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BEST ABSTRACTS SITZUNG 1

BA I - 1

Incidence and predictors of left atrial thrombus prior to catheter ablation of atrial fibrillation: a multicenter study

D. Scherr, J. Ebner, M, Manninger, B. Ohnewein, H. Brussee, A. Klein, E. Betaglia, I. Deisenhofer, C. Grebmer, M. Shinsuke, I. Yoshido, H. Calkins, J. Marine

Klinische Abteilung für Kardiologie, Medizinische Universität Graz
Cleveland Clinic, Cleveland, USA
Ospedale Civile, Mirano, Italy
Deutsches Herzzentrum, München, Germany
Kinki Univ School of MedicineYokosuka, Yokosuka, Japan
Johns Hopkins University, Baltimore, USA

Background: Transesophageal echocardiography (TEE) is commonly used prior to catheter ablation of atrial fibrillation (AF) in order to exclude left atrial (LA) thrombus. In patients presenting in SR or with an AF duration < 48 h, TEE is not required if the patient has been anticoagulated in the weeks prior to ablation according to recent Guidelines. However, this recommendation is only based on expert consensus. This study aimed to evaluate whether the CHA2DS2VASc score, in addition to the CHADS2 score, is useful for risk stratification with regard to the presence or absence of LA thrombus in patients prior to catheter ablation of AF.

Methods: This study included 1838 patients (60 ± 11 years; 25 % female; 42 % persistent AF) referred for AF ablation in six ablation centers. Patients were anticoagulated for at least four weeks prior to the procedure. TEE was performed in all cases within 48 h prior to ablation.

Results: Preprocedural TEE revealed LA thrombus in 30/1838 cases (1.6 %), all located in the LA appendage. Among these 30 patients, 6 had paroxysmal AF and were in SR at the time of TEE. LA thrombus was present in 0.3, 2.0, and 3.7 % of patients with CHADS2 scores of 0, 1, and ≥ 2, and in 0.4, 2.5, 2.9, and 5.7 % of patients with CHA2DS2VASc scores of 0/1, 2, 3, and ≥ 4, respectively. (Both $p < 0.001$) In multivariate analysis, a CHADS2 score ≥ 2, a CHA2DS-2VASc score ≥ 4, and female gender remained significant predictors of LA thrombus (All $p < 0.01$). A CHA2DS2VASc cutoff ≥ 2 stratified patients with CHADS2 scores 0/1 into 2 groups with clinically significant different thrombus rates (3.6 vs. 0.2 %; $p < 0.01$).

Conclusions: Despite oral anticoagulation, there is a small but significant risk of LA thrombus by TEE prior to AF ablation even in patients presenting in SR. The CHADS2 and CHA2DS2VASc scores are useful predictors of an increased risk for pre-procedural LA thrombus. In these patients, TEE should definitely be performed prior to AF ablation. The CHA2DS2VASc score also identifies patients at very low risk for LA thrombus.

BA I - 2

ST-segment depression resolution predicts infarct size and reperfusion injury in ST-elevation myocardial infarction: insights from a cardiac magnetic resonance multicenter study

S. J. Reinstadler, A. Baum, K.-P. Rommel, S. Desch, B. Metzler, J. Poess, H. Thiele, I. Eitel

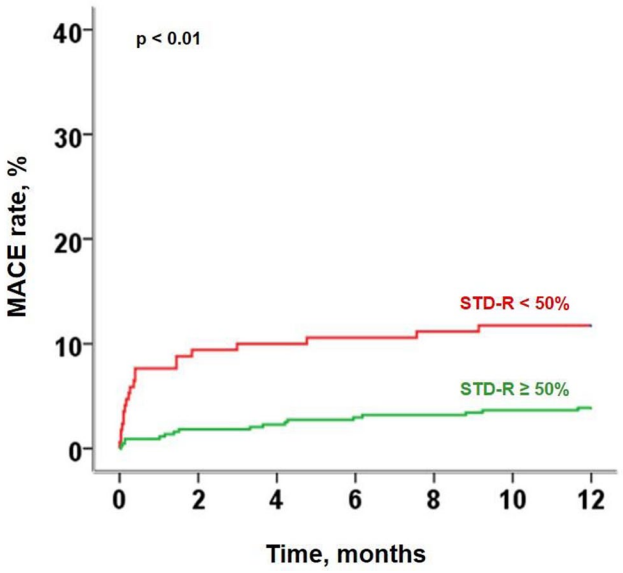
Universitätsklinik für Innere Medizin III (Kardiologie), Medizinische Universität Innsbruck, Innsbruck, Austria
University of Leipzig, Leipzig, Germany
University Heart Center Lübeck, Lübeck, Germany

Background: ST-elevation myocardial infarction (STEMI) is frequently associated with reciprocal ST-segment depression in contralateral ECG leads. However, the relationship of resolution of ST-segment depression (STD-R) with myocardial and microvascular damage is unknown and the potential prognostic value incompletely understood. The aim of this study was to evaluate the association between the STD-R and markers of myocardial injury visualized by cardiac magnetic resonance (CMR) imaging as well as to determine the prognostic impact of STD-R in patients with acute reperfused STEMI.

Methods: We enrolled 661 STEMI patients in this multicenter CMR study. STD-R, defined as either complete (≥ 50 %) or incomplete (< 50 %), was determined 90 min after primary percutaneous coronary intervention (PCI). Patients underwent CMR imaging in median 3 [2–4] days after the infarction. Major Adverse Cardiac Events (MACE) was defined as a composite of death, reinfarction and new congestive heart failure within 12 months after enrollment.

Results: Patients with STD-R < 50 % ($n = 170$, 25.7 %) had a significantly larger area at risk ($p = 0.01$), larger infarct size ($p = 0.02$), larger microvascular obstruction ($p = 0.01$), lower myocardial salvage index ($p = 0.03$), and a lower left ventricular ejection fraction ($p < 0.01$). Incomplete STD-R was significantly related with a reduced MACE-free survival (log-rank $p < 0.01$) (Fig. 1). In multivariate Cox regression analysis, STD-R < 50 % emerged as an independent predictor of MACE at 12 months (hazard ratio = 3.20 [95 % CI 1.68–6.11], $p = 0.01$) after adjusting for clinical variables.

Conclusion: Patients with acute STEMI and incomplete STD-R after PCI show a more pronounced myocardial as well as microvascular damage as detected by CMR with subsequent independent prognostic information on hard clinical events over a 12 months follow-up period.



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BA I - 3

Cardiac injury in neoplasia and association with cardiovascular hormones

N. Pavo, M. Hülsmann, C. Adlbrecht, M. Raderer, S. Neuhold, G. Goliasch, G. Strunk, H. Gisslinger, G. Kornek, S. Zöchbauer-Müller, C. Marosi, C. Zielinski, R. Pacher

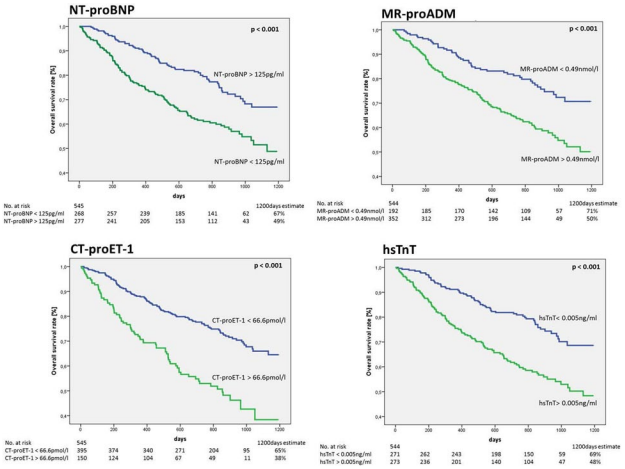
AKH, Kardiologie, Medizinische Universität Wien, Vienna, Austria
Complexity Research Austria, Vienna, Austria

Introduction: Patients with malignancies display elevated levels of B-type natriuretic peptide (BNP) and hs-TnT without clinical manifestation of cardiac disease. This study aimed to evaluate the impact of circulating cardiovascular hormones and hs-TnT on mortality in neoplastic disease.

Methods: We prospectively enrolled a total of 555 consecutive patients with primary diagnosis of neoplastic disease and without prior cardiotoxic anticancer therapy or signs of infection. NT-proBNP, MR-proANP, MR-proADM, CT-proET-1, Copeptin, hs-TnT, IL-6 and CRP were measured. Patients were followed up median 25 months (IQR 16–31 months). The primary endpoint was all-cause mortality. Cox regression analysis was performed in order to investigate the prognostic values of cardiovascular hormones and hs-TnT on survival. Correlation with the inflammatory markers was tested by means of a multiple linear regression model.

Results: During follow-up 186 (34 %) patients died. NT-proBNP, MR-proANP, MR-proADM, CT-pro-ET-1 and hs-TnT levels were elevated in patients with neoplastic disease and rose with tumor stage. All markers were significant predictors of mortality with hazard ratios per IQR of 1.54 (95 %CI 1.24–1.90; $p<0.001$) for NT-proBNP, 1.40 (95 %CI 1.10–1.79; $p<0.01$) for MR-proANP, 1.31 (95 %CI 1.19–1.44; $p<0.001$) for MR-proADM, 1.21 (95 %CI 1.14–1.30; $p<0.001$) for CT-proET-1, 1.22 (95 %CI 1.04–1.42; $p=0.014$) for Copeptin and of 1.21 (95 %CI 1.13–1.32; $p<0.001$) for hs-TnT, independent of age, gender, entity of neoplastic disease, tumor stage, and prevalence of cardiac comorbidities. Kaplan-Meier analysis confirmed the discriminatory power of neurohormones and hs-TnT on survival (Figure). Moreover NT-proBNP, MR-proANP, MR-proADM and hs-TnT displayed a significant correlation with IL-6 and CRP.

Conclusions: Circulating levels of cardiovascular peptides like NT-proBNP, MR-proANP, MR-proADM, CT-pro-ET-1 and hs-TnT are elevated in an unselected population of patients with neoplastic disease prior to induction of anticancer therapy. The aforementioned markers and Copeptin are strongly related to all-cause mortality suggesting the presence of subclinical functional and morphologic myocardial damage in the natural progression of neoplastic disease.



BA I - 4

Early electrical performance of a novel leadless transcatheter pacemaker system: Data from the Micra clinical study

C. Steinwender, S. Hönig, T. Lambert, J. Kammler, M. Grund, H. Blessberger, K. Saleh, A. Nahler, S. Schwarz, V. Gammer, B. Wichert-Schmitt, C. Eppacher, A. Kypta

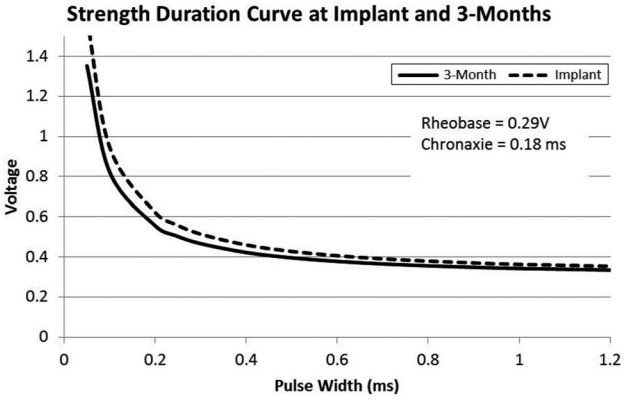
Interne 1– Kardiologie, AKH, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Austria
Medtronic Inc., Mounds View, USA

Introduction: The longevity of Micra® transcather pacing system is of special interest. The objective was to describe pacing thresholds at implant and at Month 3 (M3) with focus on the strength duration curve, longevity and threshold >1.0V.

Methods: Threshold (T), impedance (Z), percentage (%VP) and heart rate (HR) were analyzed in 60 patients at implant and M3. The strength-duration curve including rheobase and chronaxie was determined based on pacing thresholds at 0.24, and 1.0 ms pulse width using the Lapicque equation, thresholds at 0.4 ms were also collected. The longevity was estimated from the M3 threshold, %VP, HR, and Z.

Results: Sixty patients completed the M3 follow-up. Nearly all patients (59/60) were programmed to the nominal 0.24 ms pulse width. T at implant was 0.57 ± 0.31 V at 0.24 ms; 0.46 ± 0.29 V at 0.4 ms; and 0.37 ± 0.22 V at 1.0 ms. T at M3 was 0.51 ± 0.22 V at 0.24 ms; 0.43 ± 0.18 V at 0.4 ms; and 0.34 ± 0.13 V at 1.0 ms. There was a trend towards lower T at M3 vs. implant ($p=0.057$). The M3 rheobase = 0.29 V and chronaxie = 0.18 ms (Figure). Maximum pacing T was 2.0 V at implant and 1.25 V at M3. Four patients had T > 1.0 V at implant, T decreased in all below 1.25 V at M3. In one patient the T increased to 1.25 V at M3 (0.38 V increase). Maximum T increase was 0.38 V at M3. At M3, Z = 618 ± 130 Ohms (min. 444–max. 1002), %VP = 49.0 ± 37.9 % (0–100), HR = 72.4 ± 10.6 bpm (49–104). Based on the M3 threshold and pacing conditions, the mean longevity was at 12.6 ± 1.4 years, with 95 % of the patients over 10 years. Lowest estimated longevity was 8.6 years.

Conclusions: Pacing threshold of the Micra pacemaker is low at implant and stable at M3. Estimated longevity of the device is comparable with current VVI pacemaker systems.



BA I - 5

Experimental model of left ventricular hypertrophy, diastolic dysfunction and secondary pulmonary hypertension for translational research

J. Winkler, N. Pavo, K. Zlabinger, D. Macejovska, J. Bergler-Klein, G. Maurer, M. Gyöngyösi

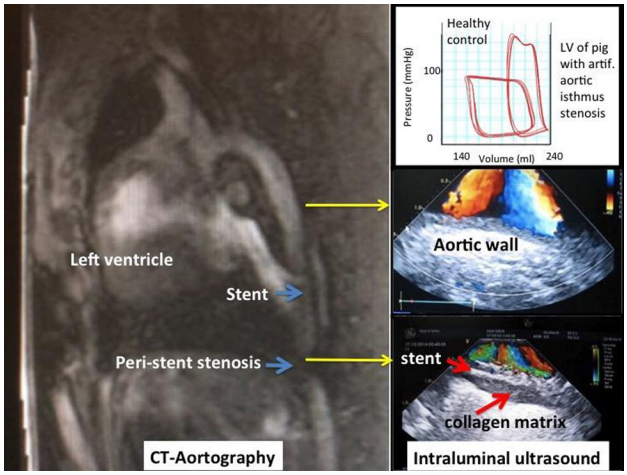
Klinik für Innere Medizin II, Department für Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: Knock-out animals or surgical partial occlusion of the thoracic aorta of pigs with abrupt increase in pre-occlusion pressure are used to model left ventricular hypertrophy (LVH) and fibrosis. We have previously reported the large animal model of artificial aortic isthmus stenosis induced by percutaneous implantation of undersized peripheral bare metal stents (BMS) in aorta descendent of juvenile pigs as the constant size of stent in growing pigs results in an antegrad partial obstruction of the aortic flow with gradual increase in afterload. After refinement of our method, we could successfully create chronic LVH, diastolic dysfunction and secondary pulmonary hypertension for translational research.

Methods: Domestic pigs (male, 15 kg, $n=10$) underwent BMS implantation of the descending aorta. Serial aortography (computer tomography, CT), transthoracic (TTE) and intraluminal echocardiography (ILE), pressure-loop measurements (PV) and magnetic resonance imaging with late enhancement (MRI + LE) were performed to measure stenosis grade, LV systolic and diastolic function and myocardial fibrosis. LV and right ventricular (RV) and right atrial (RA) pressures were measured at 4-month FUP. PicroSirius Red staining of LV myocardial tissue was performed to quantify fibrosis.

Results: CT showed a moderate-severe diameter stenosis (58±12%) of the descendent aorta at 4-month, with persistent turbulent flow by ILE (Figure). The systolic pressure gradient between LV and aorta descendent distal to stent was 69±11 mmHg, accompanied by increased LV end-diastolic (13±17 mmHg), RA (13±5 mmHg) and RV pressure (systolic: 53±6, end-diastolic: 13±5 mmHg). PV showed typical loop of LVH with increased peak systolic pressure and decrease in stroke volume (Figure). TTE revealed severe concentric LVH (mean circumferential end-diastolic wall thickness: 19.6±2.2 mm). E/A ratio was 0.92±56, E/E' ratio 9.2±1.5. MRI resulted in 18±11% fibrosis of the LV myocardium, confirmed by histology.

Conclusion: Percutaneous artificial aortic isthmus stenosis in pigs is a useful method for translation research of LVH, diastolic dysfunction and myocardial fibrosis with consequent increase in RV and RA pressures. (This experiment was sponsored by the FIBROTARGETS EU project, Grant Agreement n° 6029047).



BA I - 6

Analysis of the coding and non-coding transcriptome following neonatal mouse myocardial infarction

B. J. Haubner, M. Adamowicz-Brice, C. Morgan, T. Aitman, J. Penninger

IMBA, Penninger Lab, Wien, Imperial College, London, UK

Background: Neonatal murine hearts heal without fibrotic scarring and cardiac dysfunction following complete ligation of the left anterior descending artery (LAD). Underlying mechanisms that lead to the transition from complete cardiac regeneration to persistent fibrotic scarring within the first week after birth are poorly defined.

Methods: Thus, we performed stranded high throughput sequencing of mRNA and small RNA (RNA-seq) of mouse left ventricle tissue to detect the physiological processes leading to the decline of the regenerative capacity 7 days post birth. Moreover, we compared LAD ligated and sham operated samples to establish the pathways, which may contribute to the regeneration process.

Results: We identified thousands of differentially regulated genes (DEG) across all physiological timepoints and between LAD ligated and sham surgery animals, predominantly mRNAs. Importantly, we only found significant DEG three days post injury in the LAD vs. sham samples. Further analysis of non-coding RNAs revealed a rapid change in microRNA expression between postnatal day 3 (P3) and P5 that associates specifically with altered expression of protein-coding genes involved in cardiomyocyte proliferation and cell adhesion. Together with a set of largely uncharacterised lncRNAs with altered expression that is shared between the physiological and post-MI myocardium, our data shows a large network of non- coding RNAs in the first week after birth. Interestingly, about 70% overlap of DEG was found between regenerating and physiolgical heart samples.

Conlusion: Systems analaysis unravels a large non-coding RNA regulatory network in physiological murine heart development and cardiac regeneration. The great overlap of DEG between physiological and regenerating samples hint at common regulatory pathways. Further candidate gene approaches are needed to confirm our results.

BEST ABSTRACTS SITZUNG II

BA II - 1

Shortening of delay times is accompanied by improvement of long-term survival in a metropolitan STEMI network

B. Jäger, S. Farhan, H. Glogar, G. Christ, R. Karnik, W. Schreiber, A. Podczeck-Schweighofer, F. Weidinger, T. Stefenelli, G. Delle-Karth, A. Laggner, G. Maurer, K. Huber

Wilhelminenspital, KIM II, Notfallmedizin, Medizinische Universität, KFJ, Kardiologie, SMZ-Ost, KH Hietzing, Vienna, Austria

Background: Hospitals participating in ST-Elevation-Myocardial Infarction (STEMI)-Networks are requested to record and monitor delay times continuously. Aim of the study was to detect changes in delay times and long-time survival from 2003 to 2009 in a local STEMI network of a metropolitan area.

Methods: Pain-to-First Medical Contact (FMC), FMC-to-Reperfusion (Rx) and total ischemic time (TIT) were documented in individuals with STEMI from 2003 to 2009 in the Vienna-STEMI-Network. In-hospital mortality, 3-year-survival data and delay times were available in a total of 2492 patients. Patients were categorized via pooling of two consecutive years in order to build four categories over time (Y03: year 2003; Y04/05: year 2004 + 2005; Y06/07: year 2006 + 2007; Y08/09: year 2008 + 2009).

Results: The rate of Primary Percutaneous Coronary Intervention (PPCI) significantly increased over time (Y03: 68.0 vs. Y08/09: 98.7%; $p<0.001$), while the proportion of patients treated with fibrinolysis (Y03: 21.1 vs. Y08/09: 0.7%; $p<0.001$) and those without reperfusion (Y03: 10.9 vs. Y08/09: 0.7%; $p<0.001$) therapy declined.

Pain-to-FMC (120 min IQR 70–191 vs. 65 min IQR 34–140; $p<0.001$), FMC-to-Rx (129 min IQR 100–169 vs. 102 min IQR 81–134; $p<0.001$) and TIT (251 min IQR 186–360 vs. 197 min IQR 135–365; $p<0.001$) were significantly shortened from Y03 to Y08/09.

In-hospital mortality constantly decreased over time (Y03: 9.3 %, Y04/05: 7.9 %, Y06/07: 7.2 %, Y08/09: 7.2 %; Y03 vs. Y08/09: $p = 0.085$). Similarly, a strong statistical trend was observed for improved 3-year survival (Y03: 85.8 %, Y04/05: 87.1 %, Y06/07: 87.8 %, Y08/09: 88.4 %; Y03 vs. Y08/09: $p = 0.077$).

Conclusion: Delay times were significantly shortened between 2003 and 2009 in the Viennese local STEMI-network. This was accompanied by a strong statistical trend for improved in-hospital and long-term survival.

BA II - 2

Immunosuppressive therapy is effective in virus-negative inflammatory cardiomyopathy

M. Seiler, P. Hörmann, E.-M. Stocker, C. Ensinger, J. Dörler, M. Frick, G. Poelzl

Innere Medizin III, Kardiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Introduction: Inflammatory cardiomyopathy (iCM) has increasingly moved into clinical focus since modern immunhistochemical and molecular biological methods allow for more precise diagnosis. Causal treatment as an adjunct to conventional therapy, however, is still controversial. We aimed to investigate the effects of standardized immunosuppressive therapy in virus-negative iCM.

Methods: In this retrospective, single-centre study, 117 consecutive patients diagnosed with virus-negative iCMP between 2002 and August 2014 (age 46 ± 12, male 81 (69 %), LV-EF 33 ± 12, LVEDD 62 ± 10, NYHA functional class I 31[26.5 %], II 46[39.3 %], III/IV 40[34.2 %], NT-proBNP 1028 [391–2971] were analyzed. Prednisone 1 mg/kg/d for 4 weeks followed by 25 mg kg/d for 5 months and azathioprine (2 mg/kg/d for 6 months) on top of conventional therapy was applied in 84 patients for 6 months. 33 patients, in whom immunosuppression was withheld because of contraindications or missing consent served as control group. The end point was defined as death from any cause, heart transplantation or ventricular assist device implantation. Analysis was performed according to the intention-to-treat principle.

Results: No significant differences at study entry were seen between groups regarding age, gender, LV-EF, LVEDD, NYHA class, NT-proBNP and neurohormonal therapy. Median follow-up time was 26 months (0–107). The endpoint was recorded in 4 patients in the treatment group and 6 patients in the control group.

In multivariate sex-stratified Cox regression analysis adjusted for age, LV-EF, and NYHA class, individuals with immunosuppressive therapy were less likely to reach the endpoint (HR 0.33 [95 %CI 0.13–0.86]; $p = 0.024$) than were individuals without immunosuppressive therapy.

Summary and conclusion: These data suggest a long-term benefit of immunosuppressive therapy in patients with virus-negative iCM. A prospective, randomized study is needed for this therapy to be definitely established in clinical practice.

BA II - 3

T1 mapping by cardiac magnetic resonance imaging: from histological validation to clinical implication

A. Kammerlander, S. Pfaffenberger, C. Zotter-Tufaro, A. Bachmann, S. Aschauer, F. Duca, B. Marzluf, K. Knechtelsdorfer, M. Wiesinger, D. Bonderman, J. Mascherbauer

Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: Diffuse myocardial fibrosis/extracellular matrix expansion is a landmark feature of heart failure. Cardiac magnetic resonance (CMR) T1 mapping has recently been developed as a non-invasive technique to estimate the extracellular volume (ECV). However, the prognostic and diagnostic validity of extracellular matrix expansion by CMR T1 mapping is not well established. In particular, validation data against myocardial biopsy and prospective prognostic data are sparse.

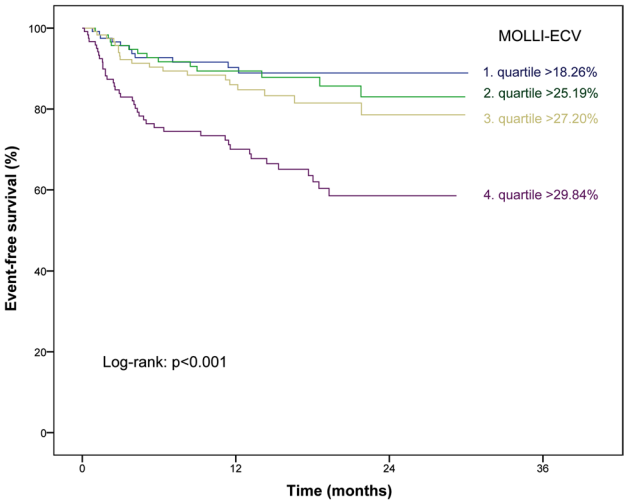
Methods: 531 consecutive patients without hypertrophic cardiomyopathy (49 % female, 57 ± 18 years old) referred to CMR were prospectively enrolled. The ECV was measured using the Modified Look-Locker Inversion recovery (MOLLI) sequence, excluding myocardial infarction.

39 patients (26 with heart failure, 9 with cardiac amyloidosis and 4 with valvular heart disease) underwent myocardial biopsy. Myocardial specimens were stained using Modified Trichrome. The ECV was histologically quantified using TissueFAXS analysis (TissueFAXS-ECV) and correlated with ECV by CMR T1 mapping (MOLLI-ECV).

For the assessment of the prognostic value of MOLLI-ECV, we investigated its association with outcome in the 531 patients (hospitalization for heart failure or cardiovascular death) by multivariable Cox-regression analysis.

Results: In myocardial specimens TissueFAXS-ECV was 33 ± 16 % and showed excellent correlation with MOLLI-ECV ($r = 0.915$, $p < 0.001$). MOLLI-ECV was 29 ± 7 % on average. When patients were divided into quartiles according to ECV (quartiles: 18.3–25.1 %, 25.2–27.1 %, 27.2–29.7 % and ≥ 29.8 %), those with higher MOLLI-ECV had a reduced event-free survival (log-rank: $p < 0.001$). By univariable Cox-regression, patients with higher MOLLI-ECV were at significantly higher risk for a cardiac event (hazard ratio 1.095 per 1 % increase, $p < 0.001$). Including cardiovascular risk factors, comorbidities, age and NT-proBNP in a multivariable Cox-regression model, MOLLI-ECV still was independently associated with outcome ($p < 0.001$), in addition to age ($p = 0.001$) and NT-proBNP level ($p = 0.016$).

Conclusion: MOLLI-ECV allows accurate non-invasive quantification of extracellular matrix expansion and is independently associated with event-free survival.



BA II - 4

Decrease in asymptomatic cerebral lesions during left atrial ablation due to improved workflow: a single center comparison

M. Derndorfer, E. Sigmund, S. Winter, W. Jauker, M. Gschwendtner, J. Aichinger, H. Pürerfellner, M. Martinek

Kardiologie 1, KH Elisabethinen Linz, Linz, Austria

Aims: Performing left atrial radiofrequency ablation during pulmonary vein isolation (PVI) has been associated with an increased risk of asymptomatic cerebral lesions. Uninterrupted oral anticoagulation (OAC) alone during procedures has not been able to completely prevent cerebral embolism. The aim of this study was to compare silent cerebral lesions in a group with an improved workflow during PVI ("new protocol") to standard ablation ("standard"). For both groups uninterrupted oral anticoagulation was obligatory. Cerebral lesions were assessed by pre- and post-procedural magnetic resonance imaging (MRI).

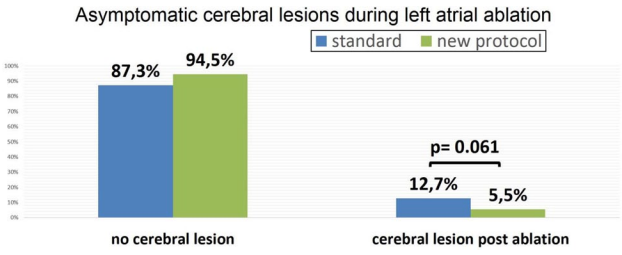
Methods and results: A total of 220 consecutive patients (110 standard, 110 new protocol) undergoing catheter ablation for paroxysmal or persistent atrial fibrillation were included in the study.

In standard procedures two initial boluses of unfractionated i.v. heparin were administered: A first "small" bolus of 3000–5000 IU before transseptal puncture (TSP), and a second bolus to add up to 100 IU/kg body weight immediately after TSP.

The new protocol consisted of a "full" initial bolus of unfractionated i.v. heparin (100 IU/kg body weight) immediately after groin venous puncture to maximize anticoagulation during TSP. Additionally modified catheter management was performed leaving blood backflow from transseptal sheaths during catheter insertion to prevent air-intake.

During all procedures the targeted activated clotting time between 300 and 400 s was maintained by a continuous i.v. heparin infusion or additional boluses as needed in both groups. Post-procedural MRI showed a trend to less cerebral lesions with the new protocol (standard: 12.7 % vs new protocol: 5.5 %, $p = 0.061$, Fig. 1). No severe complications, such as death, hemodynamically significant pericardial effusion, severe bleeding or neurological deficit occurred in both groups.

Conclusions: The new workflow-protocol during PVI shows a decrease in asymptomatic cerebral lesions. Whether this is an effect of the full-dose heparin protocol prior to TSP or due to modified catheter-handling, potentially minimizing air-embolism, should be point of further investigation.



BA II - 5

The change of mitral regurgitation severity after transfemoral vs. transapical Trans-catheter Aortic Valve Implantation (TAVI)

V. Isak, M. Mach, D. Santer, H. Pisarik, S. Folkmann, M. Harrer, J. Pollak, C. Adlbrecht, F. Veit, G. Delle Karth, M. Grabenwöger

I. Chirurgie, Abteilung für Herz- und Gefäßchirurgie, Krankenhaus Hietzing Wien, Vienna, Austria

Background: Mitral regurgitation (MR) is a frequent comorbidity in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. This population seems to have a higher mortality risk, but may also improve after an isolated surgical replacement. However, the predictors of this improvement are not well understood, and neither is the association of MR improvement and survival after TAVI. Therefore, the objective of this study is to find distinctive aspects of patients and procedures associated with MR improvement.

Methods: MR changes were assessed in all 104 patients before and after TAVI by comparing transthoracic echocardiography. Peak and mean pressure gradients across the aortic valve, the annulus diameter and the LVEF were measured as well as the color flow Doppler signal was used to determine the presence and grade of aortic regurgitation. MR was assessed by visual inspection and color-flow Doppler. The patients qualified as TAVI candidates as they had severe symptomatic aortic stenosis and were at high or prohibitive surgical risk. The transapical (TA) access route had been chosen in case of severe kinking or calcification of the iliac vessels.

Results: After the procedure, the number of patients suffering from MR was reduced from 85.3 to 62.2 % in the transfemoral (TF) TAVI population. For patients within the transapical cohort a drop from 76 to 54 % had been observed. More than half of the patients (65 %) with severe or moderate had improved in the TF-cohort vs. 50.3 % in the TA-cohort. This improvement was not influenced by the prosthetic valve type, the access type, nor the operative risk (50 % in EuroScore >20, 48.6 % in EuroScore <20). Patients with improved MR were less likely to have hypertension, diabetes and myocardial infarction. However, medical histories of COPD, coronary artery disease, coronary artery bypass graft, stroke, carotid disease, atrial fibrillation or peripheral vascular disease did not differ between patients with or without MR improvement.

No significant differences were shown between both groups concerning the post-procedural complications defined according the VARC-2 Critera and the 30-day mortality period.

Conclusion: A significant improvement of MR after TAVI could be shown in this study, especially among patients with severe MR. This improvement was independent of the aortic valve type, the prosthetic valve type, the access and the operative risk, which, however, has to be confirmed in a larger multi-center study.

BA II - 6

Indications for and experience with the use of the wearable cardioverter defibrillator in patients at high risk for sudden cardiac death: a single center experience

C. Haider, T. Odeneg, M. Manninger, D. Zweiker, J. Ebner, E. Bisping, P. Lercher, G. Prenner, B. Rotman, P. Stiegler, H. Brussee, D. Scherr

Klinische Abteilung für Kardiologie, Medizinische Universität Graz, Graz, Austria

Introduction: The wearable cardioverter defibrillator (WCD; LifeVest©) is an option for external monitoring and defibrillation in patients at high risk for sudden cardiac death (SCD) when a patient's condition delays or prohibits ICD implantation or when this high risk may be reversible. However, guidelines for the use of the WCD are not yet fully developed.

Methods: The aim of this study was to describe the indications for and experience with the use of the WCD in a tertiary cardiology center since its first use in 2012 until December 2014.

Results: Between 2012 and 2014 39 patients (64 ± 10 years; 8 female) received a WCD for a median 58 days (1–380). The most frequent indications were: Severe cardiomyopathy with recent PCI (26 %), ICD-associated infection (23 %), delay in ICD implantation (13 %), acute myocarditis (13 %), acute systemic infection with high SCD risk (8 %), severe heart failure (5 %). 13 % of patients had already experienced a malignant arrhythmia prior to the WCD. Three patients (8 %) experienced VT/VF while wearing the WCD. They received appropriate WCD shocks and subsequently underwent ICD implantation. No inappropriate WCD shock occurred. Overall, 67 % of WCD patients received an ICD after a median 57 days (3–380).

Conclusion: These data show that the WCD temporarily is a safe and effective device for patients at high SCD risk and presents an effective solution for the time until ICD implant.

Postersitzung I: Akutes Koronarsyndrom 1

I-1

Fibroblast growth factor 23 in acute myocardial infarction complicated by cardiogenic shock: a biomarker substudy of the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial

G. Fürnau, J. Pöß, D. Denks, S. Desch, G. Heine, I. Eitel, S. de Waha, G. Schuler, V. Adams, M. Böhm, H. Thiele

Klinik für Innere Medizin/Kardiologie, Universität Leipzig—Herzzentrum, University Hospital of Schleswig-Holstein, Lübeck, Universtität des SaarlandesHomburg/Saar, Saar, Germany

Introduction: Cardiogenic shock (CS) is the leading cause of death in patients hospitalized with acute myocardial infarction (AMI). Biomarkers might help in risk stratification and understanding of pathophysiology. Preliminary data suggests that patients with CS face a profound increase in the osteocyte-derived hormone fibroblast growth factor 23 (FGF-23), which acts as a negative regulator of serum phosphate levels. The present study aimed to assess the predictive role of FGF-23 for clinical outcome in a large cohort of CS patients with and without renal dysfunction.

Methods: In the randomized Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial, 600 patients with CS complicating AMI were assigned to therapy with or without IABP. Our predefined biomarker substudy included 182 patients. Blood sampling was performed in a standardized procedure at three different time points (day 1 (day of admission), day 2 and day 3). Differences in outcome of patients with FGF-23 levels < and > median were compared by log-rank testing. Stepwise logistic regression modeling was performed to identify predictors of death at 30 days and Cox regression analysis for time to death during the first year.

Results: At all three time points, nonsurvivors had significantly higher FGF-23 levels compared to survivors ($P<0.001$ for all). Patients with FGF-23 levels above the median (395 RU/mL [interquartile range 102; 2395]) were characterized by an increased 30-day mortality and 1-year mortality. In multivariable analysis FGF-23 levels remained independent predictors for 30-day (odds ratio per 10log 1.80, 95 % confidence interval (CI) 1.11–2.92; $P=0.02$) and 1-year mortality (hazard ratio 1.50, 95 % CI 1.11–2.04, $P=0.009$). After stratifying the patients according to their baseline serum creatinine levels, the negative prognostic association of increased FGF-23 was only significant in those with serum creatinine greater than median.

Conclusions: In CS, high levels of FGF-23 are independently related to a poor clinical outcome. However, this prognostic association appears only to apply in patients with impaired renal function.

I-2

Gender differences in patients with cardiogenic shock complicating myocardial infarction: a substudy of the IABP-SHOCK II-trial

G. Fürnau, K. Fengler, S. Desch, I. Eitel, S. de Waha, M. Böhm, J. Pöß, S. Schneider, G. Schuler, K. Werdan, U. Zeymer, H. Thiele

Klinik für Innere Medizin/Kardiologie, Universität Leipzig—Herzzentrum, Universitätsklinik des Saarlandes, Homburg/Saar, Saar, Germany
University Hospital of Schleswig-Holstein, Lübeck, Germany
Institut für Herzinfarktforschung, Ludwigshafen, Germany
Abteilung für Kardiologie, Martin Luther Universität Halle-Wittenberg, Halle/Saale, Germany

Background: Cardiogenic shock (CS) complicating acute myocardial infarction (AMI) is associated with high mortality. Previous studies regarding gender-specific differences in CS are conflicting and there are insufficient data for the presence of gender-associated differences in the contemporary percutaneous coronary intervention era. Aim of this study was therefore to investigate gender-specific differences in a large cohort of AMI patients with CS undergoing contemporary treatment.

Methods: In the randomized Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial, 600 patients with CS complicating AMI undergoing early revascularization were assigned to therapy with or without intra-aortic balloon pump. We compared sex-specific differences in these patients with regard to baseline and procedural characteristics as well as short- and long-term clinical outcome.

Results: Of 600 patients 187 (31 %) were female. Women were significantly older than men and had a significantly lower systolic and diastolic blood pressure at presentation ($p<0.05$ for all). Diabetes mellitus and hypertension were more frequent in women, whereas smoking was more frequent in men ($p<0.05$ for all). Women showed a higher mortality within the first day after randomization ($p=0.004$). However, after multivariable adjustment this numerical difference was no longer statistically significant. No gender-related differences in clinical outcome were observed after 1, 6 and 12 months of follow-up.

Conclusion: In this large-scale multicenter study in patients with CS complicating AMI, women had a worse-risk profile in comparison to men. No significant gender-related differences in treatment as well as short- and long-term outcome were observed.

I-3

Long-term prognostic value of growth-differentiation factor 15 in acute myocardial infarction complicated by cardiogenic shock

G. Fürnau, C. Poenisch, I. Eitel, S. de Waha, S. Desch, G. Schuler, V. Adams, K. Werdan, U. Zeymer, H. Thiele

Klinik für Innere Medizin/Kardiologie, Universität Leipzig—Herzzentrum, Leipzig, Germany
Abteilung für Kardiologie, Martin Luther University of Halle-Wittenberg, Halle/Saale, Germany
Herzzentrum, Institut für Herzinfarktforschung, Universität Heidelberg, Ludwigshafen, Universitätsspital Schleswig-Holstein, Lübeck, Germany

Purpose: Growth-differentiation factor 15 (GDF-15), a stress-responsive member of the transforming growth factor beta cytokine superfamily, has proven prognostic impact in cardiovascular disease. In acute myocardial infarction (AMI) complicated by cardiogenic shock (CS) impact on short-term the impact of GDF-15 was shown recently, but a possible long-term prognostic impact beyond the acute phase has not been investigated yet.

Methods: In 190 patients with CS complicating AMI blood samples were collected during primary percutaneous coronary intervention (PCI). The blood was centrifuged immediately and the serum was frozen at −87°C. GDF-15 was measured with a standard ELISA-Kit. All-cause mortality at 1 year was used for long-term outcome assessment.

Results: Patients with positive 1 year survival had in median significant lower levels of GDF-15 (5002 [IQR 2297;9134] vs. 10618 [IQR 6406;14458] pg/ml; $p<0.001$). GDF-15 levels above 7452 pg/ml (best cut off by Youden-index) showed higher rates of death at 1 year (71.4 vs. 34.8 %, Chi² $p<0.001$; log-rank-testing [HR 2.61 {95 %CI 1.77–3.85}; $p<0.001$]). A landmark analysis in 30 day survivors showed

a persistent discriminating effect of GDF-15 (log-rank-test day 30 to 1 year: HR 4.92 [95 %CI 2.15–11.21]; $p < 0.001$). In a multivariable stepwise Cox-regression model including all baseline variables with an univariable association to 1 year mortality ($p < 0.1$: GDF-15, age, serum creatinine and lactate, ejection fraction, sex, prior stroke, NT-ProBNP, presence of coronary 3-vessel disease, patent culprit vessel after PCI and mechanical ventilation ad admission) GDF-15, age, ejection fraction, serum lactate and a patent culprit vessel after PCI remained significant predictors of time to death (HR per 10 µg/L GDF-15 1.77 [95 %CI 1.13–2.81], $p = 0.01$). Adding GDF-15 to a model including all multivariable significant predictors resulted in a significant increase of the area under the curve for prediction of 1 year mortality (0.767 without vs. 0.817 with GDF-15, $p = 0.046$).

Conclusions: GDF-15 levels at baseline are an independent predictor of long-term mortality in acute myocardial infarction complicated by CS.

I-4

Early versus late diagnosis in patients with ST-Elevation-Myocardial Infarction: clinical characteristics and long-term-survival

B. Jäger, S. Farhan, H. Glogar, G. Christ, R. Karnik, W. Schreiber, A. Podczeck-Schweighofer, F. Weidinger, T. Stefenelli, G. Delle-Karth, A. Laggner, G. Maurer, K. Huber

Wilhelminenspital, KIM II, Notfallmedizin, Medizinische Universität, KFJ, Kardiologie, SMZ-Ost, KH Hietzing, Vienna, Austria

Background: Pre-hospital delay results in impaired outcome after ST-Elevation-Myocardial Infarction (STEMI). Pain-to-First Medical Contact (FMC) strongly depends on recognition of symptoms by the patient and willingness to attend medical help. Aim of the study was to identify factors associated with late diagnosis in STEMI.

Methods and results: Pain-to-FMC and long-term-outcome were documented in 2492 individuals presenting with STEMI from 2003 to 2009. Baseline parameters of patients with pain-to-FMC ≤60 min ("early presenters") were compared to patients in whom diagnosis was made later than 60 min of onset of pain ("late presenters").

In total, 32.6 % patients presented within 1 h of onset of pain ("early presenters"). In turn, late presenters (67.4 %) were characterized by higher age (62 ± 14 vs. 59 ± 13 years; $p < 0.0001$), higher prevalence of female sex (31.9 vs. 25.1 %; $p = 0.002$), diabetes mellitus (25.1 vs. 19.9 %; $p = 0.022$) and hypertension (57.6 vs. 50.5 %; $p = 0.007$), but lower rates of smoking (50.6 vs. 58.3 %; $p = 0.02$), dyslipoproteinemia (52.0 vs. 57.3 %; $p = 0.05$) and cardiogenic shock (8.8 vs. 11.8 %; $p = 0.042$) in univariable analysis.

After multivariable adjustment, female sex (OR 1.348; CI 1.013–1.792) and diabetes mellitus (OR 1.355; CI 1.001–1.835) were independently associated with delayed FMC in STEMI, whereas cardiogenic shock (OR 0.582; CI 0.368–0.921) was a predictor of early diagnosis.

Three-year-survival was 90.4 % and 88.7 % ($p = 0.289$) for early and late presenters, respectively. After patients with cardiogenic shock were excluded from outcome analysis, three-year-survival was significantly higher in patients with early compared to late diagnosis (96.0 and 93.0 % in early and late presenters, respectively ($p = 0.017$)).

Conclusion: In this real-world cohort of STEMI-patients, female sex and diabetes were independently associated with diagnostic lag in STEMI, whereas shock was a predictor of early diagnosis. Long-term-survival is strongly affected by an excess of cardiogenic shock in patients presenting soon after onset of pain. Special attention should be paid to avoid diagnostic delays in females and diabetics with STEMI.

I-5

Elevated levels of growth differentiation factor-15 classifies high-risk patients with acute coronary syndrome that benefit from high-dose highly efficient statins

I. Tentzeris, S. Farhan, M. Freynhofer, M. Rohla, B. Vogel, R. Jarai, S. Baumgartner-Parzer, A. Geppert, E. Wessely, M. Nürnberg, J. Wojta, K. Huber, A. Kautzky-Willer

3. Med. mit Kardiologie und internistischer Notaufnahme, Wilhelminenspital, Vienna, Austria
Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität, Vienna, Austria
Universitätsklinik für Innere Medizin III, Klinische Abteilung für Endokrinologie und Stoffwechsel, Medizinische Universität, Vienna, Austria

Background: Growth differentiation factor-15 (GDF-15) is a powerful predictor of outcome in patients after acute myocardial infarction. Statins are recommended for prevention of progression of cardiovascular disease especially after acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI).

Aim of the study was to evaluate whether GDF-15 plasma concentration at time of PCI might help to define those ACS patients who benefit from high-dose statin treatment most.

Methods: Two hundred eighty four consecutive patients, who underwent PCI and stent implantation for ACS, were included in a prospective registry from May 2009 until February 2011. Cardiovascular risk factors, co-morbidities and baseline GDF-15 levels at time of intervention were evaluated. The combined endpoint at 3 months after PCI consisted of cardiovascular death, nonfatal myocardial infarction, unstable angina, definite or probable stent thrombosis. Patients were divided into those with elevated levels of GDF-15 and those with lower in relation to the median plasma concentration. Results were compared between patients receiving high-dose, highly efficient statins (atorvastatin 80 mg or rosuvastatin 20 mg) (group A) versus patients receiving low-dose statins or who were without lipid-lowering therapy at time of discharge (group B).

Results: One hundred fifty four (54.2 %) patients had a GDF-15 levels above the median (1.21 ng/ml) and 130 (45.8 %) patients had a GDF-15 level below the median. One hundred fourteen (74 %) patients from the high GDF-15 group and 114 (87.7 %) of the low GDF-15 group received high-dose statins. In the group with high levels of GDF-15 the clinical characteristics were not significantly different between the treatment groups A and B. In the group with low levels of GDF-15 history of peripheral arterial disease, previous PCI and previous CABG were significant higher in patients of the treatment group B.

The combined endpoint was statistically lower in patients with high levels of GDF-15 in treatment group A compared to patients in treatment of group B (3.5 vs. 22.5 %, HR = 0.144; 95 % CI, 0.044–0.466; $p = 0.001$). After propensity score adjustment the results remained significant (adjusted HR for high dose statins = 0.141; 95 % CI, 0.043–0.456; $p = 0.001$). In contrast, in patients with lower levels of GDF-15 there was no significant reduction in combined endpoint rate in patients treated with high-dose statins (2.6 vs. 6.3 %, HR = 0.411; 95 % CI 0.043–3.955; $p = 0.442$).

Conclusion: In this small single-center series of 284 consecutive ACS patients undergoing PCI and coronary stenting a significant reduction in short-term combined endpoint rate could be demonstrated in patients with high levels of GDF-15 when treated with high dose, highly efficient statins as compared to patients receiving low-dose statins or no lipid lowering therapy at all. Increased GDF-15 plasma concentrations at time of PCI und stent implantation might classify high-risk ACS patients who benefit from high-dose highly efficient statins.

I-6

ATTAIN: dual antiplatelet therapy in patients presenting with acute coronary syndrome

M. Machata, F. Egger, M. Freynhofer, K. Huber, T. Weiss

3. Medizinische Abteilung mit Kardiologie und internistischer Notaufnahme, Wilhelminenspital, Vienna, Austria

Objective: Current guidelines recommend the use of dual antiplatelet therapy (DAPT) in patients with acute coronary syndrome (ACS). Whereas prasugrel and ticagrelor are favoured over clopidogrel, the latter is still frequently used—even in patients without contraindications for the more potent substances. Retrospective analysis of DAPT loading strategies in patients with ACS from our hospital has shown an underuse for both novel P2Y12 inhibitors.

The aim of this registry is to identify underlying causes for adherence or non-adherence to recent guidelines regarding initial DAPT in ACS.

Methods: In this prospective single-centre registry, all consecutive patients presenting with ACS at the emergency department will be included between November 2014 and October 2015. Pre- and intrahospital antithrombotic therapy will be assessed in order to evaluate conformity to guidelines.

Results: Of the first 60 patients presenting with ACS, 25 (41.7 %) were treated with clopidogrel, 21 (35 %) with ticagrelor and 14 (23.3 %) with prasugrel. Out of 25 patients treated with clopidogrel, one had an absolute contraindication, and 15 patients had a relative contraindication for ticagrelor or prasugrel. Accordingly, 96 % ($n=24$) of our patients were treated with clopidogrel in the absence of absolute contraindications for the administration of the novel P2Y12 inhibitors.

Conclusion: Our findings show that clopidogrel is overused in ACS patients who might profit from more potent substances such as prasugrel or ticagrelor. New P2Y12-inhibitors should not be withheld from patients without contraindications, since their superiority has been suggested in the setting of ACS. This prospective registry identifies underlying causes for the overuse of clopidogrel.

I-7

Preahospital ticagrelor versus prasugrel in st-segment elevation myocardial infarction: risk of early bleeding complications

C. Obst, F. X. Roithinger, L. Fiedler, R. Schoenbauer

Karl Landsteiner Gesellschaft, Alland, LKH Mödling, Mödling, Austria

Background: P2Y12 receptor antagonists are part of inital guideline medication for treatment of ST-Segment elevation myocardial infarction (STEMI) in terms of preventing further clot formation. Prasugrel and Ticargrelor are the main agents used. As they are combined at least with acetylsalicyl acid and heparine, risk of hemorrhagic complication exist. Whether Prasugrel or Ticagrelor, given praehospital, is superior in terms of lower early hemorrhagic complications is yet unknown.

Purpose: To determine if any of the two P2Y12 receptor antagonists has lower early bleeding complications.

Methods: We performed a restrospective analysis of 267 patients (70.0 % male, 61.6 ± 11.8 years) presenting with STEMI, who were treated with immediate percutaneous coronary intervention (PCI) in two centers. P2Y12 receptor antagonist (Ticagrelor 84.6 %) was given in the ambulance. Follow-up was 30 days after PCI. For classification of bleeding we used the Bleeding Academic Research Consortium (BARC) score.

Results: Significant differences in bleeding complications were not seen ($p=0.516$). No bleeding was observed in patients who were treated with Prasugrel. In the ticagrelor group, bleeding was seen as the following: BARC 1 = 4 patients, BARC 2 = 7 patients, BARC 3a = 1 patients. No fatal bleeding complication (BARC 5) was seen in either group. Baseline characteristics of both groups were similar (Table 1).

Conclusion: The results suggest that there exist no significant differences in terms of bleeding complications between Prasugrel and Ticagrelor. Further evaluation in larger multicenter prospective trials is needed.

I-8

Bivalirudin is not associated with lower in-hospital mortality than heparin in real-world primary PCI

M. Hasun, J. Doerler, P. Jirak, C. Wegner, G. Grimm, P. Siostrzonek, D. von Lewinski, F. X. Roithinger, W. Benzer, B. Eber, Harald Mayr, H. Alber, F. Weidinger

2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Vienna, Austria
Abteilung für Kardiologie, Universitätsklinik für Innere Medizin III, Medizinische Universität Innsbruck, Innsbruck, Austria
Wittgenstein Centre, Vienna Institute of Demography, Vienna, Austria
2. Medizinische Abteilung, Klinikum Klagenfurt am Wörthersee, Klagenfurt, Austria
Interne II, Krankenhaus der Barmherzigen Schwestern Linz, Linz, Austria
Universitätsklinik für Innere Medizin, Abteilung für Kardiologie, Medizinische Universität Graz, Graz, Austria
Innere Medizin, Landesklinikum Baden-Mödling, Baden, Austria
Abteilung für Kardiologie, Landeskrankenhaus Feldkirch, Feldkirch, Austria
Abteilung für Innere Medizin II, Kardiologie, Klinikum Wels-Grieskirchen, Wels, Austria
Abteilung für Kardiologie, Landeskrankenhaus St. Pölten, St. Pölten, Austria

Background: The HORIZONS-AMI-Trial showed reduced bleeding and mortality rates in patients undergoing primary PCI (PPCI) treated with bivalirudin compared with unfractioned heparin (UFH) and routine use of glycoprotein IIb/IIIa inhibitors (GPI). However, limited data is available to show whether bivalirudin is superior to UFH in real world PPCI. The aim of this study was to compare the in-hospital outcome of procedural anticoagulation with bivalirudin vs. UFH in PPCI for ST-elevation myocardial infarction (STEMI).

Methods: In a multicentre observational Austrian registry, 6089 patients with STEMI undergoing primary PCI between January 2010 and December 2013 were prospectively enrolled. Using multivariable logistic regression analysis, we compared in-hospital mortality of patients treated with heparin ($n=5673$) to bivalirudin ($n=416$), including GPI bail out, and heparin ($n=3533$) to bivalirudin ($n=358$), both without GPI. Baseline characteristics were similar among groups, except more comorbidities (diabetes mellitus, previous TIA/stroke, resuscitation) in patients treated with bivalirudin only ($n=86$).

Results: In-hospital mortality was not significantly different in patients receiving bivalirudin including bail out GPI compared to UFH ± GPI (OR 1.13, 95 % CI 0.62–2.04, $p=0.7$, Table 1). Furthermore, MACE (death, re-infarction and stroke) was not significantly increased in patients treated with UFH and bail out GPI (OR 1.10, 95 % Cl 0.65–1.89, $p=0.72$). In patients treated with UFH compared to those treated with bivalirudin, both without GPI, there was also no significant difference of in-hospital mortality (OR 1.68, 95 %CI 0.91–3.13, $p=0.1$) and MACE (OR 1.65, 95 %Cl 0.95–1.88, $p=0.08$).

Conclusion: In a large cohort of real world practice in PPCI, in-hospital mortality and major adverse cardiovascular events of patients treated with UFH were similar compared to patients treated with bivalirudin.

Table 1 Multivariate analysis of in-hospital mortality

Variable	OR	95% CI	*P*
Sex (m/f)	1.08	0.77 – 1.52	**0.65**
Age	1.06	1.05 – 1.08	0.00
Shock	11.8	8.4 – 16.7	0.00
Pain to catheter lab	1.05	1.03 – 1.08	**0.00**
Resuscitation	4.05	2.71 – 6.06	**0.00**
P2Y12 treatment	0.61	0.42 – 0.90	**0.01**
Diabetes	1.61	1.15 – 2.26	**0.01**
Heparin +/- GPI vs. Bivalirudin +/-GPI	1.13	0.62 – 2.04	**0.7**

Postersitzung II: Basic Science 1

II-1

Analysis of secretion profiles of pro-angiogenic paracrine factors in clinical trials of stem cell therapy for myocardial infarction

M. Lichtenauer, A. Anker, B. Wernly, M. Leisch, C. Edlinger, C. Schreiber, C. Jung, U. Hoppe

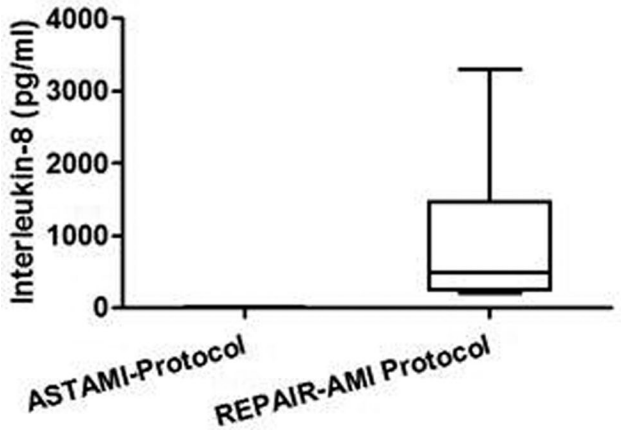
Friedrich Schiller Universität Jena, Christian Doppler Labor für Diagnose und Regeneration von Herz- und Thoraxerkrankungen, Jena, Germany
Universitätsklinik für Innere Medizin II, Kardiologie, Onkologie, Universitätsklinik für Herzchirurgie, Salzburg, Austria

Introduction: Great expectations were put on stem cell therapies for myocardial infarction (MI) over the last decade. However, inconsequent results of large clinical trials have hampered a wider application in patients who have suffered a MI. Whereas the REPAIR-AMI trial evidenced quite convincing results, no detectable effects of stem cell administration were found in the ASTAMI-trial. As paracrine mechanisms in stem cell therapy have received more and more attention recently, we sought to compare cell separation protocols of these trials with special emphasis on paracrine signaling.

Materials and methods: Mononuclear cells were obtained from peripheral blood and from bone marrow aspirates and were processed according to the ASTAMI and REPAIR-AMI protocols. In brief, cells in the ASTAMI protocol were resuspended in sodium chloride solution supplemented with 20 % of autologous plasma and were kept at 4°, whereas in the REPAIR-AMI protocol cells were cultured in X-Vivo 10 medium supplemented with 20 % serum at room temperature. Cell culture supernatants were analyzed for pro-angiogenic factors using ELISA (e.g. Interleukin-8, GRO-alpha, MCP-1, VEGF).

Results: Cells treated according to the REPAIR-AMI protocol secreted extraordinarily higher amounts of pro-angiogenic factors compared to the ASTAMI-protocol (e.g. Interleukin-8 9.7 pg/ml ± 2.9 SEM vs. 930.4 pg/ml ± 483.5 SEM, $p = 0.0022$, see Figure). Keeping cells at higher temperatures significantly boosted secretion of pro-angiogenic factors. Moreover, the addition of autologous serum was superior to plasma in further increasing the release of pro-angiogenic chemokines ($p < 0.01$).

Conclusions: Here we could show that the REPAIR-AMI protocol was by far superior regarding the secretion of pro-angiogenic factors. During the culture period these factors were enriched in great amounts in the supernatant when cells were treated in accordance to the REPAIR-AMI protocol. Based on recent studies showing that paracrine signaling represents a major influencing factor in stem cell therapy, we believe that the efficacy of clinical trials in MI patients could be increased by improved protocols for cell processing. The fact that almost no pro-angiogenic factors were present in the supernatant of cells processed according to the ASTAMI-protocol might explain the failure of the ASTAMI-trial.



II-2

Direct comparison of ischemic- vs. cryoinjury in the neonatal mouse heart

T. Schuetz, B. Kühn, J. M. Penninger, B. J. Haubner

Department of Internal Medicine III (Cardiology), Medical University Innsbruck, Innsbruck, Austria
Children's Hospital of Pittsburgh, University of Pennsylvania Medical Center Pittsburgh, Pittsburgh, USA
Institute of Molecular Biotechnology of the Austrian Academy of Sciences Vienna, Vienna, Austria

Background: We have previously shown excellent cardiac regeneration in a neonatal mouse model of myocardial infarction. The site of ischemic injury after left anterior descending artery (LAD) ligation located in the apex and anterior wall of the murine left ventricle regenerates rapidly without significant scarring. Yet, the small site of experimental ligation presents persistent fibrosis.

Methods: In order to test the hypothesis that different types of injury to the neonatal myocardium provoke different tissue responses we compared our model of neonatal LAD ligation to cryoinjury. Therefore, we subjected neonatal ICR mice to sham surgery ($n = 14$), LAD ligation ($n = 16$), and cryoinjury using a 0.5 mm ($n = 17$) and 1.5 mm ($n = 17$) metal probe cooled in liquid nitrogen.

Results: The total survival of all experimental mice was 92.2 %. We observed a trend towards increased mortality of 3.5 % in the 1.5 mm cryoinjury and LAD group compare to the 0.5 mm cryoinjury (0 %) and sham cohort (1.8 %). All three experimental models showed significant tissue damage 24 h post injury as defined by TUNEL staining. However, only the LAD ligation model displayed cleaved caspase 3 positive nuclei. In addition, cardiac function measured by echocardiography was significantly reduced in the 1.5 mm cryo and LAD group compared to the sham and 0.5 mm cryo cohort one-day post injury. Importantly, neonatal hearts subjected to LAD ligation restored cardiac function to sham levels within seven days. In contrast, experimental hearts treated with 1.5 mm cryoinjury did not recover within 30 days. This functional difference translated into histological evident transmural cardiac scars in the 1.5 mm cryo group compared to scarless healing in the LAD cohort. Even though the 0.5 mm cryo probe did not result in reduced cardiac function, fibrotic scars were found upon histological analysis.

Conclusion: The type of tissue damage to the neonatal myocardium dictates the following cardiac response. Whereas, pure necrotic stimuli e.g. cryoinjury lead to fibrotic scarring, ischemic cardiac injury leads to complete cardiac regeneration without form-

ing of a fibrotic scar. Hence, further mechanistic studies are warranted to dissect the underlying injury pathways.

II-3

Does exercise training impact clock genes in patients with coronary artery disease and type 2 diabetes mellitus?

E. Steidle, M. Schönfelder, J. Niebauer

Forschungsinstitut für Molekulare Sport- und Rehabilitationsmedizin, Paracelsus Medizinische Privatuniversität, Salzburg, Austria

Objectives: Recent findings revealed the negative effect of deregulation of the circadian rhythm on metabolic diseases like type 2 diabetes mellitus (T2DM), but limited data is available on the role of the peripheral circadian clock-machinery in metabolic diseases in humans. Physical exercise training has been shown to induce anti-diabetic and anti-atherogenic responses in skeletal muscle, but it is unknown whether it also has an impact on clock gene expression. Therefore, this study investigated whether physical exercise training alters mRNA expression of CLOCK (circadian locomoter output cycle kaput protein), PER1 (period 1), CRY2 (cryptochrome 2) und ALAS1 (aminolevulinate-delta-synthase-1) in skeletal muscle of patients with coronary artery disease and T2DM, and if so, whether this is associated with changes in metabolic and cardiovascular risk factors, proinflammatory markers, and endothelial function.

Methods: Nineteen patients with coronary artery disease and T2DM (age 64 ± 5 years) were randomized to either four weeks in-hospital exercise training, followed by a five months ambulatory exercise program or usual care. At the beginning of the study, after four weeks, and after six months parameters of metabolic and cardiovascular risk factors, and physical exercise capacity were determined. CLOCK, PER1, CRY2 and ALAS1 mRNA expression was assessed in skeletal muscle by quantitative real-time polymerase chain reaction (PCR).

Results: A time-dependent effect in gene expression was observed in CLOCK ($p = 0.013$) and ALAS1 ($p = 0.032$), while PER1 and CRY2 did not show significant changes. Furthermore, ALAS1 gene expression showed a statistically significant interaction between intervention and time ($p = 0.014$; Table 1). Significant correlations were found for PER1, CRY2 and ALAS1 expression with parameters of glycemic control, cardiovascular risk factors; proinflammatory markers, and endothelial function, as well as between each other.

Conclusion: This is the first study to analyze clock gene expression in skeletal muscle of patients with coronary artery disease and T2DM. Although there is a strong evidence for a contribution of clock genes in pathophysiological changes in T2DM, exercise training as one of the cornerstones in T2DM prevention and rehabilitation seems to exert its beneficial effects independent of putative changes of clock gene expression in human skeletal muscle.

Table 1 Gene expression analysis of clock genes referred to baseline of 19 participants at baseline after four weeks and after six months in the intervention and the control group

	Intervention group ($n = 8$)		Control group ($n = 11$)		ANOVA p	
	4 weeks	6 months	4 weeks	6 months	Time	Time x group
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
CLOCK	1.42 ± 0.96	1.83 ± 1.53	**2.05*** ± 1.52	2.17 ± 1.34	**0.014**	0.530
PER1	1.22 ± 1.42	0.63 ± 0.40	1.05 ± 0.63	1.26 ± 0.86	0.218	0.269
CRY2	1.12 ± 0.57	1.06 ± 0.32	1.04 ± 0.47	1.19 ± 0.39	0.520	0.596
ALAS1	0.85 ± 0.39	**1.93*** ± 0.81	1.15 ± 0.48	1.27 ± 0.82	**0.032**	**0.014**

Values are presented as mean ± SD. Right column presents the ANOVA *p*-values from time effect and time x group effect (interaction)
*$p < 0.05$ different from baseline

II-4

Funktionelle Effekte von Istaroxime im humanen Myokard

E. Kolesnik, M. Wallner, M. Khafaga, G. Schwantzer, M. Köstenberger, P. Curic, I. Knez, D. von Lewinski

Kardiologie, Medizinische Universität Graz, Graz, Austria
Temple University Philadelphia, Philadelphia, USA

Einleitung: Istaroxime ist eine experimentelle Substanz und wurde als Therapieoption bei systolischer und diastolischer Herzinsuffizienz entwickelt. Trotz der potentiell proarrhythmogenen Effekte von herkömmlichen Inotropika, ist deren Einsatz vor allem in der akuten kardialen Dekompensation häufig unumgänglich. Der Wirkmechanismus von Istaroxime beruht auf einer Hemmung der Natrium-Kalium-ATPase (NKA), ähnlich den jahrzehntelang bewährten Herzglykosiden. Istaroxime aktiviert zusätzlich die Sarcoendoplasmatische Reticulum Calcium ATPase (SERCA). Dieser duale Wirkmechanismus führt sowohl zu einer positiven Inotropie, als auch zu einer positiven Lusitropie, und soll das proarrhythmogene Risiko senken.

Material und Methode: Im Zuge dieser Arbeit wurden elektrisch stimulierte Muskelstreifen (Trabekel) von humanem atrialen ($n = 57$) und nicht-insuffizientem ventrikulären Gewebe ($n = 32$) mit Istaroxime und dem Herzglykosid Strophanthidin inkubiert und die darauffolgenden Änderungen der entwickelten systolischen und diastolischen Kraft, sowie der Relaxationszeit (RT50 %) gemessen. Die beiden Substanzen wurden analog auch an rechtsventrikulären Trabekeln ($n = 19$) getestet, welche von Kindern mit Fallot'scher Tetralogie (TOF) isoliert wurden, Auf Grund der rechtsventrikulären restriktiven Physiologie der TOF PatientInnen, stellt dieses Modell ein einzigartiges Modell für diastolischen Dysfunktion dar. Zusätzlich wurde die Kraft-Frequenzbeziehung (KFB; 0,5 bis 3 Hz) der einzelnen Muskelstreifen von atrialem und nicht-insuffizientem ventrikulären Gewebe in An- und Abwesenheit von 0,1 µM Istaroxime beziehungsweise Strophanthidin bestimmt und analysiert.

Ergebnisse: Sowohl Istaroxime als auch Strophanthidin übten gleichwertige, dosisabhängige positiv inotrope Effekte in humanen nicht-insuffizienten atrialen und ventrikulären Trabekeln aus. Diese inotropen Effekte waren bei einer Konzentration von 0,3 µM für beide Substanzen am stärksten ausgeprägt, höhere Konzentrationen führten jeweils zu einer Abnahme der entwickelten Kraft auf das Ausgangsniveau. In ventrikulären TOF Trabekeln konnte Istaroxime jedoch einen signifikant größeren maximalen systolischen Kraftanstieg als Strophanthidin bewirken (283 ± 26 % gegen 186 ± 21 % gemessen zur Baseline 100 %, $p = 0{,}009$)—ohne dabei die diastolische Spannung zu beeinflussen. Überraschenderweise konnte Istaroxime in keinem der drei experimentellen Modelle die Relaxationszeit signifikant gegenüber Strophanthidin oder dem Ausgangsniveau verkürzen. Ebenfalls konnten keine signifikanten Unterschiede im Effekt zwischen Istaroxime und Strophanthidin in der KFB festgestellt werden.

Diskussion: Istaroxime und Strophanthidin zeigten vergleichbare dosisabhängige positiv inotrope Effekte in humanem nicht-insuffizienten atrialen und ventrikulären Gewebe. In den TOF Trabekeln führte Istaroxime allerdings zu einer signifikant größeren maximalen Inotropie verglichen mit Strophanthidin. Auf Grund der ähnlich ausgeprägten NKA Hemmung der beiden Substanzen könnte die stärker ausgeprägte Inotropie von Istaroxime auf die zusätzliche SERCA Stimulation zurück zu führen sein. Somit könnte Istaroxime vor allem bei Vorliegen einer diastolischen Dysfunktion von Vorteil sein.

II-5

Morphological changes in aortic valves of senescent C57BL/6 mice

M. Graber, D. Lobenwein, E. Kirchmair, M. Grimm, J. Holfeld, C. Tepeköylü

Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck, Innsbruck, Austria

Introduction: Age is known as a pivotal risk factor for the development of calcific aortic valve disease (CAVD), although the exact pathomechanisms remain largely unknown. We aimed to investigate age-related morphological changes in aortic valves of senescent C57BL/6 mice.

Methods: Aortic valves from senescent C57BL/6 mice (24 months) and adult mice (12 weeks) were harvested. Paraffin sections were analyzed for valve thickness, total cell count, cells per area, valve area and atherosclerotic lesions. Six animals per group were analyzed.

Results: Senescent mice showed significantly increased valve thickness compared to adult mice (adult 75.34 ± 5.088 µm vs. senescent 105.9 ± 5.909 µm, $p = 0.0002$). In addition, the total area of the aortic valve leaflets was significantly elevated (adult 23792 ± 3289 µm^2 vs. senescent 48032 ± 5824 µm^2, $p = 0.0013$). Interestingly, adult mice showed a significantly higher number of cells per mm^2 compared to senescent mice (adult 6.312 ± 0.4308 vs. senescent 2.956 ± 0.2297, $p < 0.0001$). Furthermore, senescent aortic valves exhibited numerous atherosclerotic lesions, which were missing entirely in adult mice.

Discussion: Senescent mice show several morphological changes regarding their aortic valves compared to adult mice including increased valve thickness, larger leaflet area, lower number of cells per mm2 and numerous atherosclerotic lesions. Aged C57BL/6 mice could serve as a feasible model for elucidating the role of age in the development of CAVD.

II-6

Shock wave treatment reduces neuronal degeneration upon spinal cord ischemia via a Toll-like receptor 3 dependent mechanism

D. Lobenwein, C. Tepeköylü

Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck, Innsbruck, Austria

Objective: Paraplegia following spinal cord ischemia represents the most severe complication of aortic surgery. Shock wave treatment (SWT) was shown to induce angiogenesis and regeneration in ischemic tissue. In pre-clinical as well as clinical studies SWT had a favorable effect on ischemic myocardium. We therefore hypothesized that SWT may have a beneficial effect on spinal cord ischemia as well.

Methods: Aortic cross clamp was performed between left carotid and left subclavian artery in 10–12 weeks old male C57/Bl6 wild-type mice. Animals were randomly divided in a treatment group (SWT, 500 shock waves at 0.1 mJ/mm2, 5 Hz) and untreated controls (CTR), $n = 6$ per group. RNA expression of angiogenic and inflammatory cytokines was measured after 24 and 48 h. Immunofluorescence staining for degenerating neurons (Fluoro Jade B) and macrophages (Iba-1) was performed after 7 days. An ex-vivo spinal slice culture was performed for evaluation of Toll-like receptor (TLR) signaling. Spinal cords from wild type, TLR3 knockout and TLR4 knockout animals were cultured and set under hypoxia for 24 h. Treatment groups (SWT) received shock wave treatment following hypoxia and were cultured for another 24 and 48 h.

Results: Real-time PCR analysis revealed higher gene expression of angiogenic factors VEGF-A after 24 h (SWT 0.21 ± 0.06 vs. CTR 0.07 ± 0.01, $p = 0.028$) and 48 h (SWT 0.11 ± 0.02 vs. CTR 0.07 ± 0.01, $p > 0.05$) as well as HIF-1a after 24 h (SWT 0.11 ± 0.04 vs. CTR 0.04 ± 0.01, $p > 0.05$) and 48 h (SWT 0.09 ± 0.02 vs. CTR 0.01 ± 0, $p = 0.016$). Early increase of inflammatory mRNA expression was observed after 24 h by TNFa (SWT 0.03 ± 0.003 vs. CTR 0.005 ± 0.003, $p = 0.007$) and TGFb (SWT 0.57 ± 0.05 vs. CTR 0.17 ± 0.08, $p = 0.003$). This resulted in a markedly decreased number of degenerating neurons in the treatment group 7 days after ischemia (SWT 74.50 ± 8.14 vs. CTR 250.2 ± 42.98, $p = 0.0025$). Standardized coordination and motor tests performed at day 1, 3 and 7 postoperatively revealed a significantly better performance and outcome of the animals in the treatment group. In addition a Kaplan-Meier analysis revealed a survival benefit of SWT compared to normal animals. Effects of SWT were abolished in TLR3 knockout animals, whereas it was unchanged in TLR4 knockouts.

Conclusion: Shock wave treatment induces angiogenesis and modulates inflammation in spinal cord ischemia via the activation of TLR3. This results in a marked decrease of degenerating neurons and may therefore develop as an adjunct to the treatment armentarium for paraplegia upon aortic cross clamp.

II-7

Antimicrobial peptide LL37/RNA complexes stimulate Toll-like receptor 3 upon shock wave therapy of ischemic muscle

C. Tepeköylü, M. Graber, D. Lobenwein, E. Kirchmair, M. Grimm, J. Holfeld

Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck, Innsbruck, Austria

Introduction: Shock wave therapy (SWT) induces angiogenesis in ischemic heart disease. It is mediated via Toll-like receptor 3 (TLR3), an endosomal receptor of the innate immune system recognizing RNA. How TLR3 is activated upon SWT remains unknown. The antimicrobial peptide LL37 has been shown to be released after mechanical stress and to form complexes with RNA.

We hypothesized that mechanical stimulation upon SWT leads to LL37 release, which forms complexes with RNA and leads to activation of endosomal TLR3.

Methods: Supernatant of treated human umbilical vein endothelial cells (HUVEC) was transferred onto TLR3 reporter cells and TLR3 activation was measured. To find out whether protein/RNA complexes play a role after SWT, supernatants were treated with RNAse and proteinase. Treated HUVECs were analyzed for LL37 expression. To investigate the uptake of LL37/RNA complexes, pre-marked RNA was added to cells prior to treatment and uptake was tracked. C57BL/6 mice were subjected to hind limb ischemia and subsequently treated with SWT. Treated muscles were analyzed for LL37 expression. Laser Doppler perfusion imaging and histological quantification of vessels was performed.

Results: Supernatants of treated cells activated TLR3 reporter cells (CTR 7.346 ± 2.173 vs. SWT 146.005 ± 12.508; $p < 0.0001$). Analysis of the supernatant revealed increased RNA levels (CTR 21 ± 2.444 vs. SWT 37 ± 1.5; $p = 0.0174$). The effect could not be abolished by pre-treatment of the supernatant with RNAse, but only by a sequential digestion with proteinase and RNAse hinting strongly towards the involvement of protein/RNA complexes. Indeed, LL37 expression was significantly increased after SWT. LL37/RNA complexes could be visualized after SWT. Pre-marked RNA was added to HUVECs, followed by subsequent SWT. Cellular RNA uptake was significantly increased after SWT (CTR 31.67 ± 28.17 vs. SWT 19757 ± 1054, $p < 0.0001$). Treated muscles of C57BL/6 mice showed significantly increased expression of LL37. Finally, SWT resulted in significantly higher numbers of capillaries (SWT 1262 vs. CTR 461, $p = 0.001$) and

arterioles (SWT 461 vs. CTR 160.5, $p=0.001$) and improved limb perfusion (SWT 0.7460.01 vs. CTR 0.4860.01, $p=0.021$) in treated muscles.

Discussion: TLR3 activation upon SWT is mediated via the release of LL37. The antimicrobial peptide forms complexes with extracellular RNA and can thus stimulate endosomal TLR3. SWT subsequently induces angiogenesis in ischemic muscle and might therefore develop a potent regenerative treatment alternative for ischemic heart disease.

Postersitzung III: Basic Science 2

III-1

Exenatide exerts a PKA-dependent positive inotropic effect in human atrial myocardium

M. Wallner, E. Kolesnik, K. Ablasser, M. Khafaga, S. Ljubojevic, P. Wakula, H. Sourij, M. Kapl, B. Kuzmiski, D. Griffith, I. Knez, B. Pieske, D. von Lewinski

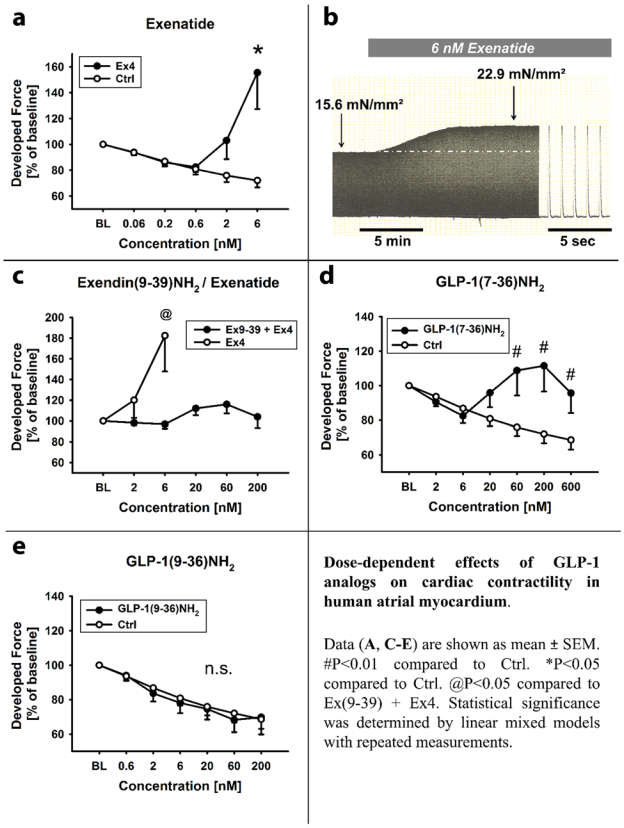
Klinische Abteilung für Kardiologie, Abteilung für Endokrinologie und Stoffwechsel, Abteilung für Herzchirurgie, Medizinische Universität Graz, Graz, Austria
Abteilung für Kardiologie, Charité-Universitaetsmedizin, Campus Virchow-Klinikum Berlin, Berlin, Germany
Cardiovascular and Metabolic Diseases Research Unit, Worldwide Research and Development, Pfizer Inc, Cambrigde, UK

Background: Glucagon-like peptide-1 receptor (GLP-1R) agonists are a rapidly growing class of drugs developed for treating type-2 diabetes mellitus. Patients with diabetes carry an up to 5-fold greater mortality risk compared to non-diabetic patients, mainly as a result of cardiovascular diseases. Although beneficial cardiovascular effects have been reported, exact mechanisms of GLP-1R-agonist action in the heart, especially in human myocardium, are poorly understood.

Material and methods: The effects of GLP-1R-agonists (exenatide, GLP-1(7–36)NH2, PF-06446009, PF-06446667) on cardiac contractility were tested in non-failing atrial and ventricular trabeculae from 72 patients. The GLP-1(7–36)NH2 metabolite, GLP-1(9–36) NH2, was also examined. In electrically stimulated trabeculae, the effects of compounds on isometric force were measured in the absence and presence of pharmacological inhibitors of signal transduction pathways. The role of β-arrestin signaling was examined using a β-arrestin partial agonist, PF-06446667. Expression levels were tested by immunoblots. Translocation of GLP-1R downstream molecular targets, Epac2, GLUT-1 and GLUT-4, were assessed by fluorescence microscopy.

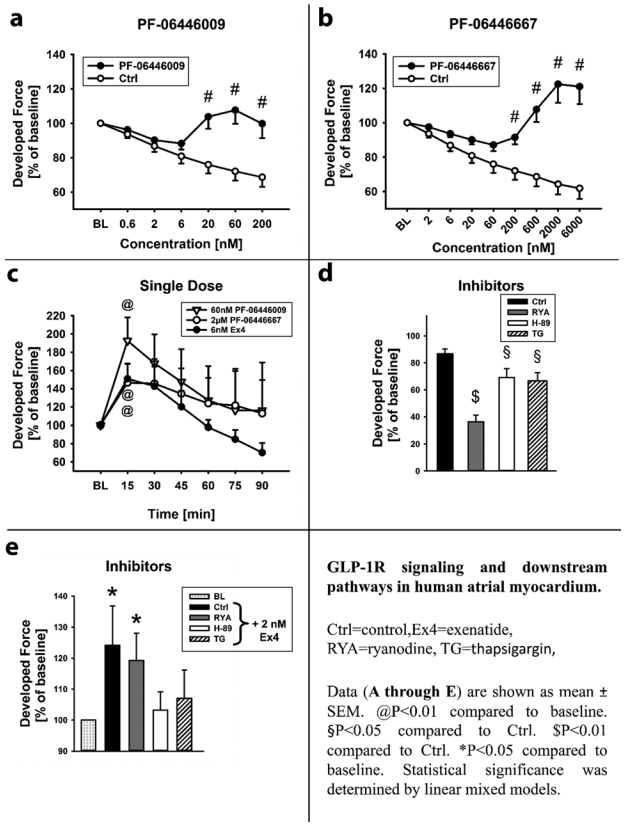
Results: All tested GLP-1R-agonists significantly increased developed force in human atrial trabeculae, whereas GLP-1(9–36) NH2 had no effect. Exendin(9–39)NH2, a GLP-1R-antagonist, and H-89 blunted the inotropic effect of exenatide. In addition, exenatide increased PKA-dependent phosphorylation of phospholamban (PLB), GLUT-1 and Epac2 translocation, but not GLUT-4 translocation. Surprisingly, exenatide failed to enhance contractility in ventricular myocardium.

Discussion: Exenatide increased contractility in a dose-dependent manner via GLP-1R/cAMP/PKA pathway and induced GLUT-1 and Epac2 translocation in human atrial myocardium, but had no effect in ventricular myocardium. Therapeutic use of GLP-1R-agonists may therefore impart beneficial effects on myocardial function and remodelling.



Dose-dependent effects of GLP-1 analogs on cardiac contractility in human atrial myocardium.

Data (**A**, **C-E**) are shown as mean ± SEM. #P<0.01 compared to Ctrl. *P<0.05 compared to Ctrl. @P<0.05 compared to Ex(9-39) + Ex4. Statistical significance was determined by linear mixed models with repeated measurements.



GLP-1R signaling and downstream pathways in human atrial myocardium.

Ctrl=control,Ex4=exenatide, RYA=ryanodine, TG=thapsigargin,

Data (**A through E**) are shown as mean ± SEM. @P<0.01 compared to baseline. §P<0.05 compared to Ctrl. $P<0.01 compared to Ctrl. *P<0.05 compared to baseline. Statistical significance was determined by linear mixed models.

III-2

CD14+CD16++CX3CR1+ monocytes are increased at the culprit lesion site of STE-ACS patients and protect from myocardial necrosis

D. Simon, A. Mangold, T. Scherz, T. Hofbauer, A. Falkinger, N. Staier, H. Heidari, J. Müller, I. Lang

Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: ST-elevation acute coronary syndrome (STE-ACS) is the leading cause of death. Mechanisms of acute plaque rupture and coronary occlusion are poorly understood. Monocytes are early inflammatory cells implicated in the pathogenesis of ACS. Monocyte subsets are divided according to their CD14:CD16 expression profile into CD14++CD16-, CD14++CD16+ and CD14+CD16++ monocytes. Especially CD14+CD16++ have been shown to play a role in tissue repair. We examined monocyte subset levels and major activation markers at the culprit lesion site (CLS) of STE-ACS patients in comparison to femoral blood. Furthermore, we correlated these data with enzymatic infarct size (creatine phosphokinase MB area under the curves [CKMB AUC]).

Methods: STE-ACS patients who underwent primary percutaneous coronary intervention at the Vienna General Hospital were consented ($n=94$). Culprit site blood was aspirated with a thrombectomy catheter and particulate thrombus material was separated. In parallel, blood was sampled from the femoral arterial sheath. Flow cytometry was employed to classify monocytes by their CD14:CD16 ratio, major activation markers (CD11a, CD11b, CD62L, CD142, CD192, HLADR, CX3CR1, TLR2, TLR4) and monocyte platelet aggregates. CKMB AUC was calculated using a trapezoidal formula. Data are expressed as median [interquartal range].

Results: Overall, monocytes are significantly decreased at the CLS compared to femoral blood. Monocyte subsets are substantially shifted at the CLS with increased levels of CD16+ subsets (CD14++CD16- femoral 92.37% [87.35–94.5] vs. CLS 89.06% [82.75–93.3], CD14++CD16+ femoral 3.92% [2.58–7.68] vs. CLS 4.82% [2.91–8.47], CD14+CD16++ femoral 3.34% [2.58–7.68] vs. CLS 4.75% [2.29–8.25], all $p<0.0001$). Increased platelet aggregation with CD16+ monocyte at the CLS could be found. Activation markers are significantly different as CX3CR1 (fractalkine receptor) is higher expressed at the CLS, while HLADR was lower. Interestingly, CX3CR1 expression of CD16+ monocytes was negatively correlated with enzymatic infarct size.

Conclusion: CD14+CD16++ monocytes with enhanced fractalkine-dependent migratory potential appear to protect from myocardial necrosis. The particular role of this monocyte subset in myocardial salvation will be investigated.

III-3

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

A. Mangold, T. Scherz, T. Hofbauer, D. Simon, H. Heidari, J. Müller, N. Staier, I. Lang

Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: ST-elevation acute coronary syndrome (STE-ACS) is among a leading cause 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+CD28 null 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+CD28 null T 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 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+CD28 null 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+CD28 null 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+CD28 null 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.

III-4

Platelet function in Chronic Thromboembolic Pulmonary Hypertension

R. Sadushi-Kolici, M.-P. Winter, C. Ay, M. Schemper, S. Panzer, T. Scherz, I. Tilea, D. Bonderman, J. Jakowitsch, N. Skoro-Sajer, B. Moser, W. Klepetko, I. Lang

Innere Medizin II, Kardiologie, Innere Medizin I, Hämatologie, Thoraxchirurgie Medizinische Universität Wien, Vienna, Austria

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a late sequelae of venous thromboembolism (VTE). However, while systematic studies of coagulation disorders have revealed an association with elevated factor VIII and lupus anticoagulant/antiphospholipid antibodies, the role of platelet function in CTEPH is poorly studied.

Methods and results: In a prospective cohort study platelet function was analyzed using cone and plate(let), and multiplate analyzer. Circulating heterotypic aggregates between leukocytes and platelets (LPA) and monocytes and platelets (MPA), platelet surface P-selectin and glycoprotein IIb/IIIa activity were measured at baseline and in response to thrombin receptor-activating peptide-6 (TRAP-6) and adenosine diphosphate (ADP) stimulation. High sensitive CRP, soluble P-selectin (sP-selectin) and soluble CD40L were determined by enzyme immuno assays.

Between June 1992 and January 2013, 176 patients with CTEPH (mean age 59.2 years, 55.7% females) were studied at baseline. 53 CTEPH patients completed a series of follow-up visits over a period of 3 ± 2 years.

In the majority of tests, platelets show a hyper-responsiveness to agonists in patients with CTEPH, both at baseline and after PEA. Soluble P-selectin ($P=0.005$) decreased significantly after pulmonary endarterectomy but did not return to normal, while hs-CRP ($P=0.035$), and D-dimer ($P=0.043$) normalized.

Conclusion: Increased platelet activatability is persistent in CTEPH, even after normalization of hemodynamics, suggesting that platelet function may play a role in the pathogenesis of the disorder, while markers of inflammatory thrombosis (hs-CRP and D-Dimer) were only transiently elevated.

III-5

Platelets are permanently activated after splenectomy

M. Gerges, C. Gerges, M. Frey, S. Panzer, I. M. Lang

Universitätsklinik für Innere Medizin II, Abteilung für Kardiologie, Medizinische Universität Wien, Vienna, Austria

Purpose: Patients after splenectomy are prone to complicated thrombosis. Recent data suggest that time to first thrombotic event or death (mainly due to "thrombotic" cardiovascular disease) may be shorter in patients after splenectomy than in matched controls. We tested the hypothesis that abnormal platelet function after splenectomy may contribute to thrombosis and delayed thrombus resolution.

Methods: In this prospective case control study, we evaluated 144 outpatients after previous splenectomy referred from 1100 primary care practitioners. 91 (63.2 %) splenectomies were due to trauma. Platelet function was measured in a subset of 36 splenectomized patients in whom splenectomy occurred after trauma, and in 7 matched non-splenectomized controls. The response to adenosine diphosphate (ADP), arachidonic acid (ASPI), protease-activated receptor (PAR)-4, and thrombin receptor activating peptide 6 (TRAP-6) was tested by multiple electrode impedance aggregometry (Multiplate). Flow cytometry was used to detect circulating monocyte-platelet aggregates (MPA) in whole blood of both subgroups. We also compared agonist (TRAP-6, PAR-4, ADP and CRP)-inducible P-selectin expression in whole blood of splenectomized versus non-splenectomized patients.

Results: During a median follow-up time of 7.9 years (25th and 75th percentile, 5.413 and 7.997 years), 10 patients (11 %) died from various causes, mainly arterial and venous thrombotic events. According to the International Classification of Diseases (ICD) an increased incidence of non-fatal thrombotic events ($n=28$) was observed in patients after splenectomy, compared with controls ($p<0.001$). Multiplate analyses revealed increased platelet activatability in splenectomized patients (97.06 ± 22.22 area under the curve, AUCs) compared with controls (80.14 ± 10.07 AUCs, $p=0.04$). Inducible P-selectin was higher in splenectomized patients (85.24 ± 19.85 %) compared with controls (62.53 ± 21.52 %, $p=0.15$). Levels of MPA [44.47 %; (11–92)] were higher than in [MPA: 31.59 %; (13–70), $p<0.001$].

Conclusions: Platelets are activated after splenectomy, with increased concentrations of MPAs, which may contribute to the high rate of vascular events in these patients.

III-6

Resolution of venous thrombosis is impaired in the absence of IgM

J. Altmann, A. Alimohammadi, I. Lang

Innere Medizin II/Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: Venous thromboembolism (VTE) is a major health problem with an annual incidence of 0.75–2.69 per 1000 individuals in the general population. Recurrence or non-resolution occurs in up to 25 % of cases. Thrombus persistence can lead to chronic thromboembolic pulmonary hypertension (CTEPH) or post-thrombotic syndrome (PTS). It is unclear which mechanisms underlie thrombus non-resultion.

One risk factor for CTEPH is splenectomy. Splenectomy was also shown to delay venous thrombus resolution in mice. Besides acting as a filter, the spleen plays an important role in B cell maturation and is required for the maintenance of peritoneal B1a cells. B1a cells spontaneously secrete IgM directed against common microbial as well as self antigens. These natural antibodies have been shown to be protective in atherosclerosis, and might also promote thrombus resolution.

Methods: To address the effect of IgM on venous thrombus resolution, we employed a mouse model of stagnant flow venous thrombosis. Mice deficient in secreting IgM (sIgM−/−) and wildtype controls (sIgM+/+) were subjected to subtotal ligation of the inferior vena cava (IVC). 3, 7, 14 or 28 days after IVC ligation, mice were sacrificed to harvest thrombi. We compared weight, length, cross-sectional area and volume of the harvested thrombi and performed histological analyses. Additionally, we used high-frequency ultrasound in a group of mice to monitor thrombus size in vivo over a time period of 28 days.

Results and conclusion: In a slow flow venous thrombosis model, sIgM−/− mice are characterized by bigger thrombi than wildtype controls and display delayed thrombus resolution. Thus, our experiments suggest an important role for natural IgM in the resolution of venous thrombosis.

III-7

The VKORC1 (−1639) G > A Promoter Polymorphism Is Associated With Elevated Systemic Arterial Blood Pressure

A. Panzenböck, C. Gerges, S. Zehetmayer, G. Endler, V. Leibetseder, T. R. Bader, C. Mannhalter, I. Lang

Department of Internal Medicine II, Division of Cardiology, Core Unit for Medical Statistics and Informatics, Clinical Institute of Medical and Chemical Laboratory Diagnostics, Center of Physiology and Pathophysiology, Department of Radiology, Medical University Vienna, Vienna, Austria

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

Methods and results: We focused on two frequent VKORC1 single nucleotide polymorphisms (SNPs), (3730) G>A polymorphism in the 3'-region and the (−1639) G>A promoter polymorphism. 1164 consecutive patients who were admitted for assessment of coronary artery disease were tested by allele specific multiplex PCR. Individuals carrying the VKORC1(−1639) A variant showed significantly elevated invasively measured systolic, diastolic and mean arterial blood pressures compared with carriers of the G allele. The (3730) SNP showed only a borderline significance for the diastolic blood pressure. No association with vascular calcification could be observed.

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

Postersitzung IV: Bildgebung

IV-1

Aortic stiffness as a predictor of high-sensitivity cardiac troponin T levels at a chronic stage after ST-segment elevation myocardial infarction

H.-J. Feistritzer, G. Klug, S. J. Reinstadler, B. Seidner, J. Mair, M. Schocke, W.-M. Franz, B. Metzler

Univ.-Klinik für Innere Medizin III, Kardiologie und Angiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Background: Aortic stiffness is associated with early pulse wave reflection resulting in an increase of cardiac afterload and impairment of coronary perfusion. Experimental data show that high left ventricular pressure due to increased aortic stiffness is associated with enhanced myocardial cell death. We investigated whether aortic stiffness is related to high-sensitivity cardiac troponin T (hs-TnT) concentrations at a chronic stage 1 year after ST-segment elevation myocardial infarction (STEMI).

Methods: Seventy-four patients underwent cardiac magnetic resonance imaging for the assessment of left ventricular function, morphology, infarct size and aortic PWV 12 months after acute STEMI. Blood samples were drawn at 12 months by peripheral venipuncture. Hs-TnT levels were measured by a commercially available immunoassay (Roche Diagnostics®).

Results: hs-TnT concentrations (6.4 ng/L, IQR 5.0–8.6) were significantly associated with age ($r=0.417$, $p<0.001$), plasma creatinine levels ($r=0.257$, $p=0.027$), high-sensitivity-C-reactive protein levels ($r=0.281$, $p=0.015$) and aortic PWV ($r=0.435$, $p<0.001$). Multiple linear regression analysis revealed aortic PWV (ß = 0.349, $p=0.014$) beside, plasma creatinine concentrations (ß = 0.288, $p=0.006$) and diastolic blood pressure (ß = 0.243, $p=0.015$) to be independently associated with hs-TnT concentrations (model: $R=0.622$, $p<0.001$).

Conclusion: The present study suggests an impact of aortic stiffness on hs-TnT concentrations at 1 year after STEMI. This might be due to subclinical myocardial damage caused by left ventricular pressure overload.

IV-2

Fetuin-A is related to infarct size, left ventricular function and remodeling after acute ST-segment elevation myocardial infarction

H.-J. Feistritzer, G. Klug, S. J. Reinstadler, M.-T. Gröber, J. Mair, A. Mayr, W.-M. Franz, B. Metzler

Univ.-Klinik für Innere Medizin III, Kardiologie und Angiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Background: Fetuin-A, an anti-inflammatory glycoprotein primarily synthesized and secreted by hepatocytes, might be involved in myocardial healing after acute infarction. We sought to investigate the relationship between plasma fetuin-A concentrations and infarct size, left ventricular (LV) function and dimensions as well as the occurrence of adverse remodeling at 4 months after acute ST-segment elevation myocardial infarction (STEMI).

Methods: In this single-center, prospective, observational study 89 patients underwent cardiac magnetic resonance imaging within the first week and 4 months after mechanical reperfusion for first STEMI. Infarct size, LV function and dimensions were assessed at both time points. Fetuin-A levels were determined from blood samples drawn at a median of 49 h (IQR 30–59 h) after STEMI by an immunofluorescent assay.

Results: Fetuin-A levels (median: 568 µg/ml, IQR 478–763 µg/ml) were significantly correlated with infarct size and LV ejection fraction (LVEF) at baseline and follow-up (all $p<0.05$). Moreover, fetuin-A was related to the increase in end-diastolic volume index ($r=-0.383$, $p<0.001$). Adding fetuin-A to a standard model consisting of cardiac troponin T, N-terminal pro-B-type natriuretic peptide, LVEF and infarct size improved the predictive value for adverse remodeling at 4 months (area under the curve = 0.803, 95 % CI 0.705–0.900 vs. area under the curve = 0.737, 95 % CI 0.614–0.861).

Conclusion: Circulating fetuin-A at day 2 after STEMI is related to acute and chronic infarct size, LV function and dimensions. In addition, it might be useful to identify patients at increased risk for adverse LV remodeling.

IV-3

Bradykardisierende Therapie mit IV Abradin und Bisoprolol vor coronarer Computer Tomographie

V. Muster, M. Wallner, A. Schmidt, M. Kapl, P. Reittner, M. Tillich, P. Brader, D. H.M. Szolar, D. von Lewinski

Kardiologie, Medizinische Universität Graz, Graz, Österreich
Temple University Philadelphia, Philadelphia, USA
Diagnostikum Graz Süd-West, Graz, Österreich

Die Computertomographische Coronarangiographie (Cardiac-CT) nimmt aufgrund besserer Bildqualität und verringerter Strahlenbelastung in den vergangenen Jahren einen immer bedeutenderen Platz in der Abklärung suspekter koronarere Herzerkrankungen (KHK) ein. Insbesondere bei Patienten mit niedriger und mittlerer Vortestwahrscheinlichkeit aber unklaren Vorbefunden kann sie mit hoher Sicherheit eine KHK ausschließen. Entscheidend für eine zufriedenstellende Bildqualität ist eine niedrige Herzfrequenz zum Zeitpunkt der Aufnahme. Hierzu werden Patienten typischerweise mit Betablocker vorbehandelt. Erste Studien haben auch die Anwendung mit dem If-Kanal Hemmer Ivabradin beschrieben.

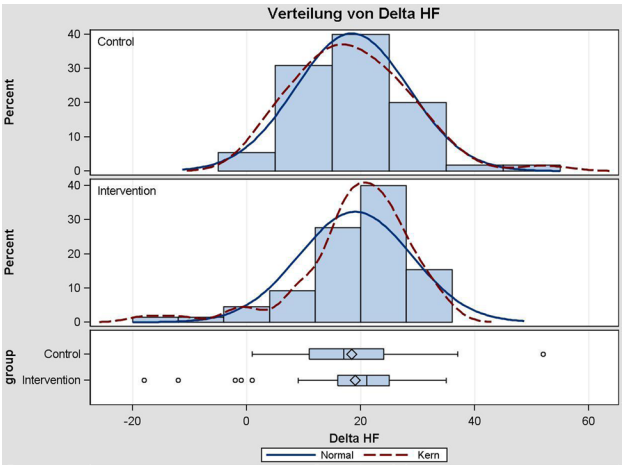
Material und Methoden: 294 Patienten wurden eine Stunde vor der Untersuchung mit strukturiertem Fragebogen, sowie Herzfrequenz- und Blutdruckmessung evaluiert. In der Interventionsgruppe (145 Patienten) wurde bei einer Herzfrequenz von 65–75/min. 10 mg Bisoprolol oral gegeben, ab einer Herzfrequenz von über 75/min. wurde zusätzlich 7,5 mg Ivabradin (65 Patienten) verabreicht. In der historischen Kontrollgruppe (149 Patienten, davon 55 mit Herzfreqnez >75/min.) wurde nur Bisoprolol gegeben. Bei Herzfrequenzen >70/min. konnte unmittelbar vor der Untersuchung noch zusätzliches Metoprolol intravenös verabreicht werden. Die Daten sind diesbezüglich kontrolliert.

Die Cardiac-CT wurde bei allen Patienten mit einem Siemens Somatom Sensation Cardiac 64 CT durchgeführt. Die Datensätze wurden anhand von archivierte MIP Bilder mit Hilfe von Siemens Syngo Plaza beurteilt.

Die statistische Analyse erfolgte mittels SAS „Statistical Analysis Software“, Version 9.2 (SAS Institute Inc., Cary, NC, USA).

Ergebnisse: Die Veränderung der Herzfrequenz während der Untersuchung war zwischen den beiden Gruppen nicht unterschiedlich ($p=0{,}6655$). Ebenso zeigten sich keine signifikanten Unterschiede für die Strahlenbelastung ($p=0{,}8885$), der Artefaktmenge ($p=0{,}5197$)oder hinsichtlich der zusätzlich notwendigen Gabe von intravenösem Betablocker. Bei keinem der Patienten kam es zu einer klinisch relevanten Bradykardiesymptomatik (Synkope, ausgeprägter Schwindel).

Diskussion: Die Gabe von Ivabradin eine Stunde vor Durchführung einer Cardiac-CT senkt weder die Herzfrequenz zusätzlich



zur Betablockergabe noch wird die Strahlendosis reduziert oder die Untersuchungsqualität verbessert.

Hintergrund ist vermutlich ein zu langsames Eintreten der Wirkung am If-Kanal, so dass im hier beschriebenen Untersuchungsablauf, der für die meisten ambulant durchgeführten Cardiac-CTs typisch ist, Ivabradin keinen Nutzen in der Vorbereitung der Cardiac-CT hat. Kurz und schnell wirksamen Betablockern sollte daher weiterhin der Vorzug gegeben werden.

IV-4

Interobserver agreement between three observers from two echocardiographic laboratories when diagnosing left ventricular noncompaction

B. Gerecke, R. Engberding, B. Grabner, C. Wandaller

2. Med. Abteilung, KA Rudolfstiftung Wien, Vienna, Austria
Klinikum Wolfsburg, Wolfsburg, Germany
Hanusch Krankenhaus Wien, Vienna, Austria

Background: Left ventricular noncompaction (LVNC) is echocardiographically characterized by an increased number of ventricular trabeculae and a two-layered myocardial structure. Interobserver agreement (IOA) of LVNC has only been studied within single echocardiographic laboratories. Aim was to assess IOA between 3 observers from 2 laboratories according to predefined criteria.

Methods: Echocardiographic recordings with and without LVNC were selected and anonymized. The "not-LVNC" cases were matched for age and systolic function. Each observer reviewed the recordings blinded to the initial diagnosis and the other observers' results. Criteria for LVNC were: 1) >3 prominent trabeculous formations, distinct from papillary muscles, false tendons or aberrant bands; 2) a noncompacted part of a two-layered myocardial structure formed by these trabeculations; 3) a ratio of >2:1 of noncompacted to compacted layer; 4) perfusion of the intertrabecular spaces from the ventricular cavity. In cases with <4 criteria, LVNC was "questionable". IOA was estimated using the kappa measure of concordance.

Results: Cine-loops of 100 patients (42 females, age 16–92 years), 50 from each center, were reviewed. In 51 patients, LVNC was the initial diagnosis. The LV enddiastolic diameter was 32–78 mm and LV ejection fraction 4–88 %. The observers agreed about presence (n=29) or absence (n=36) of LVNC and disagreed in 35 cases. Agreement was higher among the 2 observers from the same laboratory (kappa 0.793 [95 % CI 0.672;0.915]) than from different laboratories (kappa 0.628[95 % CI 0.472;0.784], kappa 0.669 [95 % CI 0.521;0.818]). The observers agreed with the initial report of LVNC-presence in 53 % and absence in 67 %. By reviewing the discordant cases, consensus was achieved about LVNC-presence (n=8) or absence (n=16), in 11 cases the diagnosis remained questionable. Discordance was due to poor image quality, lack of views in different apical planes, aberrant bands and chordae tendineae, abnormally sized or inserting papillary muscles and localized calcifications of the endocardium.

Conclusion: IOA in diagnosing LVNC was substantial. However even the application of predefined criteria yielded disagreement in 35 % and, after mutual review, still 11 % questionable cases.

IV-5

Long-term prognostic value of left ventricular ejection fraction assessed by echocardiography and magnetic resonance imaging after acute STEMI

G. Klug, S. J. Reinstadler, H.-J. Feistritzer, B. Pernter, A. Mayr, W.-M. Franz, S. Müller, B. Metzler

Medizinsche Universität Innsbruck, Innsbruck, Austria

Background: We have previously shown a moderate agreement of echocardiography and cardiac magnetic resonance (CMR) in the assessment of left ventricular ejection fraction (LVEF) after acute ST-segment elevation infarction (STEMI). We compared the prognostic value of left ventricular ejection fraction after STEMI assessed by echocardiography and CMR.

Methods: Two-hundred and two patients (mean age: 57 ± 11 years, n=27 female) with first acute STEMI were enrolled in this single-center observational study. Patients underwent CMR (median: 2.4 days) and echocardiography (median 3 days) within the first week after admission. LVEF was determined from short-axis slices with CMR and with a modified Simpson rule from apical 4-chamber echo views. Infarct size was determined from late-gadolinium enhanced (LGE) CMR. The assessment of clinical endpoints (MACE: death, myocardial reinfarction and congestive heart failure) was performed after a median of 1184 (IQR: 746–1555) days.

Results: Mean LVEF determined by echocardiography was 50 ± 10 and 52 ± 11 % as determined by CMR (paired Wilcoxon test: p=0.021). The correlation between echocardiography and CMR was moderate (r: 0.492, p<0.001). The agreement of echocardiography and CMR was higher in anterior STEMI (n=73) (r: 0.629, p<0.001) compared to non-anterior STEMI (n=105) (r: 0.279, p=0.004) (z-score: 2.92, p=0.003). A LVEF below median was associated with a significant higher event rate when assessed with echocardiography (log-rank: 0.009) or CMR (log-rank: 0.03).

Conclusion: LVEF by CMR is higher than estimated by echocardiography. The agreement of both methods is significantly higher in anterior STEMI than in non-anterior STEMI. Both methods are able to predict long-term outcome over a follow-up period >3 years.

IV-6

Prognostic value of left ventricular global function index in patients after ST-segment elevation myocardial infarction

S. J. Reinstadler, G. Klug, H.-J. Feistritzer, B. Pernter, A. Minh-Duc Tu, S. Müller, W.-M. Franz, B. Metzler

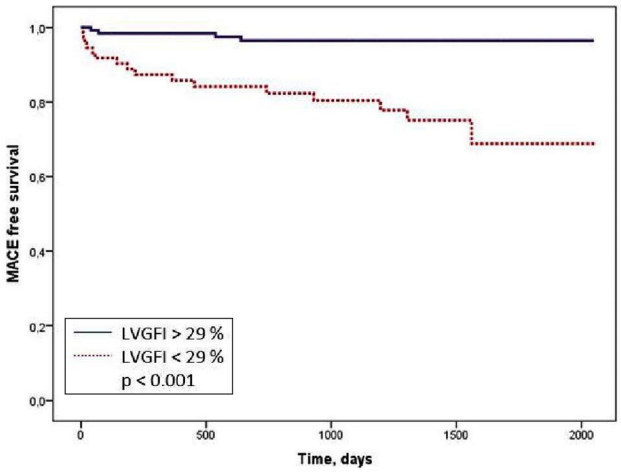
Universitätsklinik für Innere Medizin III (Kardiologie), Medizinische Universität Innsbruck, Innsbruck, Austria

Background: The left ventricular global function index (LVGFI) is a novel indicator of left ventricular performance. Its prognostic value in patients after ST-segment elevation myocardial infarction (STEMI) is unknown. We sought to evaluate the prognostic value of LVGFI measured by cardiovascular magnetic resonance (CMR) imaging after STEMI.

Methods: Two hundred eligible STEMI patients (56 ± 11 years, 16 % female) revascularized by primary percutaneous coronary intervention (PCI) were followed-up for 3.1 [2–4.1] years for major adverse cardiac events (MACE). MACE was defined as a composite of death, nonfatal myocardial re-infarction and new congestive heart failure. All patients underwent CMR imaging within 2 [2–4] days after STEMI. Late enhancement and cine images were acquired to assess myocardial injury as well as myocardial function, including LVGFI.

Results: Patients suffering a MACE event (n=20, 10 %) had a significantly lower LVGFI (p=0.001). In Kaplan-Meier analysis, a decreased LVGFI was associated with a reduced MACE-free survival (p=0.007) (Fig. 1). Multivariate Cox regression analysis revealed a decreased LVGFI as an independent predictor for MACE (hazard ratio = 5.24, 95 % CI 1.70–16.17, p=0.004) after adjusting for microvascular obstruction, multivessel disease and diabetes. In ROC analysis, LVGFI was a strong predictor for MACE (AUC = 0.73, CI 0.61–0.85). The predictive value of LVEF was similar (AUC = 0.74, CI 0.61–0.87).

Conclusion: LVGFI assessed by CMR is a strong predictor of MACE within 3 years after first STEMI.



IV-7

Pulmonary artery to aorta ratio and cardiac magnetic resonance imaging of the right heart for detecting pulmonary hypertension in heart failure with preserved ejection fraction

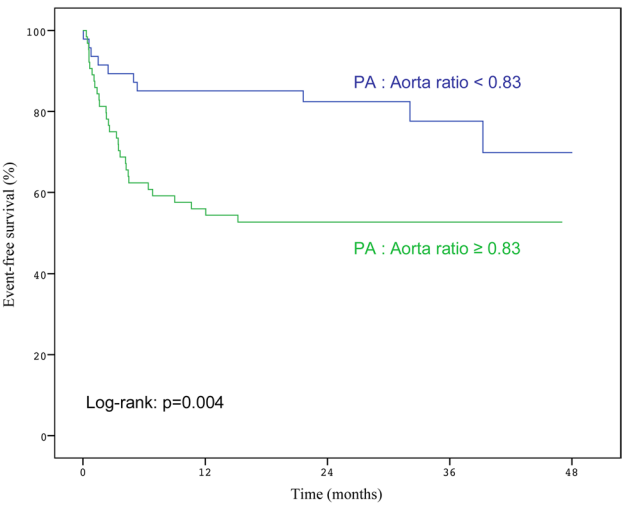
A. Kammerlander, G. Karakus, S. Aschauer, B. Marzluf, C. Zotter-Tufaro, A. Bachmann, A. Degirmencioglu, F. Duca, J. Babayev, S. Pfaffenberger, D. Bonderman, J. Mascherbauer

Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria
Acibadem Maslak Hospital, Istanbul, Turkey

Objective: Previous work indicates that dilatation of the pulmonary artery (PA) itself or in relation to the ascending aorta (PA:Ao ratio) predicts pulmonary hypertension (PH) in lung disease. Whether these results also apply for other disease entities such as heart failure with preserved ejection fraction (HFpEF) is unknown.

In the present study we evaluated the diagnostic and prognostic power of PA diameter and PA:Ao ratio on top of right ventricular (RV) size, function, and septomarginal trabeculation (SMT) thickness by cardiac magnetic resonance imaging (CMR) in HFpEF.

Methods and results: 159 consecutive HFpEF patients were prospectively enrolled. Of these, 111 underwent CMR and invasive hemodynamic evaluation.



By invasive assessment 64 % of patients suffered from moderate/severe PH (mean pulmonary artery pressure (mPAP) ≥ 30 mmHg). Significant differences between groups with and without moderate/severe PH were observed with respect to PA diameter (30.9 ± 5.1 mm vs. 26 ± 5.1 mm, $p < 0.001$), PA:Ao ratio (0.93 ± 0.16 vs. 0.78 ± 0.14, $p < 0.001$), and SMT diameter (4.6 ± 1.5 mm vs. 3.8 ± 1.2 mm; $p = 0.008$). The strongest correlation with mPAP was found for PA:Ao ratio ($r = 0.421$, $p < 0.001$). By ROC analysis the best cut-off for the detection of moderate/severe PH was found for a PA:Ao ratio of 0.83.

Patients were followed for 22.0 ± 14.9 months. By Kaplan Meier analysis event-free survival was significantly worse in patients with a PA:Ao ratio ≥ 0.83 (log rank, $p = 0.004$). By multivariable Cox-regression analysis PA:Ao ratio was independently associated with event-free survival ($p = 0.003$).

Conclusion: PA:Ao ratio is an easily measureable noninvasive indicator for the presence and severity of PH in HFpEF, and it is related with outcome.

Postersitzung V: Herzinsuffizienz 1

V-1

Cardiac hepatopathy is related to elevated central venous pressure and right ventricular dysfunction

G. Pölzl, L. Pölzl, H, Zoller, F. Plank, H. Ulmer, G. Feuchtner

Innere Medizin III, Kardiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Introduction: Cardiac hepatopathy that is characterized by elevated serum levels of cholestatic enzyms and centrilobular fibrosis is common in patients with chronic heart failure (HF). Cardiac CT and transient elastography (fibroscan) of the liver have been established for the assessment of right ventricular function and liver stiffness, respectively. We aimed to evaluate the relationship between cardiac function and hepatopathy in patients with advanced HF.

Methods: In 20 patients (56 ± 13 years, male 16 [80 %]) with severe cardiomyopathy of various etiologies hemodynamics were assessed by right heart catheterization. Prompt measurements of right ventricular ejection fraction (RV-EF) and liver stiffness (LS) were performed by cardiac CT and transient elastography (Fibroscan), respectively. Quantification of liver dysfunction was based on serum levels of GGT and bilirubin, and MELD-score. Parametric correlations were calculated using Pearson's coeffient, non-parametric correlations using Spearman's rank correlation coefficient. Multiple linear regression analyses were used to demonstrate the relationship between LS, CVP, and RV-EF.

Results: Central venous pressure (CVP) was 13 ± 6 mmHg, RV-EF 28 ± 11 %, LS 15 [IQR 7–37] kPa, GGT 128 ± 113 U/l, bilirubin 1.5 ± 1.2 mg/dl, and MELD-score 12.3 ± 4.7.

CVP was directly and RV-EF inversely correlated with LS (correlation coefficient [r] = 0.76; $p < 0.001$ and $r = -0.64$; $p < 0.01$, respectively), GGT ($r = 0.58$; $p < 0.01$, and $r = -0.53$; $p = 0.02$, respectively), bilirubin ($r = 0.53$; $p = 0.02$, and $r = -0.49$; $p = 0.03$, respectively), and MELD-score ($r = 0.57$; $p < 0.01$, and $r = -0.39$; $p = 0.09$, respectively). LS was related to GGT ($r = 0.44$; $p = 0.05$), bilirubin ($r = 0.54$; $p = 0.02$), and MELD-score ($r = 0.53$; $p = 0.02$). Multiple linear regression analysis revealed CVP (Regression coefficient [b] = –0.59 [0.02–0.16], $p = 0.02$) but not RV-EF (b = – 0.24 [– 0.06–0.02], $p = 0.30$) to be associated with FS.

Conclusions: Cardiac hepatopathy is closely related to right heart function whereby CVP rather than RV-EF accounts for an increase in liver stiffness. Whether increments in liver stiffness are associated with progression of the HF syndrome needs further evaluation.

V-2

FGF23 but not soluble klotho is associated with diasease severity and progression in chronic heart failure

G. Pölzl, P. Würtinger, J. Dörler, M. Frick, S. Gstrein, A. Griesmacher, M. Zaruba, H. Ulmer

Innere Medizin III, Kardiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Introduction: Elevated levels of the phosphatonin fibroblast growth factor 23 (FGF23) have been linked with cardiac remodeling and the advent and progression of heart failure (HF). In the kidney Klotho acts as essential coreceptor of FGF23. By contrast, circulating soluble Klotho (sKlotho), which is cleaved from the Klotho receptor appears to oppose the detrimental effects of FGF23 on the heart. We aimed to investigate the association of sKlotho with disease severity and progression in chronic HF.

Methods: Serum levels of C-term FGF23 (Ct-FGF23) and soluble Klotho (sKlotho) concentrations were measured in 287 patients with non-ischemic heart failure (age 48 ± 15 years; 69 % male; NYHA Class I 24.7 %, NYHA Class II 40.8 %, NYHA Class III/IV 34.5 %; LV-EF 32 % [IQR 21–47]; NT-proBNP 1180 ng/l [IQR 440–3128]).

Results: Median levels of Ct-FGF23 and sKlotho were 21.8 RU/ml (IQR 12.1–45.7) and 380 pg/ml (IQR 301–529), respectively. A dose-response relationship was found between median Ct-FGF23 levels and increasing NYHA class (I: 16.5 RU/ml, II: 20 RU/ml, III/IV: 38.4 RU/ml; $p < 0.001$) but not so for sKlotho (I: 380 pg/ml, II: 351 pg/ml, III/IV: 417 pg/ml; $p = 0.17$). Also, Ct-FGF23 but not sKlotho correlated with NTproBNP ($r = 0.307$, $p < 0.001$ and $r = -0.083$, $p = 0.176$).

No relationship was found for sKlotho with the combined endpoint of death or heart transplantation (hazard ratio 0.76 [0.45–1.2]; $p = 0.299$) wheras in tertile-based sex-stratified analysis, individuals in the third Ct-FGF23 tertile were 2.7 times (95 %CI 1.2–6.0; $p = 0.015$) more likely to reach an endpoint than were individuals in the first tertile.

Conclusions: In contrast to Ct-FGF23 soluble Klotho is not associated with disease severity and progression in chronic HF. Protective effects of sKlotho on the diseased heart may thus be mediated by local rather than systemic mechanisms.

V-3

Correlation between clinical response to cardiac resynchronization therapy and changes in frequency spectra of the first heart sound recorded with an endocardial acceleration sensor

D. Kiblböck, K. Höllinger, E. Zeindlhofer, A. Winter, G. Eisserer, L. Pilgerstorfer, P. Siostrzonek, J. Reisinger

Krankenhaus Barmherzige Schwestern, Kardiologie, Linz, Austria

Introduction: There is an ongoing search for early prognostic markers in patients with cardiac resynchronization therapy (CRT). We initiated this study to prove our hypothesis that dyssynchrony of the left ventricle leads to a wide frequency distribution in the endocardial acceleration signal (EAS) of the first heart sound recorded with a sensor in the tip of the right atrial lead in CRT devices and that the frequency distribution becomes narrower during clinically successfull CRT.

Methods: Fourteen 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, Kansas City cardiomyopathy questionaire (KCCQ) and echocardiographic measurements were documented at implantation (IMP), pre-hospital discharge (PHD), at 3 months (3M), at 6 months (6M) and at 12 months (12M) 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 main frequency components were calculated using a Fourier analysis.

Results: The frequency distribution became significantly narrower (IMP [mean ± SD] 21.4 ± 16.5 Hz; PHD 19.3 ± 16.3 Hz; 3M 10.2 ± 5.0 Hz; 6M 11.4 ± 4.7 Hz; 12M 11.2 ± 4.3 Hz, respectively; IMP vs. 12M, $p < 0.001$) and the power of the main frequencies increased (area under the curve at IMP 19.0 ± 17.8 mW; PHD 24.6 ± 19.9 mW; 3M 33.0 ± 23.9 mW; 6M 23.1 ± 17.0 mW; 12M 33.6 ± 29.2 mW, respectively; IMP vs. 12M, $p < 0.001$) over time. Remarkably, there is a correlation between an improvement in NYHA class, KCCQ score 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 of the first heart sound 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.

V-4

Features of myocardium remodeling and type of diastolic dysfunction in patients with anemic syndrome on a background of chronic heart failure and chronic kidney disease

G. Tytova, N. Ryndina, O. Liepieieva

Kharkiv national medical university, Kharkiv, Ukraine

Purpose: To examine the features of the remodeling of the myocardium and estimate the parameters of diastolic dysfunction in patients with anemia of varying severity that developed on the background of chronic heart failure (CHF) and chronic kidney disease (CKD).

Materials and methods: The study involved 90 patients with CHF II-IV FC (NYHA) of ischemic origin (mean age 71.42 ± 8.66 years), with anemia and CKD stage II-III. Causes of CKD were chronic pyelonephritis and diabetic nephropathy. Availability and CKD stages were determined according to the classification of the National Kidney Foundation U.S. (NKF) K/DOQ. Diagnosis of anemia was determined according to the criteria of the Medical Committee of Standards of Hematology (ICST, 1989). Mild anemia was diagnosted in 50 pts, moderate – 25 pts and severe – 12 pts. Types of remodeling were defined by Ganau classification. The nature of transmitral flow was determined by following parameters of left ventricular diastolic function: maximum peak velocity of early transmitral blood flow—E, cm/sec and the maximum speed of atrial systole—A, cm/sec;diastolic ratio—E/A.

Results: In patients with mild anemia, CHF and CKD concentric remodeling (CR) was found in 47 %, concentric hypertrophy (CG) in 53 %. The normal geometry and eccentric hypertrophy (EG) was not found in any patient. In patients with moderate anemia defined by CR in 23 % of patients, CG in 68 % pts and EG in 9 %. Study of the structural myocardial changes in patients with severe anemia showed the presence of EG in the majority of patients-72 %, CG in 28 %, CR was absent. The study of diastolic dysfunction (DD) showed the presence of transmitral flow changes in 20 % of patients, which is specific for pseudonormal type, a violation of relaxation in 80 % of patients. In patients with moderate anemia structural and functional features are characterized by heterogeneity, patients with DD type pseudonormalisation (24 %) prevailed, violation of relaxation was diagnosed in 15 % of pts, 27 % had DD of restrictive type. Patients with severe anemia mostly had restrictive type of DD

23 %, pseudonormal DD type was observed in 28 % pts, while the violation of relaxation was observed in 39 % of patients.

Conclusions: The presence of anemia in patients with CHF and CKD have a negative impact on the structural and functional parameters of the myocardium , characterized by enlargement of the heart chambers, an early type of adverse remodeling of myocardium and DD.

V-5

Affective disoders in patients with acute heart failure and acute myocardial infarction

G. Tytova, O. Liepieieva

Kharkiv national medical university, Kharkiv, Ukraine

Purpose: To investigate affective disorders in patients with acute heart failure (AHF) on a base of primary acute myocardial infarction (AMI).

Methods: 92 patients with AHF with AMI were examined. Patients were divided into 3 groups according to the AHF classification by Killip. The 1st group-22 patients with AHF class I (13 men and 9 women, 58.4 ± 6.8 years of age), the 2nd group-46 patients with AHF class II (27 men and 19 women, 59.4 ± 7.3 years), 3d group included 24 patients with AHF class III (13 men and 11 women, 63.6 ± 8.7 years). To estimate the degree of anxiety and depression scale Beck Depression Inventory was used. The evaluation was done on the 2nd day of the beginning of AHF and on 12–14th day on a background of standard therapy of the main disease, the correction of affective disorders was carried by fluoxetine use. Also on 2nd and 12–14 days from the onset of the disease in all patients were evaluated according to the Minnesota life with heart failure questionnaire (MLHFQ).

Results: During the initial testing in 1st group there were patients with predominant subdepression-15(13 ± 2 points on a Beck's scale) and 7 patients had mild depression (17 ± 2 points), in patients of the 2nd group were identified symptoms of mild depression (18 ± 1 points) in 14 patients and moderate severity depression (23 ± 3 points)-in 32 patients, in the 3rd group 10 patients had significant depression (26 ± 2 points),14 patients-severe depression (36 ± 3 points). According to MLHFQ patients of the 1st group showed 56.3 ± 3.1 points, in the 2nd group–67.8 ± 2.7 points, in the 3rd group–83.8 ± 4.9 points. Subdepressive disorders in patients did not require additional correction and regressed by usage of standard therapy of the main disease. Patients with mild, moderate and severe depression were prescibed fluoxetine at a dosage of 20, 40 and 60 mg per day, respectively. When repeated testing positive dynamics was observed in all groups as a reduction of the affective disorders by 4 points in 1st gr., by 5 points in the 2nd and in the 3d gr.-7 points. Quality of life improved in all patients mainly by psycho-emotional component: in1st group-by 64 %, in 2nd gr.-by 47 % and in the 3rd-by 38 %.

Conclusion:

1. Worsening of the depression symptoms with an increase of the AHF severity in patients with AMI was observed.
2. A direct relationship between the severity of affective disorders and decreasing of life quality in patients with AHF was found.
3. Fluoxetine can be recommended for treatment of the patients with AHF on a base of AMI due to absence of negative cardiac influence and positive effect in correction of somatogenic depressions.

Postersitzung VI: Interventionelle Kardiologie 1

VI-1

Stentrevaskularisation von signifikanten Arteria carotis interna Stenosen bei Patienten mit einem Alter über 80 Jahren- Erfolgsraten, Komplikationen und Langzeitdaten einer „Single Center" Kohorte

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

Interne 1- Kardiologie, AKH Linz, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Österreich

Einleitung: Die Stentrevaskularisation signifikanter Arteria carotis interna (ACI) Stenosen ist, in den Händen erfahrener Interventionalisten, mit geringen Komplikationsraten behaftet. Wir wollten in unserer retrospektiven Datenanalyse prüfen, ob das auch für Patienten mit einem Alter über 80 Jahre gilt.

Methoden: Zwischen Dezember 1997 und Jänner 2015 wurden 1137 Patienten (Ptn) mit 1150 signifikanten ACI Stenosen einer Revaskularisation unterzogen. 135 Ptn davon (11,7 %) waren über 80 Jahre.

Ergebnisse: 135 Ptn mit signifikanter ACI Stenose und einem Alter über 80 Jahren wurden einer Stentrevaskularisation an unserer Abteilung unterzogen. 77 (57,0 %) davon waren männlich. Das durchschnittliche Alter war 82,7 ± 2,5 Jahre. Bei 2 Ptn (1,5 %) war die Stentimplantation aus technischen Gründen nicht erfolgreich. Folgende Komorbiditäten waren erhebbar: Herzinsuffizienz 14 Ptn (10,4 %), Hypercholesterinämie 77 Ptn (57,0 %), Diabetes mellitus 31 Ptn (23,0 %), COPD 10 Ptn (7,4 %), pAVK 22 Ptn (16,3 %) und KHK bei 106 Ptn (78,5 %). Die Rate von major complications (minor stroke, major stroke, Tod) lag bei 8,9 %. Ab April 2004 wurden perinterventionell routinemäßig Filtersysteme als Embolieprotektion eingesetzt. Somit wurden 65 Ptn untere cerebraler Protektion interveniert. Dadurch kam es zu keiner Reduktion der Komplikationsrate (8,6 vs. 9,2 %).

Im Langzeitverlauf (im Mittel 33,51 Monate) kam es zu 58 Todesfällen, wobei 5 Ptn (3,9 %) an neurologischen Ereignissen, 33 Ptn (25,4 %) an kardialen Ereignissen und 20 Ptn (15,4 %) an anderen Ursachen verstarben.

Diskussion: Die interventionelle Sanierung signifikanter ACI Stenosen ist in den Händen routinierter Interventionalisten im hohen Alter mit niedrigen Komplikationsraten vergesellschaftet.

Auch im Langzeitverlauf kommt es nur selten zu neurologischen Ereignissen, wenn gleich, auch bedingt durch das Alter sowie die Komorbiditäten, die Mortalität hoch ist.

VI-2

Geschlechtsspezifische Unterschiede bei Patienten, die einer Stentrevaskularisation der Arteria carotis interna unterzogen werden- Akutergebnisse und Langzeit Follow up

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

Interne 1- Kardiologie, AKH Linz, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Österreich

Einleitung: Wir untersuchten, ob es einen geschlechterspezifischen Unterschied im Outcome bei Patienten gibt, die sich einer Intervention der Arteria carotis interna (ACI) unterziehen.

Methoden: Zwischen Dezember 1997 und Jänner 2015 wurden an unserer Abteilung bei 1137 Patienten (Ptn) 1150 signifikante ACI Stenosen mittels Stent revaskularisiert. 774 Stenosen traten bei 767

männlichen Ptn auf (Gruppe M, 67,3 %), 376 Stenosen traten bei 370 weiblichen Ptn auf (Gruppe W, 32,7 %).

Ergebnisse: In der Gruppe M war das Durchschnittsalter war 71,1 ± 33,7 Jahre, in Gruppe W 72,9 ± 47,0 Jahre. In der Gruppe M wurde 389 mal die linke sowie 385 die rechte ACI revaskularisiert. In der Gruppe W waren das in 181 Fällen die linke sowie 195 Fällen die rechte ACI.

Ab April 2004 wurden periinterventionell routinemäßig Filtersysteme als Embolieprotektion in beiden Gruppen gleich häufig eingesetzt. In der Gruppe M wurde in 464 Fällen, in der Gruppe W in 217 Fällen ein Filter verwendet ($p = 0{,}469$). In 16 Fällen der Gruppe M sowie 16 Fällen der Gruppe W war die Revaskularisation technisch bedingt nicht möglich ($p = 0{,}034$).

Die Rate von major complications (TIA, minor stroke, major stroke, Tod) war beinahe gleich, und lag in Gruppe M bei 8,3 % und in Gruppe W bei 8,5 % ($p = 0{,}889$). Im Langzeitverlauf im Mittel von 37,7 Monaten in Gruppe M zeigten sich 52 asymptomatische Restenosen >50 %, in der Gruppe W nach 38,1 Monaten 26 asymptomatische Restenosen ($p = 0{,}901$). In dieser Zeit kam es nicht signifikant unterschiedlich ($p = 0{,}180$) in der Gruppe M zu 35 Todesfällen, wobei 2 (0,3 %) davon neurologisch und 21 (2,7 %) kardial bedingt waren. 11 (1,4 %) Ptn verstarben an anderen Ursachen. In der Gruppe W waren es 24 Todesfälle, wobei 3 (0,8 %) davon neurologisch und 2 (0,5 %) kardial bedingt waren. 12 Patientinnen (3,2 %) starben an anderen Ursachen.

Diskussion: Die Rate an akuten und spät auftretenden neurologischen Komplikationen bei Patienten, die sich einer Stentrevaskularisation einer ACI Stenose unterziehen, unterscheiden sich geschlechterspezifisch nicht. Auch die Rate an Restenosen sowie Todesfällen im Langzeitverlauf sind bei männlichen und weiblichen Patienten ident. Einzig bei der Rate der technischen failures zeigten sich signifikante Unterschiede mit einer Benachteiligung des weiblichen Geschlecht bei insgesamt sehr seltenem Ereignis.

VI-3

Predictors of response to renal denervation for resistant arterial hypertension: a single centre experience

M. Rohla jr., A. Nahler, T. Lambert, C. Reiter, V. Gammer, M. Grund, H. Blessberger, J. Kammler, A. Kypta, K. Saleh, K. Huber, C. Steinwender, T. W. Weiss

3. Medizinische Abteilung Kardiologie und Notfallmedizin, Wilhelminenspital, Vienna, Austria
1. Medizinische Abteilung, Kardiologie, AKH, Linz, Austria

Background: Catheter based renal denervation (RDN) has been shown to reduce blood pressure (BP) in patients with resistant arterial hypertension (RAH). We aimed to investigate possible predictors for response to RDN.

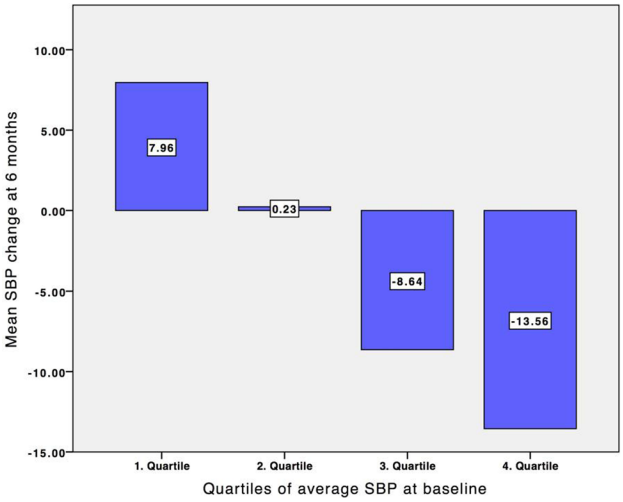
Methods: Patients suffering from RAH underwent RDN after exclusion of secondary causes of hypertension. RAH was defined by a mean systolic office BP >160 mmHg. Ambulatory blood pressure measurement (ABPM) for 24-hours was performed at baseline, 6 and 12 months after RDN. Patients were classified as responders, if the 24-hour average systolic blood pressure dropped by ≥5 mmHg after 6 months. A logistic regression model was used to analyze an association between baseline variables and response to RDN.

Results: In total, 45.6 % of patients were responders to RDN. In those patients, there was a significant reduction in ABPM values at 6 and 12 months (12 months: average systolic: −17.2 ± 9.0 mmHg, $p < 0.01$; average diastolic: −9.0 ± 11.6 mmHg, $p < 0.01$).

We identified baseline average systolic blood pressure (SBP) as the only factor associated with response to RDN.

Patients with an average SBP ≥160 mmHg (ABPM) at baseline were 3.2-times more likely to respond to RDN after 6 months.

Patients with baseline average SBP in the 3rd quartile (Q) vs. Q1 and Q4 vs. Q1 had a 8.7-fold and 13.8-fold odds ratio for response to RDN, respectively (Fig. 1).



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Conclusion: Out of a wide range of baseline variables, only highly elevated systolic ABPM values were associated with response to RDN after 6 months. One has to consider the Hawthorne effect, the regression to the mean phenomenon, the actual effect of sympathetic denervation and the interaction of therapy modification after the procedure when interpreting data from RDN registries without a control arm.

VI-4

Unterschiede in den akuten Komplikationsraten bei Patienten mit Stentrevaskularisation der Arteria carotis interna in Abhängigkeit von der Seitenlokalisation

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

Interne 1- Kardiologie, AKH Linz, Medizinische Fakultät der Johannes Kepler Universität Linz, AKH Linz, Linz, Österreich

Einleitung: Es wird vermutet, dass durch die unterschiedlichen anatomischen Zugänge zur linken bzw rechten Arteria carotis interna (ACI), unterschiedliche Komplikationsraten bei der Stentrevaskularisation entstehen.

Methoden: Zwischen Dezember 1997 und Jänner 2015 wurden 1124 Patienten (Ptn) mit signifikanter ACI Stenose einer Stentrevaskularisation an unserer Abteilung unterzogen. Jene 13, bei denen simultan beide ACI versorgt wurden, wurden aus der Analyse ausgeschlossen. In 557 Fällen (49,6 %) wurde die linke ACI (Gruppe 1), in 567 Ptn (50,4 %) die rechte ACI (Gruppe 2) interveniert.

Ergebnisse: In der Gruppe 1 waren 175 Ptn weiblich (31,4 %), das Durchschnittsalter war 71,4 ± 38,9 Jahre, in Gruppe 2 waren 189 Frauen (33,3 %), das Durchschnittsalter 71,9 ± 39,1 Jahre. Bei 13 Ptn der Gruppe 1 (2,3 %) sowie bei 19 Ptn der Gruppe 2 (3,6 %) verlief der Interventionsversuch frustran. Bei den Komorbiditäten fanden sich zwischen den Gruppen keine signifikanten Unterschiede. Der Stenosegrad konnte von 85,5 ± 10,3 % auf 3,1 ± 6,4 % in Gruppe 1, sowie von 85,9 ± 9,6 % auf 3,5 ± 7,3 % in Gruppe 2 reduziert werden. Die Stentlängen waren 27,9 ± 6,7 mm bzw 27,5 ± 9,8 mm, die Interventionsdauer war ebenfalls nicht signifikant unterschiedlich, nämlich 17,2 ± 11,4 bzw. 16,2 ± 9,8 min. Die Rate von major complications (TIA, minor stroke, major stroke, Tod) war signifikant unterschiedlich, und lag in Gruppe 1 bei 10,1 % und in Gruppe 2 bei 6,7 % ($p = 0{,}042$). Ab April 2004 wurden periinterventionell routinemäßig Filtersysteme als Embolieprotektion eingesetzt. Dadurch konnte

unabhängig von der Seitenlokalisation die Komplikationsrate gesamt signifikant von 11,1 % auf 6,5 % reduziert werden ($p = 0{,}006$). Bezogen auf die Gruppen mit (Gruppe 1: 340 Ptn, Gruppe 2: 335 Ptn) sowie ohne (Gruppe 1: 217 Ptn, Gruppe 2: 232 Ptn) Protektion, konnte links die Komplikationsrate durch den Filter signifikant von 14,8 % auf 7,1 % ($p = 0{,}003$) verringert werden, rechtsseitig war lediglich ein nicht signifikanter Trend von 7,8 % auf 6,0 % ($p = 0{,}402$) durch die Protektion erzielbar.

Diskussion: Die Komplikationsraten von Stentrevaskularisationen der ACI sind signifikant unterschiedlich, je nach dem ob die linke oder die rechte ACI interveniert wird. Möglicherweise sind Manipulationen mit dem Katheter im Bereich des Aortenbogens mit entsprechenden Ablösungen von Kalkplaques und die direkte Verbindung von Aorta zur linken ACI verantwortlich, dass es häufiger zur Embolisation von Material in das Stromgebiet der linken ACI kommt.

VI-5

Percutaneous treatment strategy in patients with severe aortic stenosis and concomitant coronary artery disease: a 30-day outcome single-center analysis

K.-P. Kresoja, R. Maier, G. Stoschitzky, J. Binder, M. Kapl, W. Marte, H. Brussee, O. Luha, A. Schmidt

Klinische Abteilung für Kardiologie, Medizinische Universitätsklinik Graz, Graz, Austria

Aims: Concomitant significant coronary artery disease (CAD) is frequent in patients with severe aortic stenosis. An area of uncertainty exists around the management of these patients. So far, the impact of a percutaneous treatment strategy (TAVI and PCI) on prognosis is unclear when compared to surgical valve replacement and CABG. In this retrospective single-center study we analyzed the outcome of patients undergoing PCI and TAVI.

Methods and results: Between November 2010 and February 2014, 42 consecutive patients from our cath-lab with severe aortic stenosis and significant CAD underwent staged PCI and TAVI (PERCUTANEOUS), as advised by the heart team. Risk score assessment revealed a logistic EuroSCORE of 19.5 ± 9.4 %, an EuroSCORE 2 of 9.9 ± 5.8 % and a STS score of 8.3 ± 4.0 %. Furthermore, the PERCUTANEOUS group was characterized by a relatively high NYHA-classification of 2.8, and atrial fibrillation was common among patients scheduled for TAVI and PCI (53.6 %). Clinical outcome at 30 days showed an overall mortality of 4.88 % and a cardiovascular mortality of 2.44 %. Acute kidney injury occurred in 9.76 %, and there was no major stroke (0 %). The 30-day combined VARC safety endpoint was relatively low in the PERCUTANEOUS group (4.88 %) compared to reported values for patients with combined surgical aortic valve replacement and bypass in the literature. Device success rate at 30 days was excellent in the PERCUTANEOUS group (Pmax 15.5 ± 5.9 mmHg) without moderate or severe aortic regurgitation or need for valvular re-intervention. Conduction disturbances requiring permanent pacemaker implantation were relatively frequent in the PERCUTANEOUS group (24.4 %). On the other hand, the percutaneous TAVI/PCI strategy resulted in a relatively short mean stay in hospital (15.9 ± 5.9d) and on intensive care unit (2.8 ± 2.46d).

Discussion: This single-center study indicates that a combined percutaneous TAVI/PCI approach in patients suffering from severe aortic stenosis and CAD is safe and comparable to published data for CABG and surgical valve replacement with respect to 30-day outcome despite a predicted higher risk in the PERCUTANEOUS group. Prospective randomized trials are warranted to confirm these preliminary data.

VI-6

Density of stent struts is a risk factor for late acquired stent malappossition in second generation drug eluting stents: a prospective, randomized comparison using Optical Coherence Tomography

C. Gangl, C. Roth, S. Scherzer, L. Krenn, D. Dalos, G. Kreiner, G. Delle-Karth, T. Neunteufl, J. Kastner, I. Lang, R. Berger

Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: Late acquired stent malapposition (LASM) is associated with a higher incidence of (very) late stent thrombosis. The impact of the stent scaffold's architecture itself—particularly in respect of stent strut density—on the incidence of LASM remains unclear.

Methods: Fifty patients with 59 lesions of interest were randomised to elective treatment with drug eluting stents either based on "Resolute Integrity" stent platform (RI, $n = 15/19$ lesions), "Multi-Link" stent platform (ML, $n = 17/20$ lesions) or "Juno" stent platform ($n = 18/20$ lesions) and underwent optical coherence tomography (OCT) direct after implantation respectively after one year. Cross-sectional OCT images were analysed at 1-mm intervals for strut count and incidence of malapposed stent struts.

Results: In total, 9 stents with LASM could be identified by optical coherence tomography whereas 50 stents did not show late acquired malappositions after one year. Both groups did not distinguish in terms of length and diameter ("LASM" vs. "no LASM": 27.11 vs. 22.4 mm; $p = 0.09$ respectively 3.1 vs. 2.9 mm; $p = 0.267$) respectively incidence of acute strut malappositions (6 vs. 23; $p = 0.299$). Remarkably, stent strut density determinded by strut count per frame (11.9 vs. 8.6; $p < 0.001$) as well as strut count normalised to diameter (11.5 vs. 9.1; $p = 0.008$) was significantly higher in stents that showed LASM compared to stents without LASM. Further, stent strut density was higher in the RI-based group compared to ML and Juno (strut count per frame: 11.4 vs. 8.6. vs. 7.36, $p < 0.001$; strut count normalised to diameter: 11.69 vs. 9.11 vs. 7.74; $p < 0.001$).

Conclusion: Stent strut density appeared higher in stents with LASM at 12 month. Stent architectures with higher strut density may induce a higher incidence of LASM after 12 month.

VI-7

Early outcomes of real-life patients treated with Everolimus-Eluting Bioresorbable Vascular Scaffolds

D. Dalos, C. Gangl, C. Roth, M. Vertesich, L. Krenn, S. Scherzer, G. Kreiner, B. Frey, J. Kastner, I. Lang, G. Delle-Karth

Univ. Klinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background and aims: Bioresorbable vascular scaffolds (BVS) represent a novelty in treating coronary artery lesions. Although BVS implantation in patients with acute coronary syndromes is getting more common, the majority of outcome data exists on stable patients. Therefore, this analysis sought to evaluate early clinical outcomes of both, stable and acute patients after treatment with BVS.

Methods and results: A total of 220 patients between October 2012 and January 2014 were eligible for BVS implantation at our institution. Mean age was 58.6 ± 11.2 years and mean follow-up duration was 306 ± 115 days. 184 (84 %) were male, 103 (47 %) underwent elective implantation of BVS, 3 (1 %) had unstable angina, 52 (24 %) for Non-ST-elevation myocardial infarction and 62 (28 %) because of ST-elevation myocardial infarction (STEMI). The overall rate of major adverse cardiac events (MACE: death, non-fatal

myocardial infarction, urgent revascularization) was 3 %, without any differences between stable and acute patients ($p = 0.34$). Acute scaffold thrombosis occurred one hour after implantation in one patient presenting with STEMI. No further scaffold thrombosis could be reported during follow-up. Re-angiography was more frequently performed for elective reasons than because of anginal pain ($n = 29$ vs. $n = 5$, $p < 0.0001$). Re-intervention because of significant in-scaffold-restenosis was required in three of these patients (9 %).

Conclusion: MACE rate at short-term follow-up in our real-life population is rather low and comparable with the ones of new-generation metallic drug-eluting stents.

Therefore, the bioresorbable vascular scaffold may be safely used in younger patients in an elective setting, as well as in acute coronary syndromes. Nevertheless, the results of large, randomized, controlled trials have to awaited in order to prove long-term safety.

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VII-1

Angiotensin inhibition and outcome after Transcatheter Aortic Valve Implantation (TAVI): influence of left ventricular ejection fraction

G. Wagner, S, Marek, L. Urbanschitz, G. Lamm, P. C. Gunacker, K. Preisl, P. Vock, H. Mayr, D. Moertl

3. Medizinische Abteilung, Abteilung für Anästhesiologie und Intensivmedizin, Universitätsklinikum St. Pölten, St. Pölten, Austria

Background: Despite advances in transcatheter aortic valve implantation (TAVI) as an option for patients with aortic stenosis at high risk for open heart surgery, the event rate with respect to hospitalizations and death remains high. Although angiotensin inhibition is a corner stone in the treatment throughout the cardiovascular continuum, the role of angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB) for cardiovascular risk reduction after TAVI is poorly understood. We investigated the influence of angiotensin inhibition on outcome after TAVI and its dependence on left ventricular ejection fraction (LVEF).

Methods: All patients discharged after TAVI at the Clinical Department of Internal Medicine III (Cardiology and Emergency Medicine), University Hospital St. Poelten, between 01/2008 and 04/2014 were included. Angiotensin inhibition was defined as the presence of an ACE-I or ARB at discharge after TAVI. Patients were stratified into those with preserved (LVEF ≥ 40 %) and those with reduced ejection fraction (LVEF < 40 %) according to pre TAVI echocardiogram. The primary endpoint was time to first unplanned hospitalization or death within one year after TAVI.

Results: 284 patients (mean age 82.1 ± 5.5 years, 61.6 % female) were discharged after TAVI. Of these, 207 (72.9 %) patients had an angiotensin inhibitor (ACE-I $n = 150$, 52.8 %; ARB $n = 57$, 20.1 %) at discharge. Within one year after discharge, 41 (14.4 %) patients died and 141 (49.7 %) were hospitalized (composite endpoint: $n = 144$, 50.7 %). In the total study population no significant influence of angiotensin inhibition on the combined endpoint was found. However, exploratory analysis revealed a significant interaction between angiotensin inhibition and LVEF ($p = 0.0112$): Angiotensin inhibition (versus no angiotensin inhibition) was associated with a significantly better outcome after TAVI in patients with reduced ejection fraction (LVEF < 40 %) whereas in patients with preserved ejection fraction (LVEF ≥ 40 %) no such influence was noted.

Conclusion: This exploratory analysis suggests improved clinical outcome with angiotensin inhibition in patients with reduced ejection fraction after TAVI, whereas no such benefit could be found in patients with preserved ejection fraction. These findings support recommendation of evidence-based angiotensin inhibition in patients with reduced ejection fraction also after TAVI, whereas the lacking effects in patients with preserved ejection fraction are in agreement with data from non-TAVI populations.

VII-2

Predictors of morbidity/mortality after Transcatheter Aortic Valve replacement (TAVI): a single-center study with up to six years follow-up

G. Wagner, S. Marek, L. Urbanschitz, G. Lamm, P. C. Gunacker, K. Preisl, P. Vock, H. Mayr, D. Moertl

2. Medizinische Abteilung, Abteilung für Anästhesiologie und Intensivmedizin, Universitätsklinikum St. Pölten, St. Pölten, Austria

Background: Transcatheter aortic valve replacement (TAVI) is a well-established treatment strategy for patients who are not suitable for surgical aortic valve replacement (SAVR). The randomized controlled PARTNER trial demonstrated significant reduction of mortality compared to medical treatment (MT), but event rate in this patient population with advanced age and several comorbidities remains high. Understanding the risk factors explaining morbidity and mortality is essential to further reduce event rates. The aim of this study was to identify predictors for long term adverse events after TAVI.

Methods: This study was designed as a retrospective, single-center, mono-cohort study. All patients with symptomatic severe aortic stenosis undergoing TAVI at the Clinical Department of Internal Medicine III (Cardiology and Emergency Medicine), University Hospital St. Poelten, between 01/2008 and 03/2014 were included. Established patient characteristics and comorbidities were selected as candidate variables for risk model in univariate and multivariate Cox models. The primary endpoint was a composite of first unplanned hospitalization and all-cause death over the complete study period.

Results: 311 patients (mean age 82.3 ± 5.5 years, 62.7 % female) undergoing TAVI (183 Medtronic CoreValve, 126 Edwards Sapien XT or 3, 2 Direct Flow Medical) were included. Median follow up was 632 days (IQR 272–1252 days). Chronic obstructive pulmonary disease (COPD, HR 1.878 [95 % CI 1.278–2.760]), diabetes (HR 1.452 [95 % CI 1.087–1.940]), and the STS score (HR 1.049 [95 % CI 1.009–1.090]) were independent predictors for the composite endpoint. Median event-free survival was 327 days (95 % CI 241–502 days) for patients with neither diabetes nor COPD, 167 days (95 % CI 95–255 days) for patients with diabetes only, 105 days (95 % CI 33–669 days) for patients with COPD only, and 44 days (95 % CI 22–168 days) for patients with both COPD and diabetes ($p < 0.0001$).

Conclusion: Our study identified COPD, diabetes and STS score as independent predictors of the composite of first unplanned hospitalization or all-cause death. If confirmed in larger patient populations, these comorbidities—COPD and diabetes—provide potential treatment targets to improve outcome after TAVI.

VII-3

Mode of death after Transcatheter Aortic Valve Implantation (TAVI) depends on left ventricular ejection fraction

G. Wagner, S. Marek, L. Urbanschitz, G. Lamm, P. C. Gunacker, K. Preisl, P. Vock, H. Mayr, D. Moertl

3. Medizinische Abteilung, Universitätsklinikum St. Pölten, St. Pölten, Austria

Background: Despite a dramatic improvement in survival in high-risk patients with severe aortic stenosis after transcatheter aortic valve replacement (TAVI), mortality remains high. To pre-

vent premature death in such a patient population, it is essential to understand the mode of death in order to define respective treatment targets. In chronic heart failure, the mode of death depends of left ventricular ejection fraction (LVEF): While patients with reduced ejection fraction (HFREF) predominantly die from heart failure associate death (progressive pump failure [PPF| or sudden cardiac death [SCD]), non-heart failure modes of death are much more important in patients with preserved ejection fraction (HFPEF). The aim of this study was to understand whether these observations also hold true after TAVI implantation.

Methods: This single-center, mono-cohort study included all patients undergoing TAVI for treatment of symptomatic severe aortic stenosis at the Clinical Department of Internal Medicine III (Cardiology and Emergency Medicine) at the University Hospital St. Poelten between 01/2008 and 03/2014. Mode of death was adjudicated by two independent observers, final classification was received by consensus reading. Adjudication was performed using medical reports, autopsy reports and personal communication with treating physicians and caregivers. LVEF was assessed by preinterventional echocardiography and dichotomized according to a cut-off of 40 %.

Results: 311 patients (mean age 82.3 ± 5.5 years, 62.7 % female) who underwent TAVI were included. Three different valve types were used: 183 self-expandable CoreValve (177 transfemoral, 6 transsubclavian), 126 balloon-expandable Edwards Sapien XT or 3 (all transfemoral) and 2 Direct Flow Medical (all transfemoral). During follow-up (median 632 days, IQR 272–1252 days) 110 patients died. LVEF had no significant influence on time to death but on mode of death: While 45 % of patients with an LVEF < 40 % died from heart failure associated reasons (sudden cardiac death 9 %, progressive pump failure 36 %), these modes of death were found in only 24 % patients with an LVEF ≥ 40 % (sudden cardiac death 9 %, progressive pump failure 15 %, $p < 0.05$).

Conclusion: Mode of death after TAVI depends on LVEF: Modes of death typically associated with HFREF are common in patients with reduced ejection fraction after TAVI and therefore might present an important and familiar treatment target. In contrast, the distribution of modes of death in TAVI patients with preserved ejection fraction might suggest similar difficulties as in common HFPEF patients when trying to further improve survival.

VII-4

Annual bleeding and vascular complications before and after implementation of a transradial cardiac catheterization programme: a retrospective, observational study in 12,745 patients

D. Kiblböck, G. Bozkaya, E. Zeindlhofer, K. Höllinger, A. Winter, M. Schmid, P. Siostrzonek

Krankenhaus der Barmherzigen Schwestern, Interne II—Kardiologie, Linz, Austria

Introduction: The transradial (TR) cardiac catheterization technique has a lower bleeding and vascular complication (VC) rate compared to the traditional transfemoral (TF) technique. TR access was implemented in our cardiac catheterization laboratory in 2011. The aim of this study was to investigate the annual bleeding and VC rate before and after the implementation of the TR cardiac catheterization programme.

Methods: All consecutive patients undergoing cardiac catheterization between January 2007 and December 2014 (diagnostic catheterization, percutaneous coronary intervention (PCI) including acute interventions in acute coronary syndrome (ACS)) were enrolled in this single-center, retrospective, observational study. Only patients undergoing transfemoral aortic valve implantation were excluded from this analysis. VC were categorized into major (retroperitoneal hematoma, pseudoaneurysm, arteriovenous fistula, hematoma diameter >5 cm, perforation and limb ischemia)

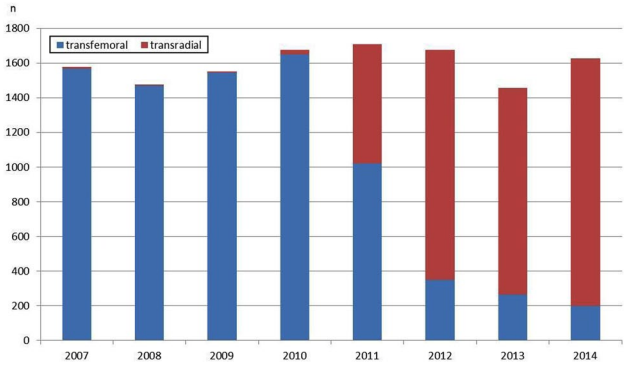


Fig. 1 Annual proportion of TF and TR access from 2007–2014

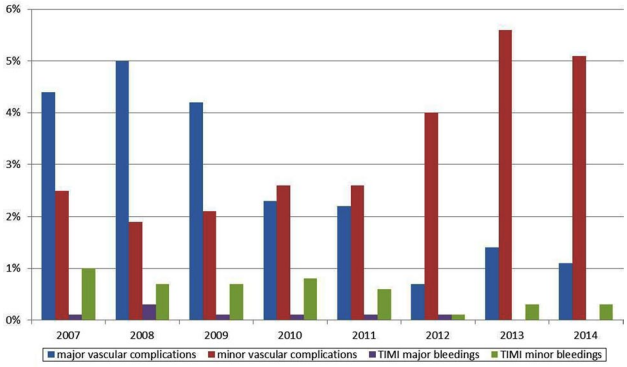


Fig. 2 Annual rate of bleedings and vascular complications 2007–2014

and minor (hematoma < 5 cm and minor bleeding at the puncture site) complications. Bleeding events were classified according to the TIMI bleeding criteria as major and minor TIMI bleedings.

Results: 12,745 patients (67.0 ± 11.9 years; female, $n = 4218$, 33.0 %; ACS, 35.4 %) underwent cardiac catheterization (TF, $n = 8459$, 63.8 %; TR, $n = 4804$, 36.2 %; PCI, $n = 5914$, 44.6 %) within the observation period. The proportion of TR procedures increased from 0.6 % in 2007 to 40.3 % with the implementation of the TR cardiac catheterization programme in 2011 and reached a proportion of 87.7 % in 2014 (Fig. 1). We observed a significant reduction of the incidence for major VC after TR implementation (Fig. 2) as follows: 2007, 4.4 %; 2008, 5.0 %; 2009, 4.2 %; 2010, 2.3 %; 2011, 2.2 %; 2012, 0.7 %, 2013, 1.4 %; 2014, 1.1 % (2007–2010 vs. 2011–2014, $p < 0.001$). There was no significant change with respect to TIMI major bleeding events (2007–2010, 0.13 %; 2011–2014, 0.05 %; $p = 0.12$), while the rate of TIMI minor bleedings significantly decreased (2007–2014, 0.8 %; 2011–2014, 0.3 %; $p < 0.001$). Only the rate of minor VC showed a significant increase (2007–2010, 2.3 %; 2011–2014, 4.2 %; $p < 0.001$). The median length of stay in hospital (2007–2010, 3 days; 2011–2014, 3 days) and the in-hospital mortality (2007–2010, 1.3 %; 2011–2014, 1.6 %; $p = 0.19$) did not change significantly after TR implementation.

Conclusion: The annual incidence of major VC and TIMI minor bleeding events significantly decreased after implementation of the TR technique in our catheterization laboratory. We did not observe a change in terms of TIMI major bleedings and in-hospital mortality. The increase of minor VC with TR did not prolong the length of in hospital stay. Therefore we conclude that the implementation of the TR access at our institution improved safety of the cardiac catheterization procedure due to a reduction of severe vascular and major bleeding complications.

VII-5

Barostimulation: therapy in patients with resistant hypertension- 6-month follow-up

T. Sturmberger, M. Kalteis, D. Debelic, H.-J. Nesser, J. Aichinger

Kardiologie, Anästhesie, KH Elisabethinen Linz, Linz, Österreich

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 patients with resistant hypertension with a 6 month follow-up.

Methods and results: We considered five patients with resistant hypertension for BAT-Implantation with a mean age of 65 years and a mean office blood pressure of 168/96 mmHg. In 3 patients renal denervation as performed previously, but they were nonresponders.

2 patients were male and mean number of antihypertensive medication was 5.5.

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 two weeks due to possible interference with wound healing. After 2 weeks the stimulator is activated and for the first 3 months, ambulatory controls have been scheduled every 4 week for modification of the device if necessary. 6 month follow-up data could be obtained in 4 patients.

After 6 months mean office blood pressure was 142/94 mmHg leading to a reduction of 26/2 mmHg to baseline.

Only in 1 patient antihypertensive medication could be reduced. No relevant complications occured unless paraesthesia on the implantion side, wich all vanished after 3 months.

Conclusion: Baroreflex Activation Therapy decreases arterial blood pressure in hypertensive patients after a follow-up of 6 Months 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.

VII-6

Echokardiografie nach TAVI mit Directflow-Prothese: Wenig Insuffizienz – hohe Gradienten

T. Sturmberger, V. Eder, C. Ebner, R. Steringer-Mascherbauer, W. Tkalec, J. Aichinger

Kardiologie, KH Elisabethinen Linz, Linz, Österreich

Hintergrund: Der Aortenklappenersatz mittels TAVI hat sich als Therapie für Patienten mit schwerer, symptomatischer Aortenklappenstenose mit hohem OP-Risiko etabliert und stellt eine Alternative zum konventionellen Aortenklappenersatz für eine ausgewählte Patientengruppe dar. Hierbei wird jedoch die native Aortenklappe nicht entfernt, sondern durch die eingebrachte Bioprothese an die Aortenwand gedrückt. Dies kann zu einem unzureichenden Anliegen der Bioprothese an den Aortenannulus führen, wodurch eine paravalvuläre Insuffizienz (PVI) entsteht, ein häufges Phänomen bei den am meisten eingesetzten TAVI-Prothesen (Edwards Sapien® und CoreValve®). Das Ausmaß der paravalvulären Insuffizienz ist mit einem erhöhten Mortalitätsrisiko assoziiert. Das Transkatheter-Aortenklappensystem von Direct Flow Medical ist ein nicht metallenes Transkatheter-Herzklappensystem. Die Bioprothese ist so konstruiert, dass sie den nativen Klappenring umgibt, damit eine Verankerung der Bioprothese sichergestellt ist und mögliche paravalvuläre Lecks, Verlagerungen oder Migrationen auf ein Mindestmaß beschränkt werden können. Wir berichten über erste Erfahrungen mit der Directflow-Prothese und postinterventionelle echokardiografische Ergebnisse.

Methode: Von Februar bis Dezember 2014 wurden in unserer Abteilung 14 Patienten mit einem mittleren Alter von 83,4 Jahren mit schwerer, symptomatischer Aortenklappenstenose einer TAVI mittels Directflow-Prothese unterzogen. Vor Entlassung der Patienten erfolgte eine Echokardiografie zur Evaluierung einer paravalvulären Insuffizienz und Bestimmung der transvalvulären Gradienten. Die Quantifizierung der paravalvulären Insuffizienz erfolgte nach den VARC 2 Kriterien mit folgender Graduierung: 1. Keine PVI; 2. triviale PVI; 3. PVI Grad I; 4. PVI Grad >II.

Resultate: Bei 13 der 14 Patienten konnte die Directflow-Prothese erfolgreich implantiert werden. Bei 1 Patientin kam es zu einer letalen Aortendissektion. Die echokardiografische Kontrolle erfolgte zwischen dem 1. und 5. postinterventionellen Tag. Bei 3/13 Patienten (23 %) konnte keine paravalvluäre Insuffizienz nachgewiesen werden. 6 Patienten (46,2 %) hatten eine triviale PVI, 3 Patienten (23 %) eine PVI Grad I und 1 Patient (7,8 %) hatte eine PVI Grad II. Somit lag bei 12 Patienten (92,2 %) eine PVI < Grad I vor. Die mittlere transvalvuläre Geschwindigkeit betrug 3,0 m/s mit einem maximalen Gradienten von 37,4 mmHg und einem mittleren Gradienten von 19,2 mmHg. Die echokardiografisch ermittelten Gradienten waren signifikant höher als die unmittelbar nach Absetzen der Klappenprothese gemessenen invasiven Gradienten (peak to peak 9 mmHg, mittlerer Gradient 8 mmHg).

Zusammenfassung: Das Auftreten einer paravalvulären Insuffizienz nach TAVI stellt einen wesentlichen Prognosefaktor dar. Die Directflow-Prothese unterscheidet sich in ihrer Konstruktion von den bislang etablierten TAVI-Prothesen. Dadurch wird eine erhebliche Reduktion einer relevanten paravalvulären Insuffizienz erreicht. Echokardiografisch auffallend sind erhöhte transvalvuläre Gradienten, welche mutmaßlich auf die Prothesenkonstruktion zurück zu führen sind und wesentlich höher sind als invasiv ermittelte Gradienten. Ursache für diese Diskrepanz sind erhöhte Ausflusstrakt-Geschwindigkeiten aufgrund des ventrikulären Klappenrings, sodass durch die vereinfachte Bernoulli-Gleichung (4 x v2) falsch hohe Gradienten errechnet werden. Es sollte daher zur Beurteilung der Prothesenfunktion der dimensionslose Index angewendet werden.

VII-7

Bleeding and vascular complications after cardiac catheterization: a retrospective comparison study of the transfemoral and transradial technique in 12,745 patients

G. Bozkaya, D. Kiblböck, E. Zeindlhofer, K. Höllinger, A. Winter, M. Schmid, P. Siostrzonek

Krankenhaus der Barmherzigen Schwestern, Interne II—Kardiologie, Linz, Austria

Introduction: Cardiac catheterization can either be performed via an access through the femoral or the radial artery. Bleeding and vascular complications (VC) at the puncture site represent important potential complications of cardiac catheterization. Although the transradial (TR) access may lead to a decrease in the rate of complications many centers still prefer the traditional transfemoral (TF) technique. At our cardiac catheterization laboratory the TR approach was introduced in 2011. The aim of this study was to compare the bleeding and VC rate for the TF and TR technique, respectively.

Methods: All consecutive patients undergoing cardiac catheterization (diagnostic catheterization, percutaneous coronary intervention (PCI) including acute intervention in patients with acute coronary syndrome (ACS)) between January 2007 to December 2014 were enrolled in this retrospective, single-center study. Only patients undergoing TF aortic valve implantation were excluded. VC were categorized into major (retroperitoneal hematoma, pseudoaneurysm, arteriovenous fistula, hematoma diameter >5 cm, perforation and limp ischemia) and minor (hematoma diameter <5 cm and minor bleeding at the puncture site) complications. Bleeding events were classified according to the TIMI bleeding criteria.

Results: 12,745 patients (67.0±11.9 years; female, 33.0%; ACS, 35.4%) underwent cardiac catheterization (TF, n=8459, 63.8%; TR, n=4804, 36.2%; PCI, n=5914, 44.6%). The success rate for the TR approach was 95.3%.The overall complication rate (bleeding and VC) was 5.7% (TF, n=520, 6.1%; TR, n=237, 4.9%; TF vs. TR, p=0.004) and was higher in patients requiring PCI (TF + PCI, n=356, 8.7%; TF + no PCI, n=164, 3.7%; TR + PCI, n=101, 5.5%; TR + no PCI, n=136, 4.6%). More complications occurred in female patients (male, n=441, 5.2%; female, n=316, 7.5%; TF + male, n=296, 5.6%; TF + female, n=224, 8.0%; TR + male, n=145, 4.5%; TR + female, 92, 6.5%) and in patients with ACS (ACS, n=331, 7.3%; no ACS, n=426, 5.2%; TF + ACS, n=247, 8.3%; TF+ no ACS, n=273, 5.4%; TR + ACS, n=84, 5.5%; TR + no ACS, n=153, 4.8%). Major VC was observed in 3.6% with the TF and in 0.6% with the TR technique. The minor VC rate was higher with 4.3% in the TR group compared to 2.5% in the TF group. Bleeding events occurred in 0.9% with the TF approach (TIMI major, n=11, 0.1%; TIMI minor, n=70, 0.8%) and in 0.1% with the TR approach (TIMI major, n=0; TIMI minor, n=3, 0.1%). The mean length of in hospital stay for patients with complications was 6.5±6.9 days in the TF group and 3.6±3.8 days in the TR group. Overall in-hospital mortality was 1.4% (TF, n=149, 1.8%; TR, n=29, 0.6%).

Conclusion: In our large, retrospective study the bleeding and major VC rate was significantly lower with the TR technique compared to the TF technique. The complication rate in the TF group was higher in female patients, in patients requiring PCI and in patients with ACS. We conclude that the TR approach is a safer procedure and should be used as the primary technique for cardiac catheterization.

Postersitzung VIII: Koronare Herzkrankheit

VIII-1

Diagnostic and prognostic value of long non-coding RNA (LIPCAR) in patients with STEMI, NSTEMI and stable coronary artery disease

G.-A. Giurgea, A. Zimba, G. Goliasch, N. Pavo, J. Bergler-Klein, G. Maurer, R. Kumarswamy, S. Batkai, T. Thum, M. Pavone-Gyöngyösi

Department of Cardiology, Medical University of Vienna, Vienna, Austria
Hannover Medical School, Hannover, Germany

Background: Long non-coding RNAs (lncRNA) belong to the non-protein coding transcriptom family and characterized by consisting of >200 nucleotids. Their role as circulating biomarker has been investigated in cancer and cardiovascular system. It has recently been shown that the circulating level of the mitochondrial lncRNA uc022bqs.1 (Long Intergenic non-coding RNA predicting cardiac remodeling, LIPCAR) was associated with development of cardiac remodeling and cardiovascular death. The aim of our study was to compare the diagnostic value of LIPCAR in patients with STEMI, NSTEMI and stable coronary artery disease (CAD) and to associate with clinical outcome at 1-year follow-up.

Methods: Sixty-one patients with either stable coronary artery disease with previous coronary intervention (group CAD, n=30), or STEMI with primary PCI (group STEMI, n=15) or NSTEMI undergoing coronary intervention (group NSTEMI, n=16) were prospectively included into the study. Clinical characteristics (age, gender, atherosclerotic risk factors, presence of peripheral artery disease or chronic renal insufficiency), and routine laboratory parameter (creatine kinase/CK/, troponin T) were measured. Cardiac adverse events (coronary revascularization, implantation of pacemaker or implantable defibrillator, hospitalization due to angina pectoris) were recorded at the 1-year clinical follow-up (FUP). LncRNAs were isolated from the plasma samples using miRNeasy kit, and the LIPCAR level was measured by quantitative real-time PCR and normalized to controls, and expressed on arbitrary scale.

Results: Group STEMI patients were younger than the patients in CAD and NSTEMI groups, and had significantly higher troponin T and CK. LIPCAR value was found significantly down-regulated in group STEMI (0.45±0.08) (mean ± SE) as compared to groups NSTEMI (0.68±0.21) or CAD (0.79±0.14). Time of plasma sampling was significantly negatively correlated with LIPCAR levels in groups STEMI and NSTEMI (p=0.018, r=0.44), suggesting an early massive down-regulation of LIPCAR in the acute phase of STEMI and NSTEMI. Patients with stable CAD and with cardiac adverse events at the follow-up had significantly higher levels of LIPCAR (1.12±0.11 vs. 0.73±0.19). Our results indicate biphasic response of LIPCAR regulation: down-regulation in acute phase of STEMI and NSTEMI, and up-regulation in chronic CAD.

In a consecutive patient cohort, LIPCAR proved to be an early discriminative diagnostic marker of STEMI versus NSTEMI, and it might be a valuable additional parameter for diagnosis and prognosis of acute or chronic CAD.

VIII-2

Hand grip strength significantly predicts cardiovascular event risk in patients with type 2 diabetes

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

VIVIT-Institute, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

Muscle fitness is an established indicator of overall health. The power of muscle strength to predict cardiovascular endpoints in patients with type 2 diabetes (T2DM) is unclear and is addressed in the present study.

We studied a high-risk cohort of 209 patients with T2DM who underwent coronary angiography for the evaluation of stable coronary artery disease (CAD). Forearm muscle dynamometry was performed to determine hand grip strength in the dominant arm the day before angiography. Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing ≥ 50 %. T2DM was diagnosed according to the ADA criteria. Prospectively, we recorded vascular events over 5.5 ± 2.2 years.

Grip strength, measured in kilograms, at baseline did not differ significantly between patients with significant CAD and those who did not have significant CAD (34 ± 12 vs. 31 ± 12 kg; $p = 0.140$). Prospectively, hand grip strength significantly predicted the incidence of major cardiovascular events ($n = 65$) after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol and HDL cholesterol (standardized adjusted HR 0.72 [0.52–0.99]; $p = 0.042$). This result was not attenuated after further adjustment for the angiographically determined baseline CAD state (HR 0.72 [0.53–0.99]; $p = 0.046$).

We conclude that hand grip strength in patients with T2DM is inversely associated with vascular events independently both from well established cardiovascular risk factors and from the angiographically determined baseline CAD state.

VIII-3

ProBNP strongly predicts future macrovascular events in angiographied coronary patients with as well as in those without type 2 diabetes

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

VIVIT-Institute, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker in various patient populations including those with congestive heart failure. The power of proBNP to predict cardiovascular events in patients with type 2 diabetes (T2DM) undergoing coronary angiography is unclear and is addressed in the present study.

We measured serum proBNP in 737 patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD). Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing ≥ 50 %. T2DM was diagnosed according to the ADA criteria. Prospectively, we recorded vascular events over 5.6 ± 2.1 years.

ProBNP was significantly higher in patients with ($n = 391$) than in subjects without significant CAD at baseline (720 ± 1358 vs. 674 ± 1606 pg/ml; $p = 0.001$). Prospectively, we recorded 183 cardiovascular events. The incidence of vascular events significantly increased over tertiles of proBNP in patients with T2DM (21.3, 30.2, and 43.5 % respectively; $p = 0.028$) was well as in subjects without T2DM (16.9, 21.2, and 29.3 %, respectively; $p = 0.015$). Concordantly, 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 patients with T2DM (standardized adjusted HR 1.50 [1.25–1.78]; $p < 0.001$) and in subjects without T2DM (HR 1.15 [1.03–1.29]; $p = 0.015$). These results were not attenuated after further adjustment for the angiographically determined baseline CAD state (HRs 1.49 [1.24–1.79]; $p < 0.001$ and 1.27 [1.13–1.43]; $p < 0.001$ in patients with T2DM and in subjects without T2DM, respectively).

We conclude that serum proBNP predicts cardiovascular events independently of established cardiovascular risk factors and of the baseline CAD state both in patients with and in subjects without T2DM.

VIII-4

Plasma chemerin is elevated in type 2 diabetes, is associated with impaired kidney function and is predictive for cardiovascular events

A. Leiherer, A. Muendlein, P. Rein, K. Geiger, P. Fraunberger, H. Drexel, C. H. Saely

VIVIT-Institute, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
Medizinisches Zentrallabor, Feldkirch, Austria

The association of the novel adipokine chemerin with cardiovascular event risk is unclear and is addressed in the present study.

We measured plasma chemerin levels in 495 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD.

Chemerin was higher in patients with type 2 diabetes mellitus (T2DM, $n = 111$) than in non-diabetic subjects (192 ± 73 vs.170 ± 65 ng/ml, $p = 0.001$). Further, chemerin was significantly and independently associated with the glomerular filtration rate (GFR) in analysis of covariance using age, sex, and BMI as covariates ($F = 49.6$, $p < 0.001$). Prospectively, we recorded 107 cardiovascular events over 3.5 years. Chemerin both univariately and after multivariate adjustment including baseline GFR significantly predicted cardiovascular events, with hazard ratios of 1.83 [95 %CI 1.19–2.83], $p = 0.006$ and 1.67 [1.05–2.67], $p = 0.030$ for the top tertile of chemerin versus the first and second tertiles, respectively. A cardiometabo-chip-analysis revealed an association of two nearby located SNPs in TP53BP1 and CAPN3 rs2444030 nominal p-value = 5.2 e-9, and rs3098423 nominal p-value = 9.6 e-8) with chemerin concentration. Haplotype analysis for these two SNPs revealed a significantly impaired GFR associated with the fully mutated haplotype compared to all other haplotypes (OR = 0.63, $p = 0.006$).

We conclude that high chemerin is characteristic of T2DM, is associated with impaired kidney function, and is predictive for cardiovascular events.

VIII-5

Single nucleotide polymorphisms at the hydroxy-methyl-glutaryl-CoA reductase gene locus significantly predict cardiovascular events in coronary patients with type 2 diabetes

A. Leiherer, A. Muendlein, C. H. Saely, E. Kinz, P. Rein, A. Vonbank, P. Fraunberger, H. Drexel

VIVIT-Institute, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
Medizinisches Zentrallabor Feldkirch, Feldkirch, Austria

Hydroxy-methyl-glutaryl-CoA reductase (HMGCR) protein catalyzes the rate-limiting step in cholesterol biosynthesis and is the major target for cholesterol-lowering drug therapy. Recently, genetic variations at that locus have been linked with lipid levels and coronary heart disease risk. The association of HMGCR gene variants with cardiovascular events in patients with type 2 diabetes (T2DM) has not yet been evaluated and is addressed in the present study.

We prospectively investigated the impact of the HMGCR tagging single nucleotide polymorphisms (SNPs) rs3761739, rs10515198, rs3846662, rs7717396, rs3846663, and rs4703670 on the incidence of vascular events in a high-risk cohort of 262 consecutive patients with T2DM undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease. Furthermore, variants rs12654264 and rs12916 were included in the present study based on previously published associations.

Table 1 HGMCR SNPs as predictors of future cardiovascular events in T2DM patients

SNP	HR [95%CI]	p-value
rs3761739	1.68 [1.04–2.73]	0.035
rs10515198	1.38 [0.78–2.42]	0.268
rs3846662	1.69 [1.16–2.44]	0.006
rs7717396	2.76 [1.21–6.30]	0.016
rs3846663	1.71 [1.19–2.47]	0.004
rs4703670	1.58 [1.03–2.42]	0.037
rs12654264	1.71 [1.19–2.47]	0.004
rs12916	1.74 [1.20–2.53]	0.003

HR hazard ratio, *SNP* single nucleotide polymorphism

As is shown in the table all variants apart from tagging variant rs10515198 significantly predicted future cardiovascular events in patients with T2DM after multivariate adjustment including LDL cholesterol and statin therapy.

We conclude that in patients with T2DM common HMGCR variants significantly predict cardiovascular events.

Postersitzung IX: Pulmonale Hypertenion 1

IX-1

Endothelin receptor blockade in heart failure with diastolic dysfunction and pulmonary hypertension (BADDHY-Trial)

B. Koller, R. Steringer-Mascherbauer, C. Ebner, T. Weber, M. Ammer, J. Eichinger, I. Pretsch, M. Herold, J. Schwaiger, H. Ulmer, W. Grander

Innere Medizin/Kardiologie, Landeskrankenhaus Hall in Tirol, Hall in Tirol, Austria
Innere Medizin II, Kardiologie, Angiologie und internistische Intensivmedizin, Krankenhaus der Elisabethinen Linz, Linz, Austria
Innere Medizin II, Kardiologie und Intensivmedizin, Klinikum Wels-Grieskirchen, Wels, Austria
Innere Medizin II, Kardiologie und Intensivmedizin, Paracelsus Medizinische Privatuniversität Salzburg, Salzburg, Austria
Innere Medizin VI, Medizinische Universität Innsbruck, Innsbruck, Austria
Department für medizinische Statistik, Informatik und Health Economy, Medizinische Universität Innsbruck, Innsbruck, Austria

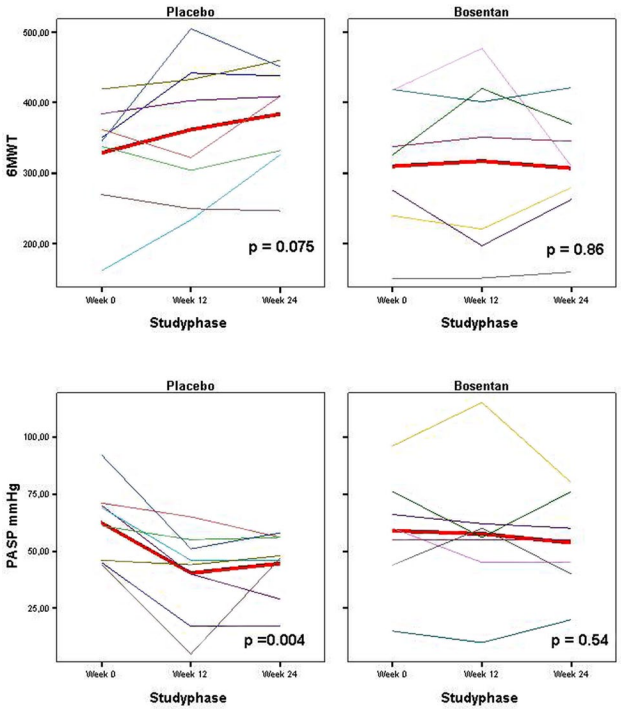
Background: About 70–83 % of patients with heart failure and preserved ejection (HFpEF) develop pulmonary hypertension (PH).

Materials and methods: In this multicentre, randomised placebo-controlled pilot trial we investigated clinical and hemodynamic effects of the endothelin-receptor blocker bosentan in patients with HFpEF and PH (PH-HFpEF). Eligible probands received either 12 weeks bosentan or placebo. At study entrance, week 12 and a follow up at week 24—a six minute walking test (6MWT), an echocardiography, and a laboratory assessment were performed, as well as the minnesota living with heart failure questionnaire and the short form 36 filled out. Right heart catheterization was conducted at screening only.

Results: The study was aborted due to an interims analysis after 20 patients had been included. 15 patients completed follow up. None of the bosentan treated patients experienced worsening of heart failure. 6MWT did not change in the bosentan group, but tentatively increased in the placebo group from 328.8 ± 79.6 m (study entrance) to 361.6 ± 98.2 mmHg (week 12) and 384.0 ± 74.9 m (week 24); $p = 0.075$ (Fig. 1). In the placebo group echocardiographic estimated systolic pulmonary artery pressure significantly decreased [62.3 ± 16.7 mmHg (study entrance), 40.4 ± 19.9 mmHg (week 12), 44.6 ± 14.5 mmHg (week 24); $p = 0.004$ (Fig. 2)] as did right atrial pressure [13.1 ± 5.3 (study entrance), 10.0 ± 3.8 (week 12), and 9.4 ± 3.2 (week 24); $p = 0.046$]. Both parameters did not change in the bosentan group.

Discussion: Endothelin receptor blockade in patients with PH-HFpEF may be safe, but does not improve exercise capacity, quality of life or echocardiographic assessed hemodynamic parameters.

Clinical trial registration: http://www.clinicaltrials.gov/ct2/show/NCT00820352?term=BADDHY&rank=1, NCT00820352.



IX-2

First promising experience with the surgical exchange of a gas-driven implantable pump in a patient with pulmonary arterial hypertension in a center having implanted more than 30 pumps

R. Steringer-Mascherbauer, V. Eder, C. Huber, J. Niel, R. Függer, J. Aichinger

Interne 2 Kardiologie/Angiologie/Intensivmedizin, Krankenhaus Elisabethinen Linz, Linz, Austria

Introduction: Intravenous (iv.) administration of treprostinil by a gas-driven implantable pump offers relevant advantages: Absence of site pain, which is frequent with subcutaneous (sc.) administration and a minimized risk of possibly life-threatening line-infections as compared to iv. administration with external pumps. As previously reported implantation is only offered to stable patients with severe site pain under sc. treprostinil. Treprostinil uptitration is done exclusively sc. at our center. Since 2010 we have successfully implanted 33 pumps. Since the first patient standard operation procedures (SOPs) for pre-, peri- and postoperative management are in use. During long-term follow-up an increased flowrate was observed leading to adoption of the refill interval. A second generation of this pump is under development. One pump twisted due to

weight reduction of the patient (20 kg) leading to difficulties in refill. Reimplantation became necessary.

Methods: First implantation was performed without any complications in October 2011 in a 30-year female PAH patient. After start of sc. treprostinil in July 2011 the patient had rapidly improved from NYHA FC III/IV to FC II but suffered from site pain. Monthly controls proved sustained parenteral prostanoid treatment improvement. For non-disease related reasons the patient lost more than 20 kg. This led to twisting of the pump complicating refill procedures until refill was impossible in March 2014. Patient was transitioned to sc treprostinil for two weeks without any problems until reimplantation. As required by our SOPs the patient was preoperatively independently assessed by the PAH specialist, surgeon and anesthesiologist. After explantation of the twisted pump the tissue encapsuling the pump was removed. A new pump was implanted.

Results: No intraoperative complications were observed. Due to the size of the wound area not surprisingly the patient postoperatively developed a clinically significant seroma. Therefore special longer needles had to be used for the next 4 monthly refills. Nevertheless the patient was highly pleased with the new pump and the refill procedures. By August 2014 the seroma resolved. Our patient is currently stable in NYHA FC II. In our cohort no other reimplantation was necessary including the pumps with increased flowrates. For these pumps adaption of the refill interval was sufficient.

IX-3

Kidney parameter changes in severe pulmonary arterial hypertension: an early hint for reevaluation of treatment decisions?

R. Steringer-Mascherbauer, V. Eder, C. Huber, J. Niel, J. Aichinger

Interne 2 Kardiologie/Angiologie/Intensivmedizin, KH Elisabethinen Linz, Linz, Austria

Introduction: Pulmonary arterial hypertension (PAH) is a progressive fatal disease. Renal dysfunction is a common finding in PAH, especially in patients with severe disease. In heart failure patients a decline in renal function is a negative prognostic marker. Recent data for PAH associated with sickle-cell disease discuss serum ureic acid as a potential prognostic marker. In severely ill patients changes in N-terminal prohormone brain natriuretic peptide (NT-proBNP) values are widely used to facilitate clinical decision making. We evaluated renal function parameters with reference to echocardiography-derived and clinical parameters in severely ill PAH patients after treatment escalation with parenteral treprostinil. Published experience on parenteral prostanoids and renal function is scarce.

Methods: At our specialized PH center data are documented in ELPHREG (Elisabethinen Linz Pulmonary Hypertension Registry). 28 consecutive PAH patients requiring treatment escalation with parenteral treprostinil were included in this evaluation. Data were assessed at beginning of treprostinil treatment (baseline) and after 12 months.

Results: Three patients were excluded from analysis (missing data at 12 months). These patients were referred to our center for treprostinil initiation and are followed up at the referring center. Complete data are available for 25 patients (f/m), aged 33–83. All but three patients received PAH-specific combination therapy. Some patients were even managed without additional diuretics. Diabetes was diagnosed in 3 patients. Table 1 shows patient specific data. Data of 23 patients revealed preserved renal function. This was observed in patients with laboratory findings in normal range as well as in patients with slight to moderate impaired renal function at baseline. One patient (No 9) expired after 12.5 months. In this patient renal function parameters started to deteriorate after 6 months, whereas NT-pro BNP values increased 2 months earlier. Patient No 6 started with a very low glomerular filtration rate (GFR) 18.1 and dialysis had to be started after 12 months. Also these NT-proBNP values started varying months before.

Conclusions: To the best of our knowledge this is the first long-term report on renal function in severely ill PAH patients treated with parenteral treprostinil. We demonstrated no influence of treprostinil therapy on renal function even in patients with pre-existing impaired kidney capacity. To gain more information on a possible prognostic impact of renal function for clinical decisions further research is warranted.

IX-4

Severe pulmonary arterial hypertension: gender therapy: a crucial point?

R. Steringer-Mascherbauer, V. Eder, C. Huber, J. Niel, J. Aichinger

Interne 2 Kardiologie/Angiologie/Intensivmedizin, KH Elisabethinen Linz, Linz, Austria

Introduction: Epidemiological data confirm female predominance in pulmonary arterial hypertension (PAH). There is the estrogen paradoxon. Beneficial or deleterious effects of estrogen in PAH are controversely discussed. Estrogen per se is negatively affecting pulmonary vasculature. Animal models however suggest a "second hit" like a change in estrogen metabolism. Smad1 deficiency and female gender have been shown to contribute to development of PAH. There is an age dependent sex effect on outcomes after high-risk pediatric cardiac surgery reflected by increased risk of death for girls in early infancy, supporting a biological effect. In adults cardiovascular stress is sex dependent. Female and male right ventricles differ in anatomy and physiology. Experimental data demonstrate sex differences in electrophysiological properties leading to higher risk of arrhythmia in women. Since 2005 PAH death rates increased in both genders however more pronounced in women. Contrarily death rates for pulmonary embolism and emphysema have significantly declined. Still it is unclear how incidence, age of onset, disease severity and prognosis are sex related or influenced by other factors such as socioeconomic impact or ethnicity. Probably there is both positive and negative estrogen influence in PAH depending on e.g. cell environment. Gender differences in PAH seem to vary in different age groups.

Methods: We evaluated severely ill PAH patients under PAH specific combination therapy including parenteral prostanoids, as due to the stage of the disease differences in e.g. right ventricular function (RVF) might be more prominent. 26 patients (17 f, 9 m) were identified in our registry. Number of children, contraceptive use and hormone replacement (HRT) therapy were evaluated in female patients, diabetes and use of psychotropic drugs in all patients. RVF was assessed by echocardiography at the start of prostanoid treatment and during routine visits to demonstrate possible gender differences in disease progression.

Results: 9 female patients had children (1–8), contraceptive use was reported by 3 women, HRT by 3 women. Diabetes and use of psychotropic drugs was present in 3 female. RVF tended to be more impaired in male patients at start of prostanoid therapy. Tailored parenteral prostanoid therapy led to comparable clinical improvement in female and male patients. Not surprisingly there was a trend towards higher prostanoid doses in men.

Conclusion: The clinical impact of gender differences in PAH remains controversial. At our center we focus on personalized, tailored PAH specific therapy including individualized parenteral prostanoid treatment.

IX-5

Levels of the soluble subform of the mechanosensing cell surface receptor PECAM-1 (platelet endothelial cell adhesion molecule-1) are elevated after acute pulmonary embolism with right heart dysfunction and CTEPH (chronic thromboembolic pulmonary hypertension)

J. Kellermair, M. Lankheit, L. Kellermair, M. K. Frey, W. Helmreich, I. M. Lang

Interne II, Klinikum Wels, Wels, Austria
CTH Universität Mainz, Mainz, Germany
Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Introduction: Platelet endothelial cell adhesion molecule-1 (PECAM-1) is a complex single-chain glycopeptid cell receptor that is involved in sensing of chronic mechanical forces arising from blood flow and sheer stress in pulmonary endothelium. In the setting of acute pulmonary embolism (PE) and chronic thromboembolic pulmonary hypertension (CTEPH) the pulmonary endothelium is exposed to significant mechanical forces due to pulmonary hypertension. A soluble subform of PECAM-1 (sPECAM-1) is generated via cell surface cleavage upon cell activation during venous thromboembolism (VTE) and can be detected via ELISA in human plasma. We suggest that sPECAM-1 plasma levels reflect the degree of mechanical force on pulmonary endothelium, thus are elevated in patients with pulmonary hypertension.

Material/methods: In the present study we determined soluble PECAM-1 plasma levels in patients with acute pulmonary embolism (baseline and 6 month follow-up, $n=132$) and CTEPH ($n=42$) to characterize the course of sPECAM-1 and assess a potential predictive value for the development of CTEPH after PE. sPECAM-1 levels were measured utilizing indirect enzyme-linked immunosorbent assay (sandwich Platinum ELISA Bender MedSystems BMS 229).

Results: Our results demonstrate that sPECAM-1 plasma levels are elevated in patients with severe pulmonary embolism with echocardiographic signs of right ventricular (RV) dysfunction, compared to patients with normal RV function after 6 months follow-up (63.62 [51.41/77.74] vs. 54.11 [43.69/67.65] ng/ml; $p=0.0253$). This difference is mainly due to a significant rise (baseline- > follow up) of sPECAM-1 plasma levels in patients with initial RV dysfunction (baseline versus follow up sPECAM-1 in patients without RV dysfunction: $p=0.8332$ and in patients with RV dysfunction $p<0.0001$).

In patients with CTEPH sPECAM-1 levels are markedly higher (83.33 [70.83/95.97] ng/ml) than in patients with acute pulmonary embolism (both baseline [$p<0.0001$] and follow up [$p<0.0001$]) and are unrelated to hemodynamic parameters evaluated during right heart catheter studies (PVR, s/d/m PAP, PCWP).

Conclusion: In our present study we demonstrate that sPECAM-1 plasma levels increase in conditions of elevated mechanical forces in the pulmonary vascular system over time, and could serve as a biomarker for the development of CTEPH after acute pulmonary embolism.

IX-6

Parenteral treprostinil induces a phenotypic shift of circulating monocyte subsets

T. Hofbauer, A. Mangold, T. Scherz, D. Simon, R. Sadushi-Kolici, I. M. Lang

Kardiologie, Medizinische Universität Wien, Vienna, Austria

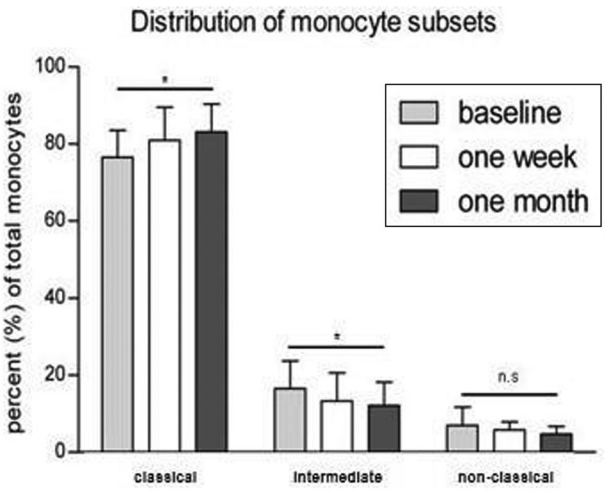
Introduction: Pulmonary hypertension (PH) is a disease of occlusive pulmonary vascular remodeling. Key histologic features are intimal fibrosis, smooth muscle cell hypertrophy, adventitial fibrosis, vascular occlusion and thrombosis. Increased pulmonary vascular resistance augments right ventricular load, and eventually leads to right heart failure. Early vascular changes have been reported to involve vascular inflammation, including mononuclear cells. We investigated monocyte subsets in patients with severe PH, prior to and after initiation of parenteral treprostinil.

Materials and methods: Peripheral blood samples were drawn prior to (baseline), one week and one month after treatment initiation in 10 treatment-naïve patients (6 females, age = 71 ± 10.1). Monocytes were characterized based on their expression of CD14 and CD16 (CD14++CD16- corresponding to classical, CD14+CD16+ corresponding to intermediate, CD14+CD16++ corresponding to non-classical monocytes), CX3CR1, HLA-DR, TLR-2, TLR-4, IL-6 and BMPR-II.

Results: Treprostinil treatment led to a shift of monocyte subsets (Figure): classical monocytes significantly increased (baseline 76.5 ± 7.1 %, one month 83.16 ± 7.24 %, $p=0.020$), whereas intermediate and non-classical monocytes decreased (baseline 16.57 ± 7.14 %, 1 month 12.12 ± 6.06 %, $p=0.049$ and baseline 6.93 ± 4.75 %, one month 4.73 ± 1.94 %, $p=0.205$). The total number of monocytes did not change. The expression of HLA-DR on classical monocytes was significantly upregulated (baseline MFI 5833 ± 1991, one month MFI 7291 ± 2534, $p=0.015$). No alterations of CXCR3, BMPRII, TLR2, TLR4 and IL-6 expressions were observed.

Discussion: In the present study, classical monocytes were shown to comprise 76.5 ± 7.1 % of total monocytes in severe PH at baseline, compared with a fraction of 85–90 % of total monocytes in normal subjects. Because classical monocytes exert phagocytic properties, removal of antigenic debris and thrombus may be delayed in PH, thus enhancing vascular occlusion.

Furthermore, our data illustrate that PH patients have a threefold higher proportion of intermediate monocytes compared with healthy controls. Because intermediate monocytes exert proangiogenic and antigen presenting functions, further experiments will focus on these properties and their involvement in occlusive vascular remodeling.



Postersitzung X: Rhythmologie 1

X-1

Increased inducibility of atrial fibrillation and impaired left atrial contractile function in a porcine model of arterial hypertension

M. Manninger, D. Zweiker, A. Alogna, G. Adlsmayr, B. Zirngast, H. Mächler, A. Lueger, U. Reiter, G. Reiter, H. Brussee, G. Antoons, H. Post, D. Scherr

Universitätsklinik für Innere Medizin, Abteilung für Kardiologie, Abteilung für Herzchirurgie, Abteilung für Radiologie, Medizinische Universität Graz, Graz, Austria
Siemens Healthcare, Vienna, Austria
Department of Physiology, UniversityMaastricht, Maastricht, The Netherlands
Campus Virchow, Abteilung für Kardiologie, Charite Universitätsmedizin Berlin, Berlin, Germany

Introduction: Arterial hypertension is the strongest risk factor for atrial fibrillation (AF). However, the underlying mechanisms are poorly understood. 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 a >40 mmHg increase of systolic blood pressure, left ventricular concentric hypertrophy, atrial and left ventricular cardiomyocyte hypertrophy, but no overt increase of atrial and left ventricular collagen content. On a cellular level, we found impaired cardiomyocyte contractility, which could be reversed by NCX-blockade.

Here, we sought to test whether these cellular findings are also reflected in vivo and if these changes render the atria more susceptible to AF.

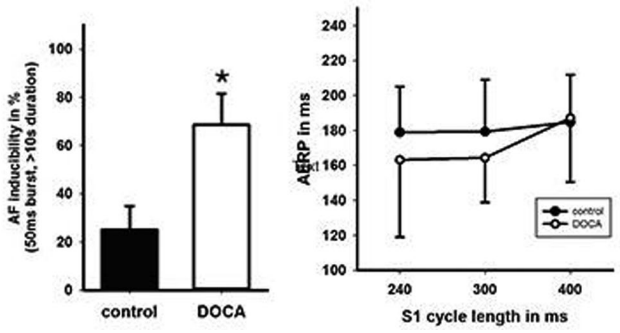
Methods: Seven healthy pigs underwent subcutaneous implantation of DOCA pellets and high-salt feeding for 12 weeks. 8 weight-matched animals (65±4 vs. 66±6 kg) served as controls. The animals were anaesthetized and instrumented with a quadripolar stimulation catheter in the high right atrium and a decapolar 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, 10s 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 10s.

After the electrophysiological study, magnetic resonance (MR) imaging was performed on 5 DOCA-treated and 7 control animals (65±2 vs. 58±9kg, n.s.) on a 3T MR scanner. To assess atrial and ventricular function, retrospectively ECG-gated, fast low angle shot (Flash) cine images were obtained under free breathing. Left ventricular (LV) volumes and mass, as well as left atrial (LA) volumes were derived by manual segmentation using the Simpson approach.

Results: AERP did not differ between both groups, but the inducibility of AF was significantly higher in DOCA treated animals compared to controls (Figure). Mean AF duration was not different between groups (DOCA: 17±2s, control: 12±5s; n.s.).

MRI in DOCA-treated animals showed no change in systolic LV function (ejection fraction (EF) 52.8±4.7 vs. 52.4±2.8 %, n.s.), increased LV mass (134±21 vs. 100±18.6 g, $p<0.01$) and impaired left atrial contractile function (total left atrial EF 38±11 vs. 55±3 % , $p<0.05$, left atrial contractile EF 23±10 vs. 38±7 %, $p<0.05$).

Conclusion: DOCA-induced arterial hypertension increases atrial susceptibility towards fibrillation at a state of impaired left atrial contractile function on cellular base and in vivo 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.



X-2

Outcome of patients with atrial fibrillation and predictors of new onset atrial fibrillation after TAVI

D. Zweiker, M. Fröschl, S. Tiede, J. Schmid, M. Manninger, H. Brussee, R. Zweiker, J. Binder, H. Mächler, R. Maier, O. Luha, A. Schmidt, D. Scherr

Klinische Abteilung für Kardiologie, Medizinische Universität Graz, Graz, Austria

Introduction: Rhythm disturbances after TAVI are common. This study investigates outcome of patients with new onset of atrial fibrillation (NOAF) after TAVI compared to outcome of patients with baseline atrial fibrillation and those with sinus rhythm.

Materials and methods: We performed a single-centre study of 113 consecutive patients undergoing TAVI with the Medtronic CoreValve prosthesis (90 % transfemoral, 10 % direct transaortic) between December 2010 and September 2012. Mean age was 82±6 years, 63 % were female. EuroScore II predicted a 30-day mortality of 9.4 % and the German AV Score was 11.7 %. Patients were divided into a sinus rhythm group ($n=63$, 56 %) and baseline atrial fibrillation group ($n=50$, 44 %) according to clinical records and baseline electrocardiograms. Preprocedural pacemaker incidence was 11 % ($n=6$) in the sinus rhythm group and 16 % ($n=8$) in baseline atrial fibrillation group. After the procedure, patients were monitored by telemetry during their intensive care stay and electrocardiograms were recorded daily. NOAF was defined as any episode of atrial fibrillation occurring in the sinus rhythm group after TAVI procedure before discharge from hospital. All patients were followed up for one year.

Results: NOAF occurred in 8 (13 %) of patients with prior sinus rhythm. Pre-existing anticoagulation and previous valve surgery were factors associated with NOAF ($p=0.041$ for both). Thirty-day mortality was 1.6, 0.0 and 4.0 % in the sinus rhythm, NOAF and baseline atrial fibrillation groups ($p=0.683$), respectively. Pacemaker implantation rate in the first postprocedural year was 11, 25 and 16 % in the sinus rhythm, NOAF and baseline atrial fibrillation groups ($p=0.817$). NOAF was not associated with higher mortality or morbidity, or longer hospitalization. However, baseline atrial fibrillation patients had significantly higher 1-year mortality (baseline atrial fibrillation 22 % vs. sinus rhythm 13 %, $p=0.033$) than patients without baseline atrial fibrillation.

Discussion: This study shows that NOAF is common after TAVI, but is not associated with higher mortality. Baseline atrial fibrillation is, however, associated with higher 1-year mortality.

X-3

Clinical experience using a new fluoroscopy integrated catheter tracking system (Mediguide) for ablation of ventricular tachycardia: a case matched comparison

M. Derndorfer, E. Sigmund, G. Kollias, S. Winter, J. Aichinger, H. Pürerfellner, M. Martinek

Kardiologie 1, KH Elisabethinen Linz, Linz, Austria

Background: Mediguide (MG) represents a new catheter tracking system integrated into the C—arm of a standard fluoroscopic unit. After recording of short fluoro loops (usually RAO, LAO), the tip of MG—enabled catheters is precisely visualized within these, allowing nonfluoroskopic tracking in an integrated 3D environment (NavX).

Objective: We assessed system feasibility, safety and intraprocedural MG related parameters for radiofrequency (RF)ablation of ventricular tachycardias (VT) in patients with structural heart disease (SHD) or idiopathic VT.

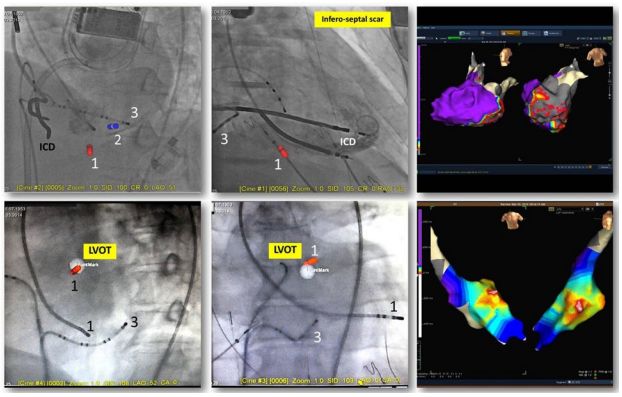
Methods: 63 consecutive VT patients (21 MG—system, 42 non—MG [“conventional”] using a standard 3D system) were ret-

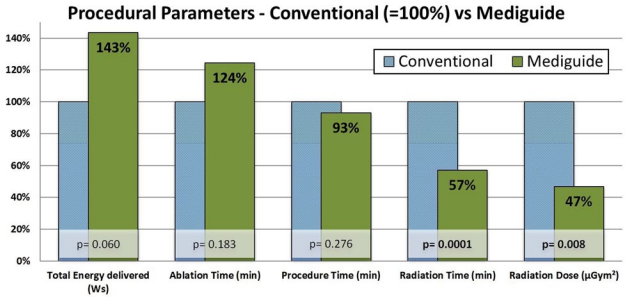
rospectively compared in a 2:1, closely case matched comparison. 13 patients (61.9 %) in the MG—group and 23 patients (54.7 %) in the conventional group showed SHD and 8 (MG) vs. 19 (conventional) idiopathic VT. 10 (MG, 47.6 %) vs. 25 (conventional, 59.5 %) patients had a history of recurrent ICD/CRTD shocks. Procedural parameters were compared between both groups. The endpoint of noninducibility was used for all patients.

Results: Mean fluoro time (15 ± 8.39 vs. 8.6 ± 3.83 min, $p = 0.0001$) and radiation dose (3.733 ± 3.429 vs. 1.747 ± 1.770 µGym^2, $p = 0.008$) were significantly reduced by the use of MG. Mean procedure duration using MG could be reduced by 16 min (n.s.).

54.5 % of the fluorotime an 58.3 % of fluoro dosage in the MG group was acquired in "nonMG—dependent" situations (positioning of conventional reference catheters, performing transseptal punctures) situations (positioning of conventional reference catheters, introducing sheaths, performing transseptal punctures) showing a great additional potential in further decreasing fluoro-time if more specialized MG tools were available. No major complications occurred in both groups.

Conclusions: The use of the novel MG system is feasible and safe in VT ablation, significantly reducing fluoro time and radiation dose compared to standard 3D systems.





X-4

Cardiotoxic effects of chemotherapy on cardiac conduction system leading to pacemaker or implantable cardioverter defibrillator implantation

A. Zimba, F. Rauscha, M. Andreas, C. Khazen, G. Laufer, G. Maurer, J. Bergler-Klein, M. Pavone-Gyöngyösi

Department of Cardiology, Medical University of Vienna, Vienna, Austria

Background: Chemotherapy with/without radiotherapy might cause cardiotoxic effects on cardiomyocytes, resulting in decrease of left ventricular function and development of heart failure. Less is known about the toxic effects of anticancer drugs on the human heart conduction system. We aimed to investigate the indications of implantation of pacemaker (PM) or implantable cardioverter-defibrillator (ICD) and the incidence of exchange of electrode or pulse-generator in patients receiving chemotherapy.

Methods: All patients who received a PM/ICD between 2001 and 2011 at the Medical University of Vienna were included in the present analysis. Patients with malign tumors of the thorax requiring chemotherapy with/without radiotherapy were selected and analyzed separately. The selected patients were divided into two groups: patients who required PM/ICD during/after chemotherapy with or without radiotherapy (Group 1, $n = 30$) and patients who already had PM/ICD 46 ± 37 months before chemotherapy (Group 2, $n = 34$). Age, gender, indication of PM/ICD implantation, type of PM/ICD and the sensing and pacing data as well as electrode impedance data were recorded.

Results: Between 2001 and 2011, a total number of 2938 PM with additional 304 cardiac resynchronization therapy system (CRT) (77.3 %) and 950 ICDs (22.7 %) were implanted. The mean age of all patients was 68 ± 16 years; 65.2 % of patients were male. The mean age of Groups 1 and 2 were 69 ± 9 and 65 ± 12 years, and there were 50 and 68 % male patients in the Groups 1 and 2, respectively. The incidence of PM or ICD implantation were 96.7 and 3.3 % in Group 1, in contrast to 70.6 and 29.4 % in Group 2. In Group 1, the main indications for PM implantation were sick sinus syndrome (36.4 %) and AV block II and III (36.7 %), in contrast to the Group 2 patients (26.4 and 14.9 %, respectively). Regular control of the PM/ICD showed no difference in electrode status between the groups. Fifteen patients (50 %) in the Group 1 required PM/ICD implantation already during the chemotherapy. The rate of pulse-generator exchange was increased in the Group 2 (41 %), compared to patients in Group 1 (10 %) ($p = 0.019$).

Discussion: The high percentage of patients who required a device implantation during anticancer therapy underlines a potential toxic effect of chemotherapy on the cardiac conduction system. Pulse-generator exchanges were increased in the group who received cancer therapy after implantation, which may indicate a higher required workload of the device. Our data suggest the toxic effect of the anticancer drugs not only on the cardiomyocytes, but also on the cardiac conduction system.

X-5

Häufigkeit von pathologischen Befunden in der prä- und postinterventionellen Gastroösophagoduodenoskopie bei Patienten mit Pulmonalvenenisolation

C. Neuhold, H. Keller, T. Mraz, M. Wurm, T. Pachofszky, T. Pulgram, C. Madl, F. Weidinger, E. Gatterer

2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien, Österreich
St. Jude Medical Austria, Wien, Österreich

Einleitung: Die Pulmonalvenenisolation (PVI) hat sich bei therapieresistentem Vorhofflimmern als effektive Methode erwiesen. Ösophagoatriale Fisteln durch thermische Läsionen stellen mit 0,04 % eine seltene, jedoch eine der gefährlichsten Komplikationen dar. Um mögliche pathologische Veränderungen des Ösophagus, Magens oder Duodenums vor oder nach der PVI zu erfassen, wurden unsere Patienten einen Tag prä- und postinterventionell einer diagnostischen Gastroösophagoduodenoskopie unterzogen.

Methodik: Von August 2010 bis Oktober 2014 wurde bei 136 Patienten in der Rudolfstiftung eine bilaterale antrale PVI durchgeführt, davon waren 112 Ersteingriffe, nur diese wurden ausgewertet. Eine standardisierte komplette Gastroösophagoduodenoskopie wurde am prä- und postinterventionellen Tag durchgeführt. Während der PVI erhielten 111 der 112 Patienten eine ösophageale Temperatursonde (St. Jude Medical), die Temperatur im Ösophagus während der Ablation wurde kontinuierlich erfasst, und die

Energieabgabe bei Überschreiten von 39°, bzw. ab 2014 38,5° sofort unterbrochen.

Ergebnisse: Neunundvierzig Patienten hatten paroxysmales und 63 Patienten persistierendes Vorhofflimmern. Das Durchschnittsalter der Patienten war 59,4 (32–83) Jahre, 25 der 112 Patienten waren Frauen (22,3 %).

Von den 112 Patienten wurden 101 postinterventionell gastroösophagoduodenoskopiert (90 %). Dabei hatten 25 der 101 Patienten (24,9 %) sowohl vor der PVI als auch danach einen makroskopisch unauffälligen Befund. Bei 13 Patienten fand sich vor der PVI ein Normalbefund, nachher jedoch eine neu aufgetretene Pathologie: erosive Gastritis ($n=1$), Antrumgastritis ($n=2$), Refluxösophagitis ($n=2$), (Ösophagusläsionen ($n=3$). Ein Pat. hatte schon vor der PVI eine Ösophagusläsion, möglicherweise durch die präinterventionelle transösophageale Echokardiographie bedingt.

Vierundsiebzig der 112 Patienten (66 %) hatten bereits bei der präinterventionellen Gastroösophagoduodenoskopie eine oder mehrere klinisch makroskopische Pathologien (die wichtigsten waren: Hiatushernie ($n=36$), Antrumgastritis ($n=11$) Schleimhauterosionen im Magen ($n=9$), Varixknoten bzw. Ösophagusvarizen ($n=8$), Refluxösophagitis ($n=8$), Barrettösophagus ($n=7$), Magenerythem ($n=5$), Magenpolypen ($n=3$).

Neue Ösophagusläsionen wurden am Tag nach der PVI bei 12 von 101 Patienten nachgewiesen. Drei davon waren sicher mechanisch durch die Ösophagussonde bedingt, bei den übrigen 9 lag der dringende Verdacht auf eine thermische Läsion nahe. Alle Patienten erhielten 2 x täglich PPIs. Bei fünf Patienten wurde sicherheitshalber eine Nahrungskarenz verordnet. Bis auf einen Patienten wurden diese nochmals gastroskopiert, in all diesen Fällen kam es zur kompletten Abheilung der Läsionen. Auch der Patient, der nicht nachgastroskopiert wurde, blieb klinisch völlig unauffällig.

Diskussion: Bei unseren PVI-Patienten betrug die Prävalenz von Pathologien in der präinterventionellen Gastroösophagoduodenoskopie 66 %. Die Inzidenz von Ösophagusläsionen (thermisch oder mechanisch), die direkt durch den Eingriff bedingt waren, betrug 12 %. Die interdisziplinäre Zusammenarbeit mit den Gastroenterologen hat sich als essentiell erwiesen und erfolgt an unserer Abteilung routinemäßig.

X-6

„Synchrones Pacing“ als neue Methode zur Hochfrequenzablation des cavotrikuspiden Isthmus bei typischem Vorhofflattern

A. Simon, E, Gatterer, C. Neuhold, H. Keller, H. Domanovits, M. Wurm, F. Weidinger

Universitätsklinik für Notfallmedizin, Medizinische Universität Wien, Wien, Österreich
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien, Österreich
St. Jude Medical, Wien, Österreich

Einleitung: Die Standardmethode der Ablation von typischem Vorhofflattern – die Ablation des rechtsatrialen Isthmus (CTI) – zielt darauf ab, eine kontinuierliche Verödungslinie zwischen Trikuspidalannulus und Vena Cava Inferior mit Erreichen eines bidirektionalen Blocks zu etablieren. Da rezenten, elektrophysiologischen Studien zufolge dieser Isthmus nicht, wie bisher angenommen, durch eine diffuse Leitungsstruktur, sondern durch distinkte Leitungsbündel in variabler Ausprägung charakterisiert ist, wurde im Rahmen dieses Pilotprojektes eine Methode klinisch getestet, mit welcher eine signalgesteuerte Ablation dieser Leitungsstrukturen möglich ist.

Material und Methode: Mit Hilfe einer in dieser Indikation bisher nicht beschriebenen Stimulationsart, dem „Synchronen Pacing“, wurden mit dem Ablationskatheter während synchroner Stimulation vom distalen Bipol eines Halo-Katheters und dem proximalen Bipol des Sinus Coronarius (CS)-Katheters charakteristische Signale registriert und punktuell abliert, bis der bidirektionale Block nachweisbar war. Die für die Studie in Frage kommenden Patienten wurden konsekutiv in zwei Gruppen randomisiert. In Gruppe A erfolgte die Ablation herkömmlich, in Gruppe B wurden die Patienten mit der neuen Methode behandelt. In beiden Gruppen erfolgte der Eingriff unter Sinusrhythmus, da dies eine Voraussetzung für die Anwendung des „Synchronen Pacings“ darstellt. Als Endpunkte dienten die Parameter Gesamtdauer aller Energieabgaben, Durchleuchtungszeit, Durchleuchtungsdosis und Prozedurdauer. Alle Patienten wurden zur Evaluierung des anhaltenden Therapieerfolges einem Follow-up unterzogen. Um die Ablationspunkte darzustellen, wurde das 3D Mappingsystem Ensite NavX (St. Jude Medical) verwendet.

Ergebnisse: Im Zeitraum von Juni 2011 bis April 2013 wurden 15 Patienten randomisiert und behandelt. Ein bidirektionaler Isthmusblock wurde in der Synchro-Gruppe in allen sieben Fällen erreicht, in der konventionell behandelten Gruppe konnte in einem Fall nur ein frequenzabhängiger Block erzielt werden. Bezüglich der Parameter Gesamtdauer aller Energieabgaben, Durchleuchtungszeit, Durchleuchtungsdosis und Prozedurdauer fanden sich keine signifikanten Unterschiede. Ein Patient aus der konventionellen Gruppe erlitt nach primär erfolgreicher Intervention ein typisches Vorhofflatterrezidiv und wurde einer neuerlichen Isthmusablation unterzogen (mittlerer Beobachungszeitrum des Follow-up =29,1 Monate). In der Synchro-Gruppe trat kein Rezidiv auf. Abb. 1 zeigt den exemplarischen Fall eines Patienten nach kompletter Isthmusablation, Abb. 2, jenen eines Patienten nach punktueller Ablation (erfolgte Energieabgaben mitdargestellt).

Diskussion: Die Ergebnisse des Pilotprojekts stehen im Einklang mit rezent publizierten Daten anderer Arbeiten: um einen anhaltenden bidirektionalen Isthmusblock zu erreichen, ist es nicht notwendig, die gesamte anatomische Linie vom Trikuspidalring bis zur Vena Cava Inferior zu ablieren. Zusätzlich konnte gezeigt werden, dass die Methode des „Synchronen Pacings“ ein effektives Verfahren darstellt, um die für die Isthmusleitung verantwortlichen Strukturen rasch lokalisieren und ablieren zu können.

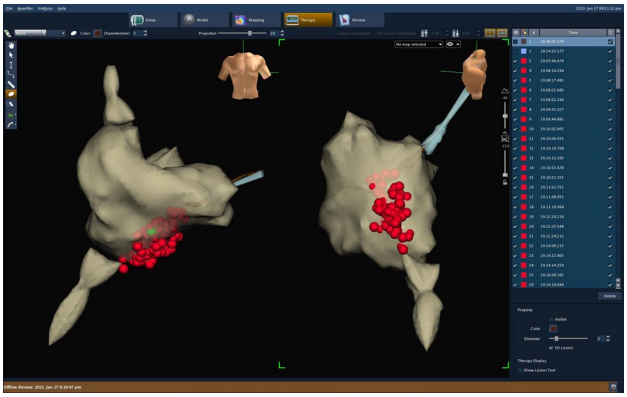


Abb. 1 Ansicht im dreidimensionalen Mapping nach erfolgten Energieapplikationen. Der gesamte cavotrikuspide Isthmus wurde abliert (rote Markierungen)

Energieabgabezeit (Sek)	Prozedurdauer (Min)	Durchleuchtungszeit (Min)	Bestrahlungsdosis (mGy)
1030	81	953	818

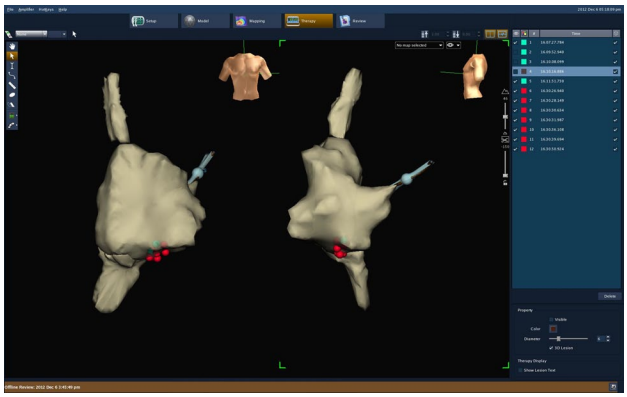


Abb. 2 Ansicht im dreidimensionalen Mapping nach erfolgten Energieapplikationen. Grün der Punkt an dem die charakteristischen Signale lokalisiert wurden, rot die Hochfrequenzabgabe am Ort des vermuteten Bündels

Energieabgabezeit (Sek)	Prozedurdauer (Min)	Durchleuchtungszeit (Min)	Bestrahlungsdosis (mGy)
60	40	477	95

X-7

Atrial flutter ablation in a patient with dextrocardia and persistent left superior vena cava

L. Teischinger, M. Derndorfer, E. Sigmund, S. Winter, J. Aichinger, H. Pürerfellner, M. Martinek

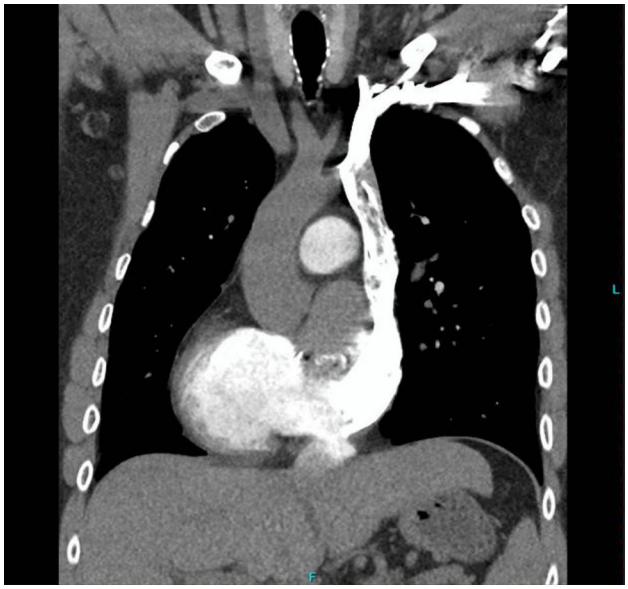
Kardiologie 1, KH Elisabethinen Linz, Linz, Austria
Interne/3. Medizinische Abteilung, Universitätsklinikum St. Pölten, St. Pölten, Austria

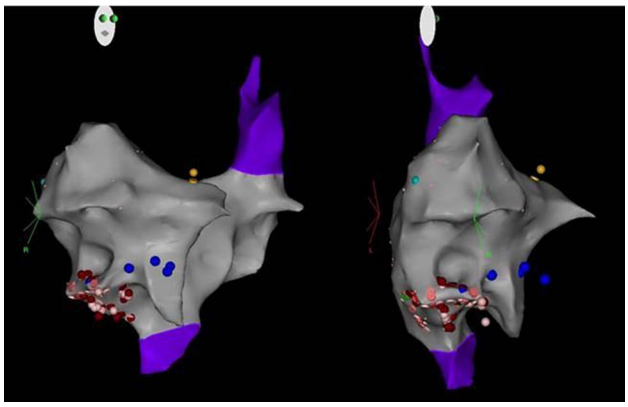
Introduction: A 45 year old male with a history of persistent atrial flutter and negative F waves in leads II, III, aVF and dextrocardia was referred for flutter ablation. His past medical history includes a closure of an atrial septal defect during childhood. Paroxysmal atrial flutter has been documented for 15 years; 1 year ago he underwent electrocardioversion with an early recurrence of atrial flutter, neither responding to Amiodarone nor to Sotalol. He was highly symptomatic with palpitations, progressive loss of exercise capacity and dyspnoea on exertion. A previous ablation attempt (without comprehensive imaging) was unsuccessful.

Methods and results: A pre-interventional CT reconstruction showed a persistent left vena cava superior draining into a massively dilated coronary sinus and a significantly enlarged right atrium (Fig. 1). A transvenous access was performed using the right femoral and left subclavian vein, a standard CS-catheter and decapolar diagnostic catheter were placed in the coronary sinus and along the lateral wall of the right atrium.

Entrainment from the cavotricuspid isthmus as well as a propagation-map using 3D electro-anatomical mapping (CARTO 3®, Fig. 2) were performed confirming typical atrial flutter with counterclockwise rotation around the tricuspid valve. Radiofrequency ablation was performed at the cavotricuspid isthmus resulting in arrhythmia termination and bidirectional isthmus block.

Conclusions: To the best of our knowledge, no case report on atrial flutter ablation in a patient with dextrocardia and persistent left vena cava superior has been presented yet. Accurate preparation and pre-interventional imaging is essential for a successful procedure in patients with challenging thoracic anatomy.





X-8

Pulmonalvenenisolationen mittels Kryoballon der zweiten Generation: Sechsmonats Follow-up mittels Loop Recorder und CARTO® 3

L. Teischinger, C. Plass, N. Doruska, H. Mayr, B. Frey

3. Medizinische Abteilung, Universitätsklinikum St. Pölten, St. Pölten, Austria

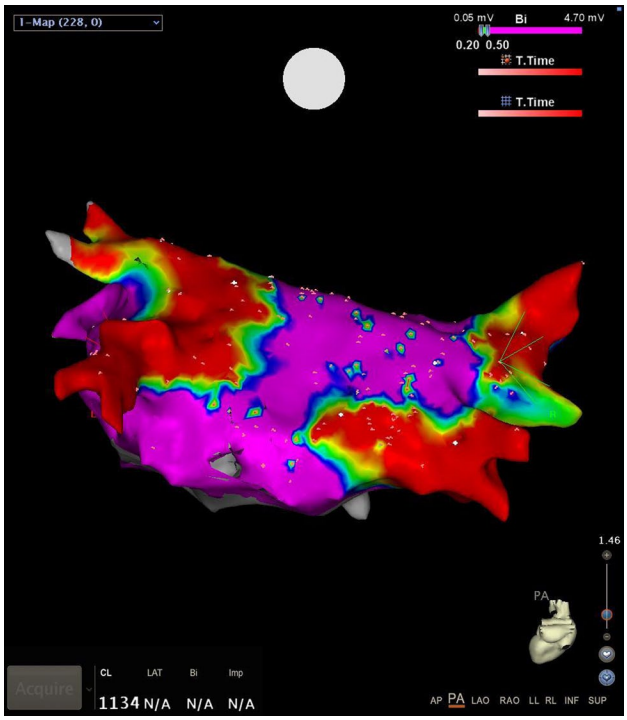
Einleitung: Der 28 mm Kryoballon der zweiten Generation ist ein neues Tool zur Pulmonalvenenisolation in Patienten mit symptomatischem Vorhofflimmern. Um diese Technik in unseren Patienten umfassend zu evaluieren, wurde bei allen Patienten der Herzrhythmus permanent monitiert.

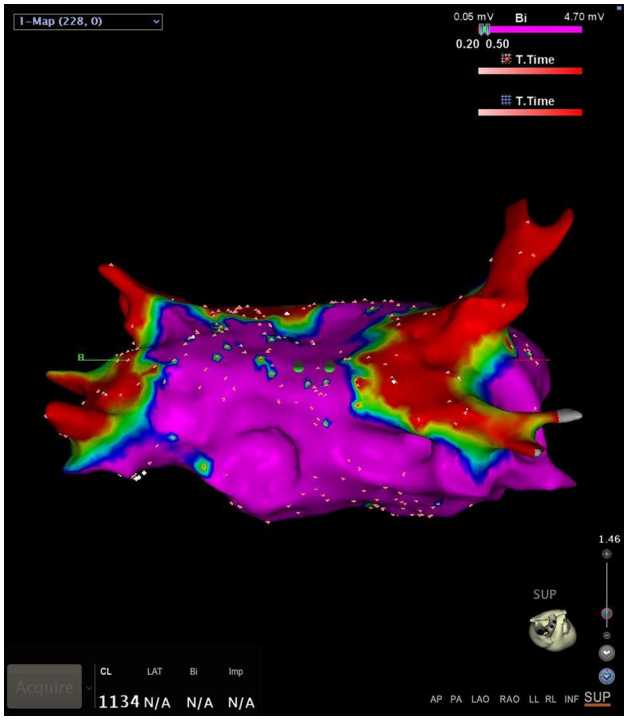
Methodik: Die Isolation der Pulmonalvenen erfolgte unter Verwendung eines 28 mm Kryoballons in 26 Patienten mit symptomatischem Vorhofflimmern (1 long-standing persistierend, 6 persistierend, 19 paroxysmal). Weitere Läsionen bzw. Linien wurden nicht durchgeführt. 4 Patienten hatten einen DDD Schrittmacher implantiert, in 22 Patienten wurde 1 Woche vor Ablation ein Reveal LINQ® implantiert. Als Rezidiv wurde jegliche atriale Arrhythmie >30 sec definiert, als Blanking Periode 3 Monate. Allen symptomatischen Pat. wurde ein Redo unter Verwendung von CARTO® 3 angeboten.

Ergebnisse: Im 6 Monats Follow-up fand sich in 6/26 (23 %) Patienten ein Rezidiv. 2 Rezidive waren persistierend und symptomatisch (beide in Patienten mit initial persistierendem Flimmern),

4 Rezidive waren paroxysmal, davon 2 symptomatisch, und 2 asymptomatisch. Die AFIB Burden war < 1,2 % in allen Patienten mit paroxysmalem Rezidiv.

CARTO® 3 Re-mapping mit SmartTouch® Katheter (contact force >7 g) bei 3 symptomatischen Patienten (1 oligosymptomatischer Patient lehnte ein Redo ab) zeigte bei einem Patienten 1 rekonnektierte Pulmonalvene (in Summe 1/12 Venen rekonnektiert), bei einem Patienten 1 inkomplette Ablation eines Antrum einer Pulmonalvene und bei einem Patienten vollständig isolierte Antra und Pulmonalvenen (in Summe 10/12 Antra und Venen dicht). Die low voltage area (0,5 mV bipolar) nach Isolation reichte in den 10 Antra ca. 2 cm in das linke Atrium hinein.





Diskussion: Follow-up mittels Loop Recorder zeigte eine hohe Erfolgsquote mit minimaler AFIB Burden. 50 % der Rezidive von paroxysmalem Vorhofflimmern würden ohne permanentem Monitoring unentdeckt bleiben. Eine Redo Strategie mit ausschließlicher Pulmonalvenen Re-isolation wird möglicherweise keine wesentliche Verbesserung der Langzeit-Erfolgsquote bringen.

Postersitzung XI: Risikofaktoren/Stoffwechsel/Lipide 1

XI-1

Coronary artery disease as a risk factor for developing type 2 diabetes mellitus

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

VIVIT-Institute, Academic Teaching Hospital Feldkirch, Austria

Diabetes mellitus is a major risk factor for coronary artery disease (CAD); whether conversely CAD confers an increased risk for diabetes is unclear.

We prospectively recorded incident diabetes over 6.1 ± 3.7 years in 829 consecutive non-diabetic Caucasian patients undergoing coronary angiography for the evaluation of stable CAD, covering 5057 patient years.

During follow-up, diabetes was newly diagnosed in 133 patients, i.e. in 16 % of the study population or in 2.6 % per year. Patients with significant CAD ($n = 444$) when compared to subjects who did not have significant CAD at the baseline angiography were at a strongly increased diabetes risk (20.3 vs. 11.2 %; $p < 0.001$). The relationship between CAD and incident diabetes was confirmed after multivariate adjustment including metabolic syndrome status (OR 1.85 [1.23–2.79], $p = 0.003$).

We conclude that the presence of CAD indicates a strongly increased risk for incident diabetes. Repeated diabetes screening of coronary patients and targeted programs to prevent diabetes in these high-risk patients are warranted.

XI-2

Monacolin K- die pflanzliche Alternative?

S. Charwat-Resl, W. Helmreich, M. Suppan, A. Zittmayr, M. Eber, B. Eber

Angiologie, AKH Wien, Innere Medizin II, Klinikum Wels-Grieskirchen, Wels, Austria

Einleitung: Es ist inzwischen gut belegt, dass ein erhöhter LDL-Cholesterinspiegel (LDL-C) der Hauptrisikofaktor für die Entwicklung einer Atherosklerose ist. Weiters wurde wiederholt gezeigt, dass eine LDL-Cholesterinsenkung dieses Risiko minimieren kann. Monacolin K und 13 andere Monacoline sind die Wirkstoffe eines Nahrungsergänzungsmittels aus fermentiertem rotem Hefereismehl (Monascus purpureus), das ebenfalls über die LDL-C-Senkung diese Risikoverminderung verspricht.

Methode: Im vorliegenden Register wurde der Effekt einer einmal täglichen Reismehl-Kapselgabe (ArterinR) auf die Gesamtcholesterin-, LDL- und HDL-Cholesterin- sowie Triglyceridspiegel im Serum unter Alltagsbedingungen untersucht. Zum Vergleich zwischen Ausgangswerten und Serumspiegeln nach 6 Monaten wurden T-Tests verwendet.

Ergebnisse: 22 Patienten (w:m = 15:7, Alter 61,5 ± 9,3 Jahre) in ambulanter kardiologischer Betreuung wurden konsekutiv eingeschlossen. 15 Patienten nahmen das Präparat zur Primärprävention

Tab. 1 Entwicklung des Lipidprofils nach Monacolin K – Einnahme über 6 Monate

	Start	6 Wochen	6 Monate	*p* – Wert (6 Mo vs. Start)
Gesamtcholesterin [mg/dl]	245,95 ± 35,41	198,82 ± 33,90	202,09 ± 36,29	< 0,0001
LDL – Cholesterin [mg/dl]	149,67 ± 41,27	104,53 ± 29,46	106,44 ± 34,62	< 0,0001
HDL – Cholesterin [mg/dl]	61,55 ± 19,16	65,95 ± 20,50	67,26 ± 23,02	ns
Triglyceride [mg/dl]	166,95 ± 109,47	142,05 ± 72,71	132,57 ± 73,14	ns
HbA1c [%]	5,80 ± 0,17	5,73 ± 0,18	5,79 ± 0,19	ns

ein, die restlichen 7 zur Sekundärprävention bei Statin-Unverträglichkeit. Bei 3 Patienten bestand eine Ko-Medikation mit Ezetimib. Die Effekte auf das Lipidprofil sind in Tab. 1 dargestellt. Die Wirkungen waren in allen Patientengruppen vergleichbar. Folgende Parameter wurden durch die ArterinR-Einnahme nicht signifikant beeinflusst: Körpergewicht, HbA1c, CPK, Nierenparameter.

Schlussfolgerung: Die Einnahme von Monacolin K führt zu einer signifikanten Senkung des Gesamt-Cholesterins und LDL-C, aber zu keiner signifikanten Beeinflussung des HDL-Cholesterins oder der Triglyceride nach einer Einnahme über 6 Monate. Daher scheint eine Gabe bei Patienten, bei denen (noch) keine Indikation für ein rezeptpflichtiges Statin besteht, die eine Medikamenteneinnahme ablehnen oder eine Statin-Unverträglichkeit haben, gerechtfertigt, auch wenn Endpunktstudien bislang fehlen.

XI-3

Microvascular function in women with former gestational diabetes

S. Charwat-Resl, R. Yarragudi, M. Heimbach, K. Leitner, G. Giurgea, M. Müller, R. Koppensteiner, M. Gschwandtner, A. Kautzky-Willer, O. Schlager

Universitätsklinik für Innere Medizin II, Abteilung für Angiologie,Medizinische Universität Wien, Vienna, Austria

Introduction: Gestational diabetes (GDM) affects up to 6% of all pregnancies and bears a 7.5 fold risk for the development of type 2 diabetes mellitus. Furthermore, it has been shown that GDM increases the risk for macrovascular complications such as myocardial infarction, peripheral artery disease and stroke even in the absence of overt diabetes. No data exist on the long-term effects of GDM on microvascular dysfunction, a well-established pathology in diabetes.

Methods: We sought to investigate microvascular function by post-occlusive reactive hyperemia (PORH) using laser Doppler fluxmetry. Therefore, skin perfusion under resting conditions (baseline perfusion), after suprasystolic inflation of an upper arm cuff (biological zero) and after release of cuff pressure (peak perfusion) as well as time to peak perfusion and the time between peak perfusion and the return to baseline perfusion (recovery time) were recorded. Otherwise healthy study participants were recruited from the 10-years-follow-up-visit of the "Viennese Post-Gestational Diabetes Project". A statistical analysis using Mann-Whitney-U test was performed to identify a significant difference in baseline perfusion, biological zero, peak perfusion, time to peak perfusion and recovery time in females after at least one GDM-pregnancy compared to females without GDM-pregnancy.

Results: 44 females with a history of GDM in at least one pregnancy (age 45.7 ± 4.4 years) and 32 females with a history of pregnancy without GDM (age 42.8 ± 5.3 years) were included in this study. Microvascular function was studied 13.5 ± 4.1 years after index pregnancy. All demographic parameters as well as comorbidities were similar in both groups. Microvascular function in females with a history of GDM was not impaired in comparison with females with no history of GDM (see Table 1).

Table 1 Comparison of perfusion parameters measured by Laser Doppler fluxmetry between post-GDM females and females without a history a GDM

Post-GDM	No GDM	p-value
Baseline perfusion [AU]	0.30 IQR 0.21–0.34	0.26 IQR 0.21–0.32 ns
Biological zero [AU]	0.11 IQR0.08–0.14	0.11 IQR 0.08–0.13 ns
Peak perfusion [AU]	1.30 IQR 0.92–1.63	1.39 IQR 0.95–1.67 ns
Time to peak perfusion [sec]	12 IQR 8–14	11.5 IQR 9–15 ns
Recovery time [sec]	71.5 IQR 50.7–100.3	74.5 IQR 37.8–96.3 ns

Conclusion: While GDM has been shown to potentially cause macrovascular damage, there appear to be no long-term effect on microvascular function 10 years after GDM.

XI-4

Prevalence of (un)diagnosed cardiovascular risk factors and metabolic syndrome with comparison of FRS, PROCAM, SCORE, and ASCVD risk equation models in an Austrian workplace

B. Rittmannsberger, M. Luger, E. Luger, S. Dämon, J. Höfler, L. Angelmaier, K. Maschke, C. Sakho, A. Pfeiffenberger, M. Schätzer, M. Lechleitner, F. Hoppichler

SIPCAN, Special Institute for Preventive Cardiology & Nutrition, Salzburg, Salzburg, Austria
Medizinische Universität Wien, Vienna, Austria
Abteilung für Innere Medizin, Krankenhaus der Barmherzigen Brüder Salzburg, Salzburg, Austria
Abteilung für Innere Medizin im Landeskrankenhaus Hochzirl, Zirl, Austria

Background: The high prevalence of cardiovascular disease (CVD) mortality is mainly due to the increase of risk factors. Nevertheless, these risk factors are modifiable and might be preventable. This investigation aims to evaluate the prevalence of (un)diagnosed CVD risk factors in employees within a health-check- program in an Austrian company.

Methods: In 704 employees demography, anthropometry, blood pressure (RR), lipids, blood glucose and 10-year-CVD risk were assessed between 2006 and 2013 from a workplace health program, which is called the "SIPCAN health-check-program" (Special Institute for Preventive Cardiology And Nutrition). SIPCAN is an Austrian independent and non-profit organization. To estimate the 10-year-CVD risk, the Framingham Risk Score (FRS), Prospective Cardiovascular Münster Study (PROCAM), Systematic Coronary Risk Evaluation (SCORE), and absolute risk for AtheroSclerotic CardioVascular Disease (ASCVD) equations were used. The International Diabetes Federation (IDF) global consensus was used to define metabolic syndrome (MeS).

Results: Mean (SD) age was 37 (10) years with 19.6% women and median BMI of 25.0 (17.4–44.3) kg/m2. Additionally, median waist circumference (WC) of both female and male workers was below 88 and 102 cm [81.0 (64.0–124.0) and 93.0 (65.0–155.0) cm; $p < 0.001$] although it was above the reference values according to IDF definition (female ≤ 80 cm, male ≤ 94). Furthermore, both median systolic and diastolic RR levels were above the optimum values [134.5 (100.0–183.0) and 83.0 (61.0–120.0)]. 12% demonstrated obesity, 38% overweight, 18–44% abdominal obesity, and 19% MeS. We found a significant difference in undiagnosed com-

pared to diagnosed hypertension (47 vs. 14 %; $p < 0.001$). Increasing age was a significant predictor of MeS [OR (95 % CI) = 1.08 (1.06–1.10); $p < 0.001$]. 7–12 % had intermediate and 3–28 % high 10-year-CVD risk, depending on the different equations (Fig. 1). 79 % demonstrated at least one risk factor.

Conclusions: In summary, we detected a high prevalence of risk factors particularly elevated RR and abdominal obesity. Regarding the use of risk estimation models, the same population should be used in which the equation was developed and validated. Therefore, in our evaluation, the PROCAM and SCORE equations might be appropriate choices as they were validated in samples of healthy employees or general population, respectively. Due to the high prevalence of (un)diagnosed CVD risk factors, workplace health prevention programs should aim in initially identifying risk factors and subsequently improve nutritional habits and physical activity.

XI-5

Rolle von Faktor-V-Leiden und Prothrombinvariante als Marker zur Prädiktion von Mortalität in der Ludwigshafen Risk and Cardiovascular Health Study (LURIC)

G. Delgado de Moissl, R. Siekmeier, B. K. Krämer, W. März, M. Kleber

Bundesinstitut für Arzneimittel u Medizinprodukte, Bonn, Deutschland
Medizinische Klinik V, Medizinische Fakultät Mannheim, Universität Heidelberg, Mannheim, Deutschland
Drug Regulatory Affairs, Pharmazie, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Deutschland
Klinisches Institut für Medizinische und Chemische Labordiagnostik, Medizinische Universität Graz, Graz, Österreich

Einleitung: Faktor-V-Leiden und die Prothrombinvariante sind die bekanntesten genetischen Veränderungen im Gerinnungssystem und wichtige prädiktive Marker für das Auftreten von venösen Thrombosen und Lungenembolien. Die Rolle dieser Varianten als Risikofaktoren eines Myokardinfarktes wird kontrovers diskutiert. Ziel dieser Studie war die Untersuchung der Bedeutung beider Veränderungen für die Risikoprädiktion bei Teilnehmern der Ludwigshafen Risk and Cardiovascular Health Study (LURIC).

Material und Methoden: Die Bestimmung der Allele erfolgte mittels PCR in 3316 Studienteilnehmern, die über 10 Jahre hinweg (Median) beobachtet wurden. Die Assoziation von Faktor-V-Leiden und Prothrombinvariante mit prävalenter Erkrankung und Mortalität wurde mittels SPSS v22 analysiert, wobei homo- und heterozygote Patienten jeweils zusammengefasst wurden.

Ergebnisse: Faktor-V-Leiden fand sich bei 265 Patienten (8 %, davon 5 homozygot), während bei 111 Patienten (3,3 %, davon 1 homozygot) eine Prothrombinvariante vorlag. Während des Beobachtungszeitraums starben 622 Patienten, davon 42 Patienten mit Faktor-V-Leiden und 15 Patienten mit Prothrombinvariante durch ein kardiovaskuläres Ereignis. Weder Faktor-V-Leiden noch die Prothrombinvariante waren mit der kardiovaskulären Mortalität assoziiert. Beim prävalenten Myokardinfarkt fanden sich ebenfalls keine signifikanten Unterschiede. Demgegenüber fand sich nur bei Männern, (nicht jedoch Frauen) ein Zusammenhang zwischen dem Vorliegen der Varianten und der Anamnese einer venösen Thrombose oder Lungenembolie (Faktor-V-Leiden, Männer: OR: 2,21 (95 % KI: 1,04–4,70), Frauen: 1,78 (0,60–5,26); Prothrombinvariante, Männer: 2,38 (1,39–4,10), Frauen: 1,65 (0,86–3,16)). Eine Stratifizierung nach koronararterieller Erkrankung (CAD) zeigte dabei sowohl bei Faktor-V-Leiden als auch bei der Prothrombinvariante ein erhöhtes Risiko bei Vorliegen einer CAD (Faktor-V-Leiden: 1,69 (0,63–4,49); Prothrombinvariante: 2,05 (1,07–3,92)).

Diskussion: Die Ergebnisse bestätigen die Bedeutung von Faktor-V-Leiden und Prothrombinvariante für das Auftreten venöser Thrombosen und Lungenembolien. Auffällig ist dabei das vermehrte Auftreten beider Erkrankungen bei Männern mit nachgewiesener koronararterieller Erkrankung (CAD > 20 %) und Vorliegen der genetischen Varianten. Demgegenüber geht weder das Vorliegen von Faktor-V-Leiden noch das Vorliegen einer Prothrombinvariante mit einer Zunahme des Risikos für das Auftreten eines Myokardinfarktes einher. Dies weist auf eine höhere Bedeutung des Vorliegens dieser Veränderungen für venöse thromboembolische Erkrankungen hin, schließt jedoch umgekehrt deren mögliche Relevanz bei Vorliegen weiterer Risikofaktoren auch bei arteriellen Erkrankungen wie z. B. Myokardinfarkt nicht aus, so dass ggf. eine Bestimmung im Rahmen der kardiovaskulären Diagnostik erfolgen sollte.

XI-6

Aortic stiffness predicts cardiovascular events in patients undergoing coronary angiography

L. Liebenberger, J. Kellermair, S. Sartori, S. Charwat-Resl, M. Suppan, B. Eber, T. Weber

Interne II, Klinikum Wels-Grieskirchen, Wels, Austria

Background: Aortic stiffness, non-invasively estimated as carotid-femoral pulse wave velocity (PWV), is a strong independent predictor of cardiovascular events in the general population, in hypertensives, renal patients and in the elderly. Its prognostic value in coronary patients has never been assessed, nor the prognostic value of invasively measured, true aortic PWV.

Methods: We measured aortic PWV from ascending aorta to the bifurcation during catheter pullback in patients undergoing angiographic assessment for suspected coronary artery disease (CAD). Patients were followed, using hospital records, telephone interviews with general practitioners, and a national mortality registry (Statistics Austria).

Results: We included 870 patients (mean age 63 years, 37 % female, 76 % hypertensives, 20.5 % diabetics, significant CAD 46 %, mean EF 68 %, mean aortic PWV 9.0 m/sec). After a mean follow-up of 51 months, 46 patients had died, 26 suffered from a myocardial infarction, 29 from a stroke, 68 underwent coronary revascularisation, and 182 had reached the combined endpoint (death, myocardial infarction, stroke, coronary revascularization, carotid or peripheral revascularisation and hospitalisation due to heart failure).

In univariate analysis, an increase in 1 SD of PWV (2.5 m/sec) was associated with a 59 % increase in total mortality, a 54 % increase in stroke risk, a 66 % increase in heart failure hospitalisation, and a 40 % increase in the risk of the combined endpoint ($p < 0.001$ for all, respectively). In a multivariable stepwise Cox poportional hazards model, PWV remained a significant predictor of the combined endpoint (HR 1.30, CI 1.14–1.48, $p = 0.0001$). The other significant predictors were diabetes, and presence of coronary and peripheral artery disease.

Conclusion: Aortic stiffness is an independent, significant predictor of cardiovacular events in patients undergoing coronary angiography.

Postersitzung XII: Akutes Koronarsyndrom 2

XII-1

3. Rezidiv einer Tako-Tsubo Kardiomyopathie

B. Stanic, T. Yoshida, M. Hasun, W.-B. Winkler, C. Stöllberger, F. Weidinger

2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien, Österreich

Einleitung: Die Tako-tsubo Kardiomyopathie (TTK) ist gekennzeichnet durch meist stress-induziertes Auftreten von akuten Thoraxschmerzen, reversiblen EKG-Veränderungen und regionalen Wandbewegungsstörungen ohne Koronarstenosen. Die Pathophysiologie von TTK ist unklar. Die TTK-Rezidivrate wird in der Literatur mit ca. 1,5 % pro Jahr beschrieben. Mehrmalige Rezidive bei demselben Patienten werden selten berichtet.

Fallbericht: Eine 71 jährige Patientin wird wegen thorakalen Drucks und Übelkeit, sowie mit ST Elevationen im EKG wegen des Verdachts auf akutes Koronarsyndrome aufgenommen. Anamnestisch waren schon drei ähnliche Episoden 2008, 2010 und 2012 zu erheben. 2008 und 2010 war echokardiographisch und mittels Koronarangiographie beide Male eine Tako-Tsubo Kardiomyopathie diagnostiziert worden. Anamnestisch konnten wir keine physischen oder psychischen Stressoren als Auslöser für diese Episoden finden. Der Tod des Ehegatten 2006 und die Diagnose eines Gehirntumors der Tochter 2012 wurden als Gründe für eine depressive Stimmungslage genannt. An Komorbiditäten wies sie eine COPD GOLD III, zweimalige TIA 2007, substituierte Hypothyreose nach Strumektomie, Osteoporose, sowie eine PTA der A. femoralis und A. poplitea 2009, eine arterielle Hypertonie und Nikotinkonsum mit ca. 35 packyears auf. Die Patientin stand bei Aufnahme unter einer Medikation mit Risedronat, Calcium, Amlodipin, Levothyroxin, Budesonid/Formoterol, Acetylsalicylsäure, Tiotropium und Trazodon.

Angesichts der multiplen koronaren Risikofaktoren erfolgte eine neuerliche Koronarangiographie. Es zeigte sich eine geringe Koronarsklerose mit Akinesie des Apex, der mittleren und apikalen Vorder- und Hinterwand mit einer mittel- bis höhergradig reduzierten Linksventrikelfunktion. Wir stellten die Diagnose eines 3. Rezidivs einer Tako-Tsubo Kardiomyopathie. Der Krankenhausaufenthalt wurde kompliziert durch Herzinsuffizienz und reversiblen EKG-Veränderungen mit T-Wellen Negativierung und QT-Verlängerung. Die maximale CK betrug 152 U/l, Troponin T 0,445 ng/ml und das NT-pro-BNP von 3090 ng/l. Wegen der ausgedehnten Akinesie wurde die Patientin vorübergehend mit niedermolekularem Heparin behandelt. Nach 9 Tagen zeigte das EKG einen partiellen Rückgang der negativen T Wellen und eine Normalisierung der QT Zeit. Die Echokardiographie zeigte eine Normalisierung der systolischen Linksventrikelfunktion. Die Pharmakotherapie wurde um Ramipril ergänzt, Amlodipin wurde abgesetzt. Eine Vorstellung in der psychosomatischen Herz-Ambulanz wurde angeraten.

Konklusion: Rezidivierende Episoden einer Takotsubo-Kardiomyopathie können auch ohne fassbare Stressoren auftreten. Ob eine pharmakologische oder psychotherapeutische Therapie vor den Rezidiven schützen kann ist unklar.

XII-2

Aortic stiffness as a predictor of high N-terminal pro-B-type natriuretic peptide in patients presenting with acute coronary syndrome

H.-J. Feistritzer, S. J. Reinstadler, G. Klug, A. Rederlechner, J. Mair, W.-M. Franz, B, Metzler

Univ.-Klinik für Innere Medizin III, Kardiologie und Angiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Background: Aortic stiffness is related to increased left ventricular afterload and high myocardial wall stress. This process is generally accompanied by a release of natriuretic peptides. Measurement of aortic pulse wave velocity (PWV) is the gold-standard technique to assess aortic stiffness in vivo.

In this study we sought to prospectively investigate the impact of aortic PWV on N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentrations in patients presenting with acute coronary syndrome (ACS).

Methods: In this study we included 184 consecutive ACS patients all reperfused by percutaneous coronary intervention. Assessment of aortic PWV was performed at a median of 38 h (IQR 24–57 h) after symptom onset. It is based on a transfer function from the brachial pressure waves determined by oscillometric blood pressure measurements with a common cuff. NT-proBNP values were measured serially using a commercially available enzymatic assay. Maximum value was defined as highest in the concentration time course.

Results: Mean age of the study population was 61 ± 12 years (26 % female). Maximum NT-proBNP concentrations were measured at a median of 23 h (IQR: 9–45 h) after symptom onset. Median PWV was 8.3 m/s (IQR: 7.1–9.6 m/s). Patients with a PWV above the median value were older (70 ± 7 vs. 52 ± 7 years, $p < 0.001$) and showed higher systolic blood pressure (121 ± 15 vs. 114 ± 13 mmHg, $p = 0.002$) than patients with a PWV below the median. Furthermore, patients with high PWV showed significantly higher maximum NT-proBNP concentrations (median: 867 ng/l, IQR: 361–2282 ng/l vs. median: 496 ng/l, IQR: 161–1391 ng/l, $p = 0.003$). According to multinomial binary logistic regression analysis, PWV (HR: 1.43, 95 % CI, 1.17–1.75; $p < 0.001$) beside peak cardiac troponin T levels (HR: 1.01, 95 % CI, 1.00–1.02; $p = 0.003$) and systolic blood pressure (HR: 0.97, 95 % CI, 0.94–0.99; $p = 0.005$) was an independent predictor of NT-proBNP concentrations above the median value of 736 ng/l (IQR 246–1571 ng/l).

Conclusion: In patients presenting with ACS aortic PWV is an independent predictor of increased NT-proBNP concentrations. This finding suggests a deleterious effect of high aortic stiffness on left ventricular myocardium in these patients.

XII-3

Circulating corin concentrations are related to infarct size in patients after ST-segment elevation myocardial infarction

H.-J. Feistritzer, G. Klug, S. J. Reinstadler, J. Mair, A. Mayr, G. Göbel, W.-M. Franz, B. Metzler

Univ.-Klinik für Innere Medizin III, Kardiologie und Angiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Background: Corin, a transmembrane serine protease, partially sheds from the cardiomyocyte cell surface and enters the circulation, a process that might be enhanced in the setting of myocardial injury. This study evaluated the potential association between plasma corin concentrations and myocardial infarct size (IS) measured by cardiovascular magnetic resonance (CMR) within the first week after reperfused ST-segment elevation myocardial infarction (STEMI) and 4 months thereafter.

Methods: In this observational, single-centre study, IS was determined at baseline and 4 months after STEMI using late gadolinium contrast-enhanced CMR. Corin concentrations were determined from blood samples drawn at a median of 1.9 days (IQR 1.1–3.3 days) after STEMI by an immunofluorescent assay.

Results: This study cohort included 50 patients (median age: 59 years (IQR 51–66 years); females: 7 (14 %)). Corin concentrations (median = 1084 pg/ml, IQR 841–1341) were significantly associated with 4-month IS ($r = 0.366$, $p = 0.009$) but there was only a trend to correlation with baseline IS ($r = 0.249$, $p = 0.084$). Corin was significantly correlated with maximum high-sensitivity cardiac troponin T (hs-TnT) concentrations ($r = 0.346$, $p = 0.014$). A receiver operator characteristics (ROC) model including hs-TnT provided an area under the curve (AUC) of 0.95 (95 % CI 0.89–1) for the prediction of large 4-month IS. Including corin instead of hs-TnT resulted in an AUC of 0.90 (95 % CI 0.81–0.98).

Conclusion: Circulating corin at day 2 after acute STEMI is associated with 4-month IS as assessed by CMR.

XII-4

Evaluation of the Manchester Triage System for patients with acute coronary syndrome with primary presentation in the emergency department

D. Kiblböck, K. Steinrück, W. Lang, E. Zeindlhofer, K. Höllinger, A. Winter, M. Schmid, P. Siostrzonek

Interne II—Kardiologie, Krankenhaus Barmherzige Schwestern, Linz, Austria
Medizinische Universität, Wien, Austria

Introduction: Chest pain is a frequent cause of presentation in emergency departments (ED). An early diagnosis of acute coronary syndrome (ACS), in particular in patients with ST-elevation myocardial infarction (STEMI), is crucial for treatment and prognosis. The Manchester Triage System (MTS) classifies patients based on their main symptoms into five different levels of urgency in terms of their need for assessment, irrespective of the eventual diagnosis. The aim of this study was to evaluate the MTS for patients with ACS and primary presentation in the ED.

Methods: Retrospective, single-center study of patients diagnosed with ACS (STEMI, non-STEMI, unstable angina pectoris) with primary presentation in the emergency department between January and June 2014.

Results: 148 patients (69.4 ± 14.5 years; female, $n=47$, 31.8 %; STEMI, $n=54$, 36.5 %; non-STEMI, $n=86$, 58.1 %; unstable angina pectoris, $n=8$, 5.4 %) were admitted because of ACS to the cardiac care unit and were triaged by the MTS in the ED as follows: MTS level 1 (immediate assessment), $n=1$ (0.7 %); MTS level 2 (very urgent), $n=82$ (55.4 %); MTS level 3 (urgent), $n=53$ (35.8 %); MTS level 4 (standard), $n=12$ (8.1 %), MTS level 5 (non urgent), $n=0$. While 101 patients (68.1 %) presented with chest pain, 47 patients had atypical symptoms (e.g. respiratory distress, nausea and vomiting). There was no significant difference between the mean MTS level in different types of ACS (STEMI, 2.5, 95 % CI 2.3–2.6; non-STEMI, 2.5, 95 % CI 2.4–2.7; unstable angina pectoris, 2.6, 95 % CI 2.2–3.1) or with respect to gender (male, 2.5, 95 % CI 2.4–2.6; female, 2.6, 95 % CI 2.4–2.8), age (age < 80 years, 2.5, 95 % CI 2.4–2.6; age ≥ 80 years, 2.6, 95 % CI 2.4–2.9) and diabetes status (diabetic, 2.4, 95 % CI 2.2–2.6; non diabetic, 2.6, 95 % CI, 2.2–2.7). Overall in-hospital mortality was 2.7 % ($n=4$; STEMI, $n=1$; non-STEMI, $n=3$).

Conclusion: The majority of patients with ACS and primary presentation in the ED were classified as MTS levels 1–3 (immediate to urgent assessment) in our retrospective study. We did not observe a significant difference in terms of type of ACS, gender, age and diabetes status. This data leads to the hypothesis that the MTS is a valuable triage tool for patients with ACS. Further prospective studies are needed to confirm our hypothesis.

XII-5

Fibrocytes accumulate at the culprit lesion site and display enhanced migratory and reparatory properties in ST elevation acute coronary syndrome

T. Hofbauer, A. Mangold, T. Scherz, D. Simon, V. Seidl, A. Panzenböck, N. Staier, H. Heidari, J. Müller, I. M. Lang

Kardiologie, Medizinische Universität Wien, Vienna, Austria

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 ischemic myocardium of patients. This finding was also observed in a mouse model of ischemia/reperfusion cardiomyopathy. 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. This might contribute to occlusion and consecutive reparative processes.

Methods: Blood samples from the coronary culprit lesion site (CLS) of STE-ACS patients ($n=50$, male = 78 %, mean age = 61 ± 12y) drawn in the course of primary percutaneous coronary intervention were analyzed. Blood from the femoral artery served as a peripheral control. Flow cytometry was employed to characterize fibrocytes based on their expression of Collagen-I, BMPRII, CD34, CD11b, CD13, and CD45. Data are expressed as cell count/106 CD45+ cells, mean fluorescence intensity (MFI), mean ± SD or median [IQR].

Results: Fibrocyte count is increased at the coronary site compared to femoral blood (CLS 722 [276–1298]/106 CD45+ cells vs. femoral 324 [180–589]/106 CD45+ cells, $p=0.0001$). Furthermore, CLS fibrocytes display significantly increased expression of Collagen-I (CLS MFI 19530 ± 11476 vs. femoral MFI 13241 ± 9961, $p=0.0001$). The adhesion markers CD11b and CD13 are upregulated in CLS fibrocytes compared to femoral fibrocytes (CLS MFI 73619 ± 46632 vs. femoral MFI 57375 ± 36948, $p=0.0001$ and CLS MFI 42747 ± 19065 vs. femoral MFI 29734 ± 11760, $p=0.001$, respectively). The expression of BMPRII remained unchanged.

However, in patients suffering from dyslipidemia (dyslip), BMPRII expression of fibrocytes was significantly upregulated at the femoral site (dyslip 26056 [13195–54807], no dyslip 19913 [13635–22965], $p=0.009$). The same trend was observed in CLS fibrocytes, but failed to reach statistical significance.

Discussion: The more than two-fold increase of CLS fibrocyte count compared to femoral blood is possibly due to homing to the coronary vessels in STE-ACS. This might be mediated by the upregulation of the adhesion markers CD11b and CD13 on CLS fibrocytes. Increased Collagen-I expression of fibrocytes at the CLS might reflect an increased reparative activity of fibrocytes within the coronary vessels. A general pro-inflammatory state associated with dyslipidemia might induce an upregulation of BMPRII expression of fibrocytes. This might increase the susceptibility of fibrocytes to signaling via the bone morphogenic protein-family. Further experiments will clarify the contribution of fibrocytes to STE-ACS.

XII-6

High-sensitivity troponin T for prediction of left ventricular function and infarct size one year following STEMI

S. J. Reinstadler, H.-J. Feistritzer, G. Klug, A. Rederlechner, M.-T. Gröber, C. Diem, J. Mair, W.-M. Franz, B. Metzler

Universitätsklinik für Innere Medizin III, Kardiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

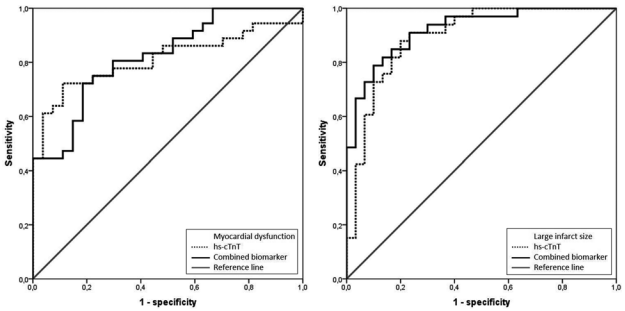
Background: Data relating high-sensitivity cardiac troponin T (hs-cTnT) to long-term myocardial function and infarct size in patients after first ST-segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI) are lacking. We aimed to evaluate the use of serial and peak concentrations of hs-cTnT for prediction of myocardial function as well as infarct size assessed by cardiac magnetic resonance imaging (CMR) one year following first STEMI.

Methods: Sixty-six patients, successfully revascularized by PCI for first-time STEMI (mean age 57 ± 11 years, 12 % females), were enrolled in this single-centre, observational study. Serial hs-cTnT levels were measured on admission, 6 h, 12 h, 24 h, and 12 months post-PCI. At the same time points, creatine kinase (CK), high-sensitivity C-reactive protein (hs-CRP) and lactate dehydrogenase (LDH) concentrations were also determined. CMR imaging was performed within the first week and 12 months thereafter.

Results: Except for admission hs-cTnT, all single time point and peak hs-cTnT concentrations showed significant correlations with left ventricular ejection fraction (LVEF: $r=-0.404$–-0.517, all $p<0.01$) and infarct size (IS: $r=0.421$–0.700, all $p<0.01$) at baseline and 12 months follow-up. Peak concentrations of CK, hs-CRP

and LDH were significantly associated with 12-month LVEF and IS (all $p<0.05$). In receiver-operator characteristics analysis, the area under the curve (AUC) of peak hs-cTnT was 0.82 (95 % CI 0.71–0.92) for the prediction of decreased LVEF (<55 %) at 12 months and 0. 89 (0.89, 95 % CI 0.81–0.97) for the prediction of large IS (>8 %) at 12 months (Fig. 1). The combination of all 4 biomarkers resulted in an AUC of 0.82 and 0.92 for the prediction at 12 months of reduced LVEF and large IS at 12 months, respectively.

Conclusion: In patients with first-time STEMI, serial and peak concentrations of hs-cTnT are closely correlated to long-term LVEF and IS. Combination of hs-cTnT with other traditional biomarkers did not add any significant prognostic value compared with hs-cTnT alone.



XII-7

Risk assessment in patients with cardiac rupture after acute myocardial infarction

P. Sulzgruber, F. El-Hamid, L. Koller, S. Forster, G. Goliasch, A. Niessner

Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: A cardiac rupture (CR) such as ventricular septal rupture (VSR), free wall rupture (FWR) or papillary muscle rupture (PMR) has a very low incidence of approximately 1 % among patients with acute myocardial infarction (AMI), but is associated with a very poor prognosis with a mortality rate between 60 and 100 %.

Methods and results: Therefore we identified 28 patients with AMI (median age of 68 years, 46.4 % male, 92.9 % STEMI) suffering from additional CR (VSR, FWR and PMR) who were admitted to the Vienna General Hospital, Austria between 1996 and 2009. Within our study 35.7 % of all patients ($n=10$) survived the initial event. After a median follow-up time of 5 years only additional 20 % of the survivors ($n=2$) died due to cardiovascular causes. Age with a hazard ratio [HR] per one standard deviation [1-SD] of 1.95 (95 % CI: 1.09–3.45, $p=0.023$), systolic blood pressure at admission with a HR per 1-SD of 0.50 (95 % CI: 0.28–0.90, $p=0.018$), Glasgow Come Scale (GCS) with a HR per 1-SD of 0.52 (95 % CI: 0.32–0.84, $p=0.007$), Simplified Acute Physiology Score (SAPS) II with a HR per 1-SD of 2.06 (95 % CI: 1.27–3.30, $p=0.003$), peak CK-MB levels with a HR per 1-SD of 1.61 (95 % CI: 1.00–2.60, $p=0.035$) and bicarbonate with a HR per 1-SD of 0.56 (95 % CI: 0.34–0.92, $p=0.020$) were risk predictors in univariate Cox regression analysis.

Conclusion: In accordance with existing literature, the mortality rate in the acute phase of AMI with CR was considerably high. However, in CR patients who survived the initial event long-term mortality was comparable to the overall AMI cohort. Intensive care assessment and markers of shock severity were identified as most important risk factors. Further studies about risk prediction in AMI patients with CR should be done in multi-center trials to receive an adequate number of patients.

Postersitzung XIII: Basic Science 3

XIII-1

Prolyl hydroxylase inhibition induces SDF-1 and CXCR4 expression to increase CXCR4+ cell homing and myocardial repair

S. K. Ghadge, T. Van Pham, M. Messner, M. Doppelhammer, B. Husse, W.-M. Franz, M.-M. Zaruba

Kardiologisches Labor/Abtlg 1-G3–024, Medical University Innsbruck, Innsbruck, Austria
Ludwig Maximilians University, München, Germany

Objective: Stabilization of the cardiac SDF-1/CXCR4 axis preserves myocardial function and attenuates ischemic cardiomyopathy. However, HIF-1α dependent SDF-1 upregulation lasts only for 48–72 h after MI limiting the targeting of regenerative cells to ischemic myocardium. To overcome this caveat, we aimed to activate the HIF-1α target genes SDF-1 and CXCR4 by stabilization of HIF-1α through inhibition of prolyl hydroxylase with the ratio to stimulate myocardial repair.

Methods: To evaluate the effects on HIF-1α mediated SDF-1 and CXCR4 expression, genetically tagged SDF1-EGFP and CXCR4-EGFP mice were subjected to optimal doses (80 mg/kg i.p.) of the prolyl hydroxylase Inhibitor dimethyloxalylglycine (DMOG). To examine the time frame of SDF-1 and CXCR4 expression in in vitro (HEK cells) and in vivo (BM & heart), DMOG was treated at different dosing regimens (50–1000 μM & 80 mg/kg i.p.) and time intervals (1–6 h). FACS and immunhistochemical analyses of CXCR4+ bone marrow (BM), peripheral blood, and heart cells as well as infarct size measurements were performed under normoxaemic and ischemic conditions with and without DMOG treatment.

Results: SDF1-EGFP mice treated with DMOG showed robust induction of SDF-1 in heart vessels. In vitro, SDF-1 was transiently upregulated within 60 min to 2 h after DMOG treatment, followed by significant decrease after 6 h. CXCR4 was significantly elevated at later time points (6 h). In vivo, CXCR4 expression was significantly upregualted in BM (6 h) after DMOG treatment. FACS analyses of transgenic CXCR4-EGFP BM and hearts revealed that CXCR4+ was frequently expressed on CD11b+ monocytes, and to a less amount on angiogenic CD31+, CD34+, c-kit+, and Flk1+ cells, as well as stem cell populations like ACC133+ and Lin-/c-kit+/Sca-1+. Treatment with DMOG revealed a robust upregulation of CXCR4+ cell populations in the ischemic heart, predominantly of angiogenic CXCR4+/CD11b+ monocytes. Further analysis of the latter showed that DMOG treatment leads to a shift of the CD206+/CD86 ratio in favor of M2 macrophages associated CD206+ subpopulation in infarcted hearts associated by attenuated infarct remodeling.

Summary and conclusion: Our data suggest that inhibition of prolyl hydroxylase may be a promising target for HIF-1a mediated SDF-1 activation to increase CXCR4+ stem cell homing and myocardial repair.

XIII-2

Increased expression of the aging related splice variant progerin in patients with cardiomyopathy

S. K. Ghadge, M. Messner, G. Pölzl, W.-M. Franz, M.-M. Zaruba

Kardiologisches Labor/Abtlg 1-G3–024, Medical University Innsbruck, Innsbruck, Austria

Objective: Defined mutations in the human lamin A gene or in enzymes processing the important nuclear membrane protein LMNA (e.g. Zmpste24) are causally involved in premature aging syndroms like progeria. The most prevalent and recurrent point mutation is depicted by a single C to T (1824) nucleotide substitu-

tion in exon 11 of the lamin A gene. This results in the activation of a cryptic splice donor site and production of a truncated prelamin A protein (LMNA Δ50 aa), also called progerin. Besides, low levels of progerin also play a prominent role in the process of aging in healthy individuals. Since LMNA mutations are associated with dilated cardiomyopathy, we aimed to address whether progerin and Zmpste24 play a role in patients with cardiomyopathy.

Methods: To quantitatively analyze the expression of progerin and Zmspte24, blood and endomyocardial biopsies ($n=6$) were obtained from non-ischemic cardiomyopathy patients. For controls, blood samples from age matched healthy individuals as well as biopsies from healthy transplanted hearts ($n=6$) were analyzed. Total mRNA was extracted and quantitative RT-PCR analyses were performed. Total LMNA expression was determined utilizing primers spanning exon 8 to 9. To specifically quantify progerin expression, we designed optimized primers spanning the splice junction site between exon-11 and 12. Progerin expression was related to total LMNA expression. Zmpste24 expression was related to housekeeping genes rpl32 and polr2a.

Results: Progerin mRNA levels were not significantly different in blood samples from controls and DCM patients (0.84 ± 0.14 vs. 0.81 ± 0.33; $p=0.67$). In contrast, progerin levels were significantly upregulated in failing hearts compared to heart biopsies derived from healthy controls after heart transplantation (1.66 ± 0.56 vs. 1.06 ± 0.07; $p=0.01$). Zmpste24 mRNA level were not significantly different between patient and control blood samples (1.31 ± 0.23 vs. 1.11 ± 0.15, $p=0.12$) and hearts (1.05 ± 0.13 vs. 1.00 ± 0.20, $p=0.62$).

Summary and conclusion: In conclusion, our preliminary data suggest that elevated levels of the aging related splice variant progerin are involved in human heart failure.

XIII-3

Klotho and FGF receptor are concomitantly expressed in human individuals with heart failure

G. Pölzl, S. Ghadge, M. Messner, E.-M. Stocker, C. Ensinger, B. Husse, M. Zaruba

Innere Medizin III, Kardiologie und Angiologie, Medizinische Universität Innsbruck, Innsbruck, Austria

Introduction: In clinical studies elevated levels of FGF23 have been linked with the advent and progression of heart failure. Klotho acts as essential coreceptor for FGF23 whereby tissue-specific expression of Klotho determines target organs of FGF23. Moreover, Klotho is an antiaging protein and actively involved in the prevention of arteriosclerosis. Previous data in mice suggest that FGF23 exerts its effects on LV hypertrophy independently of Klotho due to not detectable expression of the Klotho receptor. Since no information is available on Klotho expression in human individuals with heart failurewe aimed to investigate the cardiac expression of Klotho and FGF receptor in patients with heart failure.

Methods: Endomyocardial biopsies from patients with non-ischemic cardiomyopathy ($n=6$) and patients 3–4 weeks after successful heart transplantation ($n=6$) were analyzed for the expression of Klotho and FGF receptor. The latter were considered healthy controls after exclusion of graft rejection. Total RNA was isolated and reverse transcribed using QuantiTect RT kit. Exon spanning primers for human Klotho were designed. Using SYBR green (Applied Biosystems, USA) quantitative gene expression was calculated using the comparative ΔΔCt-method with RPL32 as a reference gene. Immunohistochemistry was performed utilizing monoclonal mouse and rabbit antibodies against FGFR and Klotho protein, respectively (Abcam, USA).

Results: Klotho mRNA and FGFR were detectable in non-ischemic cardiomyopathy and in healthy hearts by RT-PCR and immunohistochemistry. Expression of both Klotho mRNA and FGFR1 mRNA was significantly upregulatedin cardiac biopsies derived from patients suffering from non-ischemic cardiomyopathy as compared to healthy controls by quantitative RT-PCR (2.65 ± 0.70 vs. 1.32 ± 0.43; $p=0.002$, and 1.65 ± 0.43 vs. 1.08 ± 0.21; $p=0.01$, respectively). Immunohistochemically, double stainingrevealed colocalization of Klotho and FGFR in diseasedcardiomyocytes.

Summary and conclusion: We show that Klotho and FGFR are concomitantly and highly expressed in non-ischemic cardiomyopathy. Whether adverse cardiac effects of FGF23 are mediated by its coreceptor Klotho and/or cardiac expressed Klotho and its soluble ligand exerts independent effects in heart failure has to be addressed in future studies.

XIII-4

IL-33 stimulates the expression of the neuroimmune guidance cues netrin-1 and semaphorin3A by human endothelial cells

E. Montanari, Ch. Kaun, C. Lemberger, R. De Martin, G. Maurer, K. Huber, J. Wojta

Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria
Institut für Gefäßbiologie und Thromboseforschung Wien, Vienna, Austria
3. Medizinische Abteilung, Wilhelminenspital, Vienna, Austria

Background: In addition to their important function as neuroimmune guidance cues during the development of the nervous system, a role for netrin-1 and semaphorin3A in the pathogenesis of atherosclerosis has emerged. Among other effects in this disease, they were shown to inhibit the egress of macrophages from atherosclerotic plaques, thus contributing to maintenance of the chronic inflammation in such lesions. The role of interleukin (IL)-33, one of the numerous cytokines involved in this disease, is still controversially discussed, as both pro- and atherosclerotic effects could be seen. The aim of this study was to find out whether IL-33 influences netrin-1 and semaphorin3A production by human umbilical vein endothelial cells (HUVECs) in vitro.

Methods and results: Netrin-1 and semaphorin3A mRNA expression by HUVECs was up-regulated after stimulation with IL-33 at various concentrations for different periods of time with a maximum at 6 h after incubation as analysed by qRT-PCR. This effect of IL-33 on ECs seems to be mediated by NF-κB, as adenoviral overexpression of inhibitor of κBa (IκBa) or a dominant negative form of IκB kinase 2 (dnIKK2) inhibited IL-33-induced netrin-1 and semaphorin3A mRNA expression. Stimulation of netrin-1 and semaphorin3A production by IL-33 was found to be IL-1-independent as addition of IL-1 receptor antagonist (IL-1Ra) did not inhibit IL-33-induced netrin-1 and semaphorin3A mRNA up-regulation in human ECs.

Conclusion: IL-33 stimulates netrin-1 and semaphorin3A expression by human endothelial cells, an effect that appears to be independent of IL-1 and mediated by NF-κB. Through subsequent retention of macrophages in atherosclerotic lesions, which contribute to the chronic inflammation present in this disease, up-regulation of these neuroimmune guidance cues may represent another mechanism through which this cytokine contributes to the pathogenesis of atherosclerosis.

XIII-5

Hemmung der Atherosklerose durch Gliptin-Therapie im ApoE-knock-out-Mausmodell

F. Remm, C. Brenner, W.-M. Franz, N. Kränkel, U. Landmesser, K. Kuschnerus, S. Kühlenthal, L. Gross, H. Theiss

Klinik für Innere Medizin III, Kardiologisches Labor, Medizinische

Universität Innsbruck, Innsbruck, Österreich
Charité – Universitätsmedizin Berlin, Berlin, Deutschland
Ludwig-Maximilians Universität München-Großhadern, München, Deutschland

Gliptine wirken als Hemmstoffe der Dipeptidylpeptidase 4 (DPP4) und werden seit einigen Jahren klinisch zur Therapie des Diabetes mellitus Typ 2 eingesetzt. In aktuellen präklinischen Studien konnte gezeigt werden, dass Gliptine neben der blutzuckersenkenden Wirkung auch zahlreiche protektive Effekte im Kardiovaskulären System vermitteln können. In eigenen Vorarbeiten im Mausmodell konnten wir bereits nachweisen, dass eine vasoprotektive Gliptinwirkung nach Endothelschädigung über den SDF1/CXCR4-Signalweg vermittelt wird. In der vorliegenden Arbeit haben wir nun den Einfluss einer Langzeit-Gliptintherapie auf die Entstehung der Atherosklerose im ApoE k.o. Mausmodell untersucht.

Die Tiere wurden in folgenden Gruppen behandelt: Normaldiät (ND) oder hochcholesterolhaltige Diät (HD) zur Atherosklerose induktion. Die Tiere auf HD wurden weiterhin entweder mit Placebo, Sitagliptin oder Sitagliptin in Kombination mit dem CXCR4-Rezeptorblocker AMD3100 therapiert. Nach der dreimonatigen Behandlungsperiode wurde den Tieren die Aorta zu weiteren Analysen entnommen. In diesen Aorten wurde zuerst die Ausdehnung der atherosklerotischen Plaques mit Hilfe der Oil-red-O-Färbung bestimmt. Die Messung von Gesamtmakrophagengehalt und Differenzierung der Makrophagen-Subtypen (M1 und M2) erfolgte mittels FACS-Analysen. Zusätzlich wurde, um den Einfluss der Gliptintherapie auf die Differenzierung der Makrophagen detaillierter zu untersuchen, ein in-vitro Makrophagen-Differenzierungs-Assay ergänzt.

Die Ergebnisse unserer Analysen haben gezeigt, dass die Ausdehnung der atherosklerotischen Plaques bei Mäusen unter HD signifikant höher war, als bei Tieren auf ND oder auf HD unter Sitagliptintherapie. Dass diese Plaque-Reduktion vermutlich auf dem Einfluss der Gliptintherapie beruht, konnten wir durch die Blockade des SDF1/CXCR4-Weges mittels AMD3100 nachweisen. Bei Tieren auf HD mit Sitagliptintherapie und zusätzlicher ADM3100-Behandlung zeigte sich eine Plaque-Ausdehnung, die der Placebogruppe vergleichbar war. Die FACS-Analysen ergaben, dass sich der Gesamtmakrophagengehalt und die Anzahl der muralen M1-Makrophagen der einzelnen Gruppen nicht signifikant unterschied. Interessanterweise zeigte sich jedoch eine signifikante Erhöhung der M2-Makrophagen in der erkrankten Aortenwand von Tieren, die mit Sitagliptin behandelt worden waren. Weitere in-vitro-Analysen haben ergeben, dass Sitagliptin die Monozyten-Differenzierung in Richtung M2-Makrophagen verschiebt und so für die verstärkte murale Anreicherung dieses protektiven Zelltyps verantwortlich ist.

Die Langzeittherapie mit Sitagliptin stellt damit einen neuen möglichen Therapieansatz zur Prävention atherosklerotischer Erkrankungen dar.

XIII-6

Differential in vivo activation of monocyte subsets during experimental endotoxemia in humans

P. Hohensinner, B. Thaler, K. Krychtiuk, L. Koller, M. Brekalo, G. Maurer, K. Huber, B. Jilma, J. Wojta, W. Speidl

Innere Medizin II, Medizinische Universität Wien, Vienna, Austria
Wilhelminenspital Wien, Vienna, Austria

Background: Human monocytes are a heterogeneous cell population that can be divided into a classical (CM, CD14++CD16-), a non-classical (NCM, CD14+CD16+), and an intermediate subset (IM, CD14++CD16+). Monocytes are key cells in the response to sepsis.

Aims: A human endotoxemia model was used to identify monocyte subset activation under septic conditions.

Methods: Healthy volunteers ($n=12$) were injected with a bolus infusion of LPS (2 ng/kg) and blood samples were obtained before LPS injection and at 2, 6 and 24 h after injection. Whole blood samples were stained for CD14, CD16 and CD11b and were analysed with a BD FACS Canto II. Absolute cell numbers were determined using 123counting beads and a novel in situ mRNA hybridization approach to detect IL6 and IL8 specific mRNA at the single-cell level by flow cytometry was applied.

Results: The analysis of cell counts showed a drop in monocyte levels after 2 h of LPS treatment. After 6 h, CM recovered to their initial cell number whereas IM and NCM remained reduced. After 24 h, monocyte subsets were skewed towards IM, which showed a 572 % increase ($p<0.001$). In addition, IM showed the strongest upregulation of CD11b after 2 h compared to CM and NCM ($p<0.05$, $p<0.005$). After 6 and 24 h CD11b returned to baseline values albeit IM still displayed the highest baseline expression. Furthermore, IL6 and Il8 mRNA levels were enhanced after 6 h in IM to 180 % ($p<0.05$) and 240 % ($p<0.05$) respectively and NCM to 225 % ($p<0.05$) and 232 % ($p<0.05$) respectively, whereas CM response was weak to 119 % ($p<0.05$) and 142 % ($p<0.05$) respectively. After 24 h, IM and NCM mRNA levels for IL6 and IL8 mRNA return back to the baseline expression levels.

Conclusion: Our data indicate that the main responding subset of monocytes to LPS is the CD14++CD16+ intermediate subset followed by the CD14+CD16+ non-classical monocyte subset. Circulating classical monocytes showed comparably less reaction to LPS challenge in vivo.

XIII-7

Effects of acute exercise on circulating microRNA levels

B. Mayr, E. E. Müller, H. Breitenbach-Koller, M. Schönfelder, J. Niebauer

University Institute of Sports Medicine, Prevention and Rehabilitation, Research Institute of Molecular Sports Medicine and Rehabilitation, Department of Cell Biology, Paracelsus Medical University, Salzburg, Austria

Background and objective: Micro ribonucleic acids (miRNAs) are small non-coding RNA molecules that control gene expression by translational inhibition. They have been identified to play roles in a multitude of cellular functions. Recently, plasma-based circulating miRNAs and their response to physical exercise have gained increasing interest in research, but until now exercise induced modulation of miRNA flux has been explored insufficiently. The aim of the present study was to investigate the influence of an acute all-out ergometry on miRNA expression in human plasma by means of a miRNome panel.

Methods: In this study, 23 participants (12 males and 11 females) performed an all-out cycling ergometry. All plasma samples were extracted for total RNA before and after exercise. RNA pools were generated out of selected RNA samples of four male and four female participants. Each pool was screened for miRNA levels using a service whole genome miRNA-qPCR-array (Human Human panel I + II V3.M; Exiqon, Vedbaek, Denmark) analyzing 752 miRNAs.

Results: Taking into account only those miRNAs with a regulation higher than 2-fold, 87 miRNAs were found to be regulated after exercise either in females or males. Of those, 12 miRNAs were detected to be regulated in both, male and female samples. A concordant up-regulation was detected in miR-1249, miR-188–3p, miR-200c-3p, miR-27a-5p, miR-338–3p and miR-874, and a concordant down-regulation was found for miR-196b-5p, miR-26b-3p and miR-627. Three miRNAs (miR-139–3p, miR-214–3p, miR-361–3p) were counter-regulated between males and females. The highest down-regulation was found within the female pool (miR-218–5p, 33.9-fold), and the highest up-regulation after exercise was found within the male pool (miR-106b-3p, 17.7-fold). A higher number of miRNAs was expressed in male samples; but the magnitude of regulation due to exercise was higher in females.

Conclusion: In the present study, a whole genome screen revealed several circulating plasma miRNAs with expression levels changing more than 2-fold after an all-out exercise. Many of those have not been described in literature before, probably as most other studies analyzed pre-selected miRNAs. The present results suggest that there might be a gender-dependent effect of acute exercise.

Postersitzung XIV: Basic Science 4

XIV-1

Difference in MIF production by PBMC in patients with Diabetes mellitus type II

E. Simader, M. Zimmermann, A. Geßl, D. Traxler-Weidenauer, H. Brath, K. Leitner, A. Mitterbauer, O. Glück, L. Beer, H. J. Ankersmit

Chirurgie, Thoraxchirurgie, Medizinische Universität Wien, Vienna, Austria

Background: Macrophages migration inhibitory factor (MIF), as a pleiotropic cytokine, plays a critical role in several inflammatory conditions including various tumours, atherosclerosis, diabetes and obesity. MIF also influences glucose metabolism at several levels, affecting both insulin production in the pancreatic beta cell and the cells targeted by insulin and therefore plays a key role in the development of type 1 and 2 diabetes mellitus (DM).

However, the cellular source of elevated circulating MIF and the potential significance in promoting inflammation and related consequences are unknown.

A previous study reported a co-localization of infiltrated macrophages and expression of MIF in the infarct myocardium, respectively elevated plasma levels of MIF in MI patients. These results indicate that peripheral blood mononuclear cells (PBMC) constitute an important cellular source for sustained elevation of circulating MIF in diabetes patients.

Aims: The aim of this study was to analyze serum MIF levels in diabetes mellitus type II patients and serum changes caused by disease severity or medication. Using cultured peripheral blood mononuclear cells (PBMC) from DM patients, we investigated MIF secretion under physiological and inflammatory conditions.

Materials/methods: 54 subjects were enrolled in this study. We obtained serum samples and PBMCs from 15 patients with DM type 2 under medication, 11 DM type 2 patients without medication (initial diagnosis), 13 patients with impaired fasting glucose and 15 healthy controls (all groups gender and age matched). PBMC were isolated from whole blood and cultured either alone, with Lipopolysaccharide (LPS) or Phytohaemagglutinin (PHA). Supernatants were collected after 24 h of culture and concentrations of MIF were determined by enzyme-linked immunosorbent assay (ELISA).

Results: Serum concentrations of MIF and hs-CRP, a marker for the risk of cardiovascular complications, were significantly higher in DM patients than in controls.

The spontaneous production of MIF by PBMC was significantly modified by PHA and LPS in all four groups. The induction of MIF production was highest in newly diagnosed diabetes patients under LPS stimulation with significantly lower levels in the other groups (diabetes patients on medication, impaired fasting glucose or healthy controls).

Discussion: The presented data suggest that increased MIF serum levels could be mainly produced by PBMC. Moreover PBMC in diabetes patients may actually be more susceptible to infection than PBMC in control patients. This could play a role in DM patients' increased risk for chronic infections and cardiovascular complications.

Yet further studies are necessary to better understand the relevance of MIF secretion in the immune, endocrine and cardiovascular system of diabetes patients.

XIV-2

Differences in cardioprotective effects of ischemic post-conditioning and remote conditioning in porcine closed-chest reperfused myocardium

D. Macejovska, N. Pavo, K. Zlabinger, P. Ferdinandy, G. Mauer, M. Gyöngyösi

Abteilung für Kardiologie, Innere Medizin II, Medizinische Universität Wien, Vienna, Austria
Semmelweis Medical University Budapest, Budapest, Hungary

Background: Brief repetitive ischemia/reperfusion (I/R) immediately after re-opening of the occluded artery (ischemic post-conditioning, IPostC) thought to be cardioprotective due to diminish reperfusion injury, and has been successfully applied in humans. Remote ischemic conditioning (RIC) is characterized by brief cycles of I/R applied to an extracardiac organ during the prolonged ischemic event, aiming to release of antiischemic substances in larger amount. The aim of our present experiments was to elaborate the changes in gene expression profile induced by IPostC and RIC in a porcine closed chest reperfused myocardial infarction model.

Methods: Domestic pigs (group AMI, $n=6$) underwent 90-min percutaneous coronary balloon occlusion of the LAD followed by reperfusion. IPostC (group IpostC, $n=6$) was performed immediately after initiation of reperfusion by repeated 6×30 s inflation/deflation of the LAD-balloon. RIC was induced by repeated 4×5 min I/R by tourniquet occlusion of blood flow of a hind limb (group RIC, $n=6$). Animals with sham intervention served as control (group Sham, $n=4$). Animals in all groups were randomized to 3 h or 3 days follow-ups (FUPs). Transthoracic echocardiography was performed to measure left ventricular (LV) ejection fraction using Teichholz formula from the 4-chamber views. Infarct sizes were measured by MRI with late enhancement (LE) at the 3 days FUP. Gene expression profile of the ischemic infarcted area was analysed by next generation sequencing (NGS) and the overexpression or downregulation of the genes were expressed as log fold changes.

Results: Echocardiography and MRI-LE showed similarly depressed LV function in groups AMI, IPostC or RIC, both at the 3 h FUP or at the 3d FUP, as compared to group Sham. However, trend to smaller infarct size was measured in groups IPostC and RIC by MRI + LE as compared to group AMI. NGS showed totally 3861 and 3737 overexpressed genes significantly at 3 h or 3 days FUP as compared to controls with the most obvious changes of group AMI in contrast with groups IPostC and RIC (Table). IpostC and RIC resulted in a delay of gene expression changes, as only magnitude of gene expression, but not direction between groups AMI, IpostC and IRC was observed at 3 h, but several structural and ion transporter genes were downregulated in groups IPostC and RIC as compared to group AMI and Sham at the 3 days FUP (Table). These changes in gene profiling might explain the cardioprotective effect of IPostC and RIC.

Table 1 Differences n gene expression profile in group AMI, IPostC and RIC as compared to Sham group.

gene	function	description	3 hours FUP			3 days FUP		
			AMI LogFC	IPostC LogFC	RIC LogFC	AMI LogFC	IPostC LogFC	RIC LogFC
ADAM19	cellular function, structural proteins	cell adhesion, cell migration	**-2.71**	**-2.19**	-1.13	0.30	0.76	0.80
MKI67		marker of proliferation	**-3.23**	**-1.79**	-0.88	1.58	3.07	1.43
MXRA5		matrix remodeling	**-1.91**	**0.00**	-1.34	2.94	**3.90**	2.88
BGN		muscle regeneration	**-2.10**	**-1.81**	-1.28	1.46	**2.94**	1.92
THBS1		cell to cell, cell to matrix interaction	**3.13**	**5.64**	0.99	**2.75**	**4.57**	**4.05**
IFRD1		muscle cell differentiation	**2.98**	**4.82**	1.24	**1.23**	**1.63**	**1.47**
FGF13		cell proliferation	**2.22**	**2.40**	**2.44**	1.42	-0.61	0.19
MYO18B		cellular traffiking, regulatory function	0.69	**2.21**	**2.24**	**1.88**	**-1.82**	**-0.56**
ANK1		structural protein, cytosceletal element	**1.17**	**1.54**	**1.29**	1.01	**-3.61**	-2.37
TUBA8		structural protein, cytoscleletal element	**1.98**	**2.48**	**2.48**	1.07	**-3.32**	-1.84
KCNIP2	channel transport	muscle contraction, postassium transport	**2.23**	1.21	**1.84**	0.82	**-4.39**	**-3.10**
KCNJ4		potassium channel	**2.07**	**1.91**	1.65	1.52	**-3.66**	**-2.72**
SLC41A1		magnesium transporter	**1.56**	**1.95**	**1.72**	1.35	**-1.71**	-1.00
SLC30A1		zinc transporter	**2.60**	**2.38**	**1.63**	1.58	1.49	1.30
SLC25A30		mitochondrial transport of ions	**1.26**	**1.03**	0.89	0.50	**-2.51**	**-2.03**
CXCL10	immunomodulatory function	chemotactic for monocytes and T-lymphocyte	**5.18**	**5.59**	**2.29**	**3.46**	1.13	0.92
NFAT5		nuclear factor of activated T-cells	**1.75**	**2.60**	**2.10**	1.24	**1.24**	**1.44**
FCGR1A		CD64	**1.86**	**2.17**	**3.22**	**2.50**	**3.08**	**2.00**
TBX4	angiogenesis	angiogenesis, activation of transcription	**5.10**	**4.91**	**7.87**	**5.62**	**3.45**	**3.85**
VASH1		angiogenesis inhibitor	**-2.55**	**-1.66**	**-2.30**	**0.36**	**1.27**	0.49

downregulated
upregulated
significant

Discussion: Temporary genetic mapping of the ischemic area showed complex responses in IPostC and RIC. These differentially expressed factors may serve as an indicator of cardioprotection.

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XIV-3

Differential gene expression profile of intramyocardially injected mesenchymal stem cells extracted from the heart and spleen early post transplantation

A. Gugerell, D. Macejovska, M. Emmert, P. Wolint, I. Sabdyusheva, N. Pavo, G. Maurer, S. P. Hoerstrup, M. Gyöngyösi

Univ.-Klinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria
University Hospital Zurich, Zurich, Schwizerland

Introduction: The main mechanism of the improvement in cardiac function after percutaneously intramyocardially (i.m.) injected regenerative cells in the ischemic myocardium might be the paracrine effect of the directly delivered cells. Little is known, however about the genetic alterations of the host myocardium and the remote organs, where the cells wander to. Accordingly, we have investigated the transcriptome profile of the percutaneously i.m. injected porcine bone-marrow mesenchymal stem cells (pMSCs) and host myocardium and spleen.

Material and methods: pMSCs were labeled with encapsulated super-paramagnetic microspheres (MPIOs) that were co-labeled with Dragon-green fluorochromes (DGF). Closed chest, re-perfused anterior AMI was induced in domestic pigs. One month later (development of chronic LV dysfunction) MPIO/DGF-pMSCs were injected i.m. using the NOGA mapping and injection system into the border zone of infarction in 11 ± 2 locations. Three hours post transplantation cardiac and whole body MRI was performed to localize the biodistribution of the MPIO/DGF-pMSCs. Cardiac and spleen samples containing the MPIO/DGF-pMSCs and remote heart and spleen tissue samples were harvested and dissociated to obtain single cells. Using MACS-sorting and targeting the DGF, the pMSCs were separated from the cardiac (C-MPIO/DGF-pMSCs and Cardiac cells) and splenic cells (S-MPIO/DGF-pMSCs and Splenic cells) and transcriptome profiles were analyzed.

Results: MRI resulted in infarct size of 22 ± 3 % and LV EF of 42 ± 2 %. In total, 2328 genes were significantly differently expressed in the C-MPIO/DGF-pMSCs or S-MPIO/DGF-pMSCs. C-MPIO/DGF-pMSCs overexpressed several cardiac-related genes, such as tropomyozin, actin, angiopoietin, annexin, insulin-like growth factor, classified in extracellular matrix, cell adhesion, growth and metabolism gene clusters. In contrast, the S-MPIO/DGF-pMSCs expressed several genes annotated in immunglobulin or T or B-cell signaling or gastrointestinal-related clusters. No gene expression differences between the myocytes adjacent to the transplanted cells or remote cardiomyocytes, as well as in spleen (adjacent or remote) was found, indicating no paracrine effect of the pMSCs on the host myocardium during the first 3 h post transplantation.

Conclusions: I.m. transplanted pMSCs that retain in the heart or wander into a remote organ receive organ-specific signals from the host tissue. The gene expression profile of the host myocardium was not influenced in the first hours post i.m. transplantation, most probably due to the short exposition of the host tissue to the reparative cells. Longer follow-up study with refinement of this method will elaborate the genomic profile of the ischemic myocardium affected by cell-based regeneration.

XIV-4

Effect of ischemic pre-conditioning or post-conditioning on myocardial viability

N. Pavo, K. Zlabinger, D. Macejovska, G. Goliasch, J. Bergler-Klein, M. Emmert, S. P. Hoerstrup, Z. Giricz, P. Ferdinandy, G. Maurer, M. Gyöngyösi

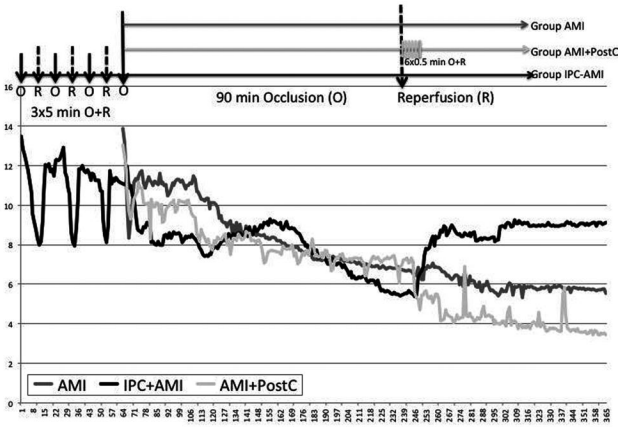
Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria
Swiss Center for Regenerative Medicine, University Hospital and University of Zürich, Zurich, Schwizerland
Semmelweis University HungaryBudapest, Budapest, Hungary

Introduction: Brief repetitive ischemia called ischemic preconditioning (IPC), or postconditioning (PostC) are powerful protective conditions against myocardial infarction (AMI)-related morbidity and mortality, yet the exact mechanisms are still unclear. We have investigated the myocardial viability using real-time detection of intracardiac ECG signal during IPC with subsequent infarction and with/without PostC.

Methods: Domestic pigs underwent 90-min percutaneous occlusion of the mid LAD followed by reperfusion (I/R), with IPC (3 × 5 min I/R) before occlusion (group IPC, $n = 6$), or with PostC (6 × 0.5 min I/R) (group PostC, $n = 4$) immediately after final reperfusion; group AMI served as control ($n = 5$) (Figure). NOGA endocardial mapping catheter was placed in the left ventricular (LV) cavity, and measured the intracardiac voltage values of a single ischemic distal anterior LV point during the entire procedure. LV function and infarct size were measured by cardiac MRI with late enhancement (LE) at the 1-month follow-up.

Results: Coronary occlusion resulted in rapid decrease in voltage values with partial recovery in the reperfusion phase during IPC. Voltage values decreased in all 3 groups during the 90-min occlusion with no recovery after release of the balloon in groups AMI and PostC; PostC did not have any beneficial effect on the myocardial viability. However, voltage values were increased in group IPC after reperfusion of the ischemic myocardium, indicating protective effect. MRI + LE resulted in significant better LV ejection fraction and smaller infarct size in group IPC as compared with groups AMI and PostC.

Conclusion: IPC but not PostC induced preservation of the myocardial viability during reperfused myocardial infarction.



XIV-5

In vivo long-term serial tracking of living mesenchymal stem cells seeded to bioengineered artificial pulmonary valves in sheep

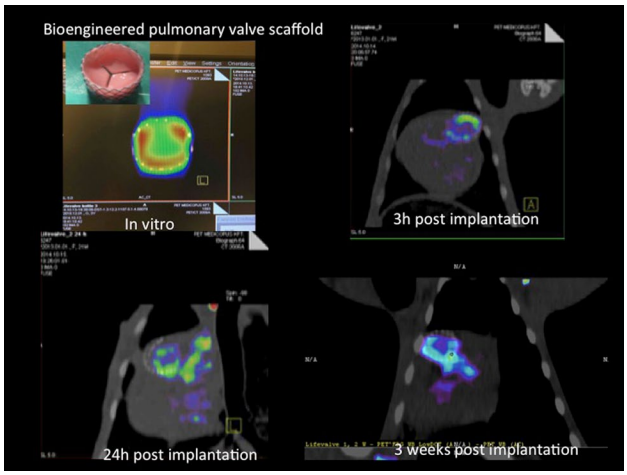
K. Zlabinger, H. Spriesterbach, L. Balkay, D. Macejovska, N. Pavo, R. Garamvölgyi, J. Bergler-Klein, J. C. Wu, G. Maurer, S. P. Hoerstrup, M. Pavone-Gyöngyösi

Universitätsklinik für Innere Medizin II, Kardiologie-Forschung, Medizinische Universität Wien, Vienna, Austria
Deutsches Herzzentrum Berlin, Berlin, Germany
PET Center of University of Debrecen, Debrecen, Hungary
University of Kaposvar, Kaposvar, Hungary
Stanford University School of Medicine,Stanford, USA
University Hospital and University Zürich, Zürich, Schwizerland

Background: Heart valve tissue engineering attracts increasing attention in pediatric cardiology due to the lack of living, non-immunogenic heart valve grafts with adaptive self-growth. The aim of the present sub-study of the LifeValve EU project was to seed the tissue engineered heart valves with transfected mesenchymal stem cells (MSCs) to enable tracking the fate of the seeded stem cells via serial in-vivo non-invasive positron emission tomography-computer tomography (PET-CT).

Methods: The bioengineered valves were air dried for one hour before the seeding procedure to facilitate cell attachment. MSCs were thawed and proliferated for one week in culture followed by a transfection with a PET-reporter gene using Lipofectamin (LTX + Plus Reagent), resulting in a transfection efficiency of 55 %. The transfected cells were seeded in a highly concentrated cell suspension to the scaffolds. Static cultivation at 37 °C and 5 % CO_2 led to successful ingrowth of the MSCs into the 3D artificial valves, resulting in an average cell number of 2 × 10^6 in each valve. The artificial valves were then implanted percutaneously into sheep in the pulmonary position under general anaesthesia (n=4), an additional sheep did not underwent valve implantation to serve as control. Then a mCi [18F]-FHBG PET tracer was produced for each procedure and serial PET-CT imaging of the sheep was performed 3 h, 6 h, 24 h and 3 weeks after the valve implantation. For the quantitative assessment of the number of cells survived in the 3D scaffold after in vivo implantation, vials containing 5 × 10^4, 2 × 10^5 and 4 × 10^5 transfected cells were mixed with the PET tracer for 1 h, then the non-bound tracer was washed out and the vials were PET-CT imaged as in vitro control.

Results: PET-CT of control vials containing transfected cells showed a dose-dependent tracer uptake in the cells in all doses. In vitro PET-CT images of the valves showed the accumulation of the seeded cells at the base of the leaflets. PET-CT images of the sheep 3 h after implantation of the "living" valve showed a clear signal of the valves with the seeded transfected cells, with a mean estimated number of survived cells of 1.2 × 10^6. Extracardiac hot spots were seen in the mediastinal lymph nodes. No meaningful decrease of the cells living in the implanted scaffold occurred at 6 or 24 h. Three weeks after valve implantation, living MSCs could be found in the valve location (estimated cell number 0.6 × 10^6) in one sheep, with some cardiac hot spots in the left ventricle. Immunfluorescense histology showed alpha-smooth muscle actin positivity on the explanted valve surface 1 month after implantation.



Conclusions: This is the first report on serial non-invasive in vivo tracking of long-term survival of MSCs seeded to 3D bioengineered valves and implanted into sheeps. A longer follow-up with a stable transfection of the cells seeded to the artificial valve and implanted in vivo will evaluate the transformation of the transplanted cells in a natural in vivo milieu. The study was supported by the LifeValve EU project.

XIV-6

Quantitative and qualitative analysis of paracrine factors released from human peripheral blood mononuclear cells in response to ionizing radiation

L. Beer, A. Mitterbauer, M. Zimmermann, A. Ellinger, F. Gruber, M. Zellner, M. Gyöngyösi, M. Mildner, H. J. Ankersmit

Universitätsklinik für Chirurgie, Thoraxchirurgie, Department of Cell Biology and Ultrastructure Research, Center for Anatomy and Cell Biology, Department of Dermatology, Research Division of Biology and Pathobiology of the Skin, Center of Physiology and Pharmacology, Institute of Physiology, Universitätsklinik für Kardiologie, Medizinische Universität Wien, Vienna, Austria

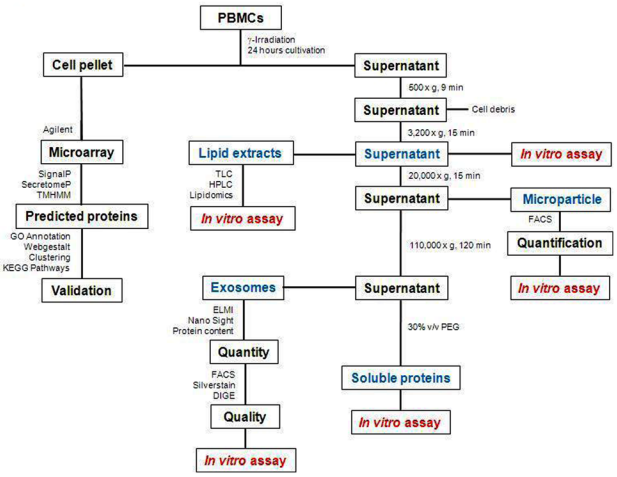
Background: Paracrine factors secreted by different cell types have been shown to exert immunological activity and affect biological processes. Depending on the cultured cell type and preconditioning strategies different soluble factors are secreted and can be detected in the cell supernatant. Our group has recently shown that paracrine factors secreted from stressed peripheral blood mononuclear cells (PBMCs) exerts pro-angiogenic, anti-aggregative, vasodilative and immune-modulating effects. The aim of the study was to identify factors present in the conditioned media of irradiated and non-irradiated cultured human PBMCs using global gene expression profiling, lipidomics and extracellular vesicle analysis. In addition we aimed to identify the biological active component using in vitro assays.

Methods: The experimental workflow is depicted in Fig. 1. Microarray analysis was performed of irradiated and non-radiated PBMCs. Bioinformatics algorithms were used to detect genes coding for secreted proteins and to uncover their biological function. Selected proteins were validated using ELISA. Secreted lipids were analyzed using thin layer chromatography and high pressure lipid chromatography. Electron microscopy, FACS, NanoSight analysis and 2D-electrophoresis were used for quantitative and qualitative analysis of microparticles and exosomes. Fibroblast and keratinocyte cell migration and activation assays were performed in order to indentify the biological active components.

Results: We observed time dependent increase of differentially expressed genes coding for secretory proteins in irradiated PBMCs in comparison to non-irradiated PBMCs. We identified several secreted factors with known cytoprotective and pro-angiogenic effects. Bioinformatics based classification of transcripts confirmed an enrichment of proteins associated with biological processes of "positive regulation of angiogenesis", "vascular wound healing", "regulation of coagulation" and "regulation of cell proliferation". Selected proteins were validated by ELISA. Irradiation of PBMCs induced the release of oxidized phospholipids. Conditioned media of irradiated PBMCs contained significantly more microparticles and exosomes. In addition the protein content of exosomes was altered in response to IR as shown by 2D-electrophoresis. Subsequently, in vitro scratch assays with fibroblasts and keratinocytes showed that exosomes and the protein fractions are the major

biological active components, responsible for the pro-angiogenic capacity. In contrast lipids and microparticles had no in vitro effects.

Conclusion: These findings highlight that ionizing radiation modulates the secretion of proteins, lipids, microparticles and exosomes in human PBMCs. Exosomes and proteins were identified as the biological active components in cell migration assays. These two components could be a valuable material for the development of safe and cell free therapies in the field of regenerative medicine.



XIV-7

Real-time imaging of healthy and ischemic porcine cardiomyocytes using living cell acquisition protocols

R. Michenthaler, K. Zlabinger, D. Macejovska, N. Pavo, A. Gugerell, J. Winkler, A. Zimba, G. Maurer, H. J. Ankersmit, M. Gyöngyösi

Universitätsklinik für Innere Medizin II, Medizinische Universität Wien, Vienna, Austria

Background: According to the 3R principles of the European Commission (replace, reduce, refine living animal experiments), in vitro cell culture methods are of enormous importance. Several rodent or human cardiomyocyte cell lines are commercially available, but currently no porcine cardiomyocyte cell lines can be purchased, even if porcine models of acute or chronic myocardial ischemia came into foreground due to direct translational value. The aim of our in vitro experiments was to follow the 3R principles, thus to establish a porcine cardiomyocyte cell culture method, investigate the behavior of these cardiomyocytes under different ischemic conditions and display the characteristics, life, proliferation, and death of these cells using real-time microscopic acquisition methodology.

Methods: Isolation of porcine cardiomyocytes out of pig myocardial tissue was performed using two different methods (isolation with digestion media containing collagenase and a primary explant culture). The cardiomyocytes were cultivated and proliferated in coated culture flasks (Medium containing FBS and antibiotics, 5% CO2, 37°C) for 3–4 weeks before executing the ischemic experiments. To confirm the cardiomyocyte specificity and characteristics αSMA, cardiac Troponin T, Connexin 43 and Vimentin immunofluorescence stainings and flow cytometry was performed. Additionally live cell imaging was implemented for 12 h to examine the real-time cardiomyocyte cell behavior using a chamber heating system combined with a gas incubation system (ibidi) on an Olympus microscope. For inducing ischemia, cardiomyocytes were treated with Cobalt(II) chloride hexahydrate (CoCl2) in different concentrations (50, 100, 200, 400, 600, 800 µM) and incubated for 2 h followed by another 24 h real-time cell imaging.

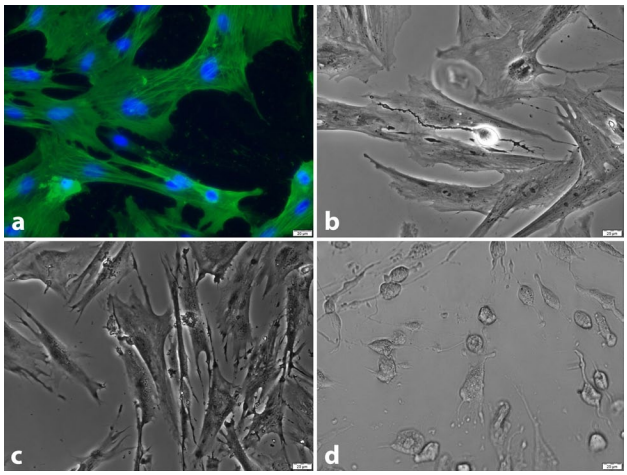


Fig. 1 A: Fluorescent staining of αSMA in cardiomyocytes (αSMA: green/FITC, nuclei: blue/DAPI), B: Phase-contrast image of cardiomyocytes under regular culture conditions (20x magnification), C: Phase-contrast image of cardiomyocytes immediately after 2 hours of incubation with CoCl2 (20x magnification), D: Phase-contrast image of the same cells 2 days after the CoCl2 treatment (20x magnification)

Results: The isolation of porcine cardiomyocytes was successful with both applied methods and no morphological differences between the cells from primary explant culture and the cells from isolation with digestion media could be observed. Typical cardiomyocyte size and morphology was confirmed via microscopy and flow cytometry methods. The cardiomyocytes showed a positive immunofluorescent staining of αSMA as well as cardiac Troponin T, Connexin 43 and Vimentin in different intensities. Real-time living cell imaging verified proliferation of the cardiomyocytes. Compared to untreated cells, differences in cell size and morphology were observed after treatment with CoCl2 in all concentrations whereas at certain concentrations cells stopped dividing (>400 µM) and eventually underwent apoptosis (>600 µM). Optimal ischemic conditions were achieved at a CoCl2 concentration of 400 µM per 5×10^4 cells.

Discussion: The successful establishment of an ischemic porcine cardiomyocyte cell culture model provides a wide area of application for in vitro investigations of ischemic circumstances or medical treatments against ischemia, while following the 3R rules. Refinement of this method, genomics, proteomics of the ischemic cells and secreted substances, including exosome analysis are planned.

Postersitzung XV: Chirurgie

XV-1

A comparison of balloonexpandable vs. selfexpandable valves in transapical transcatheter aortic valve implantation

S. Russegger, M. Mach, D. Santer, H. Pisarik, S. Folkmann, M. Harrer, J. Pollak, C. Adlbrecht, F. Veit, G. Delle Karth, M. Grabenwöger

I. Chirurgie, Abteilung für Herz- und Gefäßchirurgie, Krankenhaus Hietzing, Wien, Österreich

Zielsetzung: Die transapikale, kathetergestützte Aortenklappenimplantation (transcatheter aortic valve implantation, TAVI) hat sich in den letzten Jahren zu einer Standardtherapie in der Behandlung der schweren Aortenstenose bei Hochrisiko-Patienten entwickelt. Bei einer groben Einteilung der Klappenmodelle lassen

sich ballon- von selbst-expandierenden Klappensystemen unterscheiden. Bis jetzt liegen jedoch erst wenige Studien vor, die die unterschiedlichen Klappenmodelle miteinander vergleichen und mögliche Vorteile eines Modells aufzeigen.

Material und Methoden: Bei 156 Hochrisiko-Patienten mit schwerer Aortenstenose, die für eine transapikale TAVI in Frage kamen, wurde entweder eine selbst- (Symetis ACURATE TA™) oder eine ballon- (SAPIEN XT™ oder III™) expandierbare Prothese verwendet. Die Symetis ACURATE Klappe wurde bei 40 % ($n=27$) und die Edwards SAPIEN Klappen bei 60 % ($n=129$) der Patienten implantiert.

Ergebnisse: Das Durchschnittsalter der Patientengruppen betrug in der ACURATE-Gruppe 83,1 ± 5,4 und in der SAPIEN-Gruppe 79,8 ± 9,5 ($P<0{,}001$). Der Mean Society of Thoracic Surgeon Score betrug 7,7 ± 4,6 im Vergleich zu 8,1 ± 6.0 ($p=0{,}56$). Bei der Patientengruppe, die die selbst-expandierende Prothese implantiert bekam, kam es häufiger zu einer mehr als milden Aorten-Regurgitation (ACURATE: 5 % vs. SAPIEN: 3 %, $P=1{,}0$). Deshalb war bei diesen Patienten öfters eine Nachdilatation (40,7 vs. 14 %; $P<0{,}001$) nötig. Generell zeigen beide Klappen vergleichbar gute hämodynamische Eigenschaft und klinisches Ergebnisse. Bezogen auf device success, 30-Tage Mortalität, 1-Jahres-Überlebensrate, Notwendigkeit der Implantation eines permanenten Schrittmachers, Auftreten von kardiovaskulären Ereignissen und Blutungen konnte keine Überlegenheit eines Klappenmodells festgestellt werden.

Diskussion: Bisher haben Studien aufgezeigt, dass die ballon-expandierbare Prothese der selbst-expandierenden in einigen Punkten überlegen ist. Besonders relevant ist dabei das geringere Auftreten einer paravalvulären Klappeninsuffizienz nach Implantation eines ballon-expandierbaren Modells und daraus resultierend eine weniger häufig indizierte Nachdilation oder Implantation einer zweiten Klappe.

XV-2

Evaluation of the downstream aorta after frozen elephant trunk repair for aortic dissections in terms of diameter and false lumen status

D. Santer, G. Weiss, J.Dumfarth, H. Pisarik, M. Harrer, S. Folkmann, M. Mach, R. Moidl, M. Grabenwöger

LBC f. kardiovaskuläre Forschung, Bes. Einrichtung für biomedizinische Forschung Wien, Vienna, Austria
Department of Cardiovascular Surgery, Hospital Hietzing Wien, Vienna, Austria
Department of Cardiac Surgery, University Hospital Innsbruck, Innsbruck, Austria

Objectives: To analyse the clinical outcomes of surgical repair of DeBakey type I and III aortic dissection (AD) by using the frozen elephant trunk (FET) technique, and to evaluate the postoperative behaviour of the residual aorta.

Methods: In total, 27 consecutive patients underwent treatment of the thoracic aorta for AD with the FET technique in a tertiary-care hospital in Vienna/Austria between 2005 and 2012, and were enrolled in this case series study. All operations were performed under circulatory arrest and bilateral antegrade cerebral perfusion. During the follow-up, a clinical examination was performed as well as aortic diameters and false lumen (FL) patency evaluated by computed tomography (CT) imaging at following levels: pulmonary bifurcation, diaphragm and coeliac trunk.

Results: The mean age of the patient cohort was 56 ± 12 years; 21 patients were male. Twenty-two (82 %) and 5 (18 %) patients presented with DeBakey type I and type III AD, respectively. The hospital mortality rate was 7 % (2/28); 2 patients died due to non-aortic-related reasons during a follow-up period of 48 ± 26 months. Three (11 %) patients had a stroke, and 2 (7 %) a spinal cord injury. The follow-up CT scans revealed FL thrombosis in 96 % of the patients at the level of the pulmonary bifurcation ($P<0.001$). Distal to the stent graft, at the level of the diaphragm and coeliac trunk, FL patency was observed in 52 % ($P=0.1$) and 78 % ($P=0.6$) of the patients, respectively. The true lumen of all analysed aortic segments increased significantly while the mean aortic diameter remained stable.

Conclusions: Compared with conventional surgery for extensive ADs, the FET technique provides a high rate of FL thrombosis of the thoracic aorta.

XV-3

Is there a difference in outcome and survival after transfemoral vs. transapical transcatheter aortic valve implantation?

G. Hoti, M. Mach, H. Pisarik, S. Folkmann, M. Harrer, J. Pollak, C. Adlbrecht, F. Veit, G. Delle Karth, M. Grabenwöger

I. Chirurgie, Abteilung für Herz- und Gefäßchirurgie, Krankenhaus Hietzing Wien, Vienna, Austria

Objective: Severe aortic stenosis (AS) is the most common heart valve disease that affects the elderly population. This study aims to evaluate the postoperative complications and clinical outcomes that occur due to transfemoral aortic valve implantation (TF) and transapical aortic valve implantation (TA).

Method: In total, 325 high-risk patients with severe AS who underwent TAVI were evaluated. The high-risk is defined using the EuroSCORE and the STS. In order to assess the vessel status and determine which patients are suitable either for TF or TA, computertomography had been conducted in all patients. The TF access is preferred whenever a femoral access is feasible; however TA access applies to patients with pathological femoral arter-ies. Finally 167 patients (51.4 %) were chosen for the TF and 158 Patients (48.6 %) for the TA access. The focus was to observe the survival rate after a 30-day period, respectively after 6 and 12 months. The Kaplan-Meier-plot was used in order to estimate the survival rate.

Results: The analysis shows intraprocedural differences between both considered groups (TA vs. TF). For instance, the TA procedure requires a longer surgery, but less contrast medium and radiation exposure. However, complica-tions like cardiopulmonary bypass and cardiac depression occurred more often during the TA procedure com-pared to the TF procedure.

Furthermore, vascular complications tend to be more frequent with patients who underwent TF-TAVI. The follow-up at 30 days, 6 months and 12 months shows no significant difference between TA and TF patients. Moreover, comparing both groups, there were no differences in the causes of death, and no significant differ-ence in their frequency.

Conclusion: Both procedures have their specific access-related complications but there is no significant difference in surviv-al between the TA and TF access. In order to determine which procedure benefits the patient most, detailed and accurate preoperative screening has to be conducted in order to detect specific access-related risk factors.

XV-4

Lessons learned since TAVI became routine: TA/DA results

A. Vötsch, B. Zirngast, O. Luha, W. Marte, A. Schmidt, R. Maderthaner, O. Dapunt, H. Mächler

Division of Cardiac Surgery, Division of Anesthesiology for Cardiovascular Surgery and Intensive Care, Division of Cardiology, University Heart Center Graz, Graz, Austria
Universitätsklinik für Radiologie, Medizinische Universität Graz, Graz, Austria

Introduction: Increased patient age and multiple co-morbidities led to a change in the treatment of valvular aortic stenosis dur-

ing the last decade. TAVI has become clinical routine in most centers, requiring a heart team and preoperative planning to provide excellent outcomes.

Methods: Since 2011 cardiologists, cardiac surgeons and cardiac anesthetists form a permanent heart team at the University Heart Center Graz. Weekly interdisciplinary conferences as well as ad hoc meetings in urgent cases have been held since then deciding on more than 300 cases. Preoperative computer tomography based planning of all TA/DA TAVI cases was added in 2013 providing exact aortic root measurements, as well as optimal c-arm angulations in advance.

Results: At our center more than 1500 patients have been treated for aortic stenosis in the last five years of whom 78 % (n=1205) were treated by surgical AVR and 22 % (n=336) by TAVI. In 22 % (n=73) other than TF routes haven been used after interdisciplinary decision. Edwards Sapien XT, Edwards Sapien 3 and Symetis Acurate valves have been implanted through transapical access, Medtronic Corevalve, Edwards Sapien XT and Edwards Sapien 3 valves have been used in the direct aortic approach. Mean age at implantation of these TA and DA TAVI patients was 85 ± 5 years, 40 % of patients have been females. Device success according to VARC 2 was 94 %. Two cases of migration and embolization with the need of conversion to surgical AVR have been observed. One case of annular rupture was observed. No peri-procedural myocardial infarctions have been observed. Access site related complications occurred in 2.7 % (n=2). The need for new pacemaker implantation was 32 % (n=23). One patient suffered from perioperative stroke. 30 day mortality was 8.2 % (n=6).

Discussion: After establishing a permanent heart team all treatment options in aortic valve stenosis have been instituted as routine at our center. Non TF TAVI including preoperative CT based planning has become a routine procedure, either performed by transapical or direct aortic access by cardiac surgery trainees under guidance of senior staff members with excellent results.

XV-5

Sizing matters: the outcome of patients with patient-prosthesis mismatch after transcatheter aortic valve implantation

E. Polat, M. Mach, D. Santer, H. Pisarik, S. Folkmann, M. Harrer, J. Pollak, C. Adlbrecht, F. Veit, G. Delle Karth, M. Grabenwöger

I. Chirurgie, Abteilung für Herz- und Gefäßchirurgie, Krankenhaus Hietzing Wien, Vienna, Austria

Background: Transcatheter aortic valve implantation (TAVI) has become an important therapeutic option for high-risk patients with severe aortic valve stenosis. Patient-prosthesis mismatch (P-PM) is an important determinant of morbidity and mortality after open aortic valve replacement. The objective of our study was to evaluate P-PM incidence and its impact on survival in our center treated with TAVI.

Methods: We retrospectively analyzed transthoracal echocardiographic data of 52 consecutive patients (STS SCORE was 6.5 ± 4.3, euroSCORE II was 8.3 ± 4.1 female 56 %, age 80 ± 8 years) who underwent transapical TAVI with the Edwards Sapien (XT and III) or Symetis Accurate valves between April 2010 and December 2014. Effective orifice area was calculated using the continuity equation and indexed with body surface area (iEOA). P-PM was stratified as severe (iEOA < 0.65 cm^2/cm^2) and moderate (iEOA, 0.65–0.85 cm^2/cm^2). Midterm survival (up to 30 months) was analyzed by Kaplan-Meier curves and log-rank tests.

Results: There was no P-PM in 38 (73.1 %) patients; moderate P-PM was found in 9 (17.3 %) patients and severe P-PM in 4 (7.7 %). Thirty-day survival was 94 vs. 91 vs. 75 %. The 1 year survival was 78, 76, and 50 %. Additionally, mean survival time in patients with an ejection fraction less than 40 % was significantly shorter than in patients with an ejection fraction greater than 40 % (17 ± 8 vs. 28 ± 14 months; p=0.03). Our study revealed that patients with a larger BMI were more likely to develop a PPM (p=0.001), while the prosthesis type, the prosthesis size, the preoperative EOA and gender had no influence. The postoperative mean aortic gradient was significantly higher in patients with PPM (p=0.02). All patients showed a reduction in the left ventricular end-diastolic diameter, without significant differences between groups. There were no differences in postoperative NYHA class or quality of life between patients with or without PPM.

Conclusions: P-PM is found in patients undergoing transapical TAVI. Severe mismatch is accompanied by high early mortality, especially when combined with increased pressure gradients.

XV-6

The fate of patients with atrial fibrilation undergoing transfemoral vs. transapical transcatheter aortiv valve implantation

M. Stattmann, M. Mach, D. Santer, H. Pisarik, S. Folkmann, M. Harrer, J. Pollak, C. Adlbrecht, F. Veit, G. Delle Karth, M. Grabenwöger

I. Chirurgie, Abteilung für Herz- und Gefäßchirurgie, Krankenhaus Hietzing Wien, Vienna, Austria

Background: Atrial Fibrilation is one of the most common comorbidities among patients undergoing transcatheter aortic valve implantation (TAVI). The aim of this study was to investigate the importance of Atrial Fibrilliation as a risk factor for adverse clinical outcomes and mortality in patients selected for either transapical (TA) or transfemoral (TF) TAVI.

Methods: A total number of 325 (158 TA/167 TF) patients undergoing TAVI between April 2010 and December 2014 were included in this retrospective study, out of which 54 (TA) vs. 47 (TF) patients had a history of AF prior to surgery. The mean CHAD1DS2-VASC score amongst this group was 3.9 vs. 4.1, with a HAS-BLED bleeding score of 2.8 vs. 2.6; all of which were compared with the non-AF group. Out of the 101 patients with AF undergoing TAVI, 48 (89 %) were under long-term oral antikoagulation prior to TF-TAVI, vs. 39 (72 %) in the TA-group.

Both patients with AF and without AF had similar baseline characteristcs. Echocardiographic results were compared preoperatively as well as post-operatively. Furthermore, follow-up adverse events defined according to the VARC-2 criteria were evaluated for both groups.

Results: No difference in 30d mortality was found between groups; however, patients with baseline AF did have higher 1-year mortality (28.8 vs. 18 %, P=0.01). 5 (3.2 %) patients in the TA-group and 11 (6.6 %) in the TF group developed new, postprocedural AF during their hospital stay. Inhospital death was more frequent in patients with new, postprocedure AF, however, this difference did not reach statistical significance (p=0.22).

Risk of stroke has been identified as a risk factor in TAVI particularly for patients with AF; during a median follow-up of 30 months, there were 7 cases of stroke in the TF-group (CI, 0.86–2.19; p=0.19) and 1 case (CI, 0.79–3.01; P=0.13) in the TA-group.

No difference in the risk of other adverse events had been observed between groups.

Conclusion: Patients with AF undergoing TAVI had a higher rate of all-cause as well as cardiovascular mortality at 1 year. The type of AF does not have an influence on the outcome; however, it seems as if there is a difference in development of postprocedural AF in previously unaffected patients depending on the form of surgical access. As this study is limited by it's small study population and retrospective nature, bigger randomized trials have to be conducted to very these findings.

XV-7

The impact of chronic obstructive pulmonary disease on outcome in patients undergoing transfemoral vs. transapical transcatheter aortic valve implantation

M. Koschutnik, M. Mach, D. Santer, H. Pisarik, S. Folkmann, M. Harrer, J. Pollak, C. Adlbrecht, F. Veit, G. Delle Karth, M. Grabenwöger

I. Chirurgie, Abteilung für Herz- und Gefäßchirurgie, Krankenhaus Hietzing Wien, Vienna, Austria

Objectives: Notably, a large number of patients undergoing transcatheter aortic valve implantation (TAVI) has been diagnosed with concomitant chronic obstructive pulmonary disease (COPD) as this high risk population is generally regarded as inoperable in conventional cardiac surgery considering the clinical outcome.

The purpose of this study was to evaluate the impact of COPD on clinical outcomes in patients referred for transfemoral (TF) as well as transapical (TA) aortic valve implantation and furthermore to discuss possible advantages considering the selection of access evaluation.

Background: Limited to no data are available on long-term outcomes in COPD patients undergoing TAVI distinguishing transfemoral from transapical approach.

Methods: In total, a population of 325 patients in which TAVI procedure has successfully been performed was included in the present study: 89 (27.4 %) had concomitant COPD, whereas 236 (72.6 %) did not. Severity of airflow limitation in COPD (post-bronchodilator FEV1) was defined according to state of the art GOLD staging system: mild (FEV1 ≥ 80 % predicted), moderate (50 % ≤ FEV1 < 80 % predicted), severe (30 % ≤ FEV1 < 50 % predicted) and very severe (FEV1 < 30 % predicted) in patients with FEV1/FVC < 0.70. Furthermore, transfemoral (TF, 51.4 %) or transapical (TA, 48.6 %) approach were selected primarily depending on degree of calcification as well as kinking of iliofemoral arteries. New York Heart Association (NYHA) functional status was assessed at baseline and at 12 months follow-up. Outcome was measured and classified according to VARC-criteria. Survival was estimated by Kaplan-Meier-Plot.

Results: As analyses suggested, patients diagnosed with moderate, severe as well as very severe COPD defined by GOLD classification showed a higher mortality rate after TAVI at 12 months follow-up (25.3 %) in contrast to patients associated with mild or no COPD (18.6 %). Both populations generally feature improvement in NYHA functional class after performing TAVI procedure (81.2 %), although COPD patients experienced less progress (69.3 %). Comparing transfemoral to transapical approach in patients undergoing TAVI, analyses have shown that no significant difference on the impact of COPD on clinical outcomes can be found.

Conclusions: Preoperative COPD as common coexisting illness in patients referred for TAVI procedure is associated with a lower long-term survival rate and therefore characterizes a high-risk population. In addition, the selection of access (transfemoral vs. transapical transcatheter aortic valve implantation) does not imply a significant difference in VARC-defined clinical outcomes in COPD patients. Evaluating these results, transfemoral transcatheter aortic valve implantation cannot be considered as superior technique in treating COPD patients with aortic stenosis compared to transapical approach.

XV-8

High sensitivity troponin T plasma levels in aortic stenosis

F. Barbieri, E.-S. Thiel, P. Steidl, S. Dobner, G. Feuchtner, B. Pfeifer, J. Holfeld, M. Grimm, W.-M. Franz, S. Müller, W. Dichtl

Kardiologie, Reha-Klinik Montafon, Schruns, Austria
Universitätsklinik für Innere Medizin III, Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck, Innsbruck, Austria
UMIT, Hall in Tirol, Austria

Aim of the study: To assess the clinical implications of minimally elevated hsTnT (high sensitivity troponin T) plasma levels in patients with aortic stenosis (AS), both in the asymptomatic phase and when admitted for valve operation.

Methods: Long-term follow up data in 48 asymptomatic patients were prospectively collected in terms of survival and time to aortic valve replacement (AVR) since 2003. The impact of 8 risk factors—hsTnT, aortic valve area per body surface area (AVA/BSA), age, aortic valve and coronary calcification assessed by multi-slice computed tomography (MSCT), NTproBNP, CRP, LDL/HDL cholesterol ratio—were calculated in multivariate Cox regression analyses. 15 patients (=31 %) died and/or 31 patients (=65 %) underwent AVR during a mean follow-up of 6.7 years. The second patient cohort consisted of patients (n=695) with severe symptomatic aortic stenosis admitted for planned valve operation since 2010, when our institution started to routinely analyse hsTnT plasma levels.

Results: In asymptomatic patients, age (p=0.009) and AVA/BSA (p=0.046) were independent predictors of mortality. AVA/BSA was the expected predictor for need of AVR (p=0.001), in addition to aortic valve calcification (p=0.001) and increased CRP plasma levels (p=0.014). In contrast, hsTnT plasma levels were low at that stage (median 8.09 pg/ml) and had no influence on mortality and did not predict progression to a stage necessitating AVR. Preoperatively, median plasma levels of hsTnT strongly correlated with decreased LVEF: >50 %: 13.6 pg/ml; 35–50 %: 21.95 pg/ml; <35 %: 36.4 pg/ml (p=0.001). As compared to patients with an ECG without signs of LV hypertrophy (median 14.2 pg/ml), hsTnT plasma levels were significantly higher in patients with ECG strain (median 20.7 pg/ml) but not in patients with a positive Sokolow index without strain (median 16.65 pg/ml). Whereas no correlation between AVA/BSA and hsTnT could be detected, a subgroup analysis of patients who had undergone MSCT preoperatively showed a strong correlation between the amount of aortic valve calcification and hsTnT (p=0.001) levels. Patients with elevated hsTnT plasma levels had a three-fold higher need of postoperative permanent pacing (p=0.03).

Conclusions: Increased hsTnT plasma levels indicate myocardial dysfunction in aortic stenosis. Similar to heavy valve calcification, elevation of this routinely used laboratory parameter (above yet to be determined cut-off levels) may show the need of valve intervention to prevent further damage to the left ventricle.

Postersitzung XVI: Diverse

XVI-1

Non-occlusive mesenteric ischemia (NOMI) after out of hospital cardiac arrest: incidence and outcome of an underappreciated phenomenon

R. Wurm, A. Cho, H. Arfsten, R. van Tulder, C. Wallmüller, F. Sterz, K. Tendl, C. Adlbrecht, G. Heinz

Univ. Klinik für Innere Medizin II, Klinische Abteilung für Kardiologie, Univ. Klink für Notfallmedizin, Klinisches Institut für Pathologie, Medizinische Universität Wien, Vienna, Austria

Background: Non-occlusive mesenteric ischemia (NOMI) is characterised by hypoperfusion of the intestines without evidence of mechanical obstruction, potentially leading to extensive ischemia and necrosis. Fatality rates are ranging from 50 to 80 %. Low cardiac output appears to be a major contributing factor for this pathology.

Cardiopulmonary resuscitation (CPR) aims at restoring blood flow after cardiac arrest, but cardiac output is still limited. After successful CPR, patients are often ventilated and sedated, which impedes diagnosis of NOMI and potentially life-saving treatment.

This is the first systematic report on the incidence of NOMI in out of hospital cardiac arrest survivors.

Material and methods: A prospectively maintained database of out of hospital cardiac arrest survivors, that had successful restoration of spontaneous circulation (ROSC) and were treated at a tertiary care centre, was retrospectively screened for clinical, radiological or pathological evidence of NOMI.

Results: 2469 patients who were successfully resuscitated after out of hospital cardiac arrest between 1991 and 2014 were included into the analysis. Thirteen patients (0.5 %) suffered from NOMI and 7 of those died (54 %). NOMI was diagnosed or suspected by imaging or colonoscopy in 9 cases (70 %) and confirmed by emergency surgery in 1 case (8 %). In 3 cases (23 %) it was an incidental autopsy finding. Patients suffering from NOMI tended to have a longer duration of time until ROSC (27 vs. 20 min, $p=0.108$), had significantly higher lactate (15 vs. 8 mmol/l, $p=0.010$) and base excess levels at admission (−18 vs. −10, $p=0.002$) (Table 1).

Discussion: NOMI is a rare but life-threatening complication following successful CPR. Autopsies are usually performed when the cause of death is unclear, which is rare after CPR. Therefore, there might be a high number of undetected cases of NOMI. Lactate and base excess at admission could help to identify patients at risk for developing NOMI who might benefit from increased clinical watchfulness.

Table 1 Patient characteristics

	Cohort	NOMI	*p*-value
Number of patients	2456	13	
Male – *n* (%)	1732 (70)	10 (77)	n.s.
Medical History – *n* (%)			
Ischemic heart disease	585 (24)	5 (39)	n.s.
Previous AMI	357 (15)	3 (23)	n.s.
Diabetes mellitus	387 (16)	0 (0)	n.s.
Arterial hypertension	775 (32)	5 (39)	n.s.
Chronic heart failure	300 (12)	1 (7)	n.s.
Location of cardiac arrest – *n* (%)			n.s.
Home	1085 (44)	5 (44)	
Public space	940 (39)	1 (8)	
During transport	224 (9)	3 (23)	
Doctor's office	55 (2)	1 (8)	
Other/unknown	200 (6)	2 (15)	
Time from cardiac arrest to – median in minutes, (IQR)			
Begin of CPR	1 (0–7)	0.5 (0–6)	n.s.
ROSC	20 (10–30)	27 (13–66)	n.s.
First monitored rhythm – *n* (%)			n.s.
Ventricular fibrillation	1343 (55)	2 (17)	
Asystole	462 (19)	4 (36)	
PEA	498 (20)	5 (42)	
Unknown	123 (5)	2 (20)	
Clinical measurements at admission – median (IQR)			
pH	7 (7–7)	7 (7–7)	n.s.
Lactate (mmol/l)	8 (5–12)	15 (10.5–18.3)	0.010
Base excess	−10 (−15–−6)	−18 (−23–−14)	0.002

AMI acute myocardial infarction, *CPR* cardiopulmonary resuscitation, *ROSC* return of spontaneous circulation, *PEA* pulseless electric activity

XVI-2

Predictors of prognosis in patients surviving out-of-hospital cardiac arrest

A. Lecher, F. Fruhwald, K. Ablasser

Innere Medizin, Abteilung Kardiologie, Medizinische Universität Graz, Graz, Austria

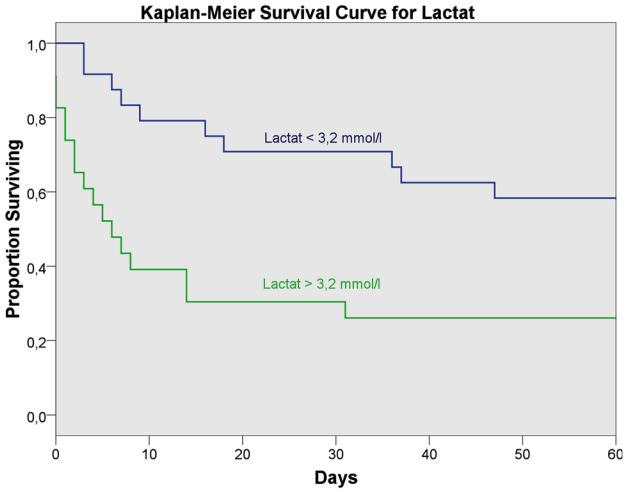
Introduction: Despite evolving therapies and interventional possibilities, out-of-hospital cardiac arrest is still associated with very high mortality even after successful resuscitation with return of spontaneous circulation (ROSC). Prediction of prognosis is not easy in these patients. Therefore, we were interested to test the ability of biomarkers to predict 60-day-mortality in patients with initially successful out-of-hospital cardiac arrest and ROSC.

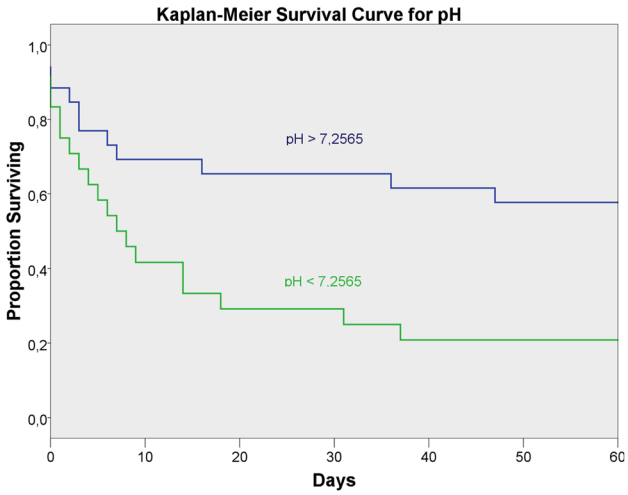
Methods: We retrospectively analysed all consecutive post-cardiac arrest (CA) patients hospitalised with ROSC between March 2013 and July 2014 at the cardiac care unit (CCU) of the Medical University Hospital Graz (Austria).

Results: Overall, 50 patients (40 male, 10 female; mean age 62.6 ± 14.5 years) were included into this analysis.

According to information gained by the emergency response team the primary rhythm was shockable in 29 patients (58 %) and non-shockable in 20 patients (40 %, including asystole and pulseless electrical activity—PEA).

The mean pH-value at CCU arrival was 7.23 ± 0.16 (min 6.73, max 7.52). Mean lactate level upon arrival was 5.88 mmol/l ± 5.79 (min 1.0, max 24), mean heart rate at arrival was 75.5 bpm ± 19.8 (min 43, max 121).





Overall, 60-day mortality was 60 % with a CCU mortality of 52 %.

Duration of treatment at CCU averaged 10.1 ± 8.9 days (min 1, max 37).

Patients with initially shockable rhythms (VF) had significantly better outcome compared to those showing non-shockable rhythms (45 vs. 75 % mortality, $p = 0.044$). In patients with VF those with a heart rate below the median of 70 bpm had a significantly better outcome than those with a HR above the median (33 vs. 64 % mortality, $p = 0.04$).

Both pH-value and lactate were predictive of mortality. Patients with a pH above the median of 7.257 had a 60-day survival of 65 % (vs. 22 % for those below the median, $p = 0.006$). Those with a lactate below median of 3.2 mmol/l had a 60-day survival of 62 % (vs. 25 % for those above the median, $p = 0.002$).

Both the initial (68.2 vs. 41.3 ng/ml, $p = 0.05$) and the maximal (123.8 vs. 49 ng/ml, $p = 0.001$) neuron-specific enolase (NSE) were predictive of survival. However, S-100 protein did not correlate with mortality.

Conclusion: The mortality of individuals who regain ROSC and arrive at the CCU after out-of-hospital CA is very high. Persons with shockable rhythm (VF) show a better outcome than patients with asystole or PEA. A high lactate level, low pH-value and (for patients with VF) high initial HR were predictors of high mortality as well as a high initial and maximum NSE level.

XVI-3

Soluble ST2 as a marker for atherosclerotic plaque vulnerability in patients with carotid stenosis

S. Stojkovic, W.-H. Eilenberg, C. Neumayer, I. Huk, K. Huber, J. Wojta, S. Demyanets

Universitätsklinik für Innere Medizin II, Kardiologie, Universitätsklinik für Chirurgie, Medizinische Universität Wien, Vienna, Austria

Background: ST2 is a member of the Toll-like/interleukin (IL)-1 receptor family. Increased levels of soluble ST2 (sST2) are recognized as a marker of poor prognosis in patients with acute myocardial infarction and heart failure.

Objective: The aim of this study was to investigate the association of sST2 plasma levels with occurrence of symptoms and plaque morphology in patients with carotid stenosis undergoing endarterectomy.

Methods: We included 136 consecutive patients undergoing carotid endarterectomy at the Medical University of Vienna. Plaque morphology was assessed by carotid ultrasound, and the patients were divided into 3 groups: having vulnerable plaque, calcified plaque or mixed plaque morphology. Furthermore, plaques were examined histologically and classified according to AHA classification Blood samples were drawn at the day of surgery prior to carotid endarterectomy. sST2 plasma levels were measured by specific ELISA.

Results: Out of 136 patients, 53 were symptomatic and 83 asymptomatic. Fifty-one patients had vulnerable atherosclerotic plaque, 59 patients had calcified plaque and 26 patients had mixed atherosclerotic plaque. There were no differences between the groups regarding age, sex, smoking, hypertension, and previous myocardial infarction. sST2 levels did not differ significantly between symptomatic and asymptomatic patients (140 ± 15 vs. 124 ± 9 pg/ml, $p = 0.327$). However, sST2 was significantly higher in patients with vulnerable atherosclerotic plaques as compared to patients with calcified plaques (164 ± 14 vs. 106 ± 9 pg/ml, $p < 0.001$). Patients with mixed atherosclerotic plaques had the tendency towards higher sST2 plasma levels (154 ± 26 pg/ml) than patients with calcified plaques ($p = 0.090$).

Conclusion: We propose sST2 as a potential marker for the vulnerability of carotid atherosclerotic plaque.

XVI-4

Identification of proto-oncogenes and genes responsible for myocardial fibrosis after anticancer treatment under experimental conditions

A. Spannbauer, K. Zlabinger, D. Macejovska, G. Maurer, J. Bergler-Klein, M. Gyöngyösi

Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: We have previously shown that liposomal encapsulation of the doxorubicin-citrat complex (Myocet® MYO) results in a less cardiotoxic effect with increased left and right ventricular ejection fraction, and less myocardial fibrosis as compared with doxorubicin (DOX). The present gene expression profiling combined with predicted protein-protein interaction analysis aimed to search genes and transcriptoms responsible for myocardial fibrosis and development of heart failure induced by anticancer treatment.

Methods: Domestic pigs were treated with either DOX ($n = 6$) or MYO ($n = 9$) in 3 cycles of cytostatic treatment of human dose. Control animals received physiologic saline infusions in 3 cycles (CO, $n = 6$). Cardiac magnetic resonance imaging (cMRI) with gadolinium late enhancement (LE) were performed at baseline and after the last dose application. The left (LV) and right (RV) ventricular ejection fraction (EF) and myocardial fibrosis was assessed by LE-cMRI images. mRNAs of myocardial samples from the left and right ventricle, and left atrium were isolated. The gene expression profile was analyzed by next generation sequencing (NGS). Predicted protein-protein interaction were constructed from the significantly over-or down-regulated genes and was displayed using the String Database.

Results: Decreased LV and RV EF was found in both DOX and MYO groups, but the pigs in MYO group showed significantly ($p < 0.05$) better LV EF (56.4 ± 5.6 vs. 41.9 ± 13.5 %) and RV EF (42.1 ± 2.8 vs. 28.9 ± 8.9 %) as compared with DOX. 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 %). LV myocardial samples showed significantly activated Ras- and inhibited p53-signaling pathways in the MYO group, which pathways play a role in cell growth regulation, proliferation and apoptosis. Functional protein association network revealed overregulation of EMILIN and SERPHIN genes both in LV and RV samples of both MYO and DOX groups, which genes are involved in biosynthetic pathway of collagen. Besides activations of tumor-suppressor genes, both DOX and MYO treatment led to upregulation of several oncogenes and proto-oncogenes, such as JUNB or BCL3 in all tissue samples, which might explain the development of secondary malignancies in patients treated with cytostatics.

Conclusions: The liposomal-encapsulated doxorubicin-citrat (MYO) proved to be less cardiotoxic as compared with DOX, resulting in better LV and RV systolic function. However, both cytostatic treatments resulted in overexpression of tissue collagen-associated genes and proto-oncogenes. Therapeutic modalities aiming gene silencing of these targeted genes during anticancer treatment might be helpful to prevent myocardial fibrosis or development of secondary malignancies.

XVI-5

Mild hypothermia (33 °C) increases the inducibility of atrial fibrillation in healthy pigs

M. Manninger, D. Zweiker, A. Alogna, B. Zirngast, H. Mächler, S. Huber, A. Lueger, B. M. Pieske, H. Brussee, H. Post, D. Scherr

Universitätsklinik für Innere Medizin, Abteilung für Kardiologie, Abteilung für Herzchirurgie, Medizinische Universität Graz, Graz, Austria

Campus Virchow, Abteilung für Kardiologie, Charite Universitätsmedizin Berlin, Berlin, Germany

Introduction: Mild hypothermia (MH, 32–34 °C) is an established therapy to improve neurological outcome and survival after cardiac arrest. However, MH also prolongs the cardiomyocyte action potential. We therefore tested the hypothesis that MH increases the inducibility of atrial fibrillation (AF).

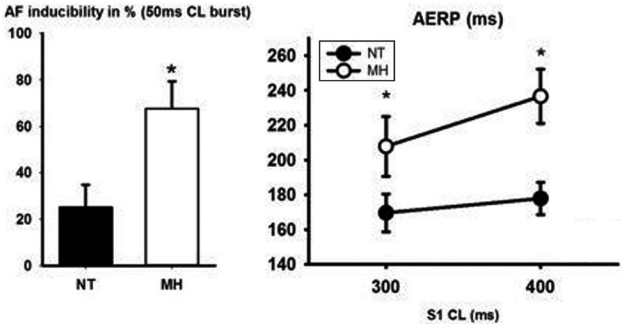
Methods: Eight healthy, anesthetized pigs (67 ± 7 kg) were instrumented with a quadripolar stimulation catheter in the high right atrium and a decapolar catheter in the coronary sinus. Measurements were performed at normothermia (NT, 38.0 °C) and at MH (33.0 °C, intravascular cooling device). At each temperature, the effective atrial refractory period (AERP) was measured with a S1S2 stimulation protocol (1 ms pulse at twice diastolic threshold at cycle lengths 400 and 300 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: During MH, AERP was significantly longer while the inducibility of AF (at a burst cycle length of 50 ms) was significantly higher compared to NT. Mean AF duration did not differ between groups (MH: 97 ± 212 s; NT: 16 ± 5 s; n.s.). Spontaneous arterial potassium levels decreased with falling temperatures (MH: 3.5 ± 0.1 mmol/L; NT: 4.0 ± 0.2 mmol/L; < 0.001).

Surface ECGs during MH showed reduced spontaneous heart rate (64 ± 9 vs. 89 ± 14 bpm, $p < 0.05$), increased PQ intervals (159 ± 24 vs. 131 ± 11 ms, $p < 0.01$), increased stim-Q intervals ($p < 0.001$ at heart rates 100/120/140 bpm), increased QRS duration ($p < 0.01$ at heart rates 100/120/140 bpm), increased QT interval ($p < 0.01$ at heart rates 100/120/140 bpm) but no change of TpTe (measure for dispersion of T-wave, n.s. at heart rates 100/120/140 bpm).

Conclusion: Our data imply that mild hypothermia represents an arrhythmic substrate rendering the atria more susceptible to AF although conduction times as well as refractory periods are increased.

Further investigations on potential electrophysiologic limits of therapeutic cooling in patients are required.



XVI-6

Ein neues Design der Bleiacrylglasscheibe verringert die Strahlenexposition des Personals bei Herzkatheteruntersuchungen und koronaren Interventionen

H. Eder, M. C. Seidenbusch, M. Treitl, P. Gilligan

Landesamt für Arbeitsmedizin, Strahlenschutz, München, Deutschland
Institut für Klinische Radiologie, Ludwig Maximilians Universität München, Deutschland
Mater Private Hospital Dublin, Dublin, Irland

Zielsetzung: Der Strahlenschutz des medizinischen Personals bei Herzkatheteruntersuchungen und koronaren Interventionen wird in der Regel durch die Anwendung einer Bleiacrylglas-Scheibe kombiniert mit einem am Tisch montierten Unterkörperschutz sicher gestellt. Ortsdosismessungen zeigten jedoch, dass diese Anordnung wegen Unterstrahlung der Scheibe durch Compton-Streustrahlung erheblich verbesserungsbedürftig ist.

Material und Methoden: 7 Szenarien wurden hinsichtlich der Exposition des Personals unter Verwendung eines anthropomorphen Alderson Rando Phantomes untersucht (Abb. 1): a) Vergrößerung der Bleiacrylglas-Scheibe b) Ergänzung der Bleiacrylglas-Scheibe durch einen flexiblen Bleilamellenvorhang auf der Unterseite; c) Verwendung abschirmender Patientenauflagen. Zur Visualisierung der Ergebnisse wurde eine Monte-Carlo Simulation durchgeführt.

Ergebnisse: Die Anwendung eines zusätzlichen, auf der Körperoberfläche des Patienten aufliegenden, flexiblen Bleilamellenvorhanges vermindert die Ortsdosisleistung am Untersucherstandort – verglichen mit der Schutzscheibe ohne Lamellenvorhang – um bis zu 87 % Die kombinierte Verwendung von Bleilamellenvorhang und Patientenauflage ermöglicht eine Reduktion der Ortsdosis im

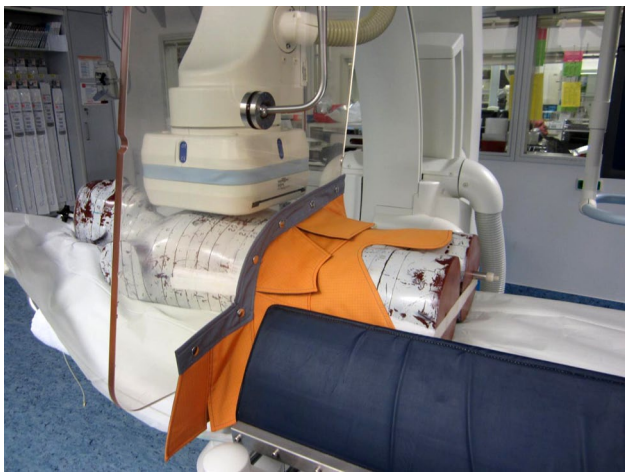


Abb. 1 Messanordnung mit dem Alderson Rando Phantom für die Messungen der Ortsdosis am Standort des Untersuchers und der Assistenz. Die Scheibe wurde optional mit einem abschirmenden Vorhang versehen. Zusätzlich bzw. optional wurde abschirmende Patientenauflagen verwendet. Der Tisch-Seitenschutz mit Aufsatz war während der gesamten Messungen in der in Abb. 1 gezeigten Position.

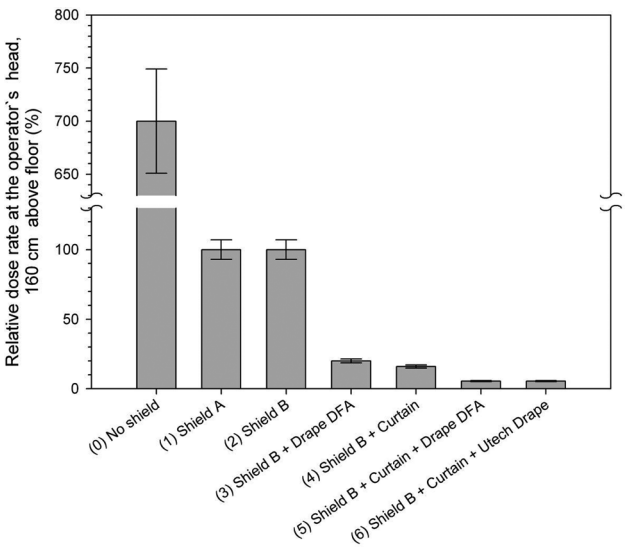


Abb. 2 Ortsdosisleistungen die in einer Höhe von 160 cm über Boden (Brusthöhe) bei 7 Szenarien am Standort des Untersuchers gemessen wurden.

Bereich Oberkörper/Schädel um bis zu 90 % (Abb. 2). Die Visualisierung mittels Monte Carlo Simulation zeigt Ergebnisse in der gleichen Größenordnung. Analoge Ergebnisse ließen sich für die Ortsdosis am Standort des Assistenzpersonals erzielen. Darüber hinaus führt die vergrößerte Scheibe zu einem besseren Schutz der Kopfregion von großen Untersuchern.

Diskussion: Die Schutzwirkung von deckenmontierten Bleiacrylglas-Schutzscheiben wurde bisher wegen des Unterstrahlungseffektes durch Compton-Streustrahlung stark überschätzt.

Die zusätzliche Verwendung eines flexiblen Bleilamellenvorhangs verbessert den Strahlenschutz des Untersuchers und insbesondere auch jener Körperbereiche, die von der Röntgenschutzkleidung nicht oder nur unzureichend bedeckt sind, wie z. B. Schädel und Augenlinsen. Ähnliche Wirkungen zeigt eine abschirmende Patientendecke. Dies ist besonders wichtig vor dem Hintergrund der demnächst zu erwartenden Verschärfung der Grenzwerte für die Augenlinse (ICRP-Empfehlung, Euratom Directive). Die Schutzwirkung unter realen klinischen Bedingungen wird derzeit in einer weiteren Studie untersucht, erste Ergebnisse liegen vor und deuten auf eine Expositionsreduzierung beim medizinischen Personal von 50 bis 70 % hin.

XVI-7

Biomarker zur Früherkennung kardiovaskulärer Erkrankungen; K-Projekt BioPersMed

C. Colantonio, M. Url-Michitsch, N. Verheyen, K. Schützenhofer, K. Kresoja, M. Kraigher-Krainer, B. Pieske, H. Brussee, A. Schmidt

Klinische Abteilung Kardiologie, Medizinische Universität Graz, Graz, Österreich

Einleitung: Die Risikostratifikation asymptomatischer Patienten mit erhöhtem kardiovaskulären Risiko erfolgt heute auf dem Boden klassischer Risikofaktoren (wie z. B. arterielle Hypertonie, Hyperlipidämie, etc.) mit Hilfe von Score-Systemen (z. B. PROCAM-Score, EURO-Score). Allerdings sind die Zuverlässigkeit und der klinische Nutzen dieser Systeme unbefriedigend. Durch neue laborchemische und biophysikalische Biomarker könnte die Früherkennung und Risikostratifikation verbessert werden. Allerdings liegen derzeit keine Modelle vor, in denen die Kombination neuartiger Biomarker mit etablierten Risikomarkern untersucht wurde. Im Rahmen der 2010 angelaufenen „Graz Heart Study" (GHS), die Teil des Comet-Projektes (K-Projekt) „BioPersMed" ist, ist die wichtigste Zielvorgabe, den vorhersagenden Wert bekannter und neuer Biomarker, Laborparameter, bildgebender Methoden und funktioneller Tests, für die Früherkennung kardiovaskulärer Erkrankungen zu evaluieren.

Patienten und Methodik: In die GHS werden seit Dezember 2010 prospektiv Probanden mit kardiovaskulären Risikofaktoren, aber noch keinem arteriosklerotischen Ereignis, eingeschlossen und longitudinal nachbeobachtet. Die Screening-Untersuchung wird nach 2, 4 und 6 Jahren wiederholt, dazwischen finden zusätzlich 3 Telefon-Visiten statt. Es ist geplant, diese Kohorte noch über einen weitaus längeren Zeitraum zu beobachten und zu untersuchen. In Kooperation mit der BioBank der Medizinischen Universität Graz werden Blut- und Urinproben, Speichel, sowie DNA für genetische Analysen asserviert. In einer detaillierten kardiovaskulären Phänotypisierung werden neben Routineparametern die systolische und diastolische Ventrikelfunktion, kardiovaskuläres Remodeling sowie state-of-the-art echokardiographische Parameter (strain, strain-rate) erhoben. Die vaskuläre Funktion wird umfassend u.a. durch Endothelfunktion, Pulswellenanalyse und Analyse der Intima/Media-Dicke an den Carotiden bestimmt. Die körperliche Leistungsfähigkeit wird nicht-invasiv mittels Spiroergometrie, Lungenfunktion und 6 min Gehtest erhoben. Zusätzliche Untersuchungen in Subgruppen beziehen zerebrale arteriosklerotische Ereignisse (Schädel-MRT), Augenhintergrunduntersuchung (Fundus Kamera), ambulante 24 h-Blutdruckmessung und eine umfassende Analyse von soziodemographischen Parametern und der Lebensqualität ein.

Ergebnisse: Von Dezember 2010 bis September 2014 konnten insgesamt 844 Probanden in die GHS rekrutiert werden.

Die primäre Auswertung des Basisdatensatzes (deskriptive Auswertung aller Screening-Untersuchungen) zeigt, dass die Pulswellengeschwindigkeit (PWV) an den großen Gefäßen bereits in erheblichem Maße pathologisch verändert ist. Bezogen auf kardiales Remodeling und Herzfunktion weisen ca. 30 % eine linksventrikuläre Hypertrophie und ca. 50 % eine diastolische Ventrikelfunktionsstörung auf, davon ca. 5 % klinisch signifikant. Es besteht außerdem eine signifikante positive Korrelation zwischen PWV, kardiovaskulären Risikofaktoren, Intima/Media Dicke der Carotiden, Linksventrikulärer Masse und diastolischer Ventrikelfunktion. Dies deutet auf einen direkten Zusammenhang zwischen der „Steifigkeit des Herzens" und der „Steifigkeit der Gefäße" hin.

Diskussion: Insgesamt zeigt sich, dass dieses Risikokollektiv bereits in erhöhtem Maße eine diastolische Dysfunktion, linksventrikuläre Hypertrophie und beschleunigte PWV's aufweist, was für Remodeling-Zeichen am Herzen und an den Gefäßen spricht.

XVI-8

Diabetes awareness among coronary artery disease patients differs significantly between men and women

C. H. Saely, D. Zanolin, A. Vonbank, G. Naerr, H. Drexel

VIVIT-Institute, Academic Teaching Hospital Feldkirch, Feldkirch, Austria
Private University of the Principality of Liechtenstein, Triesen, Austria

We aimed at investigating diabetes awareness among men and women with established coronary artery disease (CAD).

We enrolled a total of 814 consecutive patients with angiographically proven CAD, 587 men and 227 women. Fasting glucose and HbA1c were measured and oral glucose tests were performed in all patients who did not report a history of diabetes.

Overall, 74 men and 28 women (12.6 and 12.3 %, respectively) reported a history of diabetes. Based on glucose criteria only (fasting plasma glucose ≥ 126 mg/dl or glucose ≥ 200 mg/dl 2 h after a 75 g oral glucose challenge), diabetes was newly diagnosed in 33 men and 3 women (5.6 and 1.3 %, respectively); when also HbA1c values ≥ 6.5 % were considered for diabetes diagnosis, diabetes was newly diagnosed in 67 men and 13 women (11.4 and 5.7 %, respectively). Thus, among those with diabetes, the proportion of newly diagnosed diabetes was higher in men than in women both when only glucose criteria and also when additionally the HbA1c criterion was applied for the diagnosis of diabetes (30.8 vs. 9.7 %; $p = 0.007$ and 47.5 vs. 31.7 %; $p = 0.014$; respectively).

We conclude that among CAD patients with diabetes significantly more women than men are aware of their condition.

Postersitzung XVII: Herzinsuffizienz 2

XVII-1

Age-dependency of cardiac and neuromuscular findings in adults with left ventricular hypertrabeculation/noncompaction

B. Gerecke, G. Blazek, M. Gessner, K. Bichler, C. Wegner, J. Finsterer

2. Med. Abteilung, Krankenanstalt Rudolfstiftung, Vienna, Austria
Klinikum Wolfsburg, Wolfsbug, Germany

Hanusch Krankenhaus, Vienna, Austria
Landesklinikum Mödling, Mödling, Austria

Left ventricular hypertrabeculation/noncompaction (LVHT) is diagnosed in all ages and is frequently associated with neuromuscular disorders (NMDs).

Aim of the study was to compare LVHT-patients depending on the age at diagnosis. Included were 232 LVHT-patients (72 females, mean age 52 ± 17) diagnosed from 1995 to 2014 in 1 echocardiographic laboratory. In 2014, their survival was assessed. Neurologically investigated were 76 % of the patients revealing specific NMDs in 18 %, unspecific NMD in 60 % and normal findings in 22 %. Fourty-five patients (19 %) received electronic devices: Implantable cardioverter defibrillators (ICDs) 26 patients, combined with a cardiac resynchronization system (CRT) ($n = 14$) or an antibradycardic pacemaker ($n = 1$); antibradycardic pacemaker ($n = 8$), CRT ($n = 4$), implantable loop recorders ($n = 4$), life vest ($n = 2$), and a left ventricular assist device as bridging to transplantation ($n = 1$). During 72 follow-up-months, the mortality was 4.9 %/year. In younger age groups more patients were referred because of syncope or palpitations whereas in older age groups more patients were referred for heart failure. Classical cardiovascular risk factors like hypertension and diabetes, and coronary artery stenosis were rare in the young age groups whereas they were more prevalent in higher age groups. Differences between age groups were found regarding cardiac symptoms, NMDs, ECG-findings, rate of device implantation and mortality but not in location and extension of LVHT. None of the neurologically investigated patients ≥ 70 years was neurologically normal. Prevalence of heart failure, ECG-abnormalities and mortality were highest in the oldest age group.

In conclusion, LVHT has to be considered as an echocardiographic diagnosis in all age groups. The morphologic pattern of LVHT is similar whereas clinical manifestations and prognosis are variable among age groups.

XVII-2

Aortic pulse pressure is inversely associated with the risk of hospitalisation for heart failure in patients with cardiomyopathy

S. Charwat-Resl, L. Liebenberger, J. Kellermair, S. Sartori, M. Suppan, S. Parragh, B. Hametner, S. Wassertheurer, B. Eber, T. Weber

Innere Medizin II mit Kardiologie und Intensivmedizin, Klinikum Wels-Grieskirchen, Wels, Austria
Austrian Institute of Technology, Vienna, Austria

Background: Pulse pressure (PP) is determined by the interplay between the elastic properties of the aorta and the left ventricle. In populations with normal systolic function, PP is directly related to cardiovascular outcomes. We have previously shown an inverse relationship between indices of left ventricular function and PP in patients with cardiomyopathy.

Methods: We measured aortic PP invasively in patients with severly impaired systolic function undergoing coronary angiography. In addition, aortic PP was estimated on the next day, using radial tonometry, calibrated with brachial blood pressure, and a transfer function (SphygmoCor system). Patients were followed, using hospital records, telephone interviews with general practitioners, and a national mortality registry (Statistics Austria).

Results: We included 82 patients (8 women, 19 diabetics, 35 had coronary artery disease, mean EF was 28 %, mean NT-proBNP 3554 pg/ml). After a mean follow up of 3.4 years, 18 patients were hospitalized due to a worsening of heart failure.

Invasive and non-invasive aortic PP was positively related to EF (determined from echo or cineangiogram) with $R = 0.41$–0.69 ($p < 0.05$ for all combinations, respectively) and inversely related to left ventricular dimensions (enddiastolic and endsystolic volumes; determined from echo or cineangiogram) with $R = -0.28$–-0.47 ($p < 0.05$ for all combinations, respectively).

In univariate analysis, invasive aortic PP (HR per 10 mm Hg increase 0.74, CI 0.56–0.98, $p = 0.036$) as well as non-invasively determined aortic PP (HR per 10 mm Hg increase 0.43, CI 0.23–0.82, $p = 0.01$) were inversely associated with the risk of heart failure hospitalisation. In stepwise multiple Cox proportional hazards models, including age, gender, EF, and non-invasively estimated filling pressures (E/E'), invasive as well as non-invasive PP remained significantly and inversely associated with the risk of heart failure hospitalisation.

Conclusions: In patients with severe impairment of left ventricular systolic function, a lower aortic PP is associated with a worse left ventricular function and with an increased risk for heart failure hospitalisation.

XVII-3

NYHA functional class predicts outcome in patients with heart failure and preserved ejection fraction

D. Dalos, J. Mascherbauer, C. Zotter-Tufaro, A. Kammerlander, S. Aschauer, F. Duca, A. Bachmann, D. Bonderman

Univ. Klinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: In patients suffering from heart failure with preserved ejection fraction (HFpEF) dyspnea represents a leading symptom. Cardiac and extra-cardiac factors determining NYHA functional class in HFpEF patients have not been studied so far.

Objectives: To identify hemodynamic and other patient-related parameters associated with NYHA functional class and to determine whether NYHA class is related with outcome.

Methods: Consecutive patients with confirmed HFpEF were enrolled in this prospective registry. The primary outcome was defined as hospitalization due to heart failure and/or death for cardiac reasons. A multiple cox regression model was performed to define predictors of outcome, multivariable regression models were calculated to identify determinants of NYHA class.

Results: Between January 2011 and December 2014, 193 patients were included, of which 64 (33.2 %) reached the combined endpoint after a median follow-up of 21.9 ± 13.1 months. NYHA functional class was found to be an independent predictor of outcome (HR 2.621, $p < 0.001$). A number of clinical (age, $p = 0.007$), laboratory (pro-brain-natriuretic-peptide, $p < 0.001$), echocardiographic (early mitral valve flow velocity/mitral peak velocity of late filling, $p = 0.031$) and hemodynamic variables (diastolic pulmonary artery pressure, $p = 0.002$) were identified as determinants of NYHA functional class.

Conclusion: In patients with HFpEF, NYHA functional class is influenced by a variety of cardiac and non-cardiac parameters and is an independent predictor of outcome.

XVII-4

Postoperative cardiac rehabilitation after implantation of left ventricular assist devices: are there gender differences?

C. Marko, T. Lackner, E. Xhelili, M. Feilmair, D. Zimpfer, H. Schima, R. Müller, F. Moscato

Rehabilitationszentrum Felbring, Muthmannsdorf, Austria
Zentrum für Medizin, Physik und Biomedizinische Technik,Allgemeines Krankenhaus Wien, Vienna, Austria
Klinische Abteilung für Herzchirurgie, Allgemeines Krankenhaus Wien, Vienna, Austria

PensionsversicherungsanstaltWien, Vienna, Austria

Purpose: In studies concerning the postoperative rehabilitation of patients after implantation of left ventricular assist devices (LVAD) there are few data about the demographics and the outcome in women compared to men.

Methods: We retrospectively analyzed data from 104 patients (15 females, 89 males) who underwent cardiac rehabilitation between March 2010 and July 2014 after LVAD implantation. The exercise training consisted of interval bicycle training, strength training, training in walking and gymnastic groups. The change in intensity of the bicycle training (consisting of 12 modules with increasing intensity—e.g. module #1 = 1W/5W, 60s/30s to module #12 = 5W/150W, 60s/20s) as well as of strength for two muscle groups of the lower limbs were documented. Demographic data together with exercise training data and spiroergometry test data were analyzed, particularly focusing on the gender difference.

Results: Patients were admitted to the rehabilitation clinic (female vs. male) 49 ± 41 vs. 48 ± 38 days ($p = 0.442$) after LVAD implantation for a period of 31 ± 7 vs. 35 ± 9 days ($p = 0.147$). Female patients were younger than men (51 ± 15 vs. 59 ± 9 years, $p = 0{,}122$), had a lower range of comorbidities (Diabetes mellitus: 6.7 vs. 32 % $p = 0.048$, chronic obstructive pulmonary disease 7 vs. 20 % $p = 0.239$) and suffered mostly from a dilatative cardiomyopathy (60 vs. 33 % $p = 0.041$) and less from an ischemic cardiomyopathy (40 vs. 62 % $p = 0.113$). Apart from smoking, which had the same incidence in both groups (40 %) the cardiovascular risk profile was lower for women than for men (Hyperlipidämia: 27 vs. 62 % $p = 0.011$, Hypertension: 7 vs. 36 % $p = 0{,}024$).

An improvement for women at the end of the rehabilitation was observed for the intensity of the bicycle ergometer training (Module #6 ± 2 vs. #2 ± 1, $p = 0.003$), for the muscular strength (leg-press: 26 ± 12 vs. 24 ± 14 kg $p = 0.582$, leg extensor: 8 ± 5 vs. 6 ± 4, $p = 0.272$) as well as for walking- and gymnastic training.

Comparing the percentage of the reference value of peak.VO2, a better functional capacity was observed in women than in men (46 ± 14 vs. 39 ± 13 % $p = 0.079$).

Conclusions: Even if the number of women participating in the program compared to men was lower, thus limiting the study, cardiac rehabilitation demonstrated to be effective also for women. Most likely the better functional capacity of women in the percentage of the reference value is in relation to their lower range of comorbidities and lower cardiovascular risc profile compared to men.

XVII-5

Riociguat: new therapeutic approach for cardiac amyloidosis?

F. Duca, S. Aschauer, A. Kammerlander, C. Zotter-Tufaro, C. Schreiber, B. Köll, J. Mascherbauer, D. Bonderman

Kardiologie, Medizinische Universität Wien, Vienna, Austria

Background: Cardiac amyloidosis (CA) is a rare disease and represents the prototype of a restrictive cardiomyopathy.

A vast majority of affected patients present with advanced heart failure and face significant morbidity and mortality. However, an effective therapy is still lacking and a diagnosis of CA precludes patients from participation in standard heart failure clinical trials.

The solouble guanylate cyclase (sGC)—stimulator riociguat, already approved for the treatment of precapillary pulmonary hypertension, has also been shown to have favorable effects in reducing ventricular stiffness. We prospectively enrolled consecutive CA patients in a named patient use program were we tested the safety and efficacy of riociguat.

Materials and methods: CA was diagnosed based on cardiac magnetic resonance imaging and myocardial biopsy. Baseline work-up of patients and re-evaluation under therapy included the assessment of blood pressure, NYHA functional class, exercise capacity as measured by the 6-minute walk test (6MWT) as well as serum NT-proBNP.

Results: Four participants with wild-type transthyretin amyoidosis (75 % male, 25 % female mean age 80 ± 7.7 years) were included in the named-patient use program with a mean treatment time of 120 ± 80 days. Our preliminary findings indicate that application of riociguat in CA patients is safe. Systolic blood pressure 130 mmHg ± 23 vs. 124 ± 13 mmHg; ($p = 0.72$) and diastolic blood pressure 84 mmHg ± 7 vs. 80 mmHg ± 5; ($p = 0.27$) basically remained unchanged from baseline values. Despite a small patient number, considerable effects could be encountered with respect to outcome measures. At baseline three patients presented with NYHA II and one patient presented with NYHA III 2.25 ± 0.5. Under treatment one patient improved from NYHA III to NYHA II. The other patients remained clinically stable with no change in NYHA class 2 ± 0; ($p = 0.32$). 6MWT improved from 285 ± 153 m to 330 m ± 1169; ($p = 0.2$). NT-proBNP levels decreased from 4603 pg/ml ± 3630 to 3476 pg/ml ± 2999; ($p = 0.14$).

Discussion: Our preliminary data from a named patient use program indicate that riociguat treatment is safe in patients with CA. More information is necessary to support the evidence that riociguat may relieve the burden of disease associated with CA.

Postersitzung XVIII: Interventionelle Kardiologie 3

XVIII-1

Effekt der perkutanen renalen Denervation auf Entzündungszeichen bei Patienten mit therapieresistenter arterieller Hypertonie im Langzeitverlauf

A. Nahler, V. Gammer, T. Lambert, C. Reiter, J. Kammler, H. Blessberger, S. Schwarz, M. Grund, M. Rohla, T. Weiss, K. Huber, C. Steinwender

Interne 1 – Kardiologie, Allgemeines Krankenhaus Linz, Linz, Österreich
3. Medizinische Abteilung – Kardiologie, Wilhelminenspital Wien, Wien, Österreich

Hintergrund: Die perkutane Denervation des renalen sympathischen Nervengeflechtes (PRD) stellt eine erfolgsversprechende Behandlungsmöglichkeit bei Patienten mit einer therapieresistenten arteriellen Hypertonie (TAH) trotz mehrfacher Antihypertensiva-Therapie dar.

Allerdings gibt es vermehrt kritische Stimmen über die Effekte der PRD, im Speziellen seit der Publikation der SYMPLICITY HTN-3 Studie, welche als erste prospektive, randomisierte und verblindete Studie ihren primären Endpunkt nicht erreichte (Ein signifikanter Unterschied in der Blutdruckreduktion zwischen der behandelten und der Kontrollgruppe). Gerade aus diesem Grund wird vermehrt über andere potentiell positive Effekte der PRD diskutiert.

Seit langem sind Entzündungsparameter wie C-reaktives Protein (CRP) oder Interleukin-6 (IL-6) gut untersuchte Prädiktoren für eine erhöhte kardiovaskuläre Morbidität und Mortalität.

In den ersten wenigen publizierten Daten über einen möglichen Effekt der PRD auf Entzündungszeichen, gibt es einen positiven Trend. Allerdings fehlen bis zum jetzigen Zeitpunkt noch Langzeitdaten.

Methoden: Es wurde bei allen Patienten mit einer TAH, welche als mittlerer systolische Blutdruck (BD) >160 mmHg trotz zumindest drei unterschiedlicher antihypertensiven Medikamente und einem Diuretikum definiert wurde, nach Ausschluss einer sekundären Ursache, eine PRD durchgeführt.

Nach 6 Monaten wurden all jene Patienten mit einer Reduktion des ambulanten 24-Stunden BD um mehr als 5 mmHg systolisch als Responder klassifiziert.

Insgesamt wurden im Rahmen einer 6-, 12- und 24-Monatskontrolle neben einem ambulanten 24-Stunden BD auch die CRP und IL-6 Werte bestimmt und bezüglich eines positiven Effektes der PRD evaluiert.

Resultate: Insgesamt wurden hierfür 35 konsekutive Patienten mit einem Follow Up von 24 Monaten – 13 (37,1 %) davon Frauen – eingeschlossen. Bei diesen konnte ohne Komplikationen eine PRD durchgeführt werden. Nach den ersten 6 Monaten konnten insgesamt 16 Patienten (45,72 %) entsprechend unserer Definition als Responder klassifiziert werden. Diese Patienten hatten eine signifikante Reduktion des mittleren ambulanten 24-Stunden-BD von 18/8 mmHg nach 24 Monaten (p=0,003/0,001).

Die mittleren CRP-Level in der Responder-Gruppe waren zu Beginn 0,3[0,2; 0,6] mg/l, fielen auf 0,2[0,1; 0,5] mg/l (p=0,094) ab um allerdings bis zur 24 Monatskontrolle wieder auf 0,4[0,1; 0,6] mg/l zu steigen (p=0,16).

Ähnliches war bei den IL-6 Werten zu beobachten, wobei sich anfangs ein deutlicher Trend mit einem Abfall von 4,8[1,7; 7,3] pg/ml zu Beginn auf 2,1[1,5; 5,2] pg/ml nach 6 Monaten zeigte. Im weiteren Verlauf bis zur 24 Monatskontrolle kam es wieder zu einem Anstieg auf 3,9 [3; 7,5] pg/ml, sodass insgesamt keine signifkante Änderung stattfand (p=0,16).

Eine Korrelation zwischen des 24-Stunden BD und des CRP oder IL-6 konnte zu keiner Zeit gezeigt werden.

Konklusion: Wir konnten mit unseren Daten keinen Effekt der PRD auf Entzündungszeichen bei Patienten mit einer TAH zeigen.

XVIII-2

Patients with resistant arterial hypertension: is there an effect of percutaneous renal denervation on inflammation markers in responders?

A. Nahler, T. Lambert, V. Gammer, S. Schwarz, H. Blessberger, J. Kammler, C. Reiter, M. Rohla, K. Huber, C. Steinwender

Interne 1 – Kardiologie, Allgemeines Krankenhaus Linz, Linz, Austria
3. Medizinische Abteilung—Kardiologie, WIlhelminenspital Wien, Vienna, Austria

Background: Renal denervation (RDN) of sympathetic nerves is a promising treatment option in patients with a resistant arterial hypertension (RAH).

Since publication of the Simplicity HTN-3 trial, which failed it's primary endpoint (significant differences of blood pressure reductions between the treatment and the sham-controlled group), all possible effects of RDN are a matter of debate.

Inflammation parameters such as C-reactive protein (CRP) and Interleukin-6 (IL-6) are well known predictors for an increased cardiovascular morbidity and mortality. However only few data on possible effects of RDN on inflammatory parameters are published so far, showing a benefit of RDN.

Methods: Patients with RAH, defined as mean systolic office blood pressure (BP) >160 mmHg despite therapy with at least three different antihypertensive drugs, were treated with a RDN after exclusion of secondary causes of hypertension.

Patients were classified as responders if the 24-hour average systolic BP dropped by ≥5 mmHg after 6 months.

The levels of IL-6 and CRP were evaluated along with ambulatory BP measurements after 3, 6, 9 and 12 months and were analyzed for the responder group to have a population with evident RDN effect.

Results: We included 186 patients with RAH, who were treated with RDN. After 6 months 51.8 % were classified as responders. Those had a median systolic/diastolic ambulatory BP drop from 149/91 mmHg at baseline to 130/80 mmHg after 6 months (p<0.01).

Median CRP levels in responders were 0.3 [0.1; 0.6] mg/l at baseline and 0.3 [0.1; 0.5] mg/l after 12 months of follow-up (p=0.31).

In responders, median IL-6 levels were 4.5 [1.6; 6.8] pg/ml at baseline and 4.1 [2.5; 5.6] pg/ml after 12 months (p=0.33). IL-6 and CRP levels had no significant difference at any point in time.

Additionally, in responders there was a weak but significant correlation between IL-6 levels and elevated average systolic BP(r2=0.37, p=0.01) , and with elevated systolic daytime BP (r2=0.36, p=0.01) and systolic nighttime BP (r2=0.37, p=0.01) at baseline. However, after 6 and 12 months of follow-up, there were no correlations between IL-6 levels and BP.

No correlation between CRP levels and BP was found at any time of the study.

Conclusions: By our data we did not observe an effect of RDN on inflammatory parameters in patients with resistant arterial hypertension.

XVIII-3

Everolimus-eluting bioabsorbable vascular scaffold and personalised platelet inhibition: no scaffold thrombosis in a single centre registry with 223 consecutive patients

G. Christ, T. Hafner, M. Francesconi, A. Podczeck-Schweighofer

5. Med/Kardiologie, SMZ-Süd/KFJ, Vienna, Austria

Objective: Percutaneous coronary intervention (PCI) with implantation of everolimus-eluting bioabsorbable vascular scaffolds (BVS) is believed to represent a paradigm shift from sole vessel lumen opening to vascular restoration therapy with potential improvement in long-term outcome. However, reports on higher rates of scaffold thrombosis are raising some safety concerns. The value of personalising dual antiplatelet therapy (DAPT) to overcome high on-treatment platelet reactivity (HPR) with respect to clinical outcome after BVS implantation is not known.

Methods and results: A single-centre registry of 223 consecutive PCI patients with successful BVS implantation (from October 2012 to October 2014) and personalisation of DAPT guided by multiple electrode aggregometry (Multiplate) was compiled. Our cohort included 49 % patients with acute coronary syndrome (8 % STEMI, 41 % NSTE-ACS). Due to our local age limit for BVS implantation (65y), mean age was 54 ± 8y, with 17 % females and 28 % diabetics. A total of 476 BVS were implanted (mean 2.1 ± 1.4, range 1–7; total length 47 ± 35 mm, range 12–168 mm). 84 % of patients showed a b2/c lesion morphology (incl. 9 % chronic total occlusion, 57 % bifurcations, 11 % thrombus containing). Complex bifurcation and multi vessel PCI was performed in 9 % and 28 %, respectively. HPR to adenosine diphosphate induced aggregation (≥ 50 U) occurred in 45 % of patients (69 ± 14 vs. 32 ± 10 U; p<0.001) and was successfully treated with reloading (prasugrel or ticagrelor) in all cases (22 ± 9 U; p<0.001). The cumulative incidence of major adverse cardiac events (death, myocardial infarction and clinically driven target lesion revascularisation (TLR)) was 0 % at 30 days and 3.1 % (n=7) at long-term follow up to 743 days. One myocardial infarction (0.4 %) and seven TLRs (3.1 %) occurred at a median of 294 days (range 188–646 days) after PCI, without any death or scaffold thrombosis.

Conclusions: Implantation of BVS in routine clinical practice including complex and long lesion PCI showed a very favourable early and long-term outcome up to two years in our single centre registry. No scaffold thrombosis occurred with personalisation of DAPT. A randomized multicenter trial addressing this issue seems warranted.

XVIII-4

Percutaneous coronary intervention with everolimus-eluting bioabsorbable vascular scaffolds: implantation failure, application of intravascular imaging, lesion preparation and postdilatation in a single centre registry with 231 consecutive patients

G. Christ, T. Hafner, M. Francesconi, A. Podczeck-Schweighofer

5. Med/Kardiologie, SMZ-Süd/KFJ, Vienna, Austria

Aim: Percutaneous coronary intervention (PCI) with implantation of everolimus-eluting bioabsorbable vascular scaffolds (BVS) requires a more detailed planning, including intravascular imaging, as well as lesion preparation and non-compliant balloon postdilatation due to mechanical limitations of the polylactic acid polymer. We were interested whether the application of these technical aspects as well as the incidence of implantation failures (i.e. inability of lesion crossing) changes with increasing operator experience.

Methods and results: A single-centre registry with comparison of the first 50 (cohort A) versus the following 181 consecutive patients (cohort B) with intention of BVS implantation (from October 2012 to October 2014) was compiled. Clinical baseline characteristics were statistically not different including age (54 ± 9 vs. 55 ± 8), female gender (24 vs. 15 %) and diabetes (32 vs. 27 %). STEMI (4 vs. 8 %) and stable angina patients (42 vs. 54 %) were numerically lower present in cohort A (p= ns for both). Distribution of target vessels (LAD: 62 vs. 61 %; CX: 28 vs. 27 %; RCA: 38 vs. 45 %, LM: 4 vs. 1 %) and type b2/c lesions (85 vs. 83 %) were statistically not different. Multi vessel- (23 vs. 39 %) and bifurcation PCI (51 vs. 59 %), thrombus aspiration (4 vs. 13 %) as well as mean number and length of BVS implanted (2.0 ± 1.4 vs. 2.2 ± 1.4 mm; 43 ± 33 vs. 49 ± 35 mm) showed a trend for increase in cohort B. Failure of BVS implantation (overall n = 8; 3 %) was numerically lower in cohort B (6 vs. 3 %, p= ns) and associated with higher age (62 ± 7 vs. 54 ± 8; p = 0.006) and presence of type c lesion (100 vs. 33 %; p = 0.001). Intravascular imaging was performed in 37 % of patients (96 % OCT, 4 % IVUS) with a highly significant decrease from cohort A to B (74 vs. 27 %; p < 0.001). Lesion preparation was performed in 100 % of patients. Predilatation with a balloon to scaffold ratio of 0.9 ± 0.1 was performed in 99 % (non-significantly increasing from 0.8 ± 0.1 to 0.9 ± 0.1 in cohort B) and thrombus aspiration alone in 1 %. Usage of scoring balloons or rotational atherectomy significantly increased from 11 to 35 % (p = 0.002) in cohort B. Rate of non-compliant balloon postdilatation was high (77 %) with a non-significant increase in cohort B (72 vs. 78 %).

Conclusions: While the application of intravascular imaging during BVS implantation decreased with increasing operator experience in our registry, lesion preparation with scoring balloons significantly increased, resulting in a numerical higher implantation success. The rate of non-compliant balloon postdilatation remained high, underlining its importance in BVS implantation.

XVIII-5

Individual-patient and visit-by-visit evaluation of office and ambulatory blood pressure measurements over 24 months after Renal Denervation

T. Lambert, A. Nahler, C. Reiter, V. Gammer, H. Blessberger, J. Kammler, K. Saleh, M. Grund, B. Wichert, G. Buchmayr, C. Steinwender

I. Interne Abteilung, AKH Linz, Linz, Austria

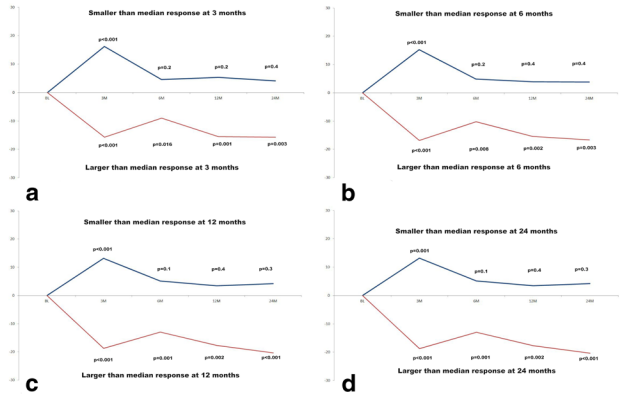
Background: Renal denervation (RDN) is a promising treatment option in addition to medical antihypertensive treatment in patients suffering from resistant hypertension. Despite the growing interest in RDN, only few long-term results are published so far.

Methods: We systematically investigated the effects of RDN on ambulatory blood pressure measurements (ABPM) for 24-hours in a consecutive series of patients with resistant hypertension out to 24 months. Office blood pressure (BP) measurements and ABPM assessment were performed at 3, 6, 12 and 24 months. Patients with an average systolic BP reduction of more than 10 mmHg in office BP 6 months after RDN were classified as responders. Additional to this classical responder concept, we categorized response to RDN by an individual-patient visit-by-visit evaluation of office BP and 24-hour-BP, separately.

Results: We included 32 patients. In 21 patients (65.6 %) we found a mean systolic BP reduction >10 mmHg in office BP six months after RDN. These patients were classified as responders. In responders, mean office BP dropped from 175.3 ± 15.9/96 ± 14.2 mmHg to 164.8 ± 24.4/93.2 ± 10.4 mmHg (p = 0.040/p = 0.323) and mean 24-hour BP in ABPM decreased from 146.8 ± 17.0/89.1 ± 11 mmHg to 136.8 ± 15.0/83.2 ± 10.7 mmHg after 24 months (p = 0.034/p = 0.014).

By the visit-by-visit evaluation, all patients were divided in larger-than-median and smaller-than-median response. Patients with a larger-than-median response had a sustained significant BP reduction, independently at which time-point we have categorized our patients.

Conclusions: In contrast to the observed variation of office BP measurements, ABPM demonstrated a reproducible and sustained significant BP reduction in patients with larger-than-median response to RDN.



XVIII-6

Instent-Restenosen nach Stentrevaskularisationen der Arteria carotis interna – Langzeitdaten einer „Single Center“ Kohorte

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

Interne 1- Kardiologie, AKH Linz, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Österreich

Einleitung: Die Stentrevaskularisation signifikanter Arteria carotis interna (ACI) Stenosen ist ein etabliertes Verfahren. Wie bei allen interventionellen Verfahren ist die Entwicklung von Instent-Restenosen (ISR) im Langzeitverlauf ein ernst zu nehmendes Problem. Wir wollten in unserer retrospektiven Datenanalyse prüfen, wie hoch die Rate an ISR in unserem Patientenkollektiv ist.

Methoden: Zwischen Dezember 1997 und Jänner 2015 wurden an unserer Abteilung 1137 Patienten (Ptn) mit 1150 signifikanten ACI Stenosen einer Stentrevaskularisation unterzogen. Postinterventionell wurden unsere Patienten mittels Ultraschall nach 1,

6 sowie 12 Monaten und dann jährlich nachkontrolliert. Eine ISR >50 % wurde als Strömungsgeschwindigkeit von >200 cm/s im Stent definiert.

Ergebnisse: Insgesamt wurden 1150 signifikante (≥80 %) ACI-Stenosen bei 1137 Patienten (Ptn, mittleres Alter 7,7 ± 38,6 Jahre) mittels Stent revaskularisiert. Die in der Anfangszeit verwendeten Technik mit ballonexpandierbaren Stents wurde im weiteren Verlauf vollständig durch die Verwendung von selbstexpandierbaren Stents ersetzt. Das Gesamtkollektiv wurde daher in zwei Gruppen aufgeteilt: In Gruppe 1 wurden ballonexpandierbare Stents (462 Stenosen, 40,2 %), in Gruppe 2 selbstexpandierbare Stents (688 Stenosen, 59,8 %) verwendet.

Im Langzeitverlauf von im Mittel 38 Monaten zeigten sich insgesamt 78 (6,8 %) Restenosen, davon 54 (11,7 %) in Gruppe 1 und 24 (3,5 %) in Gruppe 2 ($p<0,001$). Nach dem Absetzen des Stents erfolgte in 81 (17,5 %) Fällen der Gruppe 1 sowie in 564 (82 %) Fällen der Gruppe 2 eine Nachdilatation ($p<0,001$), wodurch die Restenoserate in Gruppe 1 signifikant ($p=0,037$) in Gruppe 2 jedoch nicht ($p=0,860$) gesenkt werden konnte.

Unterteilt man die Gruppe 2 je nach verwendetem Stenttyp, so wurde bei 252 (36,6 %) Stenosen ein nicht getaperter Stent (Gruppe A) und bei 436 Stenosen (63,4 %) ein getaperter Stent verwendet (Gruppe B). In Gruppe A traten 4 ISR auf, während es in Gruppe B zu 16 ISR kam ($p=0,114$).

Diskussion: Die interventionelle Sanierung signifikanter ACI-Stenosen ist mit einer niedrigen Restenoserate (6,8 % im gesamten Kollektiv) vergesellschaftet. Dies gilt vor allem für selbstexpandierbare Stents (3,5 %). Bei der Verwendung ballonexpandierbarer Stents kann eine Nachdilatation die Rate an ISR verringern. Die Verwendung von getaperten oder nicht-getaperten selbstexpandierbaren Stents hat offensichtlich keinen Einfluss auf die Restenoserate.

XVIII-7

Langzeiteffekte der renalen Denervation auf die Blutdrucklast im Tages- und Nachtintervall bei Patienten mit therapieresistenter Hypertonie

C. Reiter, T. Lambert, V. Gammer, M. Grund, H. Blessberger, J. Kammler, A. Kypta, K. Saleh, M. Rohla, T. Weiss, K. Huber, C. Steinwender

1. Interne Abteilung – Kardiologie, AKH Linz, Linz, Österreich
3. Medizinische Abteilung mit Kardiologie und internistischer Notaufnahme, Wilhelminenspital, Wien, Österreich

Einleitung: Eine vermehrte Sympathikus-Aktivität ist ein wichtiger zugrunde liegender Faktor im Rahmen der Genese einer arteriellen Hypertonie. Mittels Katheter-basierter Radiofrequenzablation der sympathischen Nervenfasern in der Adventitia der Nierenarterien (renale Denervation) kann bei Patienten mit therapieresistenter arterieller Hypertonie eine Blutdruckreduktion erzielt werden. Eine erhöhte Blutdrucklast, welche als prozentueller Anteil hypertensiver Werte definiert wird, ist sowohl im Tages- als auch Nacht-Intervall mit einer Elevation der kardiovaskulären Morbidität und Mortalität assoziiert.

Material und Methode: Patienten mit therapieresistenter arterieller Hypertonie, welche als mittlerer systolischer Blutdruck >160 mmHg nach drei Messungen in unserer Ambulanz unter laufender Einnahme von mindestens 3 Antihypertensiva – inklusive einem Diuretikum – definiert wurde, unterzogen sich nach Ausschluss sekundärer Ursachen einer renalen Denervation. Diese wurde mittels SymplicityTM RDN Catheter System (Medtronic Inc., Minneapolis, MN, USA) über einen rechtsseitigen transfemoralen Zugang durchgeführt. Ergänzend erfolgte zum Baseline-Zeitpunkt sowie nach 3, 6 und 12 Monaten unter Verwendung des „Del Mar Reynolds Medical ABPM Systems“ (Version 2.08.005) jeweils eine 24 h-Langzeit-Blutdruckmessung. Jene Patienten, welche nach 6 Monaten einen Abfall des mittleren systolischen Blutdruckwertes von mehr als 5 mmHg zeigten, wurden als Therapie-Responder klassifiziert. Die Blutdrucklast wurde dabei als der prozentuelle Anteil sämtlicher Messwerte ≥135/85 mmHg im Tages- (6:00–21:45) bzw. ≥120/70 mmHg im Nacht-Intervall (22:00–5:30) definiert und im Zuge der Kontrolluntersuchungen evaluiert.

Tab. 1 Auswertung der 24 h-Langzeitblutdruckmessung bei Therapie-Respondern

Responder ($n=41/79$)	Baseline	6 monate	*p*-Wert	12 monate	*P*-Wert
Mittlerer 24 h-Blutdruck (mmHg)	150,9/90	132,8/80,6	<0,0001	133,7/81	<0,0001
Systolische/diastolische Blutdrucklast (Tag)	75,6 %/57,1 %	29,6 %/25 %	<0,01	38,9 %/26,8 %	<0,01
Systolische/diastolische Blutdrucklast (Nacht)	100 %/62,5 %	44,4 %/25 %	<0,01	57,1 %/20 %	<0,01

Ergebnisse: Sechs Monate nach Durchführung der renalen Denervation konnten insgesamt 41 von 79 Patienten (51,9 %) als Therapie-Responder klassifiziert werden. Bei diesem Patientenkollektiv zeigte sich nach 6 Monaten (−18,1/−9,4 mmHg; $<0,0001/p<0,0001$) sowie in weiterer Folge auch nach 12 Monaten (−17,2/−9,0 mmHg; $p<0,0001/p<0,0001$) eine signifikante Reduktion des mittleren 24 h-Blutdrucks. Des Weiteren imponierte eine signifikante Verminderung der systolischen und diastolischen Blutdrucklast im Tages-(BL 75.6 %/57.1 %, nach 6M 29,6 %/25 %; $p<0,01/p<0,01$, nach 12M 38,9 %/26,8 %; $p<0,01/p<0,01$) bzw. Nachtintervall (BL 100 %/62,5 %, nach 6M 44,4 %/25 %; $p<0,01/p<0,01$, nach 12M 57,1 %/20 %; $p<0,01/p<0,01$). Im Vergleich dazu zeigten sich bei den Non-Respondern keine signifikanten Verbesserungen.

Diskussion: Im Blutdruckprofil unserer Therapie-Responder zeigte sich nach Durchführung einer renalen Denervation eine signifikant verminderte Blutdrucklast im Tages- und Nacht-Intervall sowie eine Verringerung des mittleren 24 h-Blutdruckwertes.

XVIII-8

One year clinical results of an all comers registry with a Sirolimus Eluting Stent in an Austrian population-BIOFLOW-III Satellite Austria

C. Steinwender, J. Kammler, I. Lang, M. Vertesich, G. Zenker, S. Pötz, H. Schuchlenz, D. Botegal, A. Geppert, W.-B. Winkler, M. Derntl, H. Mayr, G. Lamm, I. Jukic

Interne 1 – Kardiologie, AKH, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Austria
Internal Medicine II, Division of Cardiology, Medizinische Universität Wien, Vienna, Austria
Department of Internal Medicine, Hospital Bruck an der Mur, Bruck an der Mur, Austria
Department of Medicine II, Hospital Graz West, Graz, Austria
3. Department of Internal Medicine Cardiology and Emergency Medicine, Wilhelminen Hospital, Vienna, Austria
Department of Medicine II, Rudolfstiftung, Vienna, Austria
Department of Cardiology, Hospital of St. Pölten-Lilienfeld, St. Pölten, Austria
Department of Cardiology, Hanuschkrankenhaus, Vienna, Austria

Objective: The aim of this registry is to evaluate the clinical performance of the Orsiro Hybrid Drug Eluting Stent System in an Austrian patient population in standard clinical care.

The Orsiro is a unique hybrid solution that combines passive and active components. PROBIO passive coating encapsulates the stent and minimizes interaction between the metal stent and surrounding tissue. BIOlute active coating contains a highly biocompatible and biodegradable polymer.

Methods: Between August 2012 and June 2013, 305 subjects with 365 lesions at eight investigational sites in Austria were enrolled consecutively in this multicentric BIOFLOW-III all-comers Austrian registry using the Orsiro Hybrid Drug Eluting Stent.

Primary endpoint is Target Lesion Failure (TLF) at twelve months follow-up. Pre-specified subgroups were diabetes, small vessels, chronic total occlusion and acute myocardial infarction.

Results: Two hundred and nineteen men (71.8 %) and eighty six women were enrolled at xxx sites. The mean age was 65.3 ± 11.6, ranging from 36–90 years. The majority of subjects presented with hypertension 73 %, hypercholesteremia 71 %, smoker 54 %, and diabetes 23 %. 21 % of the lesion presented with B2/C lesions, 10 % with Bifurcation lesions and 3 % with chronic total occlusion. Moderate to severe calcification was observed in 29 % of the lesions. Acute MI was seen in 39 % of the subjects (NSTEMI 25 %, STEMI 14 %). The portion of elderly subjects (≥ 75 years) is represented by 23 %.

25 % of all subjects will be monitored and all endpoint and cardiologic related serious adverse events will be adjudicated by an independent clinical event committee. Follow-up compliance at 12-month is 87.6 %.

Conclusion: Data evaluation is still ongoing and will be available upon presentation.

Postersitzung XIX: Pulmonale Hypertension 2

XIX-1

Current treatment decisions in chronic thromboembolic pulmonary hypertension

R. Sadushi-Kolici, C. Gerges, N. Skoro-Sajer, M. Schemper, B. Moser, M. Gerges, I. Tilea, A.-M. Pistritto, W. Klepetko, I. Lang

Innere Medizin II, Kardiologie, Thoraxchirurgie, Medizinische Universität Wien, Vienna, Austria

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a late sequelae of venous thromboembolism with obstruction of pulmonary arteries by fibrotic thrombus. The treatment of CTEPH by pulmonary endarterectomy (PEA), balloon pulmonary angioplasty (BPA) or vasodilator drugs is determined by technical accessibility of thrombus, general surgical risk with overall risk-benefit ratio, and patient factors. We surveyed a CTEPH operability risk assessment in a single PEA center.

Patients and methods: Data were collected at the time of diagnosis. In addition to operability assessment by the multidisciplinary team (Figure), the European System for Cardiac Operative Risk Evaluation II (EuroScore II) was employed.

Results: Since February 1992, 425 patients (mean age 59 ± 16 years; 62 % female) were diagnosed with CTEPH. Of those 263 patients (mean age 54 ± 15 years; 58 % female) were classified as technically operable. 160 patients (mean age 68 ± 12 years; 53 % female) were classified as technically non-operable. In addition, 11 % of technically operable patients had an unacceptable surgical risk-benefit ratio and were classified as non-operable. Of those, 102 patients were treated with vasodilators. The logistic EuroScore was 6 ± 4 % in operable patients and 18 ± 3 % ($P < 0.001$) in non-operable patients.

Since April 2014, twenty-nine patients on vasodilator treatments (mean age 66 ± 13 years; 41.4 % female; 20 technically non-operable patients; 9 patients with unacceptable surgical risk-benefit ratio) underwent BPA.

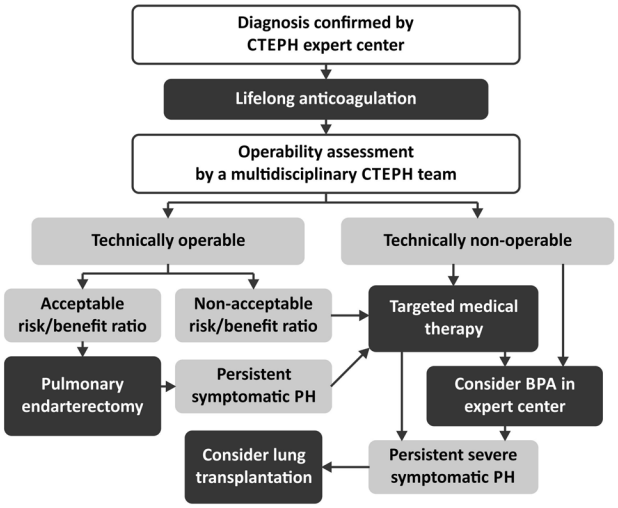


Fig. CTEPH Treatment algorithm

Conclusion: The first treatment choice for CTEPH is PEA. BPA is an emerging technique and is currently targeting non-operable patients.

XIX-2

Diastolic pressure gradient predicts outcome in patients with heart failure and preserved ejection fraction

C. Tufaro, F. Duca, A. Kammerlander, S. Aschauer, B. Koell, D. Dalos, J. Mascherbauer, D. Bonderman

Universitätsklinik für Innere Medizin II, Kardiologie, Medizinische Universität Wien, Vienna, Austria

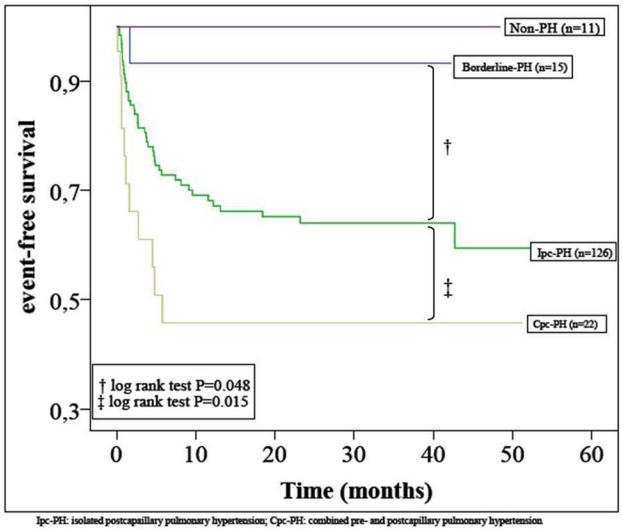
Background: Pulmonary hypertension due to heart failure with preserved ejection fraction (PH-HFpEF) is associated with poor outcome. According to the diastolic pressure gradient (DPG) with a cut-off of 7 mmHg, affected patients can be further sub-classified into isolated postcapillary PH (Ipc-PH) and combined pre- and pc-PH (Cpc-PH). However, the clinical significance and prognostic value of DPG remains to be elucidated.

Methods: Patients with HFpEF diagnosed according to current ESC guidelines were enrolled in our prospective registry. Borderline PH was defined as a mean pulmonary arterial pressure (mPAP) between 21–24 mmHg, and manifest PH was diagnosed, if mPAP ≥ 25 mmHg. DPG was calculated as difference between diastolic PAP and mean pulmonary arterial wedge pressure. Hospitalization for HF and death for cardiac reason were defined as the primary study endpoint.

Results: Between December 2010 and December 2014, 193 HFpEF patients were registered. 19 patients refused right heart catheter and were excluded. Of the remaining 174 patients, 11 (6.3 %) had no PH, 15 (8.6 %) had borderline PH and 148 (85.1 %) a manifest PH. PH patients (66 % females, mean age 70 ± 7 years) were further sub-classified into Ipc-PH ($n = 126$) and Cpc-PH ($n = 22$).

Patients with a Cpc-PH had a shorter six-minute walk distance (253.5 ± 128.7 vs. 318.4 ± 117.1 m; $p = 0.021$), a higher NT-proBNP (3816.9 ± 5977.8 vs. 1651.6 ± 1883.5 pg/ml; $p = 0.001$), larger right ventricles (42.1 ± 8.9 vs. 37.4 ± 7.1 mm, $p = 0.010$) and a lower capillary partial pressure of oxygen (63.4 ± 9.8 vs. 73.3 ± 11.6 mmHg; $p = 0.001$) compared to patients with Ipc-PH. During a median follow-up time of 25.2 months, 55 patients (33.7 %) reached the combined endpoint. DPG was found to be an independent predictor of outcome (HR 1.167, 95 % CI 1.047–1.299; $p = 0.005$). The worst outcome was recognized in the group of patients with Cpc-PH, as compared to Ipc-PH patients (log rank test, $p = 0.015$).

Conclusion: The presence of PH in HFpEF is associated with adverse outcome. The subgroup with Cpc-PH had a worse clinical status and event-free survival as compared to the remainder of the group. Although it remains unclear which subset of patients is prone to develop superimposed pulmonary vasculature remodeling, our data indicate a potential contribution of hypoxemia.



Ipc-PH: isolated postcapillary pulmonary hypertension; Cpc-PH: combined pre- and postcapillary pulmonary hypertension

XIX-3

Formation of typical vascular lesions in a new experimental model of pulmonary arterial hypertension

M.-P. Winter, A. Alimohammadi, F. Nagel, D. Santer, M. Sibilia, V. Seidl, A. Panzenböck, B. Podesser, I. Lang

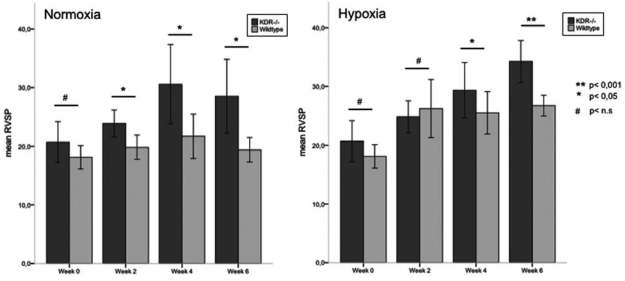
Universitätsklinik für Innere Medizin II, Kardiologie, Abteilung für Biomedizinische Forschung, Abteilung für Krebsforschung, Medizinische Universität Wien, Vienna, Austria

Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease characterized by obstruction of small pulmonary arteries leading to increased pulmonary vascular resistance. The key pathologic finding in this disease is a negative pulmonary vascular remodeling process with total vessel occlusion and a monoclonal expansion of collateral endothelial cells. It has been proposed that impaired vascular endothelial growth factor (VEGF) signaling plays a significant role in this process. Aim of our study was to investigate whether inhibition of VEGFR-2 (KDR) by direct gene manipulation may replicate classical pulmonary vasculopathy.

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

Results: There was no difference in mice might, heart weight and heart weight to body weight ratio between study and control mice. KDR knockout lead to disappearance of isolectin + microvessels. KDR-/- mice showed significantly increased right ventricular pressures (RVSP's) and Fulton indices after 4, and 6 weeks under normoxic and hypoxic conditions conditions, compared with wild type controls. There was no significant difference in systemic arterial pressure between both groups. Knockout mice showed a significant increase in pulmonary arterial wall thickness and significant increased α-SMC positive area revealed by tissue FACS. Lung histologies demonstrated neointimal thickening and vessel occlusions in lungs of KDR-/- mice resembling human pulmonary arteriopathy.

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



XIX-4

Tenascin-C deficiency and the development of Pulmonary Arterial Hypertension

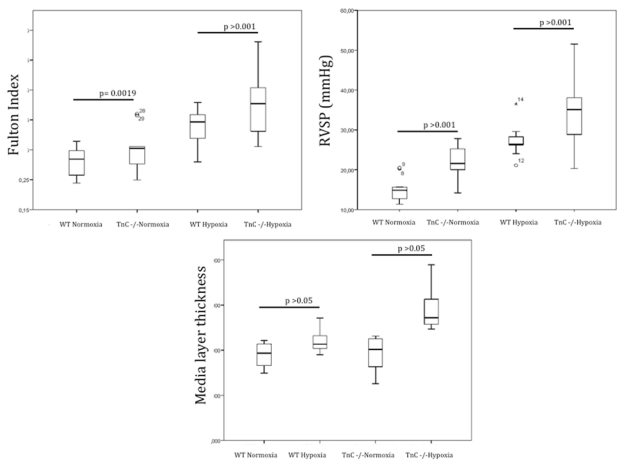
M.-P. Winter, F. Dragschitz, A. Alimohammadi, F. Nagel, V. Seidl, D. Santer, A. Panzenböck, B. Podesser, I. Lang

Abteilung für Kardiologie, Abteilung für Biomedizinische Forschung, Medizinische Universität Wien, Vienna, Austria

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 (15.2 vs. 21.95 mmHg, $p < 0.001$).



Under 4 weeks hypoxic breeding TnC KO mice revealed significantly higher right ventricular pressures (27.3 vs. 34.9 mmHg, $p<0.001$), and Fulton indices than controls (0.43 vs. 0.50, $p<0.001$). Under both normoxic and hypoxic conditions TNC KO mice revealed significant increased media thickness (Fig. 1).

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

XIX-5

Pulmonary artery occlusion waveform analysis for the assessment of small vessel disease in chronic thromboembolic pulmonary hypertension

C. Gerges, M. Gerges, P. Fesler, N. Skoro-Sajer, R. Sadushi-Kolici, P. Nierlich, B. Moser, S. Thagavi, W. Klepetko, I. M. Lang

Universitätsklinik für Innere Medizin II, Abteilung für Kardiologie, Medizinische Universität Wien, Vienna, Austria
Hôpital Lapeyronie,Montpellier, France

Purpose: Chronic thromboembolic pulmonary hypertension (CTEPH) is a common variant of pulmonary hypertension (PH). The complexity of CTEPH is that it combines a major-vessel vascular remodeling process that is amenable to pulmonary endarterectomy (PEA), with a classical small pulmonary arteriopathy that is associated with worse outcome. One of the greatest needs in the current management of CTEPH is to predict small vessel disease prior to PEA. 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 (PVR) 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 predictive value of pulmonary artery occlusion waveform analysis (PAOWA) in CTEPH patients undergoing PEA.

Methods: PAOWA was performed in 37 CTEPH patients undergoing right heart catheterization prior to PEA. Postoperative outcome was assessed by a composite of death and/or persistent/recurrent PH. Persistent/recurrent PH was defined as mean pulmonary artery pressure (mPAP) ≥25 mmHg and PVR ≥5WU measured within 4 days after PEA. Patients were followed for a median of 16.1 months (25th and 75th percentile, 8.3 and 24.5 months).

Results: 5 patients died due to right heart failure and 4 patients experienced persistent/recurrent PH. Rup% was significantly lower in patients with adverse postoperative outcomes (67 vs. 88 %, $p<0.001$). Rup% (OR 0.90 [0.84;0.96], $p=0.002$), PVR (OR 1.01 [1.00;1.01], $p=0.019$) and diastolic pulmonary vascular pressure gradient (DPG; OR 1.15 [1.02;1.30], $p=0.028$) were univariate predictors of death and/or persistent/recurrent PH. Multivariate logistic regression analysis revealed Rup% as an independent predictor of death and/or persistent/recurrent PH (OR 0.89 [0.80;0.98], $p=0.014$). Receiver operating characteristic analysis determined Rup%<82 % as a threshold that identifies patients with adverse postoperative outcomes (area under the curve 0.86, Youden index 1.70).

Conclusion: PAOWA accurately identifies patients who are at high risk of death and/or persistent/recurrent PH. Further investigations are required to clarify whether a Rup%<82 % is associated with small vessel disease in CTEPH.

XIX-6

Pulmonary hypertension in chronic heart failure: epidemiology, right ventricular function and survival

M. Gerges, C. Gerges, A. M. Pistritto, M. B. Lang, P. Trip, J. Jakowitsch, T. Binder, I. M. Lang

Universitätsklinik für Innere Medizin II, Abteilung für Kardiologie, Medizinische Universität Wien, Vienna, Austria
VU University Medical Center, Amsterdam, The Netherland

Background: Patients with pulmonary hypertension due to left heart disease (PH-LHD) and a diastolic pulmonary vascular pressure gradient (DPG) ≥7 mmHg representing PH out-of-proportion to pulmonary arterial wedge pressure, have pulmonary vascular disease and increased mortality. Little information exists on this condition.

Objectives: We investigated epidemiology, risk factors, right ventricular (RV) function and outcomes in patients with chronic heart failure (HF) and combined pre- and post-capillary PH (Cpc-PH).

Methods: The study population was identified from retrospective chart review of a clinical database of 3107 stable patients undergoing first diagnostic right heart catheterization, and from a prospective cohort of 800 consecutive patients at a national tertiary care center.

Results: In the retrospective cohort were 664 patients with systolic heart failure (SHF), and 399 patients with diastolic heart failure (DHF), 12 % of which were classified as Cpc-PH, respectively. In the prospective cohort were 172 patients with SHF (14 % Cpc-PH) and 219 patients with DHF (12 % Cpc-PH). COPD and tricuspid annular plane systolic excursion (TAPSE)/systolic pulmonary artery pressure (sPAP) ($p=0.015$) predicted Cpc-PH in SHF. Younger age ($p=0.004$), valvular heart disease ($p=0.046$) and TAPSE/sPAP predicted Cpc-PH in DHF ($p=0.016$). RV-pulmonary vascular (RV-PV) coupling was worse in Cpc-PH (Ees/Ea: SHF: 1.05±0.25; $p=0.002$; DHF: 1.17±0.27; $p=0.027$) than in those with Ipc-PH (Ees/Ea: SHF: 1.52±0.51; DHF: 1.45±0.29).

Conclusions: Cpc-PH is rare in chronic HF. RV-PV coupling is poor in Cpc-PH, and might serve as one explanation of dismal outcomes.

Postersitzung XX: Rhythmologie 2

XX-1

Angiographische Darstellung der cavotrikuspidalen Isthmusregion bei Ablation von typischem Vorhofflattern

H. Blessberger, T. Lambert, S. Hönig, M. Patrasso, K. Saleh, S. Schwarz, A. Nahler, A. Kypta, J. Kammler, C. Steinwender

I. Medizinische Abteilung mit Kardiologie, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Österreich

Hintergrund: Die cavotrikuspidale Isthmusablation ist eine etablierte Strategie zur Behandlung von isthmusabhängigem typischen Vorhofflattern. Durch starke anatomische Variationen der Isthmusregion mit Taschen, Muskelwülsten und Eustachischer bzw. Thebesischer Klappe ist der Komplexizitätsgrad des Eingriffes jedoch interindividuell sehr unterschiedlich, was sich auf die Durchleuchtungsdauer, die Strahlendosis, die primäre Erfolgsrate sowie die Rezidivrate potenziell auswirken könnte.

Methodik: Bei Patienten, die seit Februar 2013 an unserer Abteilung eine cavotrikuspidale Isthmusablation wegen eines typischen Vorhofflatterns erhielten, erfolgte vor Erstellung der Ablationslinie die angiographische Darstellung der Isthmusregion. Hierbei wurden nach dem Platzieren der Diagnostikkatheter im

rechten Vorhof (HRA-, CS- und Halo-Katheter) 12 ml eines nicht-ionischen Kontrastmittels (Visipaque® 320, GE Healthcare) im Bolus über eine im rechten Vorhof liegende 8F Schleuse (RAMP®, St. Jude Medical) verabreicht und der Isthmus dabei in RAO-Projektion gefilmt. Je nach Anatomie der Isthmusregion wurde diese als „einfach" (flache Muskelbrücke) oder „schwer" (deutliche Hügel und Täler bzw. Taschen) klassifiziert. Hierauf wurde die Ablationslinie mit einem flüssigkeitsgekühlten 4 mm Ablationskatheter (AlCath Flux®, Biotronik) unter Zuhilfenahme eines Navigationssystems (LocaLisa®, Medtronic) erstellt. Nach 30 min Observationsintervall wurde ein bidirektionaler Leitungsblock mittels septaler und lateraler Stimulation verifiziert. Beim Primäreingriff wurden Durchleuchtungsdauer, Dosisflächenprodukt sowie die primäre Erfolgsrate vermerkt. Im Februar 2015 wurden alle Patienten hinsichtlich klinischer Rezidive nachverfolgt.

Resultate: Insgesamt erhielten im Beobachtungszeitraum 85 Patienten eine cavotrikuspidale Isthmusablation. Die Anatomie von 65 Isthmen wurde als „einfach", die der restlichen 20 als „schwer" eingestuft. Hinsichtlich demographischer Daten, kardialer Risikofaktoren, Begleiterkrankungen, Nierenfunktion, Prävalenz von Schilddrüsenfunktionsstörungen oder Häufigkeit der Einnahme von Betablockern, Amiodaron oder anderen Antiarrhythmika bzw. Vorhandensein zusätzlicher bekannter Rhythmusstörungen unterschieden sich die Gruppen nicht signifikant. Alle Eingriffe waren primär erfolgreich mit dokumentiertem bidirektionalen Leistungsblock. Durchleuchtungsdauer („einfach": 14,2 ± 11,0 min, „schwer": 15,0 ± 9,4 min, $p = 0{,}77$) und Strahlendosis („einfach": 614 ± 869 µGym2, „schwer": 792 ± 826 µGym2, $p = 0{,}44$) der beiden Gruppen waren ebenfalls statistisch nicht signifikant unterschiedlich. Von den 85 Patienten erlitten 7 (8,2 %) im Nachverfolgungszeitraum von 5,1 ± 7,9 Monaten ein Vorhofflatterrezidiv. Dabei unterschied sich die Rezidivhäufigkeit hinsichtlich der anatomischen Gegebenheiten der Isthmusregion nicht (4/65 Rezidive bei „einfachem" und 3/20 bei „schwerem" Isthmus, $p = 0{,}26$).

Diskussion: In der Kohorte der Patienten mit komplexer „schwerer" Isthmusanatomie fanden sich keine statistisch signifikant verlängerte Durchleuchtungsdauer bzw. erhöhte Strahlendosis oder erhöhte Rezidivrate im Vergleich zu Patienten mit einer „einfachen" Isthmus-Morphologie. Die angiographische Darstellung der Isthmusregion als Referenz vor Erstellung der cavotrikuspidalen Ablationslinie erleichtert die Planung und technische Durchführung (Krümmungsradius des Katheters oder Anpressdruck) der Ablation und hat aus unserer Sicht maßgeblich zu diesen Ergebnissen beigetragen.

XX-2

Strahlendosisreduktion bei elektrophysiologischen Untersuchungen unter Alltagsbedingungen durch Verwendung einer neuen Detektortechnologie mit kristallinem Silizium

H. Blessberger, S. Hönig, T. Lambert, M. Patrasso, K. Saleh, S. Schwarz, A. Nahler, A. Kypta, J. Kammler, C. Steinwender

Interne I – Kardiologie, AKH, Medizinische Fakultät der Johannes Kepler Universität Linz, Linz, Österreich

Hintergrund: Längere Durchleuchtungszeiten bei elektrophysiologischen Untersuchungen (EPUs) erfordern strikte Maßnahmen zur Dosisreduktion im Sinne der Strahlenhygiene. Wir konnten im Rahmen einer experimentellen Voruntersuchung an einem Dummy (wassergefüllter Plexiglascontainer) eine 7–12fache Dosisreduktion bei der Verwendung eines kristallinen im Vergleich zu einem amorphen Silizium-Detektorsystems und Optimierung der Durchleuchtungsparameter (Röhrenstrom, Röhrenspannung, Vorfilterung, Auflösung) zeigen. Ziel dieser Erhebung war es, diese Ergebnisse mit Dosisdaten, die bei Routineuntersuchungen gewonnen wurden, zu vergleichen.

Methodik: Es wurden retrospektiv Dosisdaten der zwischen Jänner 2013 und Dezember 2014 durchgeführten EPUs erhoben, sofern diese verfügbar waren. Bis August 2013 war eine biplane Durchleuchtungsanlage mit einem amorphen Silizium-Detektorsystem in Verwendung (Gruppe 1), während danach eine monoplane Durchleuchtungsanlage mit einem kristallinen Silizium-Detektorsystem (Gruppe 2) verwendet wurde. Die Durchleuchtungszeiten, Dosisflächenprodukte und die Dosisleistung pro Minute der beiden Gruppen wurden mittels t-Test verglichen.

Resultate: Im genannten Zeitraum waren für 697 EPUs Dosisdaten verfügbar. 117 Untersuchungen, die von einem Kollegen in Einschulung ausschließlich mit der neuen Durchleuchtungsanlage durchgeführt worden waren, wurden von der Analyse ausgeschlossen, um das Ergebnis nicht zu verzerren. Von den verbleibenden 580 Untersuchungen wurden 234 (40,3 %, Gruppe 1) mit der alten und 346 (59,7 %, Gruppe 2) mit der neuen Durchleuchtungsanlage durchgeführt. Die Patienten waren im Schnitt 57 ± 16 Jahre alt, 212 (36,6 %) waren weiblich. Die Ablationseingriffe teilten sich wie folgt auf: 242 (41,7 %) Vorhofflimmern mittels Kryoballon oder robotergestützt, 97 (16,7 %) slow pathway Ablationen bei AV-nodaler Reentry-Tachykardie, 73 (12,6 %) cavotrikuspidale Isthmusablationen, 35 (6,0 %) Ablationen einer akzessorischen Leitungsbahn bei WPW-Syndrom, 17 (2,9 %) AV-Knoten Ablationen, 16 (2,8 %) ektope atriale Tachykardien, 14 (2,4 %) Ablationen einer ventrikulären Tachykardie aus dem rechten oder linken Ausflusstrakt, 6 (1,0 %) Ventrikelstimulationen, 1 (0,2 %) Ablation eines Maheim-Bündels, 18 (3,1 %) Kombinationseingriffe und 61 (10,5 %) unauffällige EPUs. Die mittleren Durchleuchtungszeiten in beiden Gruppen waren statistisch nicht signifkant unterschiedlich (Gruppe 1: 12,2 ± 9,6 min, Gruppe 2: 13,1 ± 9,9 min, $p = 0{,}285$). Das mittlere Dosisflächenprodukt war in Gruppe 2 mit einem kristallinen Silizium-Detektionssystem signifikant geringer als in Gruppe 1 mit einem amorphen Silizium-Detektionssystem (Gruppe 1: 1205 ± 1515 µGym², Gruppe 2: 592 ± 1139 µGym², $p < 0{,}00001$). Dasselbe traf auch für die Dosisleistung zu (Gruppe 1: 81,6 ± 62,0 µGym²/min, Gruppe 2: 41,2 ± 68,8 µGym²/min, $p < 0{,}00001$).

Diskussion: Die experimentell gezeigte hochsignifikante Dosisreduktion bei Verwendung einer Detektoranlage aus kristallinem Silizium konnte für die alltägliche Anwendung am Patienten mit verschiedensten elektrophysiologischen Eingriffen bestätigt werden. Das Ausmaß der Dosisreduktion ist allerdings etwas niedriger als im Vor-Experiment mit einem Dummy (7–12fache Reduktion experimentell vs. Halbierung unter Alltagsbedingungen), was aus unserer Sicht auf die individuell unterschiedliche Körperbeschaffenheit der Patienten und die begrenzte Optimierbarkeit der Durchleuchtungsparameter in der täglichen Praxis zurückzuführen ist.

XX-3

Automatic annotation algorithm (VisiTag) for pulmonray vein isolation: influence on dormant conduction and procedural time

A. Weber, J. Kosiuk, A. Bollmann, P. Sommer, B. Dinov, E. Koutalas, G. Hindricks, A. Arya

Rhythmologie, Herzzentrum Leipzig, Leipzig, Germany

Background: Incomplete transmurality or continuity of ablation lesions and resulting resumption of pulmonary vein (PV) conduction is a common mechanism of atrial fibrillation (AF) recurrence after catheter ablation. Recently an automated radiofrequency ablation annotation algorithm (VisiTag) for guidance of lesion formation has been introduced. However its clinical utility has not yet been validated.

Methods: In 14 patients (64 % male, 57 ± 9 years, 60 % persistent AF) undergoing first AF ablation the right (rPVs) and left PVs (lPVs) were randomized either to conventional ablation ($n = 14$) vs. VisiTag-guided ablation ($n = 14$). The rate of adenosine-induced

dormant PV-conduction and procedural time and ablation time needed for PV isolation were compared.

Results: Acute PV isolation was reached in all 28 PVs within mean time of 20 ± 14 min (22 ± 17 for lPVs vs. 19 ± 9 min for rPVs, $p = 0.551$). Dormant conduction have been observed in 5 PVs (18 %): 3 (21 %) in lPVs and 2 (14 %) rPVs ($p = 0.622$).

Frequency of conduction recovery was not significantly different between VisiTag-group ($n = 3$, 20 %) and conventional group ($n = 2$, 14 %) ($p = 0.622$).

There were no statistically significant differences between procedural time (22 ± 17 vs. 20 ± 10 min, $p = 0.695$) and ablation time between (684 ± 212 vs. 741 ± 204 s, $p = 0.529$) both groups.

Furthermore, no differences regarding effect of VisiTag on conduction or procedural/ablation time were observed in subgroups of lPVs and rPVs.

Conclusion: In this small group of patients undergoing AF ablation in an experienced, high-volume center an automated ablation annotation algorithm was not associated with reduction of dormant conduction rate or procedural and ablation time.

XX-4

Cardiac MRI is superior to transthoracic echocardiography as a risk stratification tool in primary prevention ICD therapy

S. Oebel, J. Kosiuk, A. Darma, J. Koch, A. Bollmann, G. Hindricks, B. Dinov

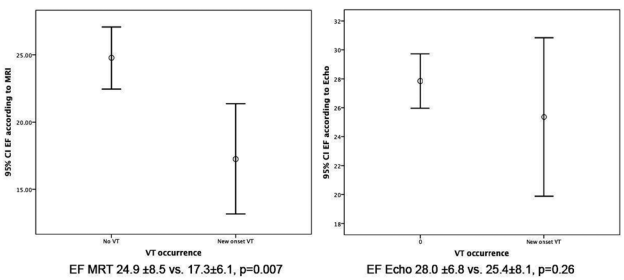
Innere Medizin, Landesklinikum Thermenregion Mödling, Mödling, Austria
Herzzentrum, Universität Leipzig, Leipzig, Germany

Introduction: Implantation of ICDs for primary prevention of ventricular arrhythmias (VA) in patients with severely reduced ejection fraction (EF) is based on the results from MADIT II study, where echocardiography, angiography and radionuclide methods were used to measure the EF. In contemporary clinical practice MRI is accepted as a gold standard for EF estimation. However, the role of MRI for guiding the ICD implantation for primary prevention is still unclear. We aimed to assess the value of EF measured in MRI compared to echocardiography for prediction of ventricular arrhythmias (VA).

Methods: In patients referred for primary prevention ICD therapy, a cardiac MRI and echocardiography were performed before implantation. Left ventricular EF was measured echocardiographically using the Simpson method by two independent investigators, as well as in the SSFP sequences in MRI. ICD devices were implanted based on the lower EF. All patients were followed for new onset VAs.

Results: Sixty-three patients (87 % male, median age 63.2 years) suffering from cardiomyopathy (59 % ischemic, 41 % dilated CMP) received an ICD device for primary prevention. During the median follow-up of 31.7 months, 17.5 % of patients developed VAs. EF measured by MRI was significantly lower in the group with new onset VA as compared to the rest (24.9 % ± 8.5 vs. 17.3 % ± 6.1, $p = 0.007$), and also remained a significant predictor of VAs in a proportional hazard regression analysis (HR 0.89, CI 95 % 0.81–0.95; $p = 0.024$). EF assessed by echocardiography showed no significant difference between patients who developed VAs and the rest (28.0 ± 6.8 vs. 25.4 ± 8.1, $p = 0.26$).

Conclusion: Cardiac MRI is superior to echocardiography to predict new-onset VAs in patients with severely impaired EF. Therefore, ICD may significantly contribute improving the risk stratification and optimizing the ICD implantation in future. Further prospective investigations are needed to demonstrate this potential superiority over transthoracic echocardiography.



EF MRT 24.9 ±8.5 vs. 17.3±6.1, p=0.007 EF Echo 28.0 ±6.8 vs. 25.4±8.1, p=0.26

XX-5

Dabigatran to reduce recurrence of atrial fibrillation after successful electrical cardioversion

C. Obst, F. X. Roithinger, L. Fiedler, R. Schoenbauer

Karl Landsteiner Gesellschaft, Alland, Austria
LKH Mödling, Mödling, Austria

Background: Electrical cardioversion (ECV) is a fast and secure method to establish sinus rhythm immediately in patients with symptomatic atrial fibrillation (AF). However recurrence rate of AF after ECV is high. Different agents such as antiarrhythmic or anti-inflammatory drugs can improve the long term rhythm outcome. Recently introduce direct thrombin inhibitor, dabigatran, has also potential antiinflammatory effect but its influence on recurrence after ECV has not yet been studied.

Characteristic	Dabigatran-etexilate (n = 78)	Phenprocoumon (n = 30)	p-value
Age (%)	64.9 ± 10.2	63.5 ± 10.3	0.516
Male (%)	54 (72.9)	20 (68.9)	0.907
Antiarrythmic therapy (%)	43 (55.8)	14 (46.6)	0.393
Hypertension (%)	51 (66.2)	44 (50.0)	0.121
CABG (%)	2 (2.6)	1 (0.3)	0.836
CAD (%)	14 (18.1)	3 (10.0)	0.298
Follow-UP (months)	17.4 ± 8.3	18.6 ± 9.6	0.542

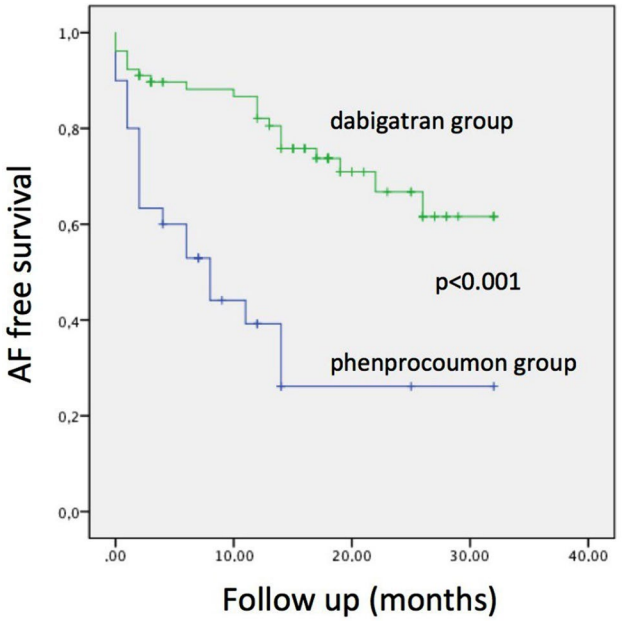


Fig. Kaplan Meier curve of dabigatran vs. phenprocoumon group

Purpose: To analyze potential effect of dabigatran on AF recurrence after ECV.

Methods: We performed an analysis of 108 patients (74 men, mean age 65 ± 10 years, 54 % on antiarrhythmic therapy, 62 % persistent AF) who underwent ECV and were anticoagulated with either dabigatran-etexilate ($n = 78$) or phenprocoumon ($n = 30$).

Results: During the mean follow up of 18 ± 9 months an AF recurrence was observed in 40 patients (37 %). Baseline characteristics of both patient groups were similar despite the fact, diabetes mellitus (29 vs. 10 %, $p = 0.045$) was more frequent in the dabigatran group (Table 1).

Although persistent AF was more frequent in patients with dabigatran (83 vs. 43 %, $p < 0.001$) the mean AF free survival was significantly longer in this group (25 ± 1 vs. 12 ± 3 months, $p < 0.001$) (Fig. 1).

In the multivariat analysis including DM, type of AF the use of dabigatran was associated with improved rhythm outcome (HR 0.24, CI 95 % 0.13–0.47, $p < 0.001$).

Conclusion: The results suggest a positive effect of dabigatran on preventing recurrence of AF after successful ECV. Further clarification of potential mechanisms and evaluation in larger multicenter trials is needed.

XX-6

Impact of sex on unfractionated heparin dosing during ablation of atrial fibrillation

C. Obst, F. X. Roithinger, L. Fiedler, R. Schoenbauer, I. Katzler

Karl Landsteiner Gesellschaft, Alland, Austria
LKH Mödling, Mödling, Austria

Introduction: Reaching adequate activated clotting time during ablation for atrial fibrillation (AF) is essential in terms of preventing thromboembolic complications and to reduce bleeding complications. The need of a gender adjusted unfractionated heparin (UFH) dosing is unknown. We therefore investigated the impact of sex, on the need to adjust UFH dosing, in terms of reaching same ACT.

Methods and results: We performed a retrospective analysis of 211 patients (71.8 % male) who underwent ablation of atrial fibrillation and were treated with either Dabigatran-etexilate or Phenprocoumon before. Our target of >350 s ACT (mean 352.0 s) was reached by using UFH. Needed UFH dose to reach defined ACT was 48.3 ($p = 0.005$; 95 % CI 15.2–81.6) international Units (I.U.) per kg for a female patient with a bolus of 8675 I.U. vs. 101.5 ($p < 0.001$; 95 % CI 60.2–142.8) I.U. per kg for male individuals with a bolus of 5143 I.U. ($p < 0.001$).

Conclusion: The results suggest the usefulness of establishing a sex adjusted UFH dosing regime, by also taking into account which oral anticoagulation was used before ablation of atrial fibrillation, to perform an optimal intraoperative coagulation management.

XX-7

Echocardiography predictors for recurrence after catheter ablation of atrial fibrillation

V. Eder

Kardiologie, KH Elisabethinen Linz, Linz, Austria

Background: Catheter ablation (CA) is an effective and potentially curative treatment in patients with atrial fibrillation (AF) to restore sinus rhythm (SR). However, the recurrence rate after CA remains unsatisfactory and the CA is an expensive procedure with potentially critical complications. Thus, it is crucial to identify those patients who are most likely to benefit from AF ablation with respect to restoration of SR. The reported predictors of recurrence after CA are the presence of hypertension, long duration of AF, prolonged procedural time, enlarged LA diameter, or increased LA volume and decreased left atrial (LA) function or decreased left atrial appendage (LAA) emptying velocity (LAV). However echocardiographic parameters for assessing SR maintenance after CA are not accurately defined. The aim of this study was to assess the echocardiographic predictors for the recurrence of AF after CA. We testet the hypothesis if the presence of left ventricular diastolic dysfunction (LVDD) is related to AF recurrence.

Methods and results: A total of 138 patients (74 % males, mean age 59.1 years) with persistent or paroxysmal nonvalvular AF who had undergone CA in our institution between January 2013 and March 2014 were included. In our cohort 89 patients (65 %) underwent CA for the first time, 49 patients (35 %) underwent multiple procedures, the last in the period between January 2013 and March 2014. Transthoracic and transesophageal echocardiography was performed in all patients before the procedure. Left ventricular diastolic function was evaluated according to the ratio of the mitral inflow early filling velocity to the velocity of the early medial mitral annular ascent (E/e') measured on pulsed wave and tissue Doppler assessments in all patients. The LAA velocity profiles were obtained by pulsed-wave Doppler interrogation 1 cm within the orifice of the LAA.

The follow-up strategy after CA included clinical follow up, 12-lead electrocardiography (ECG) and 24-h ECG 3 and 6 months after CA.

Results: During the follow up period 92 (67 %) patients remained in SR after the final procedure. AF recurred in 46 (33 %) patients. We observed that the presence of left ventricular diastolic dysfunction was the best predictor of AF recurrence. The presence of LVDD was increasingly more likely in patients who required repeated ablations. Depressed left ventricular ejection fraction was not associated with AF relapse. In our restrospective study patients with decreased LAV (<40 cm/sec) were more likely to have AF recurrence.

Conclusion and discussion: In our institute CA ablation strategies could achieve SR maintenance in 92 patients (67 %), 16 % of all patients underwent multiple procedures. Our results indicate that elevated left ventricular (LV) filling pressure estimated by raised Doppler E velocity to tissue Doppler E' velocity ratio (E/E') and decreased LAV is associated with increased risk of AF relapse after CA. Patients with normal left ventricular diastolic function had the lowest recurrence rate. We did not find a correlation between left ventricular systolic dysfunction and AF recurrence.

Maybe patients with LVDD may derive less benefit from ablation or may require a more extensive ablation approach.

XX-8

Quality of life in patients with atrial fibrillation: a comparison of therapeutic options

M. Pfeffer, R. Schönbauer, V. Maurer, L. Fiedler, C. Obst, A. Haiden, M. Haumer, T. Bernreiter, F. X. Roithinger

Innere Medizin, Landesklinikum Mödling, Mödling, Austria

Introduction: Atrial fibrillation is the most common cardiac arrhythmia. Pulmonary vein isolation (PVI) is a general accepted first or second line interventional treatment for symptomatic atrial fibrillation. The most important indication for antiarrhythmic treatment is severity of symptoms and accordingly reduced quality of life (QoL). Aim of this study was to evaluate the improvement of QoL after PVI and compare it to improvement of QoL under medical antiarrhythmic drug (AAD) treatment.

Material and methods: 65 patients were recruited prospectively in the study after signing an informed consent. All of them answered QoL questionnaires at the time of recruitment and during follow up. QoL questionnaires included the "Atrial Fibrillation Severity Scale", "Atrial Fibrillation Symptom Checklist", "WHO-Five Well-being

Index" and the "Major Depression Inventory" which proved to be valid and specific in several studies about atrial fibrillation.

Results: 65 patients were enrolled in the study (mean age 63.72 ± 9.835; 70.8 % male). 36 patients (55.4 %) were intended to get a PVI and 29 (44.6 %) to get AAD treatment (either class Ic antiarrhythmic drug or amiodarone). There were no significant differences in patients and clinical characteristics between the two groups. 62.1 % had paroxysmal and 37.9 % had persistent atrial fibrillation. The perception of severity of illness was measured by 5 questions (subjective severity of the illness, subjective evaluation of illness progression, severity of the last episode, severity of the first episode, and subjective state of health) summarized in a score. This score was significantly lower in patients after PVI ($p = 0.018$) but not under AAD treatment ($p = 0.140$). Symptoms like uneasiness ($p < 0.001$), tachycardia ($p < 0.001$), palpitation ($p = 0.035$), pause ($p = 0.004$), dyspnea ($p = 0.002$), nausea ($p = 0.009$) and chest pain ($p = 0.047$) were significantly reduced after PVI. Under AAD treatment only dyspnea was reduced ($p = 0.013$). Physical power measured by manageable floors to walk (PVI: $p = 0.003$; AAD: 0.005) was significantly improved in both groups. In contrast to patients under AAD, patients after PVI were less limited in daily work (PVI: $p = 0.017$, ECV: $p = 0.124$).

Conclusion: In this study patients with symptomatic atrial fibrillation significantly profited after PVI concerning quality of life. In contrast patients under AAD only had improved physical power. As severity of symptoms is the main indication for antiarrhythmic treatment, the findings of this study suggest PVI as a first line treatment for symptomatic atrial fibrillation because QoL improvement is superior to AAD treatment.

Postersitzung XXI: Risikofaktoren/ Stoffwechsel/Lipide 2

XXI-1

Degree of fibrosis in non-alcoholic fatty liver disease is associated with cardiovascular risk in a large screening cohort

D. Niederseer, A. Stadlmayr, U. Huber-Schönauer, D. Lederer, W. Patsch, E. Aigner, C. Datz

Sportmedizin, Universitätsklinikum Salzburg, Salzburg, Austria
Krankenhaus Oberndorf, Salzburg, Austria

Introduction: Non-alcoholic fatty liver disease (NAFLD) and cardiovascular diseases frequently coincide due to shared risk factors. Cardiovascular events are the most common causes of death in NAFLD patients. We aimed to investigate whether established cardiovascular risk scores such as the Framingham risk score (FRS) and the Heart Score of the European Society of Cardiology (HS) are associated with the degree of fibrosis in NAFLD in a large screening cohort.

Material and methods: We investigated 2138 asymptomatic subjects (59.6 ± 10.2 years, 50 % males, BMI 27.2 ± 4.6 kg/m^2). NAFLD was diagnosed if 1. (Significantly increased echogenicity in relation to the renal parenchyma present in ultrasound) and 2. (Exclusion of viral, autoimmune, hereditary liver disease and excess alcohol consumption) were fulfilled. The FRS (ten-year risk of coronary heart disease) the HS (ten-year risk of fatal cardiovascular disease) and the NAFLD Fibrosis Score (NFS; variables: age, body mass index, diabetes, alanine aminotransferase [ALT], aspartate aminotransferase [AST], thrombocytes, albumin; F0-F2: no or little fibrosis; F3-F4: advanced fibrosis or cirrhosis) were calculated for each subject. Subsequently, NFS, FRS and HS were correlated.

Results: Of 2138 subjects, 829 (38.7 %) had NAFLD. Patients with NAFLD had a significantly higher cardiovascular risk: FRS: no NAFLD: 5.5 ± 5.2 %; NAFLD: 8.8 ± 6.5 % ($p < 0.001$); HS: no NAFLD: 2.9 ± 3.8 %; NAFLD: 3.7 ± 4.1 % ($p = 0.002$). In NAFLD subjects, NFS correlated significantly with FRS ($r = 0.18$, $p < 0.001$) and HS ($r = 0.27$, $p < 0.001$) in Spearman Rank correlation. Patients with NAFLD were grouped into three groups according their NFS: F0-F2 ($n = 663$); indifferent ($n = 155$); F3-F4 ($n = 11$). In patients with F0-F2, FRS was 8.0 ± 6.1 %; with indifferent NFS, 10.8 ± 6.4 %; and in F3-F4: 11.5 ± 5.2 %, respectively. HS showed a similar pattern: F0-F2: 3.0 ± 3.4 %; with indifferent NFS, 5.4 ± 4.5 %, and in F3-F4: 7.0 ± 5.7 %, respectively.

Discussion: In this large asymptomatic screening cohort, subjects with non-invasive indicators of advanced stages of NAFLD had an increased risk of coronary heart disease and cardiovascular outcomes. A multidisciplinary approach including hepatologists and cardiologists is important to ensure optimal care for these patients at high risk of cardiovascular disease and liver-related endpoints.

XXI-2

Different protocols of endurance training lead to comparable improvement of quality of life

M. Schönfelder, S. Amann, M. Tschentscher, H. Oberreiter, J. Eichinger, A. Egger, S. Droese, J. Niebauer

Forschungsinstitut für Molekulare Sport- und Rehabilitationsmedizin, Paracelsus Medizinische Privatuniversität, Salzburg, Austria

Objective: It was the aim of the study to assess the effect of different types of endurance training during out-patient cardiac rehabilitation on patients' health related quality of life (HRQL).

Patients and methods: MacNew—Heart Disease Health-related Quality of Life Questionnaire and Hospital Anxiety and Depression scale (HADs) were used to assess changes in health-related quality of life in 66 patients before and after 6 weeks of cardiac rehabilitation. Patients were randomized to one of three types of endurance training: continuous endurance training, high intensity interval training, and pyramid training. Two-way ANOVA for repeated measure and Chi^2 test were used to analyze changes before and after rehabilitation.

Results: All 66 cardiac patients completed exercise training sessions with an overall attendance of 99.2 %. Within 6 weeks physical work capacity (PWC) increased from 136.1 to 165.5 W (+ 22.9 %; $p < 0.001$). No statistical differences in PWC were found between the three training protocols. Fully completed questionnaires at both time points were available in 46 patients (73.9 %; 61.3 ± 11.6 years, 34 males, 12 females). ANOVA detected a strong time effect with improvements in each of the categories of the McNew (i.e. emotion, physical, social, global; all $p < 0.001$) and HADs (anxiety: $p = 0.0118$; depression: $p = 0.021$). With regard to these parameters there were no significant differences between the three different types of endurance exercise.

Conclusion: All three endurance training protocols led to a comparable and significant increase in PWC, which was associated with an increase in HRQL independent of the type of training. Our findings support a further individualization of training regimes, which may as a consequence lead to an even better compliance.

XXI-3

Different types of resistance training in type 2 diabetes mellitus: effects on specific diabetic markers in human blood

B. Reich, M. Schönfelder, K. Lampl, E. E. Müller, L. Stechemesser, J. Lang, B. Paulweber, C. Pirich, A. Egger, J. Niebauer

University Institute of Sports Medicine, Prevention and Rehabilitation, Clinic of Endocrinology and Diabetology, Department

of Internal Medicine I, Paracelsus Medical University, Institute of Nuclear Medicine and Endocrinology, Salzburg, Austria

Background and objectives: In the past decades it has been proven that resistance training exerts beneficial effects on patients suffering from type 2 diabetes mellitus. The purpose of this study was to compare the effects of either hypertrophy (HRT) or endurance (ERT) resistance training on specific diabetic parameters.

Materials and methods: In this prospective, randomized, controlled exercise trial, 32 patients suffering from type 2 diabetes mellitus executed an eight week intervention program, consisting of either HRT or ERT both in combination with aerobic exercise. Effects on glycemic control, muscle mass and strength have been reported previously. Supplementary analyses on specific diabetic parameters (insulin-like growth factor 1, cortisol, C-peptide, apolipoprotein A1 and B, high-sensitivity c-reactive protein, free fatty acids—FFA, adiponectin, leptin, resistin, plasminogen activator inhibitor-1) were conducted from conserved serum samples of 27 patients (mean age 63.7 ± 8.1 years; 12 men and 15 women).

Results: This study has found that resistance training in combination with aerobic exercise training of eight weeks led to a significant reduction of FFA levels by 13.7 % ($p = 0.011$) and C-peptide concentrations by 22.5 % ($p = 0.014$), as well as a significant increase in resistin levels by 12.1 % ($p = 0.036$). There was no difference in the effectiveness regarding changes of specific diabetic parameters between the two distinct resistance training protocols, HRT and ERT.

Conclusion: The results of this research indicate that HRT and ERT in combination with aerobic exercise training are equally effective in improving C-peptide and FFA concentrations in human blood. As a consequence, both resistance training protocols can be included in diabetic management programs.

XXI-4

Effects of winter sports and indoor training on arterial stiffness

E. E. Müller, M. Schönfelder, C. Schwarzl, S. Feuchter, B. Mayr, E. Ledl-Kurkowski, K. Kvita, S. Droese, J. Stöggl, T. Stöggl, J. Niebauer

University Institute of Sports Medicine, Prevention and Rehabilitation, Department of Sport Science & Kinesiology, Paracelsus Medical University, Salzburg, Austria
Swedish Winter Sports Research Centre, Department of Health Sciences, Mid-Sweden University, Östersund, Sweden

Background and objective: Aging or unhealthy lifestyle comes along with physiological alterations that lead to stiffening of the arteries, with subsequent vascular and heart diseases. Regular exercise can decelerate these negative effects or even bring about reversal of already impaired vascular function. To increase motivation for physical activity, especially in winter time, it is of importance to validate different sports for their preventive characteristics. Therefore, the aim of this study was to compare effects of classical indoor cycling (IC), cross-country skiing (XCS) and alpine skiing (AS) on arterial stiffness.

Methods and results: After medical examination and performance diagnostics, eighteen healthy subjects conducted one session of IC, XCS and AS each. Heart rate, oxygen uptake and blood lactate were recorded continuously or at regular intervals. Arterial stiffness was measured with the portable oscillometric device Mobil-o-Graph®. An exercise session of IC, XCS or AS induced significant reductions of the reflection coefficient ($p < 0.01$) and the amplitude of the backward pressure wave (Pb, $p < 0.01$), over-all. Individually calculated, these parameters revealed to be reduced in IC (reflection coefficient and Pb) and XCS (reflection coefficient). Central systolic blood pressure (cSBP, $p < 0.001$) and pulse wave velocity (PWV, $p < 0.01$) were reduced after the acute session of IC, but not after XCS and AS. Reductions of arterial stiffness were negatively associated with individual exercise intensities (cSBP: $r = -0.500$, $p < 0.001$; PWV: $r = -0.332$, $p < 0.05$; reflection coefficient: $r = -0.286$, $p < 0.05$), indicating that higher intensities lead to greater reductions of arterial stiffness.

Conclusion: The present study revealed arterial stiffness reducing effects for acute sessions of IC, but also for XCS. It further suggests that higher intensities lead to greater reductions of arterial stiffness.

XXI-5

Oxygen supplementation during resistance training in COPD patients. The Salzburg Chronic Obstructive Pulmonary Disease: exercise and oxygen (SCOPE-) study

E. Steidle, D. Neunhäuserer, G. Weiss, M. Schönfelder, M. Sattler, M. Studnicka, J. Niebauer

University Institute of Sports Medicine, Prevention and Rehabilitation, Department of Pulmonary Medicine, Institute of Anatomy, Paracelsus Medical University, Salzburg, Austria

Objective: Loss of skeletal muscle contributes to disease progression and reduced quality of life in patients with chronic obstructive pulmonary disease (COPD). Whereas supplemental oxygen conveys beneficial effects during endurance training, its effects during resistance training (RT) remains unknown. Thus, the purpose of this study was to elucidate the effects of oxygen supplementation during RT intervention in COPD patients.

Methods: This prospective, double-blind, randomized, cross-over intervention study (Clinicaltrials.gov: NCT01150383) randomly allocated 31 patients (female 9/male 22) with COPD into two cross-over groups ($n = 15$: oxygen followed by room air (OR) versus $n = 16$: room air followed oxygen (RO)). Ten repetition maximum (10-RM) was assessed at baseline, after six (cross-over) and twelve weeks of training. Additionally, magnetic resonance imaging, mea-

Table 1 Ten repetition maximum tests and treatment effects of oxygen supplementation

	Baseline		6 weeks		12 weeks		Treatment effect
	OR	RO	OR	RO	OR	RO	OR vs. RO
Lat pull down (kg)	37 ± 11	43 ± 11	47 ± 12	57 ± 13	53 ± 12	67 ± 14	$p = 0.482$
Shoulder press (kg)	36 ± 10	43 ± 13	47 ± 15	57 ± 14	54 ± 12	69 ± 10	$p = 0.427$
Butterfly (kg)	20 ± 10	27 ± 13	30 ± 12	41 ± 18	35 ± 11	50 ± 20	$p = 0.300$
Butterfly reverse (kg)	14 ± 7	19 ± 10	21 ± 8	29 ± 10	25 ± 9	36 ± 12	$p = 0.424$
Back extension (kg)	44 ± 12	49 ± 15	55 ± 11	64 ± 18	61 ± 11	72 ± 14	$p = 0.297$
Abdominal crunch	19 ± 6	26 ± 10	29 ± 9	37 ± 9	34 ± 9	44 ± 11	$p = 0.455$
Leg extention (kg)	27 ± 8	31 ± 12	39 ± 9	44 ± 13	43 ± 10	51 ± 12	$p = 0.203$
Leg flexion (kg)	25 ± 7	28 ± 11	33 ± 10	37 ± 13	37 ± 10	44 ± 13	$p = 0.481$

suring muscle cross-sectional area (MCSA) of leg extensor muscles, was assessed before and six weeks after training intervention.

Results: During both modalities (OR/RO) muscle strength significantly increased in all trained muscle groups (lat pull down, shoulder press, butterfly, butterfly reverse, back extension, abdominal crunch, leg extension, and leg flexion; Table 1), but no significant difference could be observed between modalities (all $p > 0.05$). Also, MCSA of leg extensor muscles detected a modest, but statistically non-significant increase during both modalities (2.3 %/2.4 %) after six weeks of training. There was a moderate correlation between MCSA and 10-RM of leg extension (OR: $r = 0.678$, $p < 0.0001$; RO: $p = 0.575$, $p < 0.001$).

Conclusions: Supplemental oxygen during six weeks of RT has no additive effect on the time-dependent increase of 10-RM. No significant increase in leg muscle CSA could be observed, possibly indicating that the increase in muscle strength is predominantly triggered by muscle fiber recruitment/inter-muscular coordination and that oxygen delivery is not the limiting factors.

XXI-6

Plasma levels of Interleukin-12p40 and Interleukin-16 correlate with anthropometrical parameters of obesity with in overweight adolescents

M. Lichtenauer, M. Franz, M. Fritzenwanger, H.-R. Figulla, N. Gerdes, C. Jung

Christian Doppler Labor für Diagnose und Regeneration von Herz- und Thoraxerkrankungen, Universitätsklinik für Innere Medizin I, Kardiologie, Friedrich Schiller University Jena, Jena, Germany
Ludwig-Maximilians Universität München, München, Germany

Introduction: The development of obesity in children and adolescents has reached almost epidemic proportions in industrialized countries of the Western world. Obesity during adolescence is an increasing problem for both the individual and health care systems alike. In western world countries childhood adiposity has reached epidemic proportion. It is known that elevated levels of pro-inflammatory cytokines can be found in the plasma of obese patients. In this study we sought to determine the relation between Interkeukin-12p40 (IL-12p40), IL-12p70 and Interleukin-16 (IL-16) in overweight adolescents.

Materials and methods: Seventy-nine male, Caucasian adolescents aged 13–17 years were included in this study. Thirty-five of them had a body-mass index (BMI) above the 90th age-specific percentile. The quantitative analysis of human TNF-alpha, IL-6, IL-10, IL-12p40, IL-12p70 and IL-16 was performed from immediately frozen heparin plasma using Luminex multiplex technology.

Results: Both IL-12p40 and IL-16 concentrations were significantly increased in overweight subjects compared to normal weight control (IL-12p40: 1086.6 pg/ml ± 31.7 pg/ml SEM vs. 1228.6 pg/ml ± 43.5 pg/ml SEM; IL-16 494.0 pg/ml ± 29.4 pg/ml SEM vs. 686.6 pg/ml ± 52.5 pg/ml SEM, $p < 0.05$ and $p < 0.01$ respectively). No differences were found for IL-12p70 (7.48 pg/ml ± 0.72 pg/ml SEM vs. 7.20 ± 1.33 pg/ml SEM, $p = 0.86$). TNF-alpha, IL-6, and Il-10 also evidenced no significant differences between the groups.

Conclusions: We found that significantly higher concentrations of IL-12p40 and Il-16 but not IL-12p70 are present in the plasma of overweight adolescents. Levels of IL-12p40 and IL-16 correlated also significantly with anthropometrical measurements of obesity such as weight, BMI and waist circumference. Based on these results we believe that the increased levels of IL-12p40 and IL-16 are associated with a permanent inflammatory response in obese individuals and could lead to the development of disease conditions related to obesity. Interestingly, other prominent inflammatory mediators such as TNF-alpha and IL-6 showed no significant differences between the two study groups. One could speculate that the IL-12p40/IL-16 axis might be a more forefront pro-inflammatory signaling pathway in the earlier stages of obesity related disease conditions as they were likely present in our cohort of adolescents compared to the inflammatory milieu found in adult patients.

Postersitzung XXII: Risikofaktoren/ Stoffwechsel/Lipide 3

XXII-1

Awareness, treatment and control of hypertension in Eastern Austria: rationale and design

M. Rohla jr., K. Huber, T. W. Weiss

3. Medizinische Abteilung Kardiologie und Notfallmedizin, Wilhelminenspital, Vienna, Austria

Background: Hypertension is the single largest contributor to mortality worldwide, accounting for 13 % of all deaths globally.

Data from cross-sectional studies and surveys indicate widely varying treatment and control rates amongst European countries, the latter ranging from 27 % (Greece, 2001) to 46 % (France, 2004).

The only available Austrian observational study (SCREEN II, 2003), including 1303 patients taking at least 30 home blood pressure (BP) readings, could show that 17 % of treated patients achieved the BP threshold.

According to this data, Austria performs substantially worse than all European, and the majority of developing countries.

This cross-sectional study aims to investigate the quality of BP control in a general population receiving medical treatment for hypertension in eastern Austria.

Methods: In total, 554 pharmacies in two Austrian provinces (rural and urban) will be enrolled to obtain data on demographics, control rates and awareness in 10,000 consecutive individuals approaching the respective pharmacies with a prescription filled for antihypertensive medication.

Using a standardized questionnaire, following variables will be assessed:

Age, gender, marital status, level of education, employment, rural or urban residence, specialty of the treating physician, cardiovascular risk factors, awareness of the disease and associated risks, antihypertensive medication, heart rate and seated BP (average of two readings).

Outcome measures: As primary outcome measure, the study will evaluate the proportion of patients with adequately controlled hypertension, applying a BP threshold of < 140/90 mmHg.

Pre-specified secondary outcomes are control rates according to age, gender, socioeconomic status, rural or urban residence, specialty of the treating physician, awareness and number of drugs taken.

Conclusion: This study aims to assess whether BP control in Austria improved compared to previous data obtained more than a decade ago and if control rates are in the range of other European countries.

XXII-2

Impaired antioxidant high-density lipoprotein function predicts poor outcome in critically ill patients

L. Schrutka, K. Distelmaier, B. Meyer, R. Wurm, G. Heinz, R. Pacher, I. M. Lang, M. Hülsmann

Innere Medizin II—Kardiologie, Medizinische Universität, Kaiser-Franz-Joseph-Spital, Vienna, Austria

Background: Oxidative stress affects clinical outcome in critically ill patients. Although high-density lipoprotein (HDL) particles are generally considered protective, deleterious properties

of HDL have been observed in patients under conditions of infection, inflammation or tissue injury. Here, we analyzed the impact of impaired antioxidant HDL capacity on 30-day mortality in an unselected cohort of critically ill patients.

Methods: We prospectively included 142 consecutive patients admitted to a university-affiliated intensive care unit (ICU). HDL antioxidant capacity was determined using a 2′,7′-dichlorodihydrofluorescein diacetate-based cell free fluorescent assay in serum samples collected at ICU admission.

Results: At the time of ICU admission, 96.5 % of enrolled ICU patients presented with pro-oxidant HDL. Antioxidant properties of HDL were independent of serum HDL-cholesterol levels ($r=-0.002$, $p=0.984$). After adjustment for the Simplified Acute Physiology Score II, cox regression analysis revealed a significant and independent association between reduced antioxidant capacity of HDL and 30-day mortality with an adjusted hazard ratio per 1-SD of 1.43 (95 % CI 1.11–1.84; $p=0.005$). Extracorporeal circulation, including renal replacement therapy and extracorporeal membrane oxygenation, was a strong and independent predictor for impaired antioxidant HDL function with an odds ratio of 2.78 (95 % CI 1.20–7.07; $p=0.006$).

Conclusions: Impaired antioxidant HDL function represents a strong and independent predictor of 30-day mortality in critically ill patients. The maintenance of HDL functions might be a promising therapeutic target in ICU patients.

XXII-3

Monocyte subset distribution in patients with stable atherosclerosis and elevated levels of Lipoprotein(a)

K. A. Krychtiuk, S. P. Kastl, S. L. Hofbauer, G. Goliasch, M. Ozsvar-Kozma, G. Maurer, K. Huber, E. Dostal, C. J Binder, S. Pfaffenberger, S. Oravec, J. Wojta, W. S. Speidl

Universitätsklinik für Innere Medizin II, Abteilung Kardiologie, Klinisches Institut für medizinisch-chemische Labordiagnostik, Medizinische Universität Wien, Vienna, Austria
Krankenanstalten Dr. Dostal, Vienna, Austria
Comenius University Bratislava, Bratislava, Slovakia

Background: Lipoprotein(a) is a pro-atherogenic plasma lipoprotein currently established as an independent risk factor for the development of atherosclerotic disease and as a predictor for acute thrombotic complications. In addition, Lp(a) is the major carrier of proinflammatory oxidized phospholipids (OxPL). Today, atherosclerosis is considered to be an inflammatory disease of the vessel wall in which monocytes and monocyte-derived macrophages are crucially involved. Circulating monocytes can be divided according to their surface expression pattern of CD14 and CD16 into at least three subsets with distinct inflammatory and atherogenic potential. Therefore, the aim of this study was to examine whether elevated levels of Lp(a) and OxPL on apolipoprotein B-100-containing lipoproteins (OxPL/apoB) are associated with changes in monocyte subset distribution.

Methods: We included 90 patients with stable coronary artery disease (CAD). Lp(a) and OxPL/apoB was measured and monocyte subsets were identified as classical monocytes (CD14++CD16−; CM), intermediate monocytes (CD14++CD16+; IM) and non-classical monocytes (CD14+CD16++; NCM) by flow cytometry.

Results: In patients with elevated levels of Lp(a) (>50 mg/dL), monocyte subset distribution was skewed towards an increase in the proportion of IM (7.0 ± 3.8 vs. 5.2 ± 3.0 %; $p=0.026$), while CM (82.6 ± 6.5 vs. 82.0 ± 6.8 %; $p=0.73$) and NCM (10.5 ± 5.3 vs. 12.8 ± 6.0; $p=0.10$) were not significantly different. This association was independent of clinical risk factors, choice of statin treatment regime and inflammatory markers. In addition, OxPL/apoB was higher in patients with elevated Lp(a) and correlated with IM but not CM and NCM.

Conclusion: In conclusion, we provide a potential link between elevated levels of Lp(a) and a proatherogenic distribution of monocyte subtypes in patients with stable atherosclerotic disease.

XXII-4

Premature myocardial infarction is strongly associated with increased levels of remnant cholesterol

G. Goliasch, F. Wiesbauer, H. Blessberger, S. Demyanets, J. Wojta, M. Schillinger, K. Huber, G. Maurer, W. Speidl

Medizinische Universität Wien, Vienna, Austria

Background: Elevated levels of remnant cholesterol have been associated with increased cardiovascular risk. The aim of this study was to investigate the role of remnant cholesterol in premature myocardial infarction (MI).

Methods and results: We prospectively enrolled 302 patients into our multicenter case-control study comprising 102 consecutive MI survivors (≤ 40 years) and 200 hospital controls. MI Patients were frequency-matched for age, gender, and center. Remnant cholesterol was calculated from standard lipid parameters. Remnant cholesterol was 1.7-fold higher in premature AMI patients compared to controls (61.1 ± 36.8 vs. 35.8 ± 16.8 mg/dL; $p<0.001$). Remnant cholesterol was the lipid fraction most strongly associated with premature myocardial infarction (OR 3.94; 95 %CI 2.61–5.96; $p<0.001$) for an increase of 1-SD. This association persisted after multi-variate adjustment with an OR of 3.34 (95 %CI 2.17–5.14; $p<0.001$) and remained statistically significant when adding triglycerides, LDL cholesterol and HDL cholesterol to the multivariate model (OR 3.37; 95 %CI 2.05–5.55). This observation was independent from clinical risk factors and plasma lipid levels.

Conclusion: Remnant cholesterol is strongly associated with premature myocardial infarction, can be easily calculated and might serve as a new potent risk marker in this young patient population.

Table 1 Logistic regression analysis assessing the association of different lipid parameters with premature myocardial infarction. Odds ratios refer to a change of 1-SD in continuous variables. Multivariate model is adjusted for age, body-mass index, hypertension, diabetes and center

	Unadjusted OR (95%CI)	*P*-value	Adjusted OR (95%CI)	*P*-value
Remnant cholesterol	3.94 (2.61–5.96)	*<0.001*	3.34 (2.17–5.14)	*<0.001*
Non-HDL cholesterol	3.01 (2.16–4.20)	*<0.001*	2.78 (1.95–3.95)	*<0.001*
Triglycerides	2.56 (1.60–4.08)	*<0.001*	2.09 (1.29–3.37)	*<0.001*
Remnant/HDL cholesterol ratio	2.41 (1.75–3.31)	*<0.001*	1.99 (1.45–2.75)	*<0.001*
Total cholesterol	2.21 (1.66–2.96)	*<0.001*	2.14 (1.56–2.93)	*<0.001*
LDL/HDL cholesterol ratio	2.03 (1.54–2.68)	*<0.001*	1.77 (1.30–2.41)	*<0.001*
LDL cholesterol	1.56 (1.20–2.02)	*0.001*	1.62 (1.21–2.16)	*0.001*
HDL cholesterol	0.63 (0.48–0.83)	*0.001*	0.77 (0.57–1.05)	0.09
Lp(a)	1.16 (0.89–1.50)	0.28	1.09 (0.82–1.45)	0.54

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Significant variation of Lipoprotein(a) plasma levels after premature myocardial infarction

G. Goliasch, F. Wiesbauer, H. Blessberger, G. Maurer, K. Derfler, W. Speidl

Medizinische Universität Wien, Vienna, Austria

Objective: Myocardial infarction (MI) in very young individuals (≤40 years) represents a rare disease with an unfavorable prognosis. Elevated levels of lipoprotein(a) [Lp(a)] are an independent risk factor for premature MI. Plasma levels of Lp(a) are to a large extent genetically determined via variation in the apolipoprotein(a) gene and remain stable with little variation over time. Recent studies have shown that Lp(a) can be substantially lowered by treatment with inhibitors of proprotein convertase subtilisin/kexin type 9 (PCSK9). However, it is not known whether Lp(a) levels in the post MI period are representative for the stable phase of the disease in these young patients.

Methods: We enrolled MI survivors (≤40 years) and measured plasma levels of Lp(a) in 40 patients during the postinfarction period (3.2±2.1 days post MI) and after one year follow-up in a stable phase of the disease.

Results: Lp(a) significantly increased from 34.0±46.3 nmol/L in the post MI period to 48.4±67.8 nmol/L ($p=0.013$) at follow-up. Interestingly, this change of Lp(a) correlated significantly with baseline levels ($r=0.61$; $p<0.0001$). The increase was only present in patients with Lp(a) levels above the median of 15 nmol/L.

Conclusion: Low levels of Lp(a) directly after premature MI could possibly be used to rule out a significant involvement of Lp(a) in the early onset of the disease and no further testing of these patients seems to be necessary. However, Lp(a)-testing should be repeated in the stable phase of the disease in patients with Lp(a) >15 nmol/L.