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Jahrestagung der Österreichischen Kardiologischen Gesellschaft 2. bis 5. Juni 2010, Salzburg

Abstracts

In alphabetischer Reihenfolge nach Gruppen und Erstautoren

Best Abstracts I **(BAI)** und Best Abstracts II **(BAII)** rot hervorgehoben

Akutes Koronarsyndrom

Endothelin Receptor Blockade in Acute ST-Segment Elevation Myocardial Infarction I-9 001

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Background Acute myocardial infarction is characterized by compromised blood flow at the epicardial as well as microvascular levels and percutaneous coronary intervention (PCI) is the treatment of choice. Endothelin (ET) has been proposed to be an important mediator of microvascular dysfunction and adverse cardiac remodeling following reperfusion in ST-elevation myocardial infarction (STEMI).

We hypothesized that periinterventional administration of an ET-A receptor antagonist (BQ-123) may improve outcome in patients with STEMI undergoing PCI.

Methods 57 posterior-wall STEMI patients were randomly assigned to receive intravenous BQ-123 at 400 nmol/minute or placebo over 60 minutes, starting immediately before PCI. The primary endpoint was microvascular perfusion, assessed by first-pass perfusion cardiac magnetic resonance imaging (MRI) calculating the time to 50 % maximal myocardial enhancement. The plasma concentration of amino-terminal pro B type natriuretic peptide (NT-proBNP) at 30 days was a secondary endpoint.

Results At 6.0 (4–11.5) days after PCI microvascular perfusion MRI demonstrated shorter perfusion delays in patients randomized to receive BQ-123 compared to patients in the control group (1.8 [0.7–3.4] seconds vs 3.3 [2.3–5.4] sec.; p = 0.005). At 30 days, no patient had died and lower NT-proBNP levels were observed in association with randomization to BQ-123 (447 [270–727] pg/mL vs 713 [309–1201] pg/mL; p = 0.150).

Conclusions Short-term ET-A receptor antagonism appears safe in acute STEMI patients undergoing primary PCI. Tissue-level perfusion measured by MRI was improved in the treated group. These findings warrant a larger trial to evaluate clinical endpoints.

Glucometabolic Derangement in Patients With Acute Hyperglycemia During Acute Coronary Syndrome I-6 002

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Aim Because it has been shown recently that acute hyperglycemia during acute coronary syndrome (ACS) is related with worse clinical outcome compared to those with normal admission glucose concentrations, we were interested in the glucometabolic status of ACS patients at admission and its relation to long-term all cause mortality.

Methods 311 patients admitted with the diagnosis ACS who underwent coronary angioplasty with stent implantation were included in the study. Patients were separated according to their glucometabolic status into those with diabetes mellitus (DM), non-diabetic patients with normal admission glucose concentrations (N-AHG) and non-diabetic patients with acute hyperglycemia (AHG). Acute hyperglycemia was defined as admission glucose (AG) concentrations ≥ 140 mg/dl. Blood samples for glucose, insulin, and proinsulin were obtained at time of admission. All cause mortality was assessed at a mean follow-up of 19 ± 13 (mean ± SD) months.

Results The patients' general characteristics (hypertension, hyperlipidemia, family history of coronary artery disease and smoking status) did not differ between groups. There were no differences in admission insulin, proinsulin as well as initial and maximum troponin I plasma levels between the 3 groups. DM and AHG groups displayed the highest AG to proinsulin ratio (AG/proinsulin) as well as insulin to proinsulin ratios compared to those from N-AHG group (p = 0.001). In a Cox-regression analysis AG/proinsulin was predictive for survival (Hazard ratio [HR] 9.04; p = 0.009) in the AHG group.

Conclusion Patients with admission hyperglycemia during ACS exhibit glucometabolic changes, which are mainly reflected by higher admission glucose to proinsulin ratio, which predicts survival.

Primärstenting bei einem Patienten mit Kearns-Sayre-Syndrom und Myokardinfarkt I-8 003

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Das Kearns-Sayre-Syndrom stellt einen seltenen Symptomkomplex dar, der verschiedene Körpersysteme betrifft und auf einer Störung des Muskelstoffwechsels, bedingt durch partielle Deletionen im mitochondrialen Erbgut (delta-mtDNA), die manchmal auch mit einer Duplikation (dup-mtDNA) assoziiert sein können, basiert. Als Folge dieser strukturellen Veränderungen der mitochondrialen DNA manifestiert sich eine schwere, vor allem neuromuskulär betonte Erkrankung, die aber auch Störungen im kardialen Reizleitungssystem, die bis hin zum kompletten AV-Block, zeigt. Koronare Herzkrankheit oder Myokardinfarkt sind in diesem Zusammenhang bislang noch nicht beschrieben.

Bei dem hier im Mittelpunkt stehenden Patienten handelt es sich um einen 45-jährigen Mann. Die ersten Manifestationen des Kearns-Sayre-Syndroms zeigten sich zwischen dem 35. und 38. Lebensjahr. In diesem Zeitraum wurden seine Symptome dieser Erkrankung erstmals zugeschrieben und die Diagnose gesichert. Der Patient wurde mit Thoraxschmerz unter notärztlicher Begleitung in die Erstaufnahme der Universitätsklinik für Innere Medizin gebracht. Relevante Vorerkrankungen: Bekanntes Kearns-Sayre-Syndrom, CPEO im Rahmen der Grunderkrankung (regelmäßige Kontrollen an der Augenklinik), Niereninsuffizienz im Stadium der kompensierten Retention, rezidivierende Synkopen, Nikotinabusus (53 py), Nykturie 2–3×, Depression, Kontrastmittelallergie.

Status und Allgemeinsymptome: 45-jähriger Patient in stark reduziertem Allgemeinzustand, wach, orientiert. Größe: 182 cm, Ge-

wicht: 85 kg, RR: 137/104, Puls: 77, Caput/Collum: Augenmuskelparese; Pulmo: hochstehende Lungenbasen, sonst Vesikuläratmung. Cor: rhythmisch, normokard. Abdomen/Extremitäten: Abdomen gebläht, Darmgeräusche lebhaft in allen 4 Quadranten, kein Druckschmerz, keine Beinödeme; Grob-Neurologisch: Schwäche des linken Armes, Augenmuskellähmung rechts > links.

Ruhe-EKG: Sinusrhythmus, Frequenz 77/min, Linkstyp, PQ-Zeit von 0,2 ms, R/S-Umschlag in V_3, ST-Streckenhebungen in II, III und AVF. Im Katheterlabor wurde eine Notfalluntersuchung mit Koronarangiographie durchgeführt. Es erfolgte eine Sofort-PTCA nach diagnostischer Sitzung (Eingefäß-PTCA) mit Rekanalisation und folgender Zweifachimplantation (Genous; Antikörper-beschichtete Stents) in der RCA. Das Delay war < 3 Stunden. Während der Untersuchung traten keine Komplikationen auf.

Procedere: Hochdosierte Statingabe für 2 Wochen (bis zur Stenteinheilung), danach weiterführende Statin-Normaldosis, Plavix 1 Tablette täglich für 28 Tage und T-ASS 100 mg als Dauertherapie.

Im Rahmen dieser Fallbesprechung stehen sich 2 Krankheitsbilder gegenüber, die sich in ihrer Ätiologie und Pathogenese deutlich voneinander unterscheiden. Einerseits eine mitochondrial vererbte, neuromuskuläre Erkrankung, die auf Basis von Defekten in der DNA zur Manifestation kommt und zu den eher selteneren Varianten des menschlichen Genoms zu zählen ist. Auf der anderen Seite findet sich die koronare Herzkrankheit. Es wird die Frage diskutiert, ob die Manifestation einer KHK in diesem speziellen Fall des 45-jährigen Patienten eine noch nicht beschriebene Facette des Kearns-Sayre-Syndroms sein könnte.

Occurrence of Acute Myocardial Infarction in Winter Tourists: Data from a Retrospective Questionnaire

I-3 **004**

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Purpose In Austria every year 15 million winter tourists arrive from November to April. Acute myocardial infarction (AMI) is the leading cause of death in western countries and may be triggered by physical exertion. The study aimed to evaluate the relationship of first physical activity and the onset of AMI in winter tourists visiting the Tyrolean alps.

Methods We carried out a retrospective analysis of consecutive patients (pts.) admitted to the Department of Internal Medicine III at the Medical University of Innsbruck with the diagnose of an acute myocardial infarction (AMI) between 2006 and 2010. We identified n = 170 pts. from abroad between November and April as potential candidates for the questionnaire. So far we successfully contacted n = 93 pts (mean age: 61 ± 10 years; 16 % female; 71 % STEMIs, 23 % known CAD). We assessed the locations of visit (sea level), duration of stay, and time-point of arrival, first sport activity and onset of symptoms. Furthermore we asked for the kind of activity during AMI, training status, preexisting heart diseases and medication as well as cardiovascular risk factors.

Results 56 % of AMIs occurred within the first two days of physical activity (first two days versus others: Z = 52.747; p < 0.0001). In tourists who suffered AMI during, or within one hour after cessation of activity, (n = 46; 50 %) the mean time from the start of the activity to the onset of symptoms was 1.9 ± 1.7 hours. 52 % of patients were performing < 2 hours of sport per week regularly before their vacation. Although the mean planned vacation time was 8 ± 4 days, only 18 % of myocardial infarctions happen after day 4 of the vacation. Moreover 40 % of the tourists suffered their AMI within the arrival day or the day after (versus others: Z = 22.753; p < 0.0001).

Conclusion The majority of AMIs in tourists happens within the first 2 days after arrival and within the first 2 days of physical activity.

One-Year Mortality in Patients Undergoing Thrombolytic Therapy for Acute ST-Elevation Myocardial Infarction with Different Post-Lytic Strategies in the VIENNA STEMI Network

I-1 **005**

B. Lanschützer, R. Jarai, L. Lanschützer, K. Kalla, G. Christ, R. Karnik, R. Malzer, G. Norman, H. Prachar, W. Schreiber, G. Unger, H. D. Glogar, A. Kaff, A. N. Laggner, G. Maurer, J. Mlczoch, J. Slany, H. S. Weber, K. Huber
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Background and Aim The role of facilitated PCI (fPCI), which is defined as a combination of thrombolytic therapy (TT) and immediate PCI in patients with acute STEMI has been discussed controversially in the past. In the Vienna STEMI registry fPCI was performed guideline-conform between 2003 and 2006. We compared the long-term clinical outcome of this therapeutic strategy to patients after successful TT, who received elective PCI (ePCI) and to non-responders to TT, who received rescue-PCI (rPCI) as well as to patients after TT who were conservatively treated without further intervention.

Methods and Targets Between 2003 and 2006, 171 patients of our registry received TT and completed a one-year follow-up. 32 patients received ePCI, 38 fPCI, 69 received rPCI, and 32 had no PCI after TT. Primary endpoint was 1-year all cause mortality.

Results 1-year mortality of patients receiving ePCI after TT was 4.0 %, patients with the need of rPCI had 5.7 %, patients after fPCI exhibited a 1-year mortality of 22.5 %, and patients who were treated conservatively after TT had a 1-year mortality of 20.5 %, respectively **(Figure 1)**.

Conclusion Although these differences were not statistically significant based on the relatively low patient number the best long-term clinical outcome was seen in patients who received elective PCI after successful TT, followed by patients with rescue PCI after initially unsuccessful TT (4.0 % vs 5.7 %; p = 0.601). Most interestingly, patients with fPCI had a much worse outcome (22.5 % 1-year mortality), which was comparable with patients who had not received any further interventional therapy after TT (20.5 %). These data confirm for the first time the negative influence of facilitated PCI on long-term clinical outcome after initial TT in patients with acute STEMI.

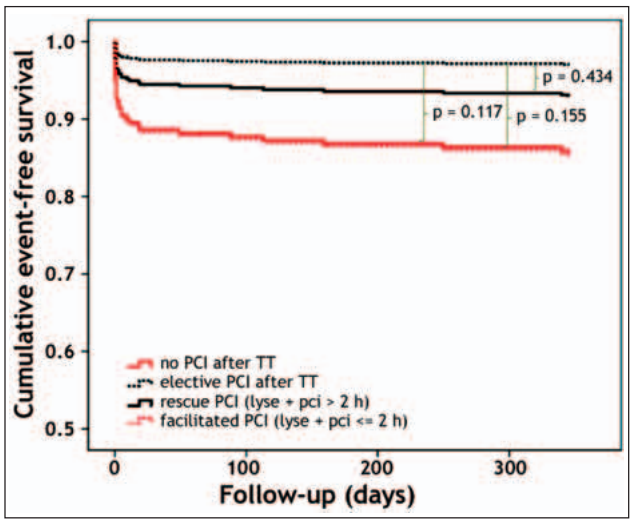

Figure 1: B. Lanschützer et al.

Amino-Terminal pro-B-Type Natriuretic Peptide but not Troponin T or C-reactive Protein Predicts the Presence of Multivessel Disease in Patients With Acute Coronary Syndromes I-7 006

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Background Multivessel disease is associated with adverse outcome after acute coronary syndromes (ACS). In addition, more complex coronary interventions may be required in patients with 2 or more diseased coronary arteries as compared to single vessel disease. Therefore we examined whether elevation of the plasma biomarkers amino-terminal pro-B-type natriuretic peptide (NT-proBNP), troponin T (TNT) or C-reactive protein (hsCRP) may be associated with the presence of multivessel disease in patients with acute chest pain.

Methods and Results We included 308 consecutive patients with acute chest pain who underwent coronary angiography for suspected ACS. We measured NT-proBNP, TNT and hsCRP at admission to the emergency department. All patients underwent coronary angiography. NT-proBNP ($p < 0.001$), TNT ($p < 0.0000001$) and hsCRP ($p < 0.05$) were significantly elevated in patients with acute myocardial infarction ($n = 240$) and all 3 markers were associated with in-hospital death ($n = 15$; NT-proBNP $p < 0.0001$; TNT $p < 0.005$; hsCRP $p < 0.05$). NT-proBNP correlated with the numbers of diseased coronary vessels ($R = 0.26$; $p < 0.000005$) whereas TNT ($R = 0.05$; $p = 0.36$) and CRP ($R = 0.09$; $p = 0.11$) did not show a significant correlation. NT-proBNP was significantly lower in ACS patients with single vessel disease (392.0, IQR 97.4–1484.0 pg/mL) as compared to patients with multivessel disease (752.8, IQR 191.0–2393.5 pg/mL; $p < 0.005$). NT-proBNP significantly predicted the presence of multivessel disease independently from clinical risk factors.

Conclusion Elevated levels of NT-proBNP are significantly associated with the presence of multivessel disease in patients with ACS. In contrast to TNT that is a marker for myocardial necrosis and hsCRP that reflects inflammatory processes, NT-proBNP, a neurohumoral marker for myocardial strain is significantly increased in the presence of multiple diseased coronary vessels during acute ischemia.

Chest Pain Unit (CPU) am Agaplesion Bethanien-Krankenhaus – Konzeption und Realisierung eines Herznotfallraums an einem Belegkrankenhaus I-5 007

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Problemstellung Zeit spielt bei der Versorgung eines akuten Herzinfarktes die entscheidende Rolle. Ziel einer CPU ist es, schnellst möglich eine effektive Therapie sicherzustellen, welche die akut lebensbedrohliche Situation und langfristige Folgeschäden vom Patienten abwendet.

Methode Die Therapie beim Herzinfarkt in Ballungsräumen ist der invasive Eingriff mittels Herzkatheter mit der Möglichkeit der Dilatation und Implantation von Gefäßstützen (Stents). Die Kombination eines räumlichen und organisatorischen Konzeptes soll die Zeit vom Eintritt des Schmerzereignisses bis zum Herzkatheter so kurz wie möglich halten. Dies geschieht unter Einbeziehung der Zentralen Rettungsstelle, des Rettungsdienstes und des Krankenhauses sowie der kardiologischen Fachärzte.

Ergebnisse Die erste Chest Pain Unit (CPU) des Agaplesion Bethanien-Krankenhauses wurde im November 2003 in einem ehemaligen Patientenzimmer des Krankenhauses eingerichtet. Seit August 2006 stehen nun 2 neue CPU-Räume in direkter Anbindung an die ebenfalls neuen Herzkatheter-Messplätze des Cardioangiologischen Centrums Bethanien (CCB) zur Verfügung. Das CCB wird von 10 Kardiologen als Medizinisches Versorgungszentrum (MVZ) betrieben. Zum Anforderungsprofil einer CPU gehört die Realisierung der Lage (freigehaltene überdachte Parkmöglichkeit), der Wege (schnellst möglicher Zugang zum Gebäude und den Durchladeaufzügen), die funktionale Raumstrukturierung (Unterteilung in administrative und Versorgungsbereiche), neueste diagnostische und therapeutische Medizintechnik, Telemetrie-Überwachung und vieles andere mehr.

Fazit Die Räume der CPU sind unter der Berücksichtigung der Wegeführung im Krankenhausbereich so gestaltet, dass eine optimale, schnelle und reibungslose Versorgung von 2 kardiologischen Notfallpatienten, die innerhalb einer Stunde eintreffen, gewährleistet werden kann.

Management bei Patienten mit Akutem Koronarsyndrom – Österreichweite Registerdaten I-4 008

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Zielsetzung Charakterisierung von Patienten, die wegen eines Akuten Koronarsyndroms (ACS) auf einer medizinischen bzw. kardiologischen Abteilung behandelt wurden; Gegenüberstellung von konservativem (medikamentösem) vs. invasivem Management mit Darstellung der medikamentösen Therapie im Krankenhaus (akut) und nach Entlassung.

Methoden Daten aus einem prospektiven österreichweiten Register aus 38 kardiologischen und medizinischen Abteilungen. Erfasst wurden demographische Merkmale, kardiovaskuläre Anamnese, TIMI-Risk-Score (IAP/NSTEMI bzw. STEMI), Begleiterkrankungen, Risikofaktoren, Laborparameter, Vortherapie und Entlassungsmedikation. Für kategorielle Variablen Angabe von Prozent und Gruppenvergleich mit Chi-Square-Test, für metrische Variablen Mittelwert ± Standardabweichung und T-Test, respektive.

Tabelle 1: R. Steinacher et al.

	Konservativ n = 124 (25,1 %)	Invasiv n = 371 (74.9 %)	p-Wert
Alter	71,9 ± 12,3	63,3 ± 12,72	< 0,001
Geschlecht (♂ vs. ♀)	20,4 % vs. 35,0 %	79,6 % vs. 65 %	0,001
Eingeschränkte Nierenfunktion – Kreatinin im Serum (mg/dl)	26 % 1,20 ± 0,66	10,4 % 1,01 ± 0,29	0,001 < 0,001
Herzinsuffizienz	32,0 %	15,7 %	< 0,001
Raucher/Exraucher/ Niemalsraucher	18,7 %/17,9 %/ 51,2 %	37,2 %/21,5 %/ 37,8 %	< 0,001
Instabile Angina pectoris (% IAP)	27,4 % (39,5 %)	14,0 % (60,5 %)	0,001
NSTEMI (% NSTEMI) – TIMI-IAP/ NSTEMI-Score	52,4 % (32,0 %) 3,18 ± 1,35	37,2 % (68,0 %) 3,24 ± 1,43	0,003 n. s.
STEMI (% STEMI) – TIMI-STEMI-Risk-Score	20,2 % (12,1 %) 5,04 ± 2,63	48,8 % (87,9 %) 3,24 ± 2,24	< 0,001 < 0.001
Medikamentöses Akutmanagement			
Acetylsalicylsäure	81,7 %	90,4 %	0,010
Clopidogrel	77,1 %	95,6 %	< 0,001
UFH	19,2 %	51,9 %	< 0,001
NMH	72,7 %	58,7 %	0,012
Entlassungsmedikation			
Acetylsalicylsäure	89,2 %	99,5 %	< 0,001
Clopidogrel	74,1 %	95,9 %	< 0,001
Statine	79,7 %	92,1 %	0,001

Ergebnisse Daten von 501 Patienten wurden erfasst, 6 Patienten anhand der Ausschlusskriterien exkludiert (n = 495). In 25,1 % wurde ein konservatives Procedere eingeschlagen. **Tabelle 1** zeigt eine univariate Gegenüberstellung ausgewählter Parameter.

Fazit Patienten mit ACS, die konservativ behandelt wurden, zeigten gegenüber invasiv behandelten Patienten in der Basischarakteristik und in der medikamentösen Therapie signifikante Unterschiede. In der Akutphase als auch nach Entlassung erhielten diese Patienten in geringerem Anteil eine duale Plättchenaggregationshemmung bzw. Clopidogrel.

Sex-Related Differences in Baseline Characteristics, Management and Outcomes in Patients With Acute Coronary Syndrome Without ST-Segment Elevation (NSTE-ACS) I-2 009

B. Vogel, S. Hahne, R. Jarai, K. Kalla, I. Kozanli, M. Nürnberg, A. Geppert, G. Unger, K. Huber
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Aim To detect sex-related differences in baseline characteristics, management and outcomes in patients with NSTE-ACS.

Methods Data on 813 consecutive patients admitted to our cardiology department for NSTE-ACS were analyzed. Early invasive therapy was defined as percutaneous coronary intervention during first hospital stay. A 4-year follow-up for the clinical endpoint of all-cause mortality could be obtained for 782 patients (342 women and 440 men, respectively).

Results See **Table 2** for sex-related differences in baseline characteristics. While 52.7 % of the male patients received clopidogrel at admission, it were only 43.6 % of the female patients (OR 0.69; 95 %-CI: 0.52–0.92; p = 0.011). The rate of an early invasive therapy was significantly higher among men compared with women (35.2 % vs 27.5 %; OR 0.70; 95 %-CI: 0.51–0.95; p = 0,021). After adjustment for age and comorbidity this difference was not significant anymore (OR 0.89; 95 %-CI: 0.59–1.35; p = 0,588). Short- as well as long-term mortality was found significantly higher in female compared to male patients. However, when performing a cox proportional hazard model to adjust for baseline characteristics and therapy, the worse outcome in female patients could not be detected any longer (HR 0,84; 95 %-CI: 0.62–1.12; p = 0.244).

Conclusion In patients with NSTE-ACS women are less likely to undergo an early invasive therapy in comparison to men due to their higher age and their comorbidities. After adjustment for age, comorbidity and therapy, female gender is not a predictor for worse long-term outcome.

Table 2: B. Vogel et al.

	Female (n = 342)	Male (n = 440)	p-value
Age (mean ± SD years)	75.2 ± 12.0	67.0 ± 14.0	<0.001
Age > 75 a (%)	59.9	33.0	<0.001
Elevated cardiac enzymes (%)	49.4	53.2	0.296
ST-deviations (%)	47.7	37.5	0.004
Clearence < 60 (%)	65.0	32.4	<0.001
TIMI-risk score > 3 (%)	55.0	50.5	0.210
Hypertension (%)	73.1	82.1	0.003
Hyperlipidemia (%)	50.7	61.6	0.003
DM II (%)	28.9	30.9	0.553
Adipositas (%)	51.2	64.9	<0.001
Current smoker (%)	8.4	16.8	0.001
Family history of CAD (%)	9.7	13.1	0.149
No cardiovasc. risk factor (%)	5.7	4.1	0.325
Prior MI (%)	25.4	28.8	0.301
Prior PCI (%)	12.0	18.9	0.008
Prior CABG (%)	5.8	7.8	0.296
No cardiac history (%)	58.5	55.3	0.364
Peripheral vascular disease (%)	5.7	9.6	0.047
Prior stroke (%)	11.0	12.1	0.650

Basic Science

Serum-free Cell Culture Medium Reduces Myocardial Damage After Ischemia in an Experimental Model of Myocardial Infarction: Importance for Cell Therapeutic Methods II-1 010

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Background Over the last decade cardiovascular research has focused on finding optimal specifications for cell therapeutic methods for ischemic heart disease. In most of the previous clinical trials investigating stem cell therapy after myocardial infarction (MI), cells were either suspended in saline solutions, basal cell culture media or serum-free specialty media. The best outcome and long lasting preservation of ventricular function was achieved in trials using stem cell suspensions in serum-free medium. As serum-free specialty media contrary to saline or basal media contain many human or animal proteins such as albumin, insulin and various growth factors, we hypothesized that these factors might influence the outcome after myocardial ischemia in a favorable way. Therefore we sought to authenticate this hypothesis in an experimental rat model of MI.

Methods MI was induced in Sprague-Dawley rats by ligation of the left anterior descending artery. After the onset of ischemia, 300 µl serum-free cell culture medium (UltraCulture™, Lonza, Basel, Switzerland) was injected intravenously. Sham operated and untreated animals served as controls. Histological evaluations were performed three days after MI in order to analyse the cellular infiltration in the infarcted myocardium and the extent of necrotic tissue. Parameters of ventricular function were analysed by echocardiography (ejection fraction, shortening fraction, ventricular diameters and volumes) six weeks after the onset of MI. Infarction size was evaluated by planimetry.

Results Rats injected with serum-free medium evidenced a significant reduction of infarction size (expressed as % of the left ventricle) and an improvement of post MI remodeling after 6 weeks (24 % vs 15 %; p < 0.03). Echocardiography showed a slight positive trend towards functional recovery in medium injected animals as evidenced by a reduced loss of ejection fraction (EF, 42 % in controls vs 45 % in treated animals, n = 12 per group).

Conclusions These data indicate that the administration of serum-free cell culture medium can reduce myocardial damage after ischemia and special emphasis should be put on this issue in experimental models and clinical trials of cell therapy for MI.

Porcine In-vitro-Model of Acute Aortic Dissection II-2 011

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Aims To evaluate the mechanisms of Type B dissections development depending on its position and direction in the porcine aorta.

Methods 25 aortic specimens from 120 kg domestic pigs were clamped to a circulatory model with pulsatile pump and arterial impedance. Dissection was introduced via contralateral incision site. In 10 cases the dissection was placed on the concavity and in 15 cases on the convexity of the aorta.

Results 8 aortic specimens reached requirements of the finally normalized protocol. The mean time of circulation was 47 ± 29 min. A mean pressure of 142 ± 16 mmHg and the mean flow of 4.6 ± 0.4/min were reached. The mean expansion on the dissection was 41 ± 34 mm (median 22 mm) antegrade and retrograde 17 ± 5 mm (median 15 mm). Within these preliminary results, the left subclavian artery and the arterial ligament were found to be anatomic boarders that can stop the expansion of the dissection.

Discussion Porcine aortas are suitable for dissection modeling in an in-vitro circuit, leading to similar dissections as known from clinical findings. The preliminary results suggest that the downstream development occurs faster than the upstream evolution of dissection, and that natural anatomical structures may stop or decelerate the process.

Pleiotropic Effects of Beta-Blockers Upon Subsets of the Inflammatory Cascade Elicited by Experimental Ischemia in Human Myocardial Tissue II-4 013

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Atherosclerosis is a condition which develops with age. Recent experimental evidence suggests a crucial role of T-lymphocytes in the development of atherosclerosis and acute coronary syndromes. It has been indicated that a pro-inflammatory imbalance resulting from T-cell activation could be responsible for activating the inflammatory cascade ultimately responsible for cellular injury, left ventricular dysfunction, remodeling and outcome. In the present study nebivolol is compared with another standard β-blocker, atenolol, commonly used in the treatment of myocardial ischemia.

Myocardial tissue probes derive from the right auricle of patients undergoing cardiac surgery. A small part of the right auricle is removed when the heart is put on extra-corporal circulation. This sample is then be placed in cooled Tyrode solution and hypoxia is brought about by switching 100 % oxygen to 100 % nitrogen (hypoxia) in 1 of the 2 chambers. By doing so, we are able to compare ischemic and non-ischemic tissue of the same patient. Snap frozen samples are stored at –70 °C until RNA isolation. Quality of isolated RNA is analysed by Agilent's Bioanalyzer 2100 system. Arrays are scanned with the AB1700 Chemiluminescence Array Reader and images, data are processed by PANTHER software.

After 30 minutes of myocardial hypoxia we found that gene expression related to T-cell immunity is more than 2-fold up-regulated compared to normoxic controls (25 of 185, 10.4 expected; $p \leq 0.00008$). In contrast, when 22.47 µmol nebivolol has been added to the solution, gene expression related to T-cell mediated immunity is significantly down-regulated (21 down of 249, 7.3 expected; $p \leq 0.0001$). Conversely, 15 of 21 genes down-regulated by nebivolol during experimental hypoxia have been neither up- nor down-regulated in the presence of an equipotent dose of atenolol during experimental hypoxia. Our observations are in accordance with published data indicating that nebivolol reduced the expression of pro-inflammatory genes in endothelial and vascular smooth muscle cells in vitro, whereas metoprolol did not. Similarly, carvedilol has recently been shown to attenuate inflammation.

Conclusion Nebivolol, not Atenolol, inhibits the expression of T-cell immunity related genes during experimental hypoxia. In the light of JUPITER and other recent publications on modulating inflammation by pleiotropic effects of cardiovascular drugs, the specific property of T-cell modulation by nebivolol in myocardial ischemia may warrant further attention.

Shift from Adult to Fetal Metabolic Phenotype During Experimental Ischemia Reiterates the Plasticity of the Molecular Networks Associated With Myocardial Metabolism II-3 012

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The fetal myocardial phenotype predominantly uses glucose for its metabolism, whereas the adult individual mainly metabolises fatty acids. During special conditions, like hypoxia and exercise, the adult phenotype of myocardial metabolism converts to the fetal one, again preferably using glucose as a substrate. It has been shown that a preferentially glucose oriented cardiac metabolism is beneficial in myocardial ischemia.

Our own microarray experiments confirm those data. Here we find that gene-expression of biological processes which are associated with glucose metabolism are up-regulated during hypoxia, whereas those associated with fatty acid and amino-acid metabolism are downregulated. Testing the effects of β-blockers (atenolol and nebivolol) we find a similar shift in well oxigenized preparations, suggesting that the cardiorotective action of β-blockers is brought about by a shift from adult to fetal phenotype of metabolism.

Myocardial ischemia thus increases glucose uptake through translocation of GLUT1 and GLUT4 from an intracellular compartment to the sarcolemma. This appears to be beneficial during ischemia and possibly recovery. Here we find that there is no significant regulation with and without the influence of β-blockers during myocardial ischemia – there is, however, a significant difference between the expression of GLUT1 in well oxygenised preparations with (0.087 ± 0.02) and without nebivolol (0.62 ± 0.02; ± SEM; $p \leq 0.05$). Similarly, atenolol led to an increase of GLUT1-expression in well oxygenated preparations compared to controls: 1.18 ± 0.08 and 0.62 ± 0.02 respectively (± SEM; $p \leq 0.05$). While there is no significant regulation with and without the influence of β-blockers during myocardial ischemia, there is, however, a significant difference between the expression of GLUT4 in well oxygenised preparations with (0.52 ± 0.01) and without nebivolol (0.29 ± 0.02; ± SEM; $p \leq 0.05$). Similarly, atenolol led to an increase of GLUT4-expression in well oxygenated preparations compared to controls: 0.92 ± 0.10 and 0.29 ± 0.02 respectively (± SEM; $p \leq 0.05$).

These results mirror the increased demand of glucose as a substrate in the presence of β-blockers.

Shifting myocardial metabolism to the fetal phenotype has become a new target for anti-anginal treatment in the aging heart. Either by augmentation of glucose metabolism or by inhibiting fatty acid metabolism [Metha, Jusuf et al, 2005]. The latter has been successfully targeted by drugs like trimetazidine and ranolazine [Fragasso, Int J Clin Pract 2007; El-Kady, Am J Cardiovasc Drugs 2005].

Conclusion In summary, here it has been shown for the first time that some of the anti-anginal effects of beta blockers may possibly be conveyed by their action on GLUT 1/4 expression in myocardial cells saw eel as by facilitating glucose metabolism and in turn causing a shift to the fetal phenotype of metabolism in the adult human heart.

Cardiac Release of Hypoxia-Inducible Factor-1alpha After Intracoronary and Intramyocardial Delivery of Mesenchymal Stem Cells in Experimental Myocardial Infarction X-1 014

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Background The cellular response to oxygen is a central process in the pathophysiology of several diseases, including cancer, cardiovascular disease, and stroke. This process is coordinated by the

Hypoxia-Inducible Factor (HIF)-1α, which transactivates genes encoding proteins controlling glucose metabolism, cell proliferation, and vascularization. The aim of our study was to investigate the local myocardial expression of HIF-1α 2h and 24 h after cardiac stem cell delivery in response to intracoronary or intramyocardial SC therapy in the porcine model of chronic myocardial ischemia.

Methods Closed-chest, reperfused myocardial infarction (MI) was created in domestic pigs, using 90 min percutaneous balloon occlusion of the left anterior descending coronary artery followed by reperfusion. Porcine mesenchymal stem cells (MSC) were selected from bone marrow and cultured. The MSC (9.8 ± 1.2 × 106) were delivered either intracoronary (Group IC) in the open infarct-related artery or percutaneously NOGA-guided transendocardially in the infarct border zone (Group IM) or 22 ± 4 days post-MI in the pigs. Pigs without MSC delivery served as shamcontrol (Group S). Plasma HIF-1α was measured at baseline, at 1 h and at 2 h or 24 h by ELISA-kit. Myocardial HIF-1α expression of infarcted, normal myocardium or border zone was determined by western blot.

Results The myocardial tissue HIF-1α expression of the infarcted area was higher in Group IM than in Group IC or Group S (1963 ± 586 vs 1307 ± 392 vs 271 ± 110 activity/mm^2, respectively; $p < 0.05$), while the border zone contained a similarly smaller level of HIF-1α in groups IC and IM (776 ± 335 and 767 ± 230 activity/mm^2), but still significantly higher than in Group S (355 ± 92 activity/mm^2). No significant correlation was found between the number of injected cells and myocardial or plasma HIF-1α level. Subanalysis revealed an obvious trend towards further increase in myocardial expression of HIF-1α in Group IM at 24 h, which was not observed in Group IC.

Conclusions Myocardial delivery of MSCs increases the local myocardial expression of HIF-1α in the infarcted area. Intramyocardial delivery of the MSC seems to be a more effective trigger of the release of the angiogenic factor in infarction, probably due to higher level of SC retention.

Signalling of Muscle-Specific MKK7 Knock-Out Cardiomyocytes Upon Cardiac Stress Stimuli II-5 015

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Introduction Mitogen-activated protein kinase kinase 7 (MKK7) is a well-known activator of c-Jun N-terminal kinases (JNK1, 2, and 3). We previously revealed that the muscle-specific deficiency of MKK7 results in cardiac dysfunction and decompensation upon pressure overload.

Here, we elucidated the impact of MKK7 loss on critical downstream signalling cascades involved in myocardial stress response in vivo and in vitro.

Methods Therefore, control (MKK7$^{fl/fl}$) mice and muscle-specific MKK7 knock-out (MKK7^{MKO}) rodents were sham and transaortic constriction (TAC) operated. In addition, adult mouse cardiac myocytes of both genotypes were isolated and either treated with isoproterenol, phenylephrine, or angiotensin II. After 12 hours, the hearts and cardiomyocytes were harvested, the proteins were extracted and SDS-PAGE was performed. Immunoblotting was carried out using antibodies against: phopho-JNK(T183/Y185), phospho-p38(T180/Y182), phospho-ERK(T202/Y204), phospho-AKT (S473), phospho-GSK3β (Ser9) and were normalized to the total levels of the proteins.

Results Baseline MKK7^{MKO} mice presented cardiac hypertrophy and reduced cardiac function when compared to the control group. Consistently, single cardiomyocytes of MKK7^{MKO} displayed a markedly increased cell area (MKK7$^{fl/fl}$ 2039.3 ± 116.1 μm² vs MKK7^{MKO} 2964.4 ± 182.6 μm²), cell length, and cell width.

Interestingly, phospho-JNK was not significantly reduced in MKK7^{MKO} compared to MKK7$^{fl/fl}$ rodents after sham and TAC surgery. A similar phenotype was evident after in vitro isoproterenol, phenylephrine, and angiotensin II treatment.

AKT and ERK signalling showed minor differences between MKK7^{MKO} and MKK7$^{fl/fl}$ mice in vivo. Phospho-p38 was significantly increased after 12 hours of TAC in the muscle-specific MKK7 knock-out animals. In contrast, neither kinase was unequally regulated among both genotypes in the cardiomyocyte culture experiments.

On the other hand, GSK3β was reduced phosphorylated in MKK7^{MKO} cardiomyocytes in vivo and in vitro which was pronounced after phenylephrine treatment.

Conclusion Loss of MKK7 in cardiomyocytes leads to cellular hypertrophy and cardiac dysfunction. Moreover, the canonical JNK pathway was not influenced in MKK7^{MKO} hearts during in vivo pressure overload and in vitro isoproterenol, phenylephrine, and angiotensin II treatment.

Delayed Recovery of Myocardial Blood Flow After Intracoronary Stem Cell Administration BAII 016

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Background Intracoronary stem cell (SC) transfer in patients with acute myocardial infarction (AMI) may result in reduced flow of the infarct-related artery (IRA). The aim of the present study was to compare the changes in absolute myocardial blood flow (AMF) after intracoronary or intramyocardial injections of mesenchymal SC (MSC) in closed-chest reperfused AMI in pigs.

Methods AMI was created by percutaneous balloon occlusion of the LAD in female domestic pigs. Male MSCs, transiently transfected with Luciferase (Luc-MSC) were delivered (9.6 ± 1.1 × 10^6) intracoronary in the open IRA or NOGA-guided intramyocardially 20 ± 3 days post-MI in female pigs. The AMF was measured immediately after, and 3 and 24 h post Luc-MSC delivery. In vitro bioluminescence images, quantitative real-time TaqMan PCR and tissue luciferase measurements were performed to detect the sex-mismatched MSCs.

Results The AMF decreased significantly immediately after intracoronary MSC delivery (from 56.3 ± 17.5 to 43.1 ± 12.7 ml/min; $p = 0.008$), and remained low at 3 h (43.3 ± 15.3 ml/min; $p = 0.021$) with incomplete recovery at 24 h (48.7 ± 6.9 ml/min; $p = 0.100$). In contrast, intramyocardial Luc-MSC delivery did not influence the AMF (from 55.7 ± 16.2 to 57.7 ± 15.7 ml/min), which remained constant at 3 and 24 h (51.9 ± 6.3 and 52.3 ± 15.6 ml/min, respectively). In vitro bioluminescence displayed transfected Luc-MSCs along the proximal and mid part of the LAD, with high activities in the lymph nodes and bone marrow 3 h after intracoronary delivery. Intramyocardial injections of Luc-MSC led to a cell accumulation in the infarcted area, with less tissue distribution in the remote organs. Y-chromosome-MSCs could be found in the infarcted treated area only after intramyocardial delivery (51.3 ± 27 sry copied/10^5 Luc-MSC cells at 24 h), while larger number of cells was found in the infarct border zone (50.3 ± 19 vs 17 ± 2.6 sry copied/10^5) and in the non-treated myocardium (61 ± 37 vs 2.2 ± 0.8 sry copied/10^5) after intracoronary vs intramyocardial delivery. Luciferase assay confirmed the presence of low number of Luc-MSC in the infarcted area (1.4 % vs at 5.5 % of the originally implanted cells at 24 h; $p = 0.004$) after intracoronary vs intramyocardial injections.

Conclusions Intracoronary injection of SCs results in immediate decrease of AMF, with delayed and partial recovery at 24 h. The diffusion of the SC into the injured myocardium might be hindered by the altered coronary pressure and flow conditions.

Interleukin-33 is Up-Regulated by Oncostatin M and Leptin in Human Smooth Muscle Cells In Vitro

II-6 **017**

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Background The new interleukin 1 family member interleukin 33 (IL-33) – first described in 2005 – plays an important role in different diseases. While IL-33 seems to be protective against atherosclerosis and helminthic infection, it can promote asthma, atopic dermatitis, anaphylaxis and joint inflammation. Later inflammatory effects are most likely caused by expanding T helper type 2 (Th2) cells and by activation of mast cells. Human coronary artery smooth muscle cells (HCASMC) constitutively express IL-33 mRNA. The regulation of IL-33 is poorly described and seems to differ between various cell types. The aim of our study was to investigate the regulation of IL-33 in HCASMC by the pro-inflammatory cytokine oncostatin M (OSM) and by the adipokine leptin, which both are known to be involved in the pathogenesis of atherosclerosis and metabolic syndrome.

Methods HCASMC were isolated from pieces of coronary arteries obtained from patients undergoing heart transplantation. These cells were treated with OSM at concentrations between 100 ng/ml and 0.01 ng/ml or leptin at concentrations between 500 ng/ml and 31.25 ng/ml. Specific mRNA levels for IL-33 were determined by real-time PCR. IL-33 protein in cell lysates and culture supernatants was measured by specific ELISA.

Results We found that HCASMC constitutively expressed IL-33 protein intracellular. In cell culture supernatants only trace levels of IL-33 were detected using a specific ELISA. Both OSM and leptin significantly ($p = 0.05$) increased intracellular IL-33 protein expression. IL-33 protein was increased up to 4-fold after 48 hours (h) of incubation with 100 ng/ml of OSM and up to 2-fold after 48 h of incubation with 500 ng/ml of leptin. The effects of OSM and leptin on IL-33 protein production were dose-dependent. These cytokines also upregulated mRNA specific for IL-33 in HCASMC after an incubation time of 12 h. The results were reproducible in HCASMC isolated from different donors.

Conclusions We found that IL-33 protein is expressed by human coronary artery SMC intracellular. IL-33 is up regulated by the cytokines OSM and leptin. Further investigations to understand the pathophysiological role of these regulations are warranted.

DDAH (Dimethylaminohydrolase) Expression is Decreased in the Presence of Nebivolol

X-2 **019**

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Methylation of arginine residues in proteins and subsequent proteolysis results in the liberation of free methylarginines, including asymmetric dimethylaginine (ADMA; R-Me2), an inhibitor of nitric oxide synthetases (NOS). ADMA is metabolised by dimethylarginine dimethyaminohydrolase (DDAH) to citrulline (CIT) and dimethylamine (MA). ADMA is recognised as a plasma marker of increased cardiovascular risk but it is unclear whether it ever accumulates to sufficient levels to affect NO pathways. However, it has been shown by chemical biology and gene deletion techniques that loss of DDAH function elevates plasma and tissue ADMA levels. On the other hand it is possible that a feed back mechanism exists which regulates DDAH expression upon the availability of NO. In this context, it has to be mentioned that nebivolol can stimulate an increase of endothelial NO, which becomes available at the vascular smooth muscle and induces vaso-relaxation. Nebivolol seems to interact with the endothelial NO pathway in 2 complementary ways: it increases NOS activity and reduces the NO-scavenging radical superoxide anion, by re-directing deranged NOS activity.

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

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

Gene Expression of the Na^+/Ca^{++}-Exchanger is Significantly Down-Regulated by Nebivolol Compared to Atenolol During Experimental Myocardial Ischemia

X-3 **020**

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Cellular Ca^{++}-homeostasis is largely maintained by the transmembrane Na^+/Ca^{++}-exchanger (NCX; 1SLC8A1 [Solute Carrier Family 8, member 16; NCX1]). NCX is a bidirectional transporter that normally extrudes Ca^{++} from the cell (forward mode), but also brings Ca^{++} into the cell (reverse mode) under special circumstances such as intracellular Na^+ accumulation or membrane depolarisation. Changes in NCX function may cause abnormal Ca^{++} release from the sarcoplasmic reticulum (SR) and increase the propensity to abnormal cardiac electrical activity and arrhythmias of all kinds.

Here, using microarray gene expression profiling technique, validated by real time PCR, we find that NCX1 gene expression is significantly down-regulated by nebivolol compared to atenolol in simulated ischemic/hypoxic (N_2-perfused) preparations. In the microarray preliminary analyses we found that NCX1 gene expression is significantly down-regulated by nebivolol compared to atenolol both in O_2-perfused preparations and simulated ischemia/hypoxia (N_2-perfused) preparations. In the presence of atenolol, however, down-regulation of NCX1 is only minimal **(Table 3)**.

Using real-time PCR, we have validated whether or not NCX1 gene expression is significantly down-regulated by nebivolol compared to atenolol in simulated ischemia/hypoxia (N_2-perfused) preparations. It can be seen that, without the influence of β-blockers, there is no significant regulation of NCX1-expression during myocardial ischemia. There is, however, a significant difference between the expression of NCX1during myocardial ischemia in the presence of atenolol (18.0 ± 0.6) and nebivolol (13.6 ± 0.3; ± SEM; $p < 0.05$): NCX1-expression is decreased during ischemia in the presence of nebivolol.

Here, confirmed by real time PCR, the finding that NCX1 gene expression is significantly down-regulated by nebivolol compared to

Table 3: E. Holzwart et al.

	N_2-Hypoxia		O_2-Normoxia	
	Nebivolol: Control	Atenolol: Control	Nebivolol: Control	Atenolol: Control
NCX1	0.33	0.51	0.28	0.83
NCX3	5.66	3.21	5.50	3.72

atenolol in simulated ischemia/hypoxia (N_2-perfused) preparations may argue for a higher protective, anti-ischemic but also anti-arrhythmic potential of nebivolol compared to standard β-blockers like atenolol. Especially patients with ischemia-triggered arrhythmias – patients with ischemic cardiomyopathy, not revascularized ischemia, large myocardial scars – may profit from this particular property of nebivolol over atenolol.

PDK (Pyruvate Dehydrogenase Kinase) is Down-Regulated Both in Normoxic and Hypoxic Myocardium by Nebivolol and not by Atenolol X-4 018

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Pyruvate dehydrogense kinase isoforms inhibit pyruvate dehydrogenase, which constitutes an important step in glucose metabolism. It is involved in various phenomena of aging and its expression changes with age, which is generally not well understood as yet. Cardiac metabolism of glucose is very tightly controlled in order to maintain the variable energy demand that is required by cardiac tissue. Energy metabolism of the cardiac myocyte can be regulated within seconds up to a few minutes or chronically regulated within the time frame of hours to days. Glucose metabolism is activated in early myocardial ischemia and in response to an increased need of high-energy-phosphate in the healthy heart during extreme physical activity. In myocardial ischemia, inhibition of PDK expression would be beneficial in order to shift myocardial metabolism from adult towards the fetal phenotype, thus metabolising more glucose than fat in order to preserve myocardial integrity.

Myocardial tissue probes derive from the right auricle of patients undergoing cardiac surgery. A small part of the right auricle is removed when the heart is put on extra-corporal circulation. This sample is then be placed in cooled Tyrode solution and hypoxia is brought about by switching 100 % oxygen to 100 % nitrogen (hypoxia) in 1 of the 2 chambers. By doing so, we are able to compare ischemic and non-ischemic tissue of the same patient. Snap frozen samples are stored at –70 °C until RNA isolation. Quality of isolated RNA is analysed by Agilent's Bioanalyzer 2100 system. Arrays are scanned with the AB1700 Chemiluminescence Array Reader and images, data are processed by PANTHER software.

In our microarray experiments, we find that, in particular, PDK isoform 4 is significantly less expressed under nebivolol both during O_2 perfusion and simulated ischemia, an effect practically negligible under atenolol. Here, nebivolol also exhibits a unique cardio-protective property, different from standard β-blockers.

We find that, without the influence of β-blockers, there is no significant regulation of PDK-expression during myocardial ischemia. There is just a trend towards a decrease in PDK-Gene expression. There is, however a significant difference between the expression of PDK during myocardial ischemia in the presence of atenolol (3.62 ± 0.18) and nebivolol (1.97 ± 0.06; ± SEM; $p \leq 0.05$): PDK-expression is decreased during normoxia (trend) and ischemia (significant) in the presence of nebivolol.

Here, confirmed by real time PCR, the finding that PDK gene expression is down-regulated by nebivolol compared to atenolol in normoxia (trend, not statistically significant) and simulated ischemia/hypoxia (statistically significant) may argue for a higher protective, anti-ischemic but also anti-anginal metabolic potential of nebivolol compared to standard β-blockers like atenolol. Especially patients with angina may profit from this particular property of nebivolol over atenolol.

Irradiated Apoptotic Peripheral Blood Mononuclear Cells Preserve Ventricular Function After Myocardial Infarction: Implication of the Way of Cell Administration III-7 021

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Background Acute myocardial infarction (AMI) followed by cardiac remodeling is a major cause of congestive heart failure and death. Of clinical relevance are reports that demonstrated that infusion of apoptotic cells lead to allogeneic hematopoietic cell engraftment in transplantation models and to a delay of lethal acute graft-versus-host disease by initiating immunesuppressive mechanisms. Based on these reports, we hypothesized that apoptotic cells can reduce inflammatory reactions after AMI.

Methods Immunemodulatory function of irradiated apoptotic peripheral blood mononuclear cells (PBMC) was evaluated by mixed-lymphocyte reactions (MLR) and co-culture assays using bacterial lipopolysaccharide (LPS) stimulated cells in vitro. Reverse transcription polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay were utilised to determine pro-angiogenic mediators such as Interleukin-8, Vascular endothelial growth factor and Matrix metalloproteinase-9 in viable and apoptotic PBMC. Cell suspensions of irradiated apoptotic PBMC were infused intravenously (i.v.) or injected intracardially (i.c.) in an experimental rat model of AMI. Sham operated animals and rats injected with viable cells served as controls. Cardiac function was analysed by echocardiography (e.g. ejection fraction, EF) and infarction size was determined by planimetry after 6 weeks.

Results Irradiated apoptotic PBMC attenuated immune responses as evidenced in MLR and by reduced secretion of pro-inflammatory factors in stimulation assays. Additionally, transcripts of pro-angiogenic mediators were up-regulated in apoptotic cells as seen in RT-PCR. Rats that were infused or injected with irradiated apoptotic PBMC showed enhanced homing of macrophages and endothelial progenitor cells (EPC) within 72 hours as compared to controls. Planimetric analysis showed a significant reduction of infarction size and improvement of post AMI remodeling with less signs of dilation (infarct dimension 5.8 % of left ventricle in i. v. and 9.1 % in i. c. injected rats, 24.9 % in controls; $p < 0.001$, respectively). Echocardiography revealed that ventricular function was almost preserved in both treatment groups with EF values of 53 % (i. v.) and 55 % (i. c.) in treated animals vs. 42 % in untreated controls compared to 61 % in sham operated rats ($n = 12$ per group; $p < 0.01$).

Conclusions These data indicate that irradiated apoptotic PBMC suspensions, either administered i. v. or i. c., circumvented inflammation, caused preferential homing of regenerative EPC and preserved cardiac function.

Two Receptors for PEDF, ATGL and RPSA are Expressed in Human Adult Cardiac Myocytes II-7 022

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Objective In recent years pigment-epithelium derived factor (PEDF), which was originally described as an ocular antiangiogenic factor, has been also shown to be involved in the pathogenesis of cardiovascular disease. PEDF was shown to be downregulated in cardiac myocytes by hypoxia and its expression was reduced in ischaemic hearts. However, no information is available on the presence of its receptors in the heart. The goal of this study was to study

the expression of the 2 selective receptors for PEDF, namely adipocyte triacylglycerol (ATGL) and 37/67 kDa non-integrin laminin receptor (RPSA), in human adult cardiac myocytes (HACM).

Methods HACM were isolated from explanted human hearts and cultivated. After stimulation with PEDF at a concentration of 400 ng/ml, RNA was isolated from such treated cells at 4, 12, 24 and 48 hours. Quantitative PCR analysis with specific primers was performed to detect specific mRNA for both ATGL and RPSA.

Results Quantitative PCR analysis revealed the presence of ATGL and RPSA in HACM. Stimulation of HACM with PEDF (400 ng/ml) did not regulate mRNA expression of neither ATGL nor RPSA at neither time point tested.

Conclusion We could show for the first time that mRNA specific for both receptors for PEDF, namely ATGL and RPSA, are present in HACM. However, expression of mRNA specific for ATGL or RPSA in cardiac myocytes was not affected by treatment of these cells with their ligand PEDF. Our findings indicate that 2 receptors for PEDF could be involved in the modulation of effects of PEDF on the heart.

Liver Function Tests and Hemodynamics in End-Stage Heart Failure Patients

II-8 **023**

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Purpose End-stage heart failure (HF) is frequently associated with abnormal liver function. Previous studies have demonstrated a predominantly cholestatic enzyme pattern in these patients. Whether this can be attributed to hepatic congestion and/or impaired arterial perfusion is still under debate. Hence, it was the aim of our study to analyse the association between abnormal liver function tests (LFT) and cardiac hemodynamics in end-stage HF patients.

Methods We retrospectively evaluated data from 186 adult patients with end-stage HF (57 ± 10 years, 77 % male) at time of listing for heart transplantation between 1997 and 2009. Serum levels of total bilirubin (T-Bil), γ-glutamyl transferase (GGT), alkaline phosphatase (ALP), alanine transaminase (ALT), and aspartate transaminase (AST) were registered. Hemodynamics were taken from right heart catheterization. Partial correlation coefficients adjusted for sex and age and logistic regression analyses were used to show dependencies between LFTs and cardiac hemodynamics.

Results Patients were characterized by a predominantly cholestatic enzyme pattern (prevalence of T-Bil 34 %, GGT 57 %, ALP 21 %, ALT 13 %, and AST 16 %, respectively). Cholestatic enzymes but not transaminases were significantly associated with hemodynamic indices of right heart failure (RAP, mPAP) and elevated left ventricular filling pressure (PAWP) (**Table 4**). On the contrary, neither cholestatic enzymes nor transaminases were correlated with CI. RAP remained the only independent predictor of T-Bil (r = 0.37; p = 0.028) and GGT (r = 0.44; p = 0.006) in a stepwise multiple regression analysis.

Conclusion Our findings clearly support the concept that cholestatic liver enzyme pattern is associated with hemodynamic indices of right heart failure and congestion in end-stage heart failure patients. In contrast to acute heart failure, low-output and impaired arterial perfusion appears not to essentially impact on LFT abnormalities in end-stage, although stable heart failure.

Table 4: S. Mariacher et al. Partial correlation between hemodynamics and LFTs adjusted for sex and age

		T-Bil	GGT	ALP	ALT	AST
RAP	Correlation	0.396[2]	0.438[2]	0.173	0.000	–0.005
mPAP	Correlation	0.265[2]	0.196[1]	0.222	0.095	0.062
PVR	Correlation	–0.025	0.120	0.230[1]	–0.006	–0.069
PAWP	Correlation	0.328[2]	0.196[1]	0.157	0.0092	0.026
CI	Correlation	–0.092	–0.105	–0.043	0.101	0.099

[1] Correlation is significant at the 0.05 level (2-tailed)
[2] Correlation is significant at the 0.01 level (2-tailed)

Proarrhythmic Effects of Increased Primary Bileacid Levels on Human Atrial Myocardium

X-5 **024**

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Purpose Clinical data indicates that high bileacid levels correlate with an increased incidence of cardiac arrhythmias. In vitro studies on isolated newborn rat cardiomyocytes have demonstrated the proarrhythmic potential of bileacids at pathophysiologic concentrations. The effect of high bileacid levels on human cardiac tissue, however, remains unknown. We aimed to explore the proarrhythmic effect of different primary bileacids on human cardiac tissue.

Methods Human atrial endocardial trabeculae were isolated (n = 63 from 27 patients) and electrically field stimulated (0.5 and 1 Hz) at 37 °C in modified Tyrode's solution containing 2.5 mM Ca^{2+}. Dose-response curves for the appearance of arrhythmic extra-contractions (AECs) were determined for the predominant human primary bile-acids including taurin- and glycin-conjugated cholicacid and chenodeoxycholicacid (TCA, GCA, TCDCA, GCDCA, respectively) at 10, 30, 100, 300 and 1000 µM.

Additionally, 12 trabeculae (from 6 patients) were preincubated with 1 µM BayK 8644 (L-type Ca^{2+}-channel agonist) and the incidence of AECs was compared to trabeculae treated only with TCA (control).

Results Different primary-bile acids evoked AECs (**Figure 2, Table 5**) in human atrial myocardium in a dosedependent manner. At 0.5 Hz stimulation AECs occured at lower concentrations (e.g. the EC50 for GCA treated trabeculae shifted from 262.6 µM to 24.0 µM. Arrhythmias were fully reversible by switching to bileacid free perfusate. Preincubation of trabeculae with BayK 8644 completely abolished arrhythmias upon TCA administration at 1 Hz stimulation; at 0.5 Hz AECs were significantly reduced (1.5 min^{-1} vs 22.5 min^{-1} at 300 µM; $p < 0.05$).

Conclusions Our data suggest that different primary bileacids induce AECs in human atrial myocardium.

These arrhythmias are dose-dependent and occur at pathophysiologic relevant concentrations. Higher pacing frequencies or activation of the L-type Ca^{2+}-channel with BayK 8644 reduces the incidence of AECs, indicating that shortening of diastole acts antiarrhythmic in this setting.

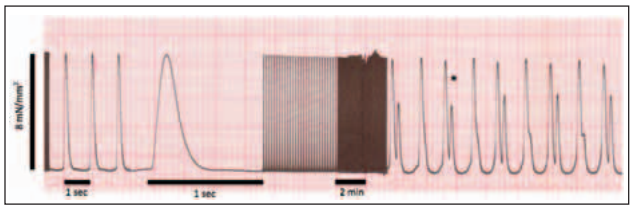

Figure 2: P. P. Rainer et al. AEC (*) at 300 µM GCA at Hz stimulation rate

Table 5: P. P. Rainer et al. Cumulative appearance of AECs at different bile acid concentrations at 1 Hz stimulation rate

Bile acid	AECs @ 100 µM (pat.)	AECs @ 300 µM (pat.)	AECs @ 1000 µM (pat.)
GCA	1/12 = 8.3 %	4/12 = 33.3 %	7/12 = 58.3 %
GCDCA	1/8 = 12.5 %	4/8 = 50 %	7/8 = 87.5 %
TCA	0	4/12 = 30.8 %	9/13 = 69.2 %
TCDCA	2/16 = 12.5 %	10/16 = 62.5 %	13/16 = 81.3 %

Administration of Anti-thymocyte Globulin (ATG) Preserves Ventricular Function After Experimental Myocardial Infarction III-8 025

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Background Despite advances in clinical interventions and drug therapy for cardiovascular disease, congestive heart failure secondary to ventricular remodeling after myocardial infarction (MI) continues to be a significant medical problem. Over the last decades research has focused on finding therapies to reduce inflammatory reactions after an ischemic event which is detrimental for a favorable outcome after MI. Of relevance are reports showing that infusion of apoptotic leucocytes or anti-lymphocyte serum after MI can reduce myocardial necrosis and preserves cardiac function. In order to corroborate this therapeutic mechanism, the utilisation of immunesuppressive agents with a comparable mechanism and proven clinical safety, such as anti-thymocyte globulin (ATG), which induces apoptosis in T cells, was evaluated in this study.

Methods MI was induced in rats by ligation of the left anterior descending artery. Initially after the onset of ischemia, rabbit ATG (10 mg/rat) was injected intravenously. Histological evaluations were performed 3 days after MI in order to analyse inflammatory cell infiltration in the infarcted myocardium. Cardiac function was analysed by echocardiography (ejection fraction, shortening fraction, ventricular diameters and volumes) 6 weeks after induction of MI. Determination of infarction size was conducted by planimetry.

Results Rats treated with ATG evidenced less myocardial necrosis, showed a significant reduction of infarction size (expressed as % of the left ventricle) and an improvement of post MI remodeling after 6 weeks ($p < 0.01$). Furthermore, echocardiography revealed an improved functional recovery in ATG injected animals as evidenced by a reduced loss of ejection fraction (EF, 42.91 % in controls vs 47.13 % in treated animals, n = 10–13 per group).

Conclusions These data indicate that ATG, a therapeutic agent successfully applied in clinical transplant immunology, can salvage ischemic myocardium and improves cardiac function after experimental MI in rats.

Reinfusion of Spleen Cells is Correcting Altered Thrombus Organisation After Splenectomy X-6 026

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Purpose Splenectomy is associated with complicated venous thromboembolism, such as recurrent deep venous thrombosis, portal vein thrombosis, and chronic thromboembolic pulmonary hypertension (CTEPH). It is believed that the loss of mechanical filtering function of the spleen permits the accumulation of senescent blood cells entailing a hypercoagulable state and altered thrombus resolution. The aim of our study was to decipher the population of spleen cells responsible for misguided thrombus resolution.

Methods We utilized a mouse model of stagnant flow venous thrombosis to characterize venous thrombus resolution. Vena cava ligation was performed 1 month after splenectomy. In defined groups, whole spleens or spleens depleted of leukocyte subpopulations were reinfused intraperitoneally into autologous mice. On days 3, 7, 14 and 28 after vena cava ligation thrombi were harvested for histology.

Results Thrombus areas of splenectomized mice were significantly larger than those of controls at all time points (ANOVA, n = 8; $p < 0.03$). Reinfusion of autologous whole spleen homogenates reconstituted a normal pattern of thrombus organisation. The depletion of neutrophils and macrophages led to a significant increase in thrombus size.

Conclusion Reinfusion of spleen cells can restore the normal process of venous thrombus organisation in a mouse model. Cells of the innate immune system appear to be key mediators of thrombus resolution.

JTV 519 verringert arrhythmogene Ca^{2+}-Freisetzungen in Na^{+}-und Ca^{2+}-überladenen Mausherzzellen – die Rolle von CaMKII III-1 027

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Einleitung In Herzmuskelzellen trägt ein Leck von intrazellulär gespeichertem Ca^{2+} durch die Ryanodinrezeptoren (RyRs) des sarkoplasmatischen Retikulums (SR) in das Zytosol während der Diastole maßgeblich zur Entstehung von Arrhythmien bei. Eine Ursache ist ein Proteinkinase A (PKA)- und/oder Ca^{2+}/Calmodulin-abhängige Proteinkinase II (CaMKII)-vermittelter Defekt der RyRs („gain-of-function defect"), z. B. bei chronischer sympathischer (beta-adrenerger) Aktivierung. JTV519 (K201), ein neuartiges Antiarrhythmikum, kann unter Bedingungen der PKA-/CaMKII-Aktivierung das RyR Ca^{2+}-Leck verringern („Ca^{2+}-Stabilizer"). Auch eine hohe zelluläre Ca^{2+}-Beladung führt zu arrhythmogener diastolischer Ca^{2+}-Freisetzung. Wir untersuchten den Einfluss von JTV519 auf das diastolische SR-Ca^{2+}-Leck in Ca^{2+}-überladenen Kardiomyozyten unabhängig von einer PKA- und CaMKII-Aktivierung.

Methoden In stimulierten ventrikulären Kardiomyozyten der Maus wurden zytosolische (Ca^{2+})-Transienten und das diastolische SR-Ca^{2+}-Leck (Ca^{2+}-Spark-Frequenz, SparkF, in s-1*pl-1) quantifiziert. Eine Na^{+}- und Ca^{2+}-Überladung wurde mit dem Na^{+}/K^{+}-ATPase-Inhibitor Ouabain (± OUAB, 100 µM × 7 min) induziert. SR (Ca^{2+}) und zelluläres (Ca^{2+}) ([Ca^{2+}] gesamt) wurden mittels Applikation von Koffein (30 mM) gemessen. Zur Blockade der CaMKII wurde KN93 (1 µM) verwendet. Die Zellen wurden ± JTV519 (1 µM, > 1 Stunde Inkubation) untersucht.

Ergebnisse In Ouabain-behandelten Zellen war die SR- (Ca^{2+}-) Beladung erhöht (7.7 ± 0.6 vs. 6.2 ± 0.5, F/F0, p = 0,07). SparkF stieg während der verlängerten Diastole signifikant von 31 ± 20 auf 85 ± 30 ($p < 0.05$). JTV519 reduzierte dieses diastolische Ca^{2+}-Leck deutlich (SparkF: 25 ± 4; $p < 0.05$), verminderte jedoch auch den Ouabain-induzierten Anstieg der SR (Ca^{2+}) (F/F0: 5.2 ± 0.3 mit JTV519 + Ouab vs. 7.7 ± 0.6 mit Ouab, $p < 0.05$). Die Analyse von Zellen mit vergleichbarem SR (Ca^{2+}) bestätigte jedoch ein signifikant geringeres diastolische Ca^{2+}-Leck in Gegenwart von JTV519 (–64 % vs. Ouabain allein). KN93 hatte keinen Einfluss auf die erhöhte SparkF mit Ouabain, sodass von einem CaMKII-unabhängigen arrhythmogenen diastolischen Ca^{2+}-Leck ausgegangen werden kann. Überraschenderweise hob KN93 jedoch die antiarrhythmische Wirkung von JTV519 auf (JTV519 + Ouabain + KN93: SparkF 89 ± 23; SR [Ca^{2+}] 6,9 ±0,5, n = 11; p = n. s. vs. Ouabain).

Schlussfolgerung JTV519 reduziert die arrhythmogene diastolische SR-Ca^{2+}-Freisetzung auch bei PKA- und CaMKII-unabhängigen diastolischen SR-Ca^{2+}-Leck. Diese Wirkung ist unabhängig von der SR-Ca^{2+}-Beladung. Die Ergebnisse unterstreichen den möglichen Nutzen diese Substanz als Antiarrhythmikum in einer Vielzahl von Bedingungen, die mit einem erhöhten zellulären Ca^{2+} einhergehen. Interessanterweise scheint unter diesen Bedingungen CaMKII eine vermittelnde Rolle hinsichtlich des Effekts von JTV519 auf das RyR-Ca^{2+}-Leck zu haben.

Regulation of Angiogenesis in Pressure-Overload Hyperthrophy III-2 028

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Objective Inadequate capillary growth in pressure-overload left ventricular hypertrophy impairs myocardial perfusion and substrate

delivery, contributing to progression and heart failure. New capillary development is tightly regulated by a variety of factors such as pro-angiogenic growth factors like Vascular Endothelial Growth Factor (VEGF) and endogenous angiogenesis inhibitors such as the splice variant of VEGF Receptor-1 (sVEGFR-1). Binding of VEGF to sVEGFR-1 restricts the amount of VEGF available for VEGFR-2 activation to induce angiogenesis. We sought to determine whether blocking of sVEGFR-1 with Placental Growth Factor (PlGF), which selectively targets sVEGFR-1, releases VEGF to induce angiogenesis and thereby delays heart failure.

Methods Pressure-overload hypertrophy was achieved by banding the descending aorta in 10-day-old rabbits. At 4 wks and 6 wks of age, hypertrophied animals were treated with intra-pericardial administration of rhPlGF (2 µg/kg). Shorting fraction (SF) determined by transthoracic echocardiography was used as a measure of contractile function. At 7 wks of age (de-compensation, heart failure), capillary density (immunohistochemistry) and VEGF release from sVEGFR-1 (ELISA) were measured in age-matched controls (C), untreated hypertrophied (H), and PlGF-treated hypertrophied hearts (PlGF). Data are expressed as mean ± SEM with ANOVA for significance testing ($p \leq 0.05$).

Results Contractile function was preserved in hypertrophied hearts treated with PlGF compared to untreated hypertrophy (PlGF: 43.4 ± 2.1 % SF vs H: 16.81 ± 1.3 % SF vs C: 42.4 ± 1.9 % SF; $p \leq 0.05$). Capillary density was significantly increased in PlGF treated vs untreated hypertrophied and control hearts (PlGF: 1.86 ± 0.07 vs H: 0.733 ± 0.02 vs C: 1 ± 0.01 capillaries/nuclei; $p < 0.001$). PlGF treated hearts showed a significant increase in free, unbound VEGF protein compared to untreated hypertrophied hearts (PlGF: 0.021 ± 0.001 vs H: 0.01 ± 0.0005 pg/ml; $p \leq 0.05$).

Conclusion These results indicate that treatment with PlGF releases sufficient VEGF from soluble VEGFR-1 to promote capillary growth and thereby preserves contractile function and delays the onset of failure in pressure-overload hypertrophy.

Progressive diastolische Dysfunktion in einem Modell des akuten ischämischen Herzversagens nach koronarer Mikroembolisation III-3 030

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Koronare Mikroembolisation (KME) bewirkt auf regionaler Ebene eine akute, progressive Reduktion der systolischen Wandverdickung. Dieser Verlust ist Folge von Ischämie und entzündlichen Prozessen. Wir haben die Effekte einer KME auf die globale linksventrikuläre (LV) Funktion untersucht.

Landwirtschaftliche Schweine (n = 6, 68 ± 2 kg) wurden ohne Eröffnung des Thorax mit Kathetern instrumentiert (Swan-Ganz-Katheter, LV-Konduktanzkatheter, rechtsatriale Schrittmachersonde, intraaortaler Ballonkatheter). Polystyrol-Mikrosphären (45 µm, n = 500.000) wurden unter Durchleuchtung wiederholt in die A. coronaria circumflexa injiziert, bis der Cardiac Power Output um mehr als 40 % reduziert war. Die Daten entsprechen den Zeitpunkten Kontrolle, nach Abschluss der KME (KME 0 h) und 6 h nach KME (KME 6 h).

Die Herzfrequenz (1/min) stieg von 88 ± 4 auf 89 ± 5 und 106 ± 9* an. Das Herzzeitvolumen (l/min) nahm von 6.3 ± 0.4 auf 4.4 ± 0.2* und 4.2 ± 0.2*, der maximale LV-Druck (mmHg) von 127 ± 6 auf 88 ± 3* und 73 ± 4*, das LV dP/dt_{max} (mmHg/s) von 2367 ± 136 auf 1471 ± 42* und 1292 ± 85* und das LV-Schlagvolumen (ml) von 72 ± 5 auf 50 ± 3* und 40 ± 2* ab. Die gemischt-venöse Sauerstoffsättigung (%) sank von 71 ± 2 auf 54 ± 2* und 48 ± 3*. Die Ejektionsfraktion (EF, %) hingegen blieb dabei unverändert (57 ± 3, 50 ± 4 und 54 ± 4; p = n. s.). Die unveränderte EF war auf eine progrediente Reduktion des LV enddiastolischen Volumens (ml) zurückzuführen (123 ± 5, 97 ± 7* und 72 ± 6*,#) (*: $p < 0,05$ vs. Kontrolle; #: $p < 0,05$ vs. KME 0 h). Die enddiastolische Druck-Volumen-Beziehung (EDPVR) wurde durch die KME fortschreitend nach links verschoben (siehe Originalregistrierungen), während die Lage der endsystolischen Druck-Volumen-Beziehung unverändert blieb.

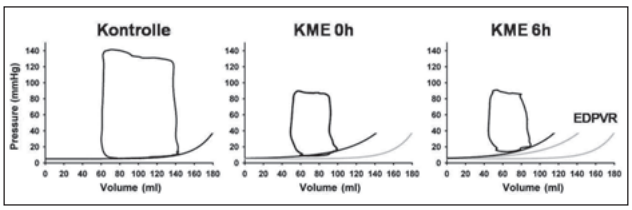

Abbildung 3: M. Schwarzl et al.

Zum akuten Herzversagen nach KME trägt eine diastolische Dysfunktion wesentlich bei; der LV ist nach KME nicht mehr in der Lage, eine adäquate Vorlast aufzunehmen. Dies resultiert auch bei unveränderter EF in einer kritisch reduzierten Pumpleistung **(Abbildung 3)**.

Accelerated Transition of Pressure Overload-Induced Cardiac Hypertrophy to Heart Failure in Mice With a Human RyR2$^{R4496C+/-}$-Mutation BAII 031

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Introduction, Background and Aims Enhanced diastolic Ca^{2+}-release (Ca^{2+}-leak) from the sarcoplasmic reticulum (SR) Ca^{2+}-release channel (ryanodine receptor, RyR2) occurs during heart failure and underlies contractile dysfunction and arrhythmias. However, it remains controversial, whether the diastolic Ca^{2+}-leak via RyR2 activates Ca^{2+}-dependent hypertrophic signalling pathways, and, thus accelerates decompensation from cardiac hypertrophy to heart failure.

Methods To assess the impact of spontaneous SR Ca^{2+}-leak on the progression of heart failure, knock-in RyR2$^{R4496C+/-}$-mice harbouring a mutated human RyR2 associated with catecholaminergic polymorphic ventricular tachycardia (CPVT), underwent minimally invasive transverse aortic constriction (TAC). Transthoracic echocardiography was performed 1 and 3 weeks post-TAC. Hearts, lungs, livers and tibias were dissected and weighed 1 and 3 weeks after TAC or sham-operated surgery. Paraffin-embedded slice sections from hearts were stained with hematoxylin/eosin and picrosirius red for examination of gross morphology and cardiac fibrosis, respectively. Experiments were performed by independent investigators blinded to the treatment and genetic background of the animals.

Results At baseline, WT and RyR2$^{R4496C+/-}$-sham hearts showed comparable gross morphology, fibrosis and cardiac function. In WT and RyR2$^{R4496C+/-}$-mice, TAC induced comparable increases in relative heart weight. However, whereas WT TAC mice exhibited concentric left ventricular hypertrophy with preserved cardiac performance 1 week after TAC, RyR2$^{R4496C+/-}$-TAC mice developed eccentric hypertrophy and significant deterioration of phenotypic changes associated with the transition to heart failure, such as chamber dilatation and left ventricular dysfunction (reduced ejection fraction). The heart failure phenotype in the RyR2$^{R4496C+/-}$-mice further deteriorated 3 weeks after aortic banding, ultimately resulting in lung oedema and increased collagen. RyR2$^{R4496C+/-}$-TAC mice died spontaneously with only 44 % alive after 4 weeks as compared to 85 % alive for WT-TAC mice.

Summary/Conclusion We conclude that increased diastolic SR Ca^{2+}-leak underlies accelerated progression from pressure overload-induced cardiac hypertrophy to heart failure in mice with CPVT. The data suggest that impaired SR Ca^{2+}-handling per se may be causally involved in the development and/or progression of heart failure.

Intrazelluläre Na^+-Homöostase bei diastolischer Funktionsstörung im Frühstadium der Herzinsuffizienz in der Maus

III-4 **032**

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Chronische sympathische Aktivierung trägt bei Patienten wesentlich zum Fortschreiten der Herzinsuffizienz bei. Im Mausmodell mit chronischer beta1-adreneger Stimulation durch kardioselektive Überexpression des humanen beta1-Adrenorezeptors (beta1TG) entwickelt sich über mehrere Monate eine schwere Herzinsuffizienz. Noch vor klinischer Manifestation der Herzinsuffizienz lässt sich in den ventrikulären Kardiomyozyten eine Erhöhung des diastolischen zytosolischen Ca^{2+}-Konzentration ($[Ca^{2+}]$diast) nachweisen, die ursächlich zur Progression der Erkrankung beiträgt. Wir konnten zeigen, dass die frühzeitig erhöhte $[Ca^{2+}]$diast mit einer verringerten Aktivität des sarkolemmalen Na^+-Ca^{2+}-Austauschers (NCX) im Vorwärtsmodus (NCXforward = Ca^{2+} Export) einhergeht. Wir untersuchten nun, ob die verminderte NCXforward-Aktivität auf eine erhöhte zytosolische Na^+-Konzentration ($[Na^+]$) zurückzuführen sein könnte.

Isolierte ventrikuläre Kardiomyozyten von jungen beta1TG- und Wildtyp-Geschwister- (WT-) Mäusen (8–9 Wochen) wurden mit dem Na^+-Indikator SBFI (10 µmol/L × 90 min) beladen.

Das SBFI-Fluoreszenzsignal wurde in intakten Kardiomyozyten kalibriert (Ratiometrie).

Zeitabhängige Veränderungen der Autofluoreszenz der Kardiomyozyten wurden in Parallelmessungen ermittelt. Die zytosolische $[Na^+]$ wurde in ruhenden und elektrisch stimulierten Kardiomyozyten (1–3 Hz) quantifiziert.

Ergebnisse Die Bindungseigenschaften von SBFI waren in betaTG und WT vergleichbar (Kd: 21,3 ± 1,6 vs. 17,5 ± 2,1 mmol/L). Wir konnten einen zeitabhängigen Abfall der Autofluoreszenz der Kardiomyozyten während der Messungen beobachten, der bei der Berechnung von $[Na^+]$ berücksichtigt wurde. In beta1TG und in WT erhöhte sich $[Na^+]$ unter Stimulation mit höherer Frequenz signifikant ($p < 0,05$). In beta1TG-Mäusen war $[Na^+]$ sowohl in ruhenden Kardiomyozyten (24,3 ± 4,5 vs. 14,2 ± 2,5 mmol/L) als auch unter Stimulation mit 1 Hz (27,6 ± 5,1 vs. 17,6 ± 3,5 mmol/L) und 3 Hz (28,6 ± 5,4 vs. 19,7 ± 4,4 mmol/L) tendenziell höher als in WT ($p = 0,21$, ANOVA, n = 14 und n = 8 Zellen resp.).

Schlussfolgerung In einem sehr frühen Stadium der Herzinsuffizienzentwicklung durch beta1-selektive adrenerge Stimulation finden sich Hinweise auf eine erhöhte zytostolische Na^+-Konzentration. Ein erhöhtes $[Na^+]$ verringert die Aktivität von NCXforward, begünstigt die Aktivität des NCX im Rückwärtsmodus (Ca^{2+}-Import) und könnte somit eine wesentliche Ursache der diastolischen Ca^{2+}-Erhöhung sein, die die Entstehung der Herzinsuffizienz in diesem Modell vorantreibt.

Deteriorated Heart Function Is Antagonized by Endurance Training in MKK7 Muscle-Knockout Mice

III-5 **033**

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Introduction C-Jun N-terminal kinases (JNK) pathway is phosphorylated by Mitogen-activated protein kinase kinase 7 (MKK7) and involved in multiple cellular functions. JNK plays an important role in cardiac stress adaptation and apoptosis, but the exact function of JNK is still controversial. Muscle restricted MKK7 knock-out ($MKK7^{MKO}$) results in a decreased cardiac function when compared to MKK7 expressing mice. $MKK7^{MKO}$ mice also develop heart failure after pathologic heart strain by transaortic constriction.

Methods $MKK7^{MKO}$ mice were generated. Hearts were characterized by heart weight to body weight ratios (HW/BW) and heart weight to tibia length (HW/TL) ratios. Cross-sectional area of cardiomyocytes was measured in HE stainings. Furthermore, 6 KO mice and 6 wild type mice were subjected to endurance training on a rodent treadmill. Training was performed daily for 4 weeks at 60–70 % of maximum running speed. Cardiac function was investigated with echocardiography and magnetic resonance imaging before, during and after training regimen.

Results Baseline $MKK7^{MKO}$ mice presented a higher HW/BW ratio, higher HW/TL ratio and reduced cardiac function ($p < 0.001$) when compared to the control group. Consistently, cross-sectional area of cardiomyocytes was markedly increased in $MKK7^{MKO}$ mice. After 4 weeks treadmill training $MKK7^{MKO}$ mice exhibited a similar significant difference in HW/BW ratio, HW/TL ratio and cross-sectional cell area when compared to control mice. However, $MKK7^{MKO}$ mice revealed a significant improvement of cardiac function ($p = 0.006$) after the training regimen (fractional shortening before training 41.1 ± 3.5 %; after training 51.1 ± 3.1 %) while no changes in cardiac function was observed in control mice (fractional shortening before training: 58.4 ± 6.1 %; after training: 57.6 ± 2.3 %). Another study group not subjected to exercise showed no change to baseline values.

Conclusion $MKK7^{MKO}$ mice present a distinct phenotype of reduced cardiac function. This was counteracted by endurance training, after which cardiac function improved to near normal functional characteristics. Hence, loss of MKK7 demonstrates to be beneficial for cardiac adaptation to physiological, but not pathological strain.

Association of the Glycoprotein130 Polymorphism G148A With Soluble Glycoprotein130 Serum Levels in Patients With Coronary Artery Disease

III-6 **034**

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Background The inflammatory cytokine interleukin-6 (IL-6) was described to be elevated in coronary artery disease (CAD) and serum levels were shown to be associated with future cardiac events and mortality. It was suggested that IL-6 exerts its pro-inflammatory actions via transsignalling, which is naturally inhibited by the soluble glycoprotein130 receptor (sgp130). Recently, the gp130 polymorphism G148A was significantly associated with a decreased risk of MI. The aim of this study was to investigate a possible influence of the gp130 polymorphism G148A on serum levels of sgp130 in patients with CAD.

Methods Serum levels of sgp130 were determined in 390 patients with CAD. DNA was extracted from whole blood and gp130 polymorphism was detected by restriction fragment length analysis.

Results 83.1 % of subjects were homozygous for the common allele (GG), 15.9 % heterozygous (GA) and 1 % homozygous for the rare allele (AA). No statistically significant difference in baseline characteristics was observed between the GG-group and the pooled GA/AA-group. Serum levels of sgp130 were significantly higher in the GA/AA-group than in the GG-group ($p = 0.018$). Sgp130 levels did not correlate with any given risk factors for CAD.

Conclusion Our results show that sgp130 serum levels are significantly elevated in patients carrying the gp130 polymorphism G148A. We speculate that the increase of sgp130 might inhibit pro-inflammatory actions of IL-6. This might contribute to the recently described decreased risk of MI in G148A-carriers.

Bildgebung

Gibt es einen Zusammenhang zwischen kardiovaskulären Risikofaktoren und dem koronaren Kalziumscore? IV-1 035

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Einleitung Obwohl Kalziumscoring in einer Population mit niedriger Vortestwahrscheinlichkeit ein anerkanntes Verfahren zur nichtinvasiven KHK-Diagnostik ist, gibt es widersprüchliche Daten über dessen Korrelation mit traditionellen Risikofaktoren. Insbesondere bei älteren Patienten zeigt die Erfahrung, dass nicht immer von einer ausgeprägten Kalzifizierung auszugehen ist. Ziel dieser retrospektiven Pilotstudie war die Untersuchung des Zusammenhangs zwischen Koronarkalzifikation, quantifiziert anhand des Agatston-Scores (AS), und etablierten kardiovaskulären Risiko- sowie demographischen Faktoren.

Methoden Zwischen Jänner 2008 und Februar 2010 wurde bei 145 PatientInnen ein Kalziumscoring durchgeführt. Bei allen wurde der AS mit einem 64- bzw. 128-Zeilen-MSCT erhoben. Die Erfassung der demographischen sowie Risikofaktoren (Alter, Geschlecht, Größe, Körpergewicht, Nikotin, art. Hypertonie, Hyperlipidämie, Diabetes mellitus [DM], Vorliegen einer CAVK) erfolgte retrospektiv anhand der Krankengeschichten. Normalverteilte Werte wurden mittels ungepaartem t-Test verglichen, nicht normalverteilte Werte mittels Mann-Whitney-Test. Mittels Uni- und Multivariatanalyse wurden unabhängige Vorhersageparameter für eine hochwahrscheinliche KHK (AS > 400) bestimmt.

Ergebnisse 119 PatientInnen (45 Frauen [37,8 %], 74 Männer [62,2 %]) wurden aufgrund der vollständig vorliegenden Information in die Studie eingeschlossen. Bei 45 PatientInnen (37,8 %) bestand zum Zeitpunkt der Untersuchung ein Nikotinabusus, bei 93 (78,2 %) fand sich ein art. Hypertonus, bei 17 (14,3 %) DM, bei 78 (65,5 %) eine Hyperlipidämie und bei 30 (25,2 %) eine CAVK. Ein signifikant höherer Agatston-Score bestand bei Hyperlipidämie (567,1 ± 982,3 vs. 185,0 ± 498,7; p = 0,021), bei Hypertonie (531,1 ± 948,0 vs. 93,6 ± 245,0; p = 0,022) sowie bei CAVK (1208,8 ± 1230,9 vs. 163,1 ± 450,4; p < 0.001). Das Vorliegen einer Hyperlipidämie oder einer CAVK war ein unabhängiger Risikofaktor für einen AS über 400 (p < 0,001 bzw. p = 0,001). Ab einem Alter von 50 Jahren war der AS signifikant erhöht (540,9 ± 938,5 vs. 18,2 ± 79,4; p < 0,001); es gab keine direkte Korrelation zwischen Alter und AS.

Schlussfolgerung Im vorliegenden Niedrig-Risiko-Kollektiv waren Hyperlipidämie, art. Hypertonie und ein Alter > 50 Jahren mit einem AS > 400 assoziiert. Das Fehlen einer direkten Korrelation zwischen Alter und AS in diesem Kollektiv deutet auf einen möglicherweise unterschätzten klinischen Stellenwert des Kalziumscorings für ältere PatientInnen hin.

Prognostische Wertigkeit der Koronar-CT-Angiographie bei Brustschmerzpatienten mit niedrigem und mittleren KHK-Risiko im Langzeitverlauf XI-1 036

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Hintergrund Die Koronar-CT-Angiographie (CCTA) ist eine etablierte Methode zum Ausschluss von Koronarstenosen. Ziel unserer Studie war es, die prognostische Wertigkeit der CCTA im Langzeitverlauf bei Patienten mit niedrigem und mittlerem KHK-Risiko zu untersuchen, bei denen wegen Brustschmerzen eine CCTA zum Ausschluss einer KHK durchgeführt wurde.

Patienten & Methodik Alle Patienten ohne kardiale Vorerkrankungen und koronare Interventionen sowie einem niedrigen bis mittleren KHK-Risiko, bei denen im Jahr 2007 an unserer Abteilung wegen Brustschmerzen eine CCTA durchgeführt wurde, wurden in einer prospektiven Datenbank erfasst. Entsprechend dem Ergebnis der CCTA wurden sie in 3 Gruppen unterteilt.

- Gruppe 1: Normales CT-Koronarangiogramm (Agatston-Score-Äquivalent = 0)
- Gruppe 2: Geringe Koronarsklerose ohne signifikante Stenose (≤ 50 % Lumeneinengung)
- Gruppe 3: Vorhandensein zumindest einer Koronarstenose mit einer Lumeneineingung von > 50 %

Bei allen Patienten der Gruppe 3 wurde nach der CCTA eine invasive Koronarangiographie und falls erforderlich eine Revaskularisation (PCI) durchgeführt. Mittels Telephoninterviews, Befragung der behandelnden Hausärzte und Meldeamtsanfragen wurden kardiale Ereignisse (kardiovaskulärer Tod, interventionelle oder operative Revaskularisation, instabile Angina, NSTEMI, STEMI) erhoben.

Ergebnisse Wir schlossen 316 Patienten in die Studie ein. Lediglich 7 Patienten (2 %) konnten nicht kontaktiert werden. Fünf Patienten (1,6 %) starben (nicht-kardiovaskuläre Todesursachen). Die mittlere Follow-up-Dauer der nachgesorgten Population (n = 309, 54 % weiblich, Alter 56 ± 12 Jahre) betrug 28 ± 5 Monate. Bei allen Patienten der Gruppe 1 (n = 174, Agatston-Score-Äquivalent = 0) und 2 (n = 99, Agatston-Score-Äquivalent 140 ± 255) traten keine kardialen Ereignisse auf (negativer prädiktiver Wert = 100 %). Bei 12 Patienten der Gruppe 3 (n = 36, Agatston-Score-Äquivalent 508 ± 634) wurden folgende kardiale Ereignisse erhoben: 7 PCIs und 5 Bypass-OPs im Anschluss an die Koronarangiographie nach CCTA, ein STEMI und 8 PCIs im Langzeit-Follow-up.

Schlussfolgerung Bei Patienten mit Brustschmerzen und niedrigem bis mittlerem KHK-Risiko sowie fehlender KHK-Anamnese kann mittels CCTA eine Population mit exzellenter Langzeitprognose (Patienten mit normalen Koronarien oder geringer Sklerose) sicher identifiziert werden.

Beurteilung der Koronararterienostien nach CoreValve®-Aortenklappenimplantation mittels 64-Zeiler-Spiral-CT-Koronarangiographie IV-2 037

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Hintergrund Vor Implantation kathetergestützter Aortenklappen hat sich die hochauflösende Spiral-Computertomographie („64-Zeiler", CT) neben transösophagealer Echokardiographie und Angiographie zur Größenbestimmung des Aortenklappenanulus bereits durchgesetzt.

Die nicht-invasive Bildgebung mittels CT-Koronararterienangiographie (CT-CA) nach perkutanem Aortenklappenersatz hat bis jetzt noch keinen gesicherten Stellenwert. Wir überprüften die Aussagekraft der CT-CA in der Evaluierung der Koronararterienostien nach erfolgtem perkutanen Klappenersatz.

Methodik Bei allen Patienten (Pat.), denen im Zeitraum von Dezember 2008–September 2009 eine perkutane Aortenklappe (CoreValve®-Klappe) implantiert wurde, wurde 3 Monate nach Implantation eine CT-CA mittels 64-Zeiler (Siemens Somatom Sensation 64 Cardiac) durchgeführt.

Die technische Durchführung erfolgte mit einer Rotationszeit von 330 ms und einer Kollimation 64 × 0,6 mm. Eine Koronarkalkbestimmung (Agatston-Kalkscore) wurde aufgrund der klappenbedingten Artefaktüberlagerungen nicht durchgeführt.

Das Hauptaugenmerk unserer Untersuchung lag darin zu evaluieren, inwieweit die Koronararterienostien durch den endoluminalen Klappenersatz beeinträchtigt waren.

Ergebnisse Insgesamt wurden 15 Pat. (8 männlich; mittleres Alter 85 ± 7 Jahre) untersucht. Bei 5 Patienten konnte eine weitere Evaluierung nicht erfolgen (3 Pat. verstarben innerhalb von 3 Monaten nach erfolgter Klappenimplantation, 1 Pat. wurde infolge eines perinterventionellen Insults und 1 Pat. wegen eines Kreatininwertes > 2 mg/dl nicht weiter evaluiert).

Die Bildqualität der CT-CA erlaubte die Evaluierung beider Ostien bei allen Pat. Hierbei zeigten sich Hauptstamm der linken Koronararterie und Ostium der rechten Koronararterie durch den endoluminalen Aortenklappenersatz nicht beeinträchtigt.

Aussagen über eventuell vorliegende Stenosen oder deren Schweregrad in der Gefäßperipherie konnten jedoch aufgrund der Artefaktüberlagerung durch liegende Schrittmachersonden (8 Pat., jeweils im Verlauf der rechten Koronararterie) und höhergradige Verkalkungen der Gefäße der alten, oft multimorbiden Pat., nicht getroffen werden.

Schlussfolgerung Nach Implantation einer CoreValve®-Aortenklappe können die Koronarostien in Hinblick auf eine eventuelle Kompromittierung durch den Klappenring gut mittels CT-CA evaluiert werden. Die Gefäßperipherie ist jedoch durch Artefaktüberlagerungen infolge der bei dieser Patientenpopulation häufigen Schrittmachersonden und höhergradigen Verkalkungen nur eingeschränkt beurteilbar.

Gibt es geschlechtsspezifische kardiovaskuläre Risikofaktoren? Ein Klärungsversuch mittels Kalzium-Scoring

IV-3 **038**

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Einleitung Der Zusammenhang zwischen kardiovaskulären Risikofaktoren und koronarer Kalzifizierung und insbesondere dessen Aufschlüsselung nach Geschlechtern ist bis dato unzureichend untersucht. Die vorliegende retrospektive Pilotstudie ging der Frage nach, ob die Koronarkalzifikation, quantifiziert anhand des Agatston-Scores (AS), bei Frauen und Männern unterschiedlich mit etablierten kardiovaskulären Risikofaktoren assoziert ist.

Methoden Zwischen Jänner 2008 und Februar 2010 wurde bei 145 PatientInnen ein Kalziumscoring durchgeführt. Bei allen wurde der AS mit einem 64- bzw. 128-Zeilen-MSCT erhoben. Die Erfassung der demographischen sowie Risikofaktoren (Alter, Geschlecht, Größe, Körpergewicht, Nikotin, art. Hypertonie, Hyperlipidämie, Diabetes mellitus [DM], Vorliegen einer CAVK) erfolgte retrospektiv anhand der Krankengeschichten. Normalverteilte Werte wurden mittels ungepaartem t-Test verglichen, nicht normalverteilte Werte mittels Mann-Whitney-Test. Die Daten wurden getrennt für Frauen und Männer untersucht.

Ergebnisse 119 PatientInnen (45 Frauen [37,8 %], 74 Männer [62,2 %]) wurden aufgrund der vollständig vorliegenden Information in unsere retrospektive Studie eingeschlossen. Das Alter betrug im Mittel bei Frauen 59,7 ± 13,4, bei Männern 59,5 ± 13,6 Jahre. Männer hatten einen tendenziell höheren AS als Frauen (548,6 ± 1003,7 vs. 249,5 ± 525,1; p = 0,067). Ab einem Alter von 50 Jahren war sowohl bei Frauen (319,7 ± 577,9 vs. 4,0 ± 12,0; p = 0,003) als auch bei Männern (670,0 ± 1079,3 vs. 28,3 ± 103,8; p < 0.001) der AS erhöht. Raucherinnen waren, wie auch Raucher, signifikant jünger als NichtraucherInnen (Frauen 53,4 ± 9,7 vs. 62,2 ± 13,9 Jahre; p = 0,031; Männer 54,6 ± 14,2 vs. 63,8 ± 12,0 Jahre; p = 0,003). Hypertoniker zeigten einen deutlichen Trend zu einem höheren AS (664,4 ± 1095,7 vs. 128,7 ± 317,6; p = 0,058), Hypertonikerinnen/Nicht-Diabetikerinnen hatten einen signifikant höheren BMI als Nicht-Diabetikerinnen (31,3 ± 6,1 vs. 26,0 ± 4,3; p = 0,032), bei Männern zeigte sich hier kein Unterschied. Bei beiden Geschlechtern fand sich kein Zusammenhang zwischen DM und dem AS. Sowohl Frauen wie auch Männer zeigten eine signifikante Assoziation von CAVK und hohem AS (Frauen 823,2 ± 617,1 vs. 143,8 ± 438,6; p = 0,01; Männer 1321,3 ± 1348,5 vs. 177,65 ± 463,1; p < 0,001).

Zusammenfassung Bei Männern zeigte sich ein Trend zu einem höheren Kalzifizierungsgrad bei Hypertonikern, ansonsten zeigten beide Geschlechter einen vergleichbaren Einfluss der Risikofaktoren auf die koronare Kalzifizierung.

Myocardium at Risk in ST-Elevation Myocardial Infarction: Comparison of T2 Edema Imaging Using Magnetic Resonance Versus Angiographic Scoring

IV-4 **039**

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Background The assessment of the area at risk (AAR) in acute myocardial infarction (AMI) with T2-weighted imaging using magnetic resonance imaging (MRI) is a relatively new method with only limited clinical data; yet, sufficient validating studies are lacking. Purpose of this trial was to assess the AAR and myocardial salvage by MRI and to compare it to the validated angiographic APPROACH-score in a large consecutive patient cohort.

Methods From November 2006 to February 2008 202 patients undergoing primary angioplasty in AMI with ST-elevation were enrolled. Myocardial salvage was assessed by MRI 2–4 days after primary PCI with measurement of the extension of myocardial edema in T2-weighted images and of infarct size with delayed enhancement imaging. Angiographic scoring was done by use of the APPROACH-score.

Results All images were assessable for measurements of the AAR, infarct size and consecutively myocardial salvage. All infarcts consistently revealed a pattern with both reversibly and irreversibly injured tissue. In contrast to the infarcted area, reversible damage was always transmural. The AAR in the MRI-studies showed a good correlation with the angiographic AAR (r = 0.870; p < 0.001). However, as shown by Bland-Altman-analyses, there was a certain bias towards an overestimation of the AAR by MRI in comparison to angiographic scoring (35.7 ± 10.9 % LV vs 28.0 ± 10.5 % LV, difference 7.7 ± 5.5; p < 0.001). The infarct size measured by MRI was 18.0 ± 11.6 % LV. The calculated myocardial salvage was 17.7 ± 11.7 % LV. The time from symptom-onset to reperfusion had a significant impact on the myocardial salvage.

Conclusion AAR measurement by MRI shows excellent correlation to the angiographic APPROACH-score with slight overestimation. This might be explained by the former validation of the angiographic score by pathological studies mostly in human hearts without recent myocardial infarction.

Kann die Analyse des globalen Strain mittels 2D-Seckle-Tracking die kardiale Magnetresonanzuntersuchung beim Screening nach kardialer Beteiligung bei Sarkoidose ersetzen?

IV-8 **040**

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Einführung Bei Patienten mit Sarkoidose kann eine kardiale Beteiligung mittels kardialer Magnetresonanzuntersuchung anhand eines subepikardialen oder transmuralen „Late enhancement" nachgewiesen werden. Wir haben untersucht, ob bei Patienten mit Sarkoidose, die mittels kardialer Magnetresonanzuntersuchung hinsichtlich einer kardialen Beteiligung gescreent wurden, das Vorhandensein und die Lokalisation eines „Late enhancement" die mittels 2D-Speckle-Tracking analysierten Strain-Qualitäten beeinflusst.

Methode In einem Zeitraum von 5 Jahren wurden 14 konsekutive Patienten mit Sarkoidose mittels kardialer Magnetresonanzuntersuchung hinsichtlich einer kardialen Beteiligung gescreent. Bei 12 Patienten wurde ein Echo durchgeführt (86 %), bei 10 Patienten (71 %) wurde der globale Strain mittels 2D-Speckle-Tracking analysiert, dabei war bei 70–90 % der langen Achsen bzw. bei 60 % der kurzen Achsen die Bildqualität so gut, dass im jeweiligen Schnitt alle Segmente mit 2D-Speckle-Tracking analysiert werden konnten. Der globale Strain wurde nur bei jenen Patienten analysiert, die eine gute Linksven-

trikelfunktion und einen normofrequenten Sinusrhythmus hatten, und bei denen im jeweiligen Schnitt alle Segmente verwertbar waren.

Ergebnisse Bei der kardialen Magnetresonanzuntersuchung fand sich bei einem Patienten ein umschriebenes subendokardiales „Late enhancement" (bei diesem Patienten wurde eine koronare Herzkrankheit angiographisch verifiziert), bei einem Patienten ein subepikardiales „Late enhancement", bei den restlichen Patienten fand sich kein „Late enhancement". Bei den Patienten ohne „Late enhancement" war der globale Strain normal (longitudinaler Strain 4-Kammerblick: 19,6 ± 2,06, longitudinaler Strain 2-Kammerblick: 17,96 ± 2,87; longitudinaler Strain 3-Kammerblick: 16,22 ± 3,90, zirkumferenzieller Strain: 18,8 ± 2,57, radialer Strain: 35,3 ± 9,39, Rotation: 7,26 ± 3,49), bei dem Patienten mit subepikardialem „Late enhancement" war der globale Strain mit Ausnahme des radialen Strain ebenfalls normal (longitudinaler Strain 4-Kammerblick: 20,4, longitudinaler Strain 2-Kammerblick: 19,0, longitudinaler Strain 3-Kammerblick: 18,1, zirkumferenzieller Strain: 19,5, radialer Strain: 22,8, Rotation: 5,4). Bei allen Patienten ohne „Late enhancement", bei denen die diastolische Funktion untersucht wurde, war die diastolische Funktion normal, bei dem Patienten mit subepikardialem „Late enhancement" fand sich eine Relaxationsstörung.

Schlussfolgerung Der Stellenwert der Analyse des globalen strain mittels 2D-Speckle-Tracking beim Screening nach kardialer Beteiligung bei kardialer Sarkoidose scheint im Vergleich mit der kardialen Magnetresonanzuntersuchung eher gering, die Fragestellung sollte anhand einer größeren Fallzahl untersucht werden.

Kann die Analyse des globalen Strain mittels 2D-Speckle-Tracking die kardiale Magnetresonanzuntersuchung bei der Differenzierung zwischen Linksventrikelhypertrophie ohne intramurale Fibrose, Linksventrikelhypertrophie mit intramuraler Fibrose und Amyloidose ersetzen? IV-6 042

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Einführung Aufgrund von Unterschieden zwischen der Faserarchitektur von subendokardialem, intramuralem und subepikardialem Myokard wird vermutet, dass subendokardiale Pathologien andere Strain-Qualitäten beeinflussen als intramurale Pathologien. Bei kardialen Magnetresonanzuntersuchungen findet man ein globales subendokardiales „Late enhancement" bei kardialer Amyloidose, ein intramurales „Late enhancement" hingegen u. a. bei hypertropher Kardiomyopathie, bei Morbus Fabry sowie bei erhöhter Nachlast wie bei Aortenklappenstenose oder arterieller Hypertonie. Wir haben untersucht, ob bei Patienten, bei denen zur Abklärung einer Linksventrikelhypertrophie eine kardiale Magnetresonanzuntersuchung durchgeführt wurde, das Vorhandensein und die Lokalisation eines „Late enhancement" die mittels 2D-Speckle-Tracking analysierten globalen Strain-Qualitäten beeinflusst.

Methode In einem Zeitraum von 5 Jahren wurde bei 35 Patienten eine kardiale Magnetresonanzuntersuchung zur Abklärung einer Linksventrikelhypertrophie durchgeführt. Bei 21 Patienten (60 %) lag eine arterielle Hypertonie vor, eine Aortenklappenstenose fand sich bei keinem Patienten. Die maximale myokardiale Wandstärke der Patienten ohne „late enhancement", mit intramuralem „late enhancement" bzw mit globalem subendokardialem „Late enhancement" betrug 18,13 ± 5,89 mm, 25,67 ± 5,68 mm bzw. 20,5 ± 0,71 mm. Bei 28 Patienten (80 %) wurde der globale Strain mittels 2D-Speckle-Tracking analysiert, dabei war bei 75–82 % der langen Achsen bzw. bei 54 % der kurzen Achsen die Bildqualität so gut, dass im jeweiligen Schnitt alle Segmente mit 2D-Speckle-Tracking analysiert werden konnten. Der globale Strain wurde nur bei jenen Patienten analysiert, die eine gute Linksventrikelfunktion und einen normofrequenten Sinusrhythmus hatten, und bei denen im jeweiligen Schnitt alle Segmente verwertbar waren.

Ergebnisse Zwischen Patienten ohne „Late enhancement" bzw. Patienten mit intramuralem „Late enhancement" fand sich kein signifikanter Unterschied hinsichtlich des globalen Strain (longitudinaler Strain 4-Kammerblick: 17,2 ± 3,35 bzw. 20,5 ± 3,99 [p = 0,09], longitudinaler Strain 2-Kammerblick: 17,99 ± 3,10 bzw. 19,37 ± 6,40 [p = 0,29], longitudinaler Strain 3-Kammerblick: 18,54 ± 2,49 bzw. 17,0 ± 5,37 [p = 0,25], zirkumferenzieller Strain: 16,2 ± 6,43 bzw. 16,6 ± 4,24 [p = 0,47], radialer Strain: 28,57 ± 15,9 bzw. 12,45 ± 2,19 [p = 0,11], Rotation: 7,19 ± 4,04 bzw. 8,45 ± 0,92 [p = 0,34]). Bei Patienten mit globalem subendokardialem „Late enhancement" waren im Vergleich mit Patienten ohne „Late enhancement" bzw. Patienten mit intramuralem „Late enhancement" der globale longitudinale Strain und die Rotation, nicht jedoch der globale zirkumferenzielle Strain und der radiale Strain signifikant erniedrigt (longitudinaler Strain 4-Kammerblick: 6,05 ± 1,63 [p = 0,0006 bzw. 0,009], longitudinaler Strain 2-Kammerblick: 5,6 [nur 1 Wert], longitudinaler Strain 3-Kammerblick: 5,6 [nur 1 Wert], zirkumferenzieller Strain: 14,7 ± 7,07 [p = 0,39 bzw. 0,37], radialer Strain: 11,4 ± 11,8 [p = 0,10 bzw. 0,45], Rotation: 5,15 ± 1,91 [p = 0,05 bzw. 0.02]). Auffällig ist, dass – im Gegensatz zu den anderen Strain-Qualitäten – bei allen Patienten mit Linksventrikelhypertrophie der radiale Strain deutlich niedriger ist als bei Gesunden.

Schlussfolgerung Bei Patienten mit Linksventrikelhypertrophie, guter Linksventrikelfunktion und normofrequentem Sinusrhythmus finden sich im Vergleich mit Patienten ohne „Late enhancement" signifikante Veränderungen hinsichtlich des mittels 2D-Speckle-Tracking analysierten globalen Strain nur bei Patienten mit globalem subendokardialem „Late enhancement", nicht jedoch bei Patienten mit intramuralem „Late enhancement"; die Analyse des globalen Strain mit 2D-Speckle-Tracking erlaubt daher in diesem Patientengut im Gegensatz zur kardialen Magnetresonanzuntersuchung nur die Verdachtsdiagnose einer Amyloidose, nicht jedoch die Differenzierung zwischen Fehlen oder Vorhandensein einer intramuralen Fibrose.

Kann die Analyse des globalen Strain mittels 2D-Speckle-Tracking die kardiale Magnetresonanzuntersuchung bei der Differenzierung zwischen Normalbefund, Myokarditis und akutem Koronarsyndrom ersetzen? IV-5 041

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Einleitung Aufgrund von Unterschieden zwischen der Faserarchitektur von subendokardialem und subepikardialem Myokard wird vermutet, dass subendokardiale Pathologien andere Strain-Qualitäten beeinflussen als subepikardiale Pathologien. Bei kardialen Magnetresonanzuntersuchungen findet man ein subendokardiales „Late enhancement" u. a. beim akuten Koronarsyndrom, ein subepikardiales „Late enhancement" u. a. bei der Myokarditis. Wir haben untersucht, ob bei Patienten mit Verdacht auf eine Myokarditis, bei denen eine kardiale Magnetresonanzuntersuchung durchgeführt wurde, das Vorhandensein und die Lokalisation eines „Late enhancement" die mittels 2D-Speckle-Tracking analysierten globalen Strain-Qualitäten beeinflusst.

Methode In einem Zeitraum von 5 Jahren wurde bei 99 konsekutiven Patienten mit Verdacht auf Myokarditis eine kardiale Magnetresonanzuntersuchung durchgeführt. Bei 82 Patienten (83 %) wurde der globale Strain mittels 2D-Speckle-Tracking analysiert, dabei war bei 81–83 % der langen Achsen bzw. bei 52 % der kurzen Achsen die Bildqualität so gut, dass im jeweiligen Schnitt alle Segmente mit 2D-Speckle-Tracking analysiert werden konnten. Der globale Strain wurde nur bei jenen Patienten analysiert, die eine gute Linksventrikelfunktion und einen normofrequentem Sinusrhythmus hatten, und bei denen im jeweiligen Schnitt alle Segmente verwertbar waren.

Ergebnisse Zwischen Patienten ohne „Late enhancement" bzw. Patienten mit subepikardialem „Late enhancement" fand sich kein signifikanter Unterschied hinsichtlich des globalen Strain (longitudinaler Strain 4-Kammerblick: 16,65 ± 2,32 bzw. 16,67 ± 2,31 [p = 0,49], longitudinaler Strain 2-Kammerblick: 17,1 ± 2,34 bzw. 15,91 ± 2,34 [p = 0,09], longitudinaler Strain 3-Kammerblick: 16,12 ± 3,00 bzw.

16,06 ± 2,60 [p = 0,48], zirkumferenzieller Strain: 15,06 ± 2,69 bzw. 14,67 ± 5,01 [p = 0,39], radialer Strain: 38,51 ± 11,77 bzw. 37,62 ± 13,77 (p = 0,43), Rotation: 5,81 ± 1,96 bzw. 5,08 ± 1,10 [p = 0,14]). Bei Patienten mit subendokardialem „Late enhancement" war der globale Strain im Vergleich mit Patienten ohne „Late enhancement" bzw. Patienten mit subepikardialem „Late enhancement" in allen Qualitäten mit Ausnahme der Rotation signifikant erniedrigt (longitudinaler Strain 4-Kammerblick: 10,56 ± 3,01 [p = 0,00004 bzw. 0,0002], longitudinaler Strain 2-Kammerblick: 12,85 ± 4,41 [p = 0,005 bzw. 0,05], longitudinaler Strain 3-Kammerblick: 12,3 ± 2,79 [p = 0,006 bzw. 0,008], zirkumferenzieller Strain: 8,2 ± 2,12 [p = 0,001 bzw. 0,03], radialer Strain: 17,5 ± 11,31 [p = 0,01 bzw. 0,02], Rotation: 4,55 ± 1,06 [p = 0,19 bzw. 0,27]). Bei Patienten ohne „Late enhancement" und Patienten mit subepikardialem „Late enhancement" wurde der globale Strain weder durch den Delay zwischen Beginn der kardialen Symptome und Analyse des globalen Strain, den Maximalwert des Troponin I, den Wert der bei der kardialen Magnetresonanzuntersuchung erhobenen „Relative global enhancement ratio" noch durch die Zahl der vom „Late enhancement" betroffenen Segmente signifikant beeinflusst.

Schlussfolgerung Bei Patienten mit Verdacht auf Myokarditis, guter Linksventrikelfunktion und normofrequentem Sinusrhythmus finden sich im Vergleich mit Patienten ohne „Late enhancement" signifikante Veränderungen hinsichtlich des mittels 2D-Speckle-Tracking analysierten globalen Strain nur bei Patienten mit subendokardialem „Late enhancement", nicht jedoch bei Patienten mit subepikardialem „Late enhancement"; im Gegensatz zu aus theoretischen Überlegungen zur myokardialen Faserarchitektur abgeleiteten Annahmen betreffen diese Veränderungen alle Strain-Qualitäten mit Ausnahme der Rotation. Die Analyse des globalen Strain mit 2D-Speckle-Tracking erlaubt daher bei diesem Patientengut im Gegensatz zur kardialen Magnetresonanzuntersuchung nur die Verdachtsdiagnose eines akuten Koronarsyndrom, nicht jedoch die Differenzierung zwischen Myokarditis und Normalbefund.

Koronar-CT: Analyse der Zuweisungsrealität unter besonderer Berücksichtigung geschlechtsspezifischer Aspekte

IV-7 **043**

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Einleitung In den vergangenen Jahren sind viele Daten über die diagnostischen Möglichkeiten des Koronar-CT publiziert worden, wenig ist hingegen über die Zuweisungsrealität bekannt. Wir wollen mit dieser Arbeit die Zuweisungsrealität in unserem Haus analysieren, wobei wir aufgrund der geschlechtsspezifischen Unterschiede hinsichtlich der Strahlenbelastung (bei weiblichen Patienten mit höheren Äquivalenzdosen aufgrund des im Strahlengang befindlichen Brustgewebes als höher zu werten) besonders auf geschlechtsspezifische Aspekte eingehen.

Setting An unserer Institution werden seit einem Jahr Koronar-CTs auf einem Dual-Source-Scanner durchgeführt. Die Zuweisung erfolgt ausschließlich nach Begutachtung durch die (eigene) kardiologische Ambulanz oder direkt durch niedergelassene Fachärzte mit Additivfach Kardiologie. Bisher wurden 231 Koronar-CTs durchgeführt, 81 % der Patienten wurden zum Ausschluss einer KHK zugewiesen.

Patienten Patienten, die zum Ausschluss einer KHK zugewiesen wurden, waren zu 62 % weiblich, die weiblichen Patienten waren etwas älter (54,3 vs. 52,3 Jahre), die männlichen Patienten hatten im Schnitt mehr „klassische" koronare Risikofaktoren (1,56 vs. 1,01, vorwiegend bedingt durch einen höheren Anteil an Hypertonikern [65 % vs. 52 %] und Rauchern [70 % vs. 26 %]). Nur 5 % der Patienten waren asymptomatisch, bei männlichen Patienten wurde vor der Zuweisung zum Koronar-CT häufiger eine Ergometrie durchgeführt (97 % vs. 85 %).

Diagnosen Bei weiblichen Patienten fanden sich häufiger blande Koronargefäße (51 % vs. 39 %), eine KHK ohne signifikante Stenosen wurde bei weiblichen und männlichen Patienten in etwa gleich häufig diagnostiziert (32 % vs. 30 %), bei männlichen Patienten wurde häufiger der Verdacht auf signifikante Koronarstenosen erhoben (30 % vs. 17 %).

Schlussfolgerungen Wenn man davon ausgeht, dass das Ziel eines Koronar-CT einerseits die Vermeidung einer invasiven Abklärung mittels Koronarangiographie (d. h. möglichst wenige Befunde mit Verdacht auf signifikante Koronarstenosen), andererseits die Vermeidung einer „unnötigen" Strahlenbelastung (d. h. möglichst wenige Befunde mit blanden Koronargefäßen) sein sollte, bedeutet das für unsere Patientenpopulation, dass die Schwelle für die Indikation zum Koronar-CT (d. h. die Vortestwahrscheinlichkeit) bei weiblichen Patienten eher zu niedrig, bei männlichen Patienten eher zu hoch gelegen ist. Die geringere Vortestwahrscheinlichkeit war bei unseren weiblichen Patientinnen nicht nur durch das Geschlecht, sondern auch durch die geringere Häufigkeit an „klassischen" koronaren Risikofaktoren bedingt.

Cardiac Computed Tomography for the Detection of Coronary Artery Disease: An Evaluation of Appropriate Use in Patients Undergoing Invasive Coronary Angiography

BAI **044**

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Background While technology of cardiac computed tomography (CCT) is continually improving, interest in CCT proceeds to increase. Guidelines which were raised for appropriate usage underwent clinical assignment and join in more experiences. We sought to examine the implementation of these principles by applying them into real world practice.

Methods All data were collected retrospectively from patients (pts) undergoing invasive coronary angiography (CA) and pts with prior

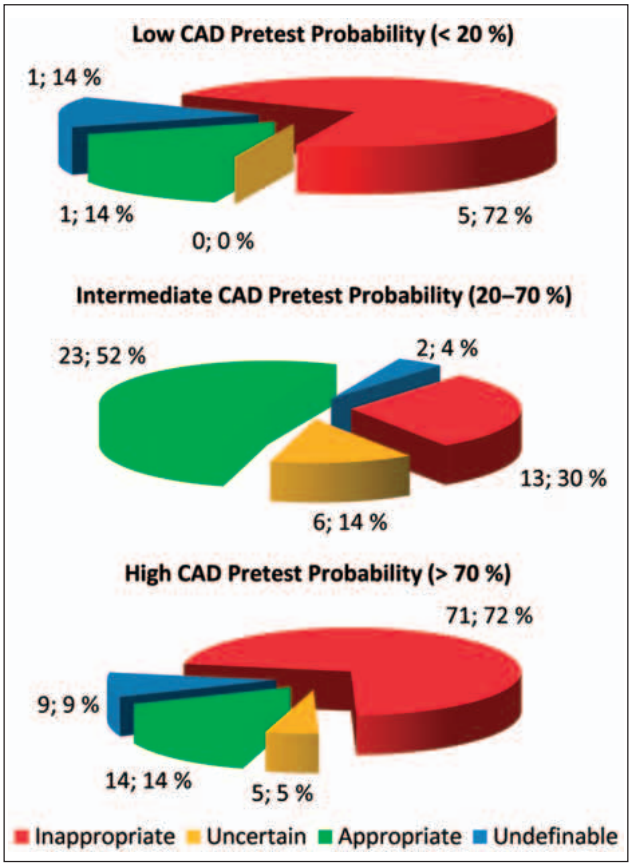

Figure 4: H. Hommel et al. Relationship between CAD pretest probability and appropriateness

stenting or bypass grafting were excluded. CCT findings were recorded at different sites and pts were referred to our institution from primary, secondary and tertiary care units. We reviewed the individual allocation to CCT and classified indications as appropriate (A), uncertain (U) or inappropriate (I) according as published criteria. If indications were not listed, they were classified as undefinable (UD). For each pt risk factors were acquired and determined with the Framingham Risk Score, additionally individual CAD pretest probabilities were evaluated and all non-invasive diagnostic, except CT data, ascertained. Clinical symptoms were categorized as given from the Canadian Cardiac Society Classification (CCSC).

Results We included 150 pts with an average age of 64.0 ± 9.9 (103 male). Overall indications were A in 25 %, U in 7 %, I in 60 % and UD in 8 %. Compared to low, intermediate and high pretest probability of CAD, A indications were 14, 52 and 14 %. U indications were 0, 14 and 5 %, I were 72, 30 and 72 % and UD were 14, 4, 9 % (**Figure 4**). The most common A indication (19.3 % of all pts, 76.3 % of total A) was for pts with equivocal stress test. A exams prevail in pts with an intermediate pretest probability (60.5 % of A). The most common I indication was for pts with a positive stress test (30.7 % of all pts, 51.7 % of total I). I exams prevail in pts with a high pretest probability (79.8 % of I). U exams were most frequent (2.7 % of all pts, 36.4 % of total U) among asymptomatic pts with moderate or high CHD risk. UD exams were limited to pts with negative results on stress test. The Framingham Risk Score was presented as low in 11.3 (male) and 19.3 % (female), as intermediate in 30.7 and 8.0 % and as high in 26.7 and 4.0 %. Pts were classified as asymptomatic (CCSC 0) in 14.7 %, as atypical angina (CCSC I) in 28.0 %, as stable (CCSC II–III) in 51.3 % and as an acute coronary syndrome (CCSC IV) in 6.0 %.

Conclusion Considering the highly selected group of pts with referral to CA, the overall appropriateness remains acceptable. The results however show a high percentage of inappropriate CCT indications especially when based on pretest probability evaluation for CAD. Therefore we conclude that the existing appropriateness criteria for the use of CCT need a more refined implementation into the practical management of pts with suspected CAD.

Determination of CMR Derived Regional and Local Aortic Pulse Wave Velocity in Healthy Volunteers and Patients with Coronary Artery Disease XI-4 045

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Background Cardiac Magnetic Resonance (CMR) is an unique method to determine regional and local aortic pulse wave velocity (PWV). Especially local elastic parameters of the ascending aorta might influence cardiac function in patients with cardiovascular diseases. So far, however, no study has investigated the use of local PWV determined by CMR in patients with coronary artery disease.

Objectives To investigate the use and reproducibility of regional and local (ascending aorta) PWV in healthy volunteers as well as in patients with coronary artery disease (CAD).

Methods We performed velocity encoded, phase contrast CMR (retrospectively ECG-gated, temporal resolution: 20 ms) in 9 healthy volunteers as well as in 6 patients with coronary artery disease (CAD). Measurements were performed at the levels of the ascending and descending thoracic, as well as the abdominal aorta. Flow-volume curves and cross-sectional area changes were determined during early systole. Regional PWV_{TT} was determined by the established Transit-Time method. Local PWV_{QA} was determined as the ratio between the flow (Q) and area (A) variations according to Vuillemonz et al. All analysis were performed in duplicate and by two different observers.

Results Healthy volunteers differed significantly from CAD patients in regional PWV_{TT} (5.34 ± 1.02 vs 10.69 ± 5.40 [m/s]; $p < 0.02$) but not in local PWV_{QA} (3.71 ± 1.09 vs 4.72 ± 1.52 [m/s]; p = n. s.). Interobserver agreement was high for PWV_{TT} (r: 0.964; $p < 0.0001$) and coefficients of variation were low (16.6 %) and without any bias (mean difference: –0.040 m/s; p = n. s.). Agreement for PWV_{QA} was low (r: 0.449; p = n. s.), the variation coefficient was high (41.8 %) but without any bias (mean difference: –0.32 m/s; p = n. s.).

Conclusion This pilot-study indicates that regional PWV_{TT} is a robust method for the assessment of CAD patients. PWV_{QA}, however, failed to detect differences in local aortic stiffness between the two studygroups and has high interobserver variations. Further studies should investigate alternative methods to assess local elastic parameters in the ascending aorta of CAD patients.

Magnetresonanztomographie des Herzens – Zuweisungsdiagnosen und Konsequenzen XI-6 047

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Hintergrund Das Herz-MR (CMR) ist ein etabliertes und wertvolles Verfahren, mit dem eine Vielfalt von kardiovaskulären Pathologien sicher diagnostiziert werden kann. Die Zuweisungsmodalitäten und Konsequenzen im klinischen Management kardiologischer Patienten aus diesen Informationen sind allerdings häufig unbekannt.

Methoden Retrospektive Datenanalyse aller an ein einzelnes Zentrum zum CMR zugewiesener Patienten. Erfassung der Zuweisungsdiagnosen und Konsequenzen. Erhoben wurden die Konsequenzen für KHK-Patienten.

1. Eine konservative Behandlungsstrategie ergab sich bei direkter Empfehlung zur konservativ-medikamentösen Therapie durch den CMR-Befund (Verzicht auf weitere Abklärung). Ausschluss eines Perfusionsdefizites/Ischämie bzw. bei avitalem Myokard bei KHK-Patienten (Verzicht auf Herzkatheter bzw. Revaskularisierung).

2. Eine neue Komorbidität im CMR mit Konsequenz in der Behandlung (z. B. Aortenaneurysma, Vitium oder TU). Eine invasive Behandlungsstrategie inklusive Revaskularisierung wurde als Konsequenz aufgrund des CMR-Befundes bei KHK-Patienten definiert, die einen Ischämienachweis bei vorhandener Vitalität zeigten.

Ergebnisse 452 CMRs wurden zwischen 2006 und 2009 durchgeführt und analysiert (mittleres Patientenalter 58 Jahre; 27,4 % Frauen). Die häufigsten Zuweisungsdiagnosen waren KHK-Patienten (57,1 %), bei 49,6 % aller Patienten war eine KHK bekannt (Z. n. Infarkt, PTCA, CABG, Z. n. Herzkatheter) mit der Fragestellung nach einem Perfusionsdefekt bzw. Vitalität, bei 7,5 % wurde ein obstruktiv wirksamen KHK vermutet (Herz-CT-Befund mit Grenzwertstenosen). 9,7 % hatten eine Myokarditis als Zuweisungsdiagnose, Kardiomyopathien in 8,7 %. Bei 24,5 % war ein kongenitales Vitium bzw. Quantifizierung von Aortenstenosen/Insuffizienzen die Zuweisungsdiagnose/Fragestellung. 411 (90,9 %) der Untersuchungen hatten eine direkte Behandlungskonsequenz. Bei 303 (66,9 %) ergab sich ein konservatives Management, bei 108 (23,8 %) ein invasives Management der Patienten. 15,9 % der Patienten mit Perfusionsdefizit wurden konservativ und 82,1 % invasiv (PTCA/CABG) behandelt. 87,5 % der Patienten mit später Kontrastmittelaufnahme (LGE) > 75 % der Wandstärke wurden konservativ, 12,5 % invasiv behandelt. In 19,6 % der Fälle mit LGE > 75 % konnte eine geplante Revaskularisierung verhindert werden.

Schlussfolgerungen Das CMR hat direkte Konsequenzen im Management kardiologischer Patienten. Die Patienten, die von invasiven Eingriffen profitieren, können durch das CMR erkannt werden. Unnötige, invasive Eingriffe können durch das CMR verhindert werden.

Stellenwert der Herz-Magnetresonanztomographie zur Risikostratifizierung der stabilen KHK XI-5 046

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Hintergrund Die Magnetresonanztomographie des Herzens (CMR) ist bei Patienten mit obstruktiv wirksamer koronarer Herzerkrankung (KHK) eine der am genauesten validierten Methoden zur Beur-

teilung der myokardialen Vitalität und/oder induzierbaren Ischämie. Ziel unserer Analyse war, die prognostische Bedeutung der CMR-Befunde bei KHK-Patienten zu untersuchen.

Methoden 258 Patienten die wegen des Verdachtes auf eine obstruktiv wirksame KHK eine Stressperfusion-CMR (MAGNETOM Espree 1.5 Tesla, Siemens; 140 µg Adenosin/min/kg KG für mindestens 3 Minuten, Kontrastmittel: Magnevist® 0,1 mmol/kg/KG) hatten, wurden einer retrospektiven Datenanalyse inklusive telephonischem Follow-up unterzogen.

Erhoben wurde das Auftreten von „major adverse cardiac events" (MACE) wie kardiale Todesfälle, Myokardinfarkte, ungeplante kardiale Hospitalisierungen oder Revaskularisierungen (PTCA/CABG). Mittels der Stress-CMR-Untersuchungen wurden das Vorhandensein eines Perfusionsdefizits (PD) und/oder des Ausmaßes einer vorhandenen, späten Kontrastmittelaufnahme („late gadolinium enhancement", LGE) auf < 75 % oder > 75 % der Wandstärke dokumentiert.

Ergebnisse Bei 228 (89 %) von 258 Patienten (mittleres Alter 65 Jahre; 28,1 % Frauen) wurden in einem mittleren Follow-up von 566 Tagen erfasst. 14,5 % der Patienten erlitten MACEs (5 Todesfälle, 5 Myokardinfarkte, 23 ungeplante kardiale Hospitalisierungen oder Revaskularisierungen). Ein PD war mit einer höheren Eventrate assoziiert (25 % vs. 14,5 % ohne PD). Die Eventrate der Gruppe mit > 75 % LGE war höher als in der mit < 75 % LGE (25,9 % vs. 7,5 %). Der negative Vorhersagewert für Tod und Myokardinfarkt bei allen Patienten ohne PD oder LGE lag bei 97,9 %.

Schlussfolgerungen Das CMR ist für die prognostische Einschätzung von Patienten mit KHK eine wertvolle Methode. Ein LGE von < 75 % ist mit einer deutlich geringeren Eventrate verbunden als ein LGE von > 75 %. Ein unauffälliges Stress-CMR geht bei KHK-Patienten mit einer exzellenten Prognose bezüglich kardiovaskulärer Morbidität und Mortalität einher.

Late Microvascular Obstruction After Acute Myocardial Infarction: Relation With Cardiac and Inflammatory Markers

XI-7 **048**

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Background Cardiac magnetic resonance imaging (CMR) permits accurate assessment of microvascular perfusion defects after acute myocardial infarction (AMI). The aim of the present study was to quantify late microvascular obstruction (l-MVO) and to correlate it with cardiac and inflammatory marker concentrations.

Methods CMR was performed in 118 consecutive patients within 8 days after successful interventional reperfused first acute ST-elevation AMI. Infarct volumes and l-MVO sizes were calculated from late enhancement (LE) sequences and functional parameters were determined from short-axis cine MR sequences. Creatine kinase (CK) and cardiac troponin T (cTnT), c-reactive protein (CRP) and fibrinogen as well as lactate dehydrogenase (LD), glutamate-oxalacetat-transaminase (GOT) and glutamate-pyruvate-transaminase (GPT) concentrations were determined serially from day 1 to day 4 after symptom onset.

Results l-MVO was detected in 66/118 patients (55.9 %) and comprised 18.2 ± 10 % of infarct size and 4.7 ± 3 % of left ventricle myocardial mass. Any single point-, peak and cumulative release concentration of cTnT (r = 0.21 to 0.81; $p < 0.03$), CK (r = 0.27 to 0.76; $p < 0.005$), CRP (r = 0.39 to 0.51; $p < 0.003$), fibrinogen (r = 0.20 to 0.39; $p < 0.03$) as well as LD (r = 0.42 to 0.82; all $p < 0.0001$) and GOT (r = 0.28 to 0.77; all $p < 0.004$) significantly correlated with l-MVO size. Receiver operating curve (ROC) analysis indicated a cut-off value of 462 U/l LD to best identify presence of l-MVO (area under the curve [AUC] 0.916; 95 %-CI: 0.86–0.96; $p < 0.0001$).

Conclusion l-MVO sizes significantly correlate with cardiac and inflammatory marker concentrations as determined early after AMI. LD concentration of > 462 U/l could help to identify patients in whom l-MVO is present.

Einfluss verschiedener Prämedikationsstrategien vor Koronar-CT-Untersuchungen auf Herzfrequenz und Blutdruck

IV-9 **049**

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Hintergrund Bildqualität und Strahlenbelastung bei Herz-CT-Untersuchungen stehen in enger Beziehung zur Herzfrequenz. In vielen Zentren wird deshalb eine orale Prämedikation mittels Betablockergabe zur Herzfrequenzreduktion durchgeführt. Wir untersuchten die Auswirkungen der verschiedenen Medikationen auf Herzfrequenz (HF) und Blutdruck (BD).

Methodik Insgesamt 220 Patienten mit einer Herzfrequenz > 60 bpm wurden vor Durchführung einer Koronar-CTA mittels oraler Gabe von Placebo, 15 mg Ivabradin, 50 mg Metoprolol oder einer Kombination (50 mg Metoprolol plus 15 mg Ivabradin) vorbereitet. Puls und BD wurden vor Prämedikation sowie unmittelbar vor der CT-Untersuchung gemessen.

Ergebnisse Der mittlere Zeitraum zwischen den beiden HF- und Blutdruckmessungen betrug 105 ± 23 Minuten. Während Placebo (–1,7 ± 5,6 bpm) nur einen geringen Einfluss auf die HF hatte, konnte die signifikant stärkste Wirkung mit der Kombination aus Ivabradin und Metoprolol (–17,4 ± 10,9 bpm) erzielt werden. Während der diastolische BD in allen Gruppen nur gering beeinflusst wurde, zeigt sich in der Ivabradin-Gruppe ein signifikant geringerer systolischer Blutdruckabfall im Vergleich zu Metoprolol oder der Kombination (–4,0 ± 13,5 mmHg vs. –13,7 ± 17,3 mmHg vs. 11,5 ± 18,9 mmHg; $p < 0.05$). Die Werte für Placebo lagen dazwischen (–10.2 ± 17,3 mmHg; p = n. s.).

Zusammenfassung Eine Kombination von Ivabradin mit Metoprolol erzielt die stärkste Herzfrequenzreduktion ohne zusätzlichen systolischen Blutdruckabfall im Vergleich zur alleinigen Betablocker-Gabe. Bei Patienten mit niedrigem Blutdruck zeigt Ivabradin alleine gegenüber dem Betablocker eine vergleichbare HF-Senkung bei deutlich geringerem Einfluss auf den Blutdruck.

High-Pitch Dual-Source-CT Allows Triple-Rule-Out With a High Accuracy and a Low Radiation-Dose in Real Life Patients: First Experience in Nonselected Symptomatic Patients

XI-2 **051**

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Objectives/Background In patients with heart rates < 60/min, multislice coronary computed tomography is associated with a high diagnostic accuracy for the exclusion and assessment of coronary artery stenoses. However radiaton exposure, especially in triple rule out (TPO) scans, are a cause of concern. The objective of this prospective evaluation was to test the diagnostic accuracy and efficiency of a new high-pitch dual-source computed tomography in non-selected symptomatic patients for the diagnosis of significant coronary stenosis, pulmonary embolism or aortic dissection (TPO).

Methods We evaluated 72 consecutive chest pain patients from our emergency department/cardiac outpatient clinic with a low to intermediate likelihood of coronary disease including patients with a previous stentimplantation, patients with heart rates > 60/min or with atrial fibrillation. CT was performed using a dual-source CT system with 2 × 128 × 0.6 mm collimation, 0.28 s rotation time and temporal resolution of 75 ms. Invasive coronary angiography (ICA) was performed in patients with significant stenosis (> 50 %) on CTCA.

Results In 70 patients (98 %) imaging was successful with diagnostic image quality for a triple-rule-out evaluation. Of 1008 coronary artery segments, 28 (3 %) were uninterpretable in 3 patients. In 39 patients (56 %) CTA could exclude a significant coronary artery stenosis but diagnosed pulmonary embolism in 2 pts. ICA was performed in 31 Patients (54 %) and analysed 434 coronary artery segments.

ICA served as golden standard. In a vessel-based analysis, sensitivity, specificity, positive predictive value, and negative predictive values of CTA were 97 %, 98 %, 93 %, and 99 %, respectively. The effective radiation dose was 3.5 ± 2 mSv.

Conclusion In real life symptomatic patients, high-pitch spiral coronary CTA provides excellent image quality to diagnose significant coronary artery stenosis at a consistent low radiation dose.

Myocardial Perfusion Szintigraphy or Stress Cardiac Magnetic Resonance: Which is the Ideal Gatekeeper for the Cathlab? An Invasive Comparison in Patients With Stable Coronary Heart Disease XI-3 050

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Introduction Current guidelines for the management of stable coronary heart disease recommend non invasive stress testing prior to cardiac catheterization and objective documentation of ischemia prior to elective PCI. However there are reports documenting a better diagnostic accuracy of cardiac stress magnetic resonance (CMR) over myocardial perfusion szintigraphy (MPS). We compared the results of these two stress imaging techniques with the invasive findings.

Method We analysed 200 consecutive patients of our cathlab-database (mean age 66.5 ± 9.8 years; 60 % men) with positive MPS (116 patients with 120 ischemic vascular territories) or stress CMR (82 patients with 91 ischemic vascular territories) with invasive angiographic findings. In patients with a mean vascular diameter (MVD) between 50 % and 75 % a fractional flow reserve (FFR) measurement was performed. A MVD > 75 % was considered as flow limiting stenosis.

Results MPS was false positive in 72 (60 % of 120 vascular territories [VT] and false negative in 10 [VT]. In 48 (40 %) patients both MPS and CA/FFR detected identical ischemic territories. On a patient basis MPS was inaccurate in 65 %. There was a poor correlation between MPS and CA/FFR (correlation coefficient: 0.45). Stress CMR was false positive in 9 (13 % of 91 [VT]) and false negative in 3 VT. In 79 (87 %) patients both CMR and CA/FFR detected identical ischemic territories. There was a good correlation between CMR and CA/FFR (correlation coeffficient: 0, 8).

Conclusion CMR is the perfusion technique with a superior diagnostic accuracy in detecting ischemia. Stress CMR can guide percutaneous intervention in patients with stable coronary artery disease according international guidelines better than MPS.

Diagnostische Genauigkeit der 64-Zeilen-MSCT-Koronarangiographie bei Patienten mit hochgradiger Koronarverkalkung XI-8 052

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Hintergrund Der Goldstandard in der Detektion von Stenosen der Herzkranzgefäße ist die invasive konventionelle Koronarangiographie. Die MSCT-Koronarangiographie (MSCT-CA) könnte als vorgeschaltete nicht-invasive Methode ermöglichen, die Zahl der invasiven Untersuchungen zu senken. Ein hoher Verkalkungsgrad der Koronararterien verursacht bei der CT-Untersuchung Artefakte, die zu falsch-positiven oder falsch-negativen Stenosebeurteilungen führen können. Unser Ziel war zu ermitteln, wie hoch die diagnostische Genauigkeit der kontrastverstärkten 64-Zeilen-MSCT-CA bei Patienten mit hochgradiger Koronargefäßverkalkung (Agatston-Score > 400) ist.

Methoden 110 Patienten mit einem Agatston-Score > 400 wurden in diese retrospektive Auswertung eingeschlossen. Alle Patienten hatten sich innerhalb eines Zeitraumes von 6 Monaten einer kontrastverstärkten MSCT-CA sowie einer konventionellen Koronarangiographie unterzogen. Patienten mit aortokoronaren Bypassgrafts und Koronarstents wurden nicht exkludiert. Die MSCT-CA-Untersuchungsbefunde wurden von 2 erfahrenen Untersuchern ausgewertet und mit den Ergebnissen der konventionellen Koronarangiographie verglichen. Die diagnostische Genauigkeit zur Erkennung einer hämodynamisch signifikanten Stenose (definiert als Durchmessereinengung von ≥ 50 %) wurde bezogen auf Koronarsegmente, Koronargefäße und auf den einzelnen Patienten ermittelt.

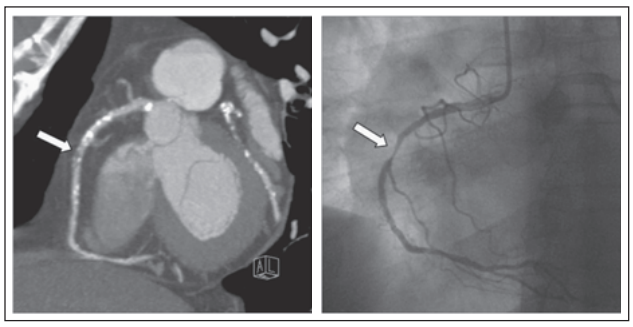

Abbildung 5: G. Steinwender et al. Signifikante Stenose in der RCA (Pfeil) dargestellt mittels MSCT-CA (links) und konventioneller Koronarangiographie (rechts)

Ergebnisse Der durchschnittliche Agatston-Score des untersuchten Patientenkollektivs lag bei 1368 ± 1105. Die KHK-Prävalenz in unserer Kohorte war sehr hoch. Bei der konventionellen Koronarangiographie wurde bei 88 % der Patienten mindestens eine signifikante Stenose detektiert. Die ermittelte Sensitivität bzw. Spezifität der MSCT-CA betrug auf Ebene der Segmente (n = 1384) 54 % bzw. 83 %, auf Ebene der Gefäße (n = 440) 80 % bzw. 70 %, auf Patientenebene (n = 110) 100 % bzw. 31 %. Der positiv-prädiktive Wert (PPW) bzw. negativ-prädiktive Wert (NPW) lag auf Segmentebene bei 52 % bzw. 85 %, auf Gefäßebene bei 74 % bzw. 77 % und auf Patientenebene bei 92 % bzw. 100 %. In unserem Patientenkollektiv bestand keine signifikante Korrelation zwischen der Anzahl der falsch beurteilten Koronarsegmente und dem Ausmaß der Koronarverkalkung.

Schlussfolgerungen Artefakte durch hochgradige Koronarkalzifikationen scheinen die Bildqualität und damit die diagnostische Genauigkeit der CT herabzusetzen. Die Durchführung einer kontrastverstärkten 64-Zeilen-MSCT-CA bei Patienten mit einem Agatston-Score > 400 ist kritisch zu hinterfragen. Es ist im Einzelfall zu entscheiden, wann eine kontrastverstärkte CT-Untersuchung indiziert ist **(Abbildung 5)**.

Left Ventricular Trabeculations and Papillary Muscles by Echocardiography and Cardiac Magnetic Resonance Imaging: A Comparative Study XI-9 053

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Introduction Left ventricular noncompaction (LVNC) is a cardiac abnormality which is increasingly diagnosed by echocardiography and cardiac magnetic resonance imaging (CMRI). However, there are various diagnostic criteria for LVNC and uncertainties regarding differentiation between normal and pathologic myocardial structures. Aim of the study was to compare the ability of echocardiography and CMRI to visualize left ventricular trabeculations (LVT) and papillary muscles (PM) by using the echocardiographic apical views and CMRI longitudinal axis views.

Methods Echocardiographic and CMRI recordings of patients who underwent both procedures within one year were blindly and independently reviewed by experts in echocardiography or CMRI. The echocardiographic apical 4-chamber, 2-chamber and 3-chamber views and CMRI longitudinal axis SSFP cine-mode views were used. The number of LVT apically of the PM was counted. Recordings with discrepant results were jointly reviewed.

Results Included were 51 patients (15 f, mean age 53 years). Indications for echocardiography were left ventricular dysfunction (n = 32), pulmonary embolism (n = 6), hypertrophic cardiomyopathy (n = 5), and others (n = 8). By echocardiography, 43 % had an enlarged left ventricle, 39 % had systolic dysfunction. LVNC was diagnosed echocardiographically in 2 patients because of 4 LVT apically of the PM. Primary agreement between echocardiography and CMRI in the number of trabeculations was achieved in 26 patients (no LVT n = 16, 1 LVT n = 7, 2 LVT n = 1, 3 LVT n=1, 4 LVT n = 1). In the remaining 25 patients the reviewers disagreed. The prevalence of LV enlargement (42 % each) or dysfunction (42 vs 35 %) was not different between the 26 cases in whom agreement and 25 patients in whom disagreement between the reviewers occurred. By jointly reviewing the discrepant cases, consensus was achieved in 20 patients. Causes for discrepancy were trabeculations diagnosed echocardiographically which turned out as papillary muscles (n = 13), muscle bands (n = 6) or wall motion abnormalities (n = 1) by CMRI. In the remaining 5 cases joint review achieved no consensus between echocardiography vs. CMRI: 1 vs. no LVT (n = 1), 1 vs 3 LVT (n = 1), 1 vs 4 LVT (n = 1), 2 vs no LVT (n = 1) and 4 vs no LVT (n = 1).

Conclusion When comparing the echocardiographic apical views with CMRI longitudinal axis views, primary agreement in the assessment of LVT is only 51 %. Echocardiography tends to misinterpret PM as LVT, most probably due to anatomic variability of PM. To better differentiate LVT from PM further echocardiographic imaging planes including atypical views have to be considered.

Chirurgie

Novel Insights Into the Mechanisms and Treatment of Intramural Hematoma Affecting the Entire Thoracic Aorta

XII-3 **056**

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Background The purpose of this study was to address a previously not described mechanism underlying intramural hematoma (IMH) of the entire thoracic aorta and to test the hypothesis whether endovascular stent graft placement in this particular mechanism could be beneficial.

Methods Within a 5-year period, we treated 8 patients with IMH affecting the entire thoracic aorta. The presumed site of initial plaque rupture was chosen as target for endovascular stent graft placement.

Results In all patients, a small atherosclerotic plaque at the free lateral wall or at the concavity of the distal aortic arch could be identified as initial site of IMH. Endovascular stent graft placement was performed successfully in all patients. By covering the suspected primary lesion, resorption of IMH especially within the ascending aorta could be achieved. Mean follow-up is 16 months (range, 1 to 25).

Conclusions Plaque rupture may be identified as the cause of IMH in a previously unrecognized subgroup of patients. If at the convexity of the distal arch, supra-aortic branches prevent retrograde extension toward the ascending aorta. If at the free lateral wall or at the concavity, IMH may affect the entire thoracic aorta, owing to the lack of the natural barrier of the supra-aortic branches. Endovascular stent graft placement of this plaque-associated IMH may be more effective and less invasive than conventional surgery to treat the entire thoracic aortic disease.

Long-term Results after TEVAR in Atherosclerotic Aneurysms Involving the Descending Aorta are not known

XII-4 **055**

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Methods Between 1996 and 2009 101 patients were analyzed. Median follow-up was 58 months (range, 9–132 months). Need for vascular transpositions to extend landing zones, in-hospital mortality, occurrence of endoleaks, reinterventions and survival were recorded.

Results 53 % of patients underwent vascular transpositions prior to TEVAR. In-hospital mortality was 4 %. Assisted primary type I and III endoleak rate was 10 %. Late type I and III endoleaks needing reintervention occurred in 14 %. Actuarial survival was 96 %, 86 % and 69 % at 1, 3 and 5 years. Event-free survival was 90 %, 82 % and 65 % at 1, 3 and 5 years. Cox proportional hazard analysis revealed a short proximal landing zone as well as a high number of prostheses as independent risk factors for early and late endoleak formation. Late endoleak formation was an independent predictor of survival.

Conclusions Long-term results of TEVAR in atherosclerotic aneurysms involving the descending aorta are excellent. Vascular transpositions broaden therapeutic options and contribute to early and late success by gaining extensive landing zones. Further clinical investigations are warranted to evaluate durability of this important tool of treating thoracic aortic disease.

Gender-Specific Risk Factors for Mortality in Patients After TEVAR

XII-2 **054**

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Aims The aim of this study was to determine gender-specific risk factors of mortality in patients after TEVAR.

Methods We retrospectively analyzed 227 consecutive patients undergoing TEVAR at our institution during a 12-year period (female 28 %, median age 67a). Clinical risk factors according to EuroSCORE stratification as well as suitability for conventional open repair according to institutional standards were recorded. Follow-up data were available in all patients.

Results Gender did not affect mortality in patients after TEVAR (p = 0,452, OR 1,48, CI: 0,75–2,91). Age turned out to be an independent risk factor in females (p = 0,002, OR 3.74, CI: 1,62–8.65) whereas suitability for open repair was an independent risk factor in males (p = 0.005, OR 0,22; CI: 0,078–0.64). Chronic pulmonary disease was a gender-independent risk factor (p = 0,036, OR 4,31; CI: 1.01–16,88).

Conclusions Males and females exhibit different risk factors after TEVAR. Advanced age is associated with increased late mortality in females whereas potential suitability for open repair – indicating a better physiologic reserve – reduces late mortality in males. The adverse impact of severe chronic pulmonary disease is balanced in both sexes.

Midterm Results After Endovascular Treatment of Acute, Complicated Type B Aortic Dissection

XII-6 **057**

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Background To assess the efficacy and midterm results of endovascular treatment of acute complicated type B dissection.

Methods Between January 2001 and February 2009, 25 patients (5 female, 20 male) with acute complicated aortic type B dissections (mean age 58, range 35–86 years), defined as either aortic rupture, malperfusion, intractable pain or uncontrolled hypertension underwent endovascular stent graft placement with either the Gore Excluder/TAG device (n = 12) or Medtronic Talent /Valiant device (n = 13). Follow-up was 100 % complete and averaged 23 ± 24 months. Mean numeric and logistic Euroscore was 11 and 32 %, respectively.

Results Technical feasibility and success with deployment proximal to the entry tear was 100 %, requiring partial or total coverage of the left subclavian artery in two patients (8 %). Hospital mortality was 16 % ± 7 % (70 % confidence limit) with 2 late deaths (17 and 18 months post implant). Causes of hospital death included rupture in 3 and cardiac arrest in one patient. None of the patients who survived the procedure developed any neurological complications. Three patients with malperfusion required branch vessel stenting. Furthermore, 3 patients developed a Type Ia Endoleak. Actuarial survival at 1 and 5 years was 84 % and 76 %, respectively. Freedom from treatment failure at 5 years (including reintervention, aortic rupture, device related complication, aortic related death, or sudden, unexplained late death) was 58 % ± 11 %.

Conclusions Endovascular stent-graft placement in acute complicated type B aortic dissection proves to be a promising alternative therapeutic treatment modality in this relatively difficult patient cohort. Refinements, especially in stent design and application, may further improve the prognosis of patients in this life-threatening situation.

Symptomatic Spinal Cord Malperfusion after Stent-Graft Coverage of the Entire Descending Aorta

XII-1 **058**

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Objectives To identify risk constellations for symptomatic spinal cord malperfusion in patients undergoing extensive stent-graft coverage of the thoracic aorta.

Methods From 1997 through 2009, 26 patients (mean age 70a) underwent extensive stent-graft coverage of the thoracic aorta. Indications for stent-graft placement were atherosclerotic aneurysms (n = 18) and penetrating atherosclerotic ulcers (PAU) (n = 8). In 16 patients a rerouting procedure was required to gain sufficient proximal landing zone length. Cerebrospinal fluid (CSF) drainage was not routinely applied due to the necessity of maintaining continuing antiplatelet therapy due to severe cardiovascular comorbidities.

Results Technical success was 100 %. 5 patients developed symptomatic spinal cord malperfusion. All symptomatic patients had impaired spinal cord blood supply by acute or chronic occlusion of at least two major blood supplying vascular territories of the spinal cord. Secondary CSF drainage improved neurologic symptoms in all patients without causing any antiplatelet therapy related collateral injury.

Conclusions Extensive stent-graft coverage of the entire thoracic aorta can be performed with a high rate of success. If collateral blood supply to the spinal cord is maintained, occlusion of the intercostal arteries does not cause symptomatic malperfusion. However, if acute or chronic occlusion of either the subclavian, lumbar or hypogastric arteries is present, likelyhood of symptomatic malperfusion dramatically increases.

Levosimendan in a Cardiac Surgical ICU

XII-7 **059**

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Background Several studies demonstrate a positive effect of levosimendan in patients undergoing cardiac surgery. Levosimendan acts positive inotropic without an increase of myocardial oxygen consumption or proarrythmic side effects. Up to now no data are available about the use of levosimendan in patients undergoing cardiac surgery in real life. Therefore, we conducted a retrospective analysis of the use of levosimendan in our cardiac surgical ICU.

Methods All patients admitted to our ICU within one year being treated with levosimendan were evaluated regarding personal data, use of levosimendan (bolus or not, start of the infusion, amount given), the combination of levosimendan with other drugs (dobutamine, norepinephrine, milrinon, vasopressin, epinephrine and beta-blocker) as well as patients ICU survival.

Results 102 out of 988 patients were treated with levosimendan (10.3 %). Mean age was 65 years (5–83), the majority was male (n = 68) with a mean ejection fraction of 37 % (12–74 %). Mean Euro Score for predicting outcome in cardiac surgery was 12 (3–20). 43 patients (42 %) underwent emergency surgery. In nearly 50 % of our patients levosimendan was started during the operation (n = 48; 47 %) and in a high proportion after the operation (n = 38; 37 %), in 97 % of the patients levosimendan was started continuously without a bolus. Virtually all patients (n = 99; 97 %) were treated with additional norepinephrine, 41 patients (40 %) with dobutamine, while other catecholamines or vasopressin were used infrequently. Interestingly, 25 patients (25 %) were on betablockers.

Overall ICU survival of levosimendan treated patients was 81 % (n = 83) with 79 % (n = 34) of emergency patients surviving ICU. Patients treated with additional dobutamine or milrinone had higher survival rates (75.6 % and 64.7 %) compared to those patients requiring epinephrine or vasopressin plus levosimendan (45 % and 31 %).

Conclusion Levosimendan is safe in patients undergoing cardiac surgery. Even in those highest risk patients with a mean Euro Score of 12 ICU survival rates were surprisingly high.

Antegrade Cerebral Protection in Thoracic Aortic Surgery: Lessons From the Past Decade

XII-5 **060**

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Objective Prolonged deep hypothermic circulatory arrest (DHCA) adversely affects outcome and quality of life in thoracic aortic surgery. Several techniques of antegrade cerebral perfusion are routinely used: bilateral selective antegrade cerebral protection (SACP) by introducing catheters in the innominate and left carotid artery, unilateral perfusion through the right axillary antegrade cerebral perfusion (RAACP) or a combination of right axillary perfusion with an additional catheter in the left carotid artery (RAACCP), resulting also in bilateral perfusion. The aim of the present study was to analyse the impact of the different approaches on the quality of life (QoL).

Methods The data of 292 patients who underwent surgery of the thoracic aorta using DHCA at our hospital between January 2004 and December 2007 have been analysed and a follow-up was performed focussing on QoL, assessed with the Short Form-36 Health Survey Questionnaire (SF-36). Results were analysed according to the type of cerebral perfusion and the duration of DHCA.

Results Patients' characteristics were similar in all groups. Of the total, 3.4 % patients underwent DHCA (average 8.3 ± 6.4 min) with-

out ACP, 45.9 % underwent SACP (average DHCA of 15.6 ± 7.1 min), 40.4 % had RAACP (average DHCA of 28.1+/-11.6 min) and 9.4 % bilateral perfusion (RAACCP) (average DHCA of 43.1 ± 16.7 min). The average follow-up was 23.2 ± 15.1 months. QoL was preserved in all groups. For DHCA above 40 min, bilateral ACP provides superior midterm QoL than unilateral RAACP (average SF-36 95.1± 44.4 vs 87.6 ± 31.3; p = 0.072).

Conclusions When midterm QoL is assessed, bilateral SACP provides the best cerebral protection for prolonged DHCA (> 40 min).

CMP

Two-Dimensional Speckle-Tracking Strain Imaging for Monitoring Enzyme Replacement Therapy in Patients with Anderson-Fabry Disease V-3 061

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Purpose Anderson-Fabry Disease (AFD) is a rare hereditary X-linked lysosomal storage disorder. It is characterized by a deficiency of alpha-galactosidase A with accumulation of globotriaosylceramide in various organs including the heart. Patients frequently develop myocardial hypertrophy with consecutive diastolic and systolic left ventricular dysfunction. Enzyme replacement therapy (ERT) has been shown to provide beneficial effects on cardiac manifestations of AFD. Calculation of global longitudinal strain (GLS) derived from echocardiographic images by speckle tracking is a new technique, which may allow monitoring of functional changes.

Methods We examined 21 patients (12 females with a mean age of 40 years, and 9 males with a mean age of 41 years) with genetically confirmed AFD. 5 women and 3 men were on ERT at study entry with a mean duration of 15.9 ± 10.5 months. 5 of these had an echocardiographic follow up (FUP), at 54.9 ± 20.6 months after start of ERT. Echocardiographic analysis was performed from digitally stored loops by a blinded observer. Thickness of the interventricular septum (IVS) and the posterior wall (PW) was measured using standard criteria. GLS was calculated from apical 4-chamber, 2-chamber- and apical long axis views using internal software.

Results In the total cohort GLS was –16.8 % ± 4.2 %. In comparison, patients with IVS < 12 mm had nonsignificantly better GLS than pts. with IVS > 12 mm (–17,7 % ± 2.2 % vs –15.8 % ± 4.0 %; p = 0.37). Correlation between GLS values and IVS was r = 0.54; p = 0.06 and between GLS and PW r = 0.58; p = 0.05. Female pts. had worse GLS than male pts. (–15.12 % ± 2.3 % vs –18.0 % ± 5.0 %; p = 0.13). Baseline GLS for pts. on ERT did not differ from those without ERT (–16.3 % ± 3.8 % vs –17.0 % ± 4.6 %; p = 0.5). At FUP, the 4 patients showing a GLS higher than –18.0 % at baseline had improved under ERT (from –15.0 % ± 3.9 % to –18.5 % ± 5.4 %; p = 0.02).

Conclusion Worse GLS values are associated with left ventricular hypertrophy in patients with Anderson-Fabry Disease. GLS improved during ERT and thus may provide a novel tool for assessment of treatment effects in such patients.

Cardiac Amyloidosis – Experience of Two Territory Care Centers in Western Austria V-2 062

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Background Amyloidosis is a systemic disease characterized by protein precipitates in different organ systems. Once the heart is involved, the disease is associated with malignant prognosis. Due to its rareness and semi-malignant character there is only limited data on cardiac amyloidosis in literature.

Methods and Results We here report on a consecutive group of 27 pts., referred to Innsbruck Medical University or Medical Private University Salzburg between 2001 and January 2010, with a mean age of 64 ± 11 years and cardiac amyloidosis evidenced by endomyocardial biopsy. By immunohistochemical analysis 1 patient was diagnosed with AA-amyloidosis, 7 pts. with ATTR-amyloidosis (1 mutant and 6 non-mutant forms) and 19 pts. with AL-amyloidosis (kappa free light-chain in 5, and lambda in 11 pts.; in 3 pts. light-chains could not be differentiated). 67 % of pts. presented in NYHA class III or IV. ECG revealed low voltage in 37 % and characteristic pseudoinfarction pattern in 67 %. Chemotherapy was applied in 16 pts. 2 pts. were treated with high-dose melphalan and consecutive autologous stem cell transplantation and 13 pts. received therapies including either melphalan, thalidomide or bortezomib. One patient was treated with R-CHOP because of underlying waldenstrom's macroglobulinemia. 4 pts. with isolated cardiac amyloidosis were listed for heart transplantation (HTx). 2 pts. were successfully transplanted and one patient died while on the waiting list. Another patient was removed from the waiting list because of progressive disease with multiorgan involvement. Mortality rate was as high as 44 % during a mean follow-up of 0.9 ± 0.8 years. A total of 52 % of pts. reached a combined endpoint of death or HTx. Median event-free survival-time was 238.0 (108.0–523.0) days.

Conclusion Cardiac amyloidosis is a rare but malignant disease with poor outcome. Although HTx in combination with chemotherapy and stem cell transplantation provides a potential curative treatment, patients frequently present in an advanced stage of the disease, in many cases too late for such an extensive approach.

Accuracy of Cardiovascular Magnetic Resonance Imaging (MRI) in Biopsy-Proven Inflammatory Cardiomyopathy BAI 063

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Purpose Inflammatory cardiomyopathy (iCMP) is a heterogenous disease and definite diagnosis is based on invasive endomyocardial biopsy (EMB). However, non-invasive cardiovascular Magnetic Resonance Imaging (CMR) may substantially add to diagnosis and assist in indicating and directing EMB. It was the aim of our retrospective analysis to evaluate the accuracy of CMR in patients with suspected iCMP as evidenced by EMB.

Methods From March 2001 to December 2009 EMB for suspected iCMP was performed in 260 patients with pre-existing CMR available in 87 patients. Of these (58 male, age 47 ± 13 yrs, NYHA I/II 63 %, NYHA III/IV 37 %) myocardial inflammation was evidenced by EMB in 14 patients. CMR studies were performed on a 1.5 Tesla scanner (Magnetom Avanto, Siemens, Erlangen, Germany). For the purpose of this analysis CMR studies were graded positive in case of concurrent evidence of myocardial edema, pericardial effusion, and late-gadolinium enhancement.

Results Based on the results of EMB, overall sensitivity of CMR to predict myocardial inflammation was 64 %, specificity 99 % (PPV 90 %, NPV 93 %). In a subgroup of patients with viral-positive iCMP (n = 6) sensitivity was as high as 83 %, specificity 99 %, as compared to patients with virus-negative iCMP (sensitivity 50 %, specificity 99 %). Sensitivity (75 %) of CMR in patients with virus-negative iCMP could be improved if diagnosis was based only on the coexistence of pericardial effusion and late-gadolinium enhancement admittedly at the expense of lower specificity (59 %).

Conclusion The predictive value of CMR in the diagnosis of myocardial inflammation clearly depends on the stringency of applied diagnostic criteria. From our data it appears that at least 2 out of 3 diagnostic criteria have to be positive for meaningful clinical decision making. Nonetheless, endomyocardial biopsy remains the gold standard in the diagnosis iCMP.

Psychologische Aspekte bei Tako-Tsubo-Syndrom

V-1 **064**

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Einleitung Das Tako-Tsubo-Syndrom (TTS) ist eine seltene Erkrankung des Myokards bei blanden Koronarien, welche vorwiegend durch das Vorhandensein eines emotionalen oder physischen Stressors ausgelöst wird [Bahlmann et al., 2007; Buchholz et al., 2007; Cattaneo et al., 2007; Devaud et al., 2007; Ferrier et al., 2007; Marchal et al., 2007; Nef et al., 2007; Nevado et al., 2007; Patane et al., 2007; Ruess et al., 2007; Yoshida et al., 2007].

Die Stressreaktion löst eine Veränderung der Hypothalamus-Hypophysen-Nebennierenrinden-Achse aus [Berg, 2005; Lahousen, Bonelli & Hofmann, 2004; Poldrack & Znoj, 2000]. Es besteht eine Assoziation zwischen der posttraumatischen Belastungsstörung (PTBS) und des Hypokortisolismus [Yehuda, 2005].

Fragestellung Ziel der Untersuchung war die Erfassung assoziierter psychologischer Aspekte (Persönlichkeitsfaktoren, chronifizierter Stress, Depression, Angst, posttraumatische Belastungsstörung, Lebenszufriedenheit) beim Auftreten eines Tako-Tsubo-Syndroms.

Material und Methoden 18 Personen mit Tako-Tsubo-Syndrom (88,9 % weiblich, Alter: M = 61,39 Jahre, SD = 10.71, Range: 35–75 Jahre) und einer gematchten Vergleichsgruppe von 18 Personen mit koronarer Herzkrankheit (KHK, 88,9 % weiblich, Alter: M = 62,72 Jahre, SD = 10,11, Range: 39–77 Jahre) wurden nach psychologischen Aspekten und kardialen Risikofaktoren untersucht. Die Parallelgruppen unterschieden sich nicht signifikant bezüglich Geschlecht, Alter und Ausmaß der emotionalen Belastung.

Zur Erfassung der Persönlichkeitsfaktoren wurden das „Big Five Inventory" und „Typ-D Personality" herangezogen. Mittels Trier-Inventar zum chronischen Stress wurde das Ausmaß von chronischem Stress erhoben. Die Ausprägung der Depression und Angst wurde mittels „Hospital Anxiety Depression Scale" operationalisiert. „Posttraumatic Stress Disorder Screen" diente zur Erfassung einer posttraumatischen Belastungsstörung. Die Lebenszufriedenheit wurde mittels Fragebogen zur Lebenszufriedenheit gemessen.

Ergebnisse Es zeigten sich keine signifikanten Unterschiede in den psychologischen Aspekten wie negative Affektivität, soziale Inhibition, chronifizierter Stress, Depression, Angst, Extraversion, Neurotizismus, Gewissenhaftigkeit, Offenheit, Verträglichkeit und allgemeine Lebenszufriedenheit zwischen Personen mit TTS und KHK.

Personen mit TTS wiesen eine signifikant höhere Inzidenzrate an PTBS auf ($c^2_{(1)} = 4{,}50$; $p = 0{,}034$).

5,6 % zeigten eine CMP (KHK: 1/TTS:1), 8,3 % (3/0) hatten eine zusätzliche Klappenerkrankung. 69,4 % (13/12) hatten einen Hypertonus, 13,9 % (3/2) einen Diabetes, 61,1 % (12/10) zeigten eine Hypercholesterinämie.

Personen mit TTS hatten signifikant geringere Triglyzeridwerte (M = 92,00, SD = 34,59, T[34] = 2,74; p = 0,010) als Personen mit KHK (M = 131,83, SD = 50,97).

Schlussfolgerung Eine Stressstörung könnte ein Tako-Tsubo-Syndrom, basierend auf einer Katecholaminstörung, induzieren.

Weiterführende Untersuchungen im Sinne von Kortisolmessungen in der Akutphase des Auftretens eines Tako-Tsubo-Syndroms würde die psychologische Hypothese, den Zusammenhang zwischen generalisierter Stressstörung und Tako-Tsubo-Syndrom, stützen.

Tako-Tsubo Cardiomyopathy in a 78 Year Old Woman Presenting With Diarrhea

V-4 **065**

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Introduction Tako-Tsubo cardiomyopathy is a relatively new clinical entity characterized by acute but rapidly reversible left ventricular systolic dysfunction. In this case we describe the diagnosis of Tako-Tsubo cardiomyopathy in the setting of a patient presenting with diarrhea.

Methods/Results We report on a 78 year old woman, who presented to the emergency department with diarrhea. The ECG was normal without ST-elevation or ST-depression. Because of the new onset of diarrhea one day ago and leucozytosis in her laboratory test the patient was diagnosed with gastroenteritis. During the course of the first night in hospital the patient reported a moderate left-sided chest discomfort and dyspnea. ECG showed significant ST-elevation in anteroseptal and inferior leads. Heart specific enzymes were only slightly elevated (CKMB maximum 2 times above normal). Imaging was collected via echocardiography and angiography. Echocardiography showed apical ballooning with severely impaired left ventricular function. Coronary angiography revealed no significant occlusion and showed left ventricular apical ballooning. Due to the patients symptoms and dynamic ST-changes in ECG resembling acute myocardial infarction, the absence of obstructive coronary disease and the typical left ventricular apical ballooning, we assumed that the patient had takotsubo cardiomyopathy.

Conclusion Tako-Tsubo cardiomyopathy can complicate several conditions and is mainly described in a setting of stress (emotional or physical). Supportive treatment leads to spontaneous, in general, rapid recovery in nearly all patients. The prognosis is excellent, and a recurrence occurs in < 10 % of patients.

Sudden Cardiac Death – Lamin A/C Mutation als Ursache einer familiären dilatativen Kardiomyopathie

V-5 **066**

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Hintergrund Bei 15–35 % aller Patienten tritt eine idiopathische dilatative Kardiomyopathie (DCM) familiär gehäuft auf, in manchen Fällen assoziiert mit einer Erkrankung der Skelettmuskulatur [1]. Bei Familien mit DCM in Kombination mit Reizleitungsstörungen sind Defekte im LMNA-Gen (kodiert die Kernhüllenproteine Lamin A und Lamin C) nachgewiesen. Über welchen Mechanismus die Mutation eine DCM bedingt, ist unklar; möglicherweise kommt es zu einer Dysfunktion der Kernmembran. Träger des mutierten Gens weisen in 92 % kardiale Arrhythmien nach dem 30. LJ und in 64 % eine Herzinsuffizienz nach dem 50. LJ auf. Der plötzliche Herztod ist die häufigste Todesursache (46 %) sowohl beim kardialen als auch beim neuromuskulären Phänotyp [2]. Innerhalb einer Familie kann der gleiche Gendefekt phänotypisch deutlich unterschiedlich auftreten.

Methode Eine 41-jährige Patientin wird bei Z. n. St. febrilis wegen Schwäche, Schwindel, Müdigkeit, Nackenschmerzen und Dysästhesien im rechten Arm stationär aufgenommen; das EKG zeigt einen LSB (0,12 sec) und einen AV-I (PQ 0,36 sec) sowie eine biphasische ST-Strecke in V1 und V2. Als einzige auffällige Laborparameter finden sich ein erhöhter CPK-Wert (176 U/l) bei negativem Troponin T sowie ein erhöhter proBNP-Wert mit 408 pg/ml. Abgesehen von Palpitationen („Pulsaussetzer") ist die Anamnese unauffällig, es besteht aber eine positive Familienanamnese hinsichtlich „Sudden Cardiac Death" (der Vater ist mit 41 Jahren und eine Schwester, die an Herzinsuffizienz litt, mit 38 Jahren plötzlich verstorben, beim 45-jährigen Bruder sind ein AV-I° [PQ 0,4 sec], ein intermittierender AV-II° und III° sowie eine ventrikuläre Extrasystolie bekannt, 2 Cousins sind im Alter von 10 und 11 Jahren an einer fraglichen Muskeldystrophie verstorben). Echokardiographisch zeigen sich ein grenzwertig großer linker Ventrikel mit paradoxer Septumbewegung und gering reduzierter LVEF (50 %), im Langzeit-EKG intermittierend ein AV-II° Wenckebach, polytope VES und ein ventrikulärer Run mit 5 Schlägen sowie Pausen bis 2,8 sec; die Spätpotentialanalyse ist positiv (QRS 138 ms, RMS40 13,6 uV, LAS40 40 ms). In einer kardialen MRT ist der linke Ventrikel gering vergrößert, es findet sich eine Fibrose des zentralen Septums ohne Zeichen einer Narbe oder Myokarditis. Bei der elektrophysiologischen Untersuchung sind die AH-Zeit (276 ms) und die HV-Zeit (61 ms) verlän-

gert und es werden nicht-anhaltende ventrikuläre Tachykardien mit max. 5 Schlägen induziert. Eine prophylaktische ICD-Implantation wird vereinbart. Drei Tage nach der Entlassung erleidet die Patientin einen Herz-Kreislauf-Stillstand und wird vom Gatten erfolgreich reanimiert. Im NA-EKG Kammerflimmern, ROSC nach 28 Minuten. Nach Intensivaufenthalt mit therapeutischer Kühlung wird nach 12 Tagen ein ICD implantiert; dabei wird auch eine molekulargenetische Untersuchung durchgeführt, wobei sich die bisher nicht beschriebene heterozygote Deletion von 3 Basen (AAG) im Exon 2 des LMNA-Gens (c.367_369del) findet. Diese Deletion führt auf Proteinebene zu einer Deletion der Aminosäure Lysin an der Position 123 der Proteinsequenz p.Lys123del. Auch beim Bruder der Patientin, der dieselbe Genmutation aufweist, wird ein ICD-System implantiert.

Schlussfolgerung Patienten mit einer Lamin A/C-Mutation haben ein hohes „Sudden Cardiac Death"-Risiko. Reizleitungsstörungen und ventrikuläre Arrhythmien lassen sich fast bei allen Patienten nachweisen, manche Patienten entwickeln eine Herzinsuffizienz. Eine frühzeitige prophylaktische ICD-Implantation scheint ungeachtet der erhaltenen LVEF indiziert.

Literatur:

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Immunosuppressive Therapy in Biopsy-Proven Virus-Negative Inflammatory Cardiomyopathy V-6 067

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Intruduction The role of immunosuppressive therapy in inflammatory cardiomyopathy is still under debate. Hence, it was the aim of our single center study to investigate the clinical effects of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy.

Materials and Methods From 2001 to 2009, 260 patients with suspected myocarditis were subjected to left ventricular endomyocardial biopsy. Virus-negative inflammatory cardiomyopathy was defined by immunohistochemical analysis quantifying the number of infiltrating activated lymphocytes (> 7/mm²) and/or leucocytes (> 14/mm²) and by histological criteria. Presence of persisting viral genomes was excluded by qualitative PCR from endomyocardial biopsies. Virus-negative inflammatory cardiomyopathy was diagnosed in 39 (15 %) patients. 29 patients were treated with azathioprine and prednisone for 6 month, in addition to optimized neurohormonal therapy for heart failure. Until now, 6-month follow-up endomyocardial biopsies are available in 12 patients; clinical 6-month follow-up information is available in another 10 patients.

Results Mean age was 47 yrs (range 18–68, 33 % female). Immunosuppressive therapy was well tolerated in all patients and resulted in an increase in left ventricular ejection fraction (25 ± 13 % vs 36 ± 14 %; p = 0.005), an improvement in NYHA Class (2.3 ± 1.0 vs 1.5 ± 0.6; p = 0.001) and a decrease in NTproBNP levels (1727 ± 2060 vs 1032 ± 1528 ng/l; p = 0.07). Hemodynamic measurements revealed an improvement of cardiac output (3.8 ± 0.9 l/min vs 4.6 ± 1.0 l/min; p = 0.01) and a decrease in pulmonary capillary wedge pressure (22 ± 10 mmHg vs 14 ± 7 mmHg; p = 0.008).

Conclusion Patients with biopsy-proven virus-negative inflammatory cardiomyopathy clearly benefit from immunosuppressive therapy. This benefit was observed in addition to conventional heart failure therapy.

Seizures May Break the Heart – an Unusual Presentation of Stress Cardiomyopathy V-7 068

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Introduction Recently, different etiologic factors, including neurologic disorders, have been described as triggers of stress cardiomyopathy. Typically, female patients in the 6th decade are affected, mostly after psychological stress situations; these patients often demonstrate apical ballooning (hence the names "broken heart syndrome" and "tako-tsubo syndrome"). We report on an unusual case of a male patient who has been presented with signs and symptoms mimicking acute myocardial infarction after repeated tonic-clonic seizures. Further investigations revealed transient midventricular ballooning in this patient, which was caused by repeated tonic-clonic seizures.

Case Report A 58-year-old man was transferred to the emergency room because of repeated tonic-clonic seizures and dizziness. As the patient cleared up, he complained of chest pain. ECG recordings showed sinus tachycardia with premature atrial complexes occurring in couplets, minimal septal ST-segment elevation and anterolateral ST-segment depression (panel A). Cardiac enzymes were elevated (creatine kinase 657 U/l (–170), CK-MB fraction of 66 U/l (–24) and troponine I 4.88 ng/ml (–0.16). Echocardiography revealed midventricular akinesia with reduced left ventricular ejection fraction (LVEF 35 %).

Cardiac catheterization was performed and ruled out significant coronary artery disease, while left ventriculography confirmed midventricular akinesia with preserved basal and apical contractility consistent with midventricular ballooning (panels B and C). NT-proBNP values rose up to 4451 pg/ml (–100); norepinephrine plasma levels were slightly elevated (648 pg/ml (–600).

Cardiac magnetic resonance imaging (Cardiac MR) confirmed midventricular ballooning without late-enhancement of myocardium after administration of contrast medium, arguing against acute myocarditis (panel D).

On follow-up one year later the patient is well, with complete resolution of ECG changes and normal LV function on echocardiography.

Conclusion In conclusion, we report the unusual case of midventricular ballooning mimicking acute myocardial infarction in a male patient with repeated seizures as trigger factor **(Figure 6)**.

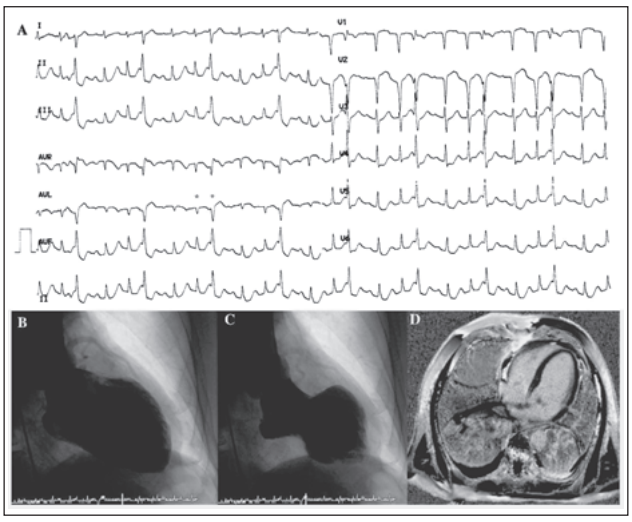

Figure 6: P. P. Rainer et al. **(A)** ECG on admission – premature atrial complexes occurring in couplets (*), minimal ST segment elevation V1–2, ST segment depression V4–6; **(B)** Ventriculography-Diastole; **(C)** Ventriculography-Systole; **(D)** Cardiac MR – no late-enhancement

Neuromuscular and Cardiac Comorbidity Determines Survival in 140 Patients With Left Ventricular Hypertrabeculation/Noncompaction V-8 069

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Background The prognosis of patients with left ventricular hypertrabeculation/noncompaction (LVHT) is controversial. We assessed cardiologic and neurologic predictors for mortality in LVHT-patients and how many received implantable cardioverters/defibrillators (ICD) or cardiac resynchronization devices (CRT).

Methods and Results Included were patients with LVHT diagnosed echocardiographically between June 1995 and May 2009. All patients underwent a baseline cardiologic examination, and were invited for a neurological investigation. During June 2009, the patients were contacted by telephone and their records were screened if they had received ICD or CRT.

In 140 patients (29 % females, mean-age 53 ± 16, range 14–94 years) LVHT was diagnosed. The neurologic investigation, carried out in 76 %, disclosed a neuromuscular disorder of definite (n = 22) or unknown (n = 68) etiology or was normal (n = 16). During a follow-up of 4.5 years the mortality was 5.7 %/year. Causes of death were heart failure (n = 11), pneumonia (n = 6), sudden cardiac death (n = 3), malignancy (n = 3), pulmonary embolism (n = 2), sepsis (n = 2), stroke (n = 2), hepatic failure (n = 1) or unknown (n = 6). Sixteen patients received devices (ICD n = 4, CRT n = 3, ICD plus CRT n = 9). Predictors for mortality were increased age (p = 0.0307), neuromuscular disorder of definite or unknown etiology (p = 0.0063), exertional dyspnea (p = 0.0018), edema (p = 0.0000), heart failure (p = 0.0002), ventricular ectopic beats (p = 0.0119), atrial fibrillation (p = 0.0000), low voltage (p = 0.0139), presence of one or more ECG abnormalities (p = 0.0420), left ventricular fractional shortening < 25 % (p = 0.0046), extension of LVHT (p = 0.0063) and LVHT affecting the lateral wall (p = 0.0110).

Conclusion Mortality in LVHT is high and due to cardiac and neuromuscular comorbidity, why monitoring and therapy, including device-therapy, should be improved.

Stroke and Embolism in Left Ventricular Hypertrabeculation/Noncompaction V-9 070

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Introduction Left ventricular hypertrabeculation/noncompaction (LVHT) is assumed to be associated with stroke or embolism (SE). It is uncertain if LVHT *per se* or if concomitant cardiac abnormalities like systolic dysfunction or atrial fibrillation (AF) contribute to SE. Aim of the study was to assess the rate, risk factors and etiology of SE in LVHT patients.

Methods Records of patients with LVHT, diagnosed between 1995 and 2009, were screened for SE. For classification of stroke-etiology, the TOAST-criteria were applied for peripheric embolism angiographic and surgical findings. Clinical, echocardiographic and electrocardiographic data were compared between patients with and without SE.

Results In 22/144 patients (15 %), stroke (n = 21) or peripheric embolism (n = 1) had occurred. The etiology of SE was cardioembolic (n = 14), atherosclerosis (n = 5) and undetermined (n = 3). SE occurred either prior (n = 14) or after (n = 8) the diagnosis of LVHT. At baseline investigation, only the prevalence of hypertension (32 vs 59 %; p < 0.05) was higher in the patients with SE. Diabetes (16 vs 27 %), heart failure (71 vs 55 %), ≥ 2 ECG-abnormalities (48 vs 50 %) and atrial fibrillation (16 vs 27 %), as well as left ventricular fractional shortening (23 vs 25) and left ventricular size (62 vs 61 mm) were not different between patients without and with SE. Among the patients with cardioembolic SE, 13/14 had either atrial fibrillation (n = 6) or systolic dysfunction (n = 11), and atrial fibrillation as well as systolic dysfunction were found in 4 patients.

Conclusion SE in LVHT is not always due to cardiogenic embolism but may be also due to atherosclerosis. Cardioembolic SE occurs only rarely in LVHT patients unless they suffer from AF or systolic dysfunction. Patients with LVHT associated with systolic dysfunction or AF should receive oral anticoagulation as primary prophylaxis against SE.

Diverse

Follow-Up of Patients With VKORC1 and CYP2C9 Polymorphisms and Phenprocoumon Therapy XIII-2 071

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Introduction Polymorphisms in the drug-targeted vitamin K epoxide reductase complex 1 (VKORC1) and in the drug metabolizing cytochrome P450 isozyme CYP2C9 affect the phenprocoumon dosage. Whether these polymorphisms affect the long-term prognosis in patients with phenprocoumon is unknown. The study aimed to assess the influence of VKORC1 and CYP2C9 polymorphisms on the incidence of stroke, bleeding and overanticoagulation.

Materials and Methods Patients genotyped in 2007 were invited for a follow-up investigation in January 2010. At that investigation the International Normalized Ratio (INR) values and weekly dosages of phenprocoumon during the year 2009 were obtained and it was asked for stroke, bleeding events and overanticoagulation.

Results Thirty-six patients (23 females) were investigated. VKORC1 polymorphisms were found in 35 patients (–1639G > A homozygous n = 8, heterozygous n = 16; 3730G > A homozygous n = 9, heterozygous n = 12; compound heterozygous n = 8). CYP2C9 variants were found in 13 patients (430C > T homozygous n = 1, heterozygous n = 8; 1075A > C heterozygous n = 4). The mean INR values were 2.4. The weekly phenprocoumon-dosage was 14.9 mg in patients without the 1639G > A VKORC1 polymorphism, 12,1 mg in heterozygeous, 7,5 mg in patients homozygeous for –1639G > A, 8 mg in patients without 3730G > A polymorphism, 13.5 mg in patients heterozygeous and 15,8 mg in patients homozygous for 3730G > A. The phenprocoumon dosages to achieve therapeutic INR were lower in patients with than without CYP2C9 variants. Two patients had a stroke and 2 patients had bleeding events. One stroke patient was heterozygous for the –1639G > A, the other homozygous for the 3739G > A VKORC1 polymorphism; and no CYP2C9 variants were found. Both patients with bleeding events were heterozygous for the –1639G > A and 3739G > A VKORC1 polymorphism, and one heterozygous for the 1075A > C CYP2C9 polymorphism. Overanticoagulation with an INR > 5 occurred in 3 patients. Two of them were homozygous and one heterozygous for the 3730G > A VKORC1 polymorphism, and all were heterozygous for the 1075A > C CYP2C9 polymorphism.

Conclusion From these limited experiences it seems that polymorphisms in VKORC1 and CYP2C9 genes do not influence the rate of bleeding, stroke or overanticoagulation during INR guided oral phenprocoumon therapy.

Medizinische Hypnose und Raucherentwöhnung im Kontext der Beherrschung kardialer Risikofaktoren (Fallbeispiele und ausgedehnte Literaturrecherche) XIII-3 072

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In dieser Arbeit wird die Effektivität von Hypnose bei Raucherentwöhnung im Kontext der Beherrschung kardialer Risikofaktoren untersucht. Zu Beginn der Diplomarbeit wird ein umfangreicher Überblick zur Hypnose aufgezeichnet. Hypnose wird zunächst historisch eingeordnet und anschließend deren Phänomene, Techniken und Begriffe erklärt. Anschließend wird versucht, die Vielzahl ver-

schiedener grundlegender Theorien zum Thema Hypnose darzustellen und einzuordnen. Nachfolgend wird von Anwendungsmöglichkeiten und Anwendungsgebieten der Hypnose berichtet, vor allem in Bezug auf Raucherentwöhnung und kardiale Risikofaktoren. Dies wird durch Fallbeispiele genauer erläutert. Hauptziel dieser Arbeit ist es, die Wirksamkeit von Hypnosetherapie bei Nikotinabusus aufzuzeigen und das oft falsche, mystische Bild der Hypnose und falsche Vorstellungen davon zu widerlegen.

Bei Hypnose handelt es sich um einen sehr tiefen und entspannten Zustand, der sich in Alphawellen im EEG präsentiert. Seit jeher ist Hypnose eine bewährte Methode zur Unterstützung des menschlichen Wohlbefindens und der Gesundheit. Die Anwendung hypnotischer Techniken hat in den vergangenen Jahren auch in der Medizin als erfolgreiche Begleitmaßnahme, im deutschsprachigen Raum eine enorme Verbreiterung erfahren. Ärztliche Hypnose wird bei vielen medizinischen Indikationen unabdingbar und erfolgversprechend eingesetzt. Die Fallbeispiele erläutern die Effektivität bei der Hilfe zum Rauchstopp und die positive Wirkung auf alle anderen Aspekte unseres Lebens. Hypnose ist ein vollkommen natürlicher Zustand, der spontan oder von außen induziert auftreten kann. Mit zunehmender Stressbelastung und Reizüberflutung in der heutigen Zeit gewinnt die Anwendung von tranceartigen Zuständen zur Entspannung, Loslassen, Selbstwertstärkung oder Konzentration auf die verschiedensten Dinge immer mehr an Bedeutung.

Im Allgemeinen ist die Wirksamkeit einer Hypnose bei Raucherentwöhnung empirisch gut widerlegt. Sowohl bei der Reduktion von Ängsten als auch im Umgang mit Stress und anderen kardiovaskulären Risikofaktoren. Hypnose bietet eine wirkungsvolle, nebenwirkungsarme Methode, die vor allem in der Kardiologie eine Bereicherung der Therapieschemata darstellt und mehr Anklang im klinischen Bereich finden sollte.

Stability of Chemokine Levels in Serum and Plasma: Influence of Temperature and Time of Measurement

XIII-1 **073**

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Background Several previous studies have stated that chemokines, such as Interleukin-8 (IL-8), Growth-related oncogene alpha (GRO-alpha) or Monocyte chemoattractant protein 1 (MCP-1) are elevated in patients with atherosclerosis or myocardial infarction. The analysis of serum or plasma levels of these mediators has become an important issue in cardiovascular research. However, few data are available on preanalytic conditions that might influence chemokine values. Thus, the aim of this pilot study was to evaluate the impact of sampling techniques and storage conditions on chemokine concentrations.

Methods Specimen of venous blood were obtained from healthy probands (n = 7) using different blood tubes (serum, heparin plasma and EDTA plasma). Blood tubes were either centrifuged initially within 20 minutes after venipuncture and kept frozen at –80 °C until further testing or were stored at 4 °C, at room temperature (RT) or at 37 °C for up to 24 hours. Samples were evaluated for MCP-1, IL-8, GRO-alpha, Epithelial neutrophil-activating protein 78 (ENA-78) and Granulocyte chemotactic peptide-2 (GCP-2) using commercially available Enzyme-linked immunosorbent assay (ELISA) kits.

Results No differences were observed when samples were processed initially after venipuncture or within the first 4 hours when tubes kept at 4 °C. A significant difference was detected for IL-8 in serum within 4 hours when samples were stored above room temperature. This rise of serum chemokine levels culminated in a 336-fold increase for IL-8, an 85-fold increase for GRO-alpha, a 22-fold increase for ENA-78, a 17-fold increase for GCP-2 and a 44-fold increase for MCP-1 compared to basic values.

Conclusions These data indicate that chemokine levels remain stable when analysed within a short interval after venipuncture or when tubes are stored at 4 °C. When tubes were exposed to temperatures higher than 24 °C (RT), levels of measured chemokines increased dramatically. We hypothesize that initiation of the blood clotting cascade in serum tubes and higher temperatures induce a pro-inflammatory microenvironment which triggers release of chemokines from cellular compartments.

Vergleich unterschiedlicher ergometrischer Belastungsformen beim kardialen Patienten

XIII-4 **074**

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Zielsetzung In dieser Studie sollte untersucht werden, ob Unterschiede in submaximalen und maximalen Kennwerten bei der Fahrrad-, Laufband-, bzw. Armkurbelspiroergometrie von kardialen Patienten bestehen, bzw. ob Zusammenhänge unter den einzelnen Belastungsformen nachweisbar waren.

Methodik Zehn Patienten mit stabiler koronarer Herzkrankheit nahmen im Rahmen ihres Aufenthaltes in der Sonderkrankenanstalt der Pensionsversicherung in St. Radegund teil. Pro Patient wurden mindestens 3 Belastungstests durchgeführt.

Es wurden stufenförmige Belastungstests durchgeführt und die Leistung (P), Herzfrequenz (HF), Laktat (La) sowie respiratorische Parameter gemessen. Zusätzlich wurden die aerobe und die anaerobe Schwelle bestimmt.

Ergebnisse Die Maximalwerte von Fahrrad, Laufband und Armkurbel waren: P_{max}: 191 ± 29 W vs. 339 ± 52 W vs. 99 ± 9 W, HF_{max}: 140 ± 16 bpm vs. 147 ± 18 bpm vs. 141 ± 18 bpm; VO_{2max}/kg: 26,9 ± 4,8 ml/min/kg vs. 30,6 ± 5,3 ml/min/kg vs. 20,5 ± 4,2 ml/min/kg; La_{max}: 7,7 ± 2,1 mmol/l vs. 7,4 ± 1,8 mmol/l vs. 8,1 ± 1,3 mmol/l.

An der anaeroben Schwelle betrugen die Werte am Fahrrad, Laufband und der Armkurbel: P: 131 ± 24 W vs. 263 ± 45 W vs. 72 ± 36 W; HF: 121 ± 15 bpm vs. 135 ± 15 bpm vs. 113 ± 19 bmp; VO_2/kg: 20,1 ± 3,6 ml/min/kg vs. 28,3 ± 4,1 ml/min/kg vs. 15,3 ± 2,9 ml/min/kg; La: 4,2 ± 1,4 mmol/l vs. 4,8 ± 1,2 mmol/l vs. 4,4 ± 1,0 mmol.

Diskussion Zur Beurteilung der körperlichen Leistungsfähigkeit erweist sich sowohl die Fahrrad-, die Laufband-, als auch die Armkurbelspiroergometrie als geeignet. An den Maximalwerten der Leistung und der VO_{2max} zeigten sich signifikante Unterschiede bezüglich der 3 Belastungsformen, wobei die Laufbandspiroergometrie jeweils die höchsten und die Armkurbelspiroergometrie jeweils die niedrigsten Werte ergab. Die Maximalwerte der HF und des Laktats ergaben keine signifikanten Unterschiede. Die bei einer spezifischen Belastungsuntersuchung ermittelten Trainingsempfehlungen sollten nicht direkt auf andere Belastungsformen übertragen werden.

First Description of Multiple Coronary Fistula in Combination With Severe Aortic Stenosis and Ectasia

XIII-5 **075**

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Complex cardiovascular pathology often constitutes a considerable therapeutic challenge for the treating physician since published experience is scant. Here we report on a case of huge combined multiple coronary fistulae, severe aortic stenosis and aortic ectasia, which has not been reported in the literature so far.

A 68 year old patient has been brought to hospital with dyspnoea (NYHA III–IV), *de novo* persistent chest pain, radiating in his left arm and tachycardia. The patient's history was pertinent with bronchial asthma, arterial hypertension, COPD and cerebral embolism. ECG showed sinus rhythm, RBBB, VESs, T-negativity in avR; cardiac biomarkers were within the normal range. Chest x-ray demonstrated a normally sized heart with elongated and suspected aortic

ectasia. Echocardiography: LVEF and -size normal and concentric hypertrophy , minimal apical wall motion abnormality, LADD and RADD 6.0 and 5.8 cm respectively, aortic root diameter 6.4 cm, aortic valve sclerosis and stenosis (0.5 cm^2, 4.9 m/s, peak gradient 98 mmHg), the other valves and RV normal. Thoracal Contrast CT: Post-stenotic dilation of the ascending aorta (6.6 cm), aortic aneurysm verum. Coronary angiography and hemodynamics: Pressures (RA (7/5), RV (32/4), PA (28/13), PC (13/15), LV (225/17), AO (138/91), RPI 207, RP/RS (0.07); cardiac output tot (5.4), aortic VGmax (100.1), VGmean (78.5), VA 0.5 cm^2, calcified aortic valve; angiographically RCA hypoplastic, LAD and LCX minimal changes, coronary fistulae RCA ad PA and LAD ad PA; aorta ascendens and aortic arch dilated (6.8 cm); laevography: LV hypertrophy, hypokinesia in the apical segment (possibly degredation of LV wall motion secondary to steal phenomenon).

The symptoms of unstable angina as well as the apical hypokinesia have been attributed to increased O_2 demand secondary to cardiac hypertrophy and, in addition, resulting from a steal phenomenon brought about by the coronary artery fistulae. Hence, it has been decided that the patient should undergo cardiac surgery: resection and a replacement of the aortic valve and of the whole aorta ascendens was performed using Bentall technique with a valve-carrying conduit (St. Jude Medical 25 mm valve size) using Elephant Trunk Technique – complete aortic arch replacement in deep hypothermic cardiac arrest and bilateral antegrade cerebral perfusion, plus a ligature of both fistulas have been performed. The operation has been complicated by a massive bleeding from the anastomosis of the aortic trunk during the reperfusion phase. The bleeding could not be stopped and, despite maximal inotropic therapy, the patient died several hours later from low cardiac output.

While congenital as well as iatrogenic coronary fistulas are seen frequently, one finds dissenting opinions as far as the therapeutic approach is concerned. More complex cardiac pathology associated with coronary fistula has not been reported so frequently and the decision which approach to follow has remained difficult. No obvious advantage could be expected from preoperative coil embolisation. In summary, the chosen approach has been appropriate. However, the pathology of the case is complex and is generally associated with a considerable risk.

Tailored Carotid Angioplasty and Stenting. An Individual Treatment Strategy – How to do it in Practice?

XIII-7 **076**

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In Carotid Artery Stenting (CAS) 2010 there is a never ending struggle between experience-driven results and randomized evidence. The good news is that cases are safe in the majority of patients. We know from high volume-centers, that the 30 days results of all, stroke and death, which are defined by an independent neurological team, with tailored protected CAS, have an event rate in symptomatic patients of 2.7 % and in asymptomatic patients of 1.2 % [Cremonesi et al, submitted to EUJ, May 2009].

The Carotid Pathology = % Stenosis ± Symptoms and Co-Morbidity

The outcome depends on following variables:

- Clinical symptoms
- Co-morbidity
- Percentage of stenosis
- Lesion-length
- Morphology
- Echo-analysis patterns of high embolization risk (GSM)
- Vascular profile
- Lesion site characteristics
- Vascular anatomy
- Access details

In our institution careful risk-benefit evaluation is crucial. We instituted a vascular board which debates in a multidisciplinary collaboration with the neurologist, vascular surgeon, interventionist and attending physician to adopt best revascularisation-strategy. Accordingly many of the negative outcomes have seen related of poor patient selection.

The Tailored carotid angioplasty and stenting means different stenting strategies for different lesions and anatomies and different types of protection devices for different lesions and anatomies. Lesion characteristics can predict adverse outcomes after CAS. The incidence of periprocedural stroke was increased in lesions over 15 mm long, from 17 % vs 2.1 % and in ostial-centered lesions from 7.1 % vs 1.8 %.

An overview of high risk subsets shows a higher percentage of embolization in patients with soft plaques, calcified plaques, octogenarians, string-sign patients. So the angiographic string-sign formerly considered a contraindication for CAS, could safely be treated using proximal cerebral protection systems.

Stents – Using the Right Stent Stent technical features and anatomical variables should be well known. It is necessary to differentiate between soft- and hard-plaque characteristics as well as the lesion length and complexity as well as the supra-aortic trunk anatomy and the diameters of the internal and common carotid artery.

Open vs. Closed Cell Stent Geometry There are different trials to give answer if free-cell area influences the outcome in CAS. The first trial [Bosiers M. et al, Department of vascular surgery, St. Blasius, Dendermond, Belgium] shows a benefit of post-procedural events in symptomatic and asymptomatic settings with the closed cell stent design. A publication in stroke with the question does carotids stents cell design matter [Schillinger M et al. Stroke 2008; 39] shows now difference.

In vitro evaluation concerning to bending, torsion and penetration of open and closed cell stents, showing the plaque penetration is correlating to the cell size area [S. Mueller-Hulsbeck].

Carotid Stent Characteristics – 7 Characteristics of Carotid Stents.

Foreshortening The amount of foreshortening is the difference between the length of a stent prior to delivery and its lengths after deployment.

Conformability or Flexibility The flexibility of a stent is defined as its ability to conform to vessel tortuosity during deployment.

Vessel Wall Adaptability Vessel wall adaptability describes the ability of a carotid stent to adjust itself to the tapered anatomy of the region.

Wall Coverage Wall coverage is defined as the ratio between the quantities of stent material in comparison to the amount of vessel tissue.

Scaffolding Scaffolding is defined as the amount of support given to the vessel wall by a stent.

Radial Strength Radial strength refers to the amount of external pressure a stent structure can withstand without resulting in a permanent reduction in the vessel lumen.

Radial Stiffness Radial stiffness is defined as the ability of a stent to maintain its diameter when external force is applied.

Embolic Protection Devices (EPD) – Using the Right Cerebral Protection Device The risk of embolization is according to the lesion length, complexity of trunk anatomy and diameter of internal and common carotid artery. The filter pores have a size between 80 to 140 microns and so the capturing capabilities are different. Filters characterised between flexibility, track-ability, crossing profile and conformability. There are two different types of filter, the concentric and excentric filter type. Both have the same problem that in complex anatomy the wall-apposition and landingzone has a worse performance.

Multicenter trials comparing CEA and CAS are absolutely needed with the concept of a superiority trial and high technical skilled operators. The use of embolic protection devices is mandatory.

At this time we must say that the ideal EPD and stent as the combination is not available but experience with multiple systems is needed and training is crucial.

Die interventionelle Therapie des abdominellen Aortenaneurysmas im Herzkatheterlabor XIII-8 077

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Seit 3 Jahren erfolgt im Kardinal Schwarzenberg'schen Krankenhaus in Schwarzach die endovaskuläre Therapie des abdominellen Aortenaneurysmas (AAA) im Herzkatheterlabor in Kooperation mit der Gefäßchirurgie.

Das abdominelle Aortenaneurysma ist klassischer Weise eine Erkrankung älterer Männer und wies in den vergangenen Jahren eine steigende Tendenz auf. Diese Zunahme ist Ausdruck der Überalterung unserer Gesellschaft, Folge der Rauchgewohnheiten und Ergebnis des vermehrten Einsatzes bildgebender Verfahren im Rahmen von Vorsorgeuntersuchungen.

Die Indikation ist ab einem AAA-Durchmesser von 5,5 cm bzw. einer Größenzunahme von über 10 mm pro Jahr oder symptomatischen AAA gegeben.

In den Entscheidungsprozess für die jeweilige Behandlungsmethode (operativ vs. endovaskulär) bilden anatomische Voraussetzungen, der Risikostatus des Patienten sowie dessen Wunsch und die Erfahrung des Operateurs eine Rolle.

Anhand praktischer Beispiele werden Selektionskriterien für die endovaskuläre Therapie des AAA dargestellt.

Kardialer Tumor als Ursache eines thromboembolischen kardiovaskuären Insults XIII-6 078

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Anamnese Ein 63-jahriger, männlicher Patient wurde zur weiteren kardiologischen Diagnostik mit der Frage einer kardialen Embolie-quelle nach rezidivierenden transienten ischämischen Attacken und einem zerebrovaskulären Insult mit verbleibender linksseitiger Hemiparese übernommen. Eine kardiale Grunderkrankung war zur Aufnahme nicht bekannt. Fieber, Nachtschweiss oder Gewichtsverlust wurden verneint.

Diagnostik und Therapie Im Aufnahmelabor zeigte sich lediglich eine Hypercholesterinämie. Eine Erhöhung der Infektparameter oder Hinweise für einen chronischen infektiösen Prozess fanden sich nicht. In seriell abgenommenen Blutkulturen konnte kein Keimnachweis erfolgen. In einer transthorakalen Echokardiographie ergab sich eine uneingeschränkte linksventrikuläre Funktion ohne regionale Wandbewegungsstörungen. Ein ventrikulärer Thrombus konnte nicht dargestellt werden. Die Aortenklappe zeigte sich trikuspide und – wie die anderen Klappen – funktionell intakt.

Im TEE zeigte eine 10 × 6 mm messende, in den LVOT flottierende, Struktur mittlerer Echogenität am NCC der Aortenklappe.

Die präoperative Angiographie ergab eine diffuse Koronarsklerose mit einer 50 % ACD-Stenose im mittleren Drittel.

Der Patient wurde unter der Verdachtsdiagnose eines papillären Fibroelastoms den kardiochirurgischen Kollegen zur Tumorresektion vorgestellt. Der Eingriff erfolgte in minimal-invasiver Technik.

Diskussion Bei der Suche nach einer kardialen Embolie-quelle muss auch an die seltene Erscheinungsform eines papillären Fibroelastoms gedacht werden, weil – vor allem bei linksseitiger Lokalisation – eine Thromboembolierate von 25 % in 3 Jahren besteht.

Die Verdachtsdiagnose kann echokardiographisch aufgrund der typischen Morphologie gestellt und nach Resektion im Wasserbad durch das charakteristische Bild des Resektats und histologisch bestätigt werden. Es handelt sich um den zweithäufigsten benignen Tumor des Herzens. Zumeist sind die Mitral- oder Aortenklappen – in seltenen Fällen Papillarmuskel oder Atria – betroffen. Ein Rezidiv nach chirurgischer Therapie ist nicht beschrieben. Zur Abklärung zerebrovaskulärer Insulte unklarer Genese empfiehlt sich bei einer Inzidenz primär kardialer Tumore von 0,8 % eine sorgfältige kardiale Diagnostik zur Erfassung auch seltener kardioembolischer Ursachen.

Herzinsuffizienz

Electrical Optimization of Cardiac Resynchronization in Chronic Heart Failure is Associated With Improved Clinical Long-term Outcome XIV-1 079

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Background Cardiac resynchronization therapy (CRT) is an established treatment option for symptomatic chronic heart failure (CHF) patients with pharmacologic baseline therapy. Several CRT patients may have poor outcome. One reason for this may be inadequate device settings. In real-world practice, echocardiographic evaluation of atrioventricular (AV) delay is not performed in a high proportion of patients, as the effect of electrical optimization of CRT is an issue open for investigation.

Aim We performed a retrospective observational study analyzing the effect of AV-interval evaluation with echocardiography on long-term clinical outcome.

Methods and Results Mean follow-up for the 205 CHF patients was 32 (23–43) months. In the total study cohort, 124 (60.5 %) patients had reached the primary combined endpoint death or cardiac hospitalization and 59 (28.8 %) had died.

A stepwise Cox regression model including a co-morbidity score, failed AV-interval evaluation, satisfactory device function after the first implantation attempt, failure to reach 100 % of the recommended renin-angiotensin system inhibitor and β-blocker dose at follow-up and CRT device implantation compared with CRT in combination with an implanted cardioverter defibrillator (ICD) revealed that failed AV-interval evaluation (HR = 1.72 [1.19–2.49]; p = 0.004) non-optimized CHF pharmacotherapy dosages (HR = 2.12 [1.32–3.42]; p = 0.002), the presence of a CRT/ICD combination device (HR = 1.87 [1.28–2.71]; p = 0.001) and satisfactory device function after the first implantation attempt (HR = 0.44 [0.25–0.77]; p = 0.004) were associated with the primary endpoint.

Conclusion Echocardiographic evaluation of the AV-interval in patients with CRT was independently associated with improved clinical outcome, impacting on daily clinical practice of HF patient care.

Comparison of Dyssynchrony by Vectorcardiography and Echocardiography for Identification of CRT-Responders (The VEK-ECH-CRT-Pilot Trial) XIV-2 080

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Background Up to one third of patients with accepted indications for cardiac resynchronisation therapy (CRT) do not benefit from this therapy. One main reason is the lack of possibility to identify cardiac dyssynchrony (DYS) with sufficient accuracy. We compared vectorcardiographic measurements (VEC), obtained from a standard 12-lead ECG, with echocardiography (ECHO) for identification of CRT-responders.

Methods 19 pts (66.1 ± 11.7 years, 63 % ICMP, 37 % DCMP, mean NYHA class 3.0 ± 0.17, mean EF 28.1 ± 5,9 %, mean QRS duration 156 ± 23 ms) with an indication for CRT, according to current guidelines (NYHA III–IV, EF < 35 %, QRS > 120 ms) were studied at baseline (BL) and 12 weeks after implantation (FU). A

routine echo study (LV volumes, EF Simpson) and NT pro-BNP levels were collected. Indexes of DYS by VEK (TI, electrical dyssynchrony) and by ECHO (LV-PEP, IVMD, DFT) were measured. In each patient, an AV- and VV-optimization was performed within the first days after device implantation. A CRT-Responder was defined when 2 out of 3 criteria were met (FU vs. BL): functional improvement by ≥ 1 NYHA class, EF increase > 5 %, NT pro-BNP decrease > 30 %.

Results 13 out of 17 pts (76.5 %) with complete FU were CRT-responders. Patients improved their functional status, NYHA class (mean 0.9 ± 0.4; p < 0.01; 78,9 % responders) and LEF (mean 10.5 ± 5.4 %; p < 0.01; 77,8 % responders) more than their NT pro-BNP response (mean decrease in NT pro-BNP: 12.4 ± 41.1 %; p = n. s.; 33.3 % responders). 76.9 % of the CRT-responders showed signs of DYS in ECHO and 92.2 % of them had DYS in VEK. CRT improved indices of DYS in Echo and in VEK. There is a high correlation of DYS in ECHO and VEK.

Conclusions Pts with classical criteria for CRT have a high response rate if criteria of DYS are present in ECHO or VEK. CRT was associated with an improvement of DYS.

Sleep Apnea Syndrome in Patients With Stable Chronic Heart Failure XIV-3 **081**

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Rationale Treatment of congestive heart failure (CHF) has made remarkable progress over the last several years. In addition to the recommended medical and electrical therapy, new treatment strategies may include non-invasive ventilation in patients with sleep related breathing disorders (SRBD). In order to assess the extent of SRBD in patients with advanced congestive heart failure, we evaluated the prevalence of sleep apnea syndrome.

Methods A total of 106 patients (male 93; female 13) were examined with a portable overnight monitoring device. All patients suffered from stable chronic heart failure with New York Heart Association (NYHA) class III, and at least moderate to severe impaired left ventricular systolic function, and levels of proBNP greater than 300 ng/ml. Each patient was receiving the best possible treatment for chronic heart failure under current guidelines.

Results 66 patients (62.3 %) were afflicted by sleep apnea syndrome defined as apnea hypopnea index (AHI) greater than or equal to 15/h or AHI greater than or equal to 5/h and present daytime sleepiness, identified by Epworth Sleepiness Scale (ESS score greater than 7). Taking into consideration the severity of sleep apnea syndrome, 11 patients (16.7 %) presented a mild form (AHI greater than or equal to 5 and less than 15/h), 24 patients (36.3 %) exhibited moderate symptoms (AHI greater than or equal to 15 and less than 30/h) and 31 patients (47.0 %) suffered from a severe manifestation (AHI greater than or equal to 30/h). By analyzing the type of breathing disorder, we found that 35 patients (54.4 %) mainly suffered from hypopnoea, 23 patients (33.8 %) predominately exhibited central sleep apnea, and 8 patients (11.8 %) primarily experienced obstructive events.

In contrast, 40 patients (37.7 %) did not present any relevant sleep related breathing difficulty.

Conclusion Sleep related breathing disorders are common in patients with advanced congestive heart failure. Further investigation is needed to determine the impact of this concomitant feature on cardiac diseases.

Optimierte Betreuung von Herzinsuffizienzpatienten mit dem „ELICARD-Telemonitoringsystem" – Darlegung des praktischen Einsatzes anhand einer Patientenkasuistik XIV-4 **082**

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Hintergrund Die chronische Herzinsuffizienz (HI) ist eine progressive Erkrankung und hat in den vergangenen Jahrzehnten sowohl bei den Krankenhausentlassungen als auch in der Mortalitätsstatistik dramatisch zugenommen. Betroffen sind vor allem ältere Menschen, weshalb durch den demographischen Trend weiterhin mit starken Wachstumsraten zu rechnen ist. Senkung der Mortalität und Verhinderung von stationären Aufnahmen wegen kardialer Dekompensation sind ein vordringliches Behandlungsziel, da insbesondere Letztere unser Gesundheitsbudget außerordentlich belastet. Die Installierung und der Einsatz eines „Heart Failure Management Programms" zur Reduktion von Mortalität und Morbidität stellt nach den geltenden Guidelines eine dringliche Maßnahme dar, mit gleicher Evidenz wie eine optimierte neurohumorale Therapie.

Methodik Im Februar 2009 wurde für Patienten mit fortgeschrittener Herzinsuffizienz in unserem Krankenhaus, zusätzlich zur Betreuung über unsere Herzinsuffizienzambulanz, ein Telemonitoringsystem in Kooperation mit dem AIT (Austrian Institute of Technology) eingeführt. Patienten erhalten ein KeepInTouch- (KIT-) Telemonitoring-Set bestehend aus einem Blutdruckmesser (UA-767 NFC, A&D), einer Körperwaage (UC-321 A&D) plus KIT-Modul (AIT), ein Mobiltelefon (Nokia 6131 NFC), eine Patienten-Identifikationskarte sowie eine KIT-Symbolkarte zur Erfassung der Herzinsuffizienzmedikation und der subjektiven Befindlichkeit. Einmal täglich übermitteln die Patienten ihre aktuellen Daten an die Datenzentrale.

Die von AIT aufgearbeiteten Daten sind dem betreuenden Herzinsuffizienzteam über eine passwortgesicherte Homepage zugänglich. Grenzwertüberschreitungen (statische und dynamische Limits) – sogenannte „warnings" – werden zusätzlich über E-Mail mitgeteilt. Eine Ereignisliste muss täglich von einem Teammitglied abgearbeitet werden. Bei kritischen Grenzwertverletzungen werden die Patienten zusätzlich telefonisch kontaktiert. Diese werden bei der Einschulung allerdings darauf hingewiesen, dass es sich hier um kein Notfallsystem handelt und bei akuter Verschlechterung des Zustandes der Hausarzt oder das nächstgelegene Krankenhaus zu kontaktieren ist.

Ergebnis Seit Februar 2009 wurden 18 Patienten (5 Frauen, 13 Männer, mittleres Alter 73 ± 9 Jahre) in die Verwendung des ELICARD-Systems eingeschult. Alle Patienten waren bei Einschulung schwer herzinsuffizient (zumindest NYHA III) und/oder hatten in den letzten 3 Monaten vor Einschulung einen stationären Aufenthalt wegen kardialer Dekompensation.

Insgesamt wurden bisher mehr als 25.000 Datenwerte übertragen. 12 Patienten werden aktuell aktiv monitorisiert, 1 Patient ist verstorben, 1 Patient wurde herztransplantiert, 1 Patient wird nun mit Peritonealdialyse therapiert, 2 Patienten erhielten die Einschulung, wollten dann aber nicht ins System inkludiert werden. Ein Patient wollte nach 3 Monaten kein weiteres Monitoring mehr.

Patientenkasuistik Herr B. A. geboren 1927, ein Patient mit chronisch schwerer HI (NYHA Stadium III–IV), wurde am 25.02.2009 ins ELICARD-Telemonitoring eingeschult. Es gab im Beobachtungszeitraum (31 Wochen) an 47 Tagen zumindest eine Grenzwertüberschreitung (Blutdruck und/oder Körpergewicht und/oder Herzrate). Nachfolgend der Verlauf während des Telemonitorings mit Beschreibung der relevanten Grenzwertverletzungen.

Woche 4: Relevanter Gewichtsanstieg und subjektive Verschlechterung des Wohlbefindens: Steigerung der diuretischen Therapie (telefonisches Aviso) – Miteinbeziehung des Hausarztes – stationäre Aufnahme vermieden!

Woche 8: Abrupter, relevanter Herzfrequenzanstieg und subjektive Verschlechterung des Wohlbefindens: Der Patient wird ambulant

einbestellt. Ursache ist ein paroxysmal tachykardes Vorhofflimmern. Stationäre Aufnahme zur weiteren Therapie (elektr. Kardioversion, Amiodarone) – kardiale Dekompensation vermieden!

Woche 10: Geplante Kontrolle in der HI-Ambulanz, keine relevanten Grenzwertverletzungen.

Woche 15: Relevanter Gewichtsanstieg und subjektive Verschlechterung des Wohlbefindens: Steigerung der diuretischen Therapie (telefonisches Aviso) – keine stationäre Aufnahme notwendig!

Woche 17: Stationäre Aufnahme wegen subjektiver Verschlechterung – keine relevanten Grenzwertverletzungen.

Woche 18: Relevanter Gewichtsanstieg: klinisch zunehmende Beinödeme – Steigerung der diuretischen Therapie (telefonisches Aviso) – stationäre Aufnahme vermieden!

Woche 29: Relevanter Gewichtsanstieg, niedriger Blutdruck und subjektive Verschlechterung des Wohlbefindens: stationäre Aufnahme wegen kardialer Dekompensation.

Woche 31: Starker Anstieg der Herzrate und relevanter Gewichtsanstieg im Vorfeld, relevante Verminderung des systolischen Blutdrucks: stationäre Aufnahme wegen kardialer Dekompensation – Patient verstirbt in Woche 32 an der progressiven Herzinsuffizienz.

Zusammenfassung Das ELICARD-Telemonitoring ermöglicht eine engmaschige und effiziente Überwachung von Patienten mit chronischer, schwerer Herzinsuffizienz. Durch Vereinfachung der Datenerhebung („Keep in touch"-Technologie) ist es auch älteren Patienten, die ja die Hauptgruppe der chronisch Herzinsuffizienten bilden, möglich, mit diesem System umzugehen. Durch Festlegen von statischen und dynamischen Limits kann eine klinische Verschlechterung rechtzeitig erkannt und therapiert und so in einem Teil der Fälle eine stationäre Aufnahme vermieden werden.

Gamma-Glutamyltransferase (GGT) Rather than Bilirubin is of Prognostic Significance in Chronic Heart Failure

BAI 083

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Purpose Recent evidence suggests that serum levels of gamma-glutamyltransferase (GGT) and total bilirubin (T-Bil) are elevated and of prognostic significance in chronic heart failure (CHI). A head-to-head comparison of the relevance of cholestatic enzymes, however, is still pending. Hence, it was the aim of our study to compare these novel cardiovascular risk factors in heart failure.

Methods From 2000 to 2008 clinical and laboratory parameters of 1032 consecutive outdoor patients (NYHA class I 25 %, class II 46 %, class III/IV 29 %; median LV-EF 28 %) of our heart failure program were evaluated. Long-term follow-up (median 36 months) was available in 1002 patients. The primary endpoint was defined as death of any cause or heart transplantation. Univariate and sex stratified Cox proportional hazards models, adjusted for age, ischemic etiology, NYHA class, LV-EF, systolic blood pressure, heart rate, glomerular filtration rate, body mass index, DM were performed to calculate hazard ratios (HR) and 95 % confidence intervals for GGT and T-Bil.

Results Prevalence of elevated GGT was 44 % in men (GGT > 65 U/l) and 52 % in women (GGT > 38 U/L); corresponding numbers for T-Bil (> 22 µmol/L for both gender) were 18 % and 8 %, respectively. Both variables were significantly correlated with severity of heart failure as assessed by NYHA class and LV-EF. The combined endpoint was recorded in 339 patients. GGT as well as T-Bil were significantly associated with adverse outcome in univariate analyses ($p < 0.0001$ and $p = 0.013$, respectively). However, GGT (HR 1.541 [1.18–2.02]; $p = 0.002$) but not T-Bil remained an independent predictor of prognosis in the multivariate model. Proportion of explained variation showed that GGT (1.03 %) was a stronger predictor of outcome than T-Bil (0.09 %; $p = 0.0009$).

Compared to the lowest GGT quintile, adjusted HR for patients in the highest quintile was 1.71 (1.18–2.48), 1.29 (0.87–1.90) in the fourth quintile, 1.1 (0.73–1.66) in the third quintile and 1.23 (0.82–1.85) in the second quintile ($p = 0.027$). Corresponding 5 years cumulative survival/time to transplantation rates were 30 %, 41 %, 58 %, 57 %, and 64 %.

Conclusions In ambulatory patients with chronic heart failure, prevalence is high for GGT and modest for bilirubin elevations. Both variables are clearly associated with disease severity. However, only GGT is independently associated with adverse outcome. Our findings further highlight the clinical importance of GGT in cardiovascular disease.

Heart Rate and Functional Class at Referral are Predictors of Outcome in Heart Failure Patients in the Real World. Data From the Austrian Heart Failure Registry

BAII 084

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[1]Department of Cardiology, Medical University Graz; [2]Department of Medical Statistics, Informatics and Health Economics, Medical University Innsbruck; [3]Department of Cardiology, Medical University Vienna; [4]Department of Cardiology, Medical University Innsbruck; [5]Department of Internal Medicine, Hanusch-Krankenhaus, Vienna; [6]Department of Internal Medicine, Hospital Krems; [7]Department of Cardiology, Elisabethinen-Hospital Linz; [8]Department of Internal Medicine, SMZ Süd, Vienna; [9]Department of Cardiology, Private Medical University Salzburg

Purpose Elevated heart rate (70 beats per minute-bpm or more) is a predictor of impaired prognosis in patients with ischemic heart failure. The Austrian Working Group on Heart Failure has established a registry in May 2006 for all patients referred to dedicated heart failure clinics with a planned follow-up after 12 ± 3 months. Here we report an analysis of the prognostic impact of elevated heart rate at referral in a well defined cohort of heart failure patients.

Methods Between May 2006 and October 2009 1904 patients have been documented in the Austrian Heart Failure Registry. 1363 patients (72 %) had sinus rhythm at referral. Kaplan-Meier and Cox proportional hazards regression analyses were used to compare overall and cardiovascular mortality between high (70 bpm or more) and low heart-rate groups. Patients with lost-of-follow-up (n = 116) were censored at time of last contact.

Results At baseline in 793 patients (58 %) heart rate has been elevated (70 bpm or more) while in 562 patients it has been below 70 bpm, in 8 patients no baseline heart rate has been recorded. Groups were equally balanced regarding age, gender and cardiovascular risk factors with the exception of smokers (more active smokers in the high heart-rate group: 23 vs 14 %; $p = 0.001$) and valvular cause of heart failure (more frequent in the high heart-rate group: 3 % vs 1 %; $p = 0.012$). Patients in the high heart-rate group had significantly higher median NT-pro-BNP (1470 pg/ml, IQR 499–4188 pg/ml) compared to patients in the low heart-rate group (784 pg/ml, IQR 314–2162 pg/ml; $p < 0.001$). NYHA functional class III and IV has been more frequent in the high heart-rate group than in the low heart-rate group (32 % and 22 %, respectively; $p < 0.001$) while reduced left ventricular ejection fraction (39 % or less) has been more frequent in the high heart-rate group than in the low heart-rate group (71 % and 61 %, respectively; $p < 0.001$). In the high heart-rate group treatment with beta-blockers has been less frequent than in the low heart rate group (76 % and 86 %, respectively; $p < 0.01$) while dosage of β-blocker therapy has been comparable in both groups.

Of the 75 patients who died within 3.5 years 38 deaths had a cardiovascular cause with 10 deaths occurring in the low heart-rate group and 28 deaths in the high heart-rate group, respectively ($p = 0.058$). Cox proportional hazards analysis revealed that high NYHA functional class (III and IV) and elevated heart rate (70 bpm or more) were the best predictors of both overall and cardiovascular mortality.

Conclusion Higher NYHA-functional classes and elevated heart rate (70 bpm or more) are predictors of adverse outcome in chronic heart failure patients. This is an important finding as 76 % of patients in the high heart-rate group have been treated with β-blockers at doses not different from patients with low heart-rate at referral.

Blood Urea Nitrogen (BUN) Predicts All-Cause Mortality in Chronic Stable Heart Failure in Addition to Plasma Nt-proBNP and Cardiac Troponin T

XIV-7 **087**

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Background Kidney function is a strong determinant of survival of patients with chronic heart failure (CHF). Blood urea nitrogen (BUN) is shown to be a strong prognostic marker in patients with acute decompensated heart failure but its predictive power in CHF has not been investigated yet.

Methods We measured BUN, serum creatinine, troponin T and plasma Nt-proBNP concentrations in 184 patients with CHF. Patients were followed for all-cause mortality during a median time of 1,282 days. The glomerular filtration rate (eGFR) was estimated by the MDRD formula. Optimal cut-off concentrations for prediction of mortality were determined using classification and regression tree analysis.

Results During the follow-up period 64 (34 %) patients died. Plasma concentrations of Nt-proBNP ($p < 0.001$), troponin T ($p < 0.001$), BUN ($p < 0.001$) and serum creatinine ($p = 0.015$) were significantly higher and eGFR ($p = 0.008$) significantly lower in patients who died compared to those who survived. In multivariate Cox regression analysis, adjusted for age, sex, Nt-proBNP and troponin T concentrations, BUN of > 33 mg/dl (HR: 1.96; $p = 0.017$) but not eGFR of ≤ 60 ml/min/1.73 m^2 (HR: 0.73; $p = 0.25$) was a significant predictor of mortality. Higher BUN concentration was also significantly associated with outcome in the group of patients with eGFR > 60 ml/min/1.73 m^2 ($p = 0.009$). Moreover, patients with BUN concentrations of > 33 mg/dl and Nt-proBNP of > 1.760 pg/ml had substantially worse outcome than patients with either marker elevated or with both markers below the respective cut-offs ($p < 0.001$; **Figure 7**).

Conclusion In the present study we could show that in contrast to eGFR, BUN, a generally available and routinely determined marker of renal function, is a strong and independent predictor of long-term outcome in CHF in addition to plasma Nt-proBNP and cardiac troponin T levels.

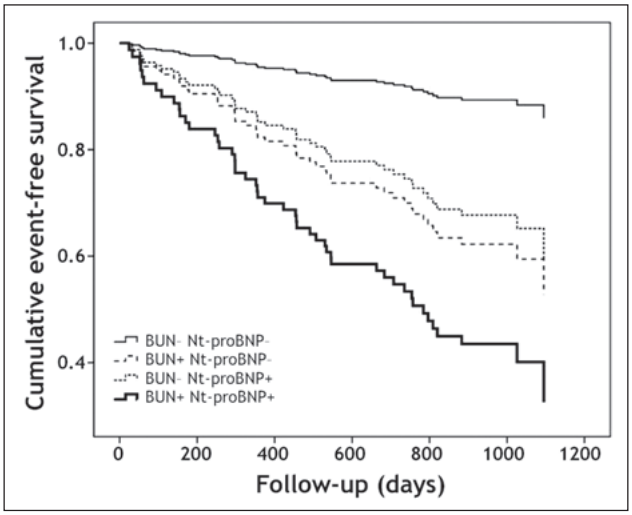

Figure 7: R. Jarai et al.

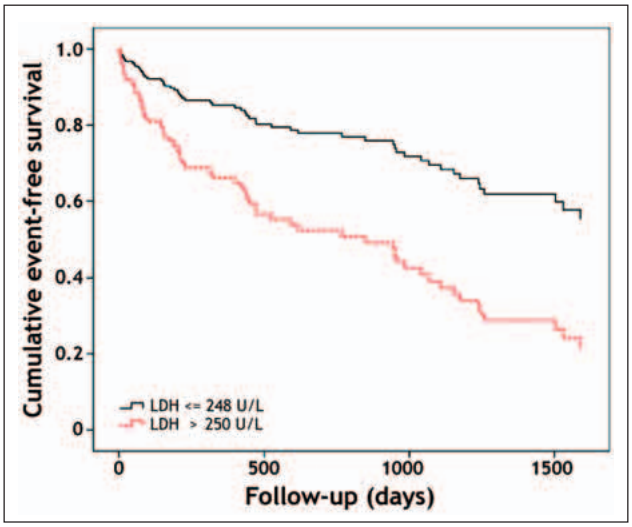

Figure 8: R. Jarai et al.

Lactate Dehydrogenase (LDH) Predicts Hospitalization Due to Cardiac Decompensation in Chronic Stable Heart Failure

XIV-9 **085**

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Background Recurrent hospitalizations due to cardiac decompensation significantly impair quality of life of patients with advanced heart failure. Reducing hospital admissions by proper identification of patient at risk might be a major step in improving not only the quality of life with chronic heart failure (CHF) but could also significantly reduce the associated financial burden on health care systems. Plasma natriuretic peptides and markers of renal function are well-established predictors of outcome in CHF. Little is known, however, about the prognostic significance of elevated liver enzymes.

Methods We measured liver enzymes (GOT, GPT, gamma-GT, ALP and LDH), serum creatinine, troponin T (4th generation assay as well as high-sensitivity assay) and plasma Nt-proBNP concentrations in 180 patients with CHF. Patients were followed for re-admission to the hospital due to cardiac decompensation. The glomerular filtration rate (eGFR) was estimated by the MDRD formula.

Results During the median follow-up time of 884 days, 71 (39 %) were re-admitted to the hospital. Plasma concentrations of Nt-proBNP ($p < 0.001$), troponin T (both with the 4th generation and the high-sensitivitiy assay: $p < 0.001$), eGFR ($p < 0.001$), LDH ($p < 0.001$), NYHA classes ($p = 0.008$) and age ($p = 0.02$) were significant predictors of re-hospitalization in univariate Cox-regression analysis. None of the other liver enzymes were related to re-hospitalization. In multivariate analysis, only Nt-proBNP (HR: 3.79; $p < 0.001$), troponin T measured with the high-sensitivitiy assay (HR: 2.26; $p = 0.011$) and LDH (HR: 2.58; $p = 0.009$; **Figure 8**) remained significantly associated with the risk of re-hospitalization.

Conclusion In the present study we could show that in the era of emerging new biomarkers an old, widely available and routinely determined biomarker, like LDH, could be used to predict outcome of patients with CHF.

Complementary Role of Copeptin and High-Sensitivity Troponin in Predicting Outcome With Stable Chronic Heart Failure

XIV-8 **086**

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Background Copeptin, the c-terminal part of the vasopressin prohormone, has elevated concentrations after myocardial infarction and predicts adverse outcome. It has been suggested that the combined determination of copeptin with cardiac troponins (cTnT) in patients with chest pain might accelerate the early diagnosis of myocardial injury. In the present study we investigated whether this complementary role of copeptin and cTnT in detecting myocardial stress

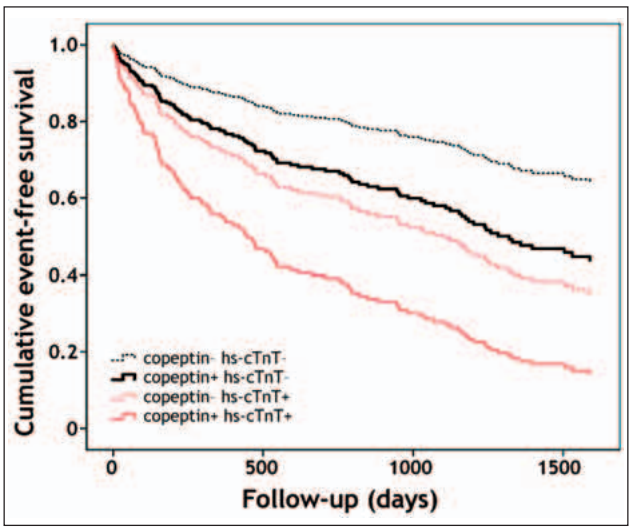

Figure 9: R. Jarai et al.

could also be used for identification of high-risk patients with chronic stable heart failure.

Methods We measured copeptin and cTnT (high-sensitivity troponin T assay) in 172 consecutive patients with stable chronic heart failure. Patients were followed for all-cause mortality and re-hospitalization due to heart failure during a median time of 796 days.

Results Plasma copeptin showed modest but significant correlation with hs-cTnT ($r = 0.4$; $p < 0.001$), age ($r = 0.36$; $p < 0.001$), creatinine ($r = 0.52$; $p < 0.001$) and Nt-proBNP ($r = 0.42$; $p < 0.001$). Both copeptin ($p = 0.002$) and hs-cTnT ($p = 0.005$) concentrations increased significantly with higher NYHA classes. 109 (58 %) patients had hs-cTnT concentrations (> 14 pg/ml) and 104 patients (55 %) had copeptin concentrations above the normal (16.4 pmol/l). In survival analysis both, elevated copeptin and hs-cTnT concentrations were significant predictors of outcome ($p < 0.001$ for both). Moreover, higher copeptin levels were related to higher risk of death or hospital re-admission both among patients with or without elevated hs-cTnT concentrations (≤ 14 pg/ml: HR 1.86; $p = 0.12$ and > 14 pg/ml: HR 1.81; $p = 0.027$; respectively). The combination of both markers showed a graded highly significant association with impaired outcome, which was independent of plasma Nt-proBNP **(Figure 9)**.

Conclusion Our data suggest that hs-cTnT and copeptin could be used in combination to predict the outcome of patients with chronic stable heart failure. Future studies should evaluate how these biomarkers might guide our therapeutic decisions and help to improve clinical outcome.

Vergleichende Prädiktion für den CRT-Response mittels invasiver, vektorkardiographischer und QRS-Dauer-Messungen BAI 088

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Einleitung Für Patienten mit schwerer Herzinsuffizienz und ventrikulären Leitungsstörungen ist die kardiale Resynchronisations-Therapie (CRT) eine akzeptierte, additive Therapie. Nicht alle CRT-versorgten Patienten profitieren davon, ca. 30 % der Patienten werden als Non-Responder eingestuft. Echokardiographische Messungen stellen Parameter für die Indikation dar, sind aber für die Responder-Prädiktion nicht valide. Ein neuer Algorithmus, basierend auf der Vektor-EKG-Analyse (VKG), kann zur Differenzierung von Respondern und Non-Respondern (NonR) beitragen. In dieser Studie wird die Effektivität des VKG-Algorithmus mit den hämodynamisch gemessenen Daten und der QRS-Dauer verglichen.

Methode Bei 126 Patienten (m 74 %, 66,6 J., QRS-Breite 161 ± 27 mm, LVEF 25 ± 6,5 %, LVEDD 67 ± 8 mm, DCMP 60 %, ICMP 40 %) wurden die EKG- und VKG-Daten prospektiv vor der CRT-Implantation aufgezeichnet. Die QRS-Dauer wurde aus 12 Ableitungen gemittelt. Über das VKG wurde die Vektorzeitfläche berechnet und das Intervall (TI) vom Maximalvektor bis zum Ende der Vektorzeitfläche bestimmt. Der TI-Wert und die QRS-Dauer wurden mit den Ergebnissen der hämodynamischen Messungen, die nach der CRT-Implantation erhoben wurden, korreliert. Invasiv, hämodynamisch wurden die Kontraktilität (LV dp/dt) und der Pulsdruck (PP) gemessen. Als positiver CRT-Response wurde eine Zunahme von > 10 % dp/dtmax und > 5 % PP, unter Stimulation gegenüber dem Ausgangswert ohne Stimulation, definiert.

Ergebnisse 25 Patienten (20 %) wurden invasiv, hämodynamisch als NonR bewertet. Für das TI ergab die ROC-Analyse, im Vergleich mit den hämodynamischen Ergebnissen, einen Cut-off-Wert von < 64 ms bei den Non-R, 19 von 25 Non-R wurden über das TI korrekt identifiziert. Die Qualitätskriterien für das TI als diagnostischer CRT-Prädiktor waren: Sensitivität 96 %, Spezifität 80 %, positiv-prädiktiver Wert 96 %, negativ-prädiktiver Wert 79 %. Für die QRS-Dauer ergab die ROC-Analyse ein Cut-off-Wert < 128 ms. Acht von 25 Non-R wurden über die QRS-Dauer (> 128 ms) identifiziert, Sensitivität 99 %, Spezifität 36 %.

Zusammenfassung Der Vergleich der hämodynamischen Daten mit dem TI-Algorithmus zeigt für diesen eine bessere Prädiktion für den CRT-Non-Response als die QRS-Dauer.

The Potential Role of Ultra-Sensitive Troponin-Determination in Chronic Stable Heart Failure XIV-5 089

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Background Patients with stable coronary artery disease (CAD) have highly a worse clinical outcome even at very low concentrations of cardiac troponin T (cTnT), which are usually undetectable with the currently used routine assays. As shown previously, increased concentrations of cTnT, as measured by routine assays, are also predictive of outcome in patients with chronic heart failure. However, it is not known to date, whether very low concentrations of cTnT, as measured with a new ultra-sensitivity assay (hs-cTnT), might be used for prediction of clinical outcome in patients with chronic stable heart failure.

Methods We measured cTnT both with a 4th generation troponin T assay as well as with an ultra-sensitivity troponin T assay (5th generation) in 186 consecutive patients with stable CHF. Patients were followed for all-cause mortality and re-hospitalization due to heart failure during a median time of 914 days.

Results 31 % of patients with normal cTnT levels by use of the commercial routine assays (cut off value > 0.01 ng/ml) had detectable cTnT levels above the normal range (> 14 pg/ml) by use of this 5th generation ultra-sensitive assay. In these patients elevated hs-

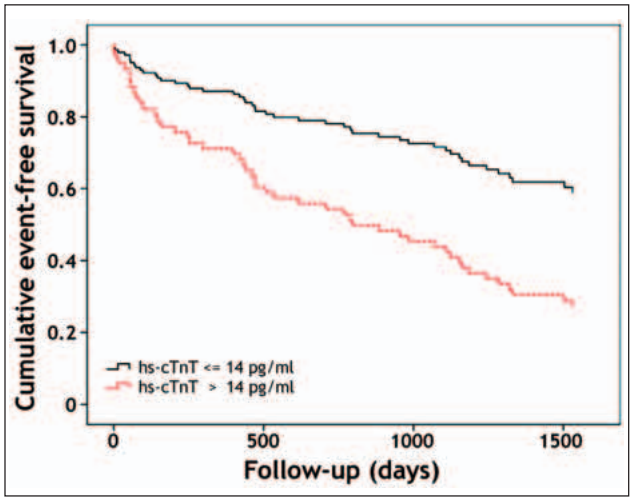

Figure 10: L. Leherbauer et al.

Table 6: D. Moertl et al.

	Placebo			1g n3-PUFA/d			4g n3-PUFA/d		
	Baseline	3 mo	p-value	Baseline	3 mo	p-value	Baseline	3 mo	p-value
LVEF (%)	25 ± 6	26 ± 5	n. s.	24 ± 8	27 ± 8	0.02	24 ± 7	29 ± 8	0.005
FMD (%)	8.5 ± 7.6	8.4 ± 4.4	n. s.	8.3 ± 5.3	10.2 ± 4.3	0.07	8.4 ± 4.8	11.6 ± 7.0	0.01
IL-6 (pg/ml)	3.6 ± 6.2	3.7 ± 6.4	n. s.	4.5 ± 6.6	1.6 ± 2.1	0.1	3.0 ± 2.9	0.7 ± 0.8	0.03

cTnT levels were significant predictors of outcome (HR: 1.08 [1.03–1.14]; p < 0.001) as hs-cTnT levels of > 14 pg/ml were associated with significantly higher risk of death or re-hospitalization due to heart failure (HR: 2.47 [1.38–4.40]; p = 0.002; **Figure 10**). This strong association between outcome and elevated hs-cTnT in survival analysis remained highly significant (HR: 2.68 [1.41–5.12]; p = 0.003) after multivariate adjustment of covariates.

Conclusion One third of patients with stable CHF and undetectable cTnT levels measured by the currently used routine assays had pathologic concentrations of hs-cTnT by use of an ultra-sensitive assay and an impaired clinical outcome. Accordingly, the use of an ultra-sensitive cTnT assay should be used for an optimal prediction of future clinical course of these patients.

Dose-Dependent Effects of Omega-3-Polyunsaturated Fatty Acids on Systolic Left Ventricular Function, Endothelial Dysfunction, and Interleukin-6 in Patients With Severe Chronic Heart Failure of Non-Ischemic Origin

XIV-6 **090**

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Background and Aim The GISSI-HF trial demonstrated a small survival advantage for supplementation with 1 g/d of omega-3 polyunsaturated fatty acids (n3-PUFA) in patients with chronic heart failure (CHF). However, benefits for other indications were achieved with higher dosages: In hypertriglyceridemia, 2-4 g/d n3-PUFA are necessary to reduce triglyceride levels. Similar dose-dependent effects were found in chronic inflammatory diseases as rheumatoid arthritis and inflammatory bowel disease. We hypothesized that such a dose-efficacy relationship for the beneficial effects of n3-PUFA also exists in chronic heart failure. Therefore, we evaluated the effects of different doses of n-3 PUFA on left ventricular ejection fraction (LVEF), flow-mediated vasodilation (FMD), and interleukin-6 in patients with severe CHF of non-ischemic origin.

Methods and Results In this randomized, double-blind, placebo-controlled three-arm trial, a total of 43 patients with severe CHF of non-ischemic origin received 1 g PUFA/day (n = 14), or 4 g PUFA/day (n = 13), or placebo (n = 16) for 3 months. N3-PUFA 1 g/d and 4 g/d significantly increased LVEF in a dose-dependent manner (**Table 6;** p = 0.03 for dose-dependent trend). FMD was increased significantly by 4 g/d, increased in trend by 1 g/d, and remained unchanged with placebo. Interleukin-6 levels were decreased significantly by 4g/d, decreased in trend by 1 g/d, and remained unchanged with placebo.

Conclusion Treatment with n-3 PUFA for 3 months leads to a dose-dependent improvement in LVEF in patients with CHF. High dose treatment with 4g n3-PUFA/d also improved endothelial function and decreased interleukin-6 levels.

Prognostic Value of Heart Rate in Chronic Heart Failure Patients With Reduced Ejection Fraction Depends on the Degree of Beta-Adrenergic Blockade

BAI **091**

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Background The BEAUTIFUL-Study has shown that a heart rate > 70 bpm is associated with a worse prognosis in patients with ischemic heart disease and reduced ejection fraction. This finding supported the rationale of the SHIfT-trial which investigates the effects of selective heart rate reduction by ivabradine on top of optimized β-blocker therapy in heart failure patients with reduced ejection fraction. Since the degree of β-blockade might influence the prognostic importance of heart rate and thus the effectiveness of selective heart rate reduction on outcome, we evaluated the prognostic power of heart rate at different levels of β-blockade.

Methods 642 chronic heart failure patients (17 % female, age 59 ± 13 y, LVEF < 40 %) were subgrouped according to their β-blocker medication in terms of percent recommended target dose: low: 6–25 % (n = 236), intermediate: 26–75 % (n = 243), high: > 75 % (n = 163).

Results 246 (38 %) patients died after a follow-up period of 60 months. β-blocker dosage was associated with lower mortality. Moreover, we found a significant, positive interaction (p = 0.026) between high heart rate and β-blocker dosage showing that the power of heart rate > 70 bpm to predict mortality increases as the β-blocker dosage increases. Although in the total population high heart rate alone was not significantly associated with mortality risk, in the subgroup of patients with highest beta blockade high heart rate was a significant predictor of mortality (HR: 1.709 [1.061–2.754]; p = 0.0276), in contrast to patients with intermediate (HR: 1.151 [0.722–1.836]; p = 0.5536) and low β-blocker dosages (HR: 0.992 [0.621–1.366]; p = 0.683).

Conclusions The prognostic importance of elevated heart rate in patients with chronic heart failure and reduced ejection fraction depends on beta-blocker dosage. The prognostic power of heart rate was only apparent in patients with highest doses of beta-blocker medication. These findings might be useful in interpreting the upcoming results of the SHIfT-Trial and in estimating the potential benefit of selective heart rate reduction in chronic heart failure.

The "Cardio-Hepatic Syndrome" in Chronic Heart Failure: Prevalence and Prognostic Significance

BAII **092**

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Background Characterization and importance of the "cardio-hepatic syndrome" in heart failure is poorly defined. We aimed to investigate the relevance of circulating liver function tests in chronic heart failure.

Methods From 2000 to 2008 clinical and laboratory variables of 1032 consecutive outdoor heart failure patients (NYHA class I 25 %, class II 46 %, class III/IV 29 %; median LV-EF 28 %) were evaluated. Follow-up (median 36 months) was available in 1002 patients. The endpoint was defined as death from any cause or heart transplantation. A forward stepwise Cox proportional hazards regression model for sex-stratified data was used.

Results Sex-specific prevalence of cholestatic enzyme elevation was 19.2 %. In contrast, prevalence of elevated transaminases (8.3 %) was in the range of a general U. S. population. All cholestatic enzymes were significantly associated with severity of heart failure (NYHA-classification, LV-EF) and signs and indices of right heart dysfunction (pulmonary artery pressure, tricuspid regurgitation, jugular venous distension, peripheral edema). The endpoint was recorded in 339 patients. T-Bil, GGT and ALP but not transaminases were associated with adverse outcome in a univariate model. Cholestatic enzyme elevation (HR 1.47 [1.12–1.91]; p = 0.005) and

GGT per log unit (HR 1.541 [1.18–2.02]; p = 0.002) as a single marker remained independent predictors of prognosis after adjusting for a wide array of other clinical and laboratory predictors.

Conclusions The "cardio-hepatic syndrome" in chronic heart failure is characterized by a predominantly cholestatic enzyme pattern, which is associated with disease severity and prognosis. GGT as a single marker is independently associated with adverse outcome. Further studies are needed to identify the exact mechanisms of interaction between heart and liver in the "cardio-hepatic syndrome".

Interventionelle Kardiologie

Effects of Unfractionated Heparin and Bivalirudin on Platelets Under High Shear Conditions in Patients Undergoing Percutaneous Coronary Intervention

VI-1 **093**

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Background Thrombin-generation and activation of platelets during percutaneous coronary intervention (PCI) play a key role for early thrombotic events. Heparin and bivalirudin are approved anticoagulants for PCI. We therefore examined the specific effects of these anticoagulants on platelet function under shear stress conditions.

Methods To simulate in vivo conditions that may precipitate a bleeding/thrombotic event, we added thrombin in vitro to blood samples from 89 patients who had been randomly assigned to receive heparin or bivalirudin for elective PCI and examined thrombin-inducible platelet function under high shear conditions.

Results Platelet adherence increased by 10 percent of baseline with heparin, but decreased by 20 % with bivalirudin (p = 0.0047). Thrombin-inducible platelet adherence and size of aggregates was equally inhibited by heparin and bivalirudin.

Conclusions Under high shear conditions as they occur in atherosclerotic vascular compartments, heparin and bivalirudin inhibit thrombin-induced platelet adherence and aggregate formation to a similar extent, while they have opposite effects on platelet adherence in the absence of thrombin.

This study was part of the doctorial thesis of NR at the Division of Blood Group Serology.

Cerebral Magnetic Resonance Imaging Unmasks Microembolic Cerebral Lesions After Transcatheter Aortic Valve Implantation

BAI **094**

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Purpose Transcatheter aortic valve implantation (TAVI) is an emerging alternative treatment option for patients with symptomatic severe aortic stenosis (AS) and high risk for operative valve replacement. However, stroke can be a catastrophic complication of TAVI. Stroke has been reported to occur in up to 6.3 % of patients undergoing TAVI. This study aimed to assess frequency and extent of subclinical microembolic cerebral lesions after TAVI.

Patients and Methods In our institution, 46 patients (15 male, 31 female; mean age 81 ± 5 years) with symptomatic severe AS underwent TAVI between July 2008 and November 2009. The self-expanding CoreValve prosthesis was implanted via transfemoral access using the current 18 French delivery catheter system. 37 patients were scheduled for cerebral diffusion-weighted magnetic resonance imaging (DW MRI) two days before and up to six days after TAVI. Nine patients were not eligible due to pacemaker implantation prior to enrolment. 25 patients underwent both pre- and postinterventional DW MRI, while twelve patients could not undergo postinterventional MRI and had to be excluded from analysis (need for permanent pacemaker implantation, n = 2; critical status, n = 5; MRI not available, n = 5).

Results Thorough physical examination did not reveal any changes in neurological status after TAVI. However, comparison of pre- and postinterventional DW MRI showed that 23 of 25 patients (92 %) had newly acquired bright lesions (p < 0.001) in accordance with subclinical cerebral embolisation: class I (1–3 new bright lesions), n = 9 (36 %); class II (4–7 new bright lesions), n = 8 (32 %); class III (≥ 8 new bright lesions or cortical infarction), n = 6 (24 %). Only in 2 patients (8 %) there was no evidence for any newly acquired bright lesion (class 0).

Conclusion TAVI with the self-expanding CoreValve® bioprosthesis is an emerging alternative treatment option for high-risk patients with symptomatic severe AS. Albeit risk of stroke is low, the vast majority of patients show newly acquired bright lesions in DW MRI compatible with subclinical cerebral embolisation. In the near future embolic protection devices along with a more detailed assessment of the aorta, improved techniques and less traumatic catheters might contribute to minimize cerebral microembolisation and even stroke.

Gender-Based Differences in Clinical Outcomes Using Dior Paclitaxel-Eluting Balloon in Coronary Artery Disease

XV-1 **095**

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Objectives The aim of our present analysis was to investigate the gender-based differences in clinical outcomes after using of paclitaxel-eluting balloon in patients with coronary artery disease (CAD).

Methods Between July 2007 and July 2009 85 patients (18 females 21.2 % and 67 male 78.8 %) were treated by dilatation of a significant coronary lesion with Dior balloon. All patients were clinically controlled 6 months after index procedure. Nonfatal acute myocardial infarction (AMI), stroke, all-cause death and target vessel revascularization (TVR) were considered as major adverse cardiac and cerebral events (MACCE) at 6-month follow-up (FUP).

Results High prevalence of coronary risk factors (88.2 % vs 89.1 % hypertension, 41.2 % vs 39 % diabetes mellitus, 100 % vs 87.7 % hyperlipidaemia, 11.8 % vs 26.2 % positive family anamnesis for coronary artery disease in female vs male patients) was documented, without significant differences between the 2 genders. The rate of previous AMI and CABG, chronic renal diseases and treatment of de novo lesion or in-stent restenosis were similar in the groups. Trend towards lower incidence of UA/NSTEMI at the clinical presentation (27.8 % vs 46.3 %; p = 0.159) was observed in females vs males. The age (58.8 ± 12.5 vs 63.2 ± 13 y), number of treated vessels (1.7 ± 1.0 vs 1.8 ± 1.0), maximal balloon diameter (2.75 ± 0.2 vs 3.06 ± 0.6 mm) and balloon inflation time (60 ± 0 vs 59 ± 21 sec) did not differ between the females and males. Intervention complication occurred in 1 female and 2 males. No acute or subacute stent thrombosis was documented. During the 6-month FUP, death occurred in 1 patient in both groups (5.6 % and 1.5 %), AMI in 0 % and 6.0 % (p = 0.288), TVR in 0 % and 17.9 % (p = 0.053) in females and males. There was neither stroke nor bleeding complications. Composite of MACCE was 5.6 % and 20.9 % in females and males (p = 0.130).

Conclusions Strong trend towards higher incidence of medium-term complications was observed in male patients as compared to females. The real clinical benefit of Dior balloon treatment for either de novo lesion or in-stent restenosis in female patients should be investigated in a larger cohort.

Tailoring Individual Antiplatelet Therapy After Coronary Stent Implantation has the Potential to Abolish Early Definitive Stent Thrombosis in Compliant Patients XV-2 096

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Context Early stent thrombosis (ST) occurs in up to 3 % of patients after coronary stent implantation and is associated with high residual platelet reactivity on standard dual antiplatelet therapy (DAP).

Objective To evaluate the capability of tailoring DAP with Multiple Electrode Aggregometry (MEA) to improve inhibition of platelet aggregation (IPA) and clinical outcome.

Setting and Patients Prospective, single-center cohort observation of 329 consecutive patients undergoing percutaneous coronary intervention (PCI) between September 24th, 2008 and January 31st, 2010. On-treatment platelet reactivity was measured by MEA, a new generation impedance aggregometer (Multiplate Analyzer, Dynabyte Medical, Munich, Germany) on average after 12 hours of loading. In case of clopidogrel non/low response (area under the curve [AUC]: > 57 U ADP-induced aggregation), individual DAP was tailored with either repeated 600mg clopidogrel loading doses (up to 3 times) until June 2009, or 60 mg prasugrel loading thereafter. 30 days follow up was obtained either by standard outpatient care, telephone contact or web.okra database search.

Main Outcome Measurement The primary end point was definitive early ST (acute or sub acute within 30 days). The secondary endpoint was defined as a composite of probable ST (according to ARC criteria) and cardiovascular death within 30 days.

Results Demographics: ACS indication for PCI (7 % STEMI, 39 % NSTEMI) was present in 46 % of the 329 consecutive patients (31 % female, 33 % diabetics, mean age 65 ± 12, range 29–90). Majority of cases (78 %) revealed a complex lesion morphology (b2/c), with LM and/or LAD PCI performed in 10 % and 58 %, respectively. Two or 3 vessel disease was treated in 53 %. On average 2.2 stents/patient (range 1–10) were implanted (total stent length 8–190 mm), 88 % of patients received DES (Xience 47 %, Resolute 22 %, Biomatrix 22 %). GP IIbIIIa inhibitors were used in 25 % of ACS patients (16 % Reopro, 9 % Integrilin).

Platelet reactivity: 12 hours after 600 mg clopidogrel loading, non- or low response occurred in 32 % of patients (AUC; 73 ± 22 U vs 28 ± 12 U; $p < 0.0001$) with a significant higher proportion of diabetics (39 % vs 28 %; $p = 0.04$) and overweights (BMI 29.5 ± 4.9 vs 28.2 ± 4.5; $p = 0.03$). Subsequently, 11 % received 60 mg prasugrel loading and 21 % 600 mg clopidogrel (up to 3 times in 3 %) to reach sufficient IPA levels (27 ± 16 U; $p < 0.0001$ vs. initial response).

Clinical endpoints: At 30 day follow-up, no primary end point occurred in patients with DAP compliance (0 %). Only 1 patient (0.3 %), discontinuing DAP on the 27th day after PCI, experience a ST on day 32. The secondary endpoint occurred in 8 patients (2.4 %). One patient with known ischemic cardiomyopathy died suddenly 10 days after PCI for NSTEMI, which qualifies as probable ST. The other 7 patients died within the index hospitalization, due to cardiogenic shock, CPR with hypoxic brain damage or massive cerebral embolisation of a ventricular thrombus, without evidence for ST on autopsy.

Conclusions Tailoring individual antiplatelet therapy to improve IPA levels below 57 U AUC with MEA is capable of abolishing early definite ST even in a not-low risk patient cohort with complex coronary anatomy, high percentage of ACS and usage of 2nd generation DES. Further observations should prove whether this benefit extends also to long term follow up.

Routine Determination of Platelet Reactivity in Patients on Long-Term Dual Antiplatelet Therapy: The WILMAA Registry VI-2 097

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Objectives The Wilhelminenhospital Monitoring of Antiplatelet Activity (WILMAA) Registry was designed to evaluate the effects of long-term dual antiplatelet therapy (asprin and clopidogrel) on P2Y12 blockade and platelet aggregation in a routine setting.

Background Low responsiveness to clopidogrel was described in up to 50 % of patients after shortterm therapy. Antiplatelet activity of clopidogrel during long-term therapy in a stable clinical situation is still unknown. Moreover, the individual variation of the platelet reactivity indices over time has not been described so far.

Methods We performed a prospective single center registry of patients undergoing PCI and coronary stenting. All patients were on aspirin. Clopidogrel-naive patients received a loading dose of 300 or 600 mg at least 6 hours before blood sampling. Patients received dual antiplatelet therapy (clopidogrel 75 mg/day plus acetylsalicylic acid 100 mg/day) for at least 6 months. VASP phosphorylation analysis was performed by an experienced investigator (MKF) using PLT VASP/P2Y12 kits (Biocytex, Marseille, France) according to the manufacturer's instructions. In addition, the Multiplate™ (Multiple Platelet Function Analyzer, Dynabyte Medical, Munich, Germany) Clopidogrel assay was performed on all samples. Our primary analysis compared VASP-Platelet reactivity index (PRI) and Multiplate-AUC determined at baseline versus 1, 3 and 6 months, respectively.

Results In the first 63 consecutive patients enrolled, VASP-PRI was 56.92 ± 19.79 at baseline, 45.25 ± 19.93 at 1 month, 49.39 ± 23.79 at 3 months, and 52.96 ± 21.15 at 6 months ($p < 0.001$; $p = 0.006$ and $p = 0.039$ for baseline versus 1, 3 and 6 months), respectively. In contrast, Multiplate-AUC remained almost unchanged during follow-up: 35.29 ± 20.13 at baseline, 36.72 ± 19.65 at 1 month, 37.20 ± 18 at 3 months and 39.03 ± 20.78 at 6 months ($p = 0.508$; $p = 0.591$ and $p = 0.245$ for baseline vs 1, 3 and 6 months).

Conclusions VASP phosphorylation assay showed a significant improvement of P2Y12-receptor inhibition over time, whereas the results of Multiplate™ remained unchanged. Because it is expected that platelet reactivity in the early phase of ACS and/or periinterventional is increased and might therefore influence the action of clopidogrel in the respective test systems, the changes over time in the VASP assay are more reliable compared with the stable results obtained with Multiplate™. Further evaluation of the clinical usefulness of these assays in patients on long-term clopidogrel is therefore mandatory.

Comparison of Clinical Outcomes of Use of Abciximab Prior to or During Primary Angioplasty in STEMI: 10 Years Follow-Up of the Austrian Multicenter Randomized ReoPro®-BRIDGING Study VI-3 098

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Purpose We compared the 10-year clinical follow-up data of the patients enrolled in the ReoPro-BRIDGING trial, which study has investigated the effects of abciximab (ReoPro®) on early reperfusion in STEMI prior to or during primary percutaneous coronary angioplasty (pPCI).

Table 7: M. Gyöngyösi et al.

10-year FUP adverse events	Group 1 (n = 28)	Group 2 (n = 27)	p-value
Re-STEMI	0 (0 %)	3 (11.1 %)	0.070
All-cause death	1 (3.6 %)	6 (22.2 %)	0.038
TVR	2 (7.1 %)	1 (3.7 %)	0.574
Stroke	0 (0 %)	1 (3.7 %)	0.304
Re-STEMI and/or All-cause death	1 (3.6 %)	8 (29.6 %)	0.009
Composite MACCE	3 (10.7 %)	11 (40.7 %)	0.011

Methods 55 patients with STEMI were randomized either to start abciximab (0.25 mg/kg bolus followed by 10 µg/min infusion) during the organization phase for pPCI (Group 1, n = 28) or immediately after qualifying angiography but before pPCI (Group 2, n = 27). Patency of the infarct-related artery and signs of early reperfusion (ST-segment resolution, higher myocardial blush and TIMI flow grade) were determined. During the 10 years follow-up (FUP) time (mean 125 ± 8 months), the composite of cardiac and cerebrovascular adverse events (MACCE, defined as major adverse events, including all-cause death, re-STEMI, reintervention of the infarct-related artery, or stroke) were recorded.

Results No difference was found between the groups regarding the baseline parameters. The time between first bolus of abciximab and first balloon inflation of pPCI was 81 ± 15 vs 20 ± 11 min in Group 1 vs 2. The complete pre-pPCI ST-segment resolution (70 % vs 37 %; p = 0.045), TIMI flow grade 3 (30 % vs 11 %; p = 0.111) were higher, the corrected TIMI frame count (53.3 ± 35.3 vs 81.3 ± 26.8; p = 0.009) lower in Group 1 vs Group 2. Post-PCI, the myocardial blush grade (index of myocardial perfusion) was significantly higher in the Group 1 as compared to Group 2 (2.7 ± 0.7 vs 2.0 ± 1.1; p = 0.007). Major bleeding was recorded for 3.6 % and 7.4 % (p > 0.1) in Group 1 and 2. During the 10-year clinical FUP, significantly higher incidence of all-cause death, death and/or AMI and composite MACCE in Group 1 as compared to Group 2 (**Table 7**).

Kaplan-Meier survival analysis revealed a significantly better event-free 10-year survival rate (log rank test p = 0.008) for patients receiving ReoPro as an upstream therapy prior to pPCI vs ReoPro immediately before pPCI.

Conclusions The use of abciximab in the organization phase for pPCI results in signs of early recanalization of the infarct-related artery with a consequent improved myocardial tissue reperfusion which turns in a significantly better 10-year event-free survival.

X-Ray Dose, Blood Loss, Dose of Radiocontrast Agent and Renal Function in a Series of 100 Consecutive Transcatheter Aortic Valve Implantation Patients – a Single Centre Experience VI-4 099

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Purpose This observational prospective study was performed in the new field of transcatheter aortic valve implantation (TAVI) using the CoreValve® self-expanding prosthesis (Medtronic Inc., MN, USA). One goal of the study was to compare the applied X-ray dose in TAVI with diagnostic catheterisation of aortic valve stenosis in the same pts. Further we investigated blood loss, the amount of contrast agent and the influence on renal function.

Methods and Results The study population consited of 100 consecutive pts, 36 male, median age 81 (25–75 %: 77–84) y, mean weight 67 (± 12) kg who were treated between May 2007 and February 2010.

X-ray dose: Median dose-area product of X-ray in the diagnostic catheterisation was 113 (25–75 %: 71–160) Gycm² compared with 91 (55–172) Gycm² in TAVI respectively (p = 0.42).

Blood loss: Median haemoglobin decreased from 11.6 (25–75 %: 10.9–12.5) g/dl right before TAVI procedure to 9.3 (8.5–10.1) g/dl afterwards but increased again to 10.7 (10.0–11.6) g/dl upon discharge (p < 0.001). Haemorrhages according to the TIMI bleeding score "major" occurred in 5 pts, one of these experienced cerebral bleeding. Haemorrhages according to TIMI score "minor" occurred in 19 pts, all other had insignificant or "minimal" blood loss. 20 pts received red blood cell transfusions (mean 3 units).

Dose of radiocontrast agent and renal function: Median amount of contrast used was 200 (25–75 %: 160–250) ml of the non-ionic, iso-osmolar contrast agent iodixanol in the TAVI procedure compared with 180 (150–200) ml in the diagnostic catheterisation (p = 0.003). Mean glomerular filtration rate (GFR) calculated according to the MDRD formula was 56 (± 20) mlmin-1 before TAVI and decreased to 44 (± 21) mlmin-1 afterwards. Until discharge, GFR recovered significantly to 55 (± 23) mlmin-1 (p < 0.001).

Conclusion The population of TAVI pts in our institution consists widely of octogenarians with impaired red blood count and impaired renal function before intervention and is therefore on high interventional risk. X-Ray dose of the TAVI procedure is similar to those of a diagnostic catheterisation. Blood loss during TAVI is significant, but bleeding rates seem to be acceptable. Renal function during TAVI is significantly affected (most likely due to the amount of given contrast media), nevertheless pts could be discharged with restored GFR. Larger studies are needed to prove the safety of TAVI robustly regarding the investigated parameters.

Cost-Effectiveness of the Treatment of Multivessel Disease With Either Percutaneous Coronary Intervention Using Taxus Stents or Bypass Surgery 5 Years After Procedure VI-5 100

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Background The objective of the present study was to analyze the cost-effectiveness of percutaneous coronary intervention (PCI) using TAXUS stents compared to the costs of coronary artery bypass surgery (CABG) in patients with multivessel coronary artery disease (CAD) in the first 5 years after intervention.

Methods Multivessel PCI or CABG were performed in 114 (79 % male, 65 ± 12 y, 3.3 ± 1.2 Taxus stents/patients) or 93 (78 % male, 66 ± 10 y, 2.7 ± 0.9 grafts/patients) patients, respectively. Clinical outcomes, in terms of incidence of acute myocardial infarction (AMI), all-cause death, target vessel revascularization (TVR) and stroke, resource use and costs were analyzed prospectively over a 5-year follow-up (FUP) period. Overall costs consisted of the baseline costs of the index procedure (PCI or CABG), clinical and angiographic procedure-related treatments during the entire FUP. The primary endpoint was cost-effectiveness and clinical effectiveness, defined as the reduction of the composite of major adverse cardiac and cerebrovascular events (MACCE).

Results The prevalence of the risk factors for CAD including diabetes mellitus (36.8 % vs 41.9 %), hyperlipidemia (83.3 % vs 74.2 %) and smoking (28.9 % vs 30.1 %) was similar in the PCI vs CABG group, respectively. Hypertension was more common in the PCI population (87.7 %) compared to the CABG group (74.2 %; p = 0.012). During the 5-year FUP no differences in the prevalence of all-cause death (15.8 % vs 12.9 %) and stroke (0.9 % vs 3.2 %) were recorded. Trends towards higher incidence of AMI (9.6 % vs 3.2 %; p = 0.067) and AMI and/or death (24.6 % vs 15.1 %; p = 0.091) were observed in PCI patients as compared to the CABG group. The number of TVR (19.3 % vs 7.5 %; p = 0.015) and composite MACCE (36.8 % vs 18.3 %; p = 0.003) was significantly higher in the PCI group. The in-hospital costs were significantly lower in PCI patients as compared to the CABG group (11512 ± 6369 € vs 16552 ± 16633 €; p = 0.005).

Although TVR was performed more often in patients with PCI, the total costs at 5 years remained significantly lower in the PCI group (12524 ± 6901 € vs 21876 ± 16177 €; p = 0.013).

Conclusion Multivessel stenting with TAXUS stent in a real world setting led to a higher rate of TVR and composite MACCE as compared to CABG. However, the use of drug-eluting stents for multivessel PCI led to an acceptable rate of revascularization during the 5-year FUP, resulting in only moderate increase of the total costs.

AV-Block II. und III. Grades nach perkutanem Aortenklappenersatz (Core-Valve®) XV-3 101

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Hintergrund Das Auftreten höhergradiger AV-Blockierungen bei Patienten nach Aortenklappenersatz ist eine bekannte Komplikation. Die Inzidenz von AV-Blöcken nach perkutanem Aortenklappenersatz mit dem Core-Valve®-System ist unbekannt. Wir untersuchten die Inzidenz bei Patienten mit neu aufgetretenen Reizleitungsstörungen nach Core-Valve®-Implantation im Rahmen einer prospektiven Fallserie.

Methodik Im Zeitraum zwischen November 2008 und Dezember 2009 wurde am AKH Linz bei 24 Patienten (12 Patienten weiblich, mittleres Alter 84,2 ± 9,2 Jahre) ein perkutaner Aortenklappenersatz (PAKE) mit dem Core-Valve®-System durchgeführt. Als postinterventionelle Reizleitungsstörung wurden ein Linksschenkelblock, AV-Block I° [PQ > 0,24 ms], II° oder III° definiert. Drei Patienten waren zum Zeitpunkt des PAKE bereits Schrittmacher- (PM-) Träger und wurden in die Analyse nicht einbezogen.

Alle Patienten wurden mindestens 48 h postinterventionell intensivmedizinisch überwacht, bei Neuauftreten der oben definierten Reizleitungsstörungen wurde ein PM (Symphony®, Sorin®) implantiert. Bei Patienten mit AV-Block III° erfolgte eine Programmierung im DDD- bzw. im VVI-Modus (bei gleichzeitig vorliegendem Vorhofflimmern), wodurch eine permanente ventrikuläre Stimulation gewährleistet ist. Bei den übrigen Patienten wurde ein spezieller Betriebsmodus gewählt, der eine intrinsische Ventrikelerregung ermöglicht und lediglich bei Auftreten eines höhergradigen AV-Blocks automatisch in einen vorhofgestenteten ventrikelstimulierenden Modus umschaltet (AAI SafeR®). Im AAI SafeR®-Modus wird ein AV-Block III° durch 2 nicht übergeleitete atriale Impulse definiert. Drei blockierte atriale Impulse innerhalb der letzten 12 Zyklen ergeben einen AV-Block II°. Die automatisch vorgenommenen Umschaltvorgänge werden im Ereignisspeicher des PM aufgezeichnet und wurden zur Beurteilung des Auftretens eines höhergradigen AV-Blocks herangezogen.

Ergebnisse Die Klappenintervention war bei allen Patienten erfolgreich und kein Patient verstarb innerhalb der ersten 3 Wochen. Fünf der 21 analysierten Patienten (24 %) entwickelten einen AV-Block III° und wurden mit einem PM versorgt, 7 weitere Patienten (33 %) zeigten die oben definierten Reizleitungsstörungen, 6 dieser Patienten wurde ein PM implantiert der im AAI SafeR®-Modus programmiert wurde. Eine Patientin lehnte die PM-Implantation ab.

Der durchschnittliche Beobachtungszeitraum betrug 94 Tage. Alle 6 im AAI SafeR®-Modus stimulierten Patienten hatten in diesem Zeitraum Episoden mit höhergradigem AV-Block (681 Episoden mit AV-Block II° und 73 mit AV-Block III°). Bei den 9 Patienten ohne postinterventionelle Reizleitungsstörung wurde kein später auftretender AV-Block dokumentiert. Zum Zeitpunkt der 6-Monats-Kontrolle waren 3 Patienten (13 %) verstorben. Zwei Patienten (einer mit und einer ohne PM) verstarben im Rahmen eines Pumpversagens. Jene Patientin, die einer PM-Implantation nicht zugestimmt hatte, verstarb unbeobachtet zu Hause.

Schlussfolgerung Patienten, die nach PAKE mit dem Core-Valve-System® eine postinterventionelle Leitungsstörung (AV-Block I°, Linksschenkelblock) aufweisen, entwickeln in weiterer Folge häufig einen höhergradigen AV-Block. Angesichts der Invasivität und Kosten des Klappeneingriffs ist der zusätzliche Aufwand einer prophylaktischen PM-Implantation überschaubar und auch im Zweifelsfall gerechtfertigt.

Permanent Pacemaker Requirement After Transcatheter Aortic Valve Implantation XV-7 102

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Background Complete atrioventricular block is a well-known complication after transcatheter aortic valve implantation (TAVI). In the current literature, a permanent pacemaker (PM) implantation rate in the range of 19 to 35 % is reported after TAVI with the self-expanding CoreValve® bioprosthesis. After 100 revalving procedures we analyzed our own patient series regarding need for permanent PM implantation.

Patients and Methods Between May 2007 and February 2010, 100 patients (35 male, 65 female; mean age 80 ± 6 years) with symptomatic severe aortic stenosis and a logistic EuroSCORE > 20 % underwent a TAVI. All procedures were performed in the catheterization laboratory: transfemorally in 98 patients, in two patients via a left subclavian approach. A temporary PM was installed in all patients for rapid pacing during valvuloplasty and for ventricular backup pacing in case of bradycardia. After balloon valvuloplasty, the selfexpanding CoreValve® prosthesis (diameter 26 mm, n = 51; 29 mm, n = 49) was implanted using the current 18 French delivery catheter system. Postprocedurally all patients were transferred to the intermediate care unit for a 48-hour monitoring period. Only patients with symptomatic bradycardia were scheduled for permanent PM implantation according to the current guidelines.

Results Acute procedural success rate was 99 %. TAVI resulted in a significant reduction of peak and mean aortic transvalvular pressure gradients and a significant increase of calculated aortic valve area. 13 of 100 patients already had a permanent PM implantation prior to selection for TAVI and were therefore excluded from analysis. In 7 of the remaining 87 patients (8.0 %; 4 male, 3 female; mean age 79 ± 5 years) a permanent PM was implanted 2 to 7 days after TAVI due to symptomatic bradycardia. In 5 of these 7 patients a 29 mm Core-Valve® prosthesis was implanted, 1 patient was revalved with a 26 mm prosthesis, and in 1 patient the prosthesis could not be safely positioned and had to be removed before complete deployment.

Conclusion The percentage of new permanent PM implantation in our TAVI series is much lower than previously reported in the literature (8 % vs. 19–35 %). Reasons for that might be that we did not implant any PM on a prophylactic basis (i.e. new-onset left bundle branch block or asymptomatic bradycardia) or for administrative logistical purposes (i.e. to promote earlier discharge from intermediate care unit or hospital). Furthermore, we aimed at a more superior positioning of the CoreValve® prosthesis within the left ventricular outflow tract to mitigate conduction abnormalities and to reduce the need for permanent PM implantation. Finally, also prosthesis size could matter.

Effect of Gender Differences on Early and Long-Term Clinical Outcome After Percutaneous Revascularisation of Multivessel Coronary Artery Disease: Insights From the Autax Registry XV-4 103

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Introduction The aim of the Austrian Multicenter Taxus Stent Registry (AUTAX) was to conduct a multicenter prospective registry including patients with multivessel disease with/without previous PCI or concomitant cardiac surgery with possible complete revascularization by PCI and treated solely with multiple Taxus stent implantations in a "real-world" setting and to report the short (30 days), medium (6 months), and long-term (1 and 2 years) follow-up (FUP)

angiographic and clinical outcomes including late thrombosis. (ClinicalTrials.gov number NCT00738686). The present subanalysis compared the short and long-term (2-year) outcome between males and females of the AUTAX study.

Methods Patients (n = 97 female, n = 344 male, age 70 ± 11 and 63 ± 12; p < 0.001) with possible complete revascularization by PCI were prospectively included. Clinical follow-up (FUP) was 755 ± 218 days post-PCI in 95.7 %; with control angiography of 78 % at 6 months in all patients. Primary endpoint was the composite of major adverse cardiac (nonfatal acute myocardial infarction [AMI], all cause mortality, target vessel revascularization [TVR]) and cerebrovascular events (MACCE). The secondary endpoints of the study included the break-down primary endpoints at the 2-year FUP, the acute, subacute, and late thrombosis rates. Potential risk factor effects on 2-year MACCE-free survival were evaluated using multiple Cox regression models.

Results Females had significantly (p < 0.05) higher incidence of hypertension (89.7 % vs 78.8 %), but less smoking (16.5 % vs 38.1 %) or previous PCI/CABG (26.8 % vs 42.4 %) as compared with male patients. The other baseline clinical variables, Syntax score, number of implanted stents, total stent length (61 ± 23 vs 63 ± 26 mm), 2- or 3-vessel disease or left main stenosis were similar in females and males. Trend towards higher incidence of 1-month (5.2 % vs 2.9 %), 6-month (14.4 % vs 9.0 %), 1-year (19.6 % vs 14.0 %) and 2-year (22.8 % vs 17.3 %) MACCE was recorded for females. All-cause death or AMI occurred significantly more often in females during the first 6-month (7.4 % vs 3.0 %; p = 0.049) and 1-year (8.5 % vs 3.3 %; p = 0.029) with trend at 2-year FUP (8.5 % vs 3.9 %; p = 0.065) as compared with males. There was no difference between the 2 genders regarding stent thrombosis. Unstable angina/NSTEMI predicted long-term MACCE only for males (hazard ratio of 1.93 with 95 %-CI: 1.13–3.28), while no significant predictors was found for females.

Conclusions Strong trend towards worse MACCE-free survival with significantly higher incidence of mid- and long-term all-cause death or MI was documented in female patients with multivessel coronary disease treated with PCI.

Das Herz-CT-Paradoxon, von der Strahlenbelastung zur Strahlenreduktion – Optimierte PTCA nach nichtinvasiver Diagnostik mit dem neuen hochauflösenden Dual-Source-Computertomographen VI-7 104

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Ziele Das Koronar-CT (CTCA) hat sich zum Ausschluss einer KHK bei Patienten mit gering-mittlerer Vortestwahrscheinlichkeit bewährt. Die Strahlenbelastung ist allerdings Gegenstand kritischer Diskussionen. Die neue Dual-Source-CT-Technologie verspricht bei besserer Qualität eine geringere Strahlenbelastung. Ziel unserer Analyse war zu untersuchen, wieweit die Information des DSCT die Strategie der Koronarintervention und dadurch die Strahlenbelastung und Kontrastmittelmenge beeinflussen kann.

Methoden Die CTCA wurde mit einem Dual-Source-CT (Siemens Somatom Definition Flash, zeitliche Auflösung 75 ms, Gantryrotation 0,28 ms) durchgeführt. Patienten mit Herzraten > 60/min, VHFA, chronischen Verschlüssen (CTO), Stents und Mehrfgefäßerkrankungen (MVD) wurden in die Evaluierung bewusst eingeschlossen.

12 Patienten (4 Frauen; mittleres Alter 73 ± 5 Jahre) wurden aufgrund einer hochgradigen Stenose oder Verschluss in der CTCA einer invasiven CA/PTCA unterzogen. Bei 5 Patienten (42 %) lag eine komplexe KHK (CTO, MVD oder Z. n. Stentimplantation) vor. Die Strahlendosiswerte (Dosis-Längeprodukt, DLP in Gcm²) der CA/PTCA wurden berechnet und mit den Werten und Kontrastmittelmengen (KM) eines vergleichbaren Patientengutes unserer Herzkatheterdatenbank, bei denen keine DS-CT-Untersuchung vorausgegangen war, verglichen.

Ergebnisse Diagnostische Übereinstimmung wurde in 99 % aller Segmente (156/158) gefunden. Ein falsch-negativer CTCA-Befund wurde in einem „poststenotischen" Segment (subtotale LAD-Instentstenose mit TIMI-I-Flow), ein falsch-positiver Befund in einem gestenteten Segment erhoben. Die im CT gewonnene 3D-Information erlaubt dem interventionellen Kardiologen, die optimale Projektion mit dem passendem Kathetermaterial gezielt einzustellen. Die errechnete Strahlendosis der CCTA betrug auf dem Durchschnitt 3,5 ± 2 mSv (bei einer HF unter 65 wurden im Flash-Mode konstant Werte unter 1 mSv erreicht). Durch die in der CTCA gewonnen Information konnten die Strahlenbelastung und die Kontrastmittelmenge der Intervention im Vergleich zur Vergleichsgruppe signifikant (p < 0.05) reduziert werden. (DLP 99 vs. 164 Gycm², Delta 40 %; KM: 85 vs. 120 ml, Delta 33 %). Die Gesamtdosis (Strahlenbelastung von DSCT und CA/PTCA in mSv) war bei Patienten mit vorangegangenem CT deutlich niedriger als ohne CT (22,5 mSv vs. 32 mSv).

Zusammenfassung Die neue DS-CT-Technologie erlaubt nicht nur den Ausschluss einer KHK, sondern bietet dem interventionellen Kardiologen auch eine dreidimensionale Informationen über die Koronarpathologie, die zu einer deutlichen Qualitätsverbesserung mit Strahlenreduktion und Kostenersparnis im Herzkatheterlabor führt.

Clopidogrel Loading Pre-Angiography versus Peri-PCI – Impact on Clinical Outcome: a Systematic Review and Meta-Analysis XV-5 105

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Background and Aim The duration of clopidogrel pre-treatment in patients undergoing percutaneous coronary intervention (PCI) varies between hospitals and is still a matter of debate. The aim of our study was to compare the efficacy and safety of clopidogrel loading administered at 2 different time points: pre-angiography (> 2 h) or peri-PCI (< 2 h pre PCI or immediately post PCI) during follow-up period of 30 days.

Methods Systematic review and meta-analysis. A systematic literature search was performed using MEDLINE, EMBASE, CENTRAL and Web of Science for relevant articles in any language. Randomised controlled trials, post hoc analyses of randomised controlled trials and non-randomised studies were included. Outcomes evaluated were combined major adverse cardiovascular events (MACE), myocardial infarction, stent thrombosis and death. Summary estimates of the relative risks (RRs) were calculated using a random-effects model.

Results 6 studies met the selection criteria and included 6,322 patients. Clopidogrel loading pre-angiography was associated with a 52 % relative risk reduction of acute or subacute stent thrombosis compared to loading peri-PCI (RR = 0.48; CI: 0.27–0.89; p = 0.02; I^2 = 2 %). In contrast, clopidogrel loading pre-angiography was not associated with a risk reduction of MACE (RR = 0.65; CI: 0.41–1.05; p = 0.08; I^2 = 18 %), myocardial infarction (RR = 0.71; CI: 0.25–1.97; p = 0.51; I^2 = 29 %) or death (RR = 0.50; CI: 0.22–1.14; p = 0.10; I^2 = 0 %) at 30 days. Interestingly, clopidogrel loading pre-angiography neither increased the risk of major bleedings (RR = 1.69; CI: 0.68–4.21; p = 0.26; I^2 = 38 %) nor of all bleeding complications (RR = 2.14; CI: 0.53–8.75; p = 0.29; I^2 = 60 %) compared to the peri-PCI loading.

Conclusions This meta-analysis demonstrates that clopidogrel loading pre-angiography significantly reduces the rate of stent thrombosis compared to the peri-PCI loading without increase in bleeding complications.

Perkutaner Verschluss des linken Vorhofohrs bei persistierender linker oberer Hohlvene VI-6 106

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Einleitung Präsentiert wird der Fall eines Vorhofflimmerpatienten mit perkutanem Verschluss des linken Vorhofohrs bei Z. n. ASD-Verschluss, Korrektur-OP einer fehlmündenden Lungenvene und persistierender linker oberer Hohlvene

Anamnese Der 80-jährige Patient wurde nach thromboembolischem Kleinhirninsult auf dem Boden eines permanenten Vorhofflimmerns zur weiteren Therapie vorgestellt.

Der $CHADS_2$-Score betrug 4. Eine orale Antikoagulation war bei trepanationspflichtigem Subduralhämatom nicht möglich. Bekannt war eine Korrektur-OP eines ASD und einer fehlmündenden Lungenvene in die Vena cava superior sowie eine persitierende linke obere Hohlvene (PLSVC) mit Einmündung in den Sinus coronarius.

Diagnostik Die transthorakale transösophageale Echokardiographie mit Kontrastmittelapplikation über den linken Arm sowie ein Kardio-CT bestätigten die PLSVC mit dilatiertem Sinus coronarius (32 mm), einen dilatierten (RVEDD basal 59 mm) und funktionseingeschränkten (Tapse 13) rechten Ventrikel sowie eine dilatierte A. pulmonalis (51 mm). Der ostiale Diameter des linken Vorhofohrs (LAA) betrug je nach Schnittebene 17–22 mm. Intrakardiale Thromben wurden ausgeschlossen.

Therapie Der interventionelle Vorhofohrverschluss mittels 27 mm Watchman-Device erfolgte komplikationslos. Bei erschwerten Bedingungen für die transseptale Punktion und enger anatomischer Beziehung zwischen dem LAA und dem dialtierten Sinus coronarius wurde die gesamte Intervention TEE-gesteuert.

Diskussion Das Risiko eines 80-jährigen Patienten mit nicht-valvulärem Vorhofflimmern für einen thromboemboischen Insult beträgt 23 %, zu 90 % stellt das linke Vorhofohr die Emboliequelle dar.

Auch im Falle unseres Patienten muss eine kardioembolische Genese des Kleinhirninsults als am wahrscheinlichsten angesehen werden.

Eine PLSVC findet sich in 0,3 % der Bevölkerung. Zu 40 % bestehen wie auch bei unserem Patienten weitere kongenitale kardiale Anomalien. Zumeist mündet die PLSVC ohne hämodynamische Auswirkungen via Sinus coronarius in das rechte Atrium.

Die Selektion des Patienten erfolgte nach den echokardiographischen Kriterien der PROTECT-AF-Studie, in welcher der interventionelle LAA-Verschluss einer OAK hinsichtlich der Prophylaxe eines zerebrovaskulären Insults nicht unterlegen war.

Konklusion Auch bei komplexen kardialen Vorerkrankungen mit deutlichen Veränderungen der anatomischen Gegebenheiten besteht die Möglichkeit des interventionellen Vorhofohrverschlusses.

4-Y Results of Stenting of In-Stent Restenosis With Drug-Eluting Stents: Comparison Between Cypher and Taxus XV-6 107

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Background Implantation of drug-eluting stents for in-stent restenosis (ISR) led to promising results in the past years. The aim of this 3-center retrospective Austrian Registry of Treatment of ISR with DESs was to compare the long-term clinical and angiographic outcomes after Cypher vs. Taxus stent implantation in "real-world" practice.

Methods From January 2003 to March 2006, 157 consecutive patients with significant ISR were treated by implantation of either Cypher (group ISR-Cypher, n = 78, 71.8 % male, mean age 64 ± 12 years) or Taxus stent (group ISR-Taxus, n = 79, 78.5 % male, mean age 62 ± 11 years). All patients were controlled clinically 4 years after index procedure, wile clinically driven control angiography was performed in 37 % of patients. Non-fatal myocardial infarction (AMI), cerebral insult, cardiac death and target vessel revascularization (TVR) were considered as major adverse cardiac and cerebral events (MACCE). Baseline and follow-up (FUP) quantitative angiographic (QCA) parameters (minimal lumen diameter [MLD], and late lumen loss [LLL, post-procedure MLD minus FUP MLD]) were measured.

Results No significant differences were found between 2 stent groups as regards the baseline clinical (including age, gender, coronary risk factors, previous AMI, CABG, UA/NSTEMI), qualitative (location and type of lesion, number of diseased vessel) and quantitative angiographic (pre- and post-stent MLD, RD and % DS) parameters. The implanted stent size (3.0 ± 0.3 vs 3.1 ± 0.4 mm, in Cypher vs Taxus stents) and length (20.7 ± 7.2 vs 19.4 ± 6.5 mm, respectively) were similar in the groups. An ALG of 1.47 ± 0.57 vs 1.28 ± 0.69 mm in ISR-Cypher vs ISR-Taxus groups (p = 0.101) could be achieved. No intervention complication or short-term (within 30 days after stenting) MACCE occurred.

During the 4-year FUP, 1 and 4 patients (p = 0.177) died in the ISR-Cypher and -Taxus group, clinically driven TVR was performed in 19.2 % vs 22.8 % (p = 0.585), and AMI occurred in 6.4 % and 2.5 % (p = 0.239), respectively. Stroke was documented in 3.8 % vs 5.1 % (p = 0.712) in Cyper- vs Taxus-group. The composite MACCE was 23.1 % vs 29.1 % (p = 0.389) in groups ISR-Cypher vs ISR-Taxus. No late thrombosis occurred. No differences were found between the groups as regards the FUP in-stent MLD, RD and % DS. LLL was also similar in the groups (0.13 ± 0.74 vs 0.19 ± 0.74 mm; p = 0.472) in ISR-Cypher vs ISR-Taxus.

Conclusion The ISR can be treated successfully with Cypher or Taxus stents, regardless of the used DES type. The lack of late thrombosis and maintained low LLL encourage the treatment of ISR with DES.

Koronare Herzkrankheit (KHK)

Bewusstsein kardiovaskulärer Risikofaktoren, Prävention und Barrieren zur Herzgesundheit bei Frauen und Männern in Österreich VII-1 108

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Ziel Die koronare Herzkrankheit (KHK) ist in industrialisierten Ländern Haupttodesursache und damit auch in Österreich und wird von verschiedenen bekannten Risikofaktoren verursacht. Gezielte kardiovaskuläre Prävention ist eine wirkungsvolle Maßnahme, das kardiovaskuläre Risiko und damit die Mortalität zu senken. In Österreich gibt es keine Daten, die das Bewusstsein, das Präventionsverhalten sowie die Barrieren zur kardiovaskulären Prävention genderspezifisch untersuchen. Das Ziel der vorliegenden Pilotstudie war sowohl das Wissen über kardiovaskuläre Risikofaktoren als auch das individuelle Präventionsverhalten von Frauen und Männer zu untersuchen, da dieses Wissen die Basis darstellt, um effektiv Prävention betreiben zu können.

Methodik Die Datenaufnahme erfolgte mittels anonymisiertem Fragebogen bestehend aus 45 Fragen, welcher an 250 Frauen und 250 Männer ausgegeben wurde. Die gewonnenen Daten wurden mittels SPSS analysiert und verglichen.

Resultate Im Durchschnitt erreichten Frauen ein Alter von 43,4 ± 14,6 Jahren und Männer ein Alter von 54 ± 15 Jahren. 40,2 % der Frauen und 54 % der Männer waren Vollzeit beschäftigt. Obwohl Frauen ein höheres Ausbildungsniveau erreichten, verdienten 70 % < 1500 € netto pro Monat, während 80 % der Männer ein Einkommen > 1800 € erreichten. Sowohl Männer als auch Frauen hatten Defizite beim Erkennen von Risikofaktoren vor allem des Diabetes mellitus (DM), welcher nur von 22 % richtig erkannt wurde.

Das Ausbildungsniveau hatte keinen Einfluss auf die Anzahl richtig erkannter Risikofaktoren. 70 % der Männer und Frauen war bewusst, dass die KHK die Haupttodesursache in Österreich darstellt.

Die Hauptbarriere zur Vorsorge für Frauen stellt die fehlende Selbstwahrnehmung als Risikopatientin dar. Trotz des Durchschnittsalters von 43,5 ± 14,6 Jahren waren 85 % der befragten Frauen einem mittelmäßigen kardiovaskulären Risiko zuordenbar und nur 21 % der Frauen konnten ihr tatsächliches Risiko richtig einschätzen. Im Gegensatz dazu konnten Männer sich und ihr kardiovaskuläres Risiko richtig wahrnehmen.

Schlussfolgerung Das Wissen über kardiovaskuläre Risikofaktoren muss verbessert werden, vor allem bezogen auf den DM. Frauen müssen vermehrt über ihr Risikoprofil und die damit verbundenen Risiken aufgeklärt werden. Zukünftige Präventionsprogramme sollten unbedingt unter geschlechtsspezifischer Perspektive konzipiert werden, da sich der Zugang zur Prävention zwischen Männern und Frauen deutlich unterscheidet.

Optimal Treatment for Patients With Atrial Fibrillation Receiving Antiplatelet Medication After PCI

VII-2 **109**

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Background The question of optimal anticoagulation (AC) and antiplatelet (AP) treatment for patients with atrial fibrillation (AF) after PCI is unresolved and depends on individual decision-making.

Aims The aim of the study was to assess the anticoagulation treatment regimen in patients with AF in our department after PCI with stenting.

Methods A retrospective analysis of all patients who underwent PCI at our hospital between January 2002 and December 2007 was performed. The inclusion criteria were pre-existing or new onset of AF and implantation of one or more stents. Clinical follow up was performed by our research staff using the hospital database and/or contacting the general practitioner or internist in charge.

Results Over this 6 year period 2852 patients underwent PCI and a total number of 40 (1.4 %) met the inclusion criteria. The mean follow-up time was 2.6 ± 1.9 years, no patient was lost to follow-up. The mean age was 72 ± 7 years, the mean $CHADS_2$-score was 2 ± 1.2 and 14 patients (35 %) were female. After stenting, 20 patients (50 %) received antiplatelet therapy with clopidogrel and aspirin, 17 patients (42.5 %) received triple therapy (phenprocoumon/LMWH, clopidogrel, aspirin), 2 (5 %) received clopidogrel only and 1 (2.5 %) received phenprocoumon only. Four patients (10 %) experienced a minor bleeding and 1 (2.5 %) a major bleeding. During the follow-up period, 7 patients (17.5 %) died, one due to lung cancer, a second one due to myocardial infarction and 5 due to unknown causes.

Conclusion The risk-benefit ratio (thrombotic and bleeding risk) for combined antiplatelet and anticoagulation therapy in patients with AF remains unclear. More prospective data is required to achieve firm recommendations for optimal treatment.

Immediate and Early Coronary Artery Bypass Graft Surgery in Acute Myocardial Infarction: A Single Center Experience

XVI-3 **110**

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Backround Primary percutaneous coronary intervention (PCI) is a well-established therapy for acute myocardial infarction (MI), successfully restoring coronary bloodflow in 90–95 % of MI patients. Immediate or early coronary artery bypass grafting (CABG) is warranted in the setting of failed PCI in patients with hemodynamic instability and coronary anatomy amenable to surgical grafting, especially in the setting of severe 3-vessel disease and severe left main coronary artery disease. Surgical revascularization is also indicated in the setting of mechanical complications of MI, such as ventricular septal defect or free wall rupture. Although potentially life-saving, patients undergoing early CABG are traditionally associated with worse outcome than those not requiring CABG.

Methods and Results Retrospective analysis of 20 patients admitted to our hospital with acute MI from January 2006 to December 2006, who were transferred to CABG after angiography because of coronary findings not suitable for PCI. Of those, 15 patients presented with STEMI (75 %) and 5 presented with NSTEMI (25 %). 15 patients had severe 3-vessel disease including 2 patients with severe-left main artery disease. 4 patients were in cardiogenic shock at presentation. 2/4 (50 %) of those patients survived after urgent surgical revascularisation. A total of 20 patients were tranferred to CABG and surgically revascularized within 0–30 days (average 6.3 days). 9 (45 %) patients (7/9 with STEMI), were transferred from the cath-lab into the operating room for immediate CABG (< 4 hours time interval between coronary angiography and CABG). The 30-day mortality was 5 % (1/20). At 4 year follow up the overall mortality was 15 % (3/20), major adverse cerebral events were seen in 10 % (2/20) of patients and repeated revascularization took place in 5 % (1/20) of cases.

Conclusion Our single center experience shows that immediate and early CABG in patients with MI not suitable for PCI can be performed with acceptable results and good long term outcome, especially in STEMI. All patients presenting with acute MI and angiographic findings of severe 3-vessel disease, left-main artery disease and/or coronary stenosis unfit for PCI, should be reviewed by a interventional cardiologist and cardiac surgeon to determine the likelihood of safe and effective revascularisation.

Sport scheint das Erkennen einer KHK zu verzögern – Angepasste Diagnostik beim sportlichen Patienten mit Verdacht auf KHK

VII-3 **112**

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Einleitung Im „Sportland" Tirol und in der „Alpenhauptstadt" Innsbruck ist die Frage nach der Bedeutung von Sport als Einflussfaktor auf die KHK naheliegend. Der wissenschaftlich gut belegte und medial stark verbreitete Nutzen von Sport in der Sekundärprophylaxe der KHK birgt die Gefahr, bei Sportlern die Prävalenz einer KHK zu unterschätzen. Die Datenlage zum Nutzen von Sport in der Primärprophylaxe ist allerdings deutlich schlechter und bezieht sich meist auf einen aktiven und weniger auf einen sportlichen bis sehr sportlichen Lebensstil. Unsere Studie beinhaltet den Versuch einer Charakterisierung des sportlichen Patienten mit Verdacht auf KHK und soll klären, ob Sport die Wahrscheinlichkeit des Vorliegens einer KHK beeinflusst.

Methodik Nach Einverständniserklärung wurden insgesamt 53 Patienten (< 70 Jahre), die zu einer elektiven CAG bei V. a. KHK stationär aufgenommen worden waren, zu kardiovaskulären Risikofaktoren und Sport befragt. Aus dem Befund der folgenden CAG wurde dann der jeweilige Koronarstatus erfasst. Es erfolgten Vergleiche der Gruppen „Sportler" vs. „Nicht-Sportler". Die Gruppe der Sportler erhielt im Weiteren einen Fragebogen zum Thema Sport und einen Monat später eine Aktivitätsmessung mittels Akzelerometer (Aipermotion 440PC®) während eines normalen Tagesablaufes. Ein orientierender Vergleich erfolgte mit ident durchgeführten Fragebogenerhebungen und Aktivitätsmessungen an Patienten (gematcht nach Alter und Geschlecht), die ambulant zur LZ-EKG-Messung gekommen waren. Die statistische Analyse wurde mittels SPSS®, Vers. 16.0 unter Verwendung von Mittelwertsvergleichen und Chi-Quadrat-Tests durchgeführt.

Ergebnisse Bei sportlichen Patienten mit V. a. KHK (z. B. Stenokardien, path. Ergometrie, path. Koronar-CT) wurde bei vergleichbaren klassischen Risikofaktoren angiographisch häufiger eine relevante KHK (OR 2,48) und häufiger eine Mehrgefäß-KHK (OR 1,64) gefunden als bei unsportlichen Patienten. Fast ausschließlich männliche Patienten (96,9 % Männer) bezeichneten sich als „sportlich", während die Geschlechterverteilung in der Gruppe der nicht-sportlichen Patienten ausgeglichen war (52,4 % Männer). Die Gruppe der sportlichen Patienten unterschied sich weiter durch höhere Werte in der Aktivitätsmessung (PAL, kcal/h) und beschrieb häufiger „Ver-

gnügen" als Grund und körperliches Wohlgefühl als „Nutzen" der sportlichen Aktivität.

Diskussion Sportler scheinen besonders spät zur CAG zu kommen, z. B. weil sie (1) Stenokardien später wahrnehmen (Schmerztoleranz, Ischämietraining), weil sie (2) später zugewiesen werden (Stigmata „gesunder Sportler", falsch-negative Belastungsuntersuchung, Fehlen von bestimmten RF) oder weil (3) Sport unter Umständen selbst ein RF bzw. mit bestimmten RF assoziiert sein könnte (Ehrgeiz, Stress, Übertraining, Persönlichkeit, Belastungshypertonie, männliches Geschlecht). Der Nutzen von adäquat durchgeführtem Sport *per se* besteht ohne Zweifel. Sollte ein Sportler dennoch den Verdacht auf eine KHK aufweisen, scheint aus oben genannten Gründen eine besonders konsequente Abklärung indiziert zu sein, insbesondere auch bei bekanntlich erhöhtem Risiko für einen plötzlichen Herztod. Die Identifizierung eines Sportlers ergibt sich zunächst unkompliziert aus der Anamnese. Weitere Attribute können z. B. mittels spezieller Sportanamnese, Aktivitätsmessungen, Leistungsdiagnostik oder Echokardiographie erfasst werden.

Herzratenvariabilitäts-Messungen zur optimierten KHK-Risikostratifizierung VII-4 111

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Einleitung Anpassung ist eine höhere Fähigkeit, die funktionelle Kapazität voraussetzt und oft bei Krankheit vermindert ist. Die Herzratenvariabilität (HRV) misst die Anpassungsfähigkeit des Herzens an ständig veränderliche interne Einflüsse (z. B. autonome bzw. neurovegetative Modulation) und externe Einflüsse (z. B. Tageszeit, Atmung, Aktivität) durch qualitative Quantifizierung der Varianz von RR-Intervallen. Bei KHK sind kardiale Anpassungsfähigkeit und dementsprechend HRV (z. B. durch limitierte Blutversorgung) reduziert. Des Weiteren weiß man, dass bei reduzierter HRV die Prognose einer KHK schlechter ist. Unsere Arbeit soll klären, ob 2-minütige Ruhemessungen der HRV-Parameter (ApEn, SDNN, RMSSD, SD1, α1, α2, D2) einen Beitrag zur KHK-Risikostratifizierung leisten können bzw. hierbei einer einfachen Herzfrequenz-Messung (HF) überlegen sind.

Methodik Bei 131 Patienten, die zur Ergometrie bei bekannter oder vermuteter KHK kamen, wurden 2-minütige HRV-Messungen im Sitzen vor der Belastung mittels Pulsgurtmessung (Polar RS800®) durchgeführt. Zusätzlich wurden die Risikofaktoren und, falls bekannt, der Koronarstatus erfasst. Die Berechnung der HRV-Parameter erfolgte nach manueller Artefaktkorrektur mittels Kubios HRV-Software®, Version 2.0, ohne Veränderung der Standarteinstellungen. Die statistische Analyse wurde mittels SPSS®, Version 16.0 unter Verwendung von parametrischen und nicht-parametrischen Mittelwertsvergleichen durchgeführt.

Ergebnisse Im Gegensatz zur einfachen HF-Messsung lässt sich bei bestimmten HRV-Parametern (SDNN, RMSSD, SD1, D2, α1) eine negative Korrelation mit einigen kardiovaskulären Risikofaktoren (Alter, familiäre Disposition, Diabetes mellitus, art. Hypertonie, Hyperlipidämie, Übergewicht), mit Risikoscores (Procam-Schnelltest, EU-Score, Framingham-Score) und mit Auftreten und Schwere der KHK erkennen. Der Zusammenhang erscheint bei klassischen Risikofaktoren stärker (Ausnahme Nikotin) als bei weniger etablierten Risikofaktoren (Stress, Depression, Inaktivität, Hyperurikämie, Geschlecht).

Diskussion Die HRV bietet als ergänzende Methode der Risikostratifizierung Vorteile, wie z. B. hohe Sensitivität (früh verändert), unkomplizierte Messung (kostengünstig, schnell, nicht-invasiv), objektive Bestimmung (unabhängig von Immobilität, Compliance) und mögliche Quantifizierbarkeit (zur Verlaufsbeurteilung, als Biofeedback-Parameter). Nachteilig an der Methode sind z. B. geringe Spezifität (viele Einfluss- und Störfaktoren), hohe Artefaktanfälligkeit (Herzrhythmusstörungen), methodische Komplexität (mathematische Algorithmen) und problematische Vergleichbarkeit (keine existenten interindividuellen Referenzwerte). Unsere Ergebnisse geben Grund zur Annahme, dass eine HRV-Ruhemessung (z. B. integriert in ein Ergometrie-Messsystem) die KHK-Risikostratifizierung sinnvoll ergänzen könnte. Insbesondere bei intra-individuellen Verlaufsuntersuchungen dürften dabei von einem Nutzen auszugehen sein. Zur Optimierung der diagnostischen Aussagekraft besteht noch Klärungsbedarf, z. B. was Dauer der Messung (2 min vs. 5 min) und Auswahl der HRV-Parameter (linear vs. nichtlinear) betrifft. Des Weiteren sind größere und prospektive Studien zur Etablierung von Referenzwerten nötig.

CD59-Expression in Monocyte Subsets and Its Association to Coronary Arterty Disease VII-7 113

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Background Atherosclerosis is nowadays recognized as an inflammatory disease. Monocytes and monocyte-derived macrophages are involved in the initiation and early progression of atherosclerotic plaques. Different subsets of monocytes can be distinguished via the surface markers CD14 and CD16. CD16+/CD14dim monocytes are considered to be proinflammatory monocytes and high numbers of this monocyte-subtype have recently been linked to atherosclerosis.

Activation of the complement system, an important component of the innate immune system, leads to the formation of the "membrane attack complex" (MAC) and has been linked to the pathogenesis of atherosclerosis. CD59 inhibits formation of the MAC and thus attenuates atherosclerosis.

The aim of this study was to analyze the distribution of monocyte subsets in a cohort of patients with angiographically proven stable coronary artery disease, to analyze the expression of CD59 on these subsets and to examine possible associations of clinical biomarkers of cardiovascular disease with the distribution of monocyte subsets.

Methods Blood samples (EDTA) were taken from 45 patients with stable coronary artery disease prior to catheter investigation for cytometric analysis. Monocytes were classified as CD16dim/CD14+ ("normal subtype", NST), CD16+/CD14dim (inflammatory subtype, IST), CD14+/CD16+ (double positive, DST) and CD14dim/CD16dim("protective subtype", PST) and expression of CD59 on each subtype was measured. We further analyzed correlations between CRP, HbA1c, BMI and different subtypes of monocytes.

Results The protective subtype of monocytes expressed significantly higher levels of CD59 ($p < 0.0001$) than all other subtypes, the inflammatory subtype showed the lowest levels of CD59 ($p < 0.0001$). CRP correlated negatively with PST ($p = 0.006$, Spearman's Correlation Coefficient –0,409). HbA1c levels correlated positively with IST ($p = 0.011$, Spearman's Correlation Coefficient 0.474) and BMI correlated positively with DST ($p = 0.019$, Spearman's Correlation Coefficient 0.348).

Conclusion Patients with elevated HbA1c levels showed higher levels of monocytes of the inflammatory subtype. This fact could contribute to the observation that diabetics are prone to atherosclerosis. On the other hand patients with laboratory signs for inflammation as indicated by elevated CRP levels had fewer protective monocytes, which could possibly result in an increased vascular vulnerability towards complement activation in these patients.

Effect of Proton Pump Inhibitors on Clinical Outcome in Patients Treated With Clopidogrel: a Systematic Review and Meta-Analysis VII-6 114

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Objective To investigate whether PPIs negatively affect clinical outcome in patients with coronary artery disease treated with clopidogrel.

Design Systematic review and meta-analysis.

Data Sources A systematic literature search of MEDLINE, EMBASE, CENTRAL, Web of Science and meeting abstracts (ESC 2008, AHA 2008, ISTH 2009, ESC 2009, ACC Summit 2009, SCAI 2009, TCT 2009) databases for relevant articles in any language.

Data Abstraction Randomised controlled trials, post hoc analyses of randomised controlled trials and non-randomised studies reporting adjusted effect estimates were included. Outcomes evaluated were combined major adverse cardiovascular events (MACE), myocardial infarction and death. Summary estimates of the relative risks (RRs) with therapy were calculated using a random-effects model for patients with and without PPI use.

Data Synthesis Ten studies met the selection criteria and included 60,816 patients. Concomitant PPI use was not associated with an increase in the risk of MACE in randomised trials (RR = 1.08; CI = 0.81–1.44; p = 0.53). In contrast, non-randomised trials indicated that PPIs increased the relative risk of MACE by 33 % (RR = 1.33; CI = 1.14–1.55; p < 0.001). When the impact of pantoprazole and omeprazole on MACE was calculated separately, none of the two PPIs negatively affected patient's outcome. Furthermore, the concomitant PPI use was not associated with increase in risk of myocardial infarction (randomised trials: RR = 0.98; CI = 0.83–1.15; p = 0.79; non-randomised trials: RR = 1.27; CI = 0.98-1.64; p = 0.07) or death (randomised trials: RR = 0.68; CI = 0.47–0.98; p = 0.04; non-randomised trials: RR = 0.95; CI = 0.87–1.04; p = 0.30).

Conclusions This meta-analysis demonstrates the lack of evidence that concomitant PPIs harms to patients on clopidogrel. A higher rate of co-morbidities in patients with concomitant PPI and clopidogrel might be the major cause for the observed worse clinical outcome in non-randomised trials, rather than the PPI use itself.

Triglyceride Levels Predict Coronary Artery Disease Prevalence Only in Patients With Low LDL-Cholesterol – Analysis in 4324 Patients

XVI-2 **116**

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Background In 2 large secondary pravastatin prevention trials, triglyceride (TG) and high-density lipoprotein cholesterol (HDL) levels predicted recurrent events in patients with low LDL cholesterol (LDL) more effectively compared to patients with higher LDL cholesterol levels. Whether this association of TG and/or HDL levels with the incidence of events can also be applied to the prevalence of coronary artery disease (CAD) is the aim of this study.

Methods 4324 consecutive, statin-naïve patients undergoing elective coronary angiography were analysed. Coronary risk factors and ongoing medical therapy were assessed by questionnaire and by routine laboratory. Coronary angiogramms were graded by visual estimation of lumen diameter stenosis (≥ 70 % stenosis, < 70 % stenosis, no lumen irregularities) as 1-, 2- or 3-vessel disease (VD), as non-significant CAD or non-CAD.

Results LDL levels were 80.7 ± 15.6 mg/dl in patients with LDL < 100 (n = 1002 [23.2 %], low LDL group) and 140.4 ± 28.9 in patients with LDL ≥ 100 mg/dl (n = 3322 [76.8 %], high LDL group). In the low LDL group triglyceride (132.4 ± 148.8 vs 150.8 ± 96.5; p < 0.001) and HDL levels were lower (53.6 ± 19.3 vs 55.4 ± 16.3; p < 0.001) and C-reactive protein levels were higher (1.21 ± 2.9 vs 0.68 ± 1.32; p < 0.001) compared to the high LDL group. Furthermore, the low LDL group was older (64 ± 12.1 vs 62.8 ± 11.3; p < 0.001) and included more often diabetics (22.9 % vs 12.9 %; p < 0.001). Remaining risk factors as well as the prevalence of CAD (70.9 vs. 68.7 %; p = n. s.) were similar.

The association of HDL, TG and LDL levels as well as risk factors with CAD prevalence in multivariate analyses are shown in **Table 8**.

Conclusion Low LDL levels are common in statin-naïve patients undergoing elective coronary angiography. Triglyceride levels predict CAD prevalence only in patients with LDL levels below 100 mg/dl. This probably reflects the higher presence of diabetes and might be a further target for therapeutic intervention in those patients.

C-reactive Protein Levels Are Increased, but are not Predictive for Coronary Artery Disease Prevalence in Patients with Diabetes Mellitus – Analysis in 7533 Patients

XVI-1 **115**

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Background C-reactive protein (CRP) levels are independently associated with incident cardiovascular events and with coronary artery disease (CAD) prevalence. Whether the presence of diabetes influences the relation of CRP to CAD prevalence is less well known.

Methods 7533 consecutive patients undergoing elective coronary angiography were analysed. Coronary risk factors and ongoing medical therapy were assessed by questionnaire and by routine laboratory. Coronary angiogramms were graded by visual estimation of lumen diameter stenosis (≥ or < 70 % stenosis) as 1-, 2- or 3-vessel disease (VD) or as non-CAD. CRP levels were determined by immunoturbidimetric assay.

Results 1339 (17.8 %) were diabetics and 6194 (82.2 %) were non-diabetics. Patients with diabetes were older (65.6 ± 63.2 vs 63.1 ± 11.1; p < 0.001), had higher CRP (1.01 ± 2.4 vs 0.78 ± 1.9; p < 0.001) and body mass index (28.4 ± 4.5 vs 26.6 ± 4.2 kg/m²; p < 0.001) as well as lower LDL cholesterol (110.8 ± 36.9 vs 126.0 ± 37.1 mg/dl; p < 0.001), HDL cholesterol (49.5 ± 14.9 vs 55.9 ± 17.0 mg/dl; p < 0.001) and triglyceride levels (146.3 ± 97.2 vs 181.3 ± 194.0 mg/dl; p < 0.001). In addition, diabetics were more frequent on statin therapy (47.3 vs 38.4 %; p < 0.001), were more often hypertensives (87.5 vs 77.7 %; p < 0.001) and less frequent smokers (21.2 vs 25.6 %; p < 0.005). As expected, significant CAD was more prevalent in diabetics (67.5 vs 54.7 %; p < 0.001).

Table 8: M. M. Wanitschek et al. Multinominal logistic regression analysis (non-CAD vs. CAD)

	LDL < 100 mg/dl CAD vs no CAD				LDL ≥ 100 mg/dl no CAD vs CAD			
	Odds ratio	95 %-CI	Wald	p-value	Odds ratio	95 %-CI	Wald	p-value
Age (years)	1.054	(1.04–1.07)	54.9	< 0.001	1.061	(1.05–1.07)	194.4	< 0.001
Gender	2.302	(1.66–3.78)	24.7	< 0.001	2.996	(2.49–3.60)	136.9	< 0.001
HDL (mg/dL)	0.983	(0.97–0.99)	13.3	< 0.001	0.974	(0.97–0.98)	68.6	< 0.001
LDL (mg/dl)	n. s. in univariate analysis				1.009	(0.95–1.00)	29.7	< 0.001
Diabetes	2.157	(1.37–3.34)	10.9	0.001	1.937	(1.43–2.62)	18.5	< 0.001
Hypertension	1.244	(0.82–1.88)	4.5	n. s.	1.569	(1.27–1.95)	16.8	< 0.001
TG (log-transf)	4.047	(1.86–4.54)	12.5	< 0.001	1.237	(0.79–1.95)	0.82	n. s.
Crp (log-transf)	n. s. in univariate analysis				1.752	(1.44–2.14)	30.4	< 0.001
BMI (kg/m²)	0.975	(0.94–1.01)	1.8	n. s.	0.969	(0.95–0.99)	8.62	0.003

Table 9: M. M. Wanitschek et al. Multinominal logistic regression analysis (non-CAD vs. CAD)

	Diabetics				Non-Diabetics			
	Odds ratio	95 %-CI	Wald	p-value	Odds ratio	95 %-CI	Wald	p-value
Age (years)	10.32	(1.02–1.05)	16.5	< 0.001	1.039	(1.03–1.05)	159.1	< 0.001
Gender	1.927	(1.46–2.55)	21.3	< 0.001	2.895	(2.54–3.30)	254.8	< 0.001
HDL (mg/dL)	0.979	(0.97–0.99)	21.2	< 0.001	0.982	(0.98–0.99)	76.3	< 0.001
LDL (mg/dl)	n. s. in univariate analysis				n. s. in univariate analysis			
Prior statin use	0.770	(0.60–0.80)	3.9	0.047	0.539	(0.48–0.61)	101.0	< 0.001
Hypertension	1.552	(1.00–2.40)	4.5	n. s.	1.190	(1.19–1.64)	16.8	< 0.001
TG (log-transf)	n. s. in univariate analysis				1.152	(0.86–1.54)	0.89	n. s.
Crp (log-transf)	n. s. in univariate analysis				1.232	(1.23–1.59)	27.1	< 0.001
BMI (kg/m²)	0.961	(0.93–0.99)	7.1	0.008	n. s. in univariate analysis			
Fibrinogen	1.001	(1.00–1.02)	7.8	0.005	n. s. in univariate analysis			
Smoking	1.989	(1.32–3.01)	10.6	< 0.010	1.205	(1.21–1.69)	16.8	< 0.001
Family history	n. s. in univariate analysis				1.211	(1.21–1.60)	21.8	< 0.001

The multivariate association of risk factors (significant different at univariate analyses) with CAD prevalence in diabetics and non-diabetics are shown in **Table 9**.

Conclusion Risk factors independently associated with CAD prevalence are different between diabetics and non-diabetics worth considering when making therapeutic decisions. Interestingly, CRP was not related to CAD prevalence in patients with diabetes probably due to its overall higher levels in the latter.

Leitlinienkonforme Abklärung der chronisch stabilen KHK – ein Pilotprojekt VII-5 117

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Ziel In dem vorliegenden Pilotprojekt wurde der Einfluss einer leitlinienkonformen Abklärung der chronisch stabilen KHK auf die Ergebnisse und Konsequenzen der Koronarangiographie untersucht.

Methodik Gemeinsam mit Vertretern aller beteiligten Berufsgruppen wurde ein auf Evidenz basierender Algorithmus für die Abklärung der chronisch stabilen KHK definiert. Basis des diagnostischen Pfades bildeten die Erhebung der Vortestwahrscheinlichkeit (< 10 %, 10–90 %, > 90 %) anhand der Anamnese und des Risikoprofils sowie die symptomlimitierte Ergometrie. Die Entscheidung zu einer weiterführenden nicht-invasiven und invasiven Abklärung wurde ausschließlich von Kardiologen des interventionellen Zentrums getroffen. Als Kennzahlen dienten die Anzahl der Koronarangiographien, die Interventionsrate, die Ausschlussrate sowie die Anzahl der Myokardszintigraphien und Cardiac CTs.

Patienten In der ersten Auswertung des Pilotprojektes wurden 111 konsekutive Patienten (49 Frauen, 62 Männer, Altersdurchschnitt 66,8 a [32–87 a]), die zur Abklärung einer chronisch stabilen KHK zugewiesen wurden, analysiert. Patienten mit akutem Koronarsyndrom, Vitien oder Kardiomyopathien wurden ausgeschlossen.

Ergebnisse Der vorgegebene diagnostische Pfad wurde bei 48 Patienten (43 %) exakt eingehalten (Gruppe A). Bei 63 Patienten (57 %) fanden sich eine oder mehrere Abweichungen: 31 Myokardszintigraphien/Cardiac CTs vor der Zuweisung, 36 keine oder atypische Beschwerden, 16 keine Ergometrie (Gruppe B). In Gruppe A konnte bei 12 Patienten mit niedriger Vortestwahrscheinlichkeit mittels Cardiac CT eine KHK ausgeschlossen werden, eine Myokardszintigraphie wurde nie veranlasst. Bei 36 Patienten wurde eine Koronarangiographie mit folgenden Ergebnissen/Konsequenzen durchgeführt: 17 PCI, 11 CABG, 5 diffuse/inop. KHK, 3 Ausschluss einer KHK. Die Interventionsrate (PCI + CABG) betrug somit 77 %. In Gruppe B wurde bei 20 Patienten, davon bei 7 mittels Cardiac CT, auf eine invasive Abklärung verzichtet. Die Ergebnisse/Konsequenzen der Koronarangiographie bei den verbleibenden 43 Patienten waren: 8 PCI, 4 CABG, 2 diffus/inop. KHK, 29 konservativ/Ausschluss einer KHK. Die Interventionsrate betrug lediglich 28 %. Die Myokardszintigraphie zeigte nur in 5/22 Fällen eine Übereinstimmung mit der invasiven Diagnostik.

Schlussfolgerung Die Einhaltung leitlinienkonformer Algorithmen in der Abklärung der chronisch stabilen KHK führt zu einer besseren Selektion der Patienten für eine invasive Abklärung mit einer hohen Interventions- und niedrigen Ausschlussrate. Bei vielen Patienten mit niedriger Vortestwahrscheinlichkeit kann eine KHK auf nicht-invasive Weise mittels Cardiac CT ausgeschlossen werden, während die Myokardszintigraphie dafür nicht geeignet ist. Die Algorithmen wurden von den Kardiologen wesentlich häufiger befolgt als dies bei den niedergelassenen Internisten der Fall war.

Pulmonale Hypertonie

Inhaled Iloprost For Patients With Pulmonary Arterial Hypertension and Right Heart Failure VIII-2 118

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Background Pulmonary arterial hypertension (PAH) is a life-threatening condition, leading to right heart failure and death. The fact that right heart failure is associated with low systemic perfusion pressures limits the use of systemic vasodilators. As a consequence, no therapeutic recommendations exist for patients experiencing right heart failure in the course of PAH. The purpose of our study was to examine the safety and feasibility of inhaled Iloprost administration in patients with PAH and right heart failure.

Methods Between 2007 and 2008, 7 patients with PAH and clinical signs of right heart failure were enrolled. Iloprost was inhaled hourly utilizing a mobile ultrasonic nebulizer (Optineb, Nebu-Tec, Inc., Elsenfeld, Germany). Inhalation was started at a dose of 2.5 mcg and increased by 2.5-mcg-steps as long as hemodynamically tolerated. Patients were treated for 24 hours except for 6–8 hours of night rest. Efficacy and safety were determined by continuous invasive monitoring of hemodynamic parameters and systemic blood pressure.

Results After inhalation of Iloprost, cardiac output increased from 4.6 ± 1.4 l/min to 5.6 ± 1.7 l/min (p = 0.009), concomitantly, pulmonary vascular resistance decreased from 635 ± 218 dynes *s*cm-5 to 490 ± 174 dynes *s*cm-5 (p = 0.044), and serum NT-proBNP dropped from 13591 ± 10939 pg/ml to 9944 ± 8569 pg/ml (p = 0.051). Mean systemic pressure remained stable (66 ± 7 mmHg vs 69.14 ± 6.4 mmHg; p = 0.478).

Conclusion Inhaled Iloprost may offer an effective, safe, and pulmonary-selective strategy for the treatment of right heart failure in the course of PAH.

Long-Term Tolerability, Side Effects, Dosing Regimens and Survival With First-Line Subcutaneous Treprostinil for Severe Pulmonary Hypertension VIII-3 119

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Objectives To evaluate all-comers with severe pre-capillary pulmonary hypertension (PH), we report on a prospective registry of patients treated with first-line subcutaneous (sc) treprostinil, a longer-acting prostacyclin analogue.

Background Recent data suggest that contemporary treatments within randomized controlled trials (RCTs) improve outcomes in pulmonary arterial hypertension. However, RCTs are biased by stringent inclusion criteria, and are limited by pre-specified patient subsets and study durations.

Methods Prospective data were collected from advanced-stage patients with pre-capillary pulmonary hypertension, and pre-specified hemodynamic evaluations and assessment of concurrent medical events were performed. According to side effects and clinical symptoms dose adjustments were done every 3 to 6 months, including pain relief treatment. Kaplan–Meier survival estimates between 1999 and 2010 were compared with an age- and gender-matched Austrian reference population.

Results Of 104 patients, 19 patients discontinued treatment due to side effects, 77 patients were on treatment > 6 months. Feasibility, pain management and tolerability were recorded over years. Between baseline and last follow-up significant improvements occurred in six-minute walking distance, Borg Dyspnea Score, mean pulmonary arterial pressure, cardiac output, pulmonary vascular resistance and World Health Organisation functional class (WHO FC), at a median dose of 37.5 ng/kg/min. Six patients (7.8 %) underwent double lung transplantation, and 18 patients (23.4 %) died of all-cause. 25 patients (32.4 %) survived non-PH related adverse events. At one, five and 8 years, overall survival rates were 97 %, 76 % and 62 %.

Conclusion First-line treatment of severe pre-capillary PH with sc treprostinil is safe and efficacious over years, improves survival and enables survival of non-PH related events.

The Combined Use of L-arginine and Tetrahydrobiopterin Improves Hemodynamic Parameters in a Rat Model of Pulmonary Hypertension VIII-1 029

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Background and Study Aim Pulmonary arterial hypertension (PAH) is a severe condition leading to right heart failure and death within 2–3 years after diagnosis. Endothelium-dependent nitric oxide (NO)-mediated vasodilatation is impaired in patients with PAH. Endothelial nitric oxide synthase (eNOS) and its co-factor tetrahydrobiopterin (BH4) convert L-arginine to L-citrulline and NO. The aim of the present study was to investigate the effects of combination therapy with L-arginine and BH4 in a rat model of PAH.

Methods PAH was induced by unilateral left pneumonectomy and injection of monocrotaline (60 mg/kg) in 10 adult male Sprague-Dawley rats (300–350 g). 21 days after monocrotaline-injection rats were randomized into 2 treatment arms: Combination of oral L-arginine (20 mg/kg) and BH4 (300 mg/kg) or water once daily for 14 days. Hemodynamic parameters such as systolic pulmonary pressure, diastolic pulmonary pressure and mean pulmonary pressure (mPAP) were continuously recorded using implantable telemetry systems (DSI Datascience).

Results Baseline mean mPAP was 67.2 ± 12.7 mmHg in the treatment group and 55.5 ± 15.8 mmHg in the control group (p = 0.131). While in the treatment group the mean decrease in mPAP was 23.6 ± 6.4 mmHg, in the placebo group a mean decrease of 3.9 ± 18.2 mmHg was encountered (p = 0.031).

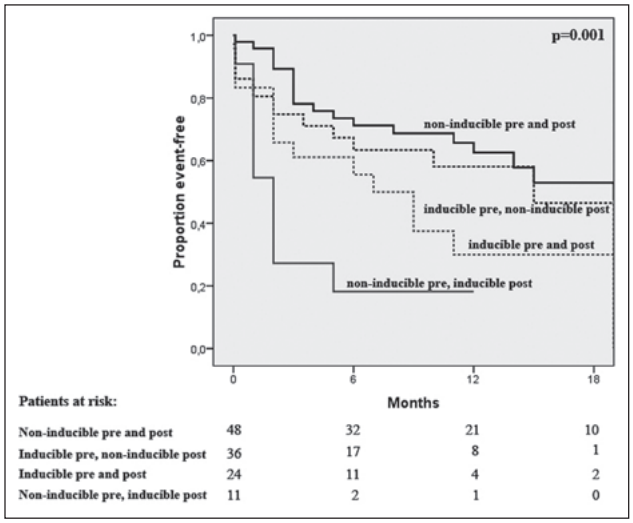

Figure 11: C. Adlbrecht et al.

Conclusion The combination therapy of L-arginine and BH4 in a rat model of severe PAH improves hemodynamic parameters.

Rhythmologie

Prognostic Value of Induction of Atrial Fibrillation Before and After Pulmonary Vein Isolation IX-1 120

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Background Catheter ablation of atrial fibrillation (AF) lacks reliable electrophysiologic endpoints. The present study investigated the prognostic value of changes in AF inducibility due to ablation.

Methods A total of 122 patients aged 59.3 ± 10.5 years undergoing pulmonary vein isolation due to paroxysmal AF were included. Two respective attempts to induce AF (> 1 minute) by decremental coronary sinus stimulation before and after ablation were performed. The mean follow-up duration was 15.7 ± 10.8 months.

Results In 37 (30.3 %) patients AF was inducible before, but not after ablation. 49 (40.2 %) were not inducible before or after the procedure, whereas 25 (20.5 %) were always found inducible. In 11 (9 %) patients AF was inducible only after ablation. Changes in inducibility achieved by catheter ablation carried prognostic value (p = 0.001; **Figure 11**). Patients with unaltered or facilitated induction of AF had the highest recurrence rate.

Conclusion The results of attempted AF induction before and after ablation have significance with respect to ablation outcome.

Noninvasive Imaging of Cardiac Electrophysiology (NICE) – Endo/Epicardial Ventricular Activation During CRT IX-2 121

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Background Noninvasive imaging of cardiac electrophysiology (NICE) is a novel imaging tool for visualization of epicardial as well as endocardial ventricular activation.

Table 10: T. Berger et al. Endocardial and epicardial left- (LV) and right-ventricular (RV) breakthroughs in milliseconds (msec) during different pacing modes.

	RV endo (msec)	RV epi (msec)	LV endo (msec)	LV epi (msec)	RV septal (msec)	LV septal (msec)
control intrinsic	12 ± 13*	19 ± 13*	17 ± 10*#	24 ± 16*#	20 ± 10*	16 ± 10*#
control RV	0 ± 1*	14 ± 6*	41 ± 13*	36 ± 16*	12 ± 11*	34 ± 11*
LBBB intrinsic	7 ± 10*	10 ± 8*	46 ± 19*#	49 ± 16*#	17 ± 12*	36 ± 13#
LBBB RV	0 ± 0*	15 ± 6*	50 ± 18*	51 ± 17*	16 ± 6*	37 ± 10
LBBB biV	16 ± 13*	28 ± 12*	17 ± 7*	1 ± 2*	30 ± 11*	40 ± 11

*: p < 0.05 during different pacing modes; #: p < 0.05 in control vs LBBB patients

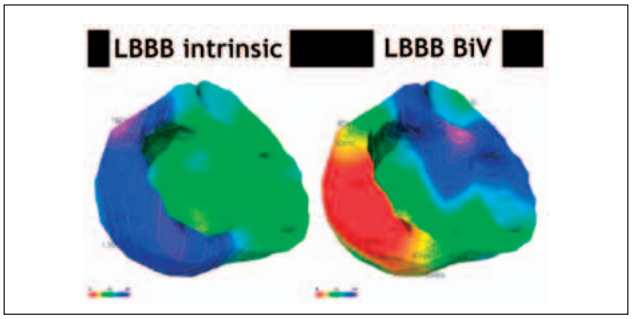

Figure 12: T. Berger et al. Ventricular activation map as obtained by NICE. Left: The blue color indicate the area of latest ventricular activation in a heart failure patient with LBBB. Right: During CRT stimulation via an epicardial LV lead in the area of latest activation reverses the activation sequence.

Methods NICE was performed in 10 patients with congestive heart failure and left bundle branch block (LBBB) undergoing cardiac resynchronization therapy (CRT) and in 10 patients without structural heart disease undergoing an EP study (control). NICE works by fusing the data from high-resolution ECG mapping and a model of individual patient's cardiac anatomy obtained by magnetic resonance imaging. The ventricular activation sequence was computed using a bidomain theory-based heart model to solve this inverse problem. Endocardial and epicardial ventricular activation were obtained during intrinsic rhythm as well as during ventricular pacing.

Results In control patients RV pacing resulted in a change of the ventricular activation sequence similar to the intrinsic activation pattern of LBBB patients. In LBBB patients biventricular pacing close to the area of latest ventricular activation resulted in a marked decrease in LV endocardial and epicardial activation times, both RV epicardial and septal breakthroughs were prolonged. Interestingly, BiV pacing in LBBB patients resulted in similar endocardial RV and LV activation times as compared to intrinsic control patients (**Table 10, Figure 12**).

Conclusion Endo- and epicardial ventricular activation can be visualized noninvasively by NICE. Deterioration of endocardial and epicardial ventricular activation in LBBB patients can be reversed by CRT. The area of latest ventricular activation can be identified by NICE which therefore may help to improve responder identification by facilitating targeted LV lead placement.

Diagnosis and Treatment of Junctional Ectopic Tachycardia in Adults

XVII-1 **122**

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Introduction Junctional ectopic tachycardia (JET) is a rare arrhythmia in grown-ups and often difficult to distinguish from AV nodal reentrant tachycardia (AVNRT). Catheter ablation of focal JET is considered difficult due to the higher risk of AV block. We present the diagnostic characteristics of this unusual arrhythmia and describe a safe and promising ablation technique.

Patients and Methods Within the last two years 103 catheter ablations of AVNRT were performed at our center, whereas only three cases were demonstrated to be JET. All patients were middle-aged women (38 to 56 yrs) with a structural normal heart and resting ECG. The clinical tachycardias were rather slow (mean heart rate 119/min) and fairly regular. All patients were symptomatic and tachycardia was terminated with adenosine in two patients, and with verapamil in one patient. After informed consent the patients underwent diagnostic four catheter electrophysiological study off antiarrhythmic drugs.

Results JET was started with incremental atrial and/or ventricular burst pacing in all three cases, requiring administration of orciprenaline in one patient. In contrast to AVNRT, JET was initiated reproducibly without a critical AH jump by atrial extrastimulation, and only one patient showed dual AV node physiology in addition. The mean CL of JET was 585 ± 85 ms. Spontaneous AV dissociation or VA Wenckebach was present during tachycardia in all patients ruling out AVNRT. An atrial premature extrastimulus was delivered on His without termination of arrhythmia in one instance. Catheter ablation was performed empirically in the posteroseptal region, moving anteriorly if the tachycardia persisted. Up to 10 RF energy impulses (50 W, 60 °C) were delivered (mean RF time 370 sec) leading to heat-induced junctional tachycardia in all cases. Selective ablation of the tachycardia focus was achieved without occurrence of transient or permanent AV block. All individuals remained free of arrhythmia and symptoms during follow-up visits up to 9 months.

Conclusion Automatic JET is an uncommon and benign type of paroxysmal supraventricular tachycardia in adults. Exact interpretation of the electrophysiological findings and pacing maneuvers is necessary to appreciate the subtle diagnostic differences between AVNRT and JET. Selective ablation of the JET focus in the slow pathway region is a safe and effective procedure replacing antiarrhythmic drug therapy.

Dronedaron bei Vorhofflimmern – erste Erfahrungen am eigenen Patientengut

IX-3 **123**

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Einleitung Dronedaron (Multaq®, Fa. Sanofi Aventis) ist ein Mehrkanalblocker, der in mehreren Studien seine Effizienz und Sicherheit bei Patienten mit nicht-permanentem VHF gezeigt hat. Seit Anfang Februar 2010 ist die Substanz in Österreich erhältlich. Wir berichten über unsere ersten Erfahrungen am KH der Elisabethinen Linz.

Methodik 22 Patienten (15 männliche/7 weibliche) im Alter von 66 ± 9,7 Jahre wurden bislang anbehandelt. 17 Patienten leiden unter paroxysmalem, 5 Patienten unter persistierendem VHF. Der durchschnittliche $CHADS_2$-Score unter den Teilnehmern beträgt 0,95 ± 0,84, das NYHA-Stadium lässt sich mit 1,32 ± 0,95 beziffern. 16 der Patienten haben echokardiographisch eine LVEF von > 50 %, 5 befinden sich in der LVEF-Gruppe zwischen 35 und 50 %. Das Serum-Kreatinin liegt im Schnitt bei 1,09 ± 0,19 mg/dl, der gemittelte linksatriale Durchmesser beträgt 40,76 ± 6,37 mm. Zu Beginn der Einnahme von Multaq® sowie zu den Follow-up werden die Teilnehmer um die Einschätzung ihrer aktuellen Lebensqualität gebeten. QOL-Werte mit durchschnittlich 6,23 ± 2,05 konnten bislang festgehalten werden. Die Zahl 1 deutet hierbei auf eine sehr schlechte, die Zahl 10 auf eine sehr gute Lebensqualität hin.

Zwei der 22 Patienten haben einen LOOP-Rekorder implantiert; 6 Patienten der beobachteten Gruppe wechseln unmittelbar, mit nur 2–3 Wochen Pause, von Sedacoron auf Multaq®.

Resultate 3-Monats-Daten hinsichtlich der therapeutischen Effizienz zur Aufrechterhaltung von SR, Hospitalisierung aus kardiovaskulärer Ursache, Proarrhythmien, Therapieabbrüchen sowie Parametern der Lebensqualität werden im Rahmen der Kardiologentagung präsentiert.

Schlussfolgerung Dronedaron wird zunehmend bei Patienten mit nicht-permanentem VHF eingesetzt. Erste Nachsorgedaten geben Auskunft über Wirksamkeit, Sicherheit und NW-Profil in einer breit gestreuten Patientenpopulation.

Appropriate Therapy But Not Inappropriate Shocks Predict Survival in Implantable Cardioverter Defibrillator Patients

IX-4 **124**

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Whereas appropriate implantable cardioverter defibrillator (ICD) therapy indicates progression of the underlying heart disease and increased mortality, inappropriate ICD shocks have been linked to a worse clinical outcome due to direct myocardial injury. In a retrospective study, 1117 recipients of an ICD were analysed with respect to appropriate/inappropriate therapies and survival. During a mean follow-up of 2.92 years, appropriate therapy occurred in 27.7 % and 54.0 % of patients who had received an ICD for primary and secondary prevention of sudden cardiac death (SCD), respectively ($p < 0.0001$). Inappropriate shock therapy occurred in 15.0 % and 25.4 % of patients who had received an ICD for primary and secondary prevention of SCD, respectively ($p = 0.122$). Appropriate ICD therapy had a strong impact on overall survival ($p < 0.0001$), and this association was found both in patients in primary ($p < 0.0001$) and secondary ($p = 0.002$) prevention of SCD. Inappropriate ICD shocks had no impact on total mortality, neither in primary nor secondary prevention of SCD. In conclusion, inappropriate shocks do not effect survival, in strong contrast to appropriate ICD therapy. Our study does not support the hypothesis that shock therapy in itself deteriorates clinical outcome. However, it confirms that appropriate ICD therapy is a warning sign and should prompt physicians to consider additional treatment stategies **(Figure 13)**.

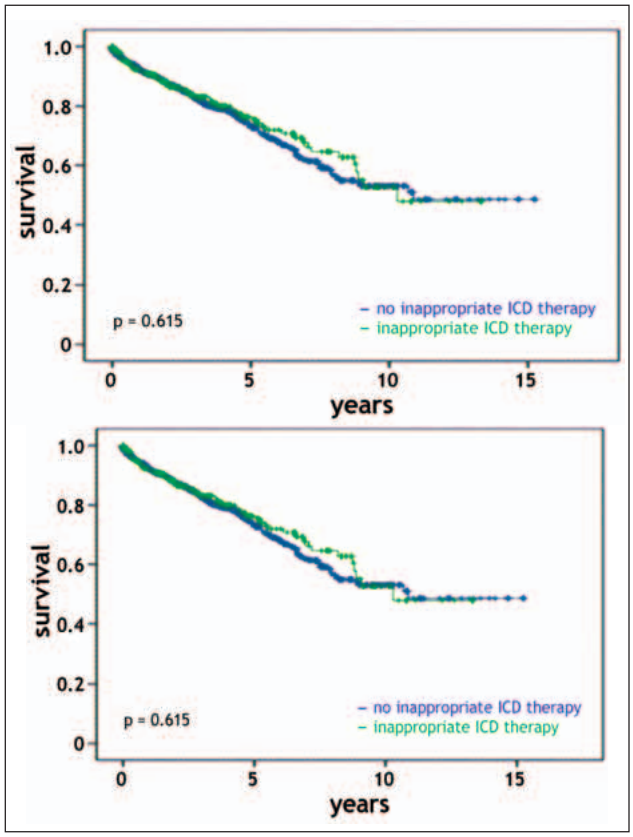

Figure 13: W. Dichtl et al.

Elevated Gamma-Glutamyltransferase in Male Implantable Cardioverter Defibrillator Patients

BAII **125**

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Aims Elevated gamma-glutamyltransferase (GGT) is a new risk factor for cardiovascular disease mortality, but its impact on ventricular tachyarrhythmia occurrence and survival in patients with an implantable cardioverter defibrillator (ICD) is unknown.

Methods and Results In a retrospective analysis, appropriate ICD therapy (both shocks and antitachycardia pacing due to ventricular tachyarrhythmias) occurred in 31.2 % of 333 male patients who had received an ICD for primary prevention (mean follow-up of 2.4 years), and in 55.4 % of 439 male patients who had received an ICD for secondary prevention (mean follow-up of 4.6 years). Compared to normal low γ-glutamyltransferase (GGT) plasma levels (< 28 U/l), risk for appropriate ICD therapy and total mortality was elevated for higher GGT categories (p for trend = 0.017 and 0.003 in primary prevention; and p = 0.006 and 0.003 in secondary prevention, respectively). In cox regression analysis, elevated GGT (> 56 U/l) remained an independent predictor of appropriate ICD therapy in primary ($p = 0.049$) but not in secondary prevention. Elevated GGT (> 56 U/l) showed a significant prognostic impact on survival in patients who had received an ICD for both primary and secondary prevention (p = 0.039 and 0.009, respectively).

Conclusions Elevation of GGT is an important prognostic parameter in male ICD patients. A possible role of GGT for improved patient selection for ICD therapy deserves further investigation **(Table 11)**.

Table 11: W. Dichtl et al.

	Appropriate ICD therapy						Survival					
	Primary prevention			Secondary prevention			Primary prevention			Secondary prevention		
Risk factor	**HR**	**CI**	**p**	**HR**	**CI**	**p**	**HR**	**CI**	**p**	**HR**	**CI**	**p**
Ischemic etiology	0.688	0.45–1.04	0.078	1.310	0.98–1.75	0.067	0.876	0.49–1.56	0.660	2.402	1.48–3.90	< 0.001
BUN > 25 mg/dl	1.451	0.90–2.35	0.128	1.819	1.27–2.61	0.001	1.785	0.96–3.33	0.069	1.977	1.24–3.14	0.004
Age > 70 a	1.034	0.60–1.77	0.902	1.507	1.08–2.11	0.016	0.664	0.28–1.59	0.359	2.336	1.53–3.56	< 0.001
Atrial fibrillation	1.116	0.74–1.69	0.605	1.083	0.81–1.45	0.592	1.906	1.03–3.52	0.039	1.020	0.67–1.54	0.926
QRS > 120 ms	1.762	1.01–2.86	0.019	1.375	1.04–1.83	0.027	2.658	1.24–5.70	0.012	1.981	1.28–3.06	0.002
NYHA > II°	1.084	0.68–1.73	0.733	0.881	0.64–1.22	0.443	1.191	0.62–2.28	0.599	1.643	1.08–2.50	0.021
GGT ≥ 56 U/l	1.575	1.00–2.48	0.049	1.160	0.87–1.56	0.323	2.072	1.14–3.78	0.039	1.762	1.16–2.69	0.009

Prescription Frequency of P-Glycoprotein-Affecting Drugs in Atrial Fibrillation IX-5 126

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Introduction Vitamin-K-antagonists (VKA) are well established for prevention of stroke or embolism in atrial fibrillation (AF)-patients. Despite their effectivity VKA are underused in AF-patients, especially in patients who would need it most urgently like patients with advanced age, previous stroke, epilepsy, or dementia. If VKA are used, the patients are only 50–65 % of the time within the therapeutic international normalised ratio (INR) range. Reasons for the underuse of VKA comprise concerns about bleeding risk, frailty with a tendency to falls, interactions with drug and food, genetic polymorphisms affecting VKA metabolism, patients' adherence and frequent laboratory monitoring. Thus, there is a desire for anticoagulant agents which would overcome these obstacles by being effective, safe and convenient to use.

Dabigatran is a new oral thrombin-inhibitor. Boehringer Ingelheim supported a recently published study, designed as a noninferiority trial, in which fixed doses of dabigatran – 110 mg or 150 mg twice daily – were compared with adjusted-dose warfarin in 18.113 AF patients. The authors present dabigatran as a drug with a similar effect as warfarin for stroke prevention but with a lower complication rate.

One of the expected advantages of dabigatran should be its lack of drug-drug interactions. However, dabigatran-absorption is dependent on the P-glycoprotein (P-gp) system in the gut which is influenced by drugs and food components. The relevance of this interaction is largely unknown. The aim of the study was to assess the prescription frequency of drugs affecting the P-gp activity in unselected consecutive hospitalized patients with AF.

Methods and Results Hundred consecutive patients (47 females, mean age 74 ± 12 y) with AF hospitalized between December 2009 and January 2010 were included. Drugs known to affect P-gp activity were identified according to the literature. For all patients, the $CHADS_2$-score was calculated and the prescribed medication was obtained at baseline. Heart failure was present in 53, hypertension in 70, diabetes in 33 and prior stroke in 14 patients. The mean $CHADS_2$-score was 2.4 ± 1.4, 0 in 8 patients, 1 in 20 patients, 2 in 27 patients, 3 in 24 patients, 4 in 14 patients, 5 in 5 patients and 6 in 2 patients. 42 patients took at least one P-gp-affecting drug, and 5 of them took two P-gp-affecting drugs. The prescribed P-gp-affecting drugs were simvastatin (n = 22), amiodarone (n = 8), vitamin E (n = 8), carvedilol (n = 4), diltiazem (n = 2), dipyridamol (n = 1), propranolol (n = 1) and verapamil (n = 1).

Conclusions Comedication with P-gp-affecting drugs is frequent in hospitalized patients with AF. More information on the clinical relevance of these drug-drug interactions is warranted before dabigatran is widely used for stroke prevention in clinical practice.

QT-verlängernde Medikamente und ihre Auswirkungen auf den klinischen Alltag IX-6 127

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Hintergrund Die Verlängerung des QT-Intervalls wird häufig durch Medikamente verursacht und kann zu Torsade-de-pointes-(TDP-) Arrhythmien führen. Wir gingen der Frage nach, welche Medikamente an unserer Abteilung verschrieben werden, die zu einer Verlängerung des QT-Intervalls führen können.

Methodik Von 102 Patienten (43 % weibliche Patientinnen) wurde die Krankengeschichte überprüft, die aktuelle Medikation erhoben, ein 12-Kanal-EKG angefertigt und ein anamnestisches Gespräch geführt. Die Anamnese erhob das Vorhandensein folgender Erkrankungen oder Umstände: Hypertonie, bekannte KHK, Gehirntumor, kongenitales LQTS, weiters ob die Patienten innerhalb der vergangenen 4 Wochen eine subarachnoidale Blutung, ein Schädel-Hirn-Trauma oder einen Insult hatten. Palpitationen und Synkopen, die durch ein verlängertes QT-Intervall oder durch eine TDP-Arrhythmie verursacht werden können, wurden ebenfalls erfragt. Weiters wurden das Alter, die Serumelektrolytwerte (Kalium und Kalzium), der Glukosespiegel und der BMI erhoben. Die QT-Zeit wurde aus dem EKG der Patienten vermessen. Sofern die Herzfrequenz zwischen 60 und 100 Schlägen pro Minute war, kam die Korrekturformel von Bazett ($QT/\sqrt{RR}$) zum Einsatz, lag die Herzfrequenz über oder unterhalb dieses Bereichs, wurde die Formel von Fridericia ($QT/\sqrt[3]{RR}$) verwendet. Für die statistische Auswertung wurden der t-Test für den Mittelwertvergleich, der Mann-Whitney-U-Test für Gruppenvergleiche verwendet. Um eine mögliche Korrelation zu finden, wurde der Korrelationskoeffizient nach Spearman verwendet.

Resultate Das Durchschnittsalter des Kollektivs betrug 67,6 (± 12,9) Jahre. Die Formel von Bazett kam bei 71,6 % aller Patienten zur Anwendung, bei den übrigen Patienten wurde die Formel von Fridericia verwendet. Der Mittelwert der QTc-Zeit aller Patienten lag bei 412 msec. Die durchschnittliche QTc-Zeit der weiblichen Patienten betrug 413 msec, 2 der Patientinnen hatten eine QTc-Zeit über 470 msec und lagen somit über dem geschlechtsspezifischen Grenzwertbereich. Bei den männlichen Patienten betrug der Mittelwert der QTc-Zeit 411 msec, hier hatten 3 der Patienten eine QTc-Zeit von über 450 msec, die als Obergrenze für Männer gilt. Von allen untersuchten Patienten hatten 41,2 % eine Komorbidität, 46 % 2 Komorbiditäten und 2 % 3 Komorbiditäten. An insgesamt 100 Patienten wurden 704 verschiedene Medikamente verschrieben, die sich aus 159 verschiedenen Wirkstoffen zusammensetzen. 16 dieser Wirkstoffe (10 %) können laut Literatur zu einer Verlängerung des QT-Intervalls führen, 38 Patienten (37,3 %) erhielten solche Medikamente.

Die erhobenen Daten ließen keinen signifikanten Zusammenhang zwischen der Länge des QTc-Intervalls, der Komorbidität, dem Geschlecht der untersuchten Personen und den eingenommen Medikamenten erkennen.

Schlussfolgerung Trotz der Häufigkeit (37 %) potenziell QT-verlängernder Medikamente in einem internistischen Patientenkollektiv zeigte sich nur ein geringer Anteil an tatsächlich verlängertem QT-Intervall im EKG.

Klinisch relevante supraventrikuläre Tachykardien bei Patienten mit implantiertem Defibrillator IX-7 128

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LKH St. Pölten

Hintergrund Eine supraventrikuläre Tachykardie (SVT) bei Patienten (Pat.) mit implantiertem Defibrillator (ICD) ist von prognostischer Relevanz. Zum einen kann sie zum inappropriaten Schock führen, zum anderen können lang dauernde Phasen zur zunehmenden Herzinsuffizienz führen. Beide klinischen Situationen sind mit einer erhöhten Mortalität verbunden.

Methode Im Zeitraum von 01.01.2009–31.12.2009 wurde an einem Zentrum mit ca. 950 betreuten ICD-Pat. prospektiv bei allen Pat. mit symptomatischer SVT oder asymptomatischer SVT aber mit hoher Arrhythmielast im ICD-Holter eine elektrophysiologische Untersuchung (EPS) durchgeführt. Ausgeschlossen wurden Pat. mit Vorhofflimmern als Indexarrhythmie im ICD-Holter sowie Pat., die keine invasive Diagnostik oder Therapie wünschten (n = 16). Die Nachbeobachtungszeit war 3 Monate.

Ergebnisse Bei 14 Pat. wurden 15 SVT im ICD-Holter diagnostiziert. Letztlich nach Zusammenschau aller Befunde (ICD-Holter, EKG, EPS) wurden sie wie folgt klassifiziert: 6 ektope atriale Tachykardien (EAT), 7 Vorhofflattern (AFL), 2 Vorhofflimmern (AFIB). Die Indexarrhytmie wurde in 6/12 Pat. mit 2-Kammer-ICD korrekt klassifiziert, nach elektrophysiologischer EGM-Begutachtung in 11/12 Pat. Bei 2 Pat. mit 1-Kammer-ICD wurden beide Indexarrhythmien sowohl vom ICD als auch vom Elektrophysiologen falsch klassifiziert.

Zusätzlich zur Indexarrhythmie hatten 12/14 Pat. AFIB, 3/14 Pat. hatten 3 unterschiedliche SVT, 9/14 Pat. hatten 2 unterschiedliche SVT. 7 Pat. erlitten einen inappropriaten Schock (4/6 EAT, 2/7 AFL, 1/2 AFIB).

In der EPS wurde bei 2 Pat. AFIB als Indexarrhythmie identifiziert, allerdings konnten 4/6 EAT trotz Katecholamininfusion nicht ausgelöst werden.

Die Ablation war in 7/8 Pat. erfolgreich. Bei erfolgreich ablierten Patienten trat kein Rezidiv auf, ebenso bei 2/4 nicht induzierbaren EAT.

Zusammenfassung (1) klinisch relevante SVT sind bei ICD-Patienten selten, führen aber häufig zu einem inappropriaten Schock. (2) Die EGM der 2-Kammer-ICD sind bei der Klassifizierung der Tachykardie wertvoll. (3) Die Ablation ist hochwirksam, falls die Indexarrhythmie ausgelöst werden kann.

VWF and ADAMTS13 Levels in Atrial Fibrillation After Cardioversion XVII-2 129

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Background The von Willebrand factor (VWF) plays an essential role in platelet adhesion and thrombus formation. It is stored in the form of multimers in platelets and endothelium from which it is released during injury or inflammation. This multimer is degraded into less active forms by ADAMTS13, which is responsible for the optimal size-distribution of VWF. Recent studies have demonstrated that ADAMTS13 has anti-inflammatory effects and reduces platelet adhesion and aggregation.

Patients with atrial fibrillation (AF) exhibit higher plasma VWF and lower ADAMTS13 antigen levels compared to control subjects. A significant correlation of these biomarkers with left atrial dimensions and left atrial appendage flow velocity suggests a possible link to higher risk of intra-atrial thrombus formation. Thus we were interested in investigating plasma concentrations of VWF and ADAMTS13 before and after CV.

Design and Methods In this observational study, we determined plasma levels of VWF and ADAMTS13 in 82 patients before, immediately after and 24 hours after CV.

Results No significant difference between mean levels of VWF before (1193 ± 397 mU/ml) and immediately after CV (1171 ± 383 mU/ml) could be shown. After 24 hours, however, a significant increase in VWF levels (1253 ± 429 mU/ml; p = 0,002) was evident. In contrast, ADAMTS13 levels decreased to a significant extent immediately after CV (59.0 ± 15.2 vs. 55.1 ± 15.8 %; p < 0.0001), whereas 24 hours later the ADAMTS13 levels again were no longer different to those at baseline. A Cox regression analysis revealed that patients in the highest tertile of ADAMTS13 levels (> 65.25 %) 24 hours after successful CV had a significantly lower rate of recurrent AF within one year after CV (p = 0.008).

Conclusion The regulation of VWF and its cleaving protease ADAMTS13 after CV might play a critical role in producing a prothrombotic milieu immediately after CV. Since high ADAMTS13 plasma concentrations are associated with a reduction of recurrent episodes of AF, it might also be used for prediction of recurrence of AF.

Neue Parameter zum Nachweis oder Ausschluss einer Präexzitation im Oberflächen-EKG IX-8 130

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Einleitung Das Wolff-Parkinson-White- (WPW-) Syndrom wird als Kombination aus QRS-Verbreiterung, kurzer PQ-Zeit im EKG und rezidivierenden Tachykardien definiert. Die Diagnose eines WPW-Syndroms ist essenziell, da betroffene Patienten nicht nur zu AV-Reentry-Tachykardien und Vorhofflimmern (VHF) neigen, sondern auch ein Risiko für das Auftreten des plötzlichen Herztodes durch sehr schnelle ventrikuläre Überleitung von VHF über die akzessorische Bahn besteht. Vor allem bei sehr gering ausgeprägter Prä-Exzitation ist die Diagnose oder der Ausschluss eines WPW-Syndroms allerdings oft schwierig. Wir suchten daher nach neuen Parametern im Oberflächen-EKG, mit denen die Diagnose oder der Ausschluss einer Präexzitation erleichtert wird.

Methode Wir analysierten die Ruhe-EKGs von 189 Patienten mit einem WPW-Syndrom im Sinusrhythmus, bei denen zwischen 1997 und 2007 an unserer Abteilung eine Ablationsbehandlung einer akzessorischen Bahn durchgeführt wurde. Als Kontrolle wurden die EKGs von 198 Patienten verwendet, bei denen zwischen 2004 und 2007 eine AVNRT behandelt und in der EPS das Vorliegen einer antegrad oder retrograd leitenden akzessorischen Bahn ausgeschlossen wurde. Wir analysierten die Amplituden aller Teile des QRS-Komplexes jeder Ableitung des 12-Kanal-EKGs, dazu wurden Herzfrequenz, PQ-Zeit, QRS-Breite und Lagetyp bestimmt. Die Unterschiede zwischen den beiden Gruppen wurden mit U-Tests und ROC-Kurven (zur Bestimmung von Cut-offs) berechnet. Darüber hinaus wurden Sensitivität und Spezifität, sowie die Likelihood-Ratio für jeden Parameter errechnet. Anschließend wurde durch Kombination der besten Parameter ein erster Algorithmus entwickelt.

Resultate Aus allen EKG-Parametern wurden 12 identifiziert, die sich in den beiden Gruppen signifikant unterschieden (AUC > 0,7 bzw. < 0,3): Für ein WPW-Syndrom sprachen wie erwartet eine QRS-Breite > 103 ms und eine PQ-Zeit < 135 ms. Des Weiteren fanden sich auch signifikante Unterschiede in den Parametern Q in aVR (Cut-off > 0,8 mV), R (Cut-off > 0,8 mV) oder S (Cut-off < 0,5 mV) in V2, R (Cut-off > 1,3 mV) oder S (Cut-off < 0,5 mV) in V3, R (Cut-off > 2,0 mV) und S (Cut-off < 0,5 mV) in V4, als auch R (Cut-off > 1,9 mV) in V5 identifiziert. Dazu sprachen noch das Vorhandensein einer vorhandenen Q-Zacke in V5 oder V6 gegen ein WPW-Syndrom. Zum Ausschluss des WPW-Syndroms wurden die 5 stärksten Parameter (QRS-Breite, PQ-Zeit, R in Ableitung V2 und V4 sowie eine Q-Zacke in V6) kombiniert. Wenn 4 dieser 5 Parameter nicht vorhanden waren, konnte ein WPW mit einer Sensitivität von 96 % bei einer Spezifität von 83 % ausgeschlossen werden.

Zusammenfassung Wir konnten zeigen, dass bei einem WPW-Syndrom mehr Veränderungen im Oberflächen-EKG auftreten als von der etablierten Definition bekannt ist. Mithilfe des neu entwickelten Algorithmus könnte es zukünftig möglich sein, eine Prä-Exzitation im Oberflächen-EKGs besser auszuschließen und damit unnotwendige invasive Untersuchungen zur Risikostratifizierung zu vermeiden.

Significant Reduction in BNP-Levels After Successful Catheter Ablation in Patients With Paroxysmal or Short Persistent Atrial Fibrillation at Six-Months-Follow-up XVII-4 131

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Purpose It has reported previously that primarily elevated N-terminal pro-brain natriuretic peptide levels (BNP) decrease in patients with atrial fibrillation (AF) within 1 month of pulmonary vein isolation (PVI). The purpose of our study was to examine the development of BNP levels after successful PVI in terms of 6 months-outcome.

Methods In 110 patients (mean age of 61 ± 9 years) undergoing successful PVI for drug-resistant highly symptomatic paroxysmal or shortly persistent AF, BNP levels were analyzed the day before, 30 days after and 6 months after the procedure, respectively. Based on a personal log of duration and frequency of symptoms and repetitive 24h-ECG recordings, patients were divided into 2 groups: 70 patients (64 %) had clinical success, and 40 patients (36 %) had clinical failure. Clinical demographic and procedural data were similar in both groups. Of note, all patients had lone AF without any clinical signs of congestive heart failure.

Results Baseline BNP levels were similar in both groups with a median of 204 pg/ml (mean 314 ± 341 pg/ml) vs 203 pg/ml (mean 454 ± 619 pg/ml; p = 0.14). After 30 days, patients who had a clinical successful procedure showed a trend in decrease of BNP levels

compared to those patients with clinical failure with a median of 157 pg/ml (mean 301 ± 523 pg/ml) vs 292 pg/ml (mean 531 ± 621 pg/ml; p = 0.057). After 6 months, a further reduction of BNP levels could be observed in clinical successful treated patients compared to patients with clinical failure, in whom a further increase over time could be detected: 141 pg/ml (249 ± 322 pg/ml) vs 256 pg/ml (578 ± 727 pg/ml). This difference reached statistic significance between the 2 groups (p = 0.008).

Conclusion Similar to previous observations, BNP levels after successful PVI decreased only in patients with clinical success during follow-up. However, our study revealed a long-term effect showing a further decrease after 6 months whereas BNP levels showed even a further increase during the 6 month follow-up-period in patients without clinical success. This observation points to an underestimated impact of AF concerning congestive heart failure even in patients without regarding symptoms.

Wie viele Patienten mit primärprophylaktischer ICD-Indikation können von einer kardialen Resynchronisationstherapie profitieren? XVII-5 **132**

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Hintergrund Die Therapie der Wahl bei Patienten mit hochsymptomatischer Herzinsuffizienz trotz optimierter medikamentöser Therapie und bestehender Dyssynchronie ist die primärprophylaktische Implantation eines Kardioverter-Defibrillators inklusive kardialer Resynchronisation (CRT-D). Rezente Untersuchungen wie MADIT CRT und REVERSE zeigten, dass auch Patienten mit milder Herzinsuffizienz (NYHA II) von einer begleitenden Resynchronisationstherapie profitieren können. Über die Anzahl an Patienten, die dafür in Frage kommen, sind nur spärliche Daten vorliegend.

Methoden In diese retrospektive Untersuchung wurden alle Patienten, denen im Zeitraum vom 01.01.2003 bis 31.12.2009 ein ICD aus primärprophylaktischer Indikation implantiert wurde, herangezogen. Für die Analyse wurden nur Patienten mit ischämischer und dilatativer Kardiomyopathie (CMP) eingeschlossen. Die Datenerhebung erfolgte vor der geplanten Aggregatimplantation.

Ergebnisse Im Beobachtungszeitraum wurden insgesamt 546 ICD-Implantationen durchgeführt, davon 274 (50,2 %) aus primärprophylaktischer Indikation (Einkammer-ICD 29,6 %, Zweikammer-ICD 22,6 %, CRT-D 47,8 %). Das Alter der Patienten betrug 64 ± 11 Jahre, die Ätiologie war in 51,8 % ischämischer, in 48,2 % dilatativer Genese. Die mittlere linksventrikuläre Auswurffraktion betrug 25,0 ± 6,2 %, die QRS-Breite 144 ± 36 ms und bei 65 % der Patienten lag eine NYHA-Klasse > NYHA II vor (17,6 % davon hatten einen QRS-Komplex < 120 ms). 96 Patienten hatten geringe Beschwerden (NYHA I–II); die QRS-Dauer war bei 33,3 % < 120 ms und bei 45,8 % ≥ 150 ms.

Zusammenfassung Die Implantation eines zusätzlichen kardialen Resynchronisationssystems bei Patienten mit gering symptomatischer Herzinsuffizienz und einem QRS-Komplex > 150 ms würde eine Steigerung von 34 % bedeuten. Kalkuliert für unser Patientenkollektiv wären 2 von 3 Patienten mit einem prophylaktischen CRT-D-System zu versorgen.

Die methodologische Entwicklung der Radiofrequenzablation von Vorhofflimmern in den Jahren 2000–2009 am Beispiel der Elektrophysiologie der Elisabethinen Linz XVII-3 **133**

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Einleitung Die Radiofrequenzablation (RFA) von Vorhofflimmern (VHF) wird nun seit 10 Jahren an der Elektrophysiologie der Elisabethinen Linz erfolgreich angewendet. Ziel dieser Darstellung ist die Aufarbeitung der Entwicklung dieser Methode in den Jahren nach der Erstbeschreibung, die Darstellung wichtiger „Meilenstein"-Studien sowie deren Einfluss auf die tägliche Praxis in unserem Elektrophysiologielabor. Zusätzlich sollen Verbesserungen der Methode aufgezeigt werden, welche zu einer deutlichen Abnahme relevanter Komplikationen Jahr für Jahr geführt haben und welche Thema einiger wissenschaftlicher Arbeiten unseres Labors waren.

Methodik 700 konsekutive Patienten (80 % männlich, 56 ± 10 Jahre) mit medikamentös therapierefraktärem und hochsymptomatischem VHF (2,8 ± 1,3 unwirksame antiarrhythmische Medikamente) wurden zwischen Dezember 2000 und November 2009 bei den Elisabethinen Linz einer linksatrialen RFA unterzogen. Alle demographischen **(Tabelle 12)** sowie prozedurbezogenen Daten wurden im zeitlichen Kontext gegenübergestellt. Bei einer Anzahl von 1,3 ± 0,5 Prozeduren pro Patient ergibt sich eine Gesamtzahl von 952 VHF-Ablationen **(Abbildung 14)**.

Ergebnisse Gemeinsamer Endpunkt aller RFA-Prozeduren für VHF ist nach wie vor die elektrische Diskonnektion der Pulmonalvenen (PV). Wurde zu Beginn noch eine segmental ostiale PV-Isolation durchgeführt, wird heute eine weite, zirkumferenzielle Isolationslinie zur Vermeidung von PV-Stenosen bevorzugt, um PV-Stenosen zu vermeiden (**Abbildung 15**, Komplikationen). Die Einführung elektroanatomischer Ortungssysteme erlaubte die dreidimensionale Lokalisation des Ablationskatheters, welche davor nur fluoroskopisch erfolgte. In weiterer Folge konnten auch CT- oder Ultraschalldaten mit der elektroanatomischen Information verschmolzen werden, was zu einer Verbesserung des Prozedurerfolges führte [Martinek et al. PACE, 2007]. Schrittweise kam es zur Einführung zusätzlicher linksatrialer Linien sowie zur RFA komplex fraktionierter Elektrogramme, um den Ablationserfolg bei persistierendem und permanentem VHF zu verbessern (**Abbildung 16**, RFA). Bezüglich Antikoagulation wird die RFA seit Anfang 2009 mit ununterbrochener Marcoumartherapie (ohne „Bridging" mit niedermolekularem Heparin)

Tabelle 12: M. Martinek et al. Demographische Parameter

	2001	2005	2009	Δp# 2001 vs 2009	Gesamt (n = 952)
Frauen	21,4 %	16,9 %	21,3 %	n. s.	19,8 %
Alter	52,1 ± 10,8	56,0 ± 8,9	57,8 ± 9,1	0,009	56,1 ± 9,7
Paroxysmales Vorhofflimmern	93 %	53 %	66 %	0,0001	69,4 %
Anzahl der Ablationsprozeduren pro Patient	1,4 ± 0,5	1,2 ± 0,5	1,3 ± 0,6	n. s.	1,3 ± 0,5
Anzahl der unwirksamen Antiarrhythmika	3,3 ± 1,4	2,3 ± 1,1	2,5 ± 0,8	n. s.	2,8 ± 1,3
Strukturelle Herzerkrankung*	3,6 %	7,6 %	18,8 %	0,0001	21,8 %
Linksatrialer Diameter in mm (Echokardiographie)	39 ± 4	40 ± 5	40 ± 5	n. s.	40 ± 5
Arterielle Hypertonie	25 %	40 %	34 %	0,001	37,9 %
Diabetes mellitus	7,1 %	6,8 %	5,8 %	n. s.	6,1 %
Thromboembolische Ereignisse vor Ablation+	0 %	7,6 %	4,4 %	0,0001	5,9 %

* Dilatative Kardiomyopathie, Klappenerkrankungen > Grad I, koronare Herzerkrankung/ischämische Kardiomyopathie; + transitorisch ischämische Attacken, Insult, periphere arterielle Embolien in Zusammenhang mit Vorhofflimmern; # p-Werte für den Vergleich zwischen den Jahren 2001 und 2009

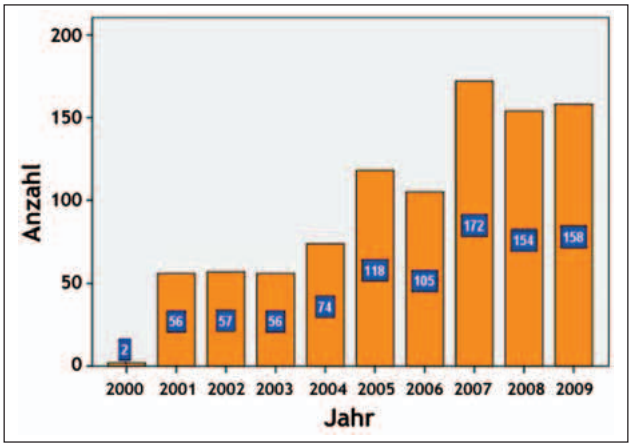

Abbildung 14: M. Martinek et al. Vorhofflimmerablationen am KH der Elisabethinen 2000–2009.

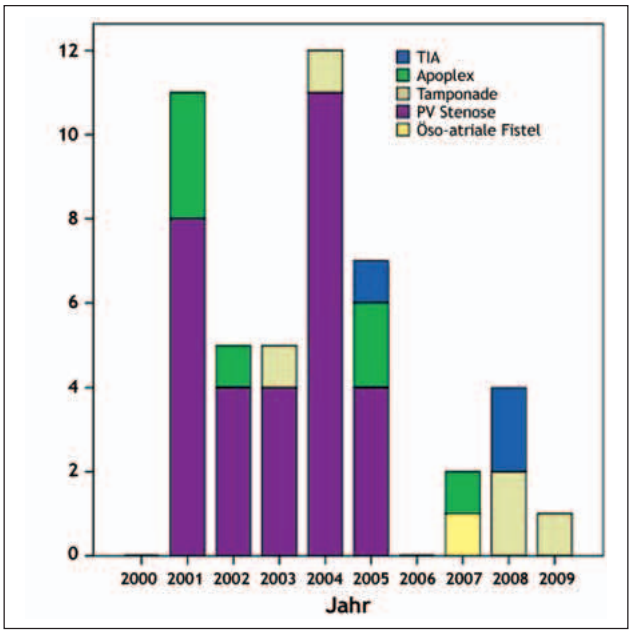

Abbildung 15: M. Martinek et al. Komplikationen

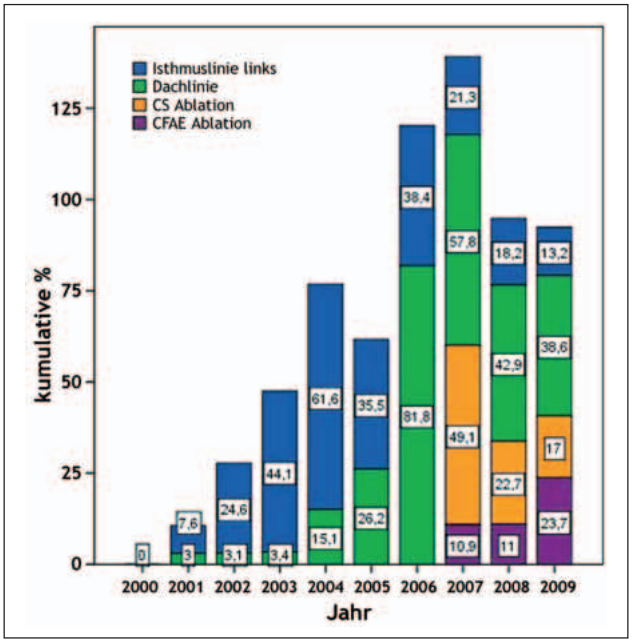

Abbildung 16: M. Martinek et al. RFA

durchgeführt, was zu einer deutlichen Abnahme postpunktioneller inguinaler Hämatome führte.

Schlussfolgerung Mit der RFA von VHF steht uns eine potenziell kurative Methode in der Therapie von VHF zur Verfügung, welche an langjährig erfahrenen Zentren mit großer Fallzahl sicher angewendet werden kann. Ständige Weiterentwicklung und Evaluierung führten an der Elektrophysiologie der Elisabethinen Linz in den vergangenen 10 Jahren zu einer Verbesserung des Prozedurerfolges bei deutlich sinkender Komplikationsrate.

Identification of Risk Factors for the Development of Esophageal Injury During Radiofrequency Catheter Ablation of Atrial Fibrillation: Procedural and Anatomical Considerations BAI 134

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Objectives The purpose of our study was to prospectively investigate the incidence of esophageal ulcerations (ESUL) in a large patient population undergoing radiofrequency catheter ablation (RFA) using a standardized ablation approach. Additionally we aimed to link demographic data and lesion sets with anatomical information given by multislice computed tomography imaging and correlate these data with the development of ESUL as no study has done as of today.

Background Atrio-esophageal fistula is an uncommon but life-threatening complication of atrial fibrillation (AF) ablation. ESUL have been proposed to be potential precursor lesions.

Methods 267 patients were included into this study consecutively screening all individuals for evidence of ESUL 24 hours after RFA of AF by endoscopy of the esophagus. A standardized ablation approach using 25W energy maximum at the posterior left atrial (LA) wall without esophagus visualization, temperature monitoring, or intracardiac ultrasound was performed.

Results In total we found 2.2 % of patients (6/267) presenting ESUL. Parameters exposing a specific patient to risk for developing ESUL were persistent AF (5/95; p = 0.023), additional RFA lines performed (roofline: 6/114; p = 0.006; LA isthmus line: 4/49; p = 0.011; Coronary Sinus: 5/66; p = 0.004), and LA enlargement (p = 0.001) leading to "sandwiching" of the esophagus between the LA and thoracic spine.

Conclusion This study is the first to link anatomical information and procedural considerations to the development of ESUL in radiofrequency ablation for AF. Furthermore, our study reveals the correlation and individual impact of these factors and introduces the concept of a "risk cascade of esophageal injury"**(Figure 17)**.

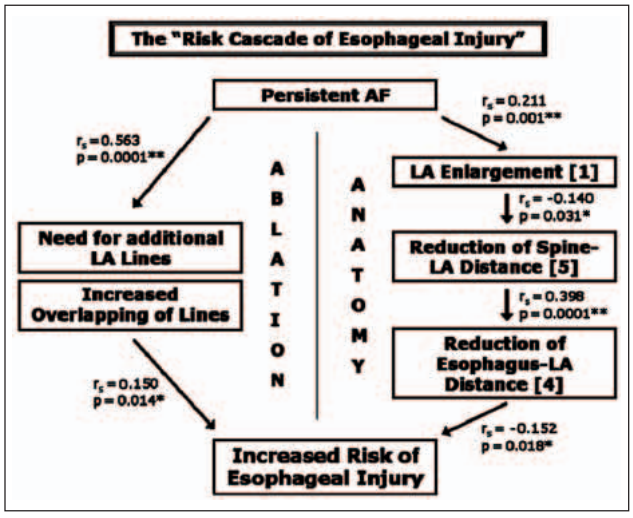

Figure 17: M. Martinek et al.

Endo- und epikardiale Substratmodifikation in der Behandlung ventrikulärer Tachykardien XVII-6 135

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Hintergrund Ventrikuläre Tachykardien (VTs) sind aufgrund ihrer hämodynamischen Auswirkungen sowie fehlender Induzierbarkeit mittels konventioneller Katheterablationstechniken teilweise nur schwer zu behandeln. Neue elektroanatomische Mappingverfahren ermöglichen die Behandlung betroffener Patienten im Sinusrhythmus. Ziel dieses Artikels ist es, unsere Erfahrung in der Modifikation des arrhythmogenen Substrats von VTs mittels endo- und epikardialen Techniken zu beschreiben.

Methoden Ausgewertet wurden die Daten von 40 konsekutiven Patienten mit Indikation zu einer katheterinterventionellen Behandlung ventrikulärer Tachyarrhythmien. Die Lokalisation der Zielregion erfolgte in Abhängigkeit der Induzierbarkeit der VTs mittels Pace-, Aktivierungs- bzw. Substratmapping.

Ergebnisse Bei 38 der 40 Patienten (Alter: 51 ± 13 Jahre; weiblich: n = 14) konnten im Rahmen von 43 Prozeduren alle klinisch relevanten der insgesamt 56 dokumentierten VTs abladiert werden. Bei einem Patienten mit vorbeschriebener mittelgradiger Mitralklappeninsuffizienz und VT-Ursprung nahe den Mitralis-Sehnenfäden wurde auf eine Ablation verzichtet. Bei einem weiteren Patienten konnte weder eine VT ausgelöst noch ein eindeutiges arrhythmogenes Substrat identifiziert werden. Es handelte sich bei 20 Patienten um rechtsventrikuläre (RV) Tachykardien und bei 20 Patienten um linksventrikuläre (LV) Tachykardien. Bei 3 Patienten war eine transthorakale epikardiale Ablation notwendig (n = 1: RV VT; n = 2: LV VT). Bei 2 der 14 Patienten mit implantierbarem Cardioverter-Defibrillator mit mehrfachen Schockabgaben in der Vorgeschichte kam es während der Nachbeobachtungszeit erneut zu antitachykarden Therapien des Aggregates (n = 1: Schock; n = 1: Antitachykardes Pacing).

Schlussfolgerung Die systematische Kombination von Pace-, Aktivierungs-, und Substratmapping ermöglicht die erfolgreiche Behandlung ventrikulärer Tachykardien mittels Katheterablation. Ein subxiphoidaler, perkutaner Zugang ermöglicht im Einzelfall die detaillierte elektroanatomische Untersuchung und Modifikation der epikardialen Oberfläche der Ventrikel.

Modulation of the Cardiac Neural Network During Atrial Fibrillation Ablation XVII-7 136

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Background The neural network formed by interconnecting neurons, axons, and autonomic ganglia recidenting on the heart has been demonstrated to be related with atrial fibrillation (AF). The aim of the present study was to investigate the anatomical and functional relationship of parasympathetic responses during AF catheter ablation.

Methods In 48 patients who underwent catheter ablation for AF we prospectively investigated the relationship between autonomic responses, their anatomical localization, and local electrogram characteristics. Parasympathetic responses were defined as transient sinus arrest, AV block, or prolongation of R-R interval > 50 %. A sympathetic response was defined as shortening of the R-R interval > 50 % during radiofrequency delivery.

Results During pulmonary vein (PV) isolation with an energy limit of 30 W an autonomic response was observed in 6 patients (12.5 %); 5 patients with a parasympathetic and 1 with a sympathetic response. In 2 patients parasympathetic responses were elicited in more than 1 site. The most common localization of the parasympathetic response was the posterior left super PV-atrial junction (n = 4) being related with sinus arrest (n = 4), AV block (n = 3), as well as R-R interval prolongation (n = 3). Postprocedural analysis demonstrated that these sites were associated with the presence of a pre-ablation high-amplitude fractionated endocardial electrogram in 3 patients which has been proposed to delineate parasympathetic innervations.

The sympathetic response was elicited during ablation at the ridge the left pulmonary veins and the left atrial appendage.

Conclusion Our findings suggest that neurons at the left superior pulmonary vein-atrial junction are involved in neural sinus node and AV node control and might release neurotransmitters during radiofrequency delivery in some patients during AF catheter ablation.

Spontane Konversion in den Sinusrhythmus nach CRT-Implantation bei Patienten mit Vorhofflimmern – Notwendigkeit der Implantation einer atrialen Sonde IX-9 137

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Hintergrund Die kardiale Resynchronisationstherapie (CRT) ist eine etablierte Therapie bei Patienten mit Herzinsuffizienz und ventrikulärer Dyssynchronie. Die aktuellen Guidelines zur Implantation berücksichtigen erstmals auch Herzinsuffizienzpatienten mit Vorhofflimmern. Die Auswirkungen der CRT auf Vorhofflimmern (VHF) sind bisher noch nicht ausreichend geklärt. Neueste Studien berichten über spontane Konversion in den Sinusrhythmus nach CRT-Implantation.

Ziel der Untersuchung war die Beurteilung der Häufigkeit von spontaner Konversion in den Sinusrhythmus bei Patienten mit Vorhofflimmern nach Implantation eines CRT-D-Systems (CRT plus Defibrillatorfunktion) zur Evaluierung der Notwendigkeit der primären Implantation einer atrialen Sonde bei diesen Patienten.

Methoden Alle Patienten, denen im Zeitraum von 2003–2008 an unserer Abteilung ein CRT-D-System implantiert wurde, sind für diese retrospektive Untersuchung herangezogen worden. Die Nachbeobachtungszeit betrug mindestens 12 Monate, der jeweils zugrundeliegende Rhythmus wurde anhand der EKG-Kontrollen im Rahmen der Nachbeobachtungen bzw. durch Auslesen der ICD-Speicheraufzeichnungen beurteilt. Vorhofflimmern war definiert als VHF mit Beginn mindestens 6 Monate vor CRT-D-Implantation.

Ergebnisse Insgesamt wurden im Beobachtungszeitraum 447 ICD-Aggregate implantiert, davon 145 (32,4 %) CRT-D-Systeme. Bei 28,3 % (41 Patienten) lag zum Zeitpunkt der Implantation VHF vor. Der mittlere Nachbeobachtungszeitraum betrug 40,0 ± 19,6 Monate. Das Alter der Patienten war 66,2 ± 9,2 Jahre, 84,1 % waren männlich, die Ätiologie war in 48,3 % ischämischer Genese. Acht Patienten (19,5 %) konvertierten im Langzeitverlauf in einen Sinusrhythmus (bei einem nach interner Schockabgabe), davon hatten 5 eine ischämische Kardiomyopathie.

Zusammenfassung Im untersuchten Kollektiv konvertierte jeder 5. Patient mit mindestens 6 Monaten bestehendem nach Implantation eines CRT-D-Systems in einen stabilen Sinusrhythmus. Die gleichzeitige Implantation einer zusätzlichen atrialen Sonde wäre daher zielführend, um sich eine eventuelle spätere Aufrüstungsoperation zu ersparen.

Incidence and Causes of Accelerated Ventricular Tachyarrhythmia in Patients With Implantable Cardioverter Defibrillator XVII-8 138

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Background Anti-tachycardia pacing (ATP) and shock delivery may induce or accelerate arrhythmia in patients with implantable cardioverter defibrillator (ICD).

Methods This retrospective analysis investigates the incidence and causes of accelerated ventricular tachyarrhythmia by ATP or shock, in a collective comprising patients with ischemic Cardiomyopathy (38 %), coronary artery disease without heart failure (27 %), non-ischemic cardiomyopathy (20 %), and other indications for ICD implantation (15 %).

Results Until December 2009, ICD was implanted in overall 1275 patients (age at implantation 59.7 ± 14.0 years; 81 % male). Within a mean follow-up period of 5.2 ± 4.0 years, intracardiac electrograms were available in 1170 patients (92 %). Overall 153 episodes of accelerated ventricular tachyarrhythmia were found in 98 patients (8.4 %). All episodes could be terminated by shock discharge. Causes of accelerated ventricular tachyarrhythmia were appropriate ATP in 137 (89 %), inappropriate ATP in 14 (9 %), appropriate shocks in 2 (1.3 %), and inappropriate shocks in 1 episode (0.7 %); 8 out of 98 patients (8.1 %) had more than one cause for acceleration. After re-programming of ATP parameters, 31 patients (31.6 %) had recurrent episodes of accelerated arrhythmia.

Conclusions Accelerated ventricular tachyarrhythmia is a frequent and serious complication of ATP, which provokes avoidable shock discharges. Despite re-programming of ATP parameters, recurrence of accelerated arrhythmia was still frequent in these patients.

Katheterablation von Vorhofflimmern mit dem Hansen® robotischen Katheter-Kontrollsystem: Erste österreichische Erfahrungen

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Hintergrund Die elektrische Isolation der Pulmonalvenen (PV) mittels Radiofrequenzstrom- (RF-) Ablation zur interventionellen Behandlung von Vorhofflimmern (AF) erfordert ausgeprägte manuelle Fertigkeiten, um eine optimale Katheterstabilität zu erreichen und setzt sowohl Patient (P) als auch Untersucher einer hohen individuellen Strahlenbelastung aus. Ein seit kurzer Zeit am Markt erhältliches robotisch über eine „dreidimensionale Maus" ferngesteuert maneuvrierbares Katheter-Kontrollsystem (KKS, Sensei®/Artisan®, Hansen Medical, Mountain View, USA) ermöglicht eine bessere Katheterbeweglichkeit und -stabilität sowie eine Reduktion der Strahlenbelastung für P und Untersucher. Wir berichten über die ersten österreichischen Erfahrungen mit dem KKS zur Katheterablation von AF.

Methodik Im November 2009 wurde an unserer Abteilung das bislang einzige nicht-magnetische KKS in Österreich installiert. Fortan wurden sämtliche P mit persistierendem AF sowie P mit AF-Rezidiv nach vorhergegangener PV-Isolation oder mit einem gemeinsamen Ostium der linken PV mit dem KKS abladiert.

Die Prozedur erfolgte stets unter Sedoanalgesie, nachdem zuvor zur anatomischen Evaluierung eine hochauflösende Spiral-CT des Herzens durchgeführt worden war. Mittels einer einfachen transseptalen Punktion und eines multipolaren Mappingkatheters (MK) wurde ein dreidimensionales anatomisches Map (EnSite NavX®, St. Jude Medical, Minneapolis, USA) erstellt und mit der CT-Anatomie fusioniert. Daraufhin wurde ein flüssigkeitsgekühlter RF-Katheter in der robotisch steuerbaren Artisan®-Schleuse (14 F) des KKS über die linke Leiste in den rechten Vorhof vorgeschoben und entlang des MK durch die transseptale Punktionsstelle in den linken Vorhof maneuvriert. Unter Kontrolle mittels des MK wurde mit dem KKS bei paroxysmalem AF eine antrale Isolation der rechten und linken PV-Paare durchgeführt, bei persistierendem AF wurde zusätzlich eine anteriore Dachlinie erstellt. Der Erfolg der Ablation wurde in Follow-ups (inklusive 48-Stunden-EKG) nach vorerst 1 und 3 Monaten beurteilt.

Ergebnisse Bis Ende Februar 2010 wurden 31 P (23 männlich, 62 ± 9 Jahre, 15 Pat. mit paroxysmalem und 16 Pat. mit persistierendem AF) mit dem KKS abladiert. Bei 26 Pat. (84 %) konnte mit dem KKS eine Isolation aller PV erzielt werden, bei 5 Pat. konnte jeweils 1 PV nicht mit dem KKS isoliert werden. Die mittlere Prozedurdauer betrug 251 ± 47 min, die mittlere Durchleuchtungszeit 30 ± 7 min (17 ± 11 min für den Untersucher am Tisch). Als Komplikation trat 1 transfusionspflichtiges Hämatom im Bereich der linken Leiste (Punktionsstele für das KKS) auf.

Die PV-Isolation mittels KKS führte bei allen bislang nachgesorgten P (Follow-up-Dauer von 3 Monaten bei 10 Pat. und von einem Monat bei weiteren 14 Pat.) zu einer objektiven und subjektiven Verbesserung der Symptomatik. Wegen des insgesamt kurzen Follow-ups wurde bislang noch keine quantitative Analyse des Ablationserfolges durchgeführt.

Schlussfolgerung Die Katheterablation von AF mit einem KKS ist mit hohen technischen Erfolgs- und niedrigen Komplikationsraten durchführbar. Eine steile Lernkurve bei der Bedienung des KKS ermöglicht von Beginn an eine dramatische Reduktion der Strahlenbelastung für den Untersucher bei akzeptabler mittlerer Prozedurdauer.

Effekt der Überprüfung auf versteckte Pulmonalvenenleitung nach Kryoballonablation bei Vorhofflimmern

XVII-9 **140**

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Einleitung Die Isolation der Pulmonalvenen (PVI) durch eine Ablationsbehandlung ist eine effektive nicht-medikamentöse Therapie bei Patienten mit paroxysmalem VH-Flimmern (PAF). Trotzdem benötigen viele Patienten auch nach primär erfolgreicher PVI wiederholte Ablations-Prozeduren, bei denen oft eine Rekonnektion der elektrischen Leitung in die Pulmonalvenen (PV) als Substrat des Rezidivs festgestellt wird. Ein systemischer Bolus von Adenosin kann die Leitung in zuvor isolierte PV vorübergehend wiederherstellen, diese „versteckte" PV-Leitung wird als Prädiktor für eine spätere Rekonnektion gewertet. Wir überprüften daher die Auswirkung dieses „Adenosin-Tests" auf prozedurale und klinische Endpunkte während und nach der Ablationsbehandlung mit der in unserem Zentrum angewandten Kryoballonablations- (CBA-) Technik.

Methoden Zwischen Mai 2008 und Dezember 2009 wurden an unserem Zentrum 50 Patienten (12 w, 38 m) mit symptomatischem PAF und ohne zugrundeliegende strukturelle Herzerkrankung mit CBA behandelt. Die Durchführung der Prozedur erfolgte mit einem Kryoballon-Katheter (Arctic Front®, Cryocath), die Isolation der PV wurde mit einem Lasso-Katheter überprüft. In 20/50 konsekutiven Patienten wurde ein Adenosin-Test (20–30 mg) durchgeführt, bei versteckter PV-Leitung erfolgten weitere CBA in der betreffenden PV. Der klinische Erfolg der Ablation wurde in Follow-ups 3, 6, 9 und 12 Monate nach der Intervention beurteilt.

Resultate Insgesamt erfolgten 658 Ablationen in 202 PV (im Mittel 3,2 CBA/PV). Durch die Behandlung konnten 197/202 PV isoliert werden, bei 6/20 Patienten (30 %) trat im Rahmen des Adenosin-Tests eine versteckte PV-Leitung auf. Die Anzahl der Ablationen im Rahmen der Prozeduren mit Adenosin-Test waren nicht signifikant höher (im Mittel 14,6 vs. 12,2 CBA; 3,7 vs. 2,9 CBA/PV), die Prozedurdauer (3,46 vs. 3,45 h) und die Durchleuchtungszeit (50,5 vs. 47,0 min) unterschieden sich nicht. Nach einem mittleren Follow-up von 254,5 Tagen führte die PVI zu einer deutlichen Reduktion der Zahl der Episoden (14,2 auf 4,2/Monat), bei 23/50 Patienten trat nach der Prozedur ohne antiarrhythmische Therapie sogar keine einzige symptomatische Episode von PAF mehr auf. Die Anzahl der Episoden von PAF war nach Durchführung des Adenosin-Tests (1,9 vs. 4,1 Episoden/Monat; $p < 0,05$) signifikant niedriger.

Zusammenfassung Bei 30 % der Patienten wurde nach PVI mit der Kryoballon-Technik eine „versteckte" PV-Leitung festgestellt und diese wurde durch weitere CBA behandelt. Der Adenosin-Test der PVI konnte den klinischen Erfolg verbessern, führte aber nicht zu einer Verlängerung der Prozedur- oder Durchleuchtungsdauer.

Risikofaktoren

Influence of Mental Stress Test on Serum Catecholamine and Endostatin Levels in Smoking, Healthy Men XVI-4 141

T. Altmann[1], S. Kampf[1], C, Biegelmayer[2], A, Handisurya[3], A. Gomari-Grisar[4], M. Fritzer-Szekeres[2], B. Meyer[5], A. Kaider[6], J. Strametz-Juranek[5]
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Background Cardiovascular diseases are the most common cause of death in industrialized countries. Arterial hypertension, obesity, hyperlipidemia, hypercholesteremia, diabetes, male gender, age, smoking, stress, and genetic factors are considered to be important risk factors for the development of atherosclerosis. A recently found potent angiostatic parameter is endostatin, a fragment of collagen XVIII, might be a new way to inhibit the progression of atherosclerosis. Multiple studies indicate that neovascularization is a key factor for plaque destabilization, plaques growth and rupture, but it still remains unclear whether angiogenesis plays a central role in the development of atherosclerosis or is the responsible element for plaque instability.

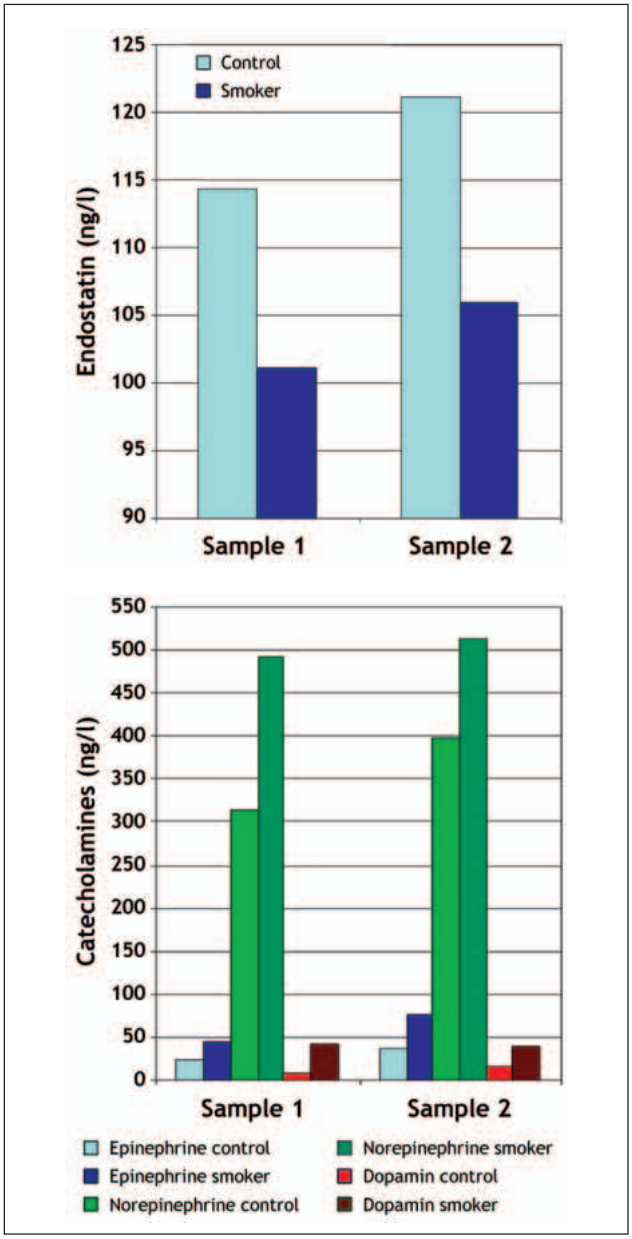

Figure 18: T. Altmann et al.

The primary goal of our study was to investigate whether mental stress leads to an altered release of endostatin and catecholamines in male smokers compared to a non-smoking control group.

Study Population and Methods A total of 37 volunteers (17 male, healthy smokers, 20 male, healthy non-smokers) were investigated during a mental stress test (Stroop-Test). Mean age was 49.5 ±7.0 years, mean BMI was 26.1 ± 2.3 kg/m². Endostatin, norepinephrine, epinephrine and dopamine were measured before starting the test (sample 1) and 5 min after ending (sample 2) the stress test. Furthermore heart rate and blood pressure were measured. Means, standard deviations and differences of all groups were calculated. Statistical significance was tested with the unpaired t-test.

Results During the mental stress test, provoked by a computer-based Stroop Test, heart-rate increased from 68.8 ± 9.3/min to 78.0 ± 13.0/min in the control group and from 66.7 ± 9.4/min to max. 72.7 ± 11.5/min in the smoking group. Blood pressure (BP) raised from 124.9 ± 9.2 mmHg to max. 135.5 ± 15.4 mmHg in the control group and from 120.0 ± 9.2 mmHg to 126.8 ± 11.3 mmHg in the smoking group. Endostatin basline levels were lower in smokers 101.1 ng/l compared to non smokers 105.9 ng/l and showed a blunted increase during mental stress compared to the control group ($p = 0.4$); although norepinephrine and epinephrine increase did not differ between the two groups statistically significant **(Figure 18)**.

Discussion Smoking is an important risk factor of cardiovascular diseases. Endostatin, as an angiostatic factor, seems to be one important atherosclerosis protective substance. This study shows, that smokers have lower baseline levels and show less increase of endostatin under mental stress, compared to non-smoking, healthy individuals. The impact of endostatin on developement of atherosclerosis and endothelial dysfunction needs to be further elucidated.

Predictive Value of Plasma von Willebrand Factor and ADAMTS13 as Markers of Endothelial Dysfunction in Patients With Atrial Fibrillation BAII 142

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Background Von Willebrand factor (VWF) plays an essential role in platelet adhesion and thrombus formation. It is degraded into smaller and less active forms by ADAMTS13. Patients with atrial fibrillation (AF) have higher plasma VWF and lower ADAMTS13 antigen levels compared to age- and sex-matched control subjects. A significant correlation of the plasma levels with echocardiographic measures of left atrial dimensions and left atrium appendage flow velocity suggests a link to higher risk of intra-atrial thrombus formation. No outcome data are available relating plasma concentrations of VWF and ADAMTS13 in patients with AF to the incidence of major adverse cardiovascular events (MACE) or all-cause death. We therefore investigated whether a high ratio of plasma levels of VWF and ADAMTS13 might predict MACE and all-cause mortality in patients with AF.

Design and Methods In this observational study, we measured plasma levels of VWF and ADAMTS13 in 284 consecutive patients with AF by means of commercially available assays and related these values to the subsequent incidence of MACE and all-cause mortality.

Results Plasma VWF/ADAMTS13 ratio was a significant predictor of MACE ($p < 0.001$) and all-cause mortality ($p < 0.001$) with a mean follow up duration of 1379 days. A Cox regression analysis revealed that patients with a VWF/ADAMTS13 ratio above the median (23.13 [IQR 16.92–34.28]) had a significantly higher risk for MACE (HR: 2.79 [95 %-CI: 1.30–5.98]; $p = 0.009$) and all-cause death (HR: 4.69 [95 %-CI: 2.24–9.81]; $p < 0.001$) compared to patients with ratios below the median.

Conclusion Among patients with AF a high ratio of VWF/ADAMTS13 is predictive for MACE and all-cause mortality. Therefore endothelial dysfunction or VWF and its cleaving protease ADAMTS13 itself might play an important role in the mechanisms behind MACE and all-cause mortality among AF patients. This might be a novel target for future treatment strategies or an additional help to risk stratification in AF patients.

Markers of Bone Metabolism in Premature Myocardial Infarction (≤ 40 years of age) XVI-8 147

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Aims Acute myocardial infarction (AMI) at young age is a rare disease with a poor prognosis. Bone metabolism parameters such as 1,25 $(OH)_2$ vitamin D_3, 25 (OH) vitamin D_3 and osteocalcin have been recently implicated in the development of coronary heart disease (CHD). We evaluated the role of these serum markers in a study population of very young AMI survivors (≤ 40 years).

Methods and Results We prospectively enrolled 302 subjects into our multi-center case control study, including 102 young myocardial infarction patients (≤ 40 years) and 200 control subjects who were frequency-matched on gender and age in an approximate 2:1 ratio per case patient. In the adjusted logistic regression analysis, elevated levels of 25 (OH) vitamin D_3 (OR per interquartile range 4.57; 95 %-CI: 2.31–9.05; $p < 0.001$) and 1,25 $(OH)_2$ vitamin D_3 (OR 3.2; 95 %-CI: 1.54–6.64; $p = 0.002$) were associated with premature AMI. Conversely, osteocalcin was inversely associated with premature myocardial infarction (OR 0.26; 95 %-CI: 0.12–0.6; $p < 0,001$). The observed associations were independent of the acute phase of myocardial infarction.

Conclusion The present study suggests that elevation of 25 (OH) vitamin D_3 and 1,25 $(OH)_2$ vitamin D_3 and a decrease in osteocalcin could play a role in the development of myocardial infarction in very young patients.

Gender effects: Nachhaltigkeit kardiovaskulärer Risikofaktoren nach kardiologischer Rehabilitation mittels eines Patientenpasses XVI-5 143

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Hintergrund Der positive Effekt eines 4-wöchigen stationären Rehabilitationsaufenthaltes auf kardiovaskuläre Risikofaktoren bei koronaren Patienten ist klar belegt. Der anhaltende Effekt, getrennt für beide Geschlechter, konnte bisher noch nicht eindeutig gezeigt werden. Durch die Implementierung eines Nachbetreuungsmoduls mittels eines Patientenpasses („St. Radegunder Gesundheitswegweiser") soll die Nachhaltigkeit einer Verbesserung kardiovaskulärer Risikofaktoren für beide Geschlechter erzielt werden.

Methoden Das Ziel der Untersuchung ist es, den Verlauf von kardiovaskulären Risikofaktoren (systolischer und diastolischer Blutdruck, Ruhepuls, Gesamtcholesterin, LDL, Körpergewicht und Anzahl der Zigaretten) des „St. Radegunder Gesundheitswegweisers" bei Frauen und Männern mit KHK in einem 1-Jahres-Verlauf an 3 Messzeitpunkten (Aufnahme, Entlassung und nach 12 Monaten) zu erfassen.

Ergebnisse Insgesamt füllten 2657 Patienten mit KHK die Patientenpässe (2000–2007) aus. Davon waren 745 Personen weiblich (28 %, Alter: 67,59 ± 9,53) und 1912 männlich (72 %, Alter: 62,94 ± 9,96).

Es zeigten sich signifikante Geschlechtsunterschiede hinsichtlich systolischem Blutdruck ($F [1/2629] = 206470,13$; $p = 0,000$), Ruhepuls ($F [1/2625] = 127929,60$; $p = 0,000$), Gesamtcholesterin ($F [1/2569] = 69113,40$; $p = 0,000$), LDL ($F [1/2518] = 32521,65$; $p = 0,000$) und Körpergewicht ($F [1/2633] = 83540,67$; $p = 0,000$) zu allen 3 Messzeitpunkten. Frauen (w) wiesen signifikant höhere Werte hinsichtlich systolischen Blutdrucks, Ruhepuls, Gesamtcholesterin und LDL auf **(Tabelle 13)**. Frauen rauchten vor dem Herzereignis signifikant weniger Zigaretten/Tag als Männer (m).

Es fanden sich signifikante Geschlechtsunterschiede (Männer vs. Frauen) in der Reduzierung des kardiovaskulären Risikoprofils (sytolischer Blutdruck: Δ15,32 ± 21,17 vs. Δ17,52 ± 22,82, Gesamtcholesterin: Δ20.77 ± 34.61 vs. Δ14.62 ± 35.09, LDL (Δ17.67 ± 28.18 vs. Δ12.41 ± 28.30, Körpergewicht: Δ2.34 ± 2.70 vs. Δ1.79 ± 3.03, Anzahl der Zigaretten/Tag (Δ25.32 ± 15.82 vs. Δ16.93 ± 12.50) zwischen Aufnahme und Entlassung.

Bei beiden Geschlechtern resultierte eine anhaltende Verbesserung (Differenz zwischen Aufnahme und 12 Monate) des diastolischen Blutdrucks ($T [2637] = -2.20$; $p = 0,027$) und des Zigarettenkonsums ($T [427] = -4.31$; $p = 0,000$), wobei Männer eine signifikant größere Reduktion des Blutdrucks (Δ4,66 ± 13,40 vs. Δ3,37 ± 13,52) und der Anzahl täglich gerauchter Zigaretten (Δ23,31 ± 16,64 vs. Δ14,85 ± 12,00) erreichten.

Die Gesamtcholesterinwerte ($T[2610] = -2.05$; $p = 0,040$) waren schlechter als bei Aufnahme, wobei sich bei Männern (Δ–4,23 ± 40,95 vs. Δ–7,91 ± 41.96) eine signifikant geringere Verschlechterung zeigte.

Konklusion Durch die Implementierung des Patientenpasses fanden sich langfristig anhaltende Effekte auf die kardiovaskulären Risikofaktoren. Das Ausmaß der Senkung der Risikofaktoren war sowohl nach Beendigung der Rehabilitationsmaßnahme als auch nach 12 Monaten zwischen den Geschlechtern unterschiedlich. Weitere Untersuchungen sollten klären, ob es geschlechtsspezifische Unterschiede in der Behandlungsqualität und/oder Compliance gibt, oder ob geschlechtsabhängige Unterschiede in den Behandlungseffekten bestehen.

Influence of Bicycle Stress Test on Plasma Catecholamine and Endostatin Levels in Smoking, Healthy Men XVI-6 144

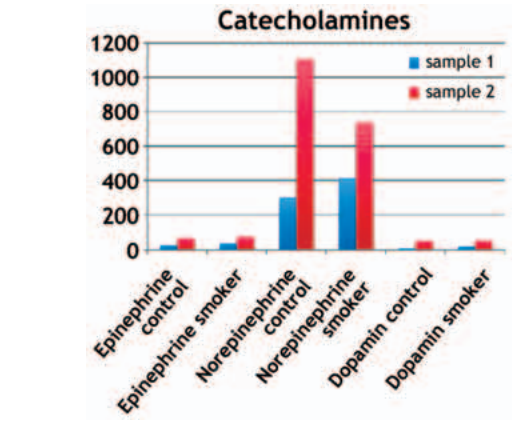
S. Kampf[1] T. Altmann[1], C. Biegelmayer[2], A. Handisurya [3], A. Gomari-Grisar[4], M. Fritzer-Szekeres[2], B. Meyer[5], A. Kaider[6], J. Strametz-Juranek[5]
[1]Students; [2]Department of Laboratory Diagnostics; [3]Department of Endocrinology; [4]Department of Angiology; [5]Department of Cardiology, Stabsstelle Gender Mainstreaming; [6]Department of Medical Statistics and Information, Medical University Vienna

Background Cardiovascular diseases are the most common cause of death in industrialized countries. Arterial hypertension, obesity, hyperlipidemia, hypercholesteremia, diabetes, male gender, age,

Tabelle 13: B. M. Harb et al.

		RRsystol	RRdiastol	Ruhepuls	Gesamtcholesterin	LDL	Körpergewicht	Zigarettenkonsum
Aufnahme	w	139,2 ± 24,5*	80,5 ± 12,4	74,8 ± 14,2*	180,4 ± 40,6*	112,4 ± 35,5*	71,4 ± 12,7*	18,5 ± 12,7*
	m	134,9 ± 21,9	80,9 ± 12,3	72,2 ± 13,9	171,0 ± 40,6	108,1 ± 34,3	82,1 ± 12,9	26,6 ± 15,9
Entlassung	w	121,6 ± 14,9*	72,7 ± 8,6	70,2 ± 11,0*	165,9 ± 35,2*	99,9 ± 29,8*	69,7 ± 12,1*	1,9 ± 3,7
	m	119,6 ± 13,7	72,1 ± 8,4	66,6 ± 10,2	150,2 ± 32,3	90,5 ± 27,3	79,8 ± 11,8	1,3 ± 3,6
12 Monate	w	131,3 ± 16,4*	77,1 ± 9,9	68,2 ± 10,0*	188,2 ± 35,5*	105,8 ± 31,9*	70,7 ± 12,3*	3,7 ± 6,2
	m	128,3 ± 14,8	76,2 ± 8,6	65,6 ± 9,0	175,1 ± 36,7	99,7 ± 30,6	81,6 ± 12,0	3,3 ± 7,0

*signifikanter Geschlechtsunterschied ($p \leq 0,01$)



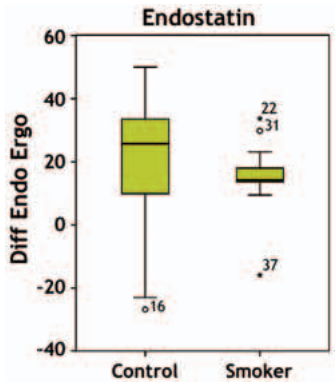


Figure 19: S. Kampf et al.

smoking, stress, and genetic factors are considered to be important risk factors for the development of atherosclerosis.

A recently found potent angiostatic parameter is endostatin, a fragment of collagen XVIII, might be a new way to inhibit the progression of atherosclerosis. Multiple studies indicate that neovascularization is a key factor for plaque destabilization, plaque growth and rupture, but it still remains unclear whether angiogenesis plays a central role in the development of atherosclerosis or is the responsible element for plaque instability.

The primary goal of our study was to investigate whether physical stress leads to an altered release of endostatin and catecholamines in male smokers compared to a non-smoking control group.

Study Population and Methods A total of 37 volunteers (17 male smokers, 20 male non-smokers) were investigated during a graded physical stress test. Mean age was 49.5 years ± 7, mean BMI was 26.1 ± 2.3. Endostatin, norepinephrine, epinephrine and dopamine were measured before starting the test and 5 min after ending the stress test. Furthermore heart rate and blood pressure were measured. Statistical significance was tested with the unpaired t-test.

Results During the graded bicycle stress test, a statistically significant increase was found for the typical stress parameter norepinephrine ($p = 0.006$) in both groups (smokers, non-smokers). Concerning endostatin, a statistically significant lower baseline level was found in the smoking group ($p = 0.021$), this group also showed statistically significant lower peak-load levels ($p = 0.006$). Serum levels of endostatin increased from 116.6 ± 16.7 at baseline to 136.6 ± 14.8 ng/ml in the control group, versus an increase of 103.3 ± 16.4 to 118.5 ± 20.8 ng/ml in the smoking group. However the verifiable increase of endostatin was not significant for both groups ($p = 0.131$) **(Figure 19)**.

Discussion Regular exercise is one of the most important lifestyle modifications in the prevention of cardiovascular diseases. Furthermore exercise leads to a hormonal response of the body and an elevation of endostatin, which is an important inhibitor of atherosclerosis. This leads to the conclusion that it plays a major part in the prevention of cardiovascular diseases. This study shows that smokers have statistically lower baseline levels and show statistically lower endostatin levels under physical exercise, compared to non-smoking, healthy individuals. Hence, the impact of endostatin on the development of atherosclerosis and endothelial dysfunction needs to be further elucidated.

Gender Distribution in Cardiac Events During Soccer World Cup 2006 in Bavaria

XVI-7 **145**

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Objective Recently, an increase in the incidence of cardiovascular events in Bavaria during FIFA Soccer World Cup 2006 (WC) has been reported. A significant pooling of cardiovascular events on days the German team played as well as on the day of the final game was shown. As watching soccer matches is predominantly popular in males, we requested data of gender distribution of acute cardiac disorders to test the hypothesis whether gender was an independent risk factor for cardiac events during WC.

Methods In order to assess acute cardiac disorders we requested data for the period of the WC (June 9–July 9, 2006) but also for control periods (May 1–July 31, 2003 and 2005; May 1–June 8, 2006 i.e. before WC and July 10–31, 2006 i.e. after WC) from the Bavarian Council for Statistics and Data Management on diagnoses. The following diagnoses were assessed: myocardial infarction (ICD-10; I 21); subsequent myocardial infarction (I 22); cardiac arrest (I 46); paroxysmal tachycardia (I 47); atrial fibrillation, atrial flutter (I 48); all remaining tachyarrhythmias (I 49).

Results Overall, no increase in cardiovascular events per day could be detected between control periods (123.7 ± 28.5) and WC (119.0 ± 28.0; $p < 0.001$) but rather a significant decrease in events occurred. No significant differences in gender distribution could be observed between control periods and WC **(Table 14)**.

Conclusion Male and female Bavarians did not differ significantly in the incidence of cardiovascular events during WC as compared to control periods, lending further support to our finding that watching soccer does not lead to an increase in cardiac events.

Table 14: D. Niederseer et. al.

	Control periods (242 days)			WC (31 days)			p-values
	total (n)	males (n; %)	females (n; %)	total (n)	males (n; %)	females (n; %)	
I21 Acute myocardial infarction	10738	6495; 60.5	4243; 39.5	1348	844; 62.6	504; 37.4	0.58
I22 Subsequent myocardial infarction	136	89; 65.4	47; 34.6	4	2; 50.0	2; 50.0	0.34
I46 Cardiac arrest	709	430; 60.7	279; 39.4	83	51; 61.5	32; 38.6	0.37
I47 Paroxysmal tachycardia	4383	2084; 47.6	2299; 52.5	546	248; 45.4	298; 54.6	0.71
I48 Atrial fibrillation and flutter	10444	5416; 51.9	5028; 48.1	1319	683; 51.8	636; 48.2	0.39
I49 Other cardiac arrhythmias	3900	1900; 48.7	2000; 50.3	390	194; 49.7	196; 50.3	0.61
Total	**30310**	**16414; 54.2**	**13896; 45.9**	**3690**	**2022; 54.8**	**1668; 45.2**	**0.72**

Shift Working is Associated With a Reduced Peripheral Endothelial Function BAII 146

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Background Shift-working is related to increased cardiovascular morbidity. Peripheral endothelial dysfunction, an inherent feature of early atherosclerosis, is suggested to be a surrogate marker of cardiovascular risk. Whether shift-working is associated with peripheral endothelial dysfunction has not been investigated so far.

Methods 48 male shift workers and 47 male day workers (mean age 43 ± 5 years) were recruited in a glas manufactory. Shift and day workers were matched according to age, body-mass-index (BMI), smoking habits, family history for premature coronary artery disease as well as the prevalence of hypercholesterolemia and hypertension.

Furthermore, sport habits were documented: no sports, regular physical activity (walking), occasional physical training (≤ 1×/week), regular physical training (2–4×/week), frequent physical training (> 4×/week).

Peripheral endothelial function was assessed using the EndoPAT technique (PAT index).

Results According to the study design no difference was found in risk factor profile between shift and day workers. Despite a higher percentage of regular physical activity among shift workers (16.7 vs 4.3 %; p = 0.05), shift working was associated with a reduced peripheral endothelial function compared to working on day shift (PAT index 1.73 ± 0.4 vs 1.94 ± 0.5; p = 0.03).

Interestingly, in the day working group participants with regular physical training (n=16) had a higher PAT index compared to those doing no sports (n = 12; PAT index 2.28 ± 0.45 vs 1.86 ± 0.51; p = 0.03); such a difference was not found in shift workers.

Conclusion A worse endothelial function was found in shift workers compared to day workers, which might explain the increased cardiovascular risk of shift working individuals.

Vascular Biology

Interleukin-33, a Novel Interleukin-1 Family Member, Is Expressed in Human Atherosclerotic Tissue and Induces Adhesion Molecules Via the NF-kappaB Pathway Resulting in Inflammatory Cell Adhesion in Human Endothelial Cells X-7 148

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Background Interleukin (IL)-33 is the most recently described member of the IL-1 family of cytokines and is a ligand of the ST2 receptor. While the effects of IL-33 on hematopoietic cells such basophils, eosinophils and mast cells have been extensively characterized, the properties of this cytokine in the vasculature are poorly investigated. Recently, IL-33 was shown to induce angiogenesis, vascular permeability and inflammatory activation in endothelial cells.

Methods Human coronary artery endothelial cells (HCAEC) or human umbilical vein endothelial cells (HUVEC) were treated with recombinant human IL-33 at concentrations between 100 ng/mL and 0.1 ng/mL for different time periods. Vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1) and E-selectin were measured by flow cytometry. Specific mRNA levels for VCAM-1, ICAM-1, E-selectin, P-selectin, L-selectin and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) mRNA expression were determined by real-time PCR. In vitro adhesion of human polymorph-nuclear leukocytes isolated from peripheral venous blood of healthy donors to the endothelial cells was determined. Quantitation of nuclear factor-κB (NF-κB) in nuclear extracts of such treated cells was performed. IL-33 mRNA and ST2 mRNA expression was also studied in human carotid endaterectomy specimens from 15 symptomatic patients.

Results We found that both HCAEC and HUVEC expressed ST2 receptor on the mRNA level. IL-33 significantly increased VCAM-1, ICAM-1 and E-selectin protein production ($p \leq 0.05$) and mRNA expression in both types of endothelial cells. IL-33 did not modulate P- and L-selectin mRNAs. ST-fusion protein abolished these effects of IL-33 on adhesion molecules expression indicating that these effects are mediated via the ST2 receptor. We also demonstrated that IL-33 promotes the adhesion of human leukocytes to monolayers of endothelial cells. IL-33 at 100 ng/mL induced translocation of NF-κB p50 and p65 subunits to the nucleus in HCAEC and HUVEC, and overexpression of a dominant negative (dn) form of IκB kinase 2 (IKK2) in HUVEC abolished IL-33-induced adhesion molecules mRNA expression. IL-33 mRNA was present in human carotid atherosclerotic plaques and significantly ($r = 0.445$; $p = 0.002$) correlated with ST2 mRNA expression.

Conclusion We found that IL-33, a novel member of the IL-1 family of cytokines, induces expression of VCAM-1, ICAM-1 and E-selectin and thus stimulates adhesion of leukocytes to human endothelial cells from both coronary artery and umbilical vein. These findings open new perspectives for the role of IL-33 in the pathogenesis of inflammatory vascular diseases.

Differential Proteomic Profiling of Coronary Stent Thrombosis Versus Atherothrombosis BAII 149

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Purpose Coronary stent implantation is reducing the risk of major adverse cardiac events. However, the occurrence of stent thrombosis (ST) remains a severe complication that results in abrupt coronary artery closure and acute myocardial infarction (AMI). The underlying molecular and cellular mechanisms of ST are not fully understood.

Methods We compared thrombus aspirated from the site of plaque rupture of 34 patients with ST and 39 patients with AMI due to atherosclerotic occlusion within a native coronary artery (time from first medical contact to balloon inflation 89 ± 12 vs 81 ± 16 minutes) by proteomic profiling.

Results While leukocytes were low at the culprit site in ST (–0.48 ± 2.45 G/L), they accumulated at the site of atherosclerotic plaque rupture (1.71 ± 4.41 G/L; p = 0.019). In contrast to native thrombus, stent thrombus was characterized by high levels of von Willebrand factor, and platelet specific proteins e.g., Platelet glycoprotein I beta and Platelet glycoprotein IX and Platelet factor IV. Local complement activation was not detected in ST, with low levels of C-reactive protein, serum amyloid P, cell adhesion molecules, and low levels of other mediators of inflammation.

Conclusion Our results demonstrate different proteomic patterns in stent thrombus compared with native coronary artery thrombus, displaying proteins involved in platelet aggregation rather than inflammation.

Response to Aspirin in Diabetic and Non-Diabetic Patients With Peripheral Arterial Disease X-8 150

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Objective To investigate whether low response to aspirin may contribute to the higher rate of restenosis in diabetic patients.

Background The long-term therapeutic success of stent angioplasty in diabetic patients is limited by a higher rate of restenosis compared with non-diabetic patients.

Patients and Methods In 42 patients with peripheral arterial disease (PAD; mean ± SD age, 69 ± 10) with normal glucose tolerance

(NGT: n = 13) or impaired glucose tolerance (IGT: n = 9) or manifest diabetes (DM: n = 20) scheduled for femoropoliteal stent-angioplasty, response to aspirin was determined by measuring urinary 11-dehydro-thromboxane B2 (d-TXB2). Urinary d-TXB2 excretion in the highest quartile was defined as low response to aspirin. The corresponding cut-off value was d-TXB2 ≥ 92 ng/mmol creatinine.

Results Low response to aspirin was found more frequent in DM-patients (n = 10; 50 %; $p < 0.05$) than in NGT- patients (n = 1; 7.7 %) or IGT patients (n = 1; 11 %). One-year restenosis rates in DM-, IGT- and NGT-patients were 60 %, 22.2 % and 16.7 %, respectively. The percentage of instent restenosis was significantly higher in patients with low response to aspirin compared with aspirin responders ($p < 0.014$).

Conclusion Low response to aspirin is more frequently observed in patients with manifest diabetes compared to patients with normal or only impaired glucose tolerance and may at least in part contribute to the increased rate of restenosis after femoropopliteal angioplasty and stenting.

Vitien

Infective Endocarditis in a 49 Year Old Man With Previously Undiagnosed Bicuspid Aortic Valve

VIII-5 **151**

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Introduction Infective endocarditis is a challenging diagnosis having many presentations ranging from an indolent infection to septicemia with life-threatening systemic embolizations. A case of infective endocarditis presenting with recurrent fever over several months in a patient with previously undiagnosed bicuspid aortic valve is described.

Methods/Results We describe a case of a 49 year old man presenting to the emergency department with complaints of recurrent fever (max. 102.6 °F), with chills on and off and fatigue for about three to four months. Several hospital visits over the past months could not detect any relevant clinical pathologies for his medical condition. A previously acquired PET/CT showed no areas of significant inflammation. On cardiac auscultation significant findings included a Grade III diastolic heart murmur, heard best at the left sternal border. Transthoracic echocardiographic imaging showed a severely destructed, bicuspid aortic valve with severe aortic insufficiency and multiple, dull vegetations (max. 15 mm). Further trans-esophageal echocardiography showed the destructed aortic valve and in addition involvement of the anterior mitral valve leaflet with valve perforation and moderate mitral regurgitation. 3/3 blood-cultures were positive for Streptococcus constellatus. The patient was started on daptomycin and amikacin and admitted to the cardiothoracic ward for early valve-resection.

Conclusion Infective endocarditis is an important consideration in the differential diagnosis for any individual presenting with recurrent fever and fatigue as it causes significant morbidity and mortality.

Der logistische EuroScore überschätzt bei Weitem das Risiko der 80-jährigen Kandidaten für einen Aortenklappeneingriff

BAI **152**

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Einleitung Der chirurgische Aortenklappenersatz (AKE) ist nach wie vor der Goldstandard zur Behandlung der Aortenstenose. Obwohl der AKE sehr effektiv sowohl das Überleben verlängert als auch die Symptome reduziert, werden weltweit manche ältere Pati-

enten nicht zugewiesen. Das Ziel dieser Studie ist, das Outcome der AKE-Patienten mit einem mittleren Alter von 80 Jahren zu evaluieren und mit dem EuroScore (welcher für die CABG-Patienten entwickelt wurde) zu vergleichen.

Methode 120 konsekutive Patienten (> 75 Jahre, mit und ohne einer KHK) wurden evaluiert (Cardiac® Datenbank). Durch den Datenabgleich mit dem Österreichischen Sterberegister wurde ein 100 %-Follow-up erreicht. Der lineare und logistische EuroScore (ES) wurde automatisch kalkuliert.

Ergebnisse Das mittlere Alter war 79,5 (75–89) Jahre. 12,2 % hatten eine signifikante COPD, 4,9 % wurde als Notfall operiert, 11,4 % litten präop. an einer signifikanten zerebrovaskulären Erkrankung. Der mittlere präop. Gradient war 54 mmHg (30–107 mmHg), 9 % benötigten eine zusätzlichen CABG I, 13 % eine CABG II und 16 % eine zusätzliche CABG III. Der akute prozedurale Erfolg war 100 %. Kein Patient hatte postoperativ eine Aortenklappeninsuffizienz, 3,2 % benötigten postop. einen Herzschrittmacher. 1,6 % mussten postop. dialysiert werden, 4 Patienten mussten länger als 24 h ventiliert werden, 1 Patient wurde reintubiert. Die mittlere Beatmungszeit war 7 h (1 Patient excl.), 41 % der AKE-Patienten wurden < 4 Stunden beatmet.

Der logistische ES (30-Tage-Mortalität) betrug 12,3 %, der lineare ES (30-Tage-Mortalität) 8,4 %. Die reale 30-Tage-Mortalität war 4 %, die reale 1-Jahres-Mortalität war 8,4 %.

Schlussfolgerungen Der logistische EuroScore (wie der STS-Score) überschätzt 3-fach die 30-Tage-Mortalität und ist kein sinnhaftes Tool zur präoperativen Risikoabschätzung und zur prädiktiven Identifikation von Patienten, welche für die perkutane Alternative geeignet sind. Zusätzlich berücksichtigt der EuroScore nicht die individuelle patientenbezogene Charakteristik und gibt keine Auskunft über die zu erwartende postprozedurale Lebensqualität v. a. bei Patienten an der Grauzone zur Geriatrie. Da der öffentliche Gesundheitsbereich unter einem Kostendruck leidet, wird es notwendig werden, andere Scores für österreichische Verhältnisse zu adaptieren (Duke-Activity-Status-Index). Bei der Initiierung neuer Methoden darf nicht ein schwacher prädiktiver Score zur individuellen Patientenselektion benutzt werden, sondern die Selektion der Patienten muss das zentrale Thema einer interdisziplinären Entscheidungsfindung (Kardiologe, Herzchirurg, Herzanästhesist) am Patientenbett sein.

Gender Differences in Low-Flow, Low-Gradient Aortic Stenosis VIII-4 **153**

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For the Multicenter TOPAS (Truly Or Pseudo Severe Aortic Stenosis) Study Investigators, Department of Cardiology, Medical University of Vienna; Department of Medicine, Laval University, Québec, QC, Canada

Background Patients with low-flow, low-gradient aortic stenosis (AS) represent the most challenging subset of AS. We have recently shown that decreased exercise capacity and projected aortic valve area are predictors of outcome in low flow AS. Little is known about gender differences in low flow AS and their potential implications on management strategies.

Methods 142 pts with low flow AS (valve area ≤ 1.2 cm², LV EF ≤ 40 %, mean gradient ≤ 40 mmHg) underwent dobutamine stress echocardiography (DSE) at study entry and assessment of functional capacity using the Duke Activity Status Index (DASI), 95 pts additionally underwent a 6-minute walk test (6MWT).

Results Only 36 (25 %) pts were female. Women were slightly older (74 vs 71 years; p = 0.21). Although women reported a similar symptomatic status at entry (NYHA and CCS; p = 0.20 and 0.54), females had significantly worse performance at 6MWT (202 ± 136 vs 296 ± 130 m; p = 0.008) and a lower DASI score (17 ± 10 vs 27 ± 15; p < 0.0001). There was no difference in mean gradients, EF at rest and peak DSE, and projected valve area.

Overall, 50 pts died (12 [33 %] women, 38 [36 %] men). Interestingly, follow up was significantly longer in males (471 ± 420 vs 250 ± 267 days; p = 0.004). There was no difference in the rate of aortic valve replacement (f/m 47 % vs. 47 %), and perioperative death (f/m 24 % vs 22 %). Kaplan-Meier survival curves showed a trend towards a higher mortality in women without reaching statistical significance (log rank 0.16). In pts undergoing AVR, shorter 6MWT distance predicted death only in men despite lower baseline distance in women (p = 0.02).

Conclusion Although the majority of pts with degenerative AS are female, women are significantly underrepresented in the subgroup of low flow AS. Although women present with significantly worse exercise capacity as reflected by lower DASI and 6MWT, both previously associated with worse outcome in low flow AS, there was no evidence of reduced survival. Hence, low functional capacity should not necessarily preclude consideration of AVR in women with low flow AS. The small patient number and shorter follow up time in women may have influenced our results, further investigations in larger series are required.

Grown Up Congenital Heart Disease (GUCH): Clinical Spectrum and Outcome in 462 Patients VIII-6 **154**

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Background The number of GUCH patients is growing, however data from long term follow up studies are limited.

Methods Retrospective analysis of 462 patients (252 m, 208 f; age 26.7 [18–61] y), who were seen in our GUCH unit between 2004 and 2008. The diagnosis of the congenital heart defects were classified into simple, moderate and complex categories.

Results In NYHA I, II and III were 86.1 %, 11.5 % and 2.4 % of patients. The majority has an occupation (86 %), are students or are in maternity leave (7.5 %). Patients with NYHA ≤ 2, relevant arrhythmias, cardiac medication, pacemakers or catheter interventions have more often complex than moderate or simple cardiac lesions (p < 0.001). In 76 patients 113 operations (87 repeat op.) were performed (age at op. 24.3 [18.1–43.1] y): pacemaker interventions (n = 40), RVOT reconstructions (n = 38), LVOT/aortic arch op. (n = 15), VSD/ASD closures (n = 9), AV valve reconstructions (n = 3), Fontan conversions (n = 2) and others (n = 6). There were 9 postoperative complications in 8 patients: bleeding (n = 6), complete AV block (n = 2) and SND (n = 1). Mortality was 7 %: 8 patients died 13 d (low cardiac output: n = 1) to 19.2 y (unknown cause: n = 7) postoperative. Risk factors for fatal outcome were documented postoperative dysrhythmias (SND: n = 2; atrial or ventricular non-sustained tachycardia: n = 4; intermittent atrial flutter: n =2) (p < 0.001) and male sex (n = 7; p < 0.01). Of the patients who died 4/6 with tachycardia had antiarrhythmic medication (none had ablative procedures), 4/8 had pacemaker therapy (none with tachycardia had ICD). Of these 8 patients 4 had complex and 3 had moderate cardiac lesions.

Discussion In our series most GUCH patients have no or only mild restrictions and are employed. The main part of operations in our GUCH patients are pacemaker implantations or changes and RVOT reconstructions. Documented relevant arrhythmias and male sex are significant risk factors for death. Relevant arrhythmias are atrial flutter and non-sustained atrial or ventricular tachycardia. Documented arrhythmias in patients with moderate and complex cardiac lesions have to be addressed with close follow up, regular Holter ECG and conservative treatment. Invasive antiarrhythmic therapy should be considered in selected cases.

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