Journal für
Kardiologie
Austrian Journal of Cardiology
Österreichische Zeitschrift für Herz-Kreislauferkrankungen

Jahrestagung der Österreichischen Kardiologischen Gesellschaft - 30. Mai bis 2. Juni 2012, Salzburg - Abstracts

Journal für Kardiologie - Austrian Journal of Cardiology 2012; 19 (5-6), 123-194

Krause & Pachernegg GmbH • Verlag für Medizin und Wirtschaft • A-3003 Gablitz
P.b.b. 02Z031105M, Verlagsort: 3003 Gablitz, Linzerstraße 177A/21 Preis: EUR 10,–

Veranstaltungskalender

Hybrid-Veranstaltungen der Herausgeber des Journals für Kardiologie

Finden Sie alle laufend aktualisierten Termine auf einem Blick unter

www.kup.at/images/ads/kongress.pdf

Österreichische Kardiologische Gesellschaft Jahrestagung 2012 30. Mai bis 2. Juni 2012, Salzburg

Abstracts

Poster in alphabetischer Reihenfolge: Gruppe / Erstautor
Vorträge: Best Abstracts I (BAI) und II (BAII) sind rot hervorgehoben.

Akutes Koronarsyndrom/Acute Coronary Syndrome

Decreased Interleukin-33 Serum Levels After Coronary Stent Implantation are Protective Against In-Stent Restenosis I – 4

S. Demyanets, R. Jarai, K. M. Katsaros, S. Farhan, A. Wonnerth, T. W. Weiss, G. Maurer, W. S. Speidl, J. Wojta, K. Huber
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna; 3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna

Background Restenosis after stent deployment is an overreaction of the wound healing response after vascular injury and is characterized by the sequence of inflammation, granulation, and extracellular matrix remodeling. Interleukin-33 (IL-33) is a recently described member of the IL-1 family of cytokines and is a ligand for the ST2 receptor. Circulating IL-33 was increased in patients with inflammatory disorders such as rheumatoid arthritis, systemic sclerosis, inflammatory bowel disease and liver failure. However, the predictive value of IL-33 for the development of in-stent restenosis (ISR) is not known.

Methods We included 387 consecutive patients undergoing percutaneous coronary intervention (PCI) of whom 193 had stable angina, 93 non-ST elevation myocardial infarction (NSTEMI), and 101 ST-elevation MI (STEMI), respectively. Blood was taken directly before and 24 hours after stent implantation. Plasma levels of IL-33 were measured by a specific ELISA. The presence of ISR was initially evaluated by clinical means. When presence of myocardial ischemia was suspected, coronary angiography was performed to confirm the suspected diagnosis of ISR.

Results Bare metal stents (BMS) were used in 283 and drug eluting stents (DES) were used in 104 patients. Clinical ISR was present in total in 34 patients (8.8%). IL-33 was detectable in 185 patients and was below detection limit in 202 patients. In patients with decreased IL-33 (n = 95), unchanged or non-detectable levels (n = 210) or increased levels of IL-33 after PCI (n = 82), ISR-rate was 2.1%, 9.5% and 14.6%, respectively ($p < 0.05$). Accordingly, patients with ISR showed a significant increase of IL-33 upon PCI ($p < 0.05$). This association was independent from clinical presentation and risk factors as well as numbers and type of stents.

Conclusion In patients with both stable and unstable coronary artery disease, a decrease of IL-33 serum levels after stent implantation is associated with a lower rate of in-stent restenosis.

Soluble ST2 Plasma Levels are Increased in Acute Coronary Syndromes and Predict Long-Term Mortality I – 5

S. Demyanets, R. Jarai, K. M. Katsaros, S. Farhan, A. Wonnerth, T. W. Weiss, G. Maurer, W. S. Speidl, K. Huber, J. Wojta
Department of Internal Medicine II, Medical University of Vienna; 3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna

Background ST2 is an interleukin (IL)-1receptor family member and is a receptor for IL-33. Elevated soluble ST2 (sST2) has been associated with an adverse short-term prognosis in non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation MI (STEMI), as well as long-term prognosis in patients with NSTEMI. In the present study we investigated a possible association of sST2 plasma levels and different clinical stages of coronary artery disease (CAD). In addition, we assessed the predictive value of sST2 levels in patients with stable angina, NSTEMI and STEMI.

Methods We included 373 consecutive patients with angiographically proven CAD of whom 178 had stable angina, 97 had NSTEMI, and 98 had STEMI, respectively. Patients were followed for a mean of 42 months for the occurrence of a combined clinical endpoint (all cause death, MI and rehospitalisation for cardiac causes). Plasma levels of sST2 were measured by a specific ELISA.

Results sST2 plasma levels were significantly increased in patients with STEMI (median 453, IQR 313–688 pg/mL) as compared to patients with NSTEMI (269, IQR 157–496 pg/mL; $p \leq 0.001$). In addition, patients with acute coronary syndromes showed significantly higher levels of sST2 as compared to patients with stable CAD (169, IQR 79–260 pg/mL; $p \leq 0.001$). During follow-up, 37 (9.9%) patients died. sST2 plasma levels significantly predicted mortality in the total cohort ($p < 0.05$). Cardiac events occurred in 66 (17.6%) patients. sST2 significantly predicted occurrence of the combined endpoint in patients with STEMI ($p = 0.003$), but not with NSTEMI ($p = 0.35$) or stable CAD ($p = 0.50$).

Conclusions Plasma levels of sST2 are increased in acute coronary syndromes. In addition, sST2 levels predict mortality in the total cohort and cardiac events specifically in STEMI patients.

Prasugrel versus Clopidogrel in Daily Clinical Practice in Patients Undergoing Primary PCI in the Austrian Acute-PCI Registry BAI

J. Dörler, F. X. Roithinger, M. Juhasz, W. Benzer, R. Zweiker, P. Siostrzonek, J. Auer, H. Schuchlenz, O. Pachinger, F. Weidinger
Department of Cardiology, Innsbruck Medical University; Department of Medicine, Hospital Mödling; Department of Medicine, Hospital Barmherzige Brüder Eisenstadt; Department of Interventional Cardiology, Academic Hospital Feldkirch; Department of Cardiology, Medical University Graz; Hospital Barmherzige Schwestern Linz; Department of Cardiology, St. Josef Hospital Braunau; Department of Cardiology and Intensive Care Medicine, LKH Graz-West; Department of Internal Medicine II, Rudolfstiftung Hospital Vienna

Background Prasugrel is recommended as first line drug for dual antiplatelet therapy after primary PCI (PPCI) in ST-elevation myocardial infarction (STEMI). There are few data on its use in daily practice of PPCI and clinical outcome in comparison with clopidogrel.

Methods 2454 consecutive patients with ST-elevation myocardial infarction undergoing PPCI between January 2010 and December 2011 and receiving either prasugrel or clopidogrel before arrival in the catheter laboratory were enrolled. Evaluation included baseline characteristics and in-hospital outcome. In addition, logistic regression analyses were performed to determine indicators for prasugrel treatment.

Results 2017 (82.2%) patients received clopidogrel and 437 (17.8%) received prasugrel. Patients on prasugrel were younger (56.0 yrs [49.0–64.0] vs 64.0 yrs [53.0–74.0]; $p < 0.01$), more often

male (71.1% vs 80.8%; p < 0.01) and current smokers (58.4% vs 43.3%; p < 0.01), but had less previous PCI (9.2% vs 12.5%; p = 0.04). Direct field triage was more common in the prasugrel group (73.7 vs 26.2%; p < 0.01) resulting in a shorter delay to PPCI (3.08 h [1.93–5.71] vs 3.57 h [2.23–6.69]; p = 0.01). In-hospital mortality was lower in the prasugrel group (1.8% vs 4.7%; p = 0.01) with no difference in TIMI major bleedings between prasugrel (0.2%) and clopidogrel (0.9%; p = 0.24). Multivariable logistic regression analysis revealed that age (HR 0.97; 95%-CI: 0.96–0.98 per year; p < 0.01), male sex (HR 0.69; 95%-CI: 0.51–0.94; p = 0.02) and direct field triage (HR 1.59; 95%-CI: 1.21–2.09; p = 0.01) were independent predictors of prasugrel treatment.

Conclusion In clinical practice prasugrel is predominantly used in younger male patients transferred directly from the field to PPCI. These factors may result in lower in-hospital mortality with similar TIMI major bleeding rates compared to clopidogrel.

B-Type Natriuretic Peptide and Risk of Contrast-Induced Acute Kidney Injury in Acute ST-Segment Elevation Myocardial Infarction: A Substudy from the HORIZONS-AMI Trial I – 2

R. Jarai, K. Huber, R. Mehran, G. Dangas, G. Stone
3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna, Austria; Cardiovascular Research Foundation, Lenox Hill Heart and Vascular Institute, New York, USA

Background Contrast-induced acute kidney injury (CI-AKI) after percutaneous coronary intervention (PCI) is associated with adverse short- and long-term outcomes. However, identification of patients at risk for CI-AKI is challenging. Using a large contemporary randomized trial database of patients with ST-segment elevation myocardial infarction (STEMI), we therefore sought to examine whether admission B-type natriuretic peptide (BNP) levels predict the development of CI-AKI.

Methods A total of 979 STEMI patients enrolled in the HORIZONS-AMI trial had BNP levels measured in the emergency room prior to primary PCI as part of the study protocol. CI-AKI was defined as a relative increase in serum creatinine of ≥ 25%, or an absolute increase of ≥ 0.5 mg/dL, occurring within 48 hours after contrast administration. Logistic regression analysis was used to estimate the association of admission BNP with development of CI-AKI.

Results CI-AKI occurred in 131 patients (13.3%). Baseline BNP was a significant univariable correlate of CI-AKI (OR 1.40, 95%-CI: 1.09–1.80; p = 0.009). After multivariable adjustment for clinical, laboratory and angiographic variables, BNP remained a significant independent predictor of CI-AKI (1.56 [1.16. 2.09]; p = 0.003). Significant net reclassification improvement (NRI) was achieved by addition of BNP to the current clinical risk prediction model (NRI = 0.022; p = 0.03) and to the Mehran Risk Score (NRI = 0.028; p = 0.002).

Conclusion Measurement of serum BNP at hospital admission may help identify patients who are at risk for developing CI-AKI after primary PCI in STEMI **(Figure 1)**.

Prognostic Relevance and Prediction of Contrast-Induced Acute Kidney Injury in Acute ST-Elevation Myocardial Infarction: Analysis from the HORIZONS-AMI Trial I – 3

R. Jarai, K. Huber, G. Dangas, R. Mehran, G. Stone
3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna, Austria; Cardiovascular Research Foundation, Lenox Hill Heart and Vascular Institute, New York, USA

Background and Aims There are limited data available on the short- and long-term prognostic relevance of contrast-induced acute kidney-injury (CI-AKI) in patients with ST-elevation myocardial infarction (STEMI) undergoing primary PCI. Identification of patients at risk of CI-AKI could be of major clinical importance, as starting specific therapeutic interventions prior to acute coronary angiography might prevent the development of CI-AKI.

Methods A total of 2975 STEMI patients enrolled in the HORIZONS-AMI trial had available data on serum creatinine concentrations after angiography. CI-AKI was defined as a relative increase in creatinine of ≥ 25%, or an absolute increase in creatinine of ≥ 0.5 mg/dL within 48 hours after primary PCI. We assessed cardiac mortality, non-fatal MI, target vessel (TVR) and target lesion revascularization (TLR), stent thrombosis, non-CABG related major bleeding and net adverse clinical events (NACE = MACE or major non-CABG bleeding) as a function of CI-AKI. Multivariate analyses were used to identify predictors of CI-AKI, as well predictors of the primary and secondary endpoints.

Results Patients with CI-AKI (n; %) had significantly worse outcome than patients without CI-AKI reflected by significantly higher rates of in-hospital cardiac death (5.8% vs 0.7%; p < 0.001), recurrent myocardial infarction (2.4% vs 1.1%; p = 0.0229) and bleeding rates (16.8% vs 6.9%; p < 0.001). The need for TVR (3.4% vs 1.8%; p = 0.0213) and TLR (3.4% vs 1.6%; p = 0.009) was substantially higher among patients with CI-AKI and there was a trend for higher rates of stent thrombosis, which was significantly different at 30 days (1.0% vs 0.2%; p = 0.0129). In multivariable Cox-regression analyses, CI-AKI was an independent predictor of all adjudicated endpoints with the exception of non-fatal myocardial infarction CI-AKI. In multivariate logistic regression analysis, age, low hemoglobin concentrations at admission, Killip Classification, heart rate, body mass index, creatinine clearance and history of kidney dysfunction were independent predictors of CI-AKI.

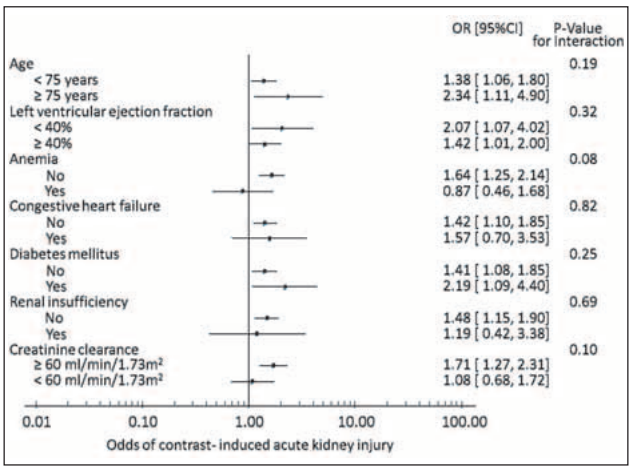


Figure 1: R. Jarai et al.

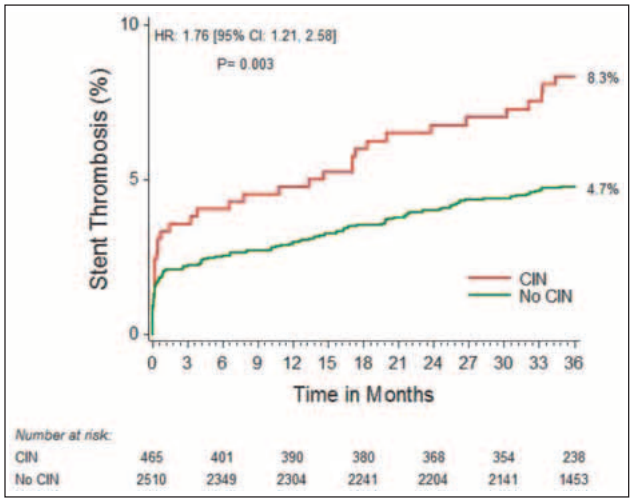


Figure 2: R. Jarai et al.

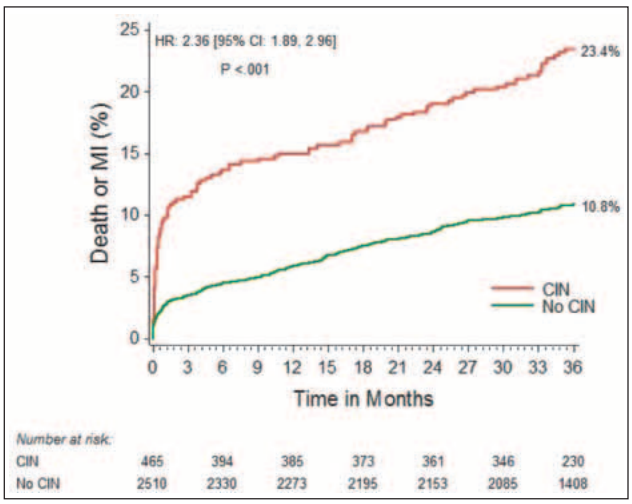


Figure 3: R. Jarai et al.

Conclusions CI-AKI is a serious complication of primary PCI, which is associated with highly impaired short- and long-term outcome, including major adverse clinical events, stent-thrombosis and bleeding complications **(Figures 2, 3)**.

Kardiogener-Schock-Register Klagenfurt XI – 5

C. Kaulfersch, G. Grimm
2. Medizinische Abteilung, Klinikum Klagenfurt

Einleitung Wir berichten über 261 Patienten, die in der Zeit von April 2007 bis Jänner 2012 mit der Diagnose kardiogener Schock an unserer Abteilung betreut wurden.

Material/Methode Retrospektive Analyse aller Patienten an unserer ICU mit der ICD-Diagnose R57.0 (kardiogener Schock). Selektion der Patienten nach der aktuellen deutsch-österreichischen S3-Leitline „kardiogener Schock".

Ergebnisse 167 (64 %) der Patienten waren Männer, 94 (36 %) Frauen. Das durchschnittliche Alter betrug 68,3 Jahre. 81 % der Patienten präsentierten sich im ischämischen Schock (davon STEMI 76 %; NSTEMI 24 %). Die 30-Tage-Mortalität aller Patienten betrug 49 % (46 % bei ischämischem Schock, 58 % bei nicht-ischämischem Schock). Die Mortalität bei NSTEMI war mit 52 % höher als bei STEMI mit 46 %. Eine IABP wurde bei 31 % der Patienten mit kardiogenem Schock implantiert. Mit IABP verstarben 39 Patienten (48 %). 181 (69 %) der Patienten wurden invasiv beatmet (Dauer median: 4,8 Tage). 22 Patienten (8 %) wurden bei Schockniere dialysiert. Die durchschnittliche Aufenthaltsdauer betrug 8,1 Tage. Es entstanden Gesamtkosten von ca. 6,372.000 Euro (ca. 24.400 Euro/Patient).

Diskussion Die Mortalität des kardiogenen Schocks bleibt trotz neuer medikamentöser und interventioneller Therapieoptionen weiterhin hoch. Unsere Daten sind vergleichbar mit jenen internationaler Studien/Register bezüglich des Endpunktes Mortalität nach kardiogenem Schock mit/ohne IABP. Daten großer randomisierter Studien bezüglich Mortalitätsvorteil bei IABP fehlen bislang (IABP-Schock-II-Studie vor Abschluss). Der kardiogene Schock bindet erhebliche Ressourcen (Diagnostik/Therapie/Pflege/Budget). Die rasche Revaskularisierung ab Diagnosestellung ist der Goldstandard bei ischämischem Schock, sowohl bei STEMI als auch NSTEMI.

Neutrophils and NETs at the Culprit Lesion Site of ST-Elevation Acute Coronary Syndrome XI – 1

A. Mangold, Th. Scherz, A. Falkinger, S. Puthenkalam, K. Distelmaier, K. Preissner, I. M. Lang
Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Austria; Institute for Biochemistry, Justus Liebig University, Giessen, Germany

Background Mechanisms of acute plaque rupture and coronary occlusion in ST-elevation acute coronary syndrome (STE-ACS) are poorly understood. In contrast to common knowledge implicating intralesional macrophages in the pathogenesis of acute coronary vascular syndromes, we hypothesize that circulating innate immune cells mediate plaque rupture and thrombotic occlusion. In former studies, we reported the accumulation of neutrophils and related proteins at the culprit lesion site. Neutrophil extracellular traps (NETS) represent an efficient effector mechanism of activated neutrophils. We aimed to characterize neutrophils in the different circulatory compartments (systemic, coronary fluidic and solid aspiration material) of STE-ACS patients.

Methods STE-ACS patients who underwent primary percutaneous coronary intervention at the Vienna General Hospital were consented (n = 70). Culprit site blood was aspirated with a thrombectomy catheter and particulate thrombus material was separated. In parallel, blood was sampled from the femoral arterial sheath. Flow cytometry was employed to evaluate neutrophils accumulating at the plaque rupture site in the fluidic and solid compartment. These results were complemented by ELISA and immunofluorescence assays.

Results Neutrophils derived from coronary thrombi are highly activated compared to systemic values (CD66b, CD11b) and form aggregates with platelets. Coronary thrombi display excessive amounts of NETs. Neutrophil-derived degradation products are predominant in coronary thrombi. MPO in coronary plasma is significantly increased. By contrast, neutrophils in fluidic compartment of culprit site aspirates show reduced expression of CD11b and form fewer aggregates.

Conclusion We report the presence of activated NET-producing neutrophils at the culprit lesion site of STE-ACS patients. NETs act as an active scaffold for the nascent coronary thrombus.

Specific Monocyte Subsets are Increased at the Culprit Lesion Site of ST-Elevation Acute Coronary Syndrome Patients XI – 2

A. Mangold, A. Falkinger, Th. Scherz, K. Distelmaier, I. M. Lang
Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna

Background ST-elevation acute coronary syndrome (STE-ACS) is the leading cause of death. Mechanisms of acute plaque rupture and coronary occlusion are poorly understood. In contrast to common knowledge implicating intralesional macrophages in the pathogenesis of acute coronary vascular syndromes, we hypothesize that circulating innate immune cells mediate plaque rupture and thrombotic occlusion. Monocytes are early inflammatory cells implicated in the pathogenesis of ACS. CD16+ monocytes represent an activated and proinflammatory subtype. In the present study, we examined the distribution and activation status of these subsets in STE-ACS.

Methods STE-ACS patients who underwent primary percutaneous coronary intervention at the Vienna General Hospital were consented (n = 40). Culprit site blood was aspirated with a thrombectomy catheter and particulate thrombus material was separated. In parallel, blood was sampled from the femoral arterial sheath. Flow cytometry was employed to classify monocytes by their CD14:CD16 ratio (CD14+CD16-, CD14+CD16+, CD14-CD16+) at the plaque rupture site, both in the fluidic and solid compartments.

Results CD14-CD16+ monocytes were selectively increased in the fluidic compartment at the culprit lesion site of STE-ACS patients. They express a distinct pattern of adhesion (CD49d, e, f,

CD142) and activation markers (TLR2, TLR4, HLA-DR) and aggregate with platelets.

Conclusion CD16-positive monocytes accumulate at the culprit lesion site in STE-ACS patients. We hypothesize that interaction with platelets induces CD16 expression initiating pro-inflammatory downstream effects, including inflammatory cell recruitment.

Vigilanz gegenüber CX-Myokardinfarkten: Erfahrungen aus einem Schwerpunktkrankenhaus XI – 7

D. Petener, P. Wexberg, M. Avanzini, W.-B. Winkler, F. Weidinger
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Einleitung Entsprechend den aktuellen ESC-Guidelines ist bei NSTEMI eine Revaskularisation innerhalb der ersten 72 Stunden vertretbar. Allerdings beobachten wir bei diesen Patienten ohne sofortige Revaskularisation immer wieder hohe Enzymverläufe trotz der vermeintlich „harmloseren" EKG-Diagnose. Wir konnten in einer früheren Untersuchung zeigen, dass auch bei NSTEMI angiographisch häufig ein Gefäßverschluss diagnostiziert wird und der Ramus circumflexus (RCX) dabei in einem hohen Prozentsatz das schuldige Gefäß darstellt, das oft in den EKG-Standardableitungen und echokardiographisch nicht eindeutig zu beurteilen ist. Ziel der vorliegenden Studie war es daher aufzuzeigen, ob unsere oben genannten Erkenntnisse über die Zeit zu einer häufigeren Revaskularisation der CX-Myokardinfarkte an unserer Abteilung führten.

Methodik 748 Patienten wurden zwischen 2006 und 2011 an unserer Abteilung im Rahmen eines akuten Myokardinfarktes einer angiographischen Abklärung unterzogen. Entsprechend der EKG-Veränderungen wurden die akuten Koronarsyndrome in STEMI und NSTEMI unterteilt. Die lokale Datenbank wurde retrospektiv hinsichtlich der Gefäßverteilung und des Risikoprofils analysiert. Die Verteilung wurde mittels Chi-Quadrat-Test statistisch ausgewertet.

Ergebnisse Das klinische Risikoprofil war zwischen STEMI und NSTEMI vergleichbar. In der NSTEMI-Gruppe stieg der Anteil des RCX als schuldiges Gefäß über die Jahre an (von 13,5 % im Jahr 2006 auf 17,1 % in 2007, auf 25,0 % in 2008) und pendelte sich in diesem Prozentsatz ein (21,1 % in 2009, 20,8 % in 2010, 23,7 % in 2011). Die Häufigkeit des RCX als schuldiges Gefäß unter den STEMIs schwankte (11,5 % in 2006, 5,4 % in 2007, 13,1 % in 2008, 17,3 % in 2009, 9,2 % in 2010, 12,0 % in 2011).

Tabelle 1: D. Petener et al.

	2006	2007	2008	2009	2010	2011
Culprit CX in NSTEMI	13,5 %	17,1 %	25,0 %	21,1 %	20,8 %	23,7 %
Culprit CX in STEMI	11,5 %	5,4 %	13,1 %	17,3 %	9,2 %	12,0 %

Diskussion An unserer Abteilung ist in der Gruppe der NSTEMIs der Anteil des RCX als schuldiges Gefäß unter den akut koronarangiographierten Patienten über die Jahre gestiegen. Ursache dafür ist vermutlich die erhöhte Vigilanz gegenüber True-Posterior-Myokardinfarkten und gegenüber der in früheren Arbeiten gezeigten Tatsache, dass viele Patienten mit NSTEMI tatsächlich Gefäßverschlüsse haben **(Tabelle 1)**.

Patients Admitted for Acute Coronary Syndrome: Current Prescription Rates of Antiplatelet Therapy and Statins XI – 4

R. Steinacher, J. Altenberger, J. Kraus, M. Pichler, U. Hoppe
Universitätsklinik für Innere Medizin II, Landeskrankenhaus Salzburg

Introduction Patients with acute coronary syndrome (ACS) present a high prevalence of cardiovascular risk factors that have been described in international registries. We report on currently observed prescription rates of antiplatelet agents and treatment with statins at time of admission within a multicenter registry upon cardiovascular risk factors in ACS patients.

Methods The Austrian ACS Survey for Cross Risk collected data on atherosclerosis risk factors, comorbidity, acute management and long term treatment in patients presenting with ACS in 38 medical centers in Austria. Documented coronary artery disease (CAD) consisted of 1 or more of the following criteria: stable angina with documented CAD, history of unstable angina, history of percutaneous coronary intervention, history of coronary artery bypass graft surgery or pervious myocardial infarction. Documented peripheral artery disease (PAD) was defined by current intermittent claudication or a history of intermittent claudication with previous angioplasty, stenting, peripheral arterial bypass graft or other intervention in-

Table 2: R. Steinacher et al. Patient Medical History and Treatment at Time of Presentation

	Overall n = 495	CAD n = 123 (24.8)	CVD n = 29 (5.9)	PAD n = 47 (9.5)	Diabetes plus Risk factors* n = 120 (24.2)
No Therapy	157 (31.7)	6 (4.9)	2 (6.9)	3 (6.3)	10 (8.3)
Antiplatelet Therapy					
– Acetylsalicylic Acid (%)	177 (35.8)	96 (78.0)	18 (62.1)	32 (66.7)	58 (48.3)
– Clopidogrel (%)	43 (8.7)	34 (27.6)	5 (17.2)	10 (20.8)	12 (10.0)
– Other Platelet Inhibitor (%)	6 (1.2)	2 (1.6)	1 (3.4)	1 (2.1)	3 (2.5)
– Dual Platelet Therapy (%)	38 (7.7)	30 (24.4)	3 (10.3)	9 (18.8)	12 (10.0)
VKA (%)	19 (3.8)	11 (8.9)	4 (13.8)	2 (4.2)	6 (5.0)
No VKA/Antiplatelet Therapy (%)	290 (58.6)	16 (13)	5 (17.2)	12 (25)	53 (44.2)
Statine (%)	145 (29.3)	75 (61.0)	16 (55.2)	23 (47.9)	57 (47.5)
Other lipid lowering agents (%)	17 (3.4)	11 (8.9)	1 (3.4)	6 (12.5)	8 (6.7)
LDL > 100 mg/dl untreated	268 (54.1)	37 (30.1)	8 (27.9)	18 (37.5)	41 (34.2)
LDL > 70 mg/dl untreated	325 (65.7)	43 (35.0)	10 (34.5)	24 (50.0)	53 (44.2)
– LDL > 100 mg/dl	– 343 (69.3)	– 70 (56.9)	– 14 (48.3)	– 31 (64.3)	– 71 (59.2)
– LDL 100–70 mg/dl	– 107 (21.6)	– 31 (25.2)	– 10 (34.5)	– 13 (27.1)	– 29 (24.2)
– LDL < 70 mg/dl	– 45 (9.1)	– 22 (17.9)	– 5 (17.2)	– 4 (8.3)	– 20 (16.7)
– HDL < 40 mg/dl	– 167 (33.7)	– 41 (33.3)	– 9 (31.0)	– 12 (25.0)	– 12 (10.0)
– HDL 40–60 mg/dl	– 260 (52.5)	– 65 (52.8)	– 16 (55.2)	– 28 (58.3)	– 60 (50.0)
– HDL > 60 mg/dl	– 68 (13.7)	– 17 (13.8)	– 4 (13.8)	– 8 (16.7)	– 48 (40)

* Risk factors include hypertension, hypercholesterolemia, current smoking, men aged 65 years or older, or women aged 70 years or older; CAD: coronary artery disease; CVD: cerebrovascular disease; PAD: peripheral artey disease; VKA: vitamin k antagonist; LDL: low density lipoprotein; HDL: high density lipoprotein

cluding amputation. Cerebrovascular disease (CVD) was defined as Carotid stenosis, a history of stroke or transient ischemic attacks. Cardiovascular risk factors were defined as diabetes, hypertension, hypercholesterolemia, current smoking, men aged 65 years or older, or women aged 70 years or older. Logistic regression was used for multivariable analysis.

Results A total of 495 ACS patients were enrolled for analysis. Mean age was 65.5 ± 13.2 years, 67.3% of patients were male; mean body mass index (BMI) was 27.2 ± 4.4 kg/m^2. Concerning relevant comorbidities 68.1% reported hypertension, 52.1% hypercholesterolemia, 24.2% diabetes, 11.5% renal insufficiency and 19.6% heart failure, respectively. A history of vascular disease was reported for a single arterial bed in 27.1% of patients, polyvascular disease in 6.3%. Prescription rates of antiplatelet therapy and statins are demonstrated in **Table 2**. A history of CAD, CVD, PAD or diabetes with additional risk factors was present in 218 individuals among whom 72 (33.0%) did not receive antiplatelet or VKA therapy. Multivariable predictors for receiving either antiplatelet or VKA therapy in the presence of overt vascular disease or diabetes with additional risk factors were older age ($p = 0.009$), a history of CAD ($p < 0.001$) and a history of PAD ($p = 0.031$). Diabetes with additional risk factors did not proof to be independently associated with use of either antiplatelet therapy or VKA in this setting.

Conclusion A substantial proportion of ACS patients present with a medical history warranting antiplatelet therapy and statin treatment. Our data suggests that in a significant proportion of patients presenting with ACS these substances were under-prescribed. To our opinion the problem exceeds compliance issues that may be reflected by low rates of patients that have refrained from all therapy. These data has to be discussed in respect to previously published reports on guideline adherence.

Diagnostic Relevance of Copeptin in Addition to High-Sensitivity Troponin I in Patients with Acute Chest Pain – Preliminary Results of the WILCOP-Registry I – 6

M. Tajsic, R. Jarai, J. Wojta, K. Huber
3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna; Department of Cardiology, Medical University of Vienna

Introduction Recent data suggest that combined measurement of copeptin and cardiac troponin T levels provides a reliable tool for early identification of patients with acute myocardial infarction. However, whether this holds true for the new high-sensitivity troponin assays is not known at present.

Material and Methods This is an ongoing prospective single-centre study of consecutive patients admitted to the emergency department (ED) of the Wilhelminenhospital with chest pain suggestive of acute coronary syndrome (ACS). The registry started in March 2011 and the present analysis reports the data of the first 577 consecutive patients. All patients had copeptin and hs-cTnI determinations at admission to the hospital. Copeptin concentrations were measured using a novel, commercially available, chemiluminescence assay (Copeptin Kryptor® developed by BRAHMS AG, Hennigsdorf, Germany).

Results Overall, 82/577 (14.2%) patients had the final diagnosis of ACS. Copeptin and hs-cTnI concentrations at admission were significantly higher among patients with proven ACS ($p < 0.001$; respectively). Accordingly, in all patients with ACS both biomarkers had good diagnostic accuracy, although c-statistics of hs-cTnI (AUC 0.918; 95%-CI) were significantly higher than that of copeptin (AUC 0.678; 95%-CI). At admission, 8/82 (12.5%) patients with ACS had hs-cTnI levels under the detection limit of the assay (0.017 ng/ml) and 15/82 (18.3%) patients had hs-cTnI within the reference range (≤ 0.056 ng/ml). This was the group of so-called

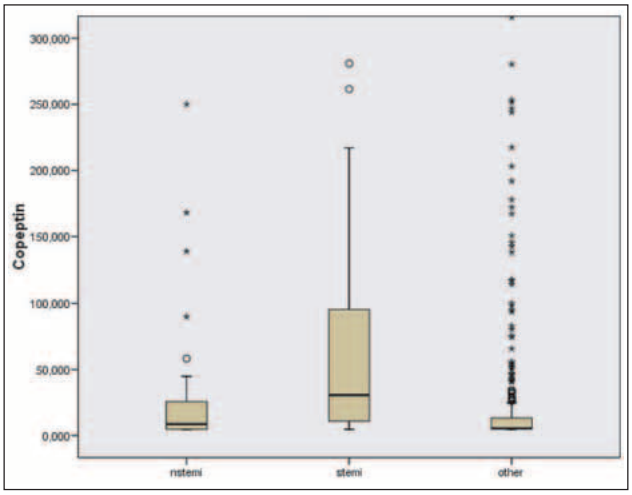


Figure 4: M. Tajsic et al.

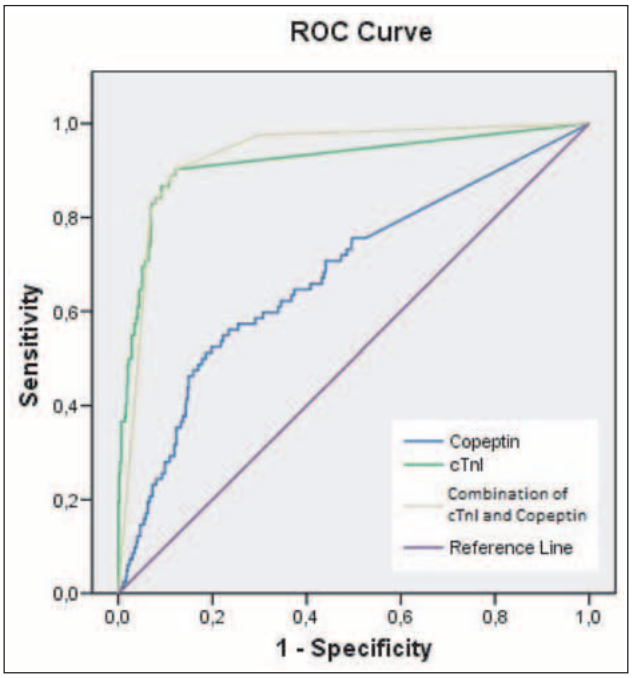


Figure 5: M. Tajsic et al.

'early presenters to ED'. In this 'early presenters' group with normal hs-cTnI concentrations, copeptin levels had good diagnostic accuracy for ACS (AUC 0.753; 95%-CI; $p = 0.001$) and in fact, more beneficial than c-statistics of hs-cTnI in the same patient group (AUC 0.704; 95%-CI; $p = 0.007$). However, among patients with already elevated levels of hs-cTnI at admission ('late presenters' group) copeptin had no diagnostic relevance (AUC 0.457; 95%-CI; $p = 0.06$). Overall, the combination of both markers resulted in an increase of diagnostic accuracy with an AUC of 0.932 (95%-CI; $p = 0.216$), compared to the c-statistics of hs-cTnI alone (AUC 0.918; 95%-CI).

Discussion Levels of hs-cTnI at admission to ED have excellent accuracy for early diagnosis of ACS. However, among the patients with initially normal hs-cTnI levels, presenting in ED in early hours after the onset of symptoms, there might be a significant diagnostic relevance of additional determination of copeptin levels, which could result in a rapid and reliable rule-out of ACS **(Figures 4, 5)**.

Akut-Koronarangiographien bei Migranten und Nicht-Migranten: Erste Ergebnisse einer prospektiven Vergleichsstudie I – 1

H. Ucar-Altenberger, D. Gündüz, E. Mulaomerovic, C. Stöllberger, W.-B. Winkler, M. Avanzini, Ch. Wegner, E. Sekulin, F. Weidinger
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Einleitung Bei Akut-Koronarangiographien ist eine Häufung junger Patienten mit Migrationshintergrund aufgefallen. Eine retrospektive Analyse hat gezeigt, dass keine Unterschiede in der Häufigkeit klassischer Risikofaktoren zwischen Migranten und Nicht-Migranten vorliegen. Dieses Phänomen weist auf ein höheres Risiko von Migranten hin, das seit November 2011 mittels einer prospektiven Studie untersucht wird. Wir berichten über die ersten Ergebnisse dieser Untersuchung.

Methode Eingeschlossen wurden konsekutive Patienten, die seit September 2011 an unserer Abteilung wegen eines akuten Koronarsyndroms akut koronarangiographiert wurden. Während des Krankenhausaufenthaltes wurden Alter, Geschlecht, Koronarangiographie-Befund, klassische Risikofaktoren und ethnische Herkunft erhoben. Als „Migranten" wurden Patienten definiert, deren Geburtsort außerhalb Österreichs lag.

Ergebnis Bisher haben wir 54 Patienten (26 % weiblich) mit einem mittleren Alter von 59 Jahren eingeschlossen. Die Koronarangiographie zeigte eine Eingefäßerkrankung bei 27 %, eine Zweigefäßerkrankung bei 24 %, eine Drei- oder Mehrgefäßerkrankung bei 41 % und keine Koronarstenosen bei 7 %. Hypertonie fand sich bei 83 %, Hypercholesterinämie bei 85 %, Nikotinkonsum bei 37 % und Diabetes mellitus bei 24 %. 23 Patienten (43 %) waren Migranten: 14 kamen aus dem ehemaligen Jugoslawien, 4 aus Nordosteuropa, 2 aus Zentraleuropa und je einer aus der Türkei, aus Bangladesh und aus Uruguay. Migranten waren jünger als Nicht-Migranten (55 vs. 61 Jahre; $p < 0,05$), waren häufiger Raucher (52 vs. 26 %; $p < 0,05$) und hatten tendenziell häufiger Hypertonie (91 vs. 77 %). Keine Unterschiede zwischen Migranten und Nicht-Migranten gab es bei Hypercholesterinämie (86 vs. 83 %), Diabetes mellitus (26 vs. 23 %) und in der Geschlechtsverteilung (Frauenanteil: Migranten 22 % vs. Österreicher 29 %). Sowohl eine koronare Eingefäßerkrankung als auch eine Zweigefäßerkrankung fand sich bei Österreichern etwas häufiger als bei Migranten (35 vs. 17 % bzw. 25 vs. 21 %) und eine Drei- oder Mehrgefäßerkrankung hatten mehr Migranten als Österreicher (52 vs. 32 %).

Schlussfolgerung Migranten, die akut koronarangiographiert werden, sind jünger als Nicht-Migranten, leiden häufiger unter koronarer Drei- oder Mehrgefäßerkrankung, unterscheiden sich aber wenig in Hinblick auf klassische Risikofaktoren, außer Nikotinkonsum. Dieses Phänomen weist auf ein höheres, möglicherweise genetisches Risiko von Migranten hin.

Patienten mit akutem Myokardinfarkt an der Universitätsklinik für Notfallmedizin – Jahresrückblick 2011 XI – 3

R. van Tulder, D. Roth, B. Heidinger, Ch. Havel, H. Herkner, W. Schreiber
Universitätsklinik für Notfallmedizin, Medizinische Universität Wien

Einleitung Die Universitätsklinik für Notfallmedizin (NFA) am Allgemeinen Krankenhaus Wien (AKH) versorgt gemeinsam mit der Universitätsklinik für Kardiologie die Patienten mit akutem Myokardinfarkt (MCI). Im Rahmen des ST-Elevation-Myocardial-Infarction (STEMI-) Netzwerkes Wien ist das Katheterlabor der Universitätsklinik für Kardiologie primärer Anlaufpunkt an Wochenenden und Feiertagen. Zusätzlich kann während der Kernarbeitszeit die NFA auf Anfrage angefahren werden. Für selbstkommende Patienten besteht ein Interventionsdienst in Rufbereitschaft.

Methoden Zur retrospektiven und deskriptiven Darstellung kommen im Folgenden prospektiv gesammelte Daten aller MCI-Patienten, die im Jahr 2011 an der NFA vorstellig wurden. Die Registrierung patientenbezogener und medizinischer Daten erfolgt logisch und physikalisch streng getrennt. Entsprechend den Cardiology Audit and Registration Data Standards (CARDS) der European Society of Cardiology (ESC) werden demographische Daten, Risikofaktoren, kardiovaskuläre Anamnese und Heimtherapie, klinische Präsentation und EKG, präklinische Therapie, Laborparameter, klinische Therapie und eventuelle Komplikationen sowie die Ergebnisse der Herzkatheteruntersuchung falls durchgeführt, gesammelt.

Ergebnisse (Tabelle 3, Abbildungen 6–12) Im Jahr 2011 wurden insgesamt 615 Patienten mit MCI an der NFA versorgt. Das Alter der Patienten lag bei einem Mean von 63 ± 14 Jahren. Nur 32 % waren weiblich (siehe demographische Information). In 75 % war die NFA die primäre Anlaufstelle für die Patienten. Die 326 (53 %) STEMIs wurden in 88 % durch den Rettungsdienst hospitalisiert. 4 % der STEMIs wurden präklinisch und 1 % innerklinisch lysiert. In 83 % wurde eine primäre perkutane Koronarintervention (PCI) durchgeführt. In 11 % der STEMIs wurde keine primäre Reperfusion angestrebt. 49 % zeigten eine Vorderwandischämie, in 46 % war die Hinterwand betroffen.

Die 274 (45 %) Non-ST-Myocardial Infarctions (NSTEMI) wurden zu 69 % durch den Rettungsdienst hospitalisiert. 45 % wurden über die NFA einem Herzkatheter zugeführt. In 2 % der MCIs konnte retrospektiv keine Zuteilung mehr in STEMI/ NSTEMI vorgenommen werden.

Zu innerklinischen Reanimationsmaßnahmen an der NFA kam es in 6 % der Fälle. Hierfür waren in 80 % Kammerflimmern oder eine

Tabelle 3: R. van Tulder et al. Demographische Daten und Risikofaktoren

Alter	63 ± 14	Weiblich	32,4 %
Diabetes mellitus	20,6 %	Body-mass-Index	27,5 ± 4,8
Hyperlipidämie	25,4 %	Anamnestisch MCI	18,7 %
Nikotinabusus	29,6 %	Anamnestisch PCI	18,7 %
Hypertonie	50,0 %	Anamnestisch CABG	5,2 %

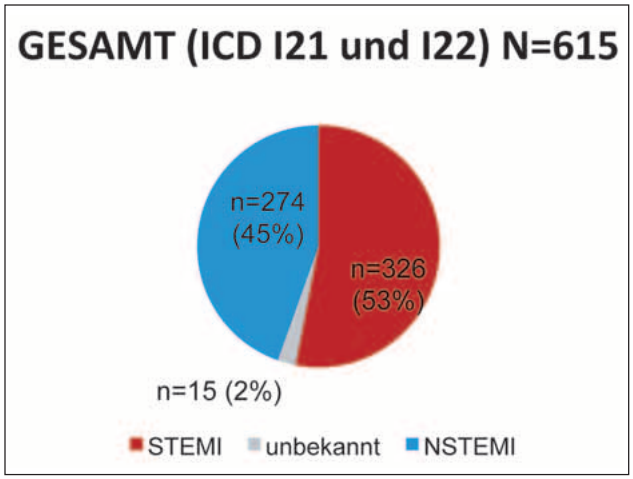


Abbildung 6: R. van Tulder et al.

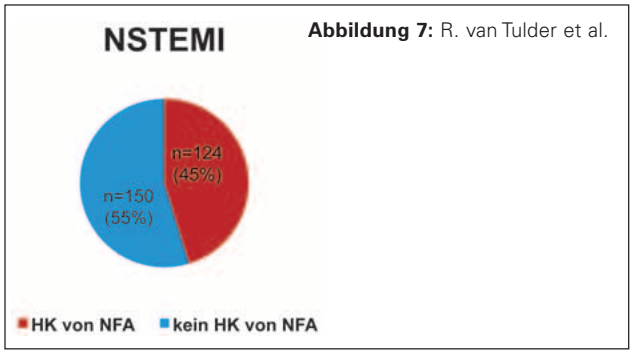


Abbildung 7: R. van Tulder et al.

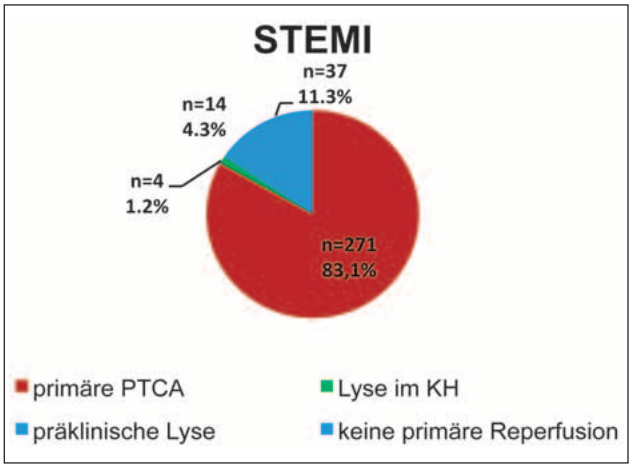


Abbildung 8: R. van Tulder et al.

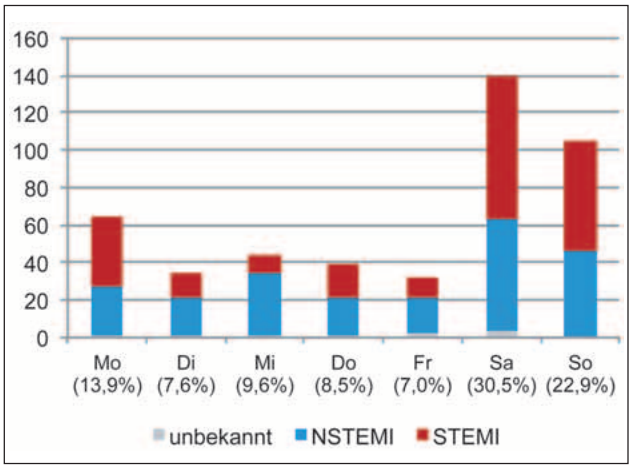


Abbildung 9: R. van Tulder et al.

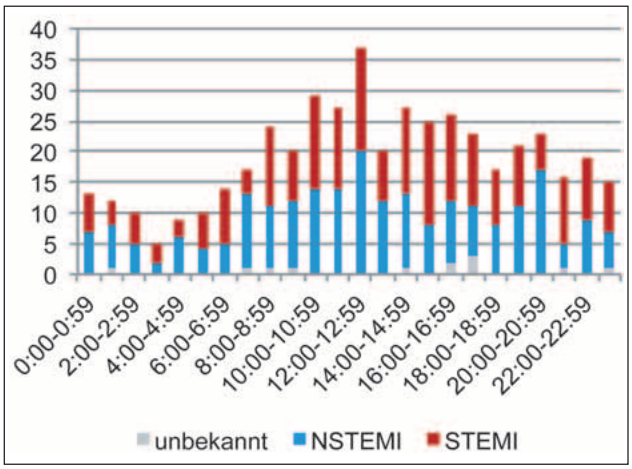


Abbildung 10: R. van Tulder et al.

ventrikuläre Tachykardie ursächlich. Die Gesamtmortalität an der NFA betrug für das Jahr 2011 2 %.

Zusammenfassung Im Jahr 2011 wurden 615 MCIs an der NFA versorgt. Das entspricht einem Zuwachs von 0,5 % im Vergleich zum Vorjahr. 53 % waren STEMIs. Insgesamt wurden 89 % einer primären Reperfusion zugeführt. Die Gesamtmortalität für den Aufenthalt an der NFA betrug für das Jahr 2011 2%.

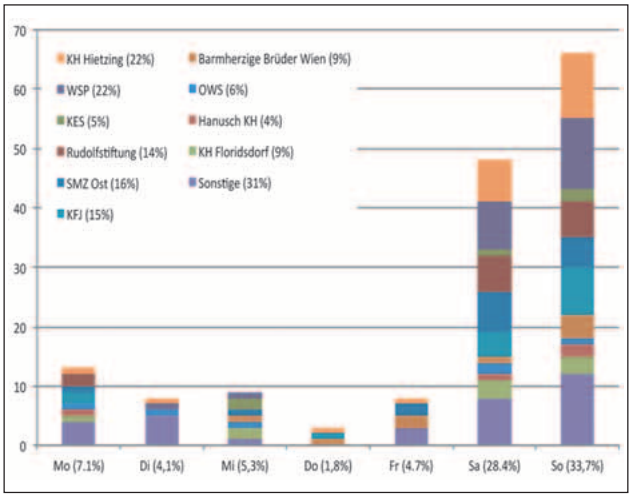


Abbildung 11: R. van Tulder et al.

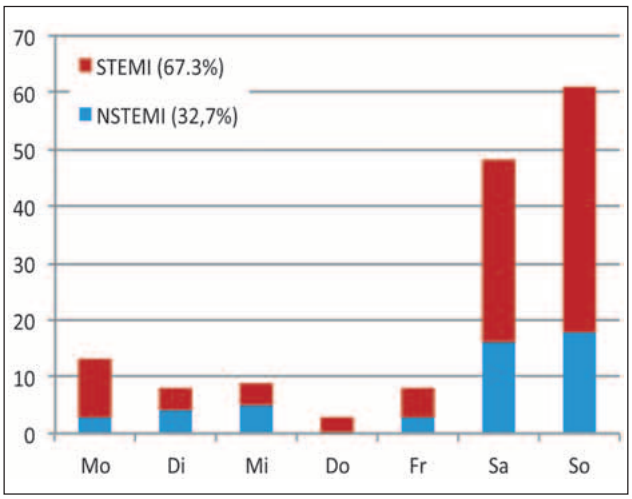


Abbildung 12: R. van Tulder et al.

Lipid Parameters in Acute Coronary Syndromes versus Stable Coronary Artery Disease in Subjects With and Without Metabolic Syndrome XI – 6

A. Vonbank, Ch. H. Saely, Ph. Rein, H. Drexel
Innere Medizin, Landeskrankenhaus Feldkirch

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

Methods We enrolled 582 patients with angiographically proven stable CAD (of whom 37.2% had the diagnosis of the MetS according to NCEP-ATPIII criteria and 182 patients with acute coronary syndromes (of whom 33.9% had MetS according to NCEP ATPIII criteria).

Results When compared to patients with stable CAD, HDL cholesterol and apolipoprotein A1 were significantly lower in patients with acute coronary syndromes among subjects with the MetS (38 ± 9 mg/dl vs 48 ± 13 mg/dl; $p < 0.001$ and 139 ± 30 mg/dl vs 14 ± 25 mg/dl; $p < 0.001$, respectively) as well as among subjects without the MetS (52.4 ± 17 mg/dl vs 60.3 ± 15 mg/dl; $p = 0.001$ and 147.3 ± 31 mg/dl vs 157.2 ± 26 mg/dl; $p = 0.003$, respectively). Analysis of covariance (ANCOVA) adjusting for age, gender, smoking, BMI, and hypertension confirmed an independent impact of the acute coronary syndrome state on these lipid parameters both among patients with the MetS and among subjects without MetS.

Total cholesterol, LDL cholesterol and apolipoprotein B neither in subjects with the MetS (182 ± 41 mg/dl vs 197 ± 48 mg/dl; p = 0.583 vs 120 ± 43 mg/dl vs 130 ± 42 mg/dl; p = 0.884 and 84 ± 23 mg/dl vs 83 ± 24 mg/dl; p = 0.834 respectively) nor among subjects without MetS (191 ± 50 mg/dl vs 193 ± 47 mg/dl; p = 0.583 vs 124 ± 42 mg/dl vs 124 ± 45 mg/dl; p = 0.884 and 84 ± 23 mg/dl vs 83 ± 24 mg/dl; p = 0.834 respectively), differed significantly between acute coronary syndromes and stable CAD patients. Furthermore, there were no significant differences in triglycerides between patients with acute coronary syndromes and patients with stable CAD, neither among subjects with the MetS (187 ± 85 mg/dl vs 184 ± 99 mg/dl; p = 0.160) nor among subjects without the MetS (114 ± 49 mg/dl vs 111 ± 67 mg/dl; p = 0.891).

Conclusion Both among patients with the MetS and among non-MetS individuals, HDL cholesterol and apolipoprotein A1 are lower in the acute coronary syndrome state than with stable CAD.

Impact of Endothelin-A Receptor Blockade on Neutrophil Activation in Patients with ST-Elevation Acute Coronary Syndrome I – 7

R. Wurm, Ch. Adlbrecht, I. Lang
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

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

Methods Patients with posterior-wall STE-ACS were randomly assigned to receive intravenous BQ-123 at 400 nmol/minute or placebo over 60 minutes, starting immediately prior to primary percutaneous coronary intervention (PCI, n = 54). Peripheral blood samples were drawn upon arrival in the catheterization laboratory (baseline) and at 24 hours after PCI. Myeloperoxidase (MPO), a marker of neutrophil activation, was measured in plasma using a commercially available ELISA assay (eBioscience, San Diego, CA, USA).

Results MPO levels at 24 hours after PCI of patients randomized to the placebo group were significantly correlated with the time from symptom onset to first balloon inflation (r = 0.455; p = 0.023), the number of affected myocardial segments assessed by magnetic resonance imaging (r = 0.572; p = 0.005) and the myocardial blush grade at the end of PCI (r = –0.524; p = 0.006). Patients randomized to receive BQ-123 demonstrated a greater reduction of MPO levels compared to placebo-treated patients (177 ng/mL reduction [IQR 103–274] for BQ-123 vs 108 ng/mL [74–147] for placebo, p = 0.006; **Figure 13**).

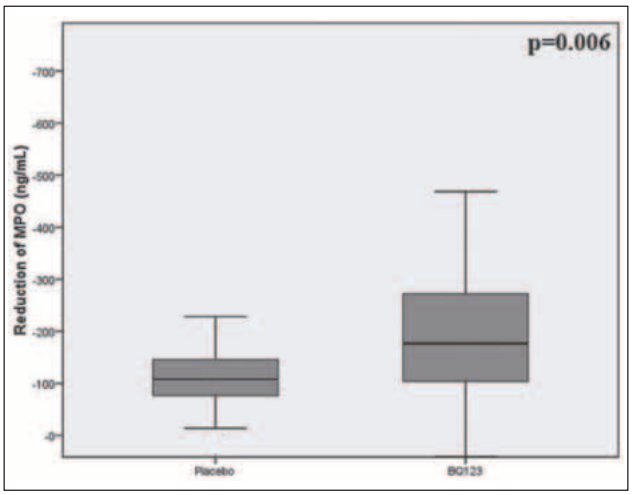


Figure 13: R. Wurm et al. Reduction of myeloperoxidase (MPO) plasma levels over the first 24 hours after percutaneous coronary intervention in patients with STE-ACS receiving an endothelin A receptor antagonist (BQ-123) or placebo.

Conclusion Short-term administration of BQ-123 reduces MPO plasma levels and possibly neutrophil activation in patients with STE-ACS. In trials with larger patient numbers this observation may translate into improved blush grade and smaller infarct size.

Basic Science

MMP-9 Released Angiogenesis Inhibitors Prevent Adaptive Capillary Growth in Hypertrophy and Contribute to Progression to Heart Failure XII – 5

K. Ablasser, A. Nikolova, P. del Nido, F. Fruhwald, B. Pieske, R. Gasser, I. Friehs
Klinische Abteilung für Kardiologie, Medizinische Universität Graz; Children's Hospital, Harvard Medical School, Boston, USA

Purpose In left ventricular pressure-overload hypertrophy, lack of adaptive capillary growth contributes to progression to heart failure. Remodeling of the hypertrophied myocardium requires proteolysis of extracellular matrix (ECM) carried out by matrix metalloproteinases (MMPs). MMPs, specifically MMP-9, are known to cleave ECM components which generate angiogenesis inhibitors (angiostatin, endostatin, tumstatin). We hypothesized that MMP-9 released anti-angiogenic factors during compensated hypertrophy, which resulted in lack of adaptive capillary growth and progression to heart failure.

Methods Newborn rabbits underwent aortic banding. At compensated hypertrophy (4 weeks) and systolic heart failure (7 weeks) myocardial tissue from banded and sham operated control animals was analyzed by immunoblotting for angiostatin, endostatin and tumstatin. MMP-9 activity was determined by zymography. A MMP-9 specific inhibitor (N- ([1,1-biphenyl]-4-ylsulfonyl)-D-phenylalanine) was administered intrapericardially to hypertrophied animals and tissue was analyzed by immunoblotting and zymography as stated above. Rabbit were followed by weekly echocardiography to determine mass/volume ratio and fractional shortening.

Results MMP-9 was activated in hypertrophied myocardium vs controls (23 ± 1 vs 17 ± 1; p = 0.04), which resulted in significantly increased levels of angiostatin (86 ± 7 vs 115 ± 10; p = 0.03), endostatin (28 ± 1 vs 33 ± 1; p = 0.02) and tumstatin (17 ± 4 vs 35 ± 6; p = 0.03). Zymography confirmed inhibition of MMP-9 (hypertrophy: 17 ± 1 vs hypertrophy+MMP-9 inhibitor: 14 ± 0.6; p = 0.01) and angiostatin, endostatin and tumstatin were down-regulated, accompanied by up-regulation of capillary density (hypertrophy: 2.99 ± 0.07 vs hypertrophy+MMP-9 inhibitor: 2.7 ± 0.05; p = 0.002). Mass/volume ratio by echocardiography, as a measure of hypertrophy, showed a significant increase in the banded group vs the sham group at week 4 (40.84 ± 0.08 vs 1,02 ± 0.04; p < 0.05), but declined significantly when the hearts dilated and went into systolic heart failure in week 7 (0.88 ± 0.04 vs 0.77 ± 0.05; p < 0.05). Inhibition of MMP-9 prevented the dilation of the left ventricle and, as confirmed by echocardiographic measurements of fractional shortening, prevented systolic heart failure after 7 weeks.

Conclusions Remodeling resulted in activation of MMP-9 which enhanced the release of angiogenesis inhibitors, angiostatin, endostatin and tumstatin. Up-regulation of angiogenesis inhibitors prevented adaptive capillary growth in pressure-overload hypertrophied myocardium. Therapeutic interventions aimed at inhibition of angiogenesis inhibitors were useful in maintaining capillary density and thereby preventing heart failure.

Influence of MicroRNA-223 Deficiency in Myocardial Ischemia-Reperfusion Injury III – 3

K. Bader, K. Streil, M. Reiner, B. Haubner, S. Leierseder, St. Engelhardt, O. Pachinger, B. Metzler
Klinische Abteilung für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck, Österreich; TU München, Deutschland

Introduction MicroRNA-223 (miR-223) is a specific microRNA which acts as a negative modulator of neutrophil activation and degradation. As upregulation of neutrophil activation is associated with increased inflammatory response, we aim to investigate the contribution of miR-223 in the regulation of neutrophil infiltration in the myocardial infarct zone following myocardial ischemia-reperfusion injury. To our knowledge, no in vivo ischemia/reperfusion model has been applied to study the detailed role of miR-223.

Material and Methods MiR-223 knockout (KO) and control wild type (WT) mice were subjected to experimental myocardial ischemia and reperfusion (m I/R). For histological evaluation of cardiac tissue damage paraffin embedded heart sections were stained with Haematoxylin and Eosin. Blood of all animals were collected from the renal vein for measurement of plasma levels of Troponin T, a marker of cardiac cellular damage. Total RNA was extracted from the area at risk (AAR) and the remote zone, respectively, and RNA quantification of TNF-alpha and IL-6 was performed by real-time PCR.

Results After 30 min ischemia and 48 h reperfusion, serum Troponin T levels were significantly increased (3306 vs 1024 pg/ml, p = 0.001, n = 9) in miR-223 KO rodents compared to WT mice. Histological analysis showed that ischemia-reperfusion resulted in marked myocardial injury in all groups of animals, but the cardiac damage was more severe in miR-223-deficient mice after 48 h of reperfusion following 30 min of ischemia. Furthermore, serum Troponin T levels were significantly increased (5476.0 vs 3250.5 pg/ml, p = 0.017, n = 9) in miR-223 KO rodents compared to WT mice after 3 h of reperfusion following 30 minutes of ischemia. Quantitative RT-PCR analysis revealed that gene expression of TNF-alpha and IL-6 was significantly higher (both, $p \leq 0.05$) in the AAR compared to the remote zone.

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

Continued Ventilation During Open Heart Surgery Attenuates Inflammatory Response II – 4

L. Beer, Th. Sezerafin, A. Mitterbauer, P. Altmann, Th. Haider, B. Seinlechner, M. Dworschak, G. Lang, W. Klepetko, H. J. Ankersmit
Universitätsklinik für Chirurgie, Abteilung für Thoraxchirurgie; Universitätsklinik für Anästhesie, Medizinische Universität Wien, Österreich; University of Debrecen, Hungary

Background Cardiopulmonary bypass, utilized in on-pump coronary artery bypass graft procedure (CABG) is known to affect cytokine release leading to a generalized endogenous immune suppression and the release of inflammation markers. We investigated whether continued ventilation on cardiopulmonary bypass induces attenuation of immune response.

Material and Methods 30 patients undergoing conventional CABG operation were randomized into a ventilated on CPB (VG) and non-ventilated (NVG) group. Venous blood was drawn preoperative, postoperative and 24, 48, 72, 96 and 120 hours after initiation of CABG operation. sST2, IL-4, IL-10, IL-13, MIP-1beta, MCP-1, Endotoxin, IgM, and IgG were measured by ELISA. An unpaired t-test or Mann-Whitney-U-test was used for statistical analysis.

Results Serum levels of sST2 increased within 24 hrs after NVG-CABG procedure. sST2 levels were significantly lower in VG group (1366.4 ± 111.9 vs 2296.3 ± 463.6 pg/ml; p = 0.033) at 24 hrs. Endotoxin levels correlated with sST2 levels (24 hrs post CABG, r = 0.723, p < 0.0001), whereas no correlation between endotoxin and IL-10 concentration was found. The mean MIP-1beta levels (pg/ml) measured 24, 48, 72 hours after CABG were significantly

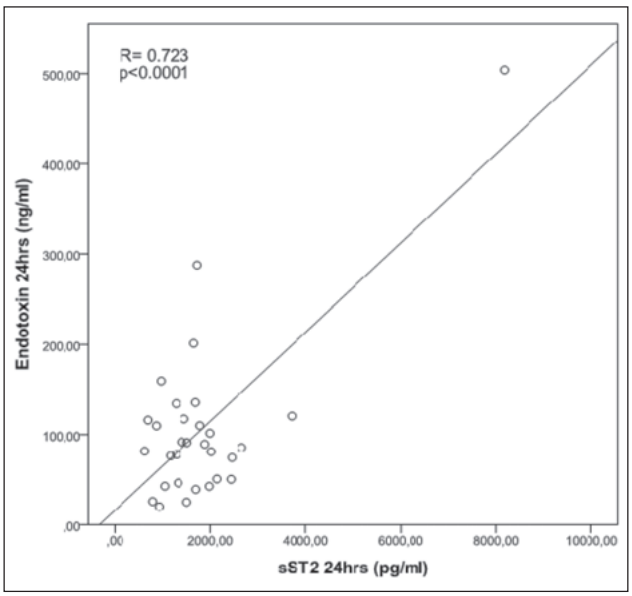


Figure 14: L. Beer et al.

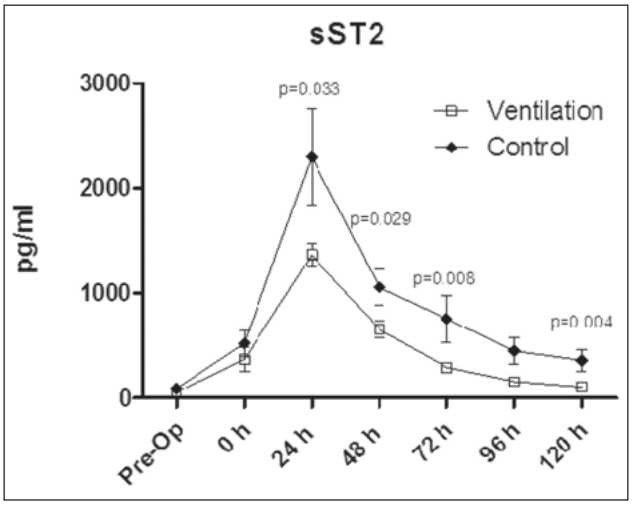


Figure 15: L. Beer et al.

lower in VG: 10.9 ± 10.0 vs 153.2 ± 153.2; p = 0.005, 16.7 ± 9.5 vs 147.9 ± 42.7 p = 0.019 and 14.2 ± 6.2 vs 97.8 ± 22.5; p = 0.005 compared to VG. NVG patients showed significantly higher MCP-1 concentration after CPB compared to VG (72 hrs, 96 hrs, 120 hrs; p < 0.05). Moreover, IL-10 levels were significantly lower in the VG as compared to NVG (10.5 ± 1.0 vs 15.3 ± 1.7 pg/ml; 24 hrs post CABG; p = 0.038). IL-13, IL-4, IgM and IgG showed now difference between the 2 groups.

Conclusion Continued lung ventilation during CABG results in a significant reduction of sST2 and IL-10 24 hours after surgery and attenuates macrophage chemotactic and inflammatory response **(Figures 14, 15)**.

LQTS Associated Caveolin-3 Mutations Differentially Regulate the Hyperpolarization-Activated Cyclic Nucleotide Gated Channel 4 II – 7

T. Darabi, D. Rottlaender, L. J. Motloch, M. Wolny, R. Larbig, S. Reda, U. C. Hoppe
Department of Internal Medicine II, Paracelsus Medical University, Salzburg, Austria; Center for Molecular Medicine, University of Cologne, Germany

Background The congenital long-QT syndrome (LQTS) is an inherited arrhythmogenic disorder. In some patients with LQTS muta-

tions of CAV3-encoded caveolin-3 were identified. In heterologeous expression these mutants increased the late sodium current. Carries of CAV3 mutants present with distinct clinical symptoms and ECG abnormalities, i. e. the CAV3 mutant T78M can be correlated to nonexertional syncope and sinus bradycardia, A85T to cardiac arrest in sleep, F97C to shortness of breath and chest pain, and S141R to nonexertional syncope. Hyperpolarization-activated cyclic nucleotide gated (HCN) channels underlie the If current and play a central role in cardiac pacemaker activity. HCN4 is known to associate with caveolin-3 to form a macromolecular complex.

Objectives To examine the effects of human LQTS-associated caveolin-3 mutations on HCN4 ion channel function and possibly indentify a link to clinical symptoms such as bradycardia.

Methods HEK293-cells were co-transfected with HCN4, and wildtype caveolin-3, a LQTS-associated CAV3 mutant (T78M, A85T, S141R or F97C) or an empty control plasmid, respectively. HCN4 currents were recorded by hyperpolarization steps from –40 mV to –170 mV for 5 seconds using the whole-cell patch-clamp technique.

Results Wildtype caveolin-3 significantly decreased HCN4 current density (–6.3 ± 1.5 pA/pF at –130 mV, n = 11) vs HCN4 alone (–20.61 ± 1.71 pA/pF, n = 10). Compared to wildtype caveolin-3 the different human LQTS-associated CAV3 mutants displayed distinct effects on HCN4 current properties. While the T78M mutation (–5.8 ± 0.9 pA/pF, n = 8) did not alter the caveolin-3 effect on HCN4 current size, the other CAV3 mutations to a various extend undermined the diminishing action of caveolin-3 on HCN4 current density (A85T –13.7 ± 2.4 pA/pF, n = 10; S141R –35.0 ± 10.4 pA/pF, n = 9; F97C –15.5 ± 3.5 pA/pF, n = 8). Moreover, the CAV3 mutants differentially modified activation kinetics of HCN4. While caveolin-3 alone had only a minor effect on HCN4 current activation (tau at –130 mV 2478 ± 441 ms and 2948 ± 355 ms without and with caveolin-3, respectively), LQTS-associated CAV3 mutants accelerated HCN4 current activation (tau at –130 mV: T78M 1653 ± 280 ms; A85T 1450 ± 339 ms; S141R 1119 ± 55 ms; F97C 1176 ± 484 ms).

Conclusions Our results indicate that HCN4 channel function is modulated by caveolin-3. LQTS-associated mutations of caveolin-3 may differentially influence pacemaker current properties, which might play a pathophysiological role in clinical manifestations of the disease.

Gene Expression of 1SLC8A1 (Solute Carrier Family 8, Member 16 – NCX1) is not Regulated During Experimental Myocardial Ischemia, but Regulation can be Elicited by Cardioprotective Drugs III – 2

R. Gasser, S. Pätzold, E. Holzwart, H. Mächler
Department of Internal Medicine, Medical University Graz

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 depolarization. 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 4)**.

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 beta-blockers, there is no significant regulation of NCX1-expression during myocardial ischemia. There is, however, a significant difference between the expression of NCX1 during 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.

Table 4: R. Gasser et al.

	N_2-Hypoxia	
	Nebivolol : Control	**Atenolol : Control**
NCX1	0.33	0.51
NCX3	5.66	3.21
	O_2-Normoxia	
	Nebivolol : Control	**Atenolol : Control**
NCX1	0.28	0.83
NCX3	5.5	3.72

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

Percutaneous Intramyocardial Delivery of Secretome of Apoptotic White Blood Cells (APOSEC) Improves Myocardial Viability and Left Ventricular Function in Experimental Ischemic Cardiomyopathy XII – 6

M. Gyöngyösi, M. Zimmermann, N. Pavo, M. Lichtenauer, G. Maurer, H. J. Ankersmit
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background Despite promising preclinical and clinical results of the cell-based therapy in chronic ischemic heart failure, the achievable benefit still remains suboptimal. We have previously shown the regenerative capacity of the secretome of the apoptotic white blood cells (APOSEC, containing a mixture of regenerative paracrine factors, such as cytokines and growth factors) in acute myocardial infarction (AMI).

Purpose In the present experiment we have investigated the effect of APOSEC on the ventricular function and myocardial ischemia in experimental ischemic cardiomyopathy.

Methods Porcine APOSEC was produced by collecting peripheral white blood cells (WBCs), followed by apoptosis induction via Caesium-137 irradiation and incubation for 24 h. Supernatants were frozen and lyophilized. Closed chest reperfused AMI was induced by 90-min occlusion of the mid LAD in 14 domestic pigs, followed by baseline cardiac magnet resonance imaging (MRI) with late enhancement (LE) at day 3. One moth later (day 30), the animals were randomized and received either porcine APOSEC (resuspended supernatant of totally 11.5× 10^12 irradiated apoptotic WBCs) (n = 7) or Medium (cell culture medium) (n = 7) using the 3D NOGA percutaneous intramyocardial injection technique in the periinfarction areas (10–13 treatment points). After 1-month follow-up (FUP) (day 60), control cardiac MRI+LE and measurements of myocardial viability via diagnostic electroanatomical mapping were performed. Gene expression of the infarction border zone and the necrotic areas were evaluated and *post hoc* validation of genes identified by microarray was performed by using quantitative real-time polymerase chain reaction (PCR).

Results APOSEC led to an improvement of left ventricular ejection fraction (45 ± 6% vs 38 ± 9%), cardiac output, cardiac index (4.1 ± 0.4 vs 3.32 ± 0.3 L/min) and to decrease in infarct size (14 ± 4% vs 20 ± 5%) ($p < 0.05$). FUP NOGA mapping revealed an increase in myocardial viability in the injected myocardial area (10.1 ± 3.0 mV vs 8.7 ± 7.1 mV; $p < 0.05$). Gene profiling analysis revealed robust significant upregulation of stem cell homing (cadherin, CXCR4 and stromal-derived factor-1) and some angiogenic factors (such as cathepsin) and myogenic genes expressing myosin and actin in the injected areas of the APOSEC, as compared with the Medium group. The angiogenic growth factor gene expression (vascular endothelial, fibroblast or insulin-like growth factor) was similar in both groups (probably due to the open infarct-related artery in both groups confirmed by FUP angiography). In the infarcted area, gene expression of troponin, myosin and actin were significantly elevated in APOSEC group, as compared with the Medium group, suggesting a regenerative process in the ischemic injured myocardium.

Conclusion "Cell-less cell therapy" proved to be effective in improvement of experimental chronic myocardial ischemia and left ventricular dysfunction, leading to a significant overexpression of myogenic and stem cell homing genes, therefore might be a promising tool in treatment of ischemic cardiomyopathy. The observed effect might be attributed to the much higher concentration of the locally acting paracrine factors as compared to that of the cell-based myocardial regenerative therapies.

Complete Cardiac Regeneration in a Mouse Model of Myocardial Infarction XII – 4

B. J. Haubner, B. Metzler, J. Penninger
IMBA Penninger Lab Innsbruck, Universitätsklinik für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck

Background Cardiac remodeling and subsequent heart failure remains a critical issue after myocardial infarction despite improved treatment and reperfusion strategies. Recently, it has been demonstrated that newborn mice retain the capacity of cardiac regeneration in an apical resection model. However, the regeneration potential of newborn hearts following myocardial infarction leading to a complex cardiac injury needs to be addressed.

Methods We established a protocol for left anterior descending artery (LAD) ligation in one-day-old mice. Using hypothermia anesthesia, the LAD was irreversibly ligated and subsequent tissue remodeling and regeneration were assessed using serial histological sectioning of the hearts combined with hematoxylin eosin (HE), Masson trichrome, immunohistochemical staining, and lineage tracking.

Results Following 24 hours of LAD ligation we found massive cardiac injury in the left ventricle. Immunohistochemical analysis demonstrated cleaved caspase 3 positive cells in the border zone of the area of infarction, confirming massive cell death. Ischemia-induced cardiomyocyte death translated in a visible area of infarction at day 4 after LAD ligation. Amazingly, hearts harvested more than 7 days of LAD ligation displayed complete regeneration and we failed to observe any obvious signs of tissue damage or scarring. Moreover, tissue regeneration translated into normal and long-term heart function as assessed by echocardiography. In contrast, LAD ligations in 7-day-old mice resulted in extensive scarring comparable to adult mice, indicating that the regenerative capacity for complete cardiac healing after heart attacks can be traced to the first week after birth.

Conclusion Here, we present for the first time a mammalian model of complete cardiac regeneration following irreversible LAD ligation. This model system provides the unique opportunity to uncover molecular and cellular pathways that can induce cardiac regeneration after ischemic injury, findings that one day could be translated to human heart attack patients.

Mitogen-Activated Protein Kinase Kinase 7 (MKK7) Couples Myocardial Ischemia/Reperfusion Stress to Necro(pto)tic Cell Death BAII

B. J. Haubner, M. Reiner, K. Streil, K. Bader, J. Voelkl, I. Kozierdazki, O. Pachinger, J. Penninger, B. Metzler
IMBA Penninger Lab Innsbruck, Universitätsklinik für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck

Background Apoptosis has long been considered the sole form of programmed cell death during development and disease. Lately, necroptosis has been implemented as a novel mode of necrotic cell death that is executed in a regulated manner. We have previously demonstrated the benefit of muscle-restricted loss of MKK7 during myocardial ischemia and reperfusion (mI/R). However, the form of cell death that is regulated by MKK7 upon mI/R is largely unknown.

Methods Therefore, we subjected muscle-restricted MKK7 knockout (MKK7fl/fl;Mck Cre, termed MKK7MKO hereafter) compared to MKK7 control (MKK7fl/fl) mice to experimental mI/R and analyzed the cardiac samples using electron microscopy (EM) and immunohistochemistry. In addition, immunoblotting was utilized in order to monitor the kinetics of MKK7 activation.

Results After 30 minutes of ischemia and 24 hours of reperfusion, MKK7fl/fl cardiac EM samples displayed large areas of damaged cardiomyocytes with a typical necrotic phenotype, including rupture of the plasma membrane and an increasingly translucent cytoplasm. In contrast, MKK7MKO EM specimen showed hardly any damaged cells within the area at risk. Typical ultrastructural characteristics found in MKK7MKO cardiomyocytes were changes of single mitochondria, previously described in the borderzone of the infarcted area. Furthermore, immunohistochemical stainings and immunoblotting for cleaved caspase 3 revealed the caspase independent cell death in our model.

Finally, c-Jun NH2-terminal protein kinase (JNK) phosphorylation, as a marker of MKK7 activity, was significantly increased in the MKK7fl/fl mice after 30 minutes of ischemia and 20 minutes of reperfusion. This mI/R stress induced JNK activation is completely lost in the MKK7MKO animals.

Conclusion Here, we demonstrate that in vivo mI/R leads to a caspase independent type of cell death with ultrastructural characteristics of necrosis. Moreover, this form of tissue injury can be experimentally regulated via the conditional knock-out of MKK7.

Recruitment and Migration of Endothelial Progenitor Cells Induced by Low Energy Shock Wave Treatment XII – 7

J. Holfeld, W. Mathes, C. Tepeköylü, K. Albrecht-Schgör, R. Kirchmair, M. Grimm
Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck

Background Shock wave therapy (SWT) was shown to enhance the recruitment of endothelial progenitor cells (EPCs) in chronic hind limb ischemia in rats. This mechanism is crucial for vasculogenesis in ischemic myocardium.

Methods The lower compartment of a transwell was filled with supernatant of hypoxic SWT treated or untreated cardiomyocytes and endothelial cells. The upper compartment was filled with EPCs. Migrated cells within the membran were stained and counted by fluorescence microscopy. ELISA of supernatant was performed for several kinds of growth factors and chemokines to detect chemotactical signals for cell recruitment.

Results Significantly higher numbers of endothelial cells were found in the lower compartment of the treatment group. Hypoxic endothelial cells secreted numerous chemokines and growth factors as stimuli for cell recruitment and homing.

Discussion SWT stimulates hypoxic endothelial cells to recruit endothelial progenitors for vasculogenesis in ischemic myocardium.

Shock Wave Treatment Enhances the Differentiation of Monocytes into M2 Macrophages Which are Crucial for Angiogenesis in Ischemic Myocardium XII – 8

J. Holfeld, C. Tepeköylü, R. Kozaryn, A. Falkner, L. Loacker, M. Grimm
Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck

Background Cardiac shock wave treatment (SWT) induces angiogenesis in ischemic heart failure. In a previous experiment our group found high numbers of macrophages in treated ischemic myocardium as shown by RM-4 immunostaining. M2 macrophages play a crucial role in angiogenesis.

Methods Peripheral blood mononuclear cells (PBMCs) were separated from donor blood by Ficoll gradient. Human umbilical vein endothelial cells (HUVECs) were isolated from umbilical cord donors. Hypoxia was induced in HUVECs for 16 hours. Thereafter cells were treated with SWT. The supernatant of treated cells was added to monocytes. Both groups were incubated with interleukin4 over 7 days. Number of M1 and M2 macrophages was determined by FACS and PCR. All other blood cells were counted with FACS or immunostaining.

Results 7 days after shock wave treatment of hypoxic endothelial cells there are significantly more macrophages in the treatment group. Surprisingly, we also found higher numbers of immune cells, e. g. natural killers, in the treatment group.

Discussion SWT stimulates ischemic endothelial cells to release growth factors that activate monocytes to differentiate into M2 macrophages which attenuate inflammation. It thereby enhances tissue regenerative processes and angiogenesis. This findings clearly explain the mechanism of increased angiogenesis after cardiac SWT in vivo.

Levosimendan Exhibits Anti-Inflammatory Effects on Human Endothelial Cells by Attenuating the Expression of Pro-Inflammatory Adhesion Molecules in vitro III – 6

K. A. Krychtiuk, L. Watzke, Ch. Kaun, S. Demyanets, J. Pisoni, St. P. Kastl, K. Huber, G. Maurer, J. Wojta, W. S. Speidl
Division of Cardiology, Department of Medicine II, Medical University Vienna; 3rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna

Purpose Levosimendan is a positive inotropic drug for the treatment of acute decompensated heart failure (HF). In clinical trials, levosimendan was shown to be effective in particular in HF due to acute myocardial infarction (AMI) and it has been demonstrated that levosimendan reduces infarct size in animal models. Neutrophil recruitment is a crucial step in tissue damage due to ischemia reperfusion injury. The aim of the present study was to examine whether levosimendan reduces the expression of adhesion molecules on endothelial cells.

Methods Human umbilical vein endothelial cells (HUVECs) were treated with 200 U/ml interleukin-1β (IL-1β) and incubated with or without levosimendan (10 μM). Expression of E-selectin, vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) was measured by flow cytometry after 8 h and by real-time PCR after 2 h, 4 h, 8 h and 24 h of incubation. HUVECs treated with IL-1β with or without co-treatment with levosimendan for 4 h were incubated with polymorphonuclear cells (PMNs) for 5 and 30 minutes to examine cell adhesion in vitro.

Results Treatment of HUVECs with IL-1β for 8 h increased expression of E-selectin, ICAM-1 and VCAM-1 (15-fold, 45-fold and 80-fold, respectively; $p < 0.05$ for all). Preincubation with levosimendan for 30 minutes down-regulated the expression of E-selectin by 65% ($p < 0.05$), ICAM-1 by 60% ($p < 0.01$) and VCAM-1 by 30% (n. s.), respectively. mRNA levels of E-selectin, ICAM-1 and VCAM-1 were highly upregulated by IL-1β treatment after 2 h, 4 h, 8 h and 24 h ($p < 0.01$). Co-treatment with levosimendan lead to a downregulation of adhesion molecules after 2 h (by 75%, $p < 0.001$ for E-selectin; by 44%, $p < 0.01$ for ICAM-1; no change for VCAM-1; respectively), 4 h (by 40%, $p < 0.05$ for E-selectin; by 17%, n. s. for ICAM-1; no change for VCAM-1; respectively) and 8 h (by 55%, $p < 0.01$ for E-selectin; by 42%, $p < 0.001$ for ICAM-1; by 32%, n. s. for VCAM-1; respectively). In vitro cell adhesion experiments showed increased adhesion of PMNs to HUVECs after treatment with IL-1β, pre-treatment with levosimendan lead to a markedly decreased number of PMNs bound to HUVECs (1130 vs 732 after 30 mins, $p < 0.01$; 302 vs 161 after 5 mins, $p < 0.001$; all values represent mean of cells that adhered to HUVECs per 250 μm^2 after washing 3 times for IL-1 vs IL-1 + levosimendan treatment).

Conclusions Levosimendan down-regulates expression of adhesion molecules in endothelial cells and decreases adhesion of PMNs. This could explain, at least in part, the beneficial effects of levosimendan after myocardial infarction due to a decrease of ischemia reperfusion injury.

Erhalt der linksventrikulären Funktion durch Anti-Thymozyten-Globulin (ATG) im Modell des experimentellen Myokardinfarkts an der Ratte durch Induktion von pro-angiogenetischen und anti-apoptotischen Mechanismen III – 8

M. Lichtenauer, G. Werba, M. Mildner, A. Baumgartner, K. Hoetzenecker, S. Nickl, L. Beer, B. K. Podesser, H. J. Ankersmit
Christian-Doppler-Labor für Diagnose und Regeneration von Herz- und Thoraxerkrankungen, Abteilung für Thoraxchirurgie, Medizinische Universität Wien

Einleitung Das ventrikuläre Remodelling nach einem Myokardinfarkt (MI) stellt ein bedeutendes medizinisches und volkswirtschaftliches Problem dar. Vorangegangene Studien zeigten, dass die Verabreichung apoptotischer Leukozyten oder Anti-Lymphozyten-Serum die kardiale Funktion nach Ischämie bewahren kann. Ziel dieser Studie war es zu evaluieren, ob Anti-Thymozyten-Globulin (ATG), als klinisch langbewährtes Medikament welches Apoptose von T-Zellen auslöst, ein vergleichbares therapeutisches Potenzial im experimentellen MI-Modell in der Ratte besitzt.

Material und Methode Herzinfarkte wurden mittels Ligatur des Ramus interventricularis anterior (RIVA) in Sprague-Dawley-Ratten induziert. Anschließend wurden 10 mg ATG pro Tier intravenös verabreicht. Drei Tage und 6 Wochen nach Induktion des Infarkts wurde das infarzierte Myokard der Tiere histologisch und immunhistologisch untersucht. Weiters wurden nach 6 Wochen kardiale Funktionsparameter erhoben. Die Ausdehnung der Infarktareale wurde mittels Planimetriesoftware berechnet. In In-vitro-Assays wurde der Einfluss von ATG auf die Sekretion diverser Zytokine, Chemokine und Wachstumsfaktoren mittels ELISA evaluiert.

Ergebnisse In vitro zeigt sich, dass ATG in Zell- und Vollblutkulturen eine hoch-signifikante Induktion der Sekretion von pro-angiogenetischen Faktoren auslöste (u. a. IL-8 und MCP-1, **Abbildung 16a, b**). Weiters fand sich eine höhere Gefäßdichte in der Peri-Infarktregion 6 Wochen nach ATG Behandlung (52 vs. 37 Gefäße pro Mikroskopfeld, $p < 0,04$). In Micro-Arrays konnte gezeigt werden, dass Kardiomyozyten, die mit ATG-konditioniertem Zellkulturüberstanden koinkubiert wurden, eine deutliche Herabregulierung von p53 zeigten.

Ratten, die mit ATG behandelt wurden, präsentierten eine signifikant geringere Infarktgröße (25 % vs. 11 %; $p < 0,01$, **Abbildung 16c–e**). Echokardiographisch konnte gezeigt werden, dass ATG-behandelte Tiere eine bessere linksventrikuläre Ejektionsfraktion aufwiesen als Tiere aus der Kontrollgruppe (53 % vs. 43 % EF; $p < 0,01$, $n = 13$ pro Gruppe, **Abbildung 16f**).

Diskussion Die vorliegenden Daten zeigen, dass ATG, ein klinisch in der Transplantationsmedizin gut erprobtes Medikament, Neo-Angiogenese induzieren, den Infarktschaden nach experimenteller Ischämie reduzieren und die kardiale Funktion erhalten kann.

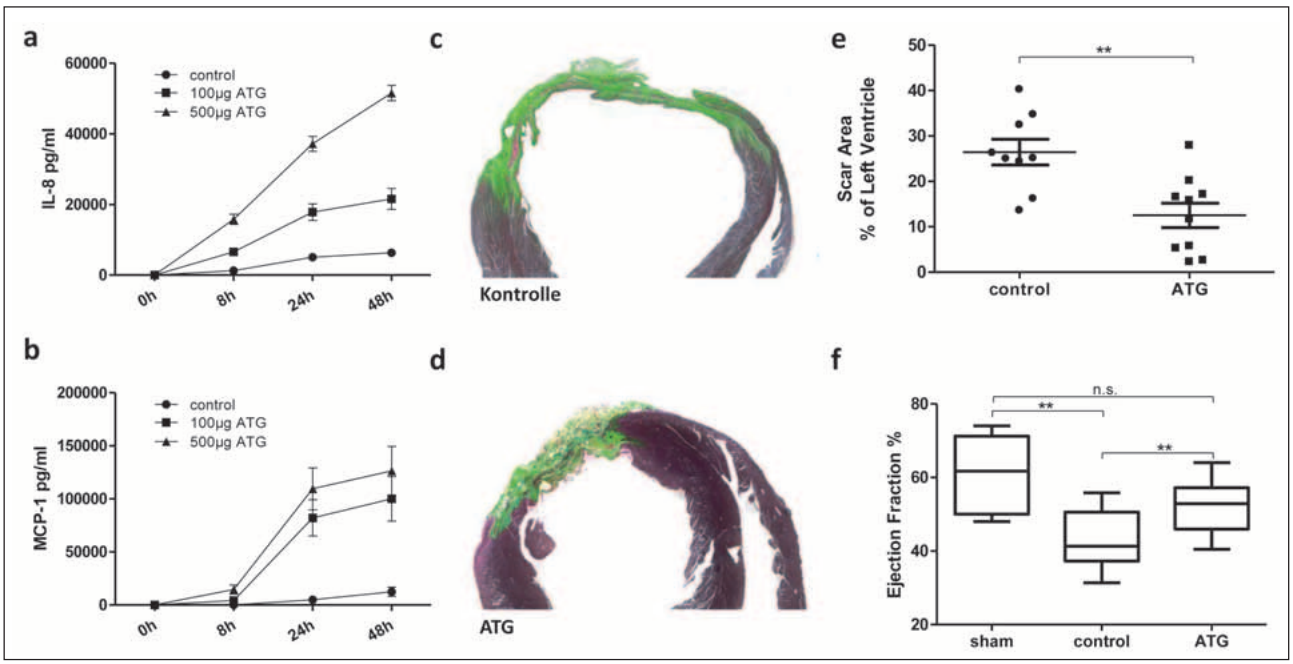


Abbildung 16: M. Lichtenauer et al.

Continued Lung Ventilation During Open Heart Surgery attenuates Systemic Heat-Shock Protein 70 Release II – 3

A. Mitterbauer, Th. Sezerafin, L. Beer, P. Altmann, Th. Haider, B. Seinlechner, G. Lang, M. Dworschak, W. Klepetko, H. J. Ankersmit
Abteilung für Thoraxchirurgie, Universitätsklinik für Chirurgie; Universitätsklinik für Anästhesie, Medizinische Universität Wien, Österreich; University of Debrecen, Hungary

Background Cardiopulmonary bypass, utilized in on-pump coronary artery bypass graft procedures (CABG) induces generalized immune suppression and release of heat shock proteins (HSP) and cc-CK18. We hypothesized that continued ventilation on cardiopulmonary bypass (CPB) induces attenuation of immune response.

Methods 30 patients undergoing conventional CABG operation were randomized into a ventilated on CPB (VG) and non-ventilated (NVG) group. Venous blood was drawn before as well as 0, 24, 48, 72, 96 and 120 hours after surgery. HSP27, HSP70, ICAM-1, IL-6, IL-8 and cc-CK18 were measured by ELISA. An unpaired t-test or Mann-Whitney-U-test was used for statistical analysis.

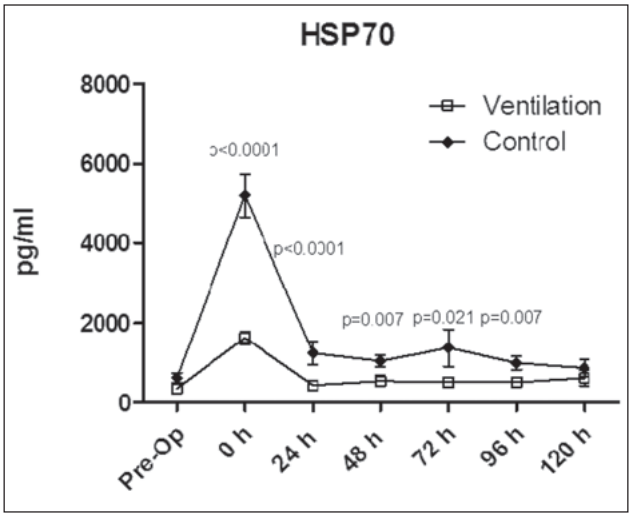


Figure 17: A. Mitterbauer et al.

Results Serum levels of HSP70 were significantly lower in VG compared to NVG after the end CABG procedure (1629.2 ± 157.1 vs 5203.5 ± 549.6 pg/ml; $p < 0.0001$). Furthermore, significant lower HSP-70 concentrations were measured 24 hours ($p < 0.0001$), 48 hours ($p = 0.007$), 72 hours ($p = 0.021$) and 96 hours ($p = 0.007$) after surgery. L-6 levels were significantly reduced in VG as compared to control group (83.1 ± 13.5 vs 110.2 ± 10.3 pg/ml, 24 hrs; $p = 0.033$). Serum IL-6 increment after CABG operation does not correlate with HSP27, 70, ICAM-1 and cc-CK18 levels indicating that HSP release and the described pro-inflammatory response after CABG were two independent events. HSP27, ICAM-1, IL-8 and cc-CK18 concentrations showed now differences between the 2 groups.

Conclusion Significantly less HSP70 was detectable in patients receiving uninterrupted lung ventilation on CPB, possibly indicating a difference in inflammatory responses, cellular stress or damage between the ventilated and non-ventilated group. These date suggest that inter-operative ventilation has a protective effect on HSP70 secretion in CABG patients (**Figure 17**).

Two Voltage-Gated Calcium Channels Regulate Calcium Uptake in Murine Cardiac Mitochondria II – 8

L. J. Motloch, D. Rottlaender, T. Gebing, M. Wolny, R. Larbig, S. Reda, U. C. Hoppe
Department of Internal Medicine II, Paracelsus Medical University, Salzburg, Austria; Center for Molecular Medicine, University of Cologne, Germany

Background Mitochondrial $Ca2^+$ handling controls the rate of mitochondrial energy (ATP) production, modulates the spatial and temporal profile of intracellular $Ca2^+$ signaling, regulates mitochondrial ROS generation, and may trigger cell death. Mitochondrial $Ca2^+$ uptake is thought to be mediated by the $Ca2^+$ uniporter (MCU) and other non specific $Ca2^+$ pathways. Recently, a MCU and a non-MCU-type mitochondrial $Ca2^+$ uptake channel were documented in human myocardium. However, existence and electrophysiological properties of calcium channels in murine cardiac mitochondria remain unclear.

Methods We isolated cardiac mitoplasts (mitochondria lacking the outer membrane) of mice and performed mitoplast-attached single-channel recordings.

Results By patch-clamping the inner membrane of these cardiac mitochondria we identified 2 different murine voltage-gated $Ca2^+$ channels, i. e. mCa1 and mCa2. Both channels differed in electro-

physiological gating parameters. In the presence of $Ca2^+$ 105 mM in the pipette solution the unitary single-channel amplitude of mCa1 (–1.16 ± 0.03 pA, at –100 mV) was higher than the amplitude of mCa2 (–0.90 ± 0.03 pA). mCa1 showed 3–5 subconductance levels, while mCa2 had only one open state. Moreover, the open probability of mCa1 (0.35 ± 0.05%) was significantly lower compared to mCa2 (0.97 ± 0.17%). Both channels could be inhibited by high concentrations of Ruthenium 360 (10 μM), while they were insensitive to blockers of other possibly $Ca2^+$-conducting mitochondrial pores.

Conclusions Single-channel properties suggest that mCa1 underlies the murine MCU. Besides the classical MCU, mitochondrial $Ca2^+$ uptake in mouse heart is mediated via a second voltage-gated $Ca2^+$ channel (mCa2) with distinct properties.

JAK3 Tag Single Nucleotide Polymorphism rs3212780 is Significantly Associated With Diabetes-Related Metabolic Phenotypes III – 4

A. Muendlein, C. Saely, S. Geller-Rhomberg, A. Leiherer, P. Rein, A. Vonbank, H. Drexel
Landeskrankenhaus Feldkirch

Background Janus kinase (JAK) 3 is involved in cytokine receptor-mediated intracellular signal transduction. Inhibition of JAK3 protects beta-cells from cytokine toxicity and has been shown to delay the onset of diabetes in the mouse model. The influence of JAK3 single nucleotide polymorphisms (SNPs) on diabetes risk or on diabetes-related metabolic traits is unknown.

Methods We therefore investigated the association of JAK3 tagging SNP rs3212780 (C > T) with metabolic phenotypes and type 2 diabetes (T2DM) in a cohort of coronary patients including 1220 non-diabetic subjects and 375 patients with T2DM, totally comprising 1595 individuals.

Results Among non-diabetic subjects SNP rs3212780 was significantly associated with HbA_{1c} (CC: 5.8 ± 0.4, CT: 5.7 ± 0.4, TT: 5.6 ± 0.4%; p = 0.001), fasting glucose (CC: 5.4 ± 0.7, CT: 5.3 ± 0.7, TT: 5.5 ± 1.1 mmol/L; p = 0.010), and HDL-cholesterol (CC: 55 ± 17, CT: 55 ± 16, TT: 51 ± 16 mg/dL; p = 0.009), as well as with total cholesterol (CC: 212 ± 44, CT: 206 ± 46, TT: 196 ± 48 mg/dL; p = 0.002) and LDL-cholesterol (CC: 134 ± 37, CT: 131 ± 40, TT: 124 ± 42 mg/dL; p = 0.013). In patients with T2DM, the JAK3 variant was significantly associated with fasting glucose (CC: 8.3 ± 2.7, CT: 8.7 ± 2.8, TT: 7.4 ± 1.9 mmol/L; p = 0.036). The association between SNP rs3212780 and T2DM did not reach statistical significance (allelic odds ratio = 1.18 [0.98–1.40]; p = 0.076).

Conclusion We conclude that JAK3 tagging SNP rs3212780 is significantly associated with phenotypes conferring an increased cardiometabolic risk, at least in non-diabetic coronary patients. The association between rs3212780 and the risk of T2DM warrants further investigation.

Effect of Paclitaxel-Eluting Balloon on Vasomotor and Endothelial Function of Porcine Peripheral Arteries, Combined with Safety and Efficacy Preclinical Studies XII – 1

C. Plass, M. Pavone-Gyöngyösi
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Introduction Drug-eluting balloon (DEB) prevents neointimal hyperplasia in coronary arteries. In contrast to the muscular type coronary vessels, the peripheral (femoral and iliac) arteries are large elastic arteries, differing from coronaries by size, relative composition of elastic and muscle tissue and by physiologic functional properties. The present study was conducted to prove the safety and efficacy of the use of the paclitaxel (PTX)-coated peripheral percutaneous balloon FREEWAY (Eurocor, Germany) in prevention of neointimal hyperplasia and to investigate the vasomotor response of the peripheral arteries to DEB use.

Methods 26 domestic pigs underwent percutaneous FREEWAY overstretch balloon dilation (1.3: 1 balloon/artery ratio) for 1 min of both iliac (6–7 mm of size, 40 mm of length) and femoral (5-6 mm of size, 40 mm of length) arteries using carotid access. Measurements of tissue PTX concentration (pre-clinical safety study) were performed by harvesting of the dilated arteries at 15 min, 1 h, 3 and 9 days follow-up (FUP). The development of neointimal hyperplasia was measured by computerized planimetry 1 month after overstretch injury in a randomized pre-clinical efficacy study. The vasomotor response of the iliac and femoral arteries was determined after 5 h, 1 and 7 days. During the FUP, the animals were treated with per os clopidogrel and aspirin.

Results The achieved tissue PTX concentration showed a significant correlation with the applied balloon inflation pressure 1 h post delivery in femoral arteries (r = 0.597; p < 0.05). The tissue PTX concentration was 433 ± 122, 185 ± 20, 4 ± 1 and 1.4 ± 0.5 ug/g in iliac arteries, and 131 ± 26, 54 ± 8, 30 ± 6 and 5.2 ± 1.7 ug/g in femoral arteries at 15 min, 1 h, 3 days and 9 days post-dilation, respectively. The injury score was similar in all arteries. The degree of neointima was small in all arteries after overstretch injury, but the difference in neointimal area was significant: 0.24 ± 0.03 vs 1.51 ± 0.48 mm^2 in femoral arteries dilated with FREEWAY or plain balloon, and 0.62 ± 0.24 vs 1.21 ± 0.04 mm^2 in iliac arteries treated with FREEWAY or plain balloon, respectively. In contrast to coronary arteries, use of DEB did not lead to addiction to vasoconstriction of the vessels, and no difference between the FREEWAY and plain balloon was observed regarding the impaired endothelium-dependent vasodilation capacity.

Conclusions FREEWAY DEB reduces effectively the neointimal hyperplasia in peripheral (iliaca and femoral) arteries, and does not lead to worse vasodilatory capacity as compared to plain balloon.

Cardiac Morphology and Function in Migfilin Deficient Mice Due to Experimental Pressure Overload II – 2

M. Reiner, K. Streil, B. J. Haubner, K. Bader, D. Moik, R. Fässler, O. Pachinger, B. Metzler
Department of Internal Medicine III/Cardiology, Innsbruck Medical University; Institute of Molecular Biotechnology Vienna, Austria; Department of Molecular Medicine, Max-Planck-Institute of Biochemistry, Martinsried, Germany

Background Migfilin, a protein associated with cell adhesions and the cytoskeleton, translocates Ca++ dependent to the nucleus and interacts with the cardiac transcription factor Csx/Nkx2-5, which is involved in cardiac development and hypertrophy by inducing gene expression of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), among others. The in vivo role of migfilin in cardiac hypertrophy and function is unknown.

Material and Methods Migfilin wild type (WT) and knock out (KO) mice were examined at baseline and further after one and three weeks of pressure overload, induced by transverse aortic constriction (TAC). To assess cardiac morphology and function, transthoracic echocardiography was performed, mean cross-sectional area of cardiomyocytes was measured in histological sections and mRNA of the cardiac hypertrophy genes ANP and BNP was quantified by rt-PCR.

Results Echocardiography at baseline showed significantly smaller hearts but normal cardiac function in migfilin KO mice. After 1 and 3 weeks of TAC, cardiac function was reduced in KO mice (FS, 1 week: 51.99% vs 55.21%, p = 0,01; 3 weeks: 49.79% vs 51.93%, p = 0,02) and murine hearts appeared to be more dilated after 3 weeks of pressure overload (End Diastolic Diameter, 3.95 mm vs 3.75 mm, p = 0,005). Mean cross-sectional area of cardiomyocytes after 1 and 3 weeks of TAC was significantly decreased in KO compared to WT mice (both, p < 0.05). Additionally, migfilin deficient mice showed decreased mRNA levels of ANP and BNP at baseline and after TAC (both, p < 0.05).

Discussion These data suggest that migfilin plays an essential role in cardiac hypertrophy since loss of migfilin in mice results in smaller hearts at baseline and reduced myocardial hypertrophy and function in association to pressure overload.

Cx43 Hemichannels of the Inner Mitochondrial Membrane Mediate Ischemic Preconditioning in Murine Cardiomyocytes II – 5

D. Rottländer, L. Motloch, M. Wolny, R. Sara, R. Larbig, U. Hoppe
Universitätsklinik für Innere Medizin II, Universitätsklinikum Salzburg, Österreich; Zentrum für Molekulare Medizin Köln, Deutschland

Background Ischemic preconditioning involves activation of multiple signaling pathways with mitochondrial ion channels as an end-effector. Recently, we demonstrated that connexin 43 (Cx43) found in the inner mitochondrial membrane, is essential for cytoprotective signal transduction onto mitoKATP channels. Since inhibition of mitoKATP channels via Cx43 by carbenoxolone and 43GAP27 implicated that Cx43 functions as a channel in mitochondria, we sought to directly record Cx43 channels in isolated mitoplasts.

Methods and Results We identified single-channel currents, which were clearly distinct from mitoKATP channels, with a mean open probability (Po, total) of 2.6 ± 0.4% (at –80 mV, n = 16) and a unitary conductance of 102.5 ± 7 pS. Notably, these channels were activated by RRNYRRNY, but not RRPPYN, with an increase of Po, total to 26.1 ± 4.7% ($p < 0.05$ vs control) without affecting channel conductance (106.1 ± 9 pS), and inhibited by 43GAP27 which suppressed Po, total and single-channel conductance to 49.1 ± 5 pS ($p < 0.05$ vs control). Single-channel properties thus supported the notion that we were recording mitochondrial Cx43 channels.

We therefore reasoned that Cx43 might be a promising target for cardioprotection circumventing possible secondary effects on other cellular functions occurring when activating multiple kinases of the upstream pathway. Thus, we determined whether the Cx43 C-terminal binding peptide RRNYRRNY confers protection in isolated cardiomyocytes or when administered systemically by intraperitoneal injection into mice. To facilitate rapid biodistribution and in vivo transduction into cardiomyocytes the peptide was conjugated to TAT47–57 as an intracellular carrier. Under normoxic conditions RRNYRRNY had no effect on the viability of isolated cardiomyocytes compared to the control peptide RRPPYN or no peptide. However, under simulated ischemia-reperfusion RRNYRRNY markedly reduced cell death versus the control peptide or no peptide. This indicated that RRNYRRNY provided protection at the single cell level independent of cell-cell coupling, i. e. gap junctions. Consistent with these in vitro results, intraperitoneal delivery of RRNYRRNY (20 nmol) 20 min prior to 30 min coronary artery ligation and subsequent 120 min reperfusion significantly reduced infarct size in wildtype mice; this protection was even more pronounced than that by ischemic preconditioning with one cycle of 10 min coronary occlusion and 10 min reperfusion. The effect of RRNYRRNY was specific, since injection of the control peptide (RRPPYN) resulted in no cardioprotection against ischemia-reperfusion injury.

Discussion For the first time we directly recorded mitochondrial Cx43 channels which were activated by RRNYRRNY. Moreover, RRNYRRNY rendered isolated cardiomyocytes in vitro and the heart in vivo resistant to ischemia/reperfusion injury, indicating that mitoCx43-mediated reduction of infarct size was not undermined by RRNYRRNY-related opening of sarcolemmal Cx43 channels. Our results demonstrate that Cx43 functions as a channel in mitochondria being an attractive target for drug development against cardiomyocyte injury.

GSK3β Transfers Cytoprotective Signaling Through Connexin 43 onto Mitochondrial ATP-Sensitive K+ Channels II – 6

D. Rottländer, L. Motloch, R. Sara, M. Wolny, K. Boengler, R. Schulz, G. Heusch, U. Hoppe
Universitätsklinik für Innere Medizin II, Universitätsklinikum Salzburg, Österreich; Zentrum für Molekulare Medizin Köln; Universität Essen; Universität Giessen, Deutschland

Background Ischemic preconditioning involves activation of signaling pathways, including activation of protein kinase C (PKC) and inhibition of glycogen synthase kinase 3beta (GSK3β). Opening of mitochondrial ATP-sensitive K+ (mitoKATP) channels has been proposed to play a critical role in ischemic preconditioning. Recently, we demonstrated that connexin 43 (Cx43) found in the inner mitochondrial membrane, is essential for cytoprotective signal transduction onto mitoKATP channels.

Objectives To dissect signal transduction targeted at mitoKATP channels and to possibly identify a functional link between mitoKATP channel activation, mitochondrial Cx43 and GSK3β activity.

Methods We used direct single-channel patch-clamp recordings of cardiac mitoplasts from C57/Bl6J mice and homozygous GSK3β-S9A mice with cardiac-specific expression of a constitutively active form of GSK3β, and performed Western blots and co-immunoprecipitation of isolated mitochondria.

Results MitoKATP channel activity was stimulated by the GSK3β small molecule inhibitor SB216763 (5 μM), which increased the open probability compared to control. The Cx43 inhibitor carbenoxolone (10 μM) and the Cx43 mimetic peptide 43GAP27 (250 μM) significantly reduced mitoKATP channel activation by SB216763, supporting the notion that GSK3 transfers cytoprotective signaling via Cx43 onto mitoKATP channels. In GSK3β-S9A mitoplasts mitoKATP currents could be recorded with similar single-channel properties as in wildtype mitochondria. Single-channel activation of mitoKATP by the PKC activator PMA was significantly attenuated in GSK3β-S9A mitoplasts. Western blot analysis revealed reduced phosphorylation of mitochondrial Cx43 at the PKC phosphorylation site Ser368 upon PMA application in mitochondria from GSK3β-S9A mice versus wildtype. Furthermore Immunoprecipitation of Cx43 from isolated mitochondria revealed a signal for GSK3β, while immunoprecipitation of GSK3β also showed a signal for Cx43, indicating an association of these proteins.

Conclusions PKC transmits a signal onto mitoKATP channels through GSK3β. This GSK3β signal transduction on mitoKATP channels is transferred via Cx43 within a multiprotein signaling module.

Angiotensin II Induces Ca2+- and IP3-Dependent Depolarisations in Mouse and Human Ventricular Cardiomyocytes II – 1

M. Sacherer, S. Ljubojevic, P. Stiegler, M. Sereinigg, B. Pieske, F. Heinzel
Klinische Abteilung für Kardiologie; Klinische Abteilung für Transplantationschirurgie, Medizinische Universität Graz

Background Angiotensin II (ATII) is a potent vasoconstrictor associated with cardiac remodeling, progression of heart failure and arrhythmia. ATII signals primarily via the Gq-coupled ATII receptor type 1 (AT1) and activates phospholipase C (PLC) signaling pathway including IP3-mediated Ca2+ release and diacylglycerol (DAG) activation of protein kinase C. Recent data suggest that DAG can directly regulate members of transient receptor potential cation (TRPC) channels family. TRPC3 was shown to form a functional complex with NCX, and its activation may lead to alterations in subcellular Na+ and Ca2+ homeostasis. On the other hand acute ATII induced IP3- mediated Ca2+ release from the SR may also play a critical role on Ca2+ hoemeostasis in cardiomyocytes (CMs). Although dysbalance in Na+ and Ca2+ concentration can lead to arrythmogenic events, no direct evidence is provided whether ATII may induce triggered cellular depolarisations and increase diastolic Ca2+ leak from the SR. Therefore, we investigated the acute effect of ATII on Ca2+ homeostasis in CMs isolated from mouse and human ventricular tissue.

Methods Cytosolic [Ca2+] (Fluo4-AM, confocally) was measured in electrically stimulated CMs from mouse (n = 41–72 cells per group) and human (n = 4 cells per group) hearts not suitable for transplantation. Amplitude of [Ca2+] transients (CaTs) and caffeine transients (CaffTs)were calculated as F/F0 and diastolic SR Ca2+ leak as frequency of sparks (SparkF, in s-1*pL-1). Arrhythmic depolarisations were identified by synchronized SR Ca2+ release (syncCR, in number*s-1) during diastole. Action potentials (Aps)

were recorded in whole cell patch clamp mode. Cells were kept in elevated [Ca2+]o (mouse: 3 mM, human: 5 mM) and ATII (100 nM) was applied for 15 min.

Results In human CMs ATII increases the incidence of arrhythmogenic diastolic Ca2+ release (SparkF: ATII vs CTRL, 292 ± 89 vs 37 ± 21; p < 0.05). In mouse cells, ATII tended to increase APD90 from 53.4 ± 6.4 to 92.4 ± 34.2 ms (p = 0.1). ATII increased CaTs amplitude from 2.7 ± 0.2 to 4.1 ± 0.3 (p < 0.05), while SparkF increased from 46 ± 21 to 269 ± 29 (p < 0.05). The incidence of syncCR increased by ATII application (0.81 ± 0.14) as compared to CTRL (0.10 ± 0.03; p < 0.05). Ouabain in combination with Na+-free external solution also lead to increased diastolic leak (SparkF: 154 ± 31; p < 0.05), but not syncCR during diastole (syncCR: 0.06 ± 0.02; n. s. vs CTRL). ATII did not change SR Ca2+ content (CaffTs: ATII vs CTRL, 6.2 ± 0.3 vs 5.5 ± 0.5; p = n. s.; subset of cells). 2-APB, a blocker of the IP3-receptor, decreased both SparkF (103.7 ± 29.29) and syncCR (0.04 ± 0.02; both p < 0.05 vs ATII alone). In cells matched for SparkF, 2-APB decreased syncCR (ATII vs ATII+2-APB; 0.63 ± 0.14 vs 0.06 ± 0.03; p < 0.05).

Conclusion ATII increases Ca2+ mediated arrhythmias in both mouse and human CM. IP3-receptor mediated signaling promotes depolarisations induced by ATII independent of SR Ca2+ leak.

Lack of Tenascin-C does not Affect Hemodynamics in Cardiac Remodeling III – 5

D. Santer, K. Trescher, F. Nagel, J. Krynicka, Ch. Kaun, M. Krssak, K. Plesch, M. Wolfsberger, B. Podesser
LBC f. kardiovaskuläre Forschung. Bes. Einrichtung für biomedizinische Forschung Vienna; Department of Cardiac Surgery, Landesklinikum St. Pölten; Division of Cardiology, Department of Medicine II; Centre of Excellence High Field MR, Department of Radiology, Medical University Vienna; Department of Paediatrics and Adolescent Medicine, Landesklinikum Wr. Neustadt

Background The extracellular matrix (ECM) protein Tenascin-C (TNC) is expressed within 24 h after myocardial infarction (MI) in the border zone between vital and infarcted myocardium. TNC affects cell attachment for reorganization in infarcted tissue. Our goal was to describe hemodynamic impacts of TNC and associations to relevant ECM proteins in cardiac remodeling using a MI model in TNC knockout mice.

Methods In A/J (WT, n = 12) and TNC-Knockout (TNC-KO, n = 13) mice left lateral thoracotomy was accomplished under isoflurane and the left anterior descending coronary artery was ligated. Ten weeks after surgery animals underwent cardiac magnetic resonance imaging (MRI). After MRI mice were anesthetized, beating hearts were rapidly excised and evaluated on the isolated working heart (WH) device for further hemodynamic measurements. Additionally, real-time PCR of TIMP 1, 2, MMP-9, and OPN expression in remodeled myocardium of WT (n = 6) and TNC-KO (n = 6) was performed.

Results MRI analyses ten weeks after MI showed no significant differences between WT and TNC-KO: Heart Rate (WT: 465 ± 13 bpm vs TNC-KO: 499 ± 10 bpm, n. s.), Ejection Fraction (WT: 34 ± 5% vs TNC-KO: 30 ± 4%, n. s.), Enddiastolic Volume (WT: 99 ± 15 µl vs TNC-KO 89 ± 13 µl, n. s.), Endsystolic Volume (WT: 73 ± 14 µl vs TNC-KO: 68 ± 13 µl, n. s.) and Stroke Volume (WT: 27 ± 2 µl vs. TNC-KO: 22 ± 2 µl, n. s.). Cardiac output and aortic flow were not significantly different in working heart mode. OPN (p < 0.01), TIMP-1 (p < 0.01), TIMP-2 (p < 0.01) and MMP-9 (p < 0.05) were downregulated in TNC-KO compared to WT.

Conclusion Our observations do not confirm direct hemodynamic effects neither in MRI nor in WH due to the lack of TNC. Future investigations have to illustrate compensatory pathways that seem to at least partially preserve TNC induced mechanisms.

Veränderung der Natriumregulation in Herzmuskelzellen im frühen Stadium der Herzinsuffizienzentwicklung der Maus XIII – 4

P. Schoenleitner, F. R. Heinzel, G. Jin, G. Unterer, B. Pieske, P. Wakula
Klinische Abteilung für Kardiologie, Ludwig-Boltzmann-Institut für Translationale Herzinsuffizienzforschung, Medizinische Universität Graz

Einleitung Erhöhte sympathische Aktivierung trägt zur Herzinsuffizienzentwicklung bei. Mäuse mit kardiospezifischer Überexpression des β1-adrenergen Rezeptors (β1-TG) entwickeln nach mehreren Monaten eine progressive Herzinsuffizienz. Eine frühe Störung der Kalziumhomöostase ist an der Entwicklung des Phänotyps ursächlich beteiligt. Schon vor dem Auftreten signifikanter kardialer Funktionsstörungen ist das zytosolische [Ca+] in β1-TG-Kardiomyozyten erhöht. Wir konnten zeigen, dass die erhöhte [Ca+] durch eine Erhöhung des zytosolischen [Na+] in Verbindung mit veränderter Na-Ca-Austauscher-Funktion verursacht wird. Der Grund für die [Na]-Erhöhung im Frühstadium des kardialen Remodellings ist unbekannt. In einem späteren Stadium wurde eine erhöhte Expression des Na+-H+-Austauschers (NHE1) beschrieben. Wir untersuchten die Expression und Regulation von Natriumtransportproteinen im Frühstadium der Herzinsuffizienzentwicklung in der β1-TG-Maus.

Methoden Proteinkonzentrationen von Natrium-Kalium-ATPase-(NKA-) Untereinheit α1 und α2, deren regulatorische Untereinheit Phospholemman (PLM), NHE1 und TRPC3 wurden in Ganzventrikelhomogenaten (GH) und Zelllysaten (ZL) von 8–12 Wochen alten β1-TG-Mäusen und deren WT-Wurfgeschwistern mittels Western-Blot bestimmt. Die Phosphorylierung von Phospholemman (Ser68) wurde via phosphorspezifischen Antikörpern in GH bestimmt und gegen GAPDH und CSQ normalisiert (arbiträre Einheiten ± SEM). Zur statistischen Auswertung der Daten wurde der t-Test verwendet. Ein Wert p < 0,05 wurde als signifikant definiert.

Ergebnisse Die Expression der physiologisch dominierenden Untereinheit NKA α1 war in jungen β1-TG- vs. WT-Mäusen sowohl in GH als auch in ZL unverändert. NKA α2 war in den GH der β1-TG-Tiere signifikant verringert (0,87 ± 0,09, n = 5 vs. 1,24 ± 0,08 in WT, n = 4; p < 0,05), in ZL zeigt sich ein ähnlicher Trend (0,76 ± 0,18, n = 4 in β1-TG vs. 1,21 ± 0,19, n = 5 in WT; p = 0,11). PLM-Expression war vermindert (0,71 ± 0,08, n = 5 vs. 1,23 ± 0,18, n = 4; p < 0,05), die Phosphorylierung von PLM signifikant erhöht (1,3 ± 0,05, n = 5 vs. 0,748 ± 0,06, n = 4; p < 0,001). Die Expression von NHE1 war in den β1-TG-Tieren, sowohl in den ZL als auch in den GH, unverändert. Die Proteinexpression des Transit-Receptor-Potential-Canonical-3- (TRPC3-) Kanals, als mögliche Ursache eines sarkolemmalen Na+-Einwärtsstroms, war in den GH signifikant verringert (0,97 ± 0,04, n = 5 vs. 1,33 ± 0,06, n = 4; p < 0,001), in den ZL konnte diese Veränderung nicht nachgewiesen werden.

Diskussion NKA-α2-Expression ist bei β1-TG-Tieren mit chronischer beta1-adreneger Stimulation frühzeitig vermindert exprimiert und könnte zur erhöhten [Na] beitragen. Die verminderte Expression und erhöhte Phosphorylierung von PLM lassen jedoch eine begleitende De-Inhibierung von NKA erwarten, die die verminderte NKA-α2-Expression kompensieren könnte.

Die unveränderte Expression der physiologischen Veränderungen der NHE1- und TRPC3-Expression können nicht als Erklärung für das erhöhte zytostolische Natrium herangezogen werden.

Deregulation of SUMO-1 and Ubc-9 Expression in Lungs from Pulmonary Hypertensive Rats XIII – 7

C. Schreiber, A. Panzenböck, M. Strobl, St. Hubmer, J. Jakowitsch, H. Bergmeister, A. Pichler, I. M. Lang, D. Bonderman
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna, Austria; Max Planck Institute of Immunobiology and Epigenetics Freiburg, Germany

Background Pulmonary arterial hypertension (PAH) results from obstruction of the pulmonary vasculature due to uncontrolled proliferation of pulmonary artery endothelial cells. On a molecular basis, reduced levels of signaling molecules that inhibit cell proliferation

have been shown. Most importantly, defective SMAD-4 signaling has been demonstrated in lungs from PAH patients and monocrotaline (MCT)-treated pulmonary hypertensive rats. SMAD-4 concentration in the nucleus is regulated via Small Ubiquitin-like Modifier-1 (SUMO-1), a posttranslational modifier of intracellular proteins. Conjugation of SUMO-1 to SMAD-4 is mediated via the enzyme Ubc-9. The aim of the present study was to study SUMO-1 and Ubc-9 expression in a rat model of pulmonary hypertension.

Methods 12 male Sprague-Dawley rats were studied before and 28 days after left unilateral pneumonectomy and MCT-exposure. Hemodynamic parameters were monitored by an implantable telemetry system (DSI Datascience, St. Paul, MN, USA). Healthy (left) and pulmonary hypertensive (right) lungs were compared with respect to SMAD-4, SUMO-1 and Ubc-9 RNA levels.

Results While there was a clear trend towards SMAD-4 down-regulation in diseased lungs (–1.1314 ± 0.509 vs 0.0 ± 0.388; p = 0.000), SUMO-1 (0.0 ± 0.608 vs 15,600 ± 1509; p = 0.015) and Ubc-9 (0.0 ± 0.639 vs 1524 ± 1461; p = 0.015) were significantly up-regulated. We found a strong negative correlation between mean pulmonary artery pressure (mPAP) and SMAD-4 (R2 = -0.490; p = 0.033) and a positive correlation between mPAP, SUMO-1 (R2 = 0.482; p = 0.027) and Ubc-9 (R2 = 0.558; p = 0.009).

Conclusion SUMO-1 and Ubc-9 expression are deregulated in lungs from pulmonary hypertensive rats and may represent novel therapeutic targets.

Mild Hypothermia Prevents Sympathetic Activation but Preserves Vascular Tone During Experimental Endotoxemia in Pigs

XII – 2

M. Schwarzl, S. Seiler, St. Huber, P. Steendijk, H. Mächler, M. Truschnig-Wilders, B. Pieske, H. Post
Klinische Abteilung für Kardiologie, Klinisches Institut für Medizinische und Chemische Labordiagnostik, Medizinische Universität Graz, Österreich; Leiden University Medical Center, Leiden, The Netherlands

Background Clinical data imply that reduced heart rate variability (HRV) predicts mortality during sepsis. Mild hypothermia (MH, 33 °C) accelerates the recovery of autonomic function after experimental cardiac arrest and resuscitation in pigs. Here, we tested the effect of MH on HRV during experimental sepsis.

Methods Acutely instrumented pigs (65 ± 2 kg) were exposed to lipopolysaccharide (LPS) infusion at 0.5 µg/kg/h for 1 h, 1 µg/kg/h for further 3 h, and followed for a total of 8 h. With the beginning of LPS infusion, pigs were assigned to either normothermia (NT, 38 °C, n = 7) or MH (33 °C, n = 6, intravascular cooling). HRV was analysed in 15-minute ECG-samples. *: p < 0.05 vs baseline, †: p < 0.05 vs NT.

Results At 8 h after onset of LPS infusion vs baseline, heart rate (bpm) increased in NT (128 ± 6* vs 97 ± 4), but decreased in MH (79 ± 4*,† vs 98 ± 4). Systemic vascular resistance decreased in NT (6.6 ± 0.4* vs 11.6 ± 0.3), but was preserved in MH (11.1 ± 1.0 † vs 12.7 ± 0.6). Time-domain parameters of HRV (SDNN, SDdeltaNN, triangular index) did not change over time and were not different between groups. However, spectral analysis of HRV revealed a different composition of underlying frequency bands: the high-frequent fraction (HF, = parasympathicus) increased in MH, but decreased in NT, whereas the ratio between low-frequent fraction and HF (LF/HF, = sympathicus) increased in NT, but not in MH **(Figure 18)**.

Conclusion The induction of MH prevents sympathetic activation during experimental sepsis and preserves vascular tone. MH may have therapeutic potential in the treatment of sepsis.

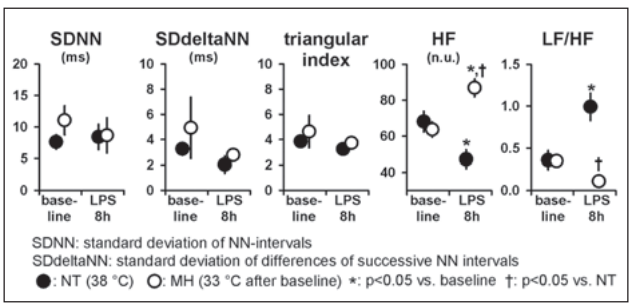


Figure 18: M. Schwarzl et al.

The Induction of Mild Hypothermia Prevents Acute Pulmonary Failure During Endotoxemia in Pigs

XII – 3

M. Schwarzl, S. Seiler, St. Huber, P. Steendijk, H. Mächler, M. Truschnig-Wilders, B. Pieske, H. Post
Klinische Abteilung für Kardiologie, Klinisches Institut für Medizinische und Chemische Labordiagnostik, Medizinische Universität Graz, Österreich; Leiden University Medical Center, Leiden, The Netherlands

Background Acute respiratory failure is a major component of multi-organ dysfunction during sepsis. The induction of mild hypothermia (MH, 33 °C) reduces whole body oxygen demand (WB-VO2) and exerts anti-inflammatory effects in experimental settings. We tested effects of MH during endotoxemia in pigs.

Methods Anesthetized pigs (65 ± 2 kg) were acutely instrumented (closed chest) with a series of catheters including an intravascular cooling device, and were ventilated in a volume controlled mode (tidal volume = 10 ml/kg, FiO2 = 50%). Respiratory rate was adjusted to keep end-tidal pCO2 at 40–45 mmHg. Endotoxemia, a model of septic shock, was induced by lipopolysaccharid (LPS) infusion at 0.5 µg/kg/h for 1 h and 1 µg/kg/h for further 3 h. With the beginning of LPS infusion, pigs were assigned to either normothermia (NT, 38 °C, n = 7) or MH (33 °C, n = 6). Data are reported at 8 h after onset of LPS-infusion vs baseline. *: p < 0.05 vs baseline, †: p < 0.05 vs NT.

Results Heart rate (bpm) increased in NT (128 ± 6* vs 97 ± 4), but decreased in MH (79 ± 4*,† vs 98 ± 4). Mean aortic pressure (mmHg) decreased in NT (53 ± 4* vs 86 ± 2) and MH (58 ± 1* vs 85 ± 2). WB-VO2 and respiratory minute volume (RMV) increased in NT but fell markedly in MH. Arterial oxygen saturation (sO2,art) fell significantly in NT but not in MH. Mixed venous sO2, a strong predictor of mortality during sepsis, decreased in NT but was preserved at baseline levels in MH.

Conclusion MH prevents acute respiratory failure during endotoxemia. This may relate to (i) reduced systemic oxygen demand with subsequently less ventilation-associated mechanical pulmonary stress and (ii) an anti-inflammatory effect of MH that preserves the lungs capability to oxygenate blood. MH may be a therapeutic option for acute pulmonary failure during sepsis **(Figure 19)**.

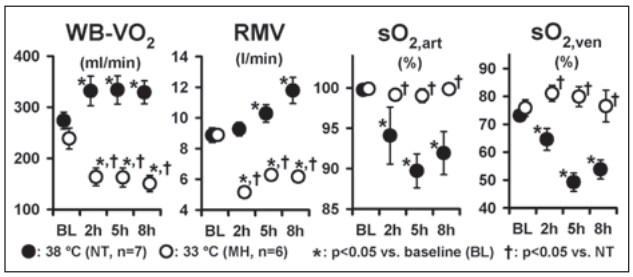


Figure 19: M. Schwarzl et al.

Modified Exhaled Nitric Oxide Measurement in Monocrotaline-Exposed Rats to Monitor Pulmonary Hypertension XIII – 6

M. S. Strobl, C. Schreiber, St. Hubmer, H. Bergmeister, I. M. Lang, D. Bonderman
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background and Aims Rats exposed to monocrotaline (MCT) are broadly used as animal model for pulmonary arterial hypertension (PAH). In analogy to human disease, right heart catheter (RHC) is the established gold standard for pulmonary pressure monitoring. Although exhaled nitric oxide (ENO) levels have been shown to correlate with pulmonary pressures in humans with pulmonary vascular disease, no link between ENO and pulmonary pressures could be established in rats. The aim of the present study was to test whether a technical modification of the NO measurement process could help generate reliable ENO values that correlate with pulmonary pressures as assessed by simultaneous RHC.

Methods 33 male Sprague-Dawley rats were studied 28 days after MCT-exposure and unilateral pneumonectomy. Hemodynamic parameters were monitored by an implantable telemetry system (DSI Datascience, St. Paul, MN, USA). ENO was measured by means of chemiluminescence (CLD 66, Eco Physics, Duernten, Switzerland) in single, conscious, spontaneously breathing rats. ENO values measured by a standard accumulation method (ENO standard) and those obtained after process modification (ENO modified) were correlated with mean pulmonary arterial pressures (mPAP).

Results After process modification, measuring errors were diminished and potential influencing factors eliminated. There was a clear correlation between ENO modified and mPAP ($p = 0.007$; $r = –0.459$), while no correlation was observed between ENO standard and mPAP ($p = 0.236$; $r = –0.212$).

Conclusion Modified non-invasive ENO measurement may be used to monitor PAH in monocrotaline-exposed rats.

Milde Hypothermie verbessert die myokardiale β-adrenerge Ansprechbarkeit und Kraft-Frequenz-Beziehung während experimentell-induzierter Sepsis im Großtiermodell XIII – 5

M. Wallner, M. Schwarzl, S. Seiler, St. Huber, P. Steendijk, H. Mächler, M. Truschnig-Wilders, B. Pieske, D. von Lewinski, H. Post
Klinische Abteilung für Kardiologie, Medizinische Universität Graz, Österreich; Medical University Leiden, The Netherlands

Einleitung Experimentell wirkt die milde Hypothermie (MH) anti-inflammatorisch. Wir prüften den Effekt der MH auf die myokardiale Kraftentwicklung in einem Modell der Sepsis bei Schweinen.

Material und Methode Unter Vollnarkose wurden 13 Hausschweine (65 ± 2 kg) mit einer Reihe von verschiedenen Kathetern (SwanGanz-Katheter, linksventrikulärer Druck-Volumen-Katheter, intraaortale Ballonpumpe und intravaskulärer Kühlkatheter) bei geschlossenem Thorax akut instrumentiert. Durch Infusion von Lipopolysaccharid (LPS) mit 0,5 µg/kg/h für 1 Stunde und 1 µg/kg/h für 3 weitere Stunden wurde ein Endotoxin-Schock induziert. Mit Beginn der LPS-Infusion wurden die Tiere entweder einer Normothermie-Gruppe (NT, 38 °C, n = 7) oder einer milden Hypothermie Gruppe (MH, 33 °C, n = 6) zugeteilt. Der Beobachtungszeitraum erstreckte sich über 8 Stunden. Im Anschluss wurden ventrikuläre Muskelstreifen isoliert, optimal vorgedehnt, mit einer modifizierten Tyrodelösung (2,5 mmol Ca^{2+}) umspült und mit 1 Hz stimuliert. Alle Muskelstreifen wurden bei 38 °C gemessen. Nach Messung der Kraftfrequenzbeziehung (KFB; 0,5–3 Hz) wurden die Muskelstreifen steigenden Isoproterenol-Konzentrationen ausgesetzt.

Ergebnisse Die hämodynamischen Analysen zeigten in beiden Gruppen eine ähnliche Beeinträchtigung der linksventrikulären Kontraktilität (dP/dt, Analyse der Druck-Volumen-Kurven), wobei in MH eine sympathische Aktivierung anders als in NT ausblieb. In vitro zeigten Muskelstreifen aus MH einen höhere Kraftentwicklung als solche aus NT: KFB: 116 ± 12 % (NT) vs. 153 ± 44 % (MH), $p < 0,05$; 10–16 mol/l Isoproterenol: 284 ± 21 % (NT) vs. 404 ± 41 % (MH); $p < 0,05$. Die logED50 % für Isoproterenol unterschied sich zwischen NT und MH nicht. Die Zeit von der maximalen Kraftentwicklung bis zur halbmaximalen Relaxation (RT50 %) war zwischen den Gruppen in beiden Protokollen nicht unterschiedlich.

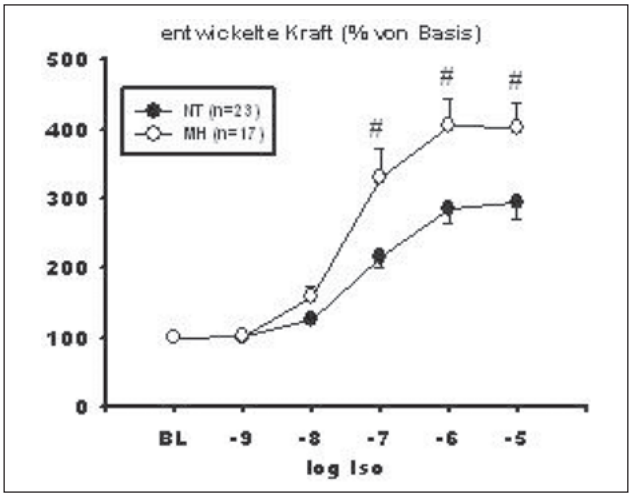


Abbildung 20: M. Wallner et al.

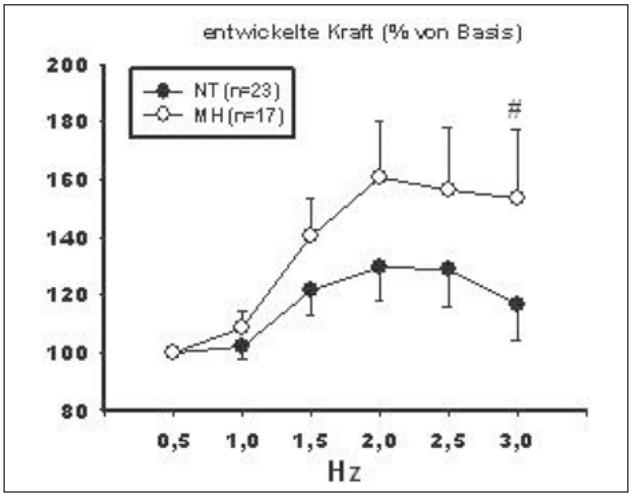


Abbildung 21: M. Wallner et al.

Diskussion Die Ergebnisse zeigen eine verbesserte Kraftentwicklung von zuvor gekühlten Muskelstreifen. Da weder die logED50 % für Isoproterenol noch Parameter der Relaxation zwischen den Gruppen verschieden waren, nehmen wir eine besser erhaltene myofibrilläre Kraftentwicklung ($Ca2^{+}$ activated force) als Mechanismus der Protektion an. MH könnte eine therapeutische Option bei septischer Kardiomyopathie darstellen **(Abbildungen 20, 21)**.

Levosimendan Modulates Inflammatory Response of Human Cardiac Myocytes in vitro III – 7

L. Watzke, K. Krychtiuk, Ch. Kaun, S. Demyanets, J. Pisoni, St. Kastl, K. Huber, G. Maurer, J. Wojta, W. Speidl
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna; 3rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna

Purpose Levosimendan is a positive inotrope drug for the treatment of acute decompensated heart failure (HF). HF is associated with an inflammatory activation of the failing myocardium. The aim of the present study was to examine whether levosimendan has anti-inflammatory effects on human adult cardiac myocytes (HACM).

Methods Primary HACM were isolated from ventricular tissue from explanted human hearts of patients undergoing heart transplantation. HACM were treated with tumor necrosis factor-α (TNF-α) (2000 U/ml) or interleukin-1 (IL-1b) (200 U/ml) and incubated with or without levosimendan (10 μM). Specific mRNA levels of IL-6 and IL-8 were determined by real-time PCR. IL-6 and IL-8 protein was measured by specific ELISA.

Results Treatment with TNF-α and IL-1-beta significantly increased mRNA and protein levels of IL-6 and IL-8 in HACM. Cotreatment with levosimendan significantly downregulated mRNA expression of IL-6 ($p < 0.05$) and IL-8 ($p < 0.05$). In addition, levosimendan decreased the effects of TNF-α on protein levels of IL-6 and IL-8 by 35% ($p < 0.05$) and 48% ($p < 0.02$). Levosimendan also reduced IL-1-beta-induced IL-6 and IL-8 by 51% ($p < 0.05$) and 60% ($p < 0.001$), respectively.

Conclusions Levosimendan downregulates expression of mRNA and protein of inflammatory modulators in cardiac myocytes in vitro. This may explain, at least in part, cardioprotective effects of levosimendan.

Methylene Blue Reduces Myocardial Contractility XIII – 3

H. Weiler, O. Moeller, M. Wohlhoefer, C. Bening, A. Abugameh, Ch.-F. Vahl
Klinik für Herz-, Thorax- und Gefäßchirurgie, Universitätsmedizin Mainz, Deutschland

Objectives Methylene blue (MB) is a dye derived from phenothiazine with pleiotropic effects. MB is administered for rescue therapy in septic shock and severe vasoplegic syndrome (VS) occurring occasionally after cardiac surgery. VS is characterized by low systemic pressure, low vascular resistance and a normal to high cardiac index neccessiting administration of vasopressors and cristalloids. Currently a controversial discussion on role of MB is ongoing. While circulatory effects are quite well examined, little is known about the influence of MB on myocardial contractility. The present study aims to evaluate the influence of MB on myocardial contractile responsiveness in an animal model excluding any preload-, afterload or humoral-related influences.

Methods The experiments were performed using isolated ventricular myocytes obtained from male, adult Wistar rats. After enzymatic isolation, cardiac myocytes were placed on the stage of an inverted microscope in a temperature regulated bath of 37 °C. The observation of cell shortening and shortening velocity – provoked by field stimulation (0,1 Hz, 20 mA) – was made by using a line camera. Cells were superperfused with carbogenated Krebs Henseleit solution (KHL). Following an equilibration period (KHL-perfusion for 2× 10 mins), MB was then added to the superperfusionsolution in clinically relevant concentrations (10-7M MB)

Results During the equilibration period cells showed constant measured parameters (cell shortening 97.9% ± 3.2%, shortening velocity 100% ± 3.6% and relaxation rate of 102.5% ± 10.6% compared to baseline). After MB treatment, we could document an early-onset decrease of cell shortening to 77.5% ± 7.5% ($p < 0.01$) after a treatment time of 20 mins compared to baseline. Shortening velocity of 83.0% ± 5.5% ($p < 0.01$) and relaxation velocity of 95.1% ± 14.8% (n. s., $p = 0.56$) diminished as well.

Conclusion Isolated administration of MB to the cardiac myocyte has important negative inotropic and lusitropic effects. When administered in septic patients MB has the potential to worsen the underlying septical cardiomyopathy as demonstrated by present data. Further evaluation is needed to identify the cellular pathways.

The Effect of the Multi Purpose Drug Tolonium Chloride on Myocardial Contractility XIII – 2

H. Weiler, O. Moeller, C. Bening, J. Jungbecker, A. Abugameh, Ch.-F. Vahl
Klinik für Herz-, Thorax- und Gefäßchirurgie, Universitätsmedizin Mainz, Deutschland

Objectives Tolonium chloride (TC) is a well-established pharmacological agent commonly used for the detection of insufficient surgical sutures as well as for exposition of body cavities. TC offers a distinct redox potential allowing the administration for therapy of methemoglobinemia. However, several case reports stressed serious cardiovascular adverse reactions, following TC application, mainly severe hypotension and cardiac arrhythmias. The study was designed, to analyze potential causes of the adverse events based on the experimental model of the isolated cardiomyocyte.

Methods Hearts of male, adult Wistar rats were rapidly excised and mounted on a Langendorffapparatus. Following enzymatic isolation, the myocytes were placed on the stage of an inverted microscope in a temperature regulated bath. The measurement of cell shortening and shortening velocity – provoked by field stimulation (0,1 Hz, 20 mA) – was made using a line camera. Measurements were performed at baseline and following TC administration. Cells were superperfused with carbogenated Krebs Henseleit solution (KHL). Following an equilibration period (KHL-perfusion for 2× 10 minutes), TC was added to the superperfusion-solution in clinically relevant concentration (10-7M TC). Proportional effects were measured (expressed as percentage).

Results During the equilibration period cells showed under steady state conditions constant measurements (cell shortening 96.7% ± 8.6%, shortening velocity of 96.9% ± 9.1% and relaxation rate of 95.4% ± 9.9% compared to baseline). Regarding the treatment effect, an early-onset decrease to 61.3% ± 17.2% ($p < 0.01$) compared to baseline of cell-shortening could be documented. Shortening velocity 77.0% ± 8.6% ($p < 0.01$) and relaxation velocity of 82.8% ± 15.5% (n. s., $p = 0.03$) decreased. Spontaneous contractions following TC treatment after a perfusion period of 20 minutes could be observed in 42.9% of all cases.

Conclusion The data shows a negative inotropic and lusitropic influence of TC on cardiac contractility. Moreover, the data demonstrates that TC administration led to spontaneous contractions/fibrillation in a subset of cases. These effects, determined without any systemic influences are in accordance with the reported clinical evidence. Further studies will analyze the underlying cellular pathways.

Schlüsselrolle von TRPC3 in der Angiotensin-II-vermittelten kardialen Dysfunktion XIII – 1

St. Wolf, B. Doleschal, M.-S. Huber, G. Wölkart, K. Groschner
Institut für Pharmazeutische Wissenschaften, Pharmakologie und Toxikologie, Karl-Franzens-Universität Graz

Hintergrund Während die Bedeutung von TRPC3 bei kardialer Hypertrophie mehrfach gezeigt wurde, ist das proarrhythmische Potenzial dieses Kationenkanals bislang unklar. Unter Verwendung eines transgenen TRPC3-überexprimierenden Mausmodells wurde die Beteiligung von TRPC3 an der Wirkung von Angiotensin II (AngII) auf das Herz untersucht.

Methoden Die Wirkung von AngII auf den linksventrikulären Druck (LVP) und das Elektrokardiogramm (EKG) wurde am Langendorff-perfundierten Herzen unter konstantem Druck untersucht. AngII-Effekte auf die zelluläre $Ca2^+$-Homöostase und Kontraktilität („sarcomer shortening“) wurden an isolierten ventrikulären Kardiomyozyten unter 1-Hz-Stimulation bei 37 °C auf einem Epifluoreszenzsetup charakterisiert.

Ergebnisse Vergleich der Wirkung von AngII (100 nM) auf kardiale Funktionen von TRPC3- (n = 5) und Wildtyp- (WT-) Mäusen (n = 5) zeigte, dass TRPC3-Überexpression die durch AngII-induzierten Störungen der Herzfunktion massiv verstärkt und auch qualitativ verändert. AngII reduzierte den LVP in TRPC3-Herzen innerhalb von 2 min auf 64 %, +dP/dt auf 50 % und -dP/dt auf 55 %, während in WT-Herzen ein positiv inotroper Effekt beobachtet werden konnte. TRPC3-Herzen (n = 6) zeigten auf AngII-Gabe (100 nM) im ECG eine akute arrhythmische Reaktion, während der Rhythmus der WT-Herzen unverändert blieb. Bei TRPC3 konnten die AngII-induzierten Arrhythmien im ECG mit Pyr3 (30 μM) unterdrückt werden.

Einzelzellmessung zeigten deutliche Unterschiede hinsichtlich der zellulären $Ca2^+$-Transienten. Die Amplitude der $Ca2^+$-Transienten in TRPC3-Myozyten ($[Ca2^+]$ F/F0 0,354 ± 0,024) waren signifikant

höher ($p < 0,05$; n = 60) als die von WT-Zellen ([Ca^{2+}] F/F0 0,262 ± 0,021). Hinsichtlich der Kontraktilität („sarcomer shortening") zeigte sich kein signifikanter Unterschied (3,8 ± 0,69 % vs. 3,52 ± 0,65 %; n = 10). Die Beladung des sarkoplasmatischen Retikulums wurde durch raschen Verabreichung von Koffein getestet und war bei TRPC3-Myozyten im Vergleich zu WT-Myozten um 40 % signifikant ($p < 0,05$; n = 43) gesteigert.

AngII-induzierte arrhythmische Aktivität und eine Erhöhung des diastolischen Ca^{2+}-Spiegel ausschließlich in TRPC3-Myozyten. Während TRPC3-Zellen einen Anstieg des diastolischen Ca^{2+} F/F0 von 0,24 ± 0,019 und 38,67 arrhythmische Ereignisse zeigten, waren bei der WT-Kontrolle keine Arrhythmien und nur ein geringer Anstieg des diastolischen Ca^{2+} F/F0 (0,24 ± 0,019) festzustellen. Pyr3 (10 µM) unterdrückte AngII-induzierte Anstiege des diastolischen Ca^{2+}-Spiegels und Arrhythmien auf das Niveau einer WT-Zelle ($p < 0,05$; n = 16). Die TRPC3-abhängige Erhöhung des diastolischen Ca^{2+} wurde durch SEA 0400 (1 µM; n = 14) und KN-93 (1 µM; n = 12) signifikant inhibiert, wobei nur SEA0400 auch die arrhythmische Ereignisse signifikant reduziert.

Konklusion Unsere Befunde zeigen, dass die kardiale Wirkung von AngII eng an die Expression von TRPC3 gebunden ist und dass TRPC-Ionenkanäle mit großer Wahrscheinlichkeit eine Schlüsselrolle in der Entstehung AngII-induzierter Arrhythmien spielen.

Frühes atriales Remodelling in einem neuen experimentellen Tiermodell des Vorhofflimmerns III – 1

D. Zweiker, M. Schwarzl, St. Huber, J. Verderber, A. Alogna, B. Pieske, H. Post, A. Lueger
Klinische Abteilung für Kardiologie, Medizinische Universität Graz

Einleitung Vorhofflimmern (VHF) kann experimentell nur an Großtieren nachgestellt werden. Wir präsentieren ein neues Modell des VHF beim Schwein und charakterisieren Parameter des frühen atrialen Remodellings.

Methoden Bei 6 Schweinen (Ausgangsgewicht 24 ± 2 kg) wurde eine 6-wöchige atriale Tachystimulation durchgeführt. Hierzu konstruierten wir ein Schrittmacheraggregat, mit welchem wir über Telemetrie (Funkstrecke 5 Meter) sowohl die Schrittmacherfunktion kontrollieren als auch ein atriales EKG übertragen konnten. Das Auftreten eines anhaltenden VHF („sustained atrial fibrillation") nach temporärem Abschalten des Aggregates wurde 3×/Woche bei wachen Tieren über einen Zeitraum von 1 Stunde überprüft. Die atriale Dimension wurden nach 2, 4 und 6 Wochen Tachystimulation durch Herzultraschall in der parasternalen Längsachse ermittelt und mit Kontrolltieren verglichen. Die atrio-ventrikuläre Überleitung wurde durch Digoxin (5 µg/kg/Tag p. o.) gebremst.

Ergebnisse Das Auftreten eines VHF stieg proportional zur Stimulationsdauer an **(Abbildung 22)**. Bereits nach 2 Wochen kam es zu einer deutlichen Dilatation der Atrien **(Abbildung 23)**. Keines der Tiere zeigte klinische Zeichen einer Herzinsuffizienz.

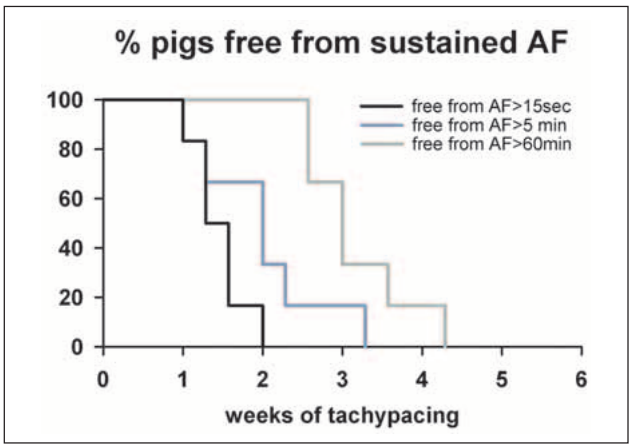


Abbildung 22: D. Zweiker et al.

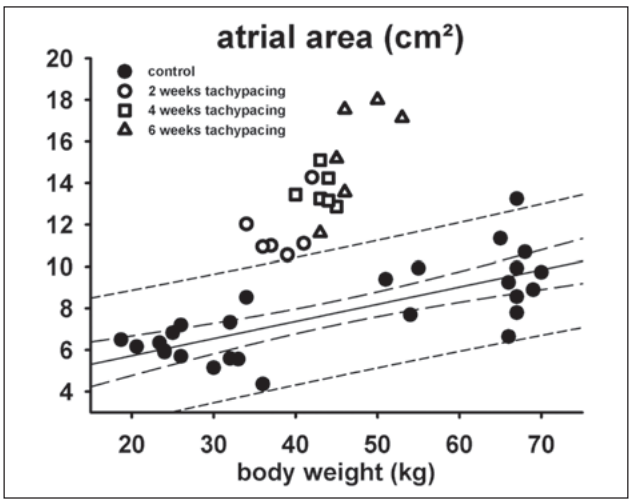


Abbildung 23: D. Zweiker et al.

Diskussion Das vorgestellte Modell erlaubt die engmaschige Abfrage des atrialen Rhythmus ohne Sedierung in tierschonender Art und Weise. Eine atriale Dilatation ist bereits nach 2 Wochen Stimulation apparent. Das Potenzial möglicherweise protektiver pharmakologischer Interventionen kann detailliert durch eine Verschiebung der Dosis-Wirkungs-Beziehung zwischen Stimulationsdauer und VHF überprüft werden. Somit ermöglicht unser Modell die systematische Testung neuer Therapieansätze zur Behandlung früher Stadien des Vorhofflimmerns.

Bildgebung/Imaging

Diastolic Retrograde Flow in the Descending Aorta by Cardiac Magnetic Resonance Imaging is Useful for the Quantification of Aortic Regurgitation IV – 2

R. Badr Eslam, St. Pfaffenberger, B. A. Marzluf, M. Frey, P. Bartko, J. Babayev, G. Maurer, J. Mascherbauer
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background Echocardiography is the current clinical routine for assessing the severity of aortic regurgitation (AR). In addition to other semiquantitative parameters, the strongest indicator for severe AR is the presence of holodiastolic retrograde flow in the descending aorta. However, bad acoustic windows frequently limit diagnostic reliability.

The aim of the present study was to compare echocardiographically assessed retrograde flow in the descending aorta with measurements by cardiac magnetic resonance imaging (CMR), which is superior in terms of image quality and reproducibility.

Methods and Results 22 consecutive patients with moderate and severe AR by echocardiography who additionally underwent CMR assessment of AR severity were included.

Patients were 53 ± 8 years old and predominantly male (18 vs 4). 14 patients were diagnosed with severe AR by echocardiography, 8 with moderate AR. In only 7 patients, pressure half times were reported (mean, 326 ± 72 ms), in the other patients pressure half times were not estimable due to jet eccentricity. In all patients the regurgitant flow in the descending aorta was assessed by echo and used for quantification of AR.

In 32% of patients, echocardiography underestimated the degree of retrograde flow, in only 5% echocardiography overestimated the severity of retrograde flow in the descending aorta.

Conclusion The assessment of diastolic retrograde flow by CMR is feasible and should complement echocardiographical workup in AR cases with unclear AR severity.

Cardiac Magnetic Resonance Imaging versus Echocardiography for Assessment of Cardiac Involvement in Pulmonary Sarcoidosis IV – 1

T. Fandl, St. Pfaffenberger, K. Vonbank, B. Marzluf, J. Mascherbauer, Th. Binder
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Study Objectives Sarcoidosis is a systemic granulomatous disease primarily affecting the lung. Cardiac involvement plays a major role for treatment decisions and prognosis, since it accounts for a majority of deaths associated with sarcoidosis. Data on prevalence of cardiac involvement in sarcoidosis patients varies depending on the patient population and diagnostic modality studied. We aimed to compare cardiac involvement diagnosed by cardiac magnetic resonance imaging (CMR) with standard echocardiography and speckle tracking echocardiography for detection of cardiac sarcoidosis in patients with pulmonary sarcoidosis.

Methods 41 patients (mean 47 years) with biopsy-proven pulmonary sarcoidosis underwent echocardiography and CMR imaging. Cardiac involvement was diagnosed if a positive late gadolinium enhancement (LE) pattern not typical for coronary artery disease on CMR was found. LE was compared to regional wall motion abnormalities on standard echocardiography and to global longitudinal peak systolic strain (GLPSS) on speckle tracking echocardiography. Additionally NT-proBNP was measured.

Results No (0%) patient revealed cardiac involvement by echocardiography while 14 (34%) patients showed a positive LE on CMR ($p < 0.001$). 4 (10.5%) patients with positive LE showed a reduced GLPSS compared to 3 (7.9%) patients without LE ($p = 0.245$). Mean NT-proBNP was higher in patients with positive LE (127 pg/ml ± 130), when compared to subjects without LE (87 pg/ml ± 80) ($p = 0.20$).

Conclusion Cardiac involvement in pulmonary sarcoidosis patients was detected in more cases by CMR than by standard echocardiography. Speckle tracking echocardiography was also more sensitive than standard echocardiography. However, cardiac involvement in a caucasian population was rare compared to previously published data based on a predominantly black-american population.

Therapeutische Konsequenzen der kardialen Magnetresonanztomographie bei koronarangiographierten Patienten IV – 8

B. Freudenthaler, P. Wexberg, A. Bastovansky, F. Weidinger, M. Avanzini
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Einleitung Die kardiale Magnetresonanztomographie (MRT) hat in den vergangenen Jahren wesentlich an Bedeutung gewonnen. Zahlreiche Daten belegen v. a. die Relevanz der Erfassung des Narbenausmaßes im Zuge des Revaskularisierungsmanagements, aber auch die höhere Genauigkeit hinsichtlich Thrombusdiagnostik und belastungsinduzierter Ischämie. Auf dieser Grundlage basierend befasst sich die nachstehende Analyse mit der therapeutischen Konsequenz im klinischen Kontext einer kardiologischen Schwerpunktabteilung.

Methoden Retrospektive Analyse von Patienten aus der lokalen MRT-Datenbank, die zwischen 2008 und 2012 an einem 1,5-Tesla-Scanner einer MRT-Untersuchung und einer Koronarangiographie zugeführt wurden. Die Befunde wurden hinsichtlich Indikationsstellung zur MRT und therapeutischer Konsequenz aufgeschlüsselt. Als therapeutische Konsequenz wurde eine Therapieentscheidung, die direkt in Folge der MRT-Untersuchung gefällt wurde, angesehen, also bei Stressuntersuchung Entscheidung zur Angiographie bzw. Revaskularisation vs. konservatives Management, bei Thrombussuche Einleiten vs. Absetzen einer oralen Antikoagulation, bei Vitalitätsfrage Planung vs. Verzicht auf Revaskularisation.

Ergebnisse In 41 Monaten wurden insgesamt 104 Patienten in unsere Studie eingeschlossen. 18 Patienten wurden (17,3 %) einem Adenosinstresstest unterzogen, davon führten 15 Untersuchungen (83,3 %) zu einer therapeutischen Konsequenz. 82 Patienten (78,8 %) wurden hinsichtlich Myokardvitalität untersucht (einschließlich 15 [18,3 %] Verlaufskontrollen), hier zeigt sich eine therapeutische Konsequenz bei 43 Untersuchungen (58,7 %). Die interkavitäre Thrombussuche (3,8 %) beeinflusste bei 3 (75 %) von 4 Patienten das weitere therapeutische Procedere.

Zusammenfassung Die Adenosinstressuntersuchungen zeigten die höchste therapeutische Relevanz, da 83,3 % der Patienten interventionell oder operativ versorgt wurden oder durch einen negativen Stresstest von einer Revaskularisierung abgesehen wurde. Im kleinen Patientenpool der interkavitären Thrombussuche wurde bei 75 % eine orale Antikoagulation eingeleitet. Aufgrund des großen Anteils an Verlaufskontrollen oder nicht-konklusiver Therapieentscheidungen ergab die Vitalitätsdiagnostik kein eindeutiges Ergebnis hinsichtlich therapeutischer Konsequenz. Hier zeigt sich, dass zahlreiche weitere Faktoren (z. B. Allgemeinzustand, Patientenwunsch, etc.) das therapeutische Vorgehen mit beeinflussen.

Intraoperative New Generation C-Arm Imaging During Cardiac Interventional Procedures: A Bridging Solution to a Hybrid Operating Room? IV – 7

G. Friedrich, Th. Schachner, L. Müller, S. Müller, O. Pachinger, Th. Bartel, M. Grimm, N. Bonaros
Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck

Objective Transcatheter valve interventions, hybrid coronary and aortic disease procedures require angiographic intraoperative imaging supporting the heart team approach. Considering limited financial and logistic possibilities of many medical centers, alternative strategies should be investigated.

Methods and Results Between 2/2001 and 7/2011, 392 patients were evaluated and treated using 4 different types of mobile c-arms: GE OEC 9800 (325), Siemens Arcadis (5), Philips Veradius (17), Ziehm RFD (45). We observed a steady increase of this imaging procedure for major cardiac procedures from 23 to 43 cases per year during the last decade ($p = 0.002$). There were 3 cases (0.8%) of system crashes, one procedure therefore deviated from a transcatheter valve implantation (TAVI) to an open surgical procedure. All other 52 TAVI procedures were completed without valve malposition or coronary obstruction. Coronary artery bypass grafts were assessed in 318 patients during implementation of new procedures (endoscopic grafting). Anastomotic or graft revision was required in 11/375 anastomoses (3%). Nitroglycerin sensitive target vessel or graft spasm was detected in 122 (33%) and 18 (5%) cases respectively. Emergency coronary intraoperative coronary angiography for signs of myocardial ischemia was performed in 14 cases (4 patients after CABG, 2 patients after AVR, 7 patients after MVR and 1 cardiac transplant recipient), in all but two patients at least one additional graft was needed. Bail out aortic stenting was needed in 7 patients and performed using conventional and digital subtraction angiography and roadmapping. Median procedure duration for coronary evaluation was 22 (10–110) minutes, fluoroscopy time was 413 (89–2282) sec, cumulative radiation (dose area product) was 46,261 (9,381–429,787) mGy/cm^2. The amount of contrast agent used was 150 (20–600) ml.

Conclusion The use of new generation mobile c-arms in the cardiac operation room is very useful for transcatheter valve and aortic interventions as well as coronary artery graft evaluation. Furthermore bail-out procedures can be successfully performed. This imaging approach may represent a bridging solution to a fully equipped hybrid interventional room.

Impact of Aortic Stiffness on NT-pro BNP Levels 4 Months After Acute STEMI IV – 5

G. Klug, M. Kremer, H.-J. Feistritzer, A. Mayr, L. Krauter, M. Schocke, Ch. Kremser, W. Jaschke, O. Pachinger, B. Metzler
Department of Internal Medicine III, Medical University Innsbruck

Objectives Chronic maladaptive remodeling of the left ventricular (LV) myocardium is associated with a significant worsening of prognosis after acute myocardial infarction (AMI) aortic pulse wave velocity (PWV) was linked to LV-geometry and -function in pa-

tients with kidney disease and non-ischemic cardiomyopathy. The role of aortic compliance after acute STEMI is so far unknown.

Methods AMI patients reperfused by primary angioplasty (n = 51, mean age: 58.0 ± 1.0 yrs, 5 female) underwent contrast enhanced cardiac MRI at a median of 2.7 days (range: 0–7 days) after the index event. Furthermore aPWV as well as aortic distensibility (DC) and compliance coefficients (CC) were determined by velocity encoded, phase contrast CMR (retrospectively ECG-gated, temporal resolution: 20 ms). Blood samples were routinely drawn. Follow-up was conducted after 4 months (median: 140, range: 92–239 days) following the same protocol (cardiac MRI, ECG, laboratory tests, history).

Results Baseline aortic aPWV (r: 0.672; $p < 0.001$), aDC (r: –0.407; $p < 0.03$) and aCC (r: –0.443; $p < 0.02$) showed moderate to good correlations to NT-pro-BNP values 4 months after STEMI. Multivariate analysis revealed aPWV beside LVEF as an independent predictor of 4-month NT-pro BNP levels after correction for age and myocardial infarct size (model r: 0.781; $p < 0.001$). Increased aPWV correlates moderately with diminished LV stroke volumes (SV, r: –0.368; $p < 0.02$) after 4 months but not with LVEF, EDV, ESV or LV-myocardial mass (all $p > 0.05$).

Conclusion Aortic stiffness (PWV, DC and CC) is associated with NT-pro-BNP levels 4 months after STEMI, suggesting a role for aortic stiffness in chronic LV-remodeling. Longer follow-up periods will show if our results translate in morphological and functional changes of the left ventricle.

Impact of Cardiovascular Risk Factors on Aortic Pulse Wave Velocity: A Comparison of Healthy Volunteers and Patients After STEMI IV – 6

G. Klug, H.-J. Feistritzer, M. Kremer, A. Mayr, L. Krauter, N. Riegler, M. Schocke, W. Jaschke, O. Pachinger, B. Metzler
Department of Internal Medicine III, Medical University Innsbruck

Objectives Aortic pulse wave velocity (aPWV, m/s) is associated with traditional cardiac risk factors and an independent prognostic parameter for future cardiac events. The association of cardiac risk factors with aPWV in patients with STEMI is not yet evaluated.

Methods 115 subjects were enrolled in this study (n = 43 controls without significant coronary heart disease CHD, n = 72 STEMI patients within 7 days of index event). Aortic aPWV was determined with velocity encoded, phase contrast cardiac MRI (retrospectively ECG-gated, temporal resolution: 20 ms). Medical history was obtained to determine pre-existing cardiovascular risk factors (hypertension, smoking, hypercholesterinaemia, family history of CVD). Blood pressure (BP) and lipid profiles were determined and ESC SCORE was calculated to quantify total cardiovascular risk.

Results In controls aPWV was correlated with age (r: 0.883, $p < 0.001$), systolic BP (sBP, r: 0.530; $p < 0.002$) and ESC SCORE (r: 0.683; $p < 0.001$) but not with diastolic BP (dBP; $p > 0.05$). In patients with recent STEMI aPWV correlated with age (r: 0627; $p < 0.001$) and ESC SCORE (r: 0.312; $p < 0.01$) but not with sBP or dBP ($p > 0.05$). In controls hypertension (5.0 ± 0.4 vs 11.1 ± 3.4 m/s; $p < 0.001$) and hypercholesterolemia (5.9 ± 2.3 vs 10.9 ± 3.8 m/s; $p < 0.001$) were associated with higher aPWV, but smoking, diabetes and positive family history were not (all $p > 0.05$). In contrast in STEMI patients subjects with hypertension and hypercholesteremia did not show higher aPWV (all $p > 0.05$). Smoking, diabetes and family history had no impact on aPWV in STEMI patients (all $p > 0.05$).

Conclusion We observed differences in the association of cardiac risk factors with aortic stiffness (aPWV) between healthy subjects and patients after acute STEMI. These results may reflect more aggressive treatment in STEMI patients and should be considered when choosing aortic stiffness as a potential therapeutic target after STEMI.

Use and Limitations of Cardiac Magnetic Resonance Derived Measures of Local Aortic Elasticity in Patients After Acute ST-Elevation Myocardial Infarction IV – 9

G. Klug, H.-J. Feistritzer, M. Kremer, U. Hecker, A. Mayr, Ch. Kremser, M. Schocke, W. Jaschke, B. Metzler
Department of Internal Medicine III, Medical University Innsbruck

Objectives Directly after acute ST-elevation myocardial infarction (STEMI), altered hemodynamics might hamper the use of Cardiac Magnetic Resonance (CMR) flow-based measures of local aortic elastic parameters. We compared the value of CMR-derived measures of aortic stiffness in healthy young volunteers, patients with coronary heart disease and patients directly after first STEMI.

Methods We performed velocity encoded, phase contrast CMR in 24 healthy volunteers as well as in 17 patients with coronary artery disease (CAD) and 29 patients with recent acute STEMI. Measurements were performed at the levels of the ascending and abdominal aorta. Regional PWVTT was determined by the established transit-time method and served as a reference standard. Local distensibility coefficients (DCascending) were determined as the product of the relative area change during systole and the pulse pressure (mmHg). Local PWVQA was determined as the ratio between the flow (Q) and area (A) variations. We evaluated hemodynamic parameters of the ascending aorta (maximal flow and flow velocities). Furthermore phase contrast CMR images were scored for their quality (from "1: good" to "5: non-diagnostic").

Results Healthy volunteers showed higher aortic elasticity determined by DCascending than patients with CHD or STEMI (7.81 ± 4.02 vs 2.76 ± 1.21 vs 4.48 ± 2.60 [10–3* mmHg]; $p < 0.001$) but did not differ form the other groups with respect on their PWVQA (3.59 ± 1.73 vs 3.06 ± 3.19 vs 2.25 ± 1.50 [m/s]). DCascending correlated inversely with age (r: –0.605; $p < 0.001$) and with the reference standard PWVTT (r: –0.538; $p < 0.005$) indicating good agreement between the 2 methods. Local PWVQA did not correlate with age (r: –0.159; p = n. s.) or PWVTT (r: –0.055; p = n. s.).

Interobserver agreement was high for the reference standard PWVTT (r: 0.915; $p < 0.001$) and for DCascending (r: 0.863; $p < 0.001$) but and only moderate for PWVQA (r: 0.398; $p = 0.003$).

STEMI and CHD patients differed from healthy volunteers in maximal achieved flow velocities (46.3 and 38.6 vs 70.8 [cm/s]; $p < 0.001$). In STEMI and CHD patients we achieved a significantly lower image quality than in healthy volunteers (3.4 and 3.4 vs 1.1; $p < 0.001$). Scored images quality correlated inversely with PWVQA (–0.326; $p < 0.01$).

Conclusion Local aortic DCascending but not PWVQA is a robust method for the assessment of local aortic parameters in STEMI patients. Reasons might be altered hemodynamics and lower image quality achieved in STEMI patients.

Diffuse Myocardial Fibrosis by Post-Contrast T1-Time is Closely Related to the Degree of Heart Failure in Heart Failure with Normal Ejection Fraction BAII

B. Marzluf, D. Bonderman, St. Pfaffenberger, E. Ringelspacher, M. Hülsmann, C. Tufaro, I. M. Lang, G. Maurer, R. Pacher, J. Mascherbauer
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Introduction Myocardial fibrosis is a histological hallmark of heart failure and an independent predictor of adverse outcome. Late gadolinium enhancement (LGE) by cardiac magnetic resonance (CMR) is a standard noninvasive tool for the identification of focal fibrosis. Diffuse fibrosis, however, cannot be quantified by LGE. Recently it was shown that diffuse myocardial fibrosis is strongly related to post-contrast longitudinal relaxation (T1) time. The aim of our study was to assess diffuse myocardial fibrosis by CMR T1 mapping in patients with serum NT-proBNP levels > 125 pg/ml and preserved left ventricular ejection fraction (EF ≥ 50%).

Methods 68 heart failure patients with normal ejection fraction and 4 healthy controls were prospectively evaluated. CMR studies

included the assessment of cardiac function and dimensions by standard cine sequences. Myocardial T1 mapping was performed 10 minutes after a gadolinium bolus using an inversion recovery sequence.

Results Serum NT-proBNP levels in patients ranged from 126 to 4239 pg/ml (mean 763 ± 864 pg/ml). Areas with LGE indicating local fibrosis in 5 patients were excluded from T1 analysis. Post-contrast T1 was significantly related to NT-proBNP ($r = –0.49$; $p < 0.0001$), EF ($r = 0.29$; $p = 0.013$) and cardiac output of the left ventricle ($r = 0.23$; $p = 0.049$). In patients with NT-proBNP levels > 500 pg/ml mean T1 was significantly shorter than in patients with NT-proBNP < 500 pg/ml (383.4 ± 55.5 vs 410.7 ± 31.0 ms; $p = 0.012$) and controls (494.0 ± 48.9 ms; $p < 0.001$). Furthermore, T1 was strongly related to degree of diastolic dysfunction by echocardiography ($p = 0.006$) and NYHA-functional class ($p = 0.003$) but independent of age, heart rate or renal function.

Conclusion Post-contrast T1 is highly correlated with NT-proBNP, cardiac function, and symptoms. Our data suggest that T1 mapping is a promising tool for the assessment of diffuse myocardial fibrosis. It appears to be closely linked to important prognostic parameters in heart failure patients.

Galectin-3: Relation to Infarction Scar and Myocardial Function After STEMI IV – 4

A. Mayr, G. Klug, K. Streil, B. Harrasser, M. Kremer, H.-J. Feistritzer, J. Mair, M. Schocke, O. Pachinger, B. Metzler
Radiologie I; Klinische Abteilung für Kardiologie, Medizinische Universität Innsbruck

Objectives Fibrosis after acute myocardial infarction (AMI) is the leading cause of heart failure and results in late enhancement of scar by cardiac magnetic resonance imaging (CMR). Galectin-3 is suggested to be involved in the development of heart failure appearing to directly mediate profibrotic pathways. The relationship between galectin-3 and the extent of myocardial infarction scar is unknown.

Methods 29 AMI patients (n = 29, mean age: 58.1 ± 10.1 yrs, 3 female) successfully reperfused by primary angioplasty underwent a 4-month (4-mo) follow-up CMR at a median of 125 days (range: 92–200 days) after the index event. Blood samples were routinely drawn at baseline and follow-up. Galectin-3 was determined from serum samples drawn at the follow-up.

Results 4-mo galectin-3 values (mean 12.29 ± 4.56 ng/ml) correlated significantly with 4-mo infarct size ($r: 0.406$; $p = 0.036$), with 4-mo NT-proBNP concentrations ($r: 0.420$; $p = 0.023$) as well as with 4-mo creatinin levels ($r: 0.486$; $p = 0.016$).

Patients with 4-mo galectin-3 concentrations above the median level of 10.86 ng/ml presented significant impaired 4-mo left ventricular ejection fractions (57.9 ± 8.3% vs 65.1 ± 5.8%; $p = 0.011$), larger mid-term infarct sizes (15.6 ± 7.8% vs 8.9 ± 6.1%; $p = 0.022$) as well as higher 4-month NT-proBNP concentrations (642.6 ± 666.0 ng/l vs 261.4 ± 183.1 ng/l; $p = 0.042$) than patients with galectin-3 concentrations below 10.86 ng/ml.

Conclusion Elevated galectin-3 levels 4 months after AMI are associated with larger infarct sizes, lower global myocardial function as well as with higher concentrations of NT-proBNP, highlighting the potential of galectin-3 as a biomarker of adverse remodeling after AMI.

Wertigkeit der Akut-Echokardiographie bei Patienten mit NSTEMI IV – 10

W. Weihs, V. Weihs, H. Schuchlenz, St. Harb, D. Botegal, G. Waltl, P. Zechner
Department für Kardiologie und Intensivmedizin, Landeskrankenhaus Graz-West

Einleitung Die Beurteilung des kardiovaskulären Risikos bei Patienten mit akutem Koronarsyndrom (ACS) ohne anhaltende ST-Hebung (NSTE) erfolgt in der Regel anhand des klinischen Status, der Anamnese, des Elektrokardiogramms (EKG) sowie der Biomarker. Die Durchführung einer Echokardiographie wird von der European Society of Cardiology (ESC) bei allen Patienten mit NSTE-ACS empfohlen. Die Wertigkeit der Echokardiographie ist jedoch zum gegebenen Zeitpunkt nicht eingehend untersucht bzw. validiert. Das Ziel der retrospektiven Studie war, die Ergebnisse der Echokardiographie bei Patienten mit erstem NSTEMI (NSTE-ACS + Troponinerhöhung) zu analysieren und mit den Ergebnissen der Koronarangiographie zu korrelieren.

Material und Methode Im Zeitraum 13 Monaten wurden von insgesamt 193 konsekutiven Patienten mit NSTEMI 51 Patienten aufgrund einer kardialen Vorerkrankung (14 PCI, 23 CABG, 14 STEMI/NSTEMI) und 24 aufgrund einer auswärts durchgeführten Echokardiographie ausgeschlossen. Bei den verbleibenden 118 Patienten wurden die Ergebnisse der Echokardiographie, des EKGs und der Koronarangiographie retrospektiv analysiert. Die echokardiographische Wandbewegungsanalyse (WMA) erfolgte anhand des 17-Segmentemodells, welche entweder dem anterioren, lateralen oder inferioren Versorgungsgebiet zugeordnet wurden. Die EKG-Veränderungen (ST-Senkung, T-Negativierung) wurden ebenfalls der anterioren (V1-V4), lateralen (V5, V6, I, aVL) und inferioren (II, III, aVF) Versorgung zugeordnet.

Ergebnisse Unter den 118 Patienten im Alter von 66,8 ± 10,3 Jahren (38–90 Jahre) befanden sich 42 Frauen und 76 Männer. Die Koronarangiographie erfolgte in 71 % < 24 h und in 91 % < 48 h nach dem Erstkontakt, wobei 56 Patienten (47 %) eine Ein-, 25 (21 %) eine Zwei-, 23 (19 %) eine Dreigefäßerkrankung, 10 (8 %) eine Hauptstammstenose und 4 (3 %) eine diffuse Koronarsklerose hatten. Bei 43 Patienten (36 %) fand sich der Verschluss zumindest eines Koronargefäßes. In 91 Fällen erfolgte eine PCI (davon in 29 Fällen > 1 Gefäß), in 16 Fällen ein CABG und in 11 Fällen eine konservative Behandlung.

Das EKG war bei 67 Patienten (57 %) unauffällig bzw. nicht interpretierbar (SM, LSB). Bei den übrigen Patienten gelang die Zuordnung der EKG-Veränderungen zum Versorgungsgebiet der betroffenen Koronargefäße lediglich in 55 %.

Die Echokardiographie wurde in 81 % < 24 h und in 96% < 48 h nach dem Erstkontakt und in 95 % < 24 h vor der Koronarangiographie vorgenommen. Die WMA war bei 34 Patienten (29 %) normal, bei 76 (64 %) pathologisch und bei 8 (7 %) nicht beurteilbar. Die regionalen Wandbewegungsstörungen zeigten in 83 % eine Übereinstimmung mit dem Versorgungsgebiet der betroffenen Koronargefäße. Bei Vorliegen von regionalen Wandbewegungsstörungen in mehreren Versorgungsgebieten fand sich in 77 % und bei Vorliegen einer hochgradig reduzierten Linksventrikelfunktion (LVEF < 30 %) in 95 % eine koronare Mehrgefäßerkrankung und/oder Hauptstammstenose.

Diskussion Patienten mit NSTEMI weisen ein sehr heterogenes kardiales Risiko auf, welches mit den herkömmlichen diagnostischen Tools, wie Klinik, EKG oder Biomarker, nur unzureichend abgeschätzt werden kann. Die Echokardiographie erlaubt eine Beurteilung des Ausmaßes und Lokalisation der Ischämie und stellt damit eine wertvolle Information vor der Intervention dar. Eine orientierende Echokardiographie sollte daher bereits zu einem sehr frühen Zeitpunkt, beispielsweise in der Notaufnahme, vorgenommen werden.

Does the Integration of Personalized Ultrasound Change Patient Management in Critical and Acute Care Medicine? IV – 3

P. Zechner, M. Campo dell' Orto, H. V. Groesdonk, F. H. Seeger, W. Weihs, R. Breitkreutz
Department of Internal Medicine, LKH Graz-West, Austria; Department of Cardiology, Kerckhoff Heart Centre Bad Nauheim; Critical Care Unit, Department of Cardiovascular Surgery, Department of Anaesthesiology, Intensive Care and Pain Therapy University of the Saarland, Medical Faculty Homburg (Saar); Department of Cardiology, Johann Wolfgang Goethe University Hospital Frankfurt am Main, Germany

Objective The aim of our study was to test the influence of personalized ultrasound (PersUS) on patient management in critical and acute care medicine.

Materials and Methods This was a prospective multicentre study in acute and critical care medicine with a total of 640 patient

ultrasound exams including 548 focused diagnostic exams and 92 interventional procedures. Five distinct sub-studies were conducted. Sub-study 1 tested, if the availability of PersUS increases the frequency of use during work shifts in an intensive care environment. The access to the PersUS device was determined randomly and the implementation pattern of PersUS, the types of indications and estimated duration of use during all work shifts were analyzed. Sub-study 2 investigated if PersUS is comparable to a high-quality mobile ultrasound device in terms of image quality and planning of selected interventions (puncture of pleural, pericardial or abdominal effusions or the urinary bladder) in intensive care patients. Sub-study 3: Four critical care physicians studied PersUS for planning an execution of ultrasound-guided needle punctures such as pleural, pericardial, abdominal or urinary bladder punctures for evacuation of fluid or inserting catheters (pleurocath, pigtail or suprapubic). They used linear analogue self-assessment to obtain semi-quantitative data of the physician's impression of (i) diagnostic quality and (ii) visual support in ultrasound-guided interventions. Sub-study 4 assessed the influence of PersUS integration on the duration of a quick-check physical examination in the emergency department. A single emergency physician used PersUS after randomisation in patients with dyspnea, thorax pain, abdominal pain or hypotension. Finally, any influence on patient management or additional information obtained due to PersUS was noted. Sub-study 5 analyzed the influence of the availability of a PersUS device during ward rounds. The PersUS device was available during wards rounds on a random basis and time between beginning and end of ward rounds was measured as well as the number of patients seen, type and length per ultrasound exam. All data was then sorted into Group A (control group) or Group B (examination with PersUS).

Results The randomized availability of PersUS increased its application in ICU work shifts more than twofold from 33 to 68 exams mainly for the detection and therapy of effusions **(Figure 24)**. Image quality and decision making was as effective as when using high-quality mobile ultrasound in a variety of intensive care patients. Diagnostic and procedural quality was rated as excellent/very good in PersUS-guided puncture in 95% of cases. In an initial quick-check physical examination of 48 randomized cases in an emergency department, PersUS extended the examination time by 100 seconds **(Figure 25a)**. However, a change of management in 6/22 (27%) cases as well as valuable additional information for immediate recognition of underlying disease in 19/22 (86%) patients was registered by the examiner. PersUS integration into 53 randomized regular ward rounds reduced average contact time per patient by 103 seconds from 8.9 to 7.2 minutes and lowered the patient referral rate to an echo lab from 20% to 2% within the study population **(Figure 25b)**.

Conclusion PersUS can be easily integrated into daily routine work of acute and critical care medicine with high diagnostic and procedural quality with few time constraints.

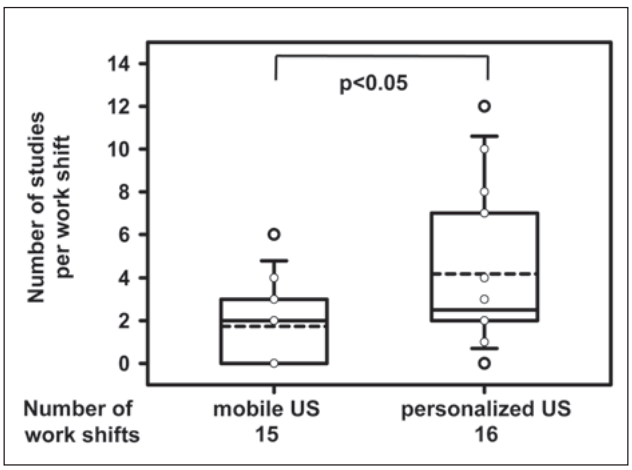


Figure 24: P. Zechner et al.

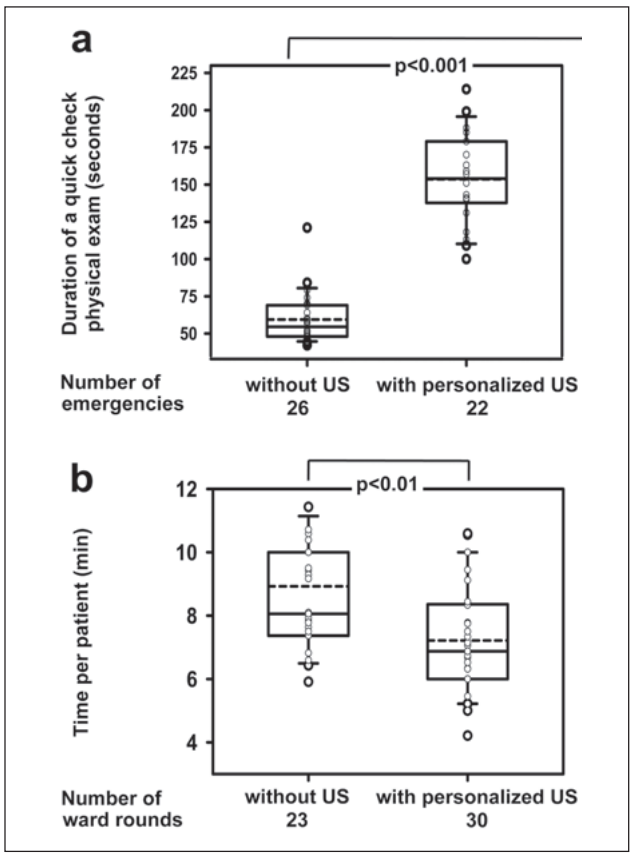


Figure 25: P. Zechner et al.

Chirurgie/Surgery

Institutional Experience with the Heartware and Heartmate II Left Ventricular Assist Device BAII

St. Mahr, F. Eskandary, J. Horvath, A. Rajek, G. Laufer, H. Schima, D. Zimpfer
Abteilung für Herzchirurgie, Medizinische Universität Wien

Background Left ventricular assist device (LVAD) implantation has become a routine therapy for patients with end-stage heart failure. This study was designed to evaluate our institutional experience with the Heartware (HVAD) and Heartmate II (HMII) LVAD in patients with end-stage heart failure.

Patients and Methods From March 2006 to January 2012 a total of 83 (male 84.1%) patients (mean age 52 ± 12 yrs.) with terminal heart failure received either a HVAD LVAD (n = 56) or a HMII LVAD (n = 27) at our department as bridge to transplant or chronic implant. Study endpoints were 30-day and in-hospital mortality. Long-term survival on the LVAD and bridge to transplant success as well differences between the 2 systems were calculated by Kaplan-Meier analysis.

Results Patients receiving a HVAD and HMII LVAD were comparable with regard to patient characteristics. Mean support time was 353 ± 400 days. Of the 83 patients included in the present analysis, 29.3% underwent cardiac transplantation, 14.6% expired on the LVAD and 56.1% continue to receive LVAD support. Thirty day (overall 6.1%; HVAD 3.6% vs HMII 13%, p = 0.149) and in-hospital mortality (overall 7.3%; HVAD 5.7% vs HMII 13%, p = 0.359) were comparable between the 2 systems. Survival or bridge to transplant success was 90% at 12 (HVAD 83.4% vs HMII 91%, log-rank = 0.114) and 85% at 24 months (HVAD 81.3% vs HMII 91%, log-rank = 0.114) respectively.

Conclusion Left ventricular assist devices have developed as an excellent treatment option for patients with terminal heart failure. The observed survival rates at 1 and 2 years challenge the results of cardiac transplantation.

Diverse/Miscellaneous

Pulswellengeschwindigkeitsmessung als prädiktiver Marker für die Entwicklung einer koronaren Herzkrankheit bei gesunden Probanden mit mindestens einem vorbekannten kardiovaskulären Risikofaktor (Comet-K-Projekt „BioPersMed") V – 7

C. Colantonio, G. Steiner, S. Pätzold, E. Kraigher-Krainer, A. Schmidt, B. Pieske
Klinische Abteilung für Kardiologie, Medizinische Universität Graz

Hintergrund Die Risikostratifikation asymptomatischer Patienten mit erhöhtem kardiovaskulären Risiko ist nach wie vor unzureichend. Etablierte Score-Systeme (z. B. EuroSCORE) stützen sich großteils auf klassische Risikofaktoren wie arterielle Hypertonie, Hyperlipidämie, Adipositas, chron. Nikotinabusus, Diabetes mellitus etc. Die Pulswellengeschwindigkeit („pulse wave velocity", PWV) an A. carotis und A. femoralis – als potenzieller prädiktiver Marker für die Früherkennung einer koronaren Herzkrankheit – wurde bislang unzureichend evaluiert.

Methodik In der K-Projekt-Kohorte (Comet-Projekt, „BioPersMed") werden seit Ende 2010 prospektiv 1000 Probanden mit kardiovaskulären Risikofaktoren, aber noch keinem atherosklerotischen Ereignis eingeschlossen und longitudinal nachbeobachtet. Neben einer umfassenden kardiovaskulären Phänotypisierung (u. a. Echokardiographie, Spiroergometrie) erfolgt die Erfassung der Endothelfunktion und der Mikrozirkulation mittels Pulswellenanalyse (A. radialis) und Pulswellengeschwindigkeitsmessung (A. carotis und A. femoralis) mittels SphygmoCor-Gerät.

Ergebnisse In einer Pilotstudie zu Zeitaufwand, Untersuchungsablauf und Compliance wurden seit Dezember 2010 240 Probanden eingeschlossen (105 Männer, 135 Frauen, Alter zwischen 45 und 75 Jahren).

In der Rangkorrelation nach Spearman zeigten sich signifikante Zusammenhänge zwischen klassischen Risikofaktoren, Parametern in Spiroergometrie sowie Echokardiographie und erhöhten Pulswellengeschwindigkeiten ($p < 0,05$ = signifikant).

Probanden mit einem BMI > 25,0 ($p < 0.001$) sowie Probanden mit einer HBA_{1c} > 6,0 ($p = 0,001$) zeigten erhöhte Pulswellengeschwindigkeiten im Vergleich zu Probanden mit BMI < 25,0 und HBA_{1c}-Werten < 6,0.

Manifeste Diabetiker ($p = 0,018$) sowie manifeste Hypertoniker ($p = 0,002$) haben eine deutlich höhere Pulswellengeschwindigkeit als gesunde Probanden.

Probanden mit diastolischer Ventrikelfunktionsstörung hatten signifikant erhöhte Pulswellengeschwindigkeiten ($p = 0,015$). Je größer E/é, desto schneller wurde auch die Pulswellengeschwindigkeit. Insbesondere konnte eine signifikante Korrelation zwischen E/é bzw. Vorhofgröße und Pulswellengeschwindigkeit beobachtet werden ($p = 0,012$).

Schlussfolgerung Unsere Daten an vermeintlich gesunden Probanden zeigen, dass die Pulswellengeschwindigkeit an den großen Gefäßen bereits in erheblichem Maße pathologisch verändert ist. Dies deutet auf einen direkten Zusammenhang zwischen „Steifigkeit des Herzens" und „Steifigkeit der Gefäße" hin.

Die Wertigkeit der PWV als Frühmarker zur Detektion kardiovaskulärer Ereignisse ist Gegenstand aktueller Studien.

Pulswellengeschwindigkeitsmessung, Echokardiographie und Spiroergometrie als Frühmarker zur Detektion eines kardiovaskulären Remodellings V – 8

C. Colantonio, G. Steiner, S. Pätzold, E. Kraigher-Krainer, A. Schmidt, B. Pieske
Klinische Abteilung für Kardiologie, Medizinische Universität Graz

Hintergrund Bisher findet die Spiroergometrie ihren Platz zur Beurteilung der Ausdauerleistungsfähigkeit, zur Messung des Energiestoffwechsels während körperlicher Belastung und zur Untersuchung der Leistungsfähigkeit des kardiopulmonalen Systems, inklusive Abklärung einer möglichen koronaren Herzkrankheit.

Die Evaluierung, ob sich kardiovaskuläre Risikofaktoren, Gefäßsteifigkeit und subklinisches kardiovaskuläres Remodelling bereits im Frühstadium in der kardiopulmonalen Leistungsfähigkeit widerspiegeln, erfolgte bisher unzureichend.

Hierzu wird der Zusammenhang zwischen Spiroergometrie und Pulswellengeschwindigkeit („pulse wave velocity", PWV) an A. carotis und A. femoralis untersucht.

Methodik Seit Dezember 2010 werden prospektiv 1000 Probanden mit kardiovaskulären Risikofaktoren (art. Hypertonie, Hyperlipidämie, Diabetes mellitus, chron. Nikotinabusus etc.), aber noch ohne manifeste koronare Herzkrankheit eingeschlossen und longitudinal nachbeobachtet. (K-Projekt-Kohorte; Comet-Projekt, „BioPersMed").

Im Rahmen der Einschluss-Untersuchungen erfolgt eine umfassende kardiovaskuläre Phänotypisierung (u. a. Echokardiographie, Intima/Media-Messung an Karotiden), die Erfassung der Endothelfunktion und der Mikrozirkulation mittels Pulswellenanalyse (A. radialis) und Pulswellengeschwindigkeitsmessung durch das SphygmoCor-Gerät sowie die Evaluierung der Leistungsfähigkeit mittels Spiroergometrie.

Ergebnisse Seit Dezember 2010 konnten im Rahmen einer Pilotstudie 240 Probanden (105 Männer, 135 Frauen, Alter zwischen 45 und 75 Jahren) untersucht werden.

Die Pulswellengeschwindigkeit (PWV) korrelierte positiv mit dem VE/VCO_2-Slope ($r = 0,287$; $p = 0,010$) und negativ mit der maximalen Sauerstoffaufnahme ($peakVO_2$; $r = –0.470$; $p < 0,001$). Das bedeutet je höher VE/VCO_2-Slope, desto schneller die PWV und je höher die $peakVO_2$, desto langsamer die PWV.

In der Echokardiographie zeigte sich, dass Probanden mit diastolischer Ventrikelfunktionsstörung höhere Pulswellengeschwindigkeiten haben als diejenigen mit normaler diastolische Ventrikelfunktion ($r = 0,241$; $p = 0,015$).

Je größer E/é, desto schneller auch die PWV und desto höher der Augmentationsindex ($p = 0,011$).

Zwischen der Dicke der posterioren Wand des linken Ventrikels und der PWV fand sich ebenfalls eine positive Korrelation ($r = 0,228$; $p = 0,021$).

Schlussfolgerung Unsere Daten an vermeintlich gesunden Probanden zeigen, dass sich die „Steifigkeit des Herzens" und die „Steifigkeit der Gefäße" bereits lang vor der Manifestation einer KHK zeigen und dass sich dies auch in der kardiopulmonalen Leistungsfähigkeit widerspiegelt.

Die Wertigkeit der PWV in Kombination mit der Spiroergometrie als Frühmarker zur Detektion einer Veränderung der kardiopulmonalen Leistungsfähigkeit sowie als Zeichen eines subklinischen kardiovaskulären Remodellings ist Gegenstand aktueller Studien.

Health-Related Quality of Life, Anxiety and Depression After PCI: Restoring a State of Equilibrium V – 6

O. Friedrich, G. Gaul, S. Höfer, J. Sipötz
Klinik für wissenschaftliche Forschung in der interventionellen Kardiologie, Hanusch-Krankenhaus, Wien

Purpose Our study aims to describe the relation of Health-Related Quality of Life (HRQoL) and Anxiety and Depression after PCI in NSTEMI patients over a 24-month follow-up period. In order to explore the potential of HRQoL and Depression/Anxiety scores as prognostic tools for adverse outcome or monitoring instruments we focus on the change in individual patients.

Methods 159 NSTEMI PCI patients (73.0% men; age: 63.8, SD: 9.2) at 7 centers in Austria completed the HADS anxiety/depression and the MacNew HRQoL questionnaire before discharge and 1, 6, 12 and 24 months after discharge.

Results MacNew HRQoL and HADS Anxiety and Depression scores are negatively correlated. Over the whole observational pe-

riod this correlation could be well described by a linear regression with MacNew Global score as dependent and HADS Total score (= HADS Anxiety + HADS Depression) as independent variable ($p < 0.001$). The coefficient of determination (R^2) of the regression equation increases drastically from 0.43 at the baseline to a level between 0.66 and 0.77 in the follow-up period (1M: 0.68; 6M: 0.77; 12M: 0.66; 24M: 0.70), which means that while at the baseline HADS Total score could explain 43% of the variance of MacNew Global score in the follow-up period between 66% and 77% could be explained.

To understand the drastic increase of the coefficient of determination it is helpful to refer to the fact that clinically relevant increase in MacNew Global score of more than 0.5 takes place in 50–60% of the patients. About one third of the patients remain stable and in about 10% a decrease of 0.5 or more is found.

Looking at the development of the regression equation for clinically relevant improving and stable patients separately it becomes clear why the increase of the explanatory power of the linear regression equation takes place: **Figure 26** shows the situation at the baseline (a) and the situation after 6 months (b). The smaller R^2 at the baseline results from a merging of 2 distinct groups, the (i) clinically relevant improving patients (brown) and (ii) stable patients (green). The coefficient of determination R^2 increases in the follow-up period because the improving patients move towards the stable patients.

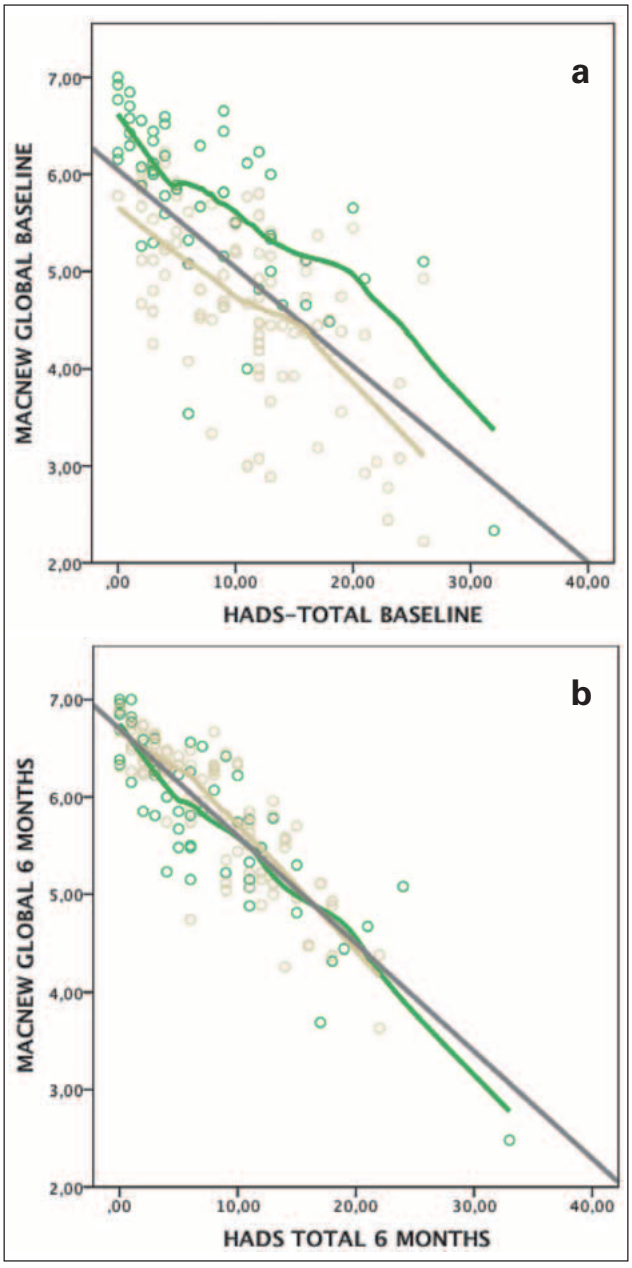


Figure 26: O. Friedrich et al.

Conclusion Our data suggest that the regression equation in the follow-up period describes a state of equilibrium: a certain degree of Quality of Life is reflected by a certain degree of mental distress. At the baseline, the manifestation of the coronary disease and/or the conditions of treatment cause an imbalance between these variables – maybe because of different temporal patterns of change in HRQoL and Anxiety and Depression scores. But not all patients experience this imbalance: it seems obvious that the improving patients must have deteriorated in the first place. We assume that the stable patents have not experienced such deterioration and are therefore not improving in the follow-up period.

In order to use MacNew and HADS as monitoring and/or prognostic tools it seems promising to refer to the state of equilibrium to define expectancy values for single patients. This approach combines MacNew and HADS and takes in consideration that more than a third of the patients seem to experience no clinically relevant change in HRQoL after PCI.

The High-Sensitive Cardiac Troponin T (hs-cTnT) Assay is Superior to its Previous Assay Generation for the Prediction of 90-Day Clinical Outcome in Ischemic Stroke XIV – 1

M. Furtner, Th. Ploner, A. Hammerer-Lercher, St. Kiechl, O. Pachinger, J. Mair
Universitätsklinik für Neurologie; Universitätsklinik für Innere Medizin III/Kardiologie; Zentralinstitut für Labordiagnostik, Medizinische Universität Innsbruck

Background Cardiac troponin T (cTnT) has been shown previously to be a predictor of stroke outcome with decision limits in the low measuring range of the assay. Recently a new high-sensitivity assay generation (hs-cTnT) has been introduced which is characterized by improved analytical sensitivity and better precision at the low measuring range. Because of more accurate measurement of low troponin concentrations, we hypothesized that this assay may be superior to its previous assay generation for prediction of stroke outcome.

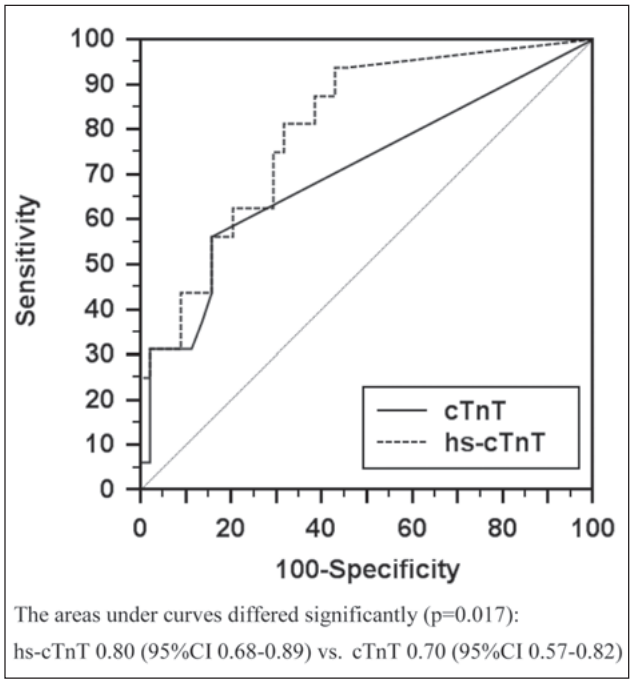


Figure 27: M. Furtner et al. Receiver operating characteristics curves for prediction of 90-day outcome in ischemic stroke.

Materials and Methods cTnT was measured by assays from Roche Diagnostics® on emergency department admission in 60 consecutive patients (35 males, age 69.4 ± 13.9 years) with ischemic stroke who were subsequently admitted to our hospital's stroke unit from beginning of March to end of April 2010. The clinical 90-day outcome of ischemic stroke patients was analyzed using the Austrian stroke registry. We used the modified Rankin scale (mRS) and Barthel index (BI) as outcome measures and defined adverse outcomes as mRSe ≥ 3 (indicating dependence or death) and/or BI < 75 points.

Results Stroke etiology was microangiopathy in 3, macroangiopathy in 17, cardiac embolism in 26, dissection in 1 and unknown in 13 patients. At 90-day follow-up, 16 (27%) patients had an adverse outcome. Receiver operating characteristic curve (ROC) analysis of the predictive performances yielded a significant better performance of hs-cTnT vs cTnT (**Figure 27**; area under curve: 0.80 vs 0.70; p = 0.017). The optimal discriminator values were 11 ng/L (detection limit of the old cTnT assay 10 ng/L) and 5.1 ng/L (detection limit of the hs-cTnT assay 5 ng/L), respectively, with the following characteristics: sensitivity 56 vs 94%, specificity 84 vs 57%, positive predictive value 57 vs 45%, and negative predictive value 84 vs 96%.

Conclusion The improvements in cTnT assay analytical sensitivity and assay precision at the low measuring range resulted in a significant improvement of cTnT as a predictor of outcome in ischemic stroke, particularly in respect of negative predictive value, for ruling out worse outcome.

Mitochondriopathie als seltene Ursache eines kardialen hypertrophen Phänotyps – ein Fallbericht XIV – 2

P. Hörmann, Ch. Fauth, J. Zschocke, S. Bösch, O. Pachinger, G. Pölzl
Abteilung für Innere Medizin III, Humangenetik, Neurologie, Medizinische Universität Innsbruck

Der Patient wurde im Alter von 36 Jahren zur Abklärung einer hypertrophen Kardiomyopathie vorgestellt, welche anlässlich einer kürzlich vorausgegangen kardialen Dekompensation erstmalig diagnostiziert wurde. Es bestand bereits seit ca. 3 Jahren eine zunehmende Leistungseinschränkung. An Vorerkrankungen konnte eine bilaterale Innenohrschwerhörigkeit mit Hörgerätversorgung seit dem 24. Lebensjahr, ein relativer Kleinwuchs sowie ein insulinpflichtiger Diabetes mellitus (ED mit 21 Jahren) erfasst werden. Weiters bestand eine okuläre Apraxie, eine mehrmals wöchentlich auftretende Cephalea sowie Z. n. fraglicher TIA. Klinisch fand sich kein Hinweis auf eine Myopathie. Die Mutter des Patienten verstarb relativ jung an einem Schlaganfall, ein Bruder des Patienten hat ebenfalls einen insulinpflichtigen Diabetes mellitus.

Echokardiographisch zeigte sich eine asymmetrische linksventrikuläre Hypertrophie ohne nachweisbare intrakavitäre Obstruktion. Die systolische LVF war deutlich eingeschränkt. In der Koronarangiographie fand sich eine wirksame Stenose eines diagonalen Astes, die Füllungsdrücke waren normal. Eine kardiale Amyloidose konnte bioptisch ausgeschlossen werden.

Die Befundkonstellation – Kardiomyopathie, insulinpflichtiger Diabetes mellitus, okuläre Apraxie, relativer Kleinwuchs, erhöhtes Laktat im Serum und Laktatpeaks in der zerebralen MRT-Spektroskopie – war hinweisend auf eine Mitochondriopathie. Die histopathologische Aufarbeitung der Endomyokardbiopsie unterstützte diese Vermutung. Die molekulargenetische Mutationsanalyse der aus dem Herzmuskelgewebe gewonnenen mitochondrialen DNA ergab eine Mutation im Gen der t-RNA für Leucin (MTTL1-Gen), m.3243A > G. Diese Mutation ist in Zusammenhang mit verschiedenen syndromalen und nicht-syndromalen Mitochondriopathien (insbesondere MELAS, Mitochondrial Encephalomyopathy, Lactic acidosis, Stroke-like episodes) beschrieben. Da die diagnostischen Kriterien für ein MELAS-Syndrom nur teilweise erfüllt waren, wurde die Diagnose einer Mitochondriopathie mit Kardiomyopathie, Schwerhörigkeit, Diabetes mellitus und okulärer Apraxie gestellt.

Eine ursächliche Therapie für diese Erkrankung ist derzeit nicht verfügbar. Manche Patienten profitieren von einer medikamentösen Therapie mit Coenzym Q10. Die Gabe bestimmter Medikamente ist kontraindiziert bzw. sollte nur unter entsprechenden Vorsichtsmaßnahmen erfolgen (z. B. Propofol, Valproin-Säure). Nach Verbesserung der LV-Funktion unter neurohumoraler Therapie ist der Patient dzt. in einem klinisch stabilen Zustand.

Der präsentierte Fall unterstreicht die Notwendigkeit einer exakten syndromologischen Charakterisierung von Patienten mit kardial hypertrophem Phänotyp sowie die Wichtigkeit der interdisziplinären Zusammenarbeit zur Diagnosefindung.

Furosemide-Induced Severe Hypokalemia with Rhabdomyolysis Without Dysrhythmia V – 4

W. Ruisz, C. Stöllberger, J. Finsterer, F. Weidinger
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Background and Objectives Hypokalemia induced by diuretic abuse is a life-threatening emergency.

Case Report A 22-year-old female nurse with a BMI of 18 suffered from myalgias, vomiting and diarrhea. Blood tests revealed hypokalemia with a lowest value of 1.1 mmol/l, moderate hyponatremia, metabolic alkalosis, mild renal insufficiency and CK elevation. The electrocardiogram showed ST-segment abnormalities and a prolonged QT interval. Since hypokalemia and alkalosis were unexplained, she was asked for diuretic-intake. She confessed that she has taken 250 mg furosemide/day for the last 4 months to improve the shape of her muscles, which she received from a physician attending the gym where she exercised. After electrolyte substitution, laboratory and electrocardiographic abnormalities regressed and no dysrhythmias were observed. Psychiatric investigation diagnosed an adjustment disorder.

Conclusion Furosemide abuse has to be considered even in underweight individuals, especially if they have a psychiatric instability or work in health care institutions. Gym-operators should be informed about the possibility of severe side effects from chronic furosemide abuse and non-indicated uncontrolled misuse has to be prohibited by responsible authorities.

Diagnostic and Therapeutic Yield of a Geriatric Assessment in Elderly Patients with Severe Aortic Stenosis Considered for Endovascular Valve Replacement: Filling Hidden Gaps of Care V – 3

Th. Schickmaier, F. Landertshammer-Gugler, J. Aichinger, Ch. Ebner, V. Eder, R. Steringer-Mascherbauer, J. Niel, W. Tkalec, Th. Sturmberger, H.-J. Nesser, H. Koller
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Aortic stenosis is almost exclusively a disease of the elderly. Older age is also associated with a significant burden of comorbidity and specific geriatric care issues. These often called "geriatric syndromes" interfere with older adults' abilities to perform basic daily activities, threaten their independence and lower their quality of life. A geriatric assessment might identify coexisting health problems and support cardiologists in treatment decisions and managing these patients.

Methods The goal of the study was to evaluate the diagnostic and therapeutic yield of a geriatric assessment through a standardized, evidence based protocol in elderly patients with severe aortic stenosis considered for aortic valve replacement for so far undetected geriatric care issues. The test instruments used included the MNA©, ADLs, IADLs, GDS, Timed Get up&Go, Chair Rising Test, the Mini Cog©, Frieds Frailty criteria and the Carlson Morbidity score.

Based on the assessment, a geriatric problem list and treatment plan was developed using a standardized intervention plan, and patients were stratified into performance categories defined as Healthy/'GoGo', Vulnerable/'SlowGo' or Frail/'NoGo'.

Results and Discussion The median number of interventions based on the geriatric assessment of 117 patients (age 81.7 ± 5.6) was 2 ± 1.4 (range 0–6), with 75 (63%) patients receiving 2 or more

interventions. Interventions most commonly suggested were medication modification (38%), physical therapy (23%) and neurocognitive evaluation (17%), followed by psychiatric evaluation (7%), dietology referral (7%), social services referral (3%) and incontinence evaluation (3%).

27 (22%) patients were classified as Frail/'NoGo', 39 (33%) as Healthy/'GoGo' and 51 (45%) as Vulnerable/'SlowGo'.

Conclusion In our cohort of geriatric patients with severe aortic stenosis considered for endovascular valve replacement, geriatric care issues and the need for interventions identified by a geriatric assessment were common. Based on the assessment 22% of the patients were stratified as physically 'frail'. Although the effects of multidisciplinary interventions have not been evaluated in this study, our findings underline the burden of geriatric care issues in patients considered for endovascular valve replacement and suggest that a specialist team approach is more likely to reach optimal treatment outcomes.

Bestehen zwischen Labortests und Schnelltests zum Nachweis von D-Dimeren Unterschiede der Produktsicherheit? – Analyse der bis Ende 2010 vom BfArM erhaltenen Meldungen V – 1

R. Siekmeier, D. Wetzel
Bundesinstitut für Arzneimittel und Medizinprodukte, Bonn, Deutschland

Einleitung Seit Implementierung der Richtlinie 98/79/EG zu In-vitro-Diagnostika (IVD) müssen Vorkommnisse und korrektive Maßnahmen zu IVD den zuständigen Behörden gemeldet werden. Für fast alle IVD ist dies das BfArM (einige Produkte aus Anhang II A und B der Richtlinie 98/79/EG fallen in die Zuständigkeit des Paul-Ehrlich-Instituts). Ziel der Studie war die Analyse der Meldungen zu D-Dimertests.

Material und Methoden Analysiert wurden alle von Anfang 1999 bis Ende 2010 eingegangenen Meldungen bezüglich Meldequelle, Patientenschädigung (PS), Häufigkeit/Art von Produktfehlern bzw. korrektiven Maßnahmen.

Ergebnisse Von 2851 Meldungen zu IVD betrafen 190 IVD zur Untersuchung der Gerinnung (6,7 % aller Meldungen zu IVD), davon 99 Tests, Kits und Reagenzien zum Gebrauch durch professionelle Anwender (3,5 %), 26 Analysengeräte und deren allgemeines Verbrauchsmaterial (0,9 %) sowie 65 Gerinnungsselbsttests (Geräte und Teststreifen, 2,3 %). Von den 99 Meldungen zu Gerinnungstests zum Gebrauch durch professionelle Anwender betrafen 14 Schnelltests (ST) und 11 Labortests (LT) zur Bestimmung von D-Dimeren. Meldungen zu ST kamen meist von Herstellern (12), seltener Behörden (1) und Anwendern (1). Auch bei LT überwogen Herstellermeldungen (6/4/1). Ein PS lag in 3 Fällen (alle ST) vor. Bei ST fand sich nur in 1 Fall (7,1 %) ein Produktfehler (Materialfehler). Kein Produktfehler bzw. Anwenderfehler fanden sich in 3 bzw. 2 Fällen. In 8 Fällen (57,1 %) blieb die Ursache unklar, da ST der Anwender nicht mehr zur Verfügung standen und Rückstellmuster eine normale Funktion zeigten. Bei LT fanden sich in 10 Fällen (90,1 %) Produktfehler, meist Produktionsfehler (6); in 1 Fall lag kein Produktfehler vor. Korrektive Maßnahmen erfolgten bei ST nur in 1 Fall (7,1 %; u. a. Rückruf). Bei LT erfolgten in 5 Fällen (45,5 %) korrektive Maßnahmen in D (5 weitere nur außerhalb D, da Produkt dort nicht im Verkehr). Bei den Maßnahmen in D handelte es sich (Mehrfachnennungen) meist um Kundeninformationen (5, obligat bei Rückruf), Änderungen in Produktion/Qualitätsmanagement (5) und Rückruf (4).

Diskussion Meldungen zu D-Dimertests stellen eine wichtige Untergruppe der Meldungen zu Gerinnungstests und -reagenzien zum Gebrauch durch professionelle Anwender dar. Die Untersuchung auf mögliche Fehlerursachen wird vor allem bei ST durch das Fehlen von Patientenproben und Teststreifen der Anwender erschwert. Als Folge der geringen Häufigkeit nachgewiesener Produktfehler finden sich bei ST seltener korrektiver Maßnahmen. Art und Häufigkeit von Produktfehlern und korrektiven Maßnahmen bei LT zur Bestimmung von D-Dimeren sind wesentlich häufiger und entsprechen denen anderer Labortests zur Gerinnungsdiagnostik. Die erhaltenen Ergebnisse zeigen deutliche Unterschiede zwischen ST und LT und belegen die Notwendigkeit und Funktion des bestehenden Systems der Marktüberwachung zur Sicherstellung und Verbesserung der Produktsicherheit von IVD.

Häufigkeit und Art von Produktfehlern und Patientenschädigungen bei Systemen zur Gerinnungsselbstmessung – Analyse der 1999 bis 2010 vom BfArM erhaltenen Meldungen V – 5

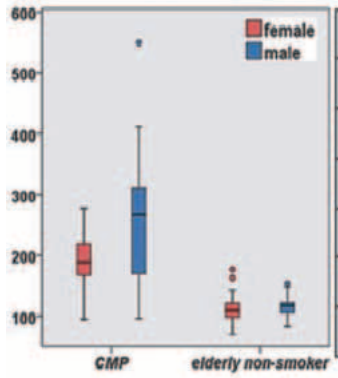
R. Siekmeier, D. Wetzel
Bundesinstitut für Arzneimittel und Medizinprodukte, Bonn, Deutschland

Einleitung Seit Implementierung der Richtlinie 98/79/EG zu In-vitro-Diagnostika (IVD) sind Vorkommnisse und korrektive Maßnahmen zu IVD den zuständigen Behörden zu melden. In Deutschland ist dies für fast alle IVD das BfArM (einige Produkte der Immunhämatologie und Infektiologie aus Anhang II A und B der Richtlinie 98/79/EG fallen in die Zuständigkeit des Paul-Ehrlich-Instituts [PEI]; zuständige Behörde für alle IVD in Österreich: BASG). Ziel dieser Studie war die Analyse der Meldungen zu Gerinnungsselbsttests (Geräte und Teststreifen) zum Gebrauch durch Patienten.

Material und Methoden Analysiert wurden sämtliche im Beobachtungszeitraum von Anfang 1999 bis Ende 2010 beim BfArM eingegangenen Meldungen in Hinblick auf Meldequelle, Patientenschädigung sowie Häufigkeit/Art von Produktfehlern bzw. korrektiven Maßnahmen.

Ergebnisse Von 2851 Meldungen zu IVD betrafen 190 IVD zur Untersuchung der Gerinnung (6,7 % aller Meldungen zu IVD), davon 99 Tests, Kits und Reagenzien zum Gebrauch durch professionelle Anwender (3,5 %), 26 Analysengeräte und deren allgemeines Verbrauchsmaterial zum Gebrauch durch professionelle Anwender (0,9 %) sowie 65 Gerinnungsselbsttests (Geräte und Teststreifen, 2,3 %) zum Gebrauch durch Patienten. Meldungen zu letzteren kamen meist von Herstellern (56; 86,2 %), seltener von Anwendern (8; 12,3 %) und Behörden (1; 1,5 %). In 31 Fällen (47,7 %) wurde eine Patientenschädigung (PS; Blutung, Apoplex, Thrombose, Embolie etc.) thematisiert. In 31 Fällen (47,7 %, davon 24 mit PS) wurde ein Produktfehler ausgeschlossen. In 16 Fällen (24,6 %, alle ohne PS) wurden Produktfehler identifiziert, meist Produktionsfehler (3), Materialfehler (2), Softwarefehler (2), Verfehlen der Spezifikation (2) und fehlerhafte Gebrauchsanweisungen (2), seltener Verpackungsfehler, Interferenzen, Kennzeichnungsfehler, mechanische und elektrische Fehler (je 1). Weiteren 2 Fällen (3,1 %, ohne PS) lagen Anwenderfehler zugrunde. In den übrigen 16 Fällen (24,6 %, davon 7 mit PS) blieb die genaue Fehlerursache unklar, da die Produkte nicht oder nur teilweise (z. B. fehlende Teststreifen des Anwenders) zur Verfügung standen und die von den Herstellern untersuchten Produkte (z. B. Rückstellmuster der betroffenen Teststreifencharge) keine Auffälligkeiten zeigten. Korrektive Maßnahmen erfolgten in 16 Fällen (24,6 %, 1 Fall mit PS) und waren meist Kundeninformation (15, obligat bei Rückruf), Rückruf (11) sowie Änderungen in Produktion/Qualitätskontrolle (6), Software (3), Gebrauchsanweisung (3), Design (2) und Kennzeichnung (1).

Diskussion Seit Beginn 1999 nimmt die Anzahl der Meldungen zu IVD kontinuierlich stark zu, was auf eine zunehmende Etablierung des Systems der Marktüberwachung hinweist. Die Analyse der Meldezahlen zu IVD zeigt, dass Gerinnungsselbsttests eine wichtige Produktgruppe innerhalb dieser Gruppe darstellen. Im Vergleich zu anderen IVD finden sich bei Gerinnungsselbsttests – evtl. als Folge der Sensibilisierung der Hersteller – häufiger Meldungen mit PS, die bei späterer Untersuchung jedoch keinen Zusammenhang zu Produktfehlern und korrektiven Maßnahmen aufweisen. Die erhaltenen Ergebnisse zeigen die Notwendigkeit und Funktion des bestehenden Systems der Marktüberwachung zur Sicherstellung und Verbesserung der Produktsicherheit von IVD.



	n	age	BMI	Endostatin
f. CHF	9	60,11 +/-17,38	29,56 +/- 5,83	191,36 +/- 52,94
m. CHF	21	67,48 +/- 11,68	27,45 +/- 4,76	263,00 +/-115,39
tot. CHF	30	65,27 +/-13,75	28,06 +/- 5,04	240,77 +/- 104,76
f. Control	25	56,00 +/- 6,01	25,36 +/- 4,69	112,33 +/- 23,59
m. Control	20	51,55 +/-7,52	26,39 +/-1,87	116,55 +/- 16,65
tot. Control	45	54,02 +/-7,04	25,85 +/-3,63	114,21 +/- 20,68

Figure 28: M. Sponder et al.

Sex Matters! Influence of Sex and Etiology on Endostatin Serum Levels in Patients with Chronic Heart Failure (CHF) XIV – 4

M. Sponder, R. Pacher, M. Hülsmann, M. Gwechenberger, J. Knoth, St. Kampf, M. Fritzer-Szekeres, B. Litschauer, J. Strametz-Juranek
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background Endostatin, a potent angiostatic factor, inhibits endothelial cell proliferation and migration and stimulates endothelial nitric oxide synthase (e-NOS). Chronic heart failure (CHF) is a vasoconstictive state associated with a significant upregulation of neurohumeral factors such as brain-natriuretic peptide (BNP), predicting morbidity and mortality in CHF patients. Therefore, the aim of the present study was to investigate the impact of sex, etiology and functional heart class in CHF on serum endostatin levels.

Material and Methods Endostatin levels were measured (ng/ml) at rest in 75 individuals, divided into 2 groups: 30 CHF-patients (17 dilatative, 13 ischemic; 9 NYHA I, 9 NYHA II, 12 NYHA III) and a control group consisting of 45 "elderly" non smokers (female vs male). In the CHF group also BNP was measured.

Results In contrast to the control group, which showed no gender specific difference in mean endostatin levels (female: 112.33 ± 23.59; male: 116.55 ± 16.65), male CHF-patients (263.00 ± 115.39) had much higher endostatin levels compared to female CHF-patients (191.36 ± 52.94). Endostatin levels in dCHF were 192.25 ± 44.85 compared to iCHF 260.69 ± 116.02. Endostatin also showed a positive correlation to BNP-levels in the CHF group ($p < 0.003$).

Conclusion

1. CHF is associated with upregulation of endostatin levels, especially in female patients
2. CHF based on ischemic heart disease is associated with higher Endo serum levels compared to DCHF
3. Furthermore, Endostatin serum levels correlate to BNP levels in CHF patients. Further studies are warranted, to investigate the impact of Endo as prognostic marker in CHF patients (**Figure 28**).

Transitioning from Subcutaneous to Intravenous Treprostinil Administered by the Implantable Infusion Pump LenusPro®: A Single-Center Pilot Study XIV – 6

R. Steringer-Mascherbauer, V. Eder, C. Huber, S. Wittrich, R. Függer, U. Fröschl, H. J. Nesser
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Introduction Parenteral Treprostinil is a mainstay in the therapy of pulmonary arterial hypertension (PAH). However, administration of parenteral prostanoids with external pump systems is technically challenging and associated with significant side effects such as infusion site pain with subcutaneous (s. c.) and possibly life-threatening catheter-related infections with intravenous (i. v.) administration. The Lenus Pro® implantable infusion pump was specifically developed to overcome the drawbacks of s. c. administration of Treprostinil. In 2010, we reported the first implantation of a Lenus Pro® pump with a filling interval of 28 days.

Methods We performed a retrospective chart analysis to assess safety and efficacy of i. v. Treprostinil delivered by Lenus Pro®. The study was approved by the local ethics committee.

Results Between September 2010 and October 2011, 14 patients underwent implantation at our center. All patients had experienced significant clinical benefits with s. c. Treprostinil but reported serious site pain associated with the change of the infusion site. Under general anesthesia, a catheter was placed in the Vena subclavia, or cephalica, according to the decision of the implanting surgeon. After preparation of the pump pocket in the abdominal wall, the pump was connected to the central venous access. To avoid overlap effects, s. c. Treprostinil was stopped one hour after connection. No intraoperative complications occurred. Postoperatively two patients developed a mild seroma, one requiring puncture. No other complications especially no infections, were observed. We have performed more than 60 refill procedures. To date one patient died during follow-up, the remaining patients are clinically stable and report an increased quality of life.

Conclusion This first pilot study demonstrates that i. v. Treprostinil, delivered by the implantable pump Lenus Pro®, is safe, effective and feasible in PAH patients transitioned from s. c. Treprostinil. Filling intervals of 28 days ensure optimal compliance and patient management. The absence of side effects such as infusion site pain is associated with a dramatic increase in quality of life.

Neurological Comorbidity Affects Prognosis in Left Ventricular Hypertrabeculation/Noncompaction XIV – 3

C. Stöllberger, G. Blazek, Ch. Wegner, J. Finsterer
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Objective Left ventricular hypertrabeculation/noncompaction (LVHT) is a cardiac abnormality which is frequently associated with neuromuscular disorders (NMD). It is unknown, if there are differences between LVHT-patients with and without NMD. Aim of the study was to compare baseline characteristics and prognosis of LVHT-patients with and without NMD.

Methods Included were patients in whom LVHT was diagnosed in one echocardiographic laboratory between June 1995 and June 2011. They underwent a baseline cardiologic examination and were invited for a neurological investigation. In June 2011, the patients were contacted by telephone and assessed if the patient was alive or not.

Results LVHT was diagnosed in 172 patients (53 female, mean age 53 ± 16 years). 123 patients (72%) were investigated neurologically. A specific NMD was diagnosed in 25: Metabolic myopathy n = 16; Leber's hereditary optic neuropathy n = 3; myotonic dystrophy n = 3; Becker muscular dystrophy n = 1; post-poliomyelitis syndrome n = 1, and Duchenne muscular dystrophy n = 1. A NMD of

unknown etiology was diagnosed in 79 patients, and the neurological investigation was normal in 19 patients. During a follow-up of 64 months the mortality was 4.84%/year. Baseline data did not differ between patients with and without NMD. No death occurred among the patients without NMD although they had a longer observation period (8 vs 4 years, p = 0.01) than patients who were not investigated neurologically.

Conclusions Presence or absence of NMD influences prognosis of LVHT-patients, why LVHT-patients should be referred to the neurologist. Presence or absence of a NMD should be considered in therapy-planning of LVHT-patients.

The proANP Increase During Exercise may Predict the PAP Increase in Connective Tissue Disease Patients at Risk of PAH XIV – 5

M. Tscherner, G. Kovacs, F. Fruhwald, R. Maier, B. Obermayer-Pietsch, V. Foris, H. Olschewski
Abteilung für Pulmologie; Abteilung für Kardiologie; Abteilung für Endokrinologie, Universitätsklinik für Innere Medizin, Medizinische Universität Graz; Ludwig-Boltzmann-Institut für Lungengefäßforschung, Graz

Background Natriuretic peptides (brain natriuretic peptide (BNP) and atrial natriuretic peptide [ANP]) are produced in cardiomyocytes of different myocardial regions. In case of dilation of the heart, BNP and ANP are excessivly released into the circulation. BNP is used as a biomarker in patients with chronic heart failure and pulmonary hypertension (PH). ANP is a marker of acute cardiac stress and may reflect actual hemodynamic changes during exercise. In connective tissue disease an excessive increase of pulmonary pressure may represent an early stage of pulmonary vascular disease and may be clinically relevant.

Patients and Methods We investigated plasma levels of proANP and NT-proBNP during right heart catheterization at rest and exercise in patients with connective tissue disease without PH. The levels at rest and during exercise were compared by Wilcoxon signed rank test. The correlations between the changes of mean PAP and NT-proBNP as well as mean PAP and proANP were calculated by Spearman's Rho test.

Results 47 patients (resting mean PAP: 16 ± 3 mmHg, mean PAP at maximal exercise: 37 ± 8 mmHg) were included. NT-proBNP and proANP significantly increased from rest to exercise (NT-proBNP rest: 91 ± 102 pg/mL, maximal exercise: 96 ± 96 pg/mL, $p < 0.001$; proANP rest: 2.43 ± 1.22 pg/mL, maximal exercise: 2.92 ± 1.33 pg/mL, $p < 0.001$). The increase in proANP levels between rest and maximal exercise significantly correlated with the increase in meanPAP ($p = 0.007$, $r = 0.404$), but there was no significant correlation for NT- proBNP ($p = 0.606$).

Conclusion Our results suggest that the exercise induced increase of proANP in patients with connective tissue disease may indicate the exercise-induced increase in PAP.

Compression-Only-CPR in Telephone-Assisted Bystanders: Is "To Push as Hard as You Can" Superior in Achieving 5–6 cm Chest Compression Depth than the Current Guideline Recommendation? A Double Randomized-Parallel-Group-Simulation-Study V – 2

R. van Tulder, D. Roth, Ch. Havel, Ph. Eisenburger, B. Heidinger, Ch. C. Chwojka, H. Novosad, F. Sterz, H. Herkner, W. Schreiber
Universitätsklinik für Notfallmedizin, Medizinische Universität Wien; Notruf NÖ, St. Pölten

Background In telephone-assisted, advanced medical priority dispatch system (AMPDS) driven, lay-rescuer, compression only cardiopulmonary resuscitation (COCPR) it remains unclear whether the instruction "push as hard as you can" improves compression depth.

Methods This was a prospective, experimental, double-blinded, randomized, controlled, parallel group study to investigate chest compressions following the instruction "push as hard as you can". Primary outcome was defined as compression depth. Secondary outcomes were defined as drawn estimation of 5 cm by every participant, exertion measured by BORG scale, modified Nine Hole Peg Test (NHPT), provider's systolic and diastolic blood pressure and the quality values measured by the Resusci® Anne skillmeter manikin.

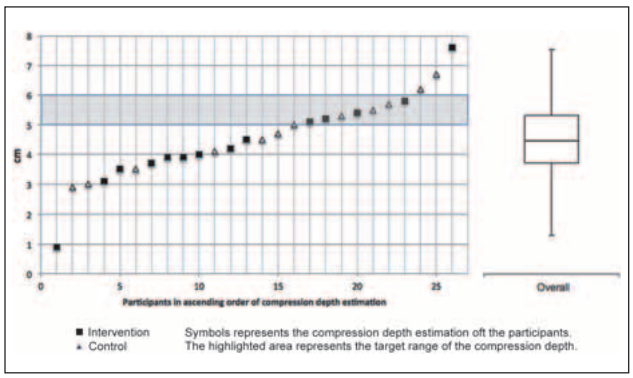


Figure 29: R. van Tulder et al. Participant estimations of compression depth.

Table 5: R. van Tulder et al. Demographic data of voluntary participants

	Control (n = 13)	Intervention (n = 13)
Female – n (%)	7 (58)	5 (38)
Age – mean ± SD	40 ± 14	33 ± 13
BMI – mean ± SD	27 ± 4	26 ± 4
FFB-Mot – mean ± SD	105 ± 14	111 ± 14
Right hander – n (%)	12 (92)	12 (92)
Smoking history – n (%)	4 (31)	8 (62)
Pack years – median (IQR)	0 (0–10)	0 (0–10)

SD = standard deviation; BMI = body mass index; FFB-Mot = physical fitness questionnaire; IQR = interquartile range

Results 13 participants were each allocated to control and intervention. 1 participant of the intervention group dropped out after minute 7 for exhaustion. Primary outcome showed a mean compression depth of 44.1 mm with an interindividual standard deviation (SDb) of 13.0 mm and an intraindividual standard deviation (SDw) of 6.7 mm for the control group versus 46.1 mm and a SDb of 9.0 mm and a SDw of 10.3 mm for the intervention group (Difference: 1.9 [–6.9 to –10.8]; $p = 0.66$). For secondary outcome participants estimated a mean of 43 ± 13 mm in control group versus 45 ± 15 mm in the intervention group ($p = 0.99$). Secondary outcome investigating exhaustion and COCPR quality values did not show any difference.

Conclusion There is no difference in compression depth, quality of COCPR or physical strain on lay-rescuers when advising "push as hard as you can" versus the standard AMPDS instruction "push down firmly 5 cm" **(Figure 29, Table 5, 6)**.

Herzinsuffizienz/Heart Failure

Schlafbezogene Atemstörungen bei Patienten mit chronischer Herzinsuffizienz und optimierter medikamentöser Therapie VI – 5

P. Dolliner, P. Ubl, L. Ringhofer, L. Stiebellehner, G. Steurer
Abteilung für Nuklearmedizin, Medizinische Universität Wien

Einleitung Ein Fortschreiten von chronischer Herzinsuffizienz (HI) kann durch wiederholt auftretende nächtliche Atemstörungen begünstigt werden. Das insuffiziente Myokard wird zusätzlich durch ein Ansteigen der Vorlast, Nachlast und des Sympathikotonus sowie durch vermehrt auftretende Arrhythmien beeinträchtigt. Aus

Table 6: R. van Tulder et al. Secondary outcomes: Performance data measured with Resusci® Anne Skillmeter

	Intervention mean ± SD_b (SD_w)	Control mean ± SD_b (SD_w)	Difference (95 % CI)	p-value
Total External Chest Compressions (ECC)* – (n per minute)	94.5 ± 5.3 (27.6)	88.1 ± 16.0 (28.3)	6.4 (–5.0 to 17.8)	0.27
ECC – accurate* – (n per minute)	2,8 ± 5,5 (12,3)	0,34 ± 0,20 (2,0)	2,4 (–1,2 to 6,1)	0,19
ECC – too shallow* – (n per minute)	57,1 ± 40,3 (30,2)	52,6 ± 38,2 (29,0)	4,4 (–26,5 to 35,5)	0,78
ECC – too deep* – (n per minute)	33,8 ± 33,8 (16,1)	18,8 ± 32,9 (18,0)	–0,3 (–26,3 to 25,7)	0,98
ECC – correct hand position* – (n per minute)	37,3 ± 34,3 (29,3)	40,2 ± 30,6 (30,2)	–2,8 (–28,9 to 23,2)	0,83
ECC – incomplete recoiling* – (n per minute)	70,6 ± 42,8 (26,1)	80,4 ± 34,9 (92,8)	–9,8 (–44,1 to 24,5)	0,57
ECC – mean frequency* – (n per minute)	100,6 ± 18,0 (17,4)	92,8 ± 9,1 (18,3)	7,7 (–4,0 to 19,5)	0,20
ECC – compression/relaxation ratio* (%)	46,4 ± 7,6 (7,2)	47,9 ± 9,3 (7,4)	–1,4 (–8,2 to 5,3)	0,67
Mean hands off – (seconds per minute)	2,0 ± 7,3	1,9 ± 7,2	0,1 (–1,6 to 1,8)	0,94
BORG scale – at study end	15 ± 2	15 ± 3	0,1 (–1,6 to 1,8)	0,89
HR – last minute (bpm)	103 ± 16	98 ± 17	5,2 (–4,2 to 14,7)	0,28
SBP at study end (mmHg)	159 ± 10	156 ± 15	3,4 (–4,0 to 10,7)	0,37
DBP at study end (mmHg)	92 ± 6	96 ± 10	–1,3 (–6,8 to 4,3)	0,65
NHPT – at study end (seconds)	25 ± 4	27 ± 4	–1,2 (–4,1 to 1,6)	0,39

* Estimates are adjusted for panel data structure with repeated measurements. SD_b denotes between (interindividual) standard deviation of the random intercepts; SD_w denotes within cluster (intraindividual) standard deviation. Measurements denoted as "at study end" were performed immediately after participants stopped chest compression.
ECC = external chest compression; BORG = Scale of perceived exertion; HR = heart rate; bpm = beats per minute; SBP = systolic blood pressure; mmHg = millimeters mercury; DBP = diastolic blood pressure; NHPT = Nine Hole Peg Test

früher durchgeführten Studien ist eine hohe Prävalenz von Schlafapnoe bei Kardiomyopathie-Patienten bekannt. In diesen Arbeiten fanden allerdings die leitliniengerechten medikamentösen Therapieschemen kaum Beachtung. Das Ziel unserer Arbeit war die Erfassung der Häufigkeit des Schlafapnoe-Syndroms bei Patienten mit chronischem Herzversagen und optimierter medikamentöser Langzeitbehandlung.

Methoden Wir untersuchten 177 konsekutive Patienten ohne klinischen Hinweis für Schlafapnoe und zumindest mittel- bis höhergradig reduzierter linksventrikulärer Auswurfleistung und einer Erhöhung der natiuretischen Peptide (NT-pro BNP > 300 pg/ml). Patienten mit Zeichen einer dekompensierten HI oder instabilem Zustand wurden ausgeschlossen. Die Teilnehmer wurden mit nächtlicher Polygraphie, einem 5-Kanal-Aufzeichnungssystem (Embletta X10®), untersucht.

Ergebnisse 151 (85,3 %) Teilnehmer waren männlich und 26 (14,7 %) weiblich. Das mediane Alter betrug 65,1 Jahre (Spannbreite 33,1–88,2 Jahre). Etwa 2/3 der Patienten (66,3 %) hatten eine ischämische und die verbleibenden 36,7 % eine dilatative Kardiomyopathie. Die linksventrikuläre Auswurfleistung errechnete sich mit durchschnittlich 24,6 ± 13,1 %. Bei den Teilnehmern wurde ein medianes NT-pro BNP von 3320,5 pg/ml (Spannbreite 305,1–35.000 pg/ml) gemessen.

172 (97,2 %) Teilnehmer wurden mit einem ACE-Hemmer oder AT2-Blocker behandelt, 160 (90,4 %) standen unter medikamentöser Betarezeptorenblockade und 106 (60 %) nahmen regelmäßig Spironolacton ein.

Bei 88 (49,7 %) Patienten wurde ein Apnea-Hypopnea-Index (AHI) ≥ 15/Stunde Aufzeichnungszeit festgestellt. Bei diesen Patienten lag die mittlere Sauerstoffsättigung bei 92,2 %, die mittlere ereignisassoziierte Sauerstoffentsättigung betrug 7,3 % und die minimale Sauerstoffsättigung errechnete sich mit durchschnittlich 78.7 %. Durchschnittlich 72 Minuten (16,3 % der Aufzeichnungszeit) lag die Sauerstoffsättigung bei diesen Patienten unter 90 %.

Bei 61 (69,3 %) Patienten bestand das pathologisch vorherrschende Atemmuster hauptsächlich aus zentralen Ereignissen und bei den verbleibenden 26 (29,6 %) Patienten handelte es sich überwiegend um obstruktive Apnoen oder Hypopnoen im Sinne eines obstruktiven Schlafapnoe-Syndroms. Bei einem (1,1 %) Patienten konnte die Atemstörung nicht weiter klassifiziert werden.

Diskussion Bei chronischem Herzversagen ist die Prävalenz von schlafbezogenen Atemstörungen trotz evidenzbasierter optimierter medikamentöser HI-Therapie hoch. Weitere Untersuchungen sind notwendig, um Erkenntnisse über die Auswirkungen der repetitiven nächtlichen Sauerstoffabfälle auf das insuffiziente Myokard zu erlangen.

The MitraClip System in Patients after Resynchronization Therapy and Persistent Significant Mitral Regurgitation and Concomitant Heart Failure VI – 6

Ch. Ebner, Th. Sturmberger, W. Tkalec, J. Aichinger, R. Steringer-Mascherbauer, V. Eder, G. Kabicher, J. Niel, H.-J. Nesser
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Despite cardiac resynchronization therapy (CRT) significant functional mitral regurgitation (FMR) frequently persists and may lead to sustained heart failure (HF) symptoms. Surgery in most of these patients is of limited value due to high perioperative risks whereas medical treatment may fail to compensate HF symptoms. The percutaneous repair with the MitraClip system offers an additional therapeutic option in selected CRT-patients.

Methods and Results Between August 2009 and March 2012 MitraClip treatment was performed in 13 patients after previous device implantation (CRT-P or CRT-D). Indication of percutaneous catheter-based mitral valve repair with the MitraClip system was significant MR ≥ grade 3 and persistent symptoms of Heart Failure NYHA ≥ 3.

Patients mean age was 72.2 ± 7.2 yrs, 61% were male. Median time after resynchronization therapy was 53.5 months (IQR: 29–71). In 5/13 patients a CRT-D system was in place and in 30% an ischemic cardiomyopathy was the underlying pathology of mitral regurgitation. LVEF was markedly reduced in all patients (mean LVEF 26.1 ± 5.4%) and 6/13 patients even had a LVEF ≤ 25%. Accordingly the log. EuroScore was markedly elevated (mean 28.9 ± 14.2%). A single clip was successfully implanted in 11 patients (84%) whereas 1 patient received 2 clips. In one patient the clip could not be positioned appropriately, so treatment was feasible in 12/13 patients. Reduction of mitral regurgitation was obtained from grade 3.5 ± 0.3 to grade 1.4 ± 0.4. In12/13 pts. we had no major complications, only 1 patient developed cardiac tamponade treated by conservative means. ICU mean duration of stay was 2 days and total hospitalization was median 9,5 days (IQR; 7–13 days). In-hospital and 30 days mortality was zero and 12 month mortality was only 20% in this group of patients with multiple co-morbidities and without further treatment options. One patient underwent successful heart transplantation due to deterioration of heart failure even reduction of mitral regurgitation was consistent. Stage of heart failure could be reduced from mean NYHA class 3.6 to class 2.5 and also distinct reduction in NT-pro BNP levels was possible.

Conclusion Residual significant mitral regurgitation after CRT in HF patients can be treated successfully by the MitraClip system to reduce regurgitant volume. Mitral valve repair with the MitraClip

system is an attractive option in patients with significant mitral regurgitation and persistent heart failure symptoms over time despite previous cardiac resynchronization therapy.

Endomyocardial Biopsy in Unexplained New-Onset Heart Failure: Time Matters! BAII

M. Frick, F. Kellner, S. Kellner, S. Pankuweit, B. Maisch, O. Pachinger, G. Pölzl
Universitätsklinik für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck, Österreich; Universitätsklinik für Innere Medizin und Kardiologie, Universität Marburg, Deutschland

Background The role of endomyocardial biopsy (EMB) in the evaluation of patients with non-ischemic cardiomyopathy (CMP) is still under debate. A recent AHA/ESC consensus document suggests to perform EMB in "unexplained new-onset heart failure of 2 weeks to 3 months duration", although the scientific evidence for this recommendation is scarce. The objective of this retrospective study was to evaluate the impact of this time frame and to identify prognostic parameters in patients with suspected inflammatory cardiomyopathy.

Methods 272 patients (mean age 45 ± 13 years), who underwent EMB between March 2001 and November 2010 at the Department of Cardiology at Innsbruck Medical University, were enrolled in this study. Patients with a history of heart transplantation and those suffering from systemic diseases (amyloidosis, sarcoidosis) were excluded. Work up of biopsy specimens included immunohistology for the assessment of myocardial inflammation and PCR for the detection of virus persistence. The combined endpoint was defined as death for any reason, heart transplantation, assist device implantation or hospitalization for acute heart failure Mean follow-up was 32 ± 26 months.

Results Time from diagnosis of CMP to EMB was significantly higher in patients with events compared to those without (18 months vs 6 months; $p < 0.001$). Patients with NYHA-class III and IV suffered significantly more often from a cardiovascular event compared to those in NYHA-class I and II (33% vs 16%; $p = 0.007$). Presence of bundle branch block (rate of events 32% vs 19%; $p = 0.047$) and unspecific ST segment changes at time of first presentation (80% vs 63%; $p = 0.016$) were associated with poor outcome.

In multivariate analyses evidence of inflammation alone ($p = 0.038$) or in combination with viral persistence ($p = 0.025$) was associated with worse outcome only in patients presented within 3 months of unexplained new-onset heart failure. On contrast, EMB results did not impact on outcome in patients who presented after 3 months of new-onset heart failure.

Conclusion Our data suggest, that time from diagnosis to EMB, NYHA class as well as ECG changes are associated with worse outcome. In multivariate analyses we found that EMB-results had only an impact on prognosis if patients underwent biopsy within 3 months after new-onset of heart failure symptoms. Consequently, our study supports the time frame suggested by the AHA/ESC consensus statement on EMB.

Outcome ein Jahr nach CRT-Implantation in Österreich BAI

F. Fruhwald, B. Strohmer
Universitätsklinik für Innere Medizin, Medizinische Universität Graz; Paracelsus Medizinische Privatuniversität Salzburg

Einleitung Entsprechend der europäischen Herzinsuffizienz-Guidelines von 2008 ist die Cardiale Resynchronisationstherapie (CRT) ein etabliertes Verfahren zur Behandlung von Herzinsuffizienz in den NYHA-Stadien III und IV bei Patienten mit vergrößertem Durchmesser des linken Ventrikels (LVEDD > 55 mm) und eingeschränkter linksventrikulärer Auswurffraktion (LVEF < 35 %). Das CRT-Survey, eine gemeinsame Initiative der Heart Failure (HFA) sowie der Heart Rhythm Association (EHRA) der ESC, hat in den Jahren 2008/2009 die in Europa gelebte Wirklichkeit im Hinblick auf diese Therapieform abgebildet und nach 1 Jahr das Outcome der Patienten erhoben. Wir berichten hier über die Daten der österreichischen Zentren.

Methodik Alle zwischen 1.11.2008 und 30.6.2009 an den 10 teilnehmenden Zentren implantierten CRT-Systeme wurden zusammen mit den Ausgangs- sowie Outcomedaten erhoben. Es wurden lediglich Patienten dokumentiert, die ihr Einverständnis dazu gegeben hatten.

Ergebnisse 155 Patienten (117 männlich, 38 weiblich) mit einem mittleren Alter von 68 ± 10 Jahren (31–86) wurden inkludiert, wovon sich 144 Patienten einem elektiven Eingriff unterzogen haben. Es fanden sich folgende NYHA-Klassen: NYHA 1/2/3/4 bei 3/31/110/11 Patienten. 96 Patienten hatten Sinusrhythmus, Vorhofflimmern wurde bei 58 Patienten (37 %) dokumentiert. Die Breite des QRS-Komplexes betrug 158 ± 34 ms (80–250). Eine echokardiographische Untersuchung war bei 146 Patienten vorhanden, wobei der LVEDD 65 ± 9 mm (45–98) und die LVEF 27 ± 8 % (10–50) betrug.

Die Eingriffe wurden überwiegend von Chirurgen durchgeführt (n = 109), Elektrophysiologen und interventionelle Kardiologen waren ca. zu 1/3 (n = 35 resp. n = 21) die Implanteure. Es wurden überwiegend CRT-D (n = 120) implantiert, lediglich 35 Patienten (23 %) erhielten einen CRT-P. *Post implantationem* betrug die Breite des QRS-Komplexes 141 ± 27 ms (80–204). 148 Patienten (95 %) wurden mit einem ACE-Hemmer oder Angiotensin-Rezeptor-Blocker entlassen, 133 (86 %) mit einem Betablocker, 125 (81 %) mit einem Diuretikum und 71 (46 %) mit einem Aldosteron-Antagonisten.

Nach 12 ± 3 Monaten waren 15 Patienten (10 %) verstorben, 53 (37 %) wurden rehospitalisiert, überwiegend wegen Herzinsuffizienz. Komplikationen am Device waren bei 18 Patienten (13 %) dokumentiert, wobei Sondendislokationen (n = 5), Sondenmalfunktionen (n = 5) und Phrenikusstimulation (n = 6) am häufigsten auftraten. Erfreulicherweise wurde keine Infektion beobachtet. Appropriate Schocks waren in 6 Fällen, inappropriate in 5 Fällen sowie appropriates antitachykardes Pacing (ATP) in 13 Fällen nachweisbar. Die NYHA-Klassen zeigten einen eindeutigen Shift in Richtung leichtere Herzinsuffizienz: NYHA 1/2/3/4 fand sich bei 49/73/13/7 Patienten. 96 Patienten wurden durch das CRT-Gerät stimuliert, überwiegend im DDD- (n = 61) oder im VVI-Modus (n = 28). Die LVEF war im Mittel auf 38 ± 10 % (10–50) angestiegen, der Ventrikeldurchmesser auf 60 ± 9 mm (42–91) zurückgegangen. Das mediane NT-pro-BNP war von 2203 vor der Implantation auf 997 pg/ml gesunken.

Schlussfolgerung Die österreichischen Daten des CRT-Survey zeigen, dass die Indikation zur Implantation großzügig und nicht immer im Gleichklang mit den Guidelines gestellt wird. Die Herzinsuffizienz konnte durch die CRT in Kombination mit einer optimalen medikamentösen Therapie deutlich gemildert werden, dies wurde sowohl subjektiv (NYHA-Klasse) als auch objektiv (NT-pro-BNP). Nichtsdestotrotz ist bei diesen chronisch kranken Patienten mit einer beträchtlichen Rehospitalisierungsrate sowie einer 1-Jahres-Mortalität von 10 % zu rechnen.

Institutional Experience with Extracorporeal Membrane Oxygenation Support for Right Ventricular Failure After Left Ventricular Assist Device Implantation VI – 9

St. Mahr, F. Eskandary, J. Horvath, A. Rajek, G. Laufer, H. Schima, D. Zimpfer
Abteilung für Herzchirurgie, Medizinische Universität Wien

Background Right ventricular failure complicating left ventricular assist device implantation (LVAD) has a poor outcome. This study was designed to determine the success of extracorporeal membrane oxygenation support (ECMO) for the treatment of right ventricular failure after LVAD implantation.

Methods From December 2008 to August 2011 13 patients (mean age 56 yrs, male 92,3%) undergoing LVAD implantation at our department received an ECMO for therapy refractory right ventricular failure. In 11 patients the ECMO was implanted at the time of LVAD implantation due to inability to wean from CPB. In 2 patients

the ECMO was implanted preoperatively for therapy refractory biventricular failure and continued postoperatively for right ventricular failure.

Results After recovery of right ventricular function, the ECMO was successfully explanted in 10 of 13 patients (77%). Three patients (23%) expired while on ECMO support. Mean duration of ECMO support was 3 days. On patient died despite successful ECMO weaning as a consequence of non-device related sepsis. Interestingly, mortality was higher in those patients receiving the ECMO prior to LVAD implantation (50%), as compared to those receiving the ECMO after inability to wean from cardiopulmonary bypass (27%, $p < 0.05$). Overall in-hospital mortality was 30.7%.

Conclusion ECMO facilitates recovery of right ventricular function after LVAD implantation complicated by perioperative right ventricular failure. Nevertheless, perioperative mortality remains high, especially in those patients receiving the ECMO preoperatively for biventricular support.

Häufigkeit, Relevanz und Prognose von Elektrolytstörungen bei Herzinsuffizienzpatienten VI – 4

M. Niederau, L. Stadlmüller, C. Colantonio, F. Fruhwald
Abteilung für Kardiologie; Institut für Medizinische Informatik, Statistik und Dokumentation, Medizinische Universität Graz

Einleitung Die Niere spielt bei Herzinsuffizienz im Elektrolythaushalt die zentrale Rolle was Regulation und Aufrechterhaltung von konstanten Elektrolytspiegeln betrifft. Hier greifen auch einige für Herzinsuffizienz verwendete Medikamente an.

Methoden Es wurden die lokalen Daten aus dem Herzinsuffizienzregister der Arbeitsgruppe Herzinsuffizienz (AG-HI) der Österreichischen Kardiologischen Gesellschaft (ÖKG) herangezogen. Patienten, die erstmalig in einer Spezialambulanz vorstellig wurden, wurden nach Einholen des Einverständnisses in diesem Register dokumentiert. Nach 12 Monaten wurde ein Follow-up erhoben. Anhand der Natrium- und Kaliumwerte der Erstuntersuchung wurden die Patienten in Gruppen eingeteilt: Normalgruppe, Hypo-/Hypernatriämie, Hypo-/Hyperkaliämie sowie deren Kombinationen. Die Hypokaliämie, Hypernatriämie und Hyperkaliämie mit gleichzeitiger Hypernatriämie wurden aufgrund des geringen Vorkommens (n = 1) nicht berücksichtigt.

Resultate Das Patientenkollektiv bestand im Zeitraum von 2006–2010 aus 228 Patienten (189 Männer, 39 Frauen, mittleres Alter 60 ±13 Jahre). Die medikamentöse Therapie bei Erstuntersuchung bestand aus ACE-Hemmer bei 175 Patienten (77 %), Angiotensin-Rezeptor-Blocker bei 36 Patienten (16 %), Angiotensin-Rezeptor-Blocker oder ACE-Hemmer bei 207 Patienten (91 %), Diuretika bei 166 Patienten (73 %), Aldosteron-Antagonisten bei 132 Patienten (58 %) und Betablocker bei 205 Patienten (90 %). Der Großteil der Patienten war mit NYHA-Klasse II (44 %) und III (37 %) klassifiziert.

Insgesamt wiesen 43 Patienten (19 %) eine Elektrolytstörung bei Erstuntersuchung auf. Ein statistisch signifikanter Zusammenhang zwischen NYHA-Stadium und dem Vorhandensein von Elektrolytstörungen konnte nicht gefunden werden (p = n. s.).

Nach 12 Monaten waren 17 Patienten verstorben, 15 aus der Gruppe mit normalen Elektrolyten und 2 aus der Gruppe mit Elektrolytstörungen (p = n. s.), wobei letztere aus der Gruppe mit Hyponatriämie sowie Hyponatriämie plus Hyperkaliämie stammten. Insgesamt wurden 111 Patienten rehospitalisiert, wobei mit 48 % aus der Normalgruppe und 51 % aus der Gruppe mit Elektrolytstörungen kein signifikanter Unterschied zu finden war (p = n. s.). Die Patienten mit Elektrolytstörungen waren im Mittel länger rehospitalisiert als Patienten mit normalen Elektrolyten.

Ein möglicher Zusammenhang einer Niereninsuffizienz (eGFR < 50) und der Entwicklung einer Hyperkaliämie ließ sich statistisch nicht belegen (p = n. s.).

Im Hinblick auf Medikamentendosierungen mit möglichem Einfluss auf die Elektrolyte konnte folgendes beobachtet werden: Spironolacton wurde in der Gruppe der kombinierten Elektrolytstörungen in einer höheren Dosierung verordnet als in der Normalgruppe (59 mg/d vs. 38 mg/d), dieser Unterschied war allerdings nicht statistisch signifikant. Dagegen wurde Furosemid in der Gruppe der Hyponatriämie wesentlich höher dosiert als in der Normalgruppe (69 mg/d vs. 43 mg/d; p = 0,0064).

Diskussion Elektrolytstörungen sind ein relativ häufiger Befund bei Patienten mit Herzinsuffizienz. Solche Patienten sind länger rehospitalisiert als Patienten mit normalen Elektrolyten, vor allem, wenn eine Hyperkaliämie oder eine kombinierte Hyponatriämie/Hyperkaliämie vorliegt. Ein möglicher Zusammenhang mit der medikamentösen Therapie der Erkrankung liegt nahe, da einzelne Elektrolytstörungen mit signifikant höheren Dosierungen von Diuretika einhergehen als in der Normalgruppe.

Why Heart Failure Treatment Is Not Prescribed to Heart Failure Patients. Data from the EuroHeart Failure Survey-III at an Austrian University Heart Failure Clinic VI – 8

V. Platzer, K. Ablasser, F. Fruhwald
Universitätsklinik für Innere Medizin, Medizinische Universität Graz

Introduction The number of patients with heart failure is growing steadily in the Western world. Although the European Society of Cardiology (ESC) has published guidelines for the optimal treatment of heart failure it can be difficult to put this recommendation into practice. Therefore, the ESC has initiated the EuroHeart Failure Survey (EHFS)-III with the aim to get information about real world reasons for not prescribing recommended heart failure therapies

Patients and Methods After giving written informed consent patients with chronic heart failure have been asked in accordance with the structured case report form provided by the ESC at baseline. After 12 months a follow-up is planned. Here we report the first data from an Austrian university heart failure clinic taking part in the EHFS-III.

Results 33 patients (8 female, 25 male; median age: 56 years) have been included in the EHFS between October 2011 and February 2012. 25 patients (76%) are treated with ACE-inhibitors (ACEI), 8 patients (24%) with Angiotensin-receptor-blockers (ARB), 31 patients (94%) with beta-blockers (BB) and 27 patients (82%) were treated with Aldosteron-antagonists (AldoA).

Of the 25 patients treated with an ACEI 8 (32%) were on recommended daily dose while 9 (36%) could not be further uptitrated due to symptomatic hypotension.

Of the 8 patients treated with an ARB 3 (38%) had reached maximum dose while another 3 (38%) could not undergo further optimisation due to hypotension. Of the 31 patients treated with a BB 7 (23%) were on ESC-recommended daily dose while 16 (52%) could not be further uptitrated due to bradyarrhythmia or symptomatic hypotension. Of the 27 patients treated with AldoA 8 (30%) had reached optimal dose while 6 (22%) could not attain target dose due to hyperkalemia and in 13 (48%) patients no reason was specified.

Conclusion Only a minority of chronic heart failure patients is on ESC-recommended daily dose of medication. The reasons for not reaching target dose can mostly be attributed to specific side effects of the drugs used.

Auswirkung verschiedener Stimulationsvektoren bei der CRT auf echokardiographische und vektorkardiographische Parameter VI – 3

G. Saurer, B. Anelli-Monti, W. Koglek, W. Weihs
Department für Kardiologie und Intensivmedizin, LKH Graz-West; Klinikum Klagenfurt am Wörthersee, Klagenfurt

Einleitung Die CRT weist eine hohe Nonresponderrate von bis zu 30 % auf. Eine Ursache liegt in der suboptimalen Lage der linksventrikulären Sonde (Koronarvenenmorphologie, Narbe, Phrenikusstimulation, hohe Reizschwelle). Mit einer quadripolaren linksventrikulären Sonde (Quartet™ von St. Jude Medical), die im Ab-

	EF	LVEDV	LVESV	SPWMD	TI
V0	29	147	104	115	65
V1	40	137	83	90	100
V3	46	126	70	30	55
V4	34	144	94	170	60
CRT off	28	174	126	280	90

Abbildung 30: G. Saurer et al.

stand von 47 mm 4 Pole aufweist, können bis zu 10 unterschiedliche Stimulationsvektoren bzw. -orte programmiert werden. Dadurch erhöhen sich die Möglichkeiten einer optimaleren biventrikulären Stimulation im Vergleich zur klassischen bipolaren linksventrikulären Sonde.

In einer Studie untersuchen wir, ob sich unterschiedliche Vektoren echokardiographisch abbilden lassen und ob eine Korrelation des besten echokardiographisch bestimmten Vektors zum Time Intervall (TI) der Vektorkardiographie (VKG) besteht. Mit der VKG lässt sich die elektrische Dyssynchronie zeitlich und räumlich darstellen. Ein TI > 65 ms im Ausgangs-EKG (ohne Stimulation) korreliert mit einem positiven CRT-Respons. Eine Verkürzung des TI nach Resynchronisation stellt einen Parameter für eine erfolgreiche CRT dar.

Methode An einem Fallbeispiel bestimmen wir echokardiographische Parameter (LV-Ejektionsfraktion in %; LV-enddiast. Volumen [LVEDV] in ml; LV-endsyst. Volumen [LVESV] in ml; „septal to posterior wall motion delay" [SPWMD] in ms;) von 5 unterschiedlichen Stimulationvektoren der quadripolaren Sonde und korrelieren sie mit dem TI (in ms) der Vektorkardiographie. Die echokardiographischen und vektorkardiographischen Daten wurden geblindet ausgewertet.

Ergebnis Der optimalste echokardiographisch bestimmte Stimulationsvektor in diesem Fallbeispiel war V3. Bei dieser Einstellung ergab sich eine Verbesserung der LVEF um 18 % im Vergleich zum nichtstimulierten linken Ventrikel und eine Verbesserung um 17 % im Vergleich zum schlechtesten Stimulationsvektor V0. Der Dyssynchronieparameter SPWMD verbesserte sich um 250 ms im Vergleich zum Ausgangswert und um 85 ms zu V0.

Das beste TI wies ebenso V3 mit einer Verbesserung auf 55 ms auf. Die geringste Verbesserung wies der Vektor V1 mit 100 ms auf. Im Vergleich zum Ausgangswert zeigte sich eine Abnahme des TI um 35 ms.

Diskussion Bei unserem Fallbeispiel kam es zu einer Verbesserung der echokardiographischen Parameter unterschiedlichen Ausmaßes bei Verwendung unterschiedlicher Stimulationsvektoren einer quadripolaren Sonde.

Es zeigte sich eine gute Übereinstimmung der mechanischen mit der elektrischen Resynchronisation. In einer Studie wird diese Beobachtung überprüft. Sollte sich die Korrelation bestätigen, könnte die Vektorkardiographie als einfache und rasche Methode zur Bestimmung des optimalen Stimulationsvektors angewendet werden (**Abbildung 30**).

Single Center Experience with Percutaneous Edge to Edge Mitral Valve Repair in High-Risk Patients

BAII

Th. Sturmberger, Ch. Ebner, W. Tkalec, J. Aichinger, R. Steringer-Mascherbauer, G. Kabicher, V. Eder, J. Niel, H.-J. Nesser
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Patients with severe symptomatic mitral regurgitation (MR) have poor prognosis in the absence of surgery. An European survey established that more than half of patients with symptomatic significant MR are not referred for surgery or are refused by cardiac surgeons, mainly due to poor LV-function and multiple comorbidities. Clinical trials with the MitraClip system showed promising results regarding feasibility and safety of this device and functional improvement of patients. We report outcomes of our patients in a so called high risk group.

Methods We included patients with symptomatic heart failure (NYHA class ≥ 3), poor LV-function (LVEF ≤ 35%) and significant MR ≥ 3, who were declined for surgery. Transthoracic echocardiography was performed before, at discharge and 3 and 6 months after the procedure. Differences in 6-min-walk test (6-MWT), NT-pro BNP, New York Heart Association (NYHA) functional class and Echoparameter were reported.

Results MitraClip procedure was performed in 21 patients with a mean age 69.6 ± 10.1 years, mean log. EuroScore 24.4 ± 13.6%, mean NYHA class 3.7 ± 0.3 and a median NT-pro BNP 4910 pg/dl (IQR 1617–12425). Mean LVEF was 26.6 ± 6.4% and mean 6-MWT distance was 208 ± 159 m. In 11 patients ischemic cardiomyopathy was the underlying pathology of MR.

The MitraClip procedure was successful in 20/21 patients. In one patient the clip could not be placed. A single clip was implanted in 18 patients (90%), whereas two clips were placed in 2 patients (10%). Severity of MR was reduced significantly in the successfully treated patients and 19/20 patients were discharged with a MR grade ≤ 2. No procedure related death occurred and only 1 patient died within 3 months.

Clinical and echocardiographic 6-month follow-up data could be obtained in 13 patients.

At 6 months, MR ≤ 2 was present in all 13 patients, and 8/13 patients were in NYHA functional class I or II. The vast majority of the latter had a LVEF ≥ 25% at baseline. Six-minute walk distance improved significantly and distinct reduction in NT-pro BNP plasma levels and LA-Index were observed.

Conclusion Percutaneous edge-to-edge valve repair with the MitraClip system in high surgical-risk patients with severe MR and poor LV-function is feasible and safe. Successful procedures lead to an improvement in functional capacity after 6 months. However, careful patient selection seems mandatory, especially in case of very advanced heart failure.

Associations of Methylarginines and Homoarginine with Diastolic Dysfunction in Patients at Cardiovascular Risk with Preserved Left Ventricular Ejection Fraction

VI – 2

A. Tomaschitz, F. Edelmann, St. Pilz, A. Meinitzer, A. Schmidt, E. Ritz, G. Gelbrich, H.-D. Düngen, K. Kienreich, R. Stahrenberg, R. Wachter, W. März, B. Pieske
Klinische Abteilung für Kardiologie; Klinische Abteilung für Endokrinologie und Stoffwechsel; Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medizinische Universität Graz Österreich; Department of Cardiology and Pneumology, University of Goettingen; Department of Nephrology, University of Heidelberg; Coordination Center for Clinical Trials, University of Leipzig; Department of Cardiology, Charité-Universitätsmedizin Berlin; Synlab Centre of Laboratory Diagnostics Heidelberg, Germany

Introduction ADMA, SDMA and homoarginine are considered to modulate nitric oxide synthesis that is crucial for cardiovascular and myocardial health. We evaluated whether asymmetric dimethylarginine (ADMA), symmetric dimethylarginine (SDMA) and homoarginine are associated with biochemical markers and echocardiographic measures of diastolic dysfunction and with glomerular filtration rate (GFR).

Materials and Methods We investigated primary care patients at cardiovascular risk with preserved left ventricular ejection fraction from the multicentre, prospective, observational DIAST-CHF study. We measured serum concentrations of ADMA, SDMA and homoarginine and performed standardized echocardiographic examinations.

Results Among 1396 patients (mean age: 65.3 ± 8.3 years; 54.6% women), diastolic dysfunction was ruled out in 261 patients (18.7%). Mild, and moderate or severe grade of diastolic dysfunction was present in 900 (64.5%), and 235 (16.8%) study participants, respectively. After adjustments for cardiovascular risk factors,

Table 7: A. Tomaschitz et al. Binary logistic analyses for presence and grade of diastolic dysfunction according to the standard deviation of ADMA, SDMA or homoarginine.

	ADMA (per SD)	SDMA (per SD)	Homorarginine (per SD)
Adjustments	**Entire study cohort (n = 1396) Odds ratios (with 95%-CI) for diastolic dysfunction**		
None	1.17 (1.01–1.34)*	1.24 (1.05–1.46)*	0.83 (0.73–0.94)#
Model 1	1.00 (0.86–1.15)	0.90 (0.77–1.05)	0.94 (0.82–1.08)
Model 2	0.97 (0.83–1.14)	0.91 (0.75–1.10)	0.86 (0.73–1.01)
Model 3	1.00 (0.84–1.18)	0.95 (0.77–1.16)	0.84 (0.72–0.99)*
Model 4	1.01 (0.85–1.19)	0.95 (0.76–1.22)	0.84 (0.72–0.99)*
Model 5	1.04 (0.87–1.25)	0.93 (0.72–1.21)	0.84 (0.71–0.99)*
	Patients with diastolic dysfunction (n = 1135) Odds ratios (with 95%-CI) for moderate or severe diastolic dysfunction		
None	1.14 (0.99–1.31)	1.03 (0.90–1.18)	1.20 (1.04–1.38)*
Model 1	1.21 (1.05–1.39)#	1.17 (1.02–1.34)*	1.12 (0.96–1.31)
Model 2	1.27 (1.09–1.49)#	1.26 (1.09–1.47)#	1.09 (0.92–1.29)
Model 3	1.19 (1.01–1.40)*	1.21 (1.03–1.42)*	1.06 (0.89–1.27)
Model 4	1.21 (1.03–1.43)	1.39 (1.14–1.69)	1.05 (0.88–1.25)
Model 5	1.11 (0.93–1.33)	1.33 (1.07–1.64)#	1.03 (0.86–1.23)

Logistic regression analyses with diastolic dysfunction as the outcome variable and ADMA, SDMA, and homoarginine (per SD) as the explanatory variable and cummulative adjustments.

Model 1 adjusted for age and sex.

Model 2 additionally adjusted for body mass index, systolic blood pressure, diabetes mellitus, LDL- and HDL-cholesterol and active smokers.

Model 3 additionally adjusted for heart rate, left ventricular hypertrophy and history of myocardial infarction.

Model 4 additionally adjusted for glomerular filtration rate.

Model 5 additionally adjusted for ADMA, SDMA, and homoarginine.

ADMA: asymmetrical dimethylarginie; SD: standard deviation; SDMA: symmetrical dimethylarginine. * $p < 0.05$; # $p < 0.01$

ADMA and SDMA were positively and homoarginine was negatively associated with N-terminal pro-B-type natriuretic peptide (NT-proBNP) and mid-regional pro-adrenomedullin (MR-proADM) ($p < 0.05$ for all). Lower homoarginine levels were an independent predictor for the presence of diastolic dysfunction and higher ADMA and SDMA levels were associated with the severity of diastolic dysfunction ($p < 0.05$ for all). ADMA was moderately and SDMA was highly significantly associated with GFR.

Discussion Our findings suggest that higher levels of ADMA and SDMA as well as lower levels of homoarginine may be associated with an adverse cardiovascular risk profile and in particular with diastolic dysfunction. Further studies should clarify the potential of these amino acids derivates for the therapy of cardiovascular diseases **(Table 7)**.

A Risk Factor-Based Porcine Model of Heart Failure with Preserved Ejection Fraction (HFPEF) VI – 1

J. Verderber, M. Schwarzl, S. Seiler, P. Steendijk, B. Pieske, H. Post
Klinische Abteilung für Kardiologie, Medizinische Universität Graz, Österreich; Leiden University Medical Center, Leiden, The Netherlands

Background Heart failure with preserved ejection fraction (HFPEF) results from the accumulation of cardiovascular risk factors. So far, no therapeutic intervention has shown to decrease mortality in HFPEF, which in part relates to the lack of suitable animal models. We aimed to model HFPEF in pigs by induced hypertension and western diet.

Methods and Results Eight landrace pigs were implanted with subcutaneous 90-day release DOCA pellets (an aldosterone analogon), and subsequently fed a high salt/high lipid/high sugar diet for 90 days (DOCA). Eight weight-matched pigs (no DOCA, regular diet) served as controls. After 90 days, tail-cuff systolic blood pressure during light sedation was 139 ± 11 mmHg in DOCA vs 95 ± 6 mmHg in control ($p < 0.05$). Echocardiography demonstrated pronounced concentric hypertrophy in DOCA. LV function was assessed during deep anesthesia by pressure-volume (PV) analysis. In DOCA vs control, baseline cardiac output (6.0 ± 0.2 vs 6.6 ± 0.5 l/min) and heart rate (95 ± 5 vs 84 ± 6 bpm) were not different, while LV ejection fraction (68 ± 3 vs 51 ± 3%) was higher ($p < 0.05$). The end-systolic and end-diastolic PV relationships (ESPVR and EDPVR) were markedly shifted leftwards in DOCA **(Figure 31)**. Right atrial pacing both at baseline and during low-dose dobutamine infusion (2.5 µg/kg/h) revealed a lower increase of cardiac output in DOCA.

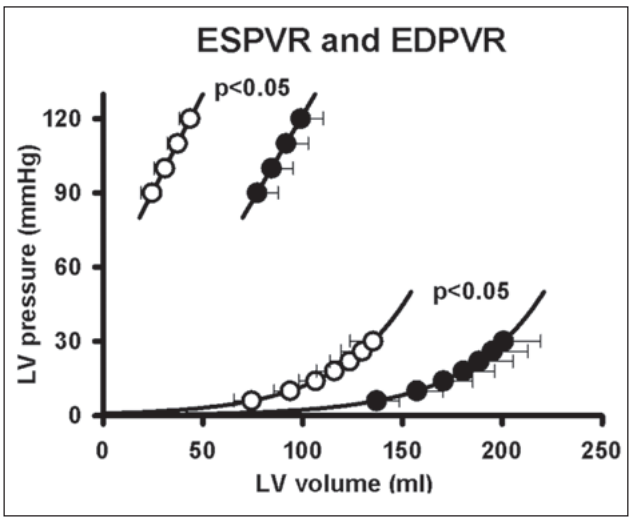


FIgure 31: J. Verderber et al.

Conclusion This risk factor based animal model for the first time reproduces two major characteristics of HFPEF: (i) a leftward shift of the ESPVR and EDPVR and (ii) a limited cardiac reserve.

Venous Congestion Rather than Low Output Predicts Hepatic and Renal Failure in CHF VI – 7

A. Von der Heidt, G. Goebel, M. Frick, G. Poelzl
Department of Internal Medicine III, Cardiology, Medical University Innsbruck

Purpose Secondary organ dysfunction such as renal and hepatic failure is an integral part of the heart failure syndrome. The underlying pathomechanisms, however, are still not well-defined. In this study we sought to investigate the impact of hemodynamic perturbations on liver and kidney function in a large cohort of chronic heart failure (CHF).

Methods Hemodynamic parameters from right heart catheterization along with liver (AP, T-Bil, GGT, GOT, GPT) and renal (serum creatinine [SCr], eGFR) function tests and clinical parameters were evaluated in a cohort of 293 patients (median age 47, NYHA class I 28,8%, II 34,8%, III/IV 35,4%; median LV-EF 28%) with CHF. Bivariate correlations and partial correlations adjusted for age and gender were performed to assess associations between hemodynamic and laboratory parameters. Univariate and multivariate regression models adjusted for age, gender, BMI, ischemic etiology, hypertension and NYHA class were created to estimate the contribution of congestion and forward failure on hepatic and renal failure.

Results Prevalence of elevated liver and kidney functions tests were as follows: AP 4,8%, T-Bil 9,2%, GGT 32,1%, GOT 23,5%, GPT 57,3%, SCr 19,1%, eGFR 16%. GGT, eGFR and SCr were strongly associated with RAP and CI ($p < 0.001$) whereas bilirubin was only correlated with RAP ($p < 0.001$). By contrast, only weak correlations were found for GPT and GOT with CI ($p < 0.05$) and AP with RAP and CI ($p < 0.05$). In multivariate regression models RAP

rather than CI was independently associated with T-Bil (RAP β = 0.232, p = 0.001; CI β = –0.025; p = 0,728), GGT (RAP β = 0.177; p = 0.012; CI β = –0.143; p = 0.058), eGFR (RAP β = –0.144; p = 0.015; CI β = 0.080; p = 0.220), and SCr (RAP β = 0.152; p = 0.013; CI β = –0.082; p = 0.225). Models for AP, GOT, and GPT were not significant.

Conclusion Our data suggest that venous congestion rather than forward failure is the hemodynamic pathomechanism contributing to hepatic and renal failure in CHF. This association holds true independent of epidemiologic and clinical parameters including etiology and severity of HF. Hence, meticulous volume management is of utmost importance in CHF.

Interventionelle Kardiologie/ Interventional Cardiology

Inzidenz von kardialen Reizleitungsstörungen und Schrittmacher-Implantation nach transfemoral-perkutanem Aortenklappenersatz (Core Valver®)

VII – 8

H. Blessberger, Th. Lambert, M. Grund, K. Kerschner, A. Kypta, B. Hartenthaler, J. Kammler, C. Steinwender, F. Leisch
I. Medizinische Abteilung mit Kardiologie, AKH Linz; Landeskrankenhaus Vöcklabruck

Hintergrund Neu aufgetretene Schenkelblöcke oder höhergradige AV-Blockierungen zählen zu den bekannten postinterventionellen Komplikationen nach transfemoral-perkutanem Aortenklappenersatz (PAKE). Die Inzidenz von postinterventionellen Schrittmacher-Implantationen aufgrund dieser neu aufgetretenen Reizleitungsstörungen wird in der Literatur mit 3–40 % angegeben.

Material und Methode Im Rahmen einer retrospektiven Beobachtungsstudie wurde die Inzidenz neu implantierter Schrittmacher an unserer Abteilung nach PAKE zwischen November 2008 und Februar 2012 erhoben. Alle Patienten wurden nach Klappenersatz mindestens 48 Stunden intensivmedizinisch mit EKG-Monitoring überwacht. Bei Neuauftreten einer höhergradigen postinterventionellen Reizleitungsstörung (Linksschenkelblock, AV-Block II.°, AV-Block III.°) wurde die Indikation zur Schrittmacher-Versorgung gestellt (Symphony®, Sorin®). Bei Patienten mit permanentem AV-Block III.° erfolgte eine DDD-/VVI-Stimulierung. Bei Patienten mit intermittierend intakter AV-Überleitung erfolgte eine Programmierung im AAI-SafeR®-Modus, der eine Eigenüberleitung erlaubt und erst bei Vorliegen eines AV-Blocks automatisch in einen vorhofgesteuerten Ventrikelstimulationsmodus wechselt. Hierbei werden ein AV-Block II.° als 3 blockierte atriale Impulse innerhalb von 12 Zyklen und ein AV-Block III.° als 2 konsekutiv nicht übergeleitete Impulse definiert. Die AV-Block-Episoden werden im Ereignisspeicher des Schrittmachers erfasst und zur Beurteilung des Vorliegens selbiger Rhythmusstörungen herangezogen.

Ergebnisse Im Beobachtungszeitraum wurden 59 Patienten mit höhergradiger Aortenklappenstenose mit einer Core Valve®-Klappe versorgt (mittleres Alter 81,8 ± 5,4 Jahre, 54 % Frauen). Der mittlere Nachbeobachtungszeitraum war 12 Monate (Interquartilen-Abstand: 3–24 Monate). Die 30-Tages-Mortalität betrug 6,8 % (4 Patienten), die 6-Monats-Mortalität 13 % (6 Patienten). Kein Patient verstarb an einem suspekt arrhythmogenen Ereignis. Sechs Patienten hatten bereits vor PAKE einen Schrittmacher erhalten und wurden von der Analyse ausgeschlossen. Von den verbleibenden 53 Patienten erhielten 27 Patienten (51 %) einen Schrittmacher (18 Patienten wegen eines höhergradigen AV-Blocks, 9 Patienten aufgrund eines neu aufgetretenen Linksschenkelblocks). Vier Patienten wurden bei AV-Block III.° und Vorhofflimmern im VVI-Modus stimuliert, von den übrigen 23 Patienten im AAI SafeR®-Modus wurden 5 Patienten (22 %) zu nahezu 100 % ventrikulär stimuliert bei permanentem AV-Block III.°, 9 Patienten (39 %) zeigten wiederholt AV-Block II.°- und -III.°-Episoden (2314 bzw. 193 Episoden). Bei 3 Patienten (13 %) mit eigener AV-Überleitung wurden im Nachbeobachtungszeitraum keine höhergradigen AV-Blockierungen vom Schrittmacher aufgezeichnet. Von den restlichen 6 Patienten waren oder sind noch keine Schrittmacherdaten verfügbar. Bei Patienten mit postinterventionell unauffälliger Reizleitung, die keinen Schrittmacher erhielten, traten auch bei weiteren Kontrollen keine AV-Blockierungen neu auf.

Diskussion Reizleitungsstörungen während der unmittelbar postinterventionellen Überwachung erlauben eine Vorhersage bezüglich höhergradiger AV-Blockierungen: Bei normalen Reizleitungsverhältnissen traten im Verlauf keine höhergradigen AV-Blockierungen neu auf. Auch bei nur intermittierend auftretendem AV-Block II.° oder III.° sollte aufgrund der nachgewiesenen häufigen Rezidive der Leitungsstörungen ein Schrittmacher implantiert werden.

Early Changes of Pulse Wave Velocity and Central Aortic Blood Pressure Parameters Following Renal Sympathetic Nervous Denervation

BAI

M. C. Brandt, S. Reda, F. Mahfoud, J. Schuler, P. Grüner, M. Böhm, U. C. Hoppe
Universitätsklinik für Innere Medizin II, Paracelsus Medizinische Privatuniversität Salzburg, Österreich; Klinik für Innere Medizin III, Universitätsklinikum des Saarlandes, Homburg/Saar, Deutschland

Background Therapy refractory hypertension causes significant structural and functional alterations not only in the heart but also in the central and peripheral vasculature. Recently, a novel technique using a tonometer sensor connected to a computer has been established to measure vascular stiffness by calculating the central aortic blood pressure curve and the pulse wave velocity from peripheral pulse recordings of the radial, carotid and femoral artery (Atcor Medical Pty Ltd., West Ryde, Australia). Clinical studies have shown prognostic relevance of the augmentative pressure and pulse wave velocity in patients with arterial hypertension. Our aim was to study the effect of sympathetic renal denervation (RDN) on central aortic pulse wave parameters and pulse wave velocity.

Results A total of 26 patients were enrolled consecutively and RDN was performed. Before and 1 month after the procedure, pulse wave studies were done. The mean age in the cohort was 64 ± 2 years, males were a majority of 69.4%. As early as 1 month post RDN, the mean blood pressure was significantly reduced (177 ± 4/95 ± 2 mmHg systolic/diastolic at baseline vs 156 ± 4/87 ± 3 mmHg at 1; p = 0.003; n = 26). The blood pressure reduction was accompanied by distinct changes of pulse wave parameters and pulse wave velocity.

The calculation of the central aortic blood pressure curve from the radial pressure recording showed a significant reduction in aortic systolic (159 ± 5 mmHg vs 144 ± 4 mmHg; p = 0.042), diastolic (95 ± 2 mmHg vs 87 ± 3 mmHg, p = 0.001) and pulse pressure (68 ± 4 mmHg vs 57 ± 3 mmHg, p = 0.036). The mean systolic pressure (141 ± 3 mmHg vs 127 ± 4 mmHg; p < 0.0001) and mean diastolic pressure (110 ± 3 mmHg vs 100 ± 3 mmHg, respectively; p < 0.0001) were also significantly reduced. Furthermore, the augmentative pressure showing early or increased pulse wave reflections causing increased cardiac workload, was significantly reduced 1 month after RDN, before (augmentative pressure 22.1 ± 2.0 mmHg vs 18.6 ± 1.8 mmHg; p = 0.042) and after correction for heart rate (augmentation index at heart rate 75/min 25.1 ± 1.5 vs 23.8 ± 1.6; p = 0.045). Consistently, an improvement of cardiac function was evident in a small but significant decrease of the ejection duration in relation to cardiac cycle length (34.6 ± 0.7 % vs 33.1 ± 0.7 %; p = 0.007).

The pulse wave velocity from the carotid to the femoral artery showed a significant reduction from 11.7 ± 0.6 m/s to 10.5 ± 0.6 m/s; p = 0.021).

Conclusion Our results show for the first time that RDN not only facilitates better peripheral blood pressure control but also causes distinct changes of central aortic blood pressure parameters. Together with better blood pressure reduction novel parameters of arterial stiffness and vascular remodeling with important clinical prognostic implications for the individual patients are improved at an early stage after RDN.

Inhibition of Platelet Aggregation by Intracoronary Bolus-Only Administration of Abciximab: Time Course and Influence of Clopidogrel versus Prasugrel Loading BAII

G. Christ, Th. Hafner, Th. Chatsakos, E. Wilhelm, M. Francesconi, A. Podczeck-Schweighofer
5. Medizinische Abteilung – Kardiologie SMZ-Süd/KFJ, Wien

Background Current acute coronary syndrome (ACS) guidelines recommend a bolus and infusion administration of the GP IIbIIIa inhibitor abciximab on top of dual antiplatelet inhibition in high risk patients undergoing percutaneous coronary intervention (PCI). Recent data suggest that an abciximab bolus-only regimen with high loading dose clopidogrel does not impair platelet inhibition throughout 24 h.

Objectives To evaluate the time course and extent of platelet inhibition by a single intracoronary abciximab bolus and the relation to co-medication with clopidogrel or prasugrel.

Patients and Methods 56 consecutive high-risk ACS patients (70% STEMI, 30% NSTEMI with visible thrombus) and intracoronary abciximab bolus administration (0.25 mg/kg) were included (55% loaded with 600 mg clopidogrel, 45% with 60 mg prasugrel). Thrombin receptor-activating peptide (TRAP) and ADP induced platelet reactivity was measured by Multiple Electrode Aggregometry (MEA; Multiplate®), at 4 h, 24 h, 3 and 6 days. Clinical outcome was evaluated at 30 days.

Results Overall platelet reactivity, measured by TRAP induced aggregation, was significantly suppressed for more than 24 h (45 ± 17 U) and returned to normal (> 84 U) only after 6 days (90 ± 26 U; $p < 0.001$). Co-medication with prasugrel significantly reduced ADP-induced ($p = 0.002$), as well as TRAP-induced ($p = 0.02$), platelet aggregation compared to clopidogrel throughout the observation period. Six patients in the clopidogrel group (19 %) were classified as nonresponder (> 49 U ADP) and switched to prasugrel (2 on day 4 and 4 on day 7; ADP pre-switch: 88 ± 25 U vs post-switch: 22 ± 10 U; $p < 0.001$). During 30 days no stentthrombosis or repeat myocardial infarction and two deaths (4%) in cardiogenic shock occurred. Significant bleeding complications were low (4%, only puncture site related: one TIMI major with red blood cell transfusion in the clopidogrel group and one TIMI minor in the prasugrel group).

Conclusion A single intracoronary abciximab bolus in combination with high loading dose of thienopyridines effectively inhibits overall platelet reactivity for more than 24 hours, suggesting no need for continuous abciximab infusion. Co-medication with prasugrel compared to clopidogrel not only reduces ADP induced platelet aggregation, but also overall platelet reactivity via a so far not known mechanism.

Single Center Experience with Paravalvular Leak Closure After Recurrent Mitral Valve Surgery XV – 7

Ch. Ebner, W. Tkalec, J. Aichinger, Th. Sturmberger, V. Eder, H.-J. Nesser
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Paravalvular leak (PVL) is a common complication after surgical valve replacement with reported incidence up to 17% for prosthetic valves in the mitral position. Although most of these leaks are clinically silent, in up to 3% of these patients reoperation is needed due to heart failure symptoms or hemolysis. Percutaneous closure of periprosthetic paravalvular leaks has been proposed as an attractive alternative to surgical closure particularly in high risk patients. Herewith we present our experience using this technique.

Methods and Results The first procedure as the first in Austria was performed in our institution on June 2010. Until November 2011 we performed 5 procedures in 4 patients (50% male) with a mean age of 65 ± 8.8 years. All of them had bileaflet mechanical prostheses and signs and/or symptoms of heart failure. Additionally hemolysis criteria were evident: hemoglobin ≤ 10 g/dl (mean 8.5 ± 1), Lactat Dehydrogenase: ≥ 600 mg/dl (median 2114, IQR 1275–4495), and haptoglobin: ≤ 10 mg/dl (mean 1 ± 1.7). All of them had at least ≥ 2 previous redo-operations of their prostheses due to paravalvular leaks and ≥ 2 blood transfusions in the past to correct anemia.

The procedure was performed under fluoroscopy and guided by 2D/3D transesophageal echocardiography (Philips IE 33) to determine the size and location of the PVLs. Duration of he procedure was mean 165 ± 49 minutes. 4/5 procedures were done using an antegrade approach via the V. fem. dext. with consecutive transseptal puncture. In 1 procedure a retrograde approach via the A. fem. dext. was choosen and passing the aortic valve. In all of the patients 2 Amplatzer Vascular Plugs III were placed followed by significant reduction of the regurgitant flow in 3/4 patients. No periprocedural complications occurred and all patients are still alive. In one of the patient a second PVL could not be closed due to anatomic conditions (introduction of the guide wire but not catheter passage); nevertheless need of blood transfusions could be reduced. 2/4 patients had an excellent result disclosing only trivial residual paraprosthetic regurgitation, significant reduction of hemolysis criteria and clinical improvement. In 1/4 patient significant paravalvular regurgitation remained and finally this patient underwent redo mitral valve replacement at risk due to symptomatic heart failure.

Conclusion Transcatheter closure of PVL after previous valve surgery can be attempted with acceptable success rates and in our series without complications. This procedure seems to be an attractive alternative in patients after previous surgical valve procedures complicated by paravalvular leaks combined with distinct hemolysis or significant mitral regurgitation. In our series this technique was exclusively performed in patients with distinct comorbidities or high surgical risk of the redo due to failed previous leak repair.

Optische Kohärenztomographie zur Beurteilung des Stentergebnisses – ein klinischer Erfahrungsbericht bei 20 Patienten VII – 6

C. Gangl, Th. Neunteufl, G. Delle-Karth, G. Kreiner, I. Lang, Ch. Roth, N. Lajic, M. Vertesich, L. Krenn, D. Bonderman, R. Berger
Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin II, Medizinische Universität Wien

Einleitung Die Kontrolle des Stent-Ergebnisses wird allgemein vor allem mittels angiographischer Beurteilung durchgeführt. Pathologien, die die angiographische Kontur nicht oder nur in geringem Ausmaß beeinflussen, können so nur schwer festgestellt werden. Mittels Optischer Kohärenztomographie (Frequency-Domain OCT) – einem Verfahren zur intravaskulären Bildgebung – können hochauflösende Bilder von der Koronararterienwand bzw. dem Inneren der Koronararterie erstellt werden, die dem intravaskulären Ultraschall im Bezug auf die Auflösung um bis zu Faktor 10 überlegen sind. Somit können Stent-Anomalien noch exakter beurteilt werden, um diese gegebenenfalls adäquat korrigieren zu können.

Material und Methoden Es wurden deskriptiv Daten von 20 Patienten ausgewertet, welche sich zwischen Mai 2010 und Mai 2011 einem interventionellen Herzkatheter-Eingriff am AKH Wien unterzogen haben. Dabei wurden die Patienten durch Randomisierung entweder mittels Xience Prime (Everolimus) oder Biomatrix Flex (Biolimus) behandelt. Nach erfolgtem Stenting und eventueller Nachdilatation nach der Entscheidung des Interventionalisten wurde abschließend von einem ausgewählten Stent eine OCT durchgeführt. Die dabei gewonnen Aufzeichnungen wurden anschließend durch einen erfahrenen Analysten mithilfe der auf dem OCT-Gerät installierten Software auf die in **Tabelle 8** angeführten Phänomene hin ausgewertet.

Ergebnisse Die Charakteristika der beiden Kohorten sind in **Tabelle 9** angeführt.

Wie in **Tabelle 8** aufgeschlüsselt, konnten bei insgesamt 11 Stents Malappositionen festgestellt werden (Biomatrix 5/Xience 6). Stent-Underexpansions konnten in insgesamt 4 (Biomatrix 2/Xience 2), asymmetrisch expandierte Stentsegmente in insgesamt in 9 implantierten

Tabelle 8: C. Gangl et al. Ergebnisse

	Biomatrix (n = 10)	Xience (n = 10)	Gesamt (n = 20)
Underexpansion	2	2	4
Most asym. Exp.	4	5	9
Edge-Diss. (prox./dist.)	–/4	1/–	1/4
Malappositionen			
keine	5	4	9
1 Segment	1	4	5
2 Segmente	2	1	3
3 Segmente	2	–	2
4 Segmente	–	1	1
Plaque-Protrusionen			
keine	1	3	4
1 Segment	4	4	8
2 Segmente	2	–	2
3 Segmente	1	1	2
4 Segmente	2	1	3
Plaque-Prolapse			
keine	1	–	1
1 Segment	1	–	1
2 Segmente	2	–	2
3 Segmente	2	2	4
4 Segmente	1	2	4
5 Segmente	3	6	9

Tabelle 9: C. Gangl et al. Kohorten-Charakteristika

	Biomatrix (n = 10)	Xience (n = 10)	Gesamt (n = 20)
Geschlecht (m/w)	6/4	9/1	15/5
Alter	55 (IQR 50,5–58)	60,1 (IQR 54–67,5)	57,7 (IQR 51,5–62,3)
Indikation (elektiv/ACS)	10/0	8/2	18/2
Stent-Lokalisationen			
LAD	5	6	11
RCA	3	2	5
CX	2	1	3
R. intermedius	–	1	1
KHK-Ausprägung			
1VD	3	4	7
2VD	3	4	7
3VD	4	2	6
Stenting-Technik			
Direct Stenting	–	5	5
Predil.	3	3	6
Postdil.	–	1	1
Pre-/Postdil.	6	2	8

Stents (Biomatrix 4/Xience 5) detektiert werden. Fünf Stents zeigten nach Implantation eine Edge-Dissection (Biomatrix 4/Xience 1).

Wie weiters in **Tabelle 8** ersichtlich, konnten in einer Vielzahl (16 von 20) der untersuchten Stents Plaque-Protrusionen (Vorwölbungen des Plaques über die Stent-Struts hinaus, ohne Kontinuitätsunterbrechung der Intima oder Plaquekappe) festgestellt werden. In 19 von 20 Patienten konnten Plaque-Prolapse in unterschiedlichen Größen und Anzahl pro Stent gefunden werden.

Konklusion Mittels OCT können viele morphologische Auffälligkeiten nach der Stent-Implantation detektiert werden, die klinische Bedeutung dieser Auffälligkeiten muss erst in Verlaufskontrollen bzw. bei größeren Patientenkollektiven untersucht werden.

Long-Term Follow-Up of Patients Treated with Combined Delivery of Intracoronary and Intramyocardial Bone-Marrow Mononuclear Cells XV – 1

E. Gieseking, B. Syeda, H. Sochor, S. Charwat, J. Bergler-Klein, G. Maurer, M. Gyöngyösi
Division of Cardiology, Department of Medicine II, Medical University Vienna

Background Between 2002 and 2006, patients with recent acute myocardial infarction (AMI) and ejection fraction (EF) between 30 and 45% were included into the MYSTAR prospective randomized study, and received combined delivery of bone-marrow mononuclear cells (BM-MNC) either 3–6 weeks (mean 32 ± 12 days, early group) or 3–4 months (mean 93 ± 15 days, late group) post AMI. The BM-MNC therapy resulted in an improvement in mean ejection fraction of 3.5% and infarct size of 3.7%.

Aim The aim of the present follow-up (FUP) study was to evaluate the long-term effect (mean 5 years) of the cardiac stem cell therapy on clinical outcome and on ventricular function and size of infarction.

Methods and Results Six patients died during the follow-up due to cardiac reasons (heart failure). Five patients were lost to FUP or refused the investigations. Patients were invited to undergo gated 99m-Tc-MIBI perfusion scintigraphy to evaluate infarct size and global EF (primary endpoint of the MYSTAR study). The further 5-year clinical follow-up (FUP) included the records of major adverse cardiac events (MACCE, defined as all-cause mortality, re-AMI, re-intervention of the infarct-related artery and stroke), implantation of automatic cardioverter-defibrillators (ICD) and hospitalization due to angina pectoris or acute or chronic heart failure.

Results Infarct size decreased non-significantly from 24.3 ± 11.6% (3 months post-stem cell therapy) to 21.0 ± 12.2% (p = 0.266) during the mean 5 years FUP. Trend towards decrease in end-diastolic volume was observed (from 209 ± 76 ml to 182 ± 69 ml; p = 0.126), suggesting reverse remodeling. EF increased significantly during the 5 years FUP (from post-stem therapy value of 41.5 ± 8.4% to 45.4 ± 9.2% at 5 years FUP) (p = 0.028). AICD was implanted in 5 patients, repeated hospitalization was necessary in 20 patients. Cumulative MACCE occurred in 10 patients, including cardiac death and reintervention (n = 4). Stroke or reinfarction did not occur.

Conclusion Combined intramyocardial and intracoronary delivery of BM-MNC led to a significant increase in global EF, and a trend towards decrease in infarct size and end-diastolic volume over a 5 years FUP, in patients with a low (30–45%) EF post-AMI.

75-jährige Patientin mit Pulmonalstenose und ausgedehnter Verkalkung an Trikuspidalring und -klappe mit resultierender hochgradiger Trikuspidalstenose VII – 1

M. Hammerer, P. Maister, K. Hergan, U. Hoppe
Universitätsklinik für Innere Medizin II; Universitätsklinik für Radiodiagnostik, Salzburger Landeskrankenhaus

Einleitung Wir berichten über eine 75-jährige Patientin mit Z. n. perkutaner Valvuloplastie der Pulmonalklappe (PK) vor 19 Jahren sowie perkutaner Valvuloplastie der Trikuspidalklappe (TK) vor 3 Jahren. Aufgrund chronisch-progredienter rechtskardialer Insuffizienz (periphere Ödeme, Hepatopathie, NYHA II–III) wurde die Indikation zu einem neuerlichen perkutanen Interventionsversuch gestellt.

Aktuelle Befunde Die Transthorakale Echokardiographie (TTE) zeigte eine Trikuspidalstenose (TS) III° **(Abbildung 32 a, c)** bei massiven para-/valvulären Verkalkungen mit exzessiver rechtsatrialer Dilatation, sowie ein kombiniertes Vitium der nur mäßig sklerosierten PK mit führender Pulmonalstenose (PS II°–III°) **(Abbildung 32 d)**. Der linkskardiale Befund war altersentsprechend unauffällig.

Die Multislice-Computer-Tomographie (CT) bestätigte die massive Verkalkung des TK-Ringes mit Fortsetzung auf den Halteapparat und die Mitralklappe (MK) **(Abbildung 32 b)**.

Die Invasivdiagnostik ergab: mittlerer Gradient über TK: 5 mmHg; mittlerer/maximaler Gradient über PK: 21/55 mmHg.

Perkutane Intervention Zunächst 2-malige PK-Valvuloplastie **(Abbildung 33 a)**. Da sich im rechtsventrikulären Ausflusstraktes (RVOT) der Eindruck einer zusätzlichen Stenosierung ergab, wurde hier diagnostisch mit sehr geringem Druck eine Ballonentfaltung ausgeführt, welche eine exzentrische kalzifizierte Obstruktion bestätigte **(Abbildung 33 b)**. In der Trikuspidalklappe erfolgte eine

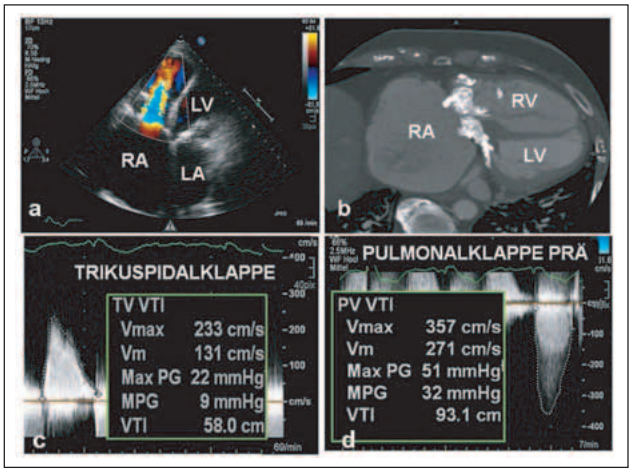


Figure 32: M. Hammerer et al.

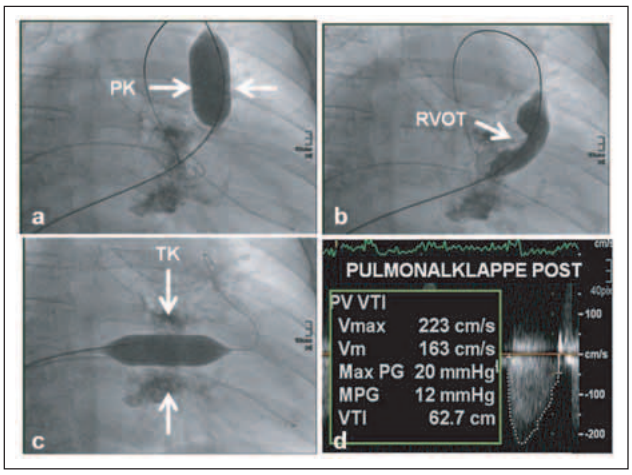


Figure 33: M. Hammerer et al.

weitere Valvuloplastie **(Abbildung 33 c)**. Von einer Doppel-Ballon-Valvuloplastie wurde aufgrund der massiven Verkalkungen Abstand genommen.

Ergebnisse Eine TTE-Kontrolle nach 2 Monaten zeigte deutlich geringere Gradienten über der PK **(Abbildung 33 d)** ohne Zunahme des Insuffizienzgrades, aber einen unveränderten Schweregrad der hämodynamisch führenden TS. Auch klinisch-anamnestisch kam es leider zu keiner relevanten Besserung. Nach multidisziplinärer Diskussion im Heart-Team wurde für ein konservativ-palliatives Vorgehen entschieden.

Diskussion TS und PS sind seltene Herzklappenerkrankungen. Eine TS ist in den allermeisten Fällen postrheumatischer Genese und ist dann in der Regel mit einer Mitralstenose assoziiert. Zweithäufigste Ätiologie einer TS und häufigste einer PS ist eine kongenitale Stenosierung oder Atresie. Wir beschreiben den äußerst ungewöhnlichen Fall einer ausgedehnten Verkalkung im Bereich der TK (mit resultierender TS III°), des TK-Ringes und des RVOT mit Ausläufern bis an die MK sowie die subvalvulären Apparate von TK und MK. Bisher beschriebene seltene Fälle ähnlicher TK-Ring-Verkalkungen (allerdings meist ohne funktionelle Beeinträchtigung) waren nahezu immer mit einer langjährig vorbestehenden chronischen Rechtsherzbelastung im Rahmen kongenitaler Vitien (PS oder ASD) assoziiert. Ein postulierter kausaler pathogenetischer Zusammenhang bleibt hypothetisch. In Anbetracht der Seltenheit dieser Entität ist jedenfalls anzunehmen, dass eine rechtskardiale Druckbelastung im Rahmen einer pulmonalen oder pulmonalarteriellen Hypertonie keine ausreichende Prädisposition darstellt. Auch bei unserer Patientin ist von einer primären (wohl kongenitalen) PS als auslösendem Faktor auszugehen.

Percutaneous Coil Embolization of a Perforated Side Branch of the Right Coronary Artery 3 Weeks After Abdominal Surgery XV – 5

R. Hemetsberger, N. Schulze-Waltrup, T. Nitschke, H. Heuer
Innere Medizin I Kardiologie, Rhythmologie, Nephrologie, St. Johannes Hospital Dortmund, Deutschland

Introduction Iatrogenic pericardial tamponade after abdominal surgery is a rare and severe complication caused by laceration of the heart through the diaphragm. Here we describe for the first time a case using percutaneous coil embolization for a perforated coronary side branch after abdominal surgery.

Methods and Results A 75-year-old female presented to our emergency department with abdominal pain 3 weeks after a laparoscopic cardiomyotomy.

The physical examination showed paleness, cold sweat, hypotension with a blood pressure of 70/50 mmHg, sinus tachycardia of 130 bpm, muffled heart sounds and hardly palpable peripheral pulses. The blood analysis revealed anemia with hemoglobin of 7.6 g/dl.

With an urgent suspicion of blood loss, first an abdominal sonography was performed and excluded free liquid in the abdominal cavity but showed a dilated vena cava (2.7 cm). A subsequent echocardiography revealed a pericardial tamponade with approximately 19 mm effusion in front of the right ventricle with typical right ventricular compression in the diastole. She was promptly transferred to our intensive care unit.

A pericardiocentesis drained initially 550 ml of hemorrhagic effusion with a hemoglobin of 12 g/dl. A pigtail-catheter was retained in order to drain the fluid. After 8 h the blood pressure decreased rapidly and an echocardiography showed a re-tamponade. The catheter was occluded with clots. A second pericardiocentesis was performed and collected 500 ml with a hemoglobin of 9 g/dl.

An emergency cardiac-CT showed a small cloud of contrast agent extravasating into the pericardial fluid. In a subsequent coronary angiogram free contrast agent extravasation from a side branch of the right coronary artery was seen, following the diagnosis of coronary artery perforation. The leakage corresponded to the inferior contrast agent dissemination at the cardiac-CT.

We decided to embolize the side branch with a fibred platinum coil using a microcatheter and a coil pusher. After exact positioning at the leakage the coil was released and 2 minutes later no extravasation was further more detected. The remaining liquid was drained and the pigtail-catheter was removed.

The patient was monitored for 2 days and was discharged at the 4th day in a stable condition.

Conclusion In this case a cardiac tamponade caused by a perforated RCA-side branch after abdominal surgery, manifested clinically after 3 weeks, was drained by pericardial puncture and treated successfully by percutaneous coil embolization of the perforated artery.

This case reflects that even 3 weeks after abdominal or oesophagogastric surgery shock symptoms should hint at a cardiac tamponade.

Patienten mit Interventionen an chronischen Koronarverschlüssen (CTO): Hohe Strahlenakkumulation durch radiologische und nuklearmedizinische Untersuchungen innerhalb eines Jahres BAI

Ch. Köllerer, C. Seelmaier, J. Schuler, U. Hoppe
Universitätsklinik für Innere Medizin, Kardiologie und Internistische Intensivmedizin, Universitätsklinikum LKH Salzburg

Einleitung Die effektive Strahlendosis einer diagnostischen Koronarangiographie beträgt durchschnittlich 3–4 mSv. Bei einer unkomplizierten Intervention erhöht sich diese Dosis um weitere 10 mSv. Bei komplexen Prozeduren (Bifurkationen, CTOs) und adipösen Patienten kann sich die Strahlendosis massiv erhöhen. Berichte von 3 Sv und mehr sind publiziert. Zusätzlich werden oft Koronar-CT (3–10 mSv) und Myokardszintigraphien (10–15 mSv) zum Vitalitätsnachweis durchgeführt. Insbesondere bei Patienten mit chroni-

schen Koronarverschlüssen (CTO) kann die Strahlendosis in der Vor- und Nachsorge erheblich akkumulieren.

Anhand eines ausgewählten CTO-Patientenkollektivs soll deren kumulative Strahlenbelastung innerhalb von 12 Monaten abgeschätzt werden.

Methodik Retrospektive Analyse aller klinischen Patientendaten aus einem monozentrischen CTO-Register hinsichtlich strahlenbelastender Untersuchungen (Röntgen-Thorax, CT, Angiographien, Szintigraphien). Es wurden alle Untersuchungen gezählt, die zum Zeitpunkt der CTO-Intervention (Indexaufenthalt) und in den nachfolgenden 12 Monaten an der Klinik durchgeführt wurden.

Ergebnisse Insgesamt wurden im Zeitraum von 04/07 bis 04/11 die Daten von 70 Patienten, die einer CTO-Katheterintervention unterzogen wurden, gesammelt und analysiert.

Beginnend vom Indexaufenthalt und in den darauffolgenden 12 Monaten wurden bei 68 Patienten (97,1 %) insgesamt 174 Röntgen-Thorax-Untersuchungen durchgeführt (durchschnittlich 2,5). Bei 15 Patienten (21,4 %) erfolgte postinterventionell eine Kontrollkoronarangiographie. 41 Patienten (58,6 %) erhielten eine Myokardszintigraphie, 2 Patienten (2,9 %) eine Lungenszintigraphie. Bei 33 Patienten (47,1 %) wurde ein Koronar-CT durchgeführt. 7 Patienten (10 %) erhielten mindestens einmal ein CT einer anderen Körperregion (11 Untersuchungen). Bei 4 Patienten (5,7 %) erfolgte eine Röntgenaufnahme einer anderen Körperregion. Insgesamt wurden bei den 70 Patienten 391 unterschiedlich strahlenbelastende Untersuchungen zusätzlich zur CTO-Intervention durchgeführt (Mittelwert 5,6).

Diskussion Bei Koronarpatienten, die eine komplexe Koronarintervention wie eine CTO-Rekanalisation erhalten, sollte nicht nur auf die Strahlenbelastung während der Intervention geachtet werden. Während eines einjährigen Follow-up wurde eine CTO-Kohorte durchschnittlich 5,5 weiteren radiologischen bzw. nuklearmedizinischen Untersuchungen ausgesetzt. Im Einzelfall kann es somit zu einer sehr hohen kumulativen Strahlenbelastung kommen.

Alle Behandelnden sollen daher jede einzelne strahlenintensive Untersuchung streng indizieren und strahlenfreie Alternativen nutzen. Die Patienten müssen in jedem Fall über die möglichen Risiken der Strahlenbelastung hingewiesen werden und die Aufzeichnung der einzelnen Untersuchungen in einem Röntgenpass ist mehr denn je anzuraten.

Incidence of Coronary Stent Fractures in Patients at High Risk VII – 5

L. C. Krenn, V. Berger-Kulemann, P. Krisai, F. Wolf, G. Delle-Karth, G. Kreiner, Ch. Roth, C. Gangl, I. Lang, H. Sochor, Th. Neunteufl, Ch. Löwe, R. Berger
Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin II; Universitätsklinik für Radiodiagnostik, Medizinische Universität Wien

Background Fracture of drug-eluting stent (DES) is regarded to play a significant role in several cases of stent thrombosis, in-stent restenosis, target lesion revascularization, myocardial infarction as well as sudden death. The rates of stent fracture diagnosed by coronary angiography (CA) seem to be underestimated (1–7%), as significantly higher rates are reported at autopsy (29%). Coronary computered tomography (CCT) may be a more accurate method for the detection of stent gaps than CA.

Aim This is the first study to prospectively evaluate the incidence of stent gaps in patients at high risk for stent fracture.

Methods Patients with two or more risk factors for stent fracture defined as (1) stent length ≥ 28 mm, (2) stent overlapping, (3) localization in the right coronary artery or saphenous vein graft and (4) vessel angulation of ≥ 75° before implantation or ≥ 45° stent angulation after implantation were invited to undergo a coronary CT angiography 6 months after the procedure. A coronary angiography including optical coherence tomography was recommended in patients with a partial or total stent gap.

Results In eleven (46%) out of 24 patients (70.8% male, mean age 63.2 ± 10 years) coronary CT revealed a stent gap. Stent fracture was suggested in 7 patients (29%), whereas a stent-gap between not exactly overlapped stents (identified by measurement of the stent-lengths) was diagnosed in 4 patients (17%). In the following CA all stent gaps were confirmed by optical coherence tomography. In 3 patients (13%) stent gap was associated with an instent-restenosis (n = 2.8%) and a chronic total occlusion (n = 1, 4%), respectively.

Conclusion Stent gaps are a frequent phenomenon in patients at risk (46%). A stent fracture was diagnosed in 29% of patients with 43% of these patients requiring revascularisation. A larger patient population and a longer follow-up time is needed to further elucidate the clinical impact of CCT for evaluation of patients at high risk for stent fracture.

A HEART Team Approach for TAVI: Clinical Outcome of the First 32 Patients as Compared with Results of the PARTNER Trial and with the Austrian TAVI Registry VII – 2

M. Leibl, G. Unger, A. Geppert, E. Wessely, J. Falkensammer, A. Bambazek, F. Waldenberger, A. Assadian, B. Gustorff, M. Grabenwöger, K. Huber
3. Medizinische Abteilung, Kardiologie, Gefäßchirurgie, Anästhesie, Wilhelminenspital, Wien; Herzchirurgie Krankenhaus Hietzing, Wien

Background In the past, transcutaneous aortic valve implantation (TAVI) has shown to restore valvular function in inoperable high-risk patients with severe aortic valve stenosis resulting in clinical improvement and patient survival as compared to a conservative strategy. This method has been investigational for many years and was usually associated with a learning curve in the early phase of implementation of this method in the departments offering TAVI. We report results of the first 32 patients of our TAVI program, which started 8/2010 after extensive education of the responsible interventionists at specialized centers and with the help of an experienced proctor for the first 15 patients to avoid complications in the "learning phase". Moreover, optimized techniques and surroundings (e. g. preparation and closure of the femoral artery by a vascular surgeon, presence of an anesthesiologist and a cardiac surgeon during the whole procedure, stand-by of a mobile heart lung unit with technician) were organized from the very beginning of this method. Our peri-procedural, short- and long-term results are compared with those achieved in larger patient cohorts (PARTNER Trial, PT; and Austrian TAVI Registry, ATR), respectively.

Methods Between 8/2010 and 1/2012, 32 high-risk patients (Euro SCORE 26.6 ± 12.4%) with a mean age of 83 ± 5 years, who were not eligible for cardiac surgery by decision of the cardiac surgeon (MG), received a Medtronic CoreValveTM at our department. We analyzed the clinical outcome during the peri-procedural phase as well as at 30 days and after one year.

Results Baseline echocardiographic parameters before implantation of the CoreValveTM revealed a mean transvalvular pressure of 45.4 ± 14.3 mm Hg (PT: 44.5 mm Hg; ATR: 53.6 mmHg), a mean aortic valve area (AVA) of 0.7 ± 0.2 cm^2 (PT: 0.6 cm^2; ATR: 0.6 cm^2), and a mean LVEF of 48.9 ± 10.2% (PT: 53.9 %; ATR: not available). Echocardiographic assessment after TAVI revealed a mean transvalvular pressure of 8,7 ± 3,9 mm Hg (PT: 11,1 mm Hg; ATR: 9.67 mm Hg), a mean AVA of 2.2 ± 0.9 cm^2 (PT: 1.5 cm^2; ATR: 1.94 cm^2), and a mean LVEF of 50,7 ± 8,8% (PT: 57,9; ATR: not available]. Major bleeding from the femoral artery (n = 3; 9.4%; PT: 16.2%, ATR: 6%), stroke or TIA (n = 1; 3.1%; PT: 6.7%, ATR: 3.2%) and post-procedural complete AV block requiring pacemaker implantation (n = 2; 6.3%; PT: 3.4%, ATR: 23.2%) represented peri-procedural complications. Moreover, 11 additional patients (34.4%), who developed post-procedural left or right bundle branch block, also received a pacemaker as a precaution (total PM rate after TAVI: 40.6%). No patient died during or immediately after the procedure. Short-term all-cause mortality at 30 days was 6.3% (PT: 3.4%; ATR: not available). All-cause mortality after 1 year (5/11 patients) was 45.5%. Of all deaths about 2/3 were non-cardiovascular indicating the specific high-risk and multimorbid population included for TAVI procedures at our institution.

Conclusion These data confirm experience from other groups that TAVI can be successfully initiated and performed without a "learn-

ing curve" if a close cooperation within a HEART team including different specialties is organized. This success encourages to further extending our program.

Post-Procedural Atrial Fibrillation After Transcatheter Aortic Valve Implantation versus Surgical Aortic Valve Replacement XV – 6

L. J. Motloch, D. Rottländer, S. Reda, R. Khatib, R. Larbig, U. C. Hoppe
Department of Internal Medicine II, Paracelsus Medical University, Salzburg

Background Transcatheter aortic valve implantation (TAVI) represents an alternative option for elderly with severe aortic valve stenosis who are denied surgical aortic valve replacement (SAVR) due to high perioperative risk. The impact of TAVI on post-procedural atrial fibrillation is undefined.

Methods In a single-centre analysis we assessed clinical data, preoperative risk scores (STS-Score, logistic EuroSCORE), pre-procedural ECGs and 72-hour post-procedural rhythm monitoring of 170 patients undergoing TAVI (n = 84) or SAVR (n = 86). In a subanalysis transapical (n = 43) and transfemoral TAVI (n = 41) were compared.

Results Expectedly, TAVI patients were significantly older, presented with more severe symptoms, had higher STS-Scores, higher logistic EuroSCOREs and revealed more frequently intermittent atrial fibrillation compared to SAVR patients. Despite this more compromised health state, prevalence of post-procedural atrial fibrillation was significantly lower in the TAVI group (6.0% vs 33.7% after SAVR; $p < 0.05$). More than 2/3 of TAVI patients but no SAVR patient with atrial fibrillation in pre-procedural ECGs had stable sinus rhythm during 72 hour post-procedural monitoring. Notably, no atrial fibrillation was observed after transfemoral TAVI. While atrial fibrillation onset in the SAVR group predominantly occurred on postoperative day 3, atrial fibrillation onset after transapical TAVI was obtained within the first 24 hours after the intervention.

Conclusion Our results indicate that TAVI compared to SAVR reduces the risk of peri-procedural atrial fibrillation. Furthermore, pre-procedural atrial fibrillation may be converted into sinus rhythm particularly after transfemoral TAVI suggesting an impact of decreased intracardiac pressures in the absence of adverse peri-procedural factors that might promote atrial fibrillation.

Drug-eluting Stent versus Bare-metal Stent nach koronarer Rotablation XV – 9

L. Pilgerstorfer, H. Kratzer, E. Zeindlhofer, A. Winter, M. Gattermeier, K. Höllinger, D. Kiblböck, D. Szücs, A. Gierlinger, M. Schmid, Ch. Steiner, P. Siostrzonek
Interne II, KH Barmherzige Schwestern, Linz; Landesklinikum Mostviertel, Waidhofen a. d. Ybbs

Einleitung Die Rotablation (RA) stellt bei starker koronarer Gefäßverkalkung eine wichtige interventionelle Therapieoption dar. Die Behandlung langer Gefäßsegmente mittels RA ist mit einer hohen Restenoserate assoziiert. Drug-eluting Stents (DES) könnten gerade nach RA gegenüber Bare-metal Stents (BMS) vorteilhaft sein.

Material und Methoden Wir erfassten alle Patienten, die in unserem Katheterlabor in den Jahren 2000–2010 einer RA mit Stent-Implantation unterzogen worden waren und bei denen eine Reangiographie nach 6 Monaten verfügbar war. Von diesen insgesamt 91 Patienten hatten 52 Pat. DES und 39 Pat. BMS erhalten. Als primärer Endpunkt wurden die Instent-Restenose und die Target-Vessel-Restenose nach 6 Monaten gewählt, sekundäre Endpunkte waren Myokardinfarkt und Tod nach 6 Monaten.

Ergebnisse DES- und BMS-Patienten waren in Hinblick auf Alter (71,0 ± 9,6 vs. 72,1 ± 8,8 a), Geschlecht (Männer: 69,2 % vs. 69,2 %) und kardiovaskuläre Risikofaktoren (Diabetes: 40 % vs. 26 %; p = 0,17) vergleichbar. Die Stentlänge betrug bei Pat. mit DES und BMS 31 ± 15,9 und 25,1 ± 13.9 mm (p = 0,078), der mittlere Stentdiameter 3,1 ± 0,28 und 3,5 ± 0,4 mm (p < 0,001). In der angiographischen 6-Monats-Kontrolle hatten 26,5 % der Pat. mit DES und 46,8 % der Pat. mit BMS eine Instent-Restenose (p = 0,06). Die Target-Vessel-Restenose betrug 40,8 % für Pat. mit DES und 65,6 % für Pat. mit BMS (p = 0,011). Restenosen außerhalb des Stent-Segmentes traten bei Pat. mit DES und BMS in 14,2 % bzw. 18,8 % (p = 0,59) auf.

Sekundäre Endpunkte traten selten auf und waren in den Gruppen nicht-signifikant unterschiedlich (Infarkt 2/51 nach DES und 2/39 nach BMS, Tod bei 1/51 nach DES und 2/39 nach BMS.

Diskussion Die klinische Ereignisrate 6 Monaten nach RA ist bei Verwendung von DES und BMS niedrig. Restenosen sind nach langstreckiger RA und Stentimplantation häufig und nicht nur auf die gestenteten Segmente beschränkt. DES reduzieren gegenüber BMS nach RA die Rate an Instent-Restenosen, aber nicht die Stenoserate in Segmenten ohne Stentabdeckung.

Mesh Covered Stents and Myocardial Blush in STEMI Patients XV – 3

N. Preis, J. Sipötz, O. Friedrich, M. Winkler, G. Gaul
2. Medizinische Abteilung, Hanusch-Krankenhaus, Wien

Background Our single centre retrospective trial sets out to examine the outcome of PCI in STEMI patients using a mesh covered stent device designed to provide embolic protection compared to a control group in with conventional stent devices. Endpoints were myocardial blush measured by a quantitative method, TIMI after PCI, ST-segment elevation resolution, and 6 months mortality.

Method Our trial included 58 single vessel interventions after acute STEMI. In 24 patients the mesh covered stent was deployed, the control group included 34 patients.

Myocardial reperfusion after PCI was assessed by Myocardial Blush Grade (MBG) and by using the Quantitative Blush Evaluator (QuBE) a computer program created by Vogelzang et. al. (2009) providing a quantitative measure for myocardial blush. To apply the QuBE to our angiographic data we modified the method calculating the increase in grey value in the filling phase of the vessel, only. The modified QuBE value is significantly correlated with MBG ($p < 0.001$) and ST-elevation resolution ($p = 0.02$). Complete ST-segment resolution was defined as a resolution of more than 70% 60–90 minutes after PCI.

Results We found a non-significant trend of better TIMI flow grade and MBG after PCI in patients treated with mesh covered stents (TIMI 2: 8.3%, 3: 91.7%; MBG 2: 8.3%, 3: 91.7%) compared to the control group (TIMI 1: 2.9%; 2: 17.7%, 3: 79.4%; MBG 1: 8.8%; 2: 17.7%; 3: 73.5%). Quantitative measured myocardial blush was significantly better (median: 5, q1/q3: 4/7 vs median: 3.5, q1/q3: 2/6; $p < 0.001$). No significant difference was found with respect to ST-segment elevation resolution and 6 months.

Table 10: N. Preis et al. Outcome Parameters

	Mesh covered stent (n = 24)	Conventional stent device (BMS or DES) (n = 34)	p
TIMI			
1	0.0 %	2.9 %	
2	8.3 %	17.7 %	0.139*
3	91.7 %	79.4 %	
MBG			
1	0.0 %	8.8 %	
2	8.3 %	17.7 %	0.064**
3	91.7 %	73.5 %	
Modified QuBE			
Median	5	3.5	
Q1	4	2	<0.001***
Q3	7	6	

* TIMI 3 vs TIMI 1/2 (Fisher Exact Test); ** MBG 3 vs MBG 1/2 (Fisher Exact Test); *** Mann-Whitney-U-Test

Conclusion At the current stage our trial suggests, the deployment of mesh covered stents results in better myocardial reperfusion in STEMI-patients compared to conventional stent devices. It may be assumed that covering a stent with a mesh may protect against distal embolization in thrombus burden. Further randomized research is needed **(Table 10)**.

Local versus General Anesthesia for Transfemoral Aortic Valve Implantation VII – 9

S. Reda, L. J. Motloch, D. Rottländer, R. Larbig, J. Strauch, T. Wahlers, U. C. Hoppe
Klinik für Innere Medizin II/Kardiologie, Universitätsklinikum Salzburg, Österreich; Universitätsklinik für Herz- und Thoraxchirurgie, Bochum; Universitätsklinik für Herz- und Thoraxchirurgie, Köln, Deutschland

Background Transcatheter aortic valve implantation (TAVI) represents a novel option for elderly with severe aortic valve stenosis who are denied surgical aortic valve replacement due to high perioperative risk. While transfemoral TAVI generally is being performed in general anesthesia (GA), TAVI under local anesthesia plus mild sedation (LAPS) might be an effective and safe alternative.

Methods In a 3 year single-centre analysis we assessed clinical data, preoperative risk scores (STS-Score), echocardiography, periprocedural data and labor costs in 74 patients undergoing transfemoral TAVI under GA (n = 33) and LAPS (n = 41).

Results Patients who underwent TAVI in LAPS presented significantly more often with pulmonary hypertension and impaired renal function, and tended to have a higher STS-Score and more severe symptoms (higher NYHA class) versus the GA group. There were no significant differences in procedure-related 30-day mortality or complications between groups. The peak systolic and mean central aortic pressure were significantly higher in the LAPS group, while at the same time these patients required significantly less often periprocedural adrenergic support. There was no significant difference between intervention time and fluoroscopy time. However, total procedure time was significantly shorter and labor costs were lower in the LAPS group. Patients who underwent TAVI in LAPS could be mobilized significantly earlier.

Conclusion Our study indicates that TAVI under LAPS is as effective and safe as TAVI under GA. Furthermore total procedure time and labor costs could be reduced by LAPS. Mobilization of patients could be achieved earlier. We therefore consider LAPS to be favorable in patients undergoing transfemoral TAVI.

Contrast Agent and Radiation Exposure in Revascularization of Chronic Total Occlusions: Magnetic Navigation versus Conventional Percutaneous Coronary Intervention VII – 3

S. Scherzer, R. Berger, L. Krenn, A. Kaider, G. Delle Karth, Th. Neunteufl
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Introduction Aim of this trial was to compare magnetic navigation system (MNS) and conventional approach in revascularization of coronary chronic total occlusions (CTO).

Methods Forty symptomatic patients with CTO were randomized to MNS or conventional approach for antegrad crossing of the occluded vessel. Crossing success, crossing time, radiation exposure, and contrast media usage were directly compared using intention-to-treat and per protocol analysis. In the per protocol analysis each study group included patients with cross over after failing wire-crossing in the original group.

Results In the intention-to-treat analysis wire-crossing and revascularization were successful in a comparable number of CTOs using MNS (n = 9/9) and the conventional approach (n = 13/12). Crossing time was significantly shorter in the MNS group (415.5 sec; IQR 211.5–497.5 sec) than in the conventional group (1131 sec; IQR 275.5–2630 sec; p = 0.03). Also radiation exposure was significantly lower in the MNS group (513.5 mGy; IQR 313–837 mGy) than in the conventional group (1346.5 mGy; IQR 520.5–4053.5 mGy; p = 0.02). Usage of contrast agent was in trend lower in the MNS group (42.4 ml; IQR 28.55–56.3 ml) than in the conventional group (116 ml; IQR 21.25–313.6 ml). However, four previously failed MNS cases were successfully crossed with a wire and revascularized using the conventional approach. Accordingly, in the per-protocol the wire-crossing rate was in trend higher using the conventional approach (17 of 31) compared to the MNS (9 of 28; p = 0.08).

Conclusion The use of MNS for wire-crossing and revascularization is feasible and can reduce crossing-time, radiation exposure, and the use of contrast agent. However, due to a better selection of crossing wires the conventional approach enables wire-crossing in cases failed by MNS and seems to be the more successful choice.

The Course of NT-proBNP in Patients who Underwent Percutaneous Transcatheter Aortic Valve Implantation VII – 4

S. Scherzer, R. Rosenhek, Th. Binder, G. Maurer, S. Sandner, G. Kreiner, W. Wisser, Th. Neunteufl, J. Bergler-Klein
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background Natriuretic peptides have been shown to predict outcome in patients with severe aortic stenosis before and after aortic valve replacement. The aim of this study was to evaluate the course of N-terminal pro B-type natriuretic peptide (NT-proBNP) in patients who underwent percutaneous transcatheter aortic valve implantation (TAVI).

Methods Between May 2007 and January 2012, 78 symptomatic pts with severe aortic stenosis successfully underwent TAVI (55 pts received a Edwards Sapiens valve, 23 pts a CoreValve). NT-proBNP (Roche Elecsys) was assessed before and 30 days, 3, 6, and 12 months, 2 and 3 years after TAVI.

Results Patients had an age of 83 ± 6 years, the logistical EuroScore was 24.7 ± 12%, the baseline aortic valve area 0.6 ± 0.1 cm^2, and the mean gradient 59 ± 18 mmHg. Baseline NT-proBNP was significantly correlated to the logistical EuroScore (rho = 0.3; p = 0.008), but not to age. After TAVI NT-proBNP decreased in trend from 2401 pg/ml (n = 71; IQR 1223–5789) to 1593 pg/ml (n = 22; IQR 783–3505; p = 0.35) after 7 days, to 1743 pg/ml (n = 42; IQR 769,8–3945,5; p = 0.134) after 30 days, to 1525 pg/ml (n = 42; IQR 902–3714; p = 0.356) after 3 months, to 1166 pg/ml (n = 39, IQR 569–2342; p = 0.019) after 6 months, to 1451 pg/ml (n = 23, IQR 770–3971; p = 0.164) after 12 months, to 1354 pg/ml (n = 13, IQR 356–4034; p = 0.111) after 2 years and to 1186 pg/ml (n = 10; 309–2072; p = 0.690) after 3 years. The Cox regression analysis suggests baseline NT-proBNP to be a predictive marker for survival (HR 1.3; p = 0.1).

Conclusion After TAVI, NT-proBNP levels tended to decrease. Baseline NT-proBNP seems to be a predictor for outcome after TAVI. These data should be confirmed in larger patient populations.

Low-Speed Rotational Atherectomy with Substantial Debulking Improves Long-Term Outcome XV – 2

J. Sipötz, M. Winkler, O. Friedrich, G. Gaul
2. Medizinische Abteilung – Kardiologie, Hanusch-Krankenhaus, Wien

Aims Our retrospective trial aims to evaluate the longterm outcome in PCI patients undergoing a modified protocol of Rotational Atherectomy using a lower burr speed of 135 krpm in short runs, intermittent ablation and minimal deceleration (pecking technique) relative to a non-debulked control group.

Methods Out of a 6 year period we selected all patients (i. e.: 1033) treated with single vessel interventions in our cath-lab. 144 patients were excluded because of incomplete data sets. Of the resulting 889 patients 40% (i. e.: 356 patients) underwent substantial debulking. To compare long time survival between debulked and non-debulked patients we calculated Kaplan Meyer curves up to 80 months.

Results Comparing the baseline data, the non-debulked group (n = 533) was significantly younger than the debulked group (n = 356), other clinical variables did not differ significantly. The lesions in the debulked group were morphologically more severe (lesion length: 13.5 ± 10.6 mm vs 10.0 ± 7.1 mm, p < 0.001; % stenosis: 71.0 vs 68.6, p = 0.007; % ostial lesions: 17.4 vs 7.2, p < 0.001; ACC class C: 62% vs 35%, p < 0.001). The intervention resulted in a substantially greater lumen increase in the debulked group (2.3 ± 0.5 mm vs 2.2 ± 0.6 mm, p < 0.001) with a burr-to-artery ratio of 0.64 ± 0.14. Kaplan-Meier survival analysis up to 80 months between the 2 groups was identical.

To address selection bias, we used propensity-score matching based on 26 prognostically important clinical and angiographic variables resulting in the formation of 279 matched pairs (i. e.: 578 patients). Lumen gain after intervention was significantly greater in the debulked group (2.3 ± 0.6 mm vs 2.2 ± 0.5 mm, p = 0.009). In the matched group treated with rotational atherectomy survival was substantially improved (hazard ratio 0.52, confidence interval 0.32–0.85, p < 0.01).

Conclusion We have redefined the protocol of the technique of rotational atherectomy with a platform speed of 135 krpm, pecking technique and a step-up burr sizing up to a debulking burr-to-artery ratio of greater than 0.6. We hypothesize this modification might explain the equal long-term outcome in patients with worse baseline endorsed by a significant improvement when analyzed by propensity for rotational atherectomy. We explain these data by the debulking effect of atherectomy with a greater lumen gain compared to matched patients and by the introduction of a less damaging protocol.

Outcome of Left Main Percutaneous Coronary Interventions – A Single-Centre Retrospective Study XV – 4

M. Unterhuber, N. Moes, O. Pachinger, H. Alber
Universitätsklinik für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck

Background The SYNTAX study has demonstrated that percutaneous coronary interventions (PCI) of left main (LM) stenoses are feasible in patients with stable coronary artery disease. However, there is ongoing controversy about the optimal patient selection for LM-PCI. Hence, the aim of this retrospective study was to determine prognostic factors for LM-PCI which may improve patient selection in the future.

Methods 90 patients (age 69 ± 11 years) were enrolled, in whom LM-PCI was performed at our department (until march 2011). All baseline clinical characteristics as well as important laboratory values were analyzed retrospectively. Also, all cardiovascular events (all cause death, myocardial infarction, stroke, bypass-operation and repeat coronary intervention) were documented after contacting patients by letter as well as phone call. The median follow-up time was 54 months.

Results In univariate analyses several parameters (e. g. arterial hypertension, chronic kidney disease, ST-elevation myocardial infarction, EuroSCORE, stent size and type, no use of intravascular ultrasound) were associated with increased risk for cardiovascular events. In a multivariate analysis chronic kidney disease (p < 0.01), ST-elevation myocardial infarction (p < 0.01), EuroSCORE (p < 0.01), use of bare-metal stents (p = 0.05) and no use of intravascular ultrasound (p = 0.02) remained significantly associated with cardiovascular events. After publication of the SYNTAX trial the proportion of stable patients with LM-PCI significantly increased (67% vs 95%; p < 0.01) and no peri-interventional event occurred.

Conclusion Our data suggest that LM-PCI in patients with chronic kidney disease, a high EuroSCORE or during acute myocardial infarction is associated with increased cardiovascular events in the long term. The results also support the use of drug-eluting stents as well as intravascular ultrasound for post-implantation control. Finally, we could demonstrate a clinically relevant impact of the SYNTAX trial in our daily practice.

Erfolgsrate und periphere Gefäßkomplikationen nach Implementation eines transradialen Katheterprogramms XV – 8

A. Winter, D. Kiblböck, K. Höllinger, E. Zeindlhofer, L. Pilgerstorfer, U. Brunhuber, A. Schiller, D. Szücs, Ch. Steiner, L. Pilgerstorfer, A. Winter, A. Gierlinger, P. Siostrzonek
Interne II/Kardiologie, Krankenhaus der Barmherzigen Schwestern, Linz

Einleitung Wir berichten über unsere Erfahrungen bei Implementation eines transradialen (TR) Katheterprogramms in unserem Herzkatheterlabor. Die Umstellung von der transfemoralen (TF) zur TR-Technik wurde durch Untersuchungen zur Ergebnisqualität begleitet. Der vorliegende Bericht beschreibt Erfolgsrate und Häufigkeit von peripheren Gefäßkomplikationen nach TR-Gefäßzugang.

Material und Methode Die TR-Technik wurde in unserem Labor seit Jänner 2011 systematisch eingeführt. Unser standardisiertes Vorgehen umfasst die Durchführung eines Allen-Tests, die Punktion mit einer 20G-Kanüle, das Einbringen einer hydrophil beschichteten 6F-Schleuse (Radifocus II, Terumo Europe N.V., Leuven, Belgien) in Seldinger-Technik, die Applikation von 5000 E Heparin und 5 mg Verapamil, und die Verwendung von Standarddrähten und Koronarkathetern wie beim TF-Vorgehen. Nach Schleusenentfernung wird ein TR-Band (Terumo Europe N.V., Leuven, Belgien) für 4 h appliziert. Nach einem Jahr verfügen nunmehr alle 5 Katheterärzte über eine TR-Erfahrung aus über 200 Untersuchungen, davon mindestens 50 Koronarinterventionen. Zur Qualitätskontrolle wurden nun prospektiv Daten aller TR-Untersuchungen vom 1.11.2011 bis 31.1.2012 ausgewertet. Inkludiert war bei allen Patienten eine Pulskontrolle mit Duplex- und Doppler-Sonographie der A. radialis 24 h und 4 Wochen nach der Katheterprozedur.

Ergebnisse Im Zeitraum von 3 Monaten wurden 482 Pat. einer Katheteruntersuchung unterzogen, davon wurde bei 318 Pat. (66,2 %; Alter: 66,6 ± 10,8 Jahre, 70 % Männer) primär der TR-Zugang und bei 164 Pat. (33,8 %) primär der TF-Zugang verwendet. Ursachen für einen primären TF-Zugang waren eine Angiographie im Bereitschaftsdienst (n = 49), die geplante Abklärung oder Intervention bei Vitium (n = 17), ein pathologischer Allen-Test (n = 21) bzw. Arzt- oder Patientenpräferenz (n = 78). Bei 79 (34,3 %) Pat. mit TR-Zugang erfolgte eine Koronarintervention. Bei 24 Pat. (7,5 %) mit primär geplantem TR-Zugang musste auf einen TF-Zugang gewechselt werden. Ursache waren Probleme bei der Punktion bei 16 Pat., beim weiteren Vorgehen über die Armarterie bei 6 Pat. und bei der Sondierung der Koronararterien bei 2 Patienten.

Bei 2 Pat. (0,6 %) mit TR-Zugang trat eine akute gefäßbezogene Komplikation auf. Ein Pat. mit Nachblutung entwickelte ein inkomplettes Kompartmentsyndrom am Unterarm, das jedoch keiner chirurgischen Intervention bedurfte, weitere Nachblutungen waren selten und durchwegs oberflächlich und begrenzt. Die Sonographie der A. radialis nach 24 h und 4 Wochen konnte bei 222 bzw. 190 Pat. durchgeführt werden. Der Gefäßdiameter an der Punktionsstelle betrug nach 24 h 2,48 ± 0,05 mm und nach 30 Tagen 2,47 ± 0,05 mm (p = n. s.). Ein Verschluss der A. radialis wurde nach 24 h bei 4 Pat. (1,3 %; davon 1 Pat. symptomatisch) und nach 30 Tagen bei 1 Pat. (0,3 %; asymptomatisch) festgestellt.

Diskussion Die Implementation der TR-Untersuchung in unserem Herzkatheterlabor erzielte rasche Akzeptanz durch Ärzte, Pflegepersonal und Patienten. Nach Durchführung von 200 Prozeduren pro Untersucher ist die TR- Technik mit einer akzeptablen Erfolgsrate und einer geringen Komplikationsrate durchführbar.

Interventionelle Behandlung eines großen Aneurysmas der rechten Koronararterie VII – 7

E. Zeindlhofer, A. Winter, K. Höllinger, M. Schmid, P. Siostrzonek
Interne II/Kardiologie, Krankenhaus der Barmherzigen Schwestern, Linz

Wir berichten über einen 60-jährigen männlichen Patienten, der wegen einer seit 3 Monaten bestehenden Crescendo-Angina zur Koronarangiographie zugewiesen wurde. An kardiovaskulären Risikofaktoren waren eine arterielle Hypertonie, eine Hypercholesterinämie, sowie ein mehrere Jahre zurückliegender Nikotinkonsum zu

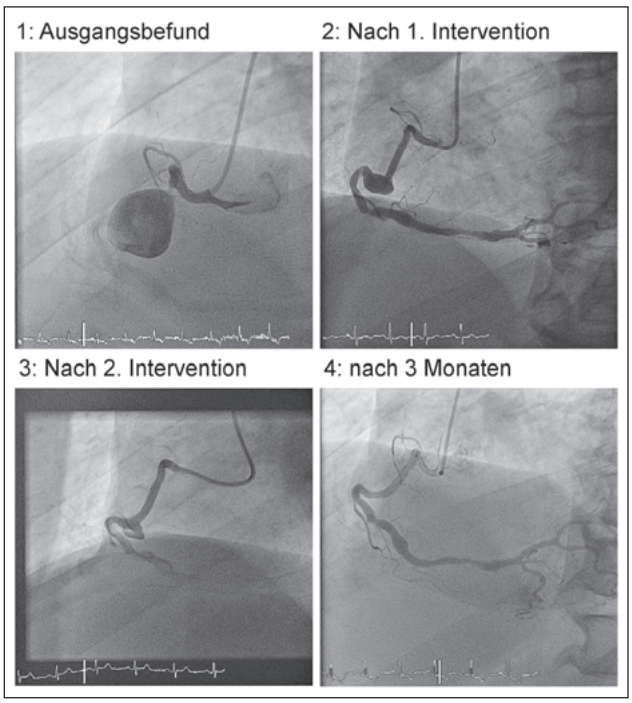


Figure 34: E. Zeindlhofer et al.

erheben. An Vorerkrankungen bestand eine operiertes abdominelles Aortenaneurysma sowie ein operiertes N. prostatae.

Die transradiale Koronarangiographie zeigte das Vorliegen einer koronaren Eingefäßerkrankung mit proximaler 90 %-RCA-Stenose sowie ein unmittelbar anschließendes poststenotisches 20 × 22 × 30 mm messendes Aneurysma **(Abbildung 34a)**. Nach Diskussion verschiedener therapeutischer Optionen sowie Aufklärung und Zustimmung des Patienten wurde ein interventioneller Therapieversuch geplant. Eine Gerinnungstherapie mit Prasugrel und Acetylsalicylsäure wurde eingeleitet. Die Intervention gestaltete sich vor allem wegen der proximalen Gefäßkrümmung schwierig. Letztlich gelang es unter Verwendung eines Guideliner-Katheters (Vascular Solutions Inc., Minneapolis, USA), 3 Stents in die proximale Stenose (Skylor 3,5 × 13 mm; Invatec, Roncadelle, Italien) und in das Aneurysma (Aneugraft 3,5 × 23 mm; ITGI Medical, Or-Akiva, Israel und M-Guard 3,5 × 18 mm; Inspire MD, Tel Aviv, Israel) vorzubringen. Allerdings erwies sich der Versuch, das Aneurysma mittels Graftstents abzudecken, nur teilweise erfolgreich, da eine distale Verankerung der Stents im Ausgang des Aneurysmas nicht erreicht werden konnte **(Abbildung 34b)**. Erst bei einer zweiten interventionellen Sitzung konnte eine komplette Überbrückung des Aneurysmas durch Implantation eines zweiten M-Guard-Stents 4,0 × 19 mm in den distalen Aneurysmateil erreicht werden **(Abbildung 34c)**. Die duale Plättchenhemmertherapie wurde fortgeführt. Der Patient ist seither kardial beschwerdefrei, die geplante Kontrollangiographie nach 3 Monaten zeigte eine vollständige Ausschaltung des Aneurysmas ohne Vorliegen von Re-Stenosen **(Abbildung 34d)**.

Verbesserungen der interventionellen Technik ermöglichen selbst bei schwierigen anatomischer Gegebenheiten die erfolgreiche Katheterbehandlung eines großen Koronararterienaneurysmas.

Austrian TAVI Registry: One-Year Experience BAI

D. Zweiker, R. Zweiker, E. Maurer, G. Lamm, M. Heigert, Th. Neunteufl, M. Leibl, E. Zeindlhofer, M. Grund, J. Pollak, W. Tkalec, O. Luha, R. Maier
Klinische Abteilung für Kardiologie, Medizinische Universität Graz; Klinische Abteilung für Innere Medizin II, Klinikum Wels-Grießkirchen; 3. Medizinische Abteilung, Landesklinikum, St. Pölten; Universitätsklinik für Innere Medizin II, Salzburger Universitätsklinikum; Klinische Abteilung für Kardiologie, Medizinische Universität Wien; Interne II/Kardiologie, Krankenhaus Barmherzige Schwestern, Linz; Interne 1, Allgemeines Krankenhaus, Linz; 4. Medizinische Abteilung mit Kardiologie, Krankenhaus Hietzing, Wien; 2. Interne/Kardiologie, Krankenhaus der Elisabethinen, Linz

Objective Transcatheter aortic valve implantation (TAVI) is a new, minimally invasive intervention for treatment of severe aortic stenosis. However, there is limited data concerning mid- and long-term outcome in a routine clinical setting. Beginning with January 1, 2011, the Austrian TAVI registry has been launched to document and assess procedure details, risks and outcome. 10 centers in Austria are currently participating in the registry.

Design and Methods In 2011, 315 patients (202 female, 113 male) were included in the registry (age 82 ± 5 years). The logistic EuroSCORE was 19.9 ± 13.5%, and the STS Risk Score (available for 123 patients) was 16.1 ± 11.1% for the female and 8.9 ± 8.7% for male patients, respectively. After baseline data assessment and documentation of the procedure itself (valve type, access site, duration, complications), follow-up visits at 1, 3, 6 and 12 months after the procedure were scheduled.

Results 282 CoreValve and 33 Sapien prostheses were implanted. Preferred access site was transfemoral (n = 285). A transapical (n = 18) or transsubclavian (n = 12) approach were used less frequently. Acute procedural success rate was 99.4%. Complications were observed in 29% of patients. Use of CoreValve was accompanied by less complications (48% vs 26%). Need for pacemaker implantation was the most common complication (n = 55, 17% overall), followed by unplanned surgery (5.4%) and peripheral vascular major bleeding (4.8%). The follow-up examinations (baseline vs 30-day follow-up) showed significant improvement of hemodynamic parameters (V_{max} 4.5 ± 0.7 m/s vs 1.9 ± 0.5 m/s, mean gradient 53 ± 17 mmHg vs 9 ± 4 mmHg, and AVA/BSA 0.4 ± 0.1 cm^2 vs 1.1 ± 0.3 cm^2; $p < 0.001$), as assessed by echocardiography. Additionally, frailty was assessed using the Karnofsky index, which showed significant improvement from 60 ± 10% to 80 ± 20%; $p < 0.001$). Periprocedural mortality was 1% (3 patients). The 30-day survival was 95.9%.

Conclusion Data of this registry prove that study results of TAVI concerning patient selection and outcome being transferred successfully into routine clinical settings. The major limitation of the presented registry is that a considerable number of patients was not included into the registry due to various reasons. To overcome this bias, the Task Force TAVI of the Austrian Society of Cardiology and the Austrian Society of Thoracic and Cardiovascular Surgery proposes a nationwide Austrian Aortic Valve Registry, which could probably start with 2013.

Koronare Herzkrankheit (KHK)/Coronary Heart Disease (CHD)

Erfolgreiche und nachhaltige Modifizierung kardiovaskulärer Risikofaktoren durch ambulante kardiologische Rehabilitation XVI – 4

J. Niebauer, K. Mayr, H. Harpf, A. Philippi, E. Huber, G. Zenker, B. Ebner, M. Wonisch, R. Pokan, W. Benzer
Universitätsinstitut für präventive und rehabilitative Sportmedizin, Paracelsus Medizinische Privatuniversität Salzburg; Cardiomed – Ambulante kardiologische Rehabilitation, Linz; Krankenanstalt Institut für Bewegungstherapie Graz; Reha-Sport-Institut Feldkirch; Ambulatorium Nord, Salzburg; Physikalisches Ambulatorium der Stadtwerke Bruck a. d. Mur; Institut für Präventiv- und Rehabilitationsmedizin Cardio-Vital-Wels; Hansa Privatklinikum Graz; Institut für Sportwissenschaften, Universität Wien; Institut für Interventionelle Kardiologie, Landeskrankenhaus, Feldkirch

Ziel Es war das Ziel dieser Studie, die Wirksamkeit der ambulanten kardiologischen Rehabilitation Phase II und Phase III nach dem Modell der Arbeitsgemeinschaft für ambulante kardiologische Rehabilitation (AGAKAR), folgend den Guidelines der Österreichischen Kardiologischen Gesellschaft (ÖKG), zu untersuchen.

Methodik Alle Ambulatorien, die Vertragspartner der Österreichischen Sozialversicherungen sind, gaben die Daten der Patienten der ambulanten kardiologischen Rehabilitation Phase II und III prospektiv in die von der AGAKAR installierte, webbasierte Datenbank ein. Insgesamt gelangten im Zeitraum 1.1.2009–30.11.2011 für die Phase II 1432 und für die Phase III 1390 vollständige Datensätze zur Auswertung.

Ergebnisse Die Patienten in der ambulanten kardiologischen Rehabilitation der Phase II konnten ihre Leistungsfähigkeit am Fahrradergometer während des 4–6-wöchigen Rehabilitationsprogramms um durchschnittlich 20,56 ± 27,72 Watt verbessern. Des Weiteren erreichte der überwiegende Teil der Patienten einen systolischen Blutdruck von < 140 mmHg (85,9 %), ein LDL < 100 mg/dl (66,8%), Triglyzeride < 150 mg/dl (70,0 %) und bei den Männer 60,8 % einen Bauchumfang < 102 cm. Am Ende der Phase III wurden die Zielwerte von einem noch größeren Teil der Patienten erreicht, wobei die Ergebnisse dann am besten waren, wenn der Phase III eine ambulante anstelle einer stationären Phase II vorausging. Bei den Frauen blieb der Bauchumfang und bei beiden Geschlechtern der Body-mass-Index beim Großteil der Patienten außerhalb der Zielwerte. Die Ergebnisse des Hospital Anxiety and Depression Scale- (HADS-) Fragebogens zeigten, dass bereits zu Beginn der ambulanten Phase II die Werte für Ängstlichkeit (HADS-A: 84,8 %) und Depressivität (HADS-D: 89,0 %) beim größten Teil der Patienten im Zielbereich lagen und im Rahmen des Rehabilitationsprogramms sich weiter verbesserten (HADS-A: 86,4 %, HADS-D: 90,8 %). Die gesundheitsbezogene Lebensqualität der Rehabilitanden verbesserte sich in allen 4 Skalen des MacNew-Fragebogens.

Schlussfolgerung Diese Daten beweisen einmal mehr und in dieser speziellen Ergebnisanalyse erstmals auch für Österreich die Wirksamkeit und Nachhaltigkeit sowohl der ambulanten kardiologischen Rehabilitation der Phase II als auch der Phase III nach dem Modell der AGAKAR und folgend den Guidelines der ÖKG. Diese Ergebnisse sollten dazu Anlass geben, die in Österreich praktizierte, evidenzbasierte und leitlinienkonforme ambulante Rehabilitation lückenlos, flächendeckend, berufsbegleitend und wohnortnah anzubieten und nicht mehr nur auf wenige Zentren zu beschränken.

Das Ausmaß der koronaren Herzkrankheit ist ein starker, unabhängiger Prädiktor der Langzeitmortalität XVI – 3

M. Rammer, T. Weber, A. Haiden, M. Porodko, E. Laßnig, M. Suppan, B. Eber
Abteilung für Innere Medizin 2, Klinikum Wels-Grieskirchen

Hintergrund Historische Studien zeigten einen Zusammenhang zwischen dem Ausmaß der koronaren Herzkrankheit (KHK), mittels Koronarangiographie (CAG) bestimmt, und der Prognose. Neuere Daten dazu stammen vorwiegend aus CT-angiographischen Studien. Die prognostische Wertigkeit der konventionellen CAG vor dem Hintergrund einer modernen Therapie der KHK ist nicht bekannt.

Wir evaluierten den prognostischen Wert des Ergebnisses einer diagnostischen CAG hinsichtlich der Langzeit-Sterblichkeit von Patienten mit klinischem Verdacht auf eine KHK.

Methodik Das untersuchte Kollektiv umfasste 1334 konsekutive Patienten (64,7 ± 11,1 Jahre, 61 % männlich), die mit Verdacht auf KHK zwischen Juli 2001 und Februar 2002 einer CAG unterzogen wurden. Die CAG-Ergebnisse wurden kategorisiert als signifikante (≥ 50%ige) Stenose in 1 (KHK 1), 2 (KHK 2), 3 (KHK 3) epikardialen Gefäßen, signifikante (≥ 50%ige) Stenose des linken Hauptstammes (HS), nicht-signifikante (< 50%ige) Stenose in zumindest einem Gefäß (Sklerose) oder unauffällige Koronarien. Endpunkt war die Gesamtsterblichkeit, die Erfassung der Endpunkte erfolgte über Krankengeschichten, telefonische Hausarzt-Interviews sowie über Daten der Statistik Austria. In multivariablen Cox-Regressions-Analysen erfolgte eine Adjustierung für Alter, Geschlecht, Cholesterin, Hypertonie, Diabetes, Kreatinin und Raucherstatus.

Ergebnisse 18,9 %, 15,9 %, 26,4 %, 20,0 %, 18,8 % der Patienten hatten unauffällige Koronarien, eine Sklerose, eine KHK 1, KHK 2 oder KHK 3/HS. Während der mittleren Nachbeobachtungszeit von 8,0 ± 2,5 Jahren betrug die Sterblichkeit 8,7 %, 17,0 %, 19,6 %, 30,7 % und 41,4 % für Patienten mit unauffälligen Koronarien, Sklerose, KHK 1, KHK 2 und KHK 3/HS. Auch nach Adjustierung für klassische Risikofaktoren blieb das KHK-Ausmaß ein unabhängiger Mortalitäts-Prädiktor ($p < 0{,}0001$).

Schlussfolgerung Auch vor dem Hintergrund einer aktuellen Therapie sind das Vorhandensein sowie das Ausmaß CAG-definierter atherosklerotischer Veränderungen Prädiktoren für die Langzeit-Mortalität unabhängig von klassischen Risikofaktoren.

Full Arterial Revascularization as a Second CABG Re-Operation XVI – 5

E. Ruttmann, V. Mühlberger, N. Fischler, A. Sakic, M. Grimm, O. Chevtchik
Department of Cardiac Surgery; Department of Cardiolgy, Innsbruck Medical University

Introduction A 67-year-old male patient presents with severe angina CCS III–IV since June 2011.

Material and Methods He underwent a CABG procedure in January 1988 receiving 2 saphenous vein grafts (SVG) to the LAD and RCA with thromb-end-arterectomy of both vessels. Due to recurrence of symptoms and occluded grafts at repeated cardiac catheterization he underwent a CABG-reoperation with 3 SVG grafts to all major coronary arteries.

He lived uneventfully until June 2011. At repeated cardiac catheterization all native coronary arteries were occluded except a 90% stenosis of a diagonal branch that failed a re-intervention. The SVG graft to the RCA was occluded, the other SVGs to LAD and CX were severely calcified with high grade stenosis. The RCA was occluded but showed excellent collaterals, ventricular function was preserved (EF = 69%).

Result In November 2011 he underwent a 2nd re-operation. Intraoperative TEE diagnosed a grade III tricuspid regurgitation that was repaired using a CE MC3 annuloplasty ring. In the previous re-operation in 1988 the left internal thoracic artery was violated in the middle segment, however, due to skeletonization reached enough length to be "recycled" as an in-situ graft to the diagonal branch. Furthermore, he received the right internal thoracic artery as an in-situ graft to the LAD and a radial graft to the CX.

The postoperative course was uncomplicated.

Conclusion Full arterial revascularization for CABG re-operations is feasible and safe and prevents from long-term SVG graft failure.

Angiopoietin-Like 4 is Elevated in Type-2 Diabetes But is Not Associated With Angiographically Determined Coronary Artery Disease XVI – 1

Ch. H. Saely, A. Muendlein, A. Vonbank, K. Geiger, P. Rein, H. Drexel
VIVIT-Institute, Innere Medizin, Landeskrankenhaus, Feldkirch

Background Angiopoietin-like 4 (ANGPTL4, fasting-induced adipose factor), a protein inhibitor of lipoprotein lipase, is synthesized and secreted during fasting in adipose tissue and the liver. Its associations with metabolic syndrome traits are uncertain, and it is not known whether it is associated with type 2 diabetes (T2DM) or coronary artery disease (CAD).

Methods We therefore measured serum ANGPTL4 in 493 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; significant CAD was diagnosed when coronary stenoses ≥ 50% were present.

Results ANGPTL4 was significantly positively correlated with age ($r = 0.177$; $p < 0.001$) and fasting glucose ($r = 0.112$; $p = 0.013$) but was not correlated with waist circumference, triglycerides, HDL cholesterol, systolic blood pressure or diastolic blood pressure. ANGPTL4 was significantly higher in patients with T2DM (n = 115) than in non-diabetic subjects (28 ± 32 vs 25 ± 38; $p = 0.032$); however, it was not significantly different between patients with significant CAD (n = 246) and individuals without significant CAD ($p = 0.112$).

Conclusion We conclude that ANGPTL4 is positively correlated with fasting glucose and elevated in T2DM but is not significantly associated with angiographically determined CAD.

Chemerin is Associated with the Metabolic Syndrome But is Not Linked to Angiographically Determined Coronary Artery Disease XVI – 2

Ch. H. Saely, A. Muendlein, A. Vonbank, K. Geiger, P. Rein, H. Drexel
VIVIT-Institute, Innere Medizin, Landeskrankenhaus, Feldkirch

Background The novel adipocytokine chemerin has been suggested to be linked to insulin resistance and to the metabolic syndrome (MetS). Its association with coronary artery disease (CAD) is unclear. We hypothesized that chemerin is associated with both angiographically determined CAD and with the MetS.

Methods We measured serum chemerin in 498 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; the MetS was defined according to NCEP-ATPIII criteria; significant CAD was diagnosed when coronary stenoses ≥ 50% were present.

Results Chemerin was higher in MetS patients (n = 150) than in subjects without the MetS (184 ± 77 vs 150 ± 62 ng/ml; $p < 0.001$). It did not differ significantly between patients with significant CAD (n = 250) and those without significant CAD ($p = 0.327$). When both, MetS and CAD status were considered, chemerin was higher in MetS patients both among those who had significant CAD (182 ± 80 vs 152 ± 60 ng/ml; $p = 0.002$) and among those who did not have significant CAD (187 ± 73 vs 148 ± 63 ng/ml; $p < 0.001$); it did not differ significantly between patients with significant CAD and subjects without significant CAD among MetS patients ($p = 0.248$) nor among subjects without MetS ($p = 0.263$). Analysis of covariance (ANCOVA) showed that from the NCEP-ATPIII metabolic syndrome traits a large waist circumference as well as elevated triglycerides were independent predictors of elevated serum chemerin ($F = 12.5$; $p < 0.001$ and $F = 8.5$; $p = 0.004$).

Conclusion We conclude that chemerin is significantly associated with the MetS but not with angiographically determined CAD. The overall association of chemerin with the MetS is carried by its association with visceral obesity and elevated triglycerides.

Pulmonale Hypertonie/Pulmonary Hypertension

Prevalence and Clinical Impact of Atrial Fibrillation Among Patients with Pulmonary Hypertension BAI

D. Rottländer, L. Motloch, R. Sara, D. Schmidt, R. Larbig, U. Hoppe
Universitätsklinik für Innere Medizin II, Universitätsklinikum Salzburg, Österreich; Universitätsklinikum Köln, Deutschland

Background Pulmonary hypertension (PH) is associated with progressive impairment of right ventricular function, reduced exercise capacity and a poor prognosis. Little is known about the prevalence, clinical manifestation and impact of atrial fibrillation (AF) on cardiac function in PH.

Objective To investigate the prevalence of AF in various forms of PH, and to assess the clinical manifestation and hemodynamic parameters in PH with AF. In a subanalysis PH due to chronic left heart failure and PH due to any other cause in the absence and presence of AF were separately compared.

Methods and Results In a 4-year single-centre retrospective analysis of 225 patients with confirmed PH of various origins, AF was prevalent in 31.3%. In patients with PH and AF, parameters of clinical deterioration (NYHA/WHO functional class, 6-minute walk distance, NT-proBNP levels) and renal function were significantly compromised compared to patients with PH and sinus rhythm (SR). Furthermore, the occurrence of AF in PH was associated with an increase of right atrial pressure (RAP) and right atrial dilatation. While no direct association was found between pulmonary artery pressure (PAP) and AF in PH, right ventricular function was reduced in AF, indicating more advanced disease. In PH due to left heart failure the prevalence of AF was particularly high (57.7% vs 22.8% in other forms of PH). In this subgroup, left atrial dilatation, increase of pulmonary capillary wedge pressure, PAP and RAP were more pronounced in AF than in SR, suggesting that more marked backward failure led to AF in this setting.

Discussion PH is associated with increased prevalence of AF. Occurrence of AF in PH indicates clinical deterioration and more advanced disease. Clinical trials to identify a beneficial therapy for AF in PH are warranted.

Factors Determining Outcome in Patients with Heart Failure and Normal Ejection Fraction BAII

C. Tufaro, J. Mascherbauer, B. Marzluf, Th. Binder, I. M. Lang, D. Bonderman
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background Patients with heart failure and normal left ventricular ejection fraction (HFNEF) face an adverse outcome. The aim of the present study was to identify factors that determine prognosis.

Methods Consecutive patients with HFNEF diagnosed according to current ESC guidelines were recruited in our prospective Viennese registry. Death and/or hospitalization for heart failure were defined as primary outcome variables. Outcome groups were compared with

Table 11: C. Tufaro et al. Independent predictors of outcome in heart failure with normal ejection fraction

	OR	95 %-CI	p-value
DM II	25.34	2.06–311.45	0.120
BMI (kg/m²)	1.25	1.00–1.56	0.048
PVR (dynes.s/cm⁵)	1.02	1.00–1.05	0.032

Results of the multivariable logistic regression model of factors determining outcome in patients with heart failure and normal ejection fraction. Data are listed as Odds Ratios (ORs), 95%-CI and p-values in the final model. DMII: Diabetes mellitus; BMI: Body mass index; PVR: pulmonary vascular resistance

respect to potential prognostic predictors using the Student's t-test. Multivariable logistic regression analysis was applied to determine whether parameters of interest were associated with adverse outcome. P < 0.05 indicated statistical significance.

Results Between December 2010 and January 2012, 49 HFNEF patients (34 f, 15 m, mean age 70 ± 8 years) were registered. After a mean follow-up of 5 ± 9 months, 14 (29 %) patients were hospitalized or died. Patients in the adverse outcome group were characterized by higher body mass index (BMI, 35 ± 7 vs 29 ± 5, p = 0.004), higher systolic pulmonary pressure on echo (sPAP in mmHg, 69 ± 15 vs 55 ± 14, p = 0.004), shorter 6-minute walk distance (6-MWD in m, 271 ± 131 vs 364 ± 100, p = 0.019), higher transpulmonary gradient (TPG in mmHg, 15 ± 4 vs 12 ± 4, p = 0.013) and a higher pulmonary vascular resistance (PVR in dynes.s/cm5, 257 ± 97 vs 198 ± 71, p = 0.030). Diabetes mellitus II (DM II, 75% vs 24%, p = 0.002) and atrial fibrillation (92% vs 51%, p = 0.013) were more prevalent among patients with adverse outcome.

In the multivariable regression model, only BMI, DM II and PVR remained independent predictors of outcome **(Table 11)**.

Discussion Presence of DM II, higher BMI and higher PVR worsen prognosis in HFNEF patients.

Rhythmologie/Rhythmology

Electroanatomic Substrate Mapping and Catheter Ablation of Right and Left Atrial Macroreentry Tachycardias VIII – 6

F. Danmayr, B. Strohmer, M. Brandt, U. Hoppe
Universitätsklinik für Innere Medizin II, PMU Klinik Salzburg

Introduction Atrial macroreentry tachycardias (AMRT) represent a spectrum of arrhythmias resulting from surgical treatment of congenital heart disease, or as a consequence of previous surgical or catheter ablations. The purpose of this retrospective study is to characterize the arrhythmogenic substrate and reentry circuits in patients with drug-resistant AMRT and to report the ablation approach guided by electroanatomic mapping.

Methods We report about a case series of 15 pts (age 56 ± 18 [21–76] yrs; male n = 10), who presented to our institution with typical (n = 9) or atypical (n = 6) atrial flutter refractory to antiarrhythmic medication. Surgically corrected congenital heart disease was present in 6 pts (ASD n = 4; VSD n = 2), a history of cardiac surgery in 3 pts (tricuspid and/or mitral annuloplasty rings n = 2, CABG+PM n = 1), previous catheter interventions in 4 pts (PVI n = 2, RA catheter ablations n = 2, LA surgical ablation n = 1) and no obvious structural heart disease in 4 pts.

Results After informed consent electrophysiological study was carried out to diagnose scar-related AMRT (CL 270 ± 50 ms). Electroanatomical mapping was performed in 14/15 patients (CARTO n = 11; NAVX n = 3). AMRT was defined to the RA in 10 pts, and to the LA in 5 pts according to concealed entrainment pacing techniques. A PPI < 30 ms and identical intracardiac activation sequence during pacing at critical sites were presumed to be part of the reentry circuit. Double loop reentry was identified in the RA (n = 4) involving the atriotomy scar and in the LA (n = 3) related to electrical silent areas or previous surgical ablations. Isolated cavotricuspid isthmus (CTI) dependent reentry was the mechanism in 3 pts only. Temperature-controlled irrigated ablation was applied to the critical isthmus of the proposed reentry circuit in the RA or LA with focal or linear lesions connecting to nearby conduction barriers. RA lesions spanned from the atriotomy scar to the IVC, SVC or TV (n = 5), LA ablations consisted of a set of lesions incorporating the septal area (n = 2), the roof and/or superior PV (n = 2) and the endo/epicardial isthmus (n = 2). In addition, standard CTI ablation was performed in 10 pts for protective reasons or due to involvement in double loop reentry. Unmappable right AMRT forms underwent an anatomically guided substrate ablation (n = 2). The endpoint of the procedure was defined as termination of the clinical AMRT (13/15 pts) and documentation of conduction block with widely split double potentials across the ablation line. One patient with ASD and previous RA substrate modifications received a pacemaker due to symptomatic sinusbradycardia following ablation. During a mean follow-up of 22 ± 18 months all pts remained free of the clinical AMRT, however 5/15 pts developed other intraatrial tachyarrhythmias, mostly atrial fibrillation.

Conclusion Patients with different pathological conditions may demonstrate similar features with respect to arrhythmogenic substrates and reentry circuits. Conduction barriers, such as postinterventional or surgical atrial scars as well as idiopathic electrical silent areas were identified as central obstacle for AMRT by electroanatomic 3D mapping. Our approach of ablating critical parts of the incisional- or scar related sites together with the CTI in the majority of patients resulted in elimination of the clinical AMRT. Over long-term we observed a moderate risk for other intraatrial tachyarrhythmias, particularly atrial fibrillation.

Katheterablation bei ventrikulären Tachykardien/Kammerflimmern mit komplexem arrhythmogenem Substrat IX – 6

M. Derndorfer, M. Martinek, E. Sigmund, Ch. Lemes, H.-J. Nesser, J. Kautzner, H. Pürerfellner
Abteilung für Kardiologie I, Krankenhaus Elisabethinen, Linz, Österreich; Department für Kardiologie, IKEM, Prag, Tschechische Republik

Einleitung Ventrikuläre Tachykardien (VT) und Kammerflimmern (VF) bei (meist) struktureller Herzerkrankung stellen komplexe Krankheitsbilder dar, die für den Patienten (Pat.) aufgrund der potentiell lebensbedrohlichen Charakteristik inkl. adäquater bzw. inadäquater Schocks des implantierten ICD-Systems eine besonders belastende Situation ergeben. Die Katheterablation stellt einen überwiegend palliativen Behandlungsansatz dar und gestaltet sich je nach zugrundeliegendem Substrat unterschiedlich komplex.

Methodik Im Krankenhaus der Elisabethinen Linz wurden in den Jahren 2007 bis 2011 insgesamt 129 Patienten **(Abbildung 35)** einer VT-Ablation unterzogen. Von diesen wurden retrospektiv 26 Pat. analysiert, bei denen ein komplexes arrythmogenes Substrat vorlag. Als Grunderkrankung wurde bei 11 Patienten eine ischämische CMP, bei 3 eine dilatative CMP, 4x eine zurückliegende Myokarditis, 2× eine ARVD und bei 6 Patienten eine idiopathische VT/VF mit rezidivierenden ICD-Schocks angegeben. Das durchschnittliche Alter der Patienten (23 m, 3 w) betrug 57 ± 12 Jahre, die LVEF vor Ablation war 43 ± 12 %, 100 % der Patienten hatten rezidivierende VT/VF-Episoden, 15 Patienten (57,7 %) teils multiple Schockabgaben durch den ICD.

Zur Charakterisierung des arrhythmogenen Substrates wurde ein 3-D-Voltagen-Map (CARTO, Fa. Biosense Webster) verwendet. 9 Pat. (34,6 %) wurden in Vollnarkose untersucht, 15 in Sedoanalgesie. Der intravasale Ultraschall kam 11× zum Einsatz, 22 Prozeduren wurden endokardial, 2 epikardial und 2 beiderorts durchgeführt. Pro Pat. konnten 2,38 ± 1,47 VT-Morphologien mit Zykluslängen zwischen 264 ms und 580 ms ausgelöst werden **(Tabelle 12)**. Die Ablation erfolgte mit einem wassergekühlten Ablationskatheter (NaviStar bzw. 4× Smart Touch, Fa. Biosense Webster). Untersucht wurden Prozedurdauer, Durchleuchtungszeit, Strahlendosis, An-

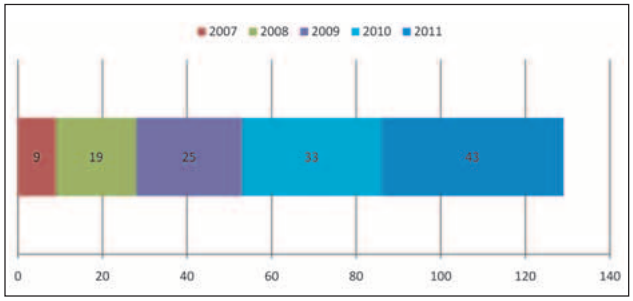


Abbildung 35: M. Derndorfer et al. VT-Ablationen im KH Elisabeth 2007–201.

Tabelle 12: M. Derndorfer et al.

Pair	Parameter	Mean	n	Std. deviation	min	max	Signifikanz
	Prozedurdauer (min)	219	25	61,72	115	330	
	Durchleuchtung (s)	14,60	23	7,17	3	33	
	Strahlendosis (cGycm²)	3062	25	2732	230	10.604	
	Ablationspunkte	20,75	24	12,29	5	51	
	Ablationszeit (s)	1019	24	648	228	2650	
	Energie gesamt (Ws)	25.845	24	17.749	5786	66.052	
	Energie max (W)	27,38	24	4,03	20	35	
	Temperatur max	37,83	24	2,14	35	44	
	VTs ausgelöst (n)	2,38	26	1,47	1	6	
	VT-Zykluslängen (ms)	367	20	80,55	264	580	
1	VTs vor Ablation (n) VTs nach Ablation (n)		26 12				CQ p = 0,000183
2	ICD-Schocks vorher (n) ICD-Schocks nachher (n)		15 3				CQ p = 0,000532

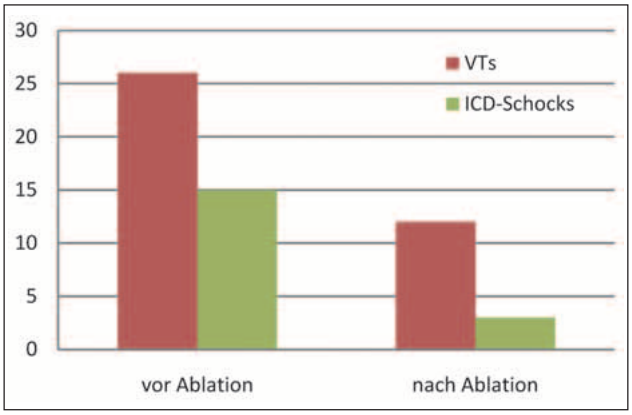


Abbildung 36: M. Derndorfer et al. VTs und ICD-Schockabgaben im Verlauf.

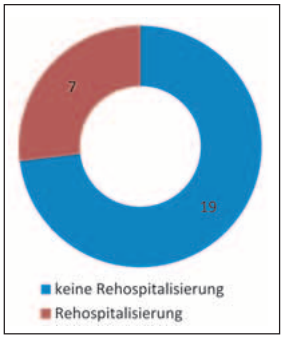


Abbildung 37: M. Derndorfer et al. Patienten mit Notwendigkeit einer Rehospitalisierung arrhythmogener Ursache nach HF-Ablation. Telefonische Abfrage im Februar 2012.

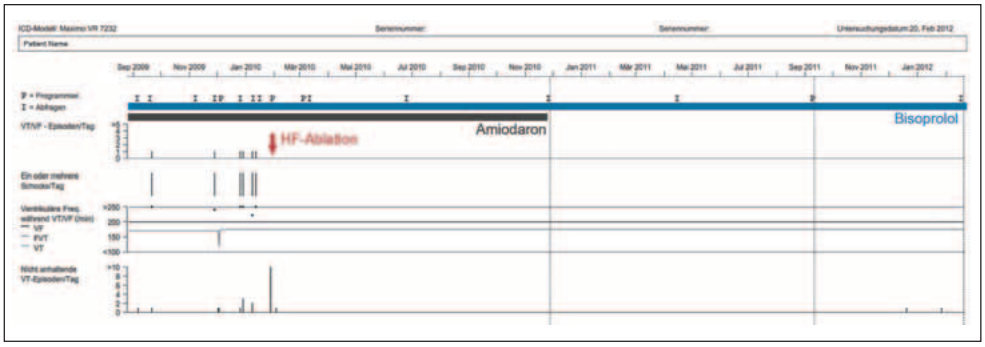


Abbildung 39: M. Derndorfer et al. Kardialer Kompass, Patientin.

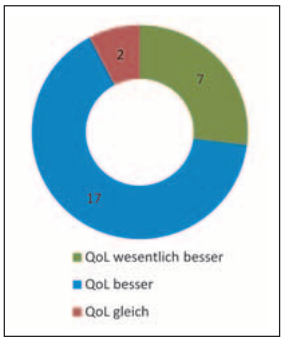


Abbildung 38: M. Derndorfer et al. Vom Patienten beurteilte Lebensqualität (QoL) nach HF-Ablation. Telefonische Abfrage im Februar 2012.

Abbildung 40: M. Derndorfer et al. Kardialer Kompass, Patient.

zahl der Ablationspunkte, die Ablationszeiten, maximale und gesamte Energieabgabe und erreichte Temperatur **(Tabelle 12)**. Die Patienten wurden 02/2012 telefonisch bzgl. VT-Rezidiven, ICD-Schocks und Veränderung der Lebensqualität (QoL) befragt.

Resultate Bei 5 Prozeduren war aufgrund VF oder hämodynamischer Intoleranz der ausgelösten VTs eine elektrische Kardioversion notwendig, 2× kamen postinterventionell zur Kreislaufstabilisierung Katecholamine zum Einsatz. Schwere Komplikation (relevanter Perikarderguss, bleibende Beeinträchtigung, Tod) wurden nicht beobachtet. Bei 18 Pat. konnte zum Prozedurende keine VT mehr induziert werden, 7× wurde aufgrund fortgeschrittener Prozedurdauer auf eine Austestung verzichtet, 1× konnte von 2 VT-Morphologien noch 1 provoziert und aufgrund ihres epikardialen Ursprunges in einer 2. Sitzung behandelt werden.

14 Patienten (53,8 %) berichteten bei einem mittleren Follow-up von 27,6 ± 16,5 Monaten hinsichtlich der VTs über Rezidiv-Freiheit und 23 Patienten (88,5 %) über Freiheit von ICD-Schocks **(Abbildung 36)**. In 19 Fällen (73,1 %) war keine Rehospitalisierung aufgrund der bekannten Arrhythmie mehr notwendig **(Abbildung 37)**, 24 Pat. (92,3 %) schilderten eine teils deutlich gebesserte QoL

(**Abbildung 38**). Zwei kardiale Kompasse implantierter ICDs zeigen Langzeitverläufe (**Abbildungen 39, 40**).

Schlussfolgerung Ablationen bei komplexem arrhythmogenem Substrat mit rezidiv. VT/VF bei Pat. mit meist signifikanter struktureller Herzerkrankung und teils multiplen ICD-Schocks sind aufwändige Interventionen, die jedoch für den Pat. eine deutliche klinische Verbesserung durch Reduktion von Arrhythmien und Schocks bewirken.

Klinische Ergebnisse mit Dronedaron (Multaq®) bei nicht-permanentem Vorhofflimmern anhand des DEMETER-Registers IX – 7

M. Derndorfer, M. Martinek, E. Sigmund, Ch. Lemes, H.-J. Nesser, H. Pürerfellner
Abteilung für Kardiologie I, Krankenhaus Elisabethinen, Linz

Einleitung Dronedaron (Multaq®, Fa. Sanofi-Aventis) ist ein Mehrkanalblocker, der in Österreich bei nicht-permanentem Vorhofflimmern (VHF) seit Anfang 02/2010 als Antiarrhythmikum zur Verfügung steht. Wir berichten über die klinischen Ergebnisse der DEMETER-Beobachtungsstudie (prospektives Register, Laufzeit von 02/2012 bis 12/2011).

Methodik An 6 österreichischen Zentren wurden 94 Patienten (Pat.) (67 m, 27 w) mit einem Alter von 65 ± 11 Jahre in die Studie aufgenommen. Als Einschlussgrund wurde bei 2 Patienten erstmaliges VHF, 68× paroxysmales VHF (72 %) und 24× persistierendes VHF (25,5 %) vermerkt, jeweils 50 % der Pat. wurden ambulant oder stationär auf Dronedaron umgestellt. Zur Baseline-Visite (BL) konnte bei 75 Pat. (80 %) Sinusrhythmus (SR) und 17× VHF (18 %), sowie 2× Vorhofflattern (VHFL) dokumentiert werden (**Abbildung 41**), echokardiographisch wurde bei 77 Pat. (82 %) eine normale und 17× (18 %) eine reduzierte LVEF zwischen 35 und 50 % berechnet. Die mittlere Vorhofsgröße lag bei 43 ± 7 mm, der $CHADS_2$-Score bei 1,3 ± 1.

Neben EKG und Labor wurden nach 3 und 6 Monaten die NYHA-Stadien erfasst und die Pat. zu ihrer aktuellen Lebensqualität (QoL) hinsichtlich des VHF befragt (0 = sehr schlecht; 10 = exzellent).

Resultate 52 von 94 Pat. (= 55 %) konnten die Studie protokollkonform abschließen, 20 Pat. waren nicht auswertbar (lost to Follow-up), bei 14 Pat. wurde ein Abbruch dokumentiert. Grund für das Ausscheiden waren bei 12 Pat. (75 %) VHF-Rezidive, 2× (13 %) eine Intoleranz gegen das Medikament (Diarrhoe), 1× Verordnungsprobleme und 2× mangelnde Compliance. Proarrhythmische Effekte oder Todesfälle traten nicht auf. 8 Pat. wurden wegen eines VHF-Rezidivs rehospitalisiert, weitere stationäre Aufnahmen aus kardiovaskulärer Ursache waren nicht notwendig. Unter Dronedaron kam es über 6 Monate zu keiner relevanten Progression von SR in ein persistierendes VHF, dies zeigten sowohl die zum FU1 und FU2 registrierten Ruhe-EKGs (**Abbildung 42**) als auch die jeweils niedrigen Raten an erforderlichen Kardioversionen (62 % der Pat. in der Anamnese, 5,3 % zum FU1, 3,8 % zum FU2). Die Leberwerte blieben über 6 Monate stabil, das Serumkreatinin stieg pharmakodynamisch erwartungsgemäß signifikant an (**Tabelle 13**). Relevante EKG-Veränderungen, insbesondere eine QTc-Verlängerung kamen nicht vor (**Tabelle 13**).

Die Herzinsuffizienzfälle unter Dronedaron (44,7 % zur BL, 26,7 % zum FU1, 23,1 % zum FU2) nahmen von Visite zu Visite viel stärker ab als zu (**Abbildung 43**). Statistisch konnte dafür (Kreuztabellenanalyse) eine tatsächliche Verbesserung des Zustandes der Pat. und nicht das Ausscheiden „schlechter" Probanden aus der Studie bestätigt werden. Entsprechend wurde von den Pat. bereits ab dem FU1 eine signifikant bessere QoL geäußert (**Abbildung 44**) und diese Entscheidung bis zum Schluss beibehalten.

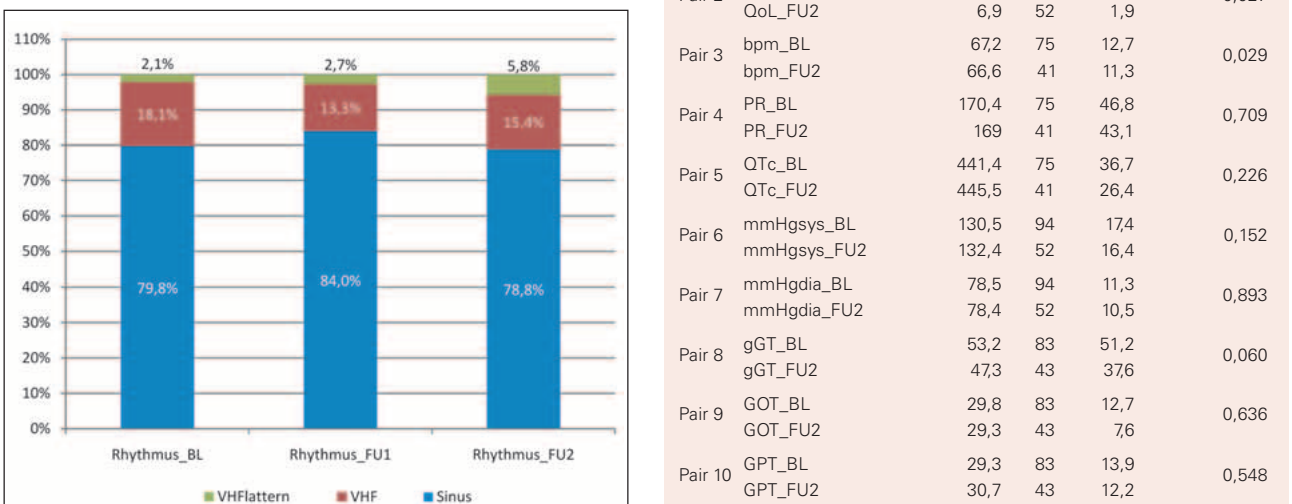


Abbildung 41: M. Derndorfer et al. Rhythmus zum Zeitpunkt des Follow-up (%).

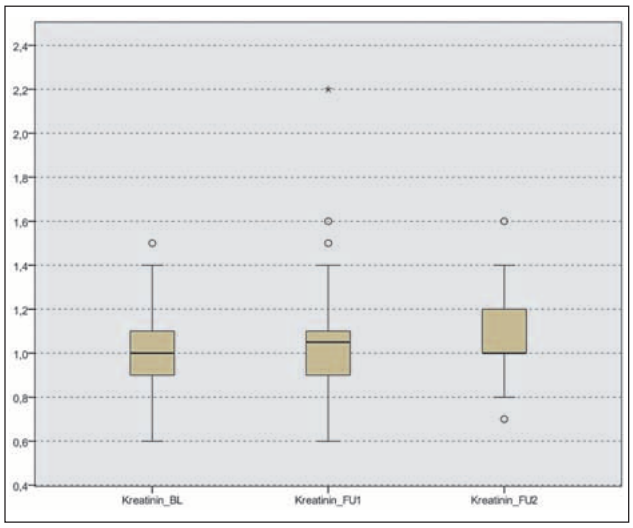


Abbildung 42: M. Derndorfer et al. Kreatinin im Verlauf – Boxplots (Median – Quartile).

Tabelle 13: M. Derndorfer et al.

Parameter		Mean	N	Std. Dev.	Sig. (2-tailed)
Pair 1	Herzinsuffizienz_BL	44,70 %	94		p < 0,001
	Herzinsuffizienz_FU2	23,10 %	52		
Pair 2	QoL_BL	6,1	94	1,9	0,027
	QoL_FU2	6,9	52	1,9	
Pair 3	bpm_BL	67,2	75	12,7	0,029
	bpm_FU2	66,6	41	11,3	
Pair 4	PR_BL	170,4	75	46,8	0,709
	PR_FU2	169	41	43,1	
Pair 5	QTc_BL	441,4	75	36,7	0,226
	QTc_FU2	445,5	41	26,4	
Pair 6	mmHgsys_BL	130,5	94	17,4	0,152
	mmHgsys_FU2	132,4	52	16,4	
Pair 7	mmHgdia_BL	78,5	94	11,3	0,893
	mmHgdia_FU2	78,4	52	10,5	
Pair 8	gGT_BL	53,2	83	51,2	0,060
	gGT_FU2	47,3	43	37,6	
Pair 9	GOT_BL	29,8	83	12,7	0,636
	GOT_FU2	29,3	43	7,6	
Pair 10	GPT_BL	29,3	83	13,9	0,548
	GPT_FU2	30,7	43	12,2	
Pair 11	Krea_BL	1	83	0,2	0,030
	Krea_FU2	1,1	43	0,2	

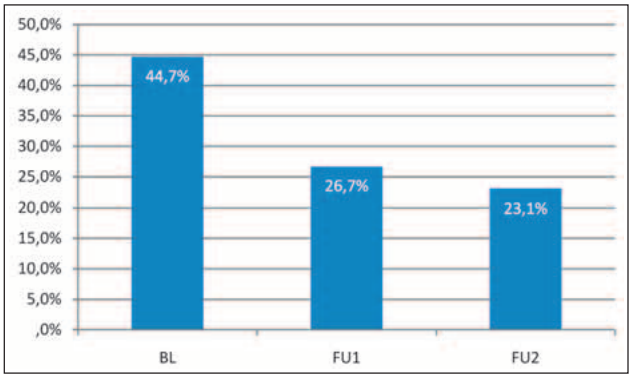


Abbildung 43: M. Derndorfer et al. Anteil der Patienten mit Herzinsuffizienz.

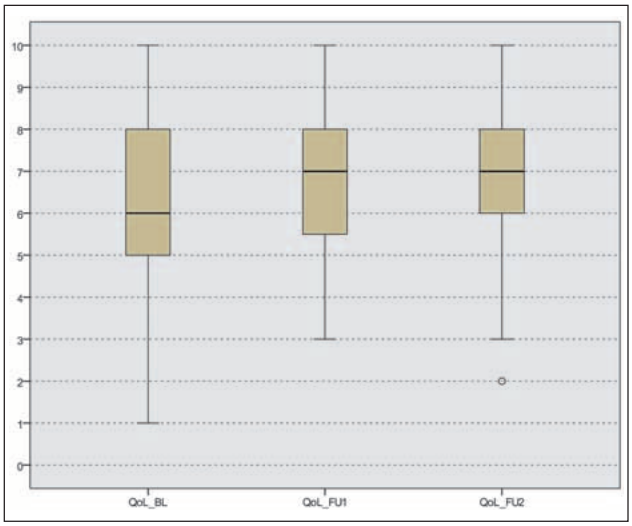


Abbildung 44: M. Derndorfer et al. Lebensqualität quantitativ – Boxplots (Median – Quartile).

Schlussfolgerung Unter Beobachtung von Klinik, EKG sowie Labor (Serumkreatinin, Leberwerte) zeigte sich Dronedaron bei nicht-permanentem VHF ohne rezente kardiale Dekompensation nebenwirkungsarm und sicher in der Anwendung. Zudem kam es zu einer signifikanten Abnahme an klinischer Herzinsuffizienz (p = 0,001) und einer signifikant gebesserten QoL der Pat. (p = 0,013, BL vs. FU1 bzw. 0,027, BL vs. FU2) **(Tabelle 13, Abbildung 43, 44)**. Anhand eines stabilen Verhältnisses an Patienten mit VHF und SR konnte unter Dronedaron über 6 Monaten keine relevante Progression von paroxysmalem in persistierendes VHF beobachtet werden.

Long-Term Outcome of Catheter Ablation of Electrical Storm Due to Monomorphic Ventricular Tachycardia in a Large Cohort of Patients with Nonischemic Cardiomyopathy BAII

L. Fiedler, B. Dinov, R. Schönbauer, A. Bollmann, P. Sommer, T. Gaspar, D. Husser-Bollmann, Ch. Piorkowski, G. Hindricks, A. Arya
Abteilung für Rhythmologie, Herzzentrum Leipzig, Deutschland

Introduction This study aimed to assess the predictors of long term outcome in patients with idiopathic dilated cardiomyopathy undergoing catheter ablation. Electrical storm due to recurrent ventricular tachycardia (VT) can adversely affect their long-term survival. This study evaluates the efficiency of the radiofrequency catheter ablation of electrical storm due to monomorphic VT in patients with idiopathic dilated cardiomyopathy and assesses predictors for recurrence.

Methods Between April 2004 and October 2011, 70 consecutive patients (83% men, mean age 59 ± 14 years) underwent 122 catheter ablation procedures, including 24 epicardial procedures, at our center.

Results The median number of inducible VTs was 2 (range 1–7, cycle length 380 ± 83 msec), mean left ventricular ejection fraction was 33.6 ± 9.95 ml. Acute complete success, defined as the lack of inducibility of any VT at the end of procedure, was achieved in 68% of patients. Eleven patients (15.7%) died during a median follow-up of 420 days (range 25–2705 days) 53% of patients were free from VT recurrence. In univariate analysis LVEF (p = 0.015), clinical VT CL (p = 0.03), and GFR (p = 0.039) were correlated with VT free survival. However, in multivariate logistic regression only female gender (p = 0.005) and left ventricular end-systolic diameter LVESD < 53 mm (0.009) were associated with VT free survival.

Conclusion VT free survival during long term follow-up in our patients cohort Catheter ablation in patients with DCM and electrical storm due to monomorphic VT, who had an ICD, prevents further VT recurrence in 53% of the patients. Female gender and LVESD are reliable markers to predict VT free survival.

Erhöhte Strahlenexposition bei Substratablation ventrikulärer Tachykardien VIII – 8

B. Frey, N. Doruska, Ch. Wollmann, M. Pribyl, P. Schlossnagl, H. Mayr
Abteilung für Kardiologie, Klinik für Innere Medizin 2, Landeskrankenhaus, St. Pölten

Einleitung Strahlendosen > 5 Gy am Referenzpunkt (Air Kerma) erhöhen das Risiko eines Strahlenschadens der Haut. Gesamtkörperdosen > 100 mSv, errechnet aus dem Dosisflächenprodukt (DFP), erhöhen nachweislich das Risiko, an einer Leukämie oder einem Lymphom oder Karzinom zu erkranken. Bezüglich der Substratablation ventrikulärer Tachykardien (VT) inklusive Mapping mittels CARTO gibt es noch kaum Daten bezüglich der zu erwartenden Strahlenexposition.

Methode Wir evaluierten die Strahlendosis in allen unseren Patienten (n = 27), bei denen von 9/2009 bis 12/2011 eine VT-Ablation (n = 28) durchgeführt wurde und verglichen die Dosis zu den letzten 28 Ablationen 2011, bei denen kein CARTO-Mapping-System verwendet wurde (Kontrollen). Indikationen zur VT-Ablation waren St. p. Herzinfarkt (n = 13), dilatative Kardiomyopathie (n = 10), arrhythmogene rechtsventrikuläre Dysplasie (ARVD) (n = 2) und idiopathische VT (n = 2). Die Kontrollen waren eine Ablation des „slow pathway" (n = 13), des rechts atrialen Isthmus (n = 10), einer fokalen atrialen Tachykardie (n = 2), einer akzessorischen Bahn (n = 2) und einer Tachykardie aus dem Ausflusstrakt bei ARVD (n = 1). In Erwartung langer Prozeduren wurde vor Beginn des VT-Ablationsprogramms das Strahlenschutzkonzept optimiert.

Ergebnisse siehe **Tabelle 14**.

Diskussion Die Strahlendosis und somit die Strahlenexposition bei Substratablation von VTs ist deutlich höher im Vergleich zu Routine-Ablationen. Kritische Werte werden nur selten erreicht, nämlich bei einem Patienten mit kombinierter endo- und epikardialer Ablation. Dies unterstreicht die klinische Bedeutung eines Konzepts zur Optimierung des Strahlenschutzes bei VT-Ablation.

Tabelle 14: B. Frey et al.

	VT	Kontrollen	p-Wert
Alter (Jahre)	64 ± 12	58 ± 16	n. s.
Geschlecht (m/w)	22/5	20/8	n. s.
Untersuchungszeit (min)	308 ± 79	163 ± 71	< 0,01
Durchleuchtungszeit (min)	55 ± 25	30 ± 30	< 0,01
DFP (cGycm²)	19.444 ± 13.331	11.793 ± 11.605	< 0,05
Air Kerma (Gy)	1,6 ± 1,07	0,94 ± 0,93	< 0,05
Air Kerma (> 5 Gy)	1	–	–
Effektive Dosis (mSv)	41 ± 28	25 ± 25	< 0,05
Effektive Dosis (> 100 mSv)	1	–	–

Endogenous tPA is an Independent Predictor of Adverse Cardiovascular Events and All Cause Mortality in Patients with Atrial Fibrillation Treated According to Guidelines VIII – 7

M. Freynhofer, S. Gruber, V. Bruno, T. Höchtl, S. Farhan, J. Wojta, K. Huber
3rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna

Background Tissue plasminogen activator (tPA) is the major activator of plasminogen, which is responsible for thrombus resolution. Patients with atrial fibrillation (AF) exhibit higher levels of endogenous tPA, suggesting a hyperfibrinolytic state due to endothelial dysfunction and clinically silent thrombus generation. tPA might help to estimate the thromboembolic risk of patients with AF. We therefore investigated whether high levels of endogenous tPA, independently of the $CHADS_2$-score, predict major adverse cardiovascular events (MACE) in patients with AF treated according to current guidelines.

Methods This prospective, longitudinal single center study included 269 patients with AF. Blood samples were analyzed for tPA-antigen concentration by means of enzyme-linked immunoassay kits.

Results Patients were followed for a median duration of 1933 (1517–2277) days. After adjustment for all univariable predictors for MACE and all-cause mortality ($p \leq 0.1$), tPA above the median of 4.22 ng/ml (HR 3.003 [95%-CI: 1.688–5.341]; $p < 0.001$ and HR 2.525 [95%-CI: 1.440–4.428]; $p = 0.001$, respectively) remained independently associated with outcome. In patients with low and intermediate risk for cardiovascular events according to the $CHADS_2$-score the addition of high tPA plasma levels (> 4.22 ng/ml) had significant impact on the patients outcome (HR 3.254 [1.129–9.378]; $p = 0.029$ and HR 2.330 [1.273–4.264]; $p = 0.006$, respectively).

Conclusion High values of endogenous tPA independently predict MACE and all-cause mortality in patients with AF. Therefore, tPA and the hyperfibrinolytic state in AF might represent an important biomarker for the development and perpetuation of vascular disease in AF patients. This might be an additional help to risk stratification in AF patients.

Renal Function, P-Glycoprotein-Affecting Drugs and Stroke Prevention in Atrial Fibrillation XVII – 1

F. Höllerl, C. Stöllberger, J. Finsterer, F. Weidinger
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Introduction Dabigatran is an oral thrombininhibitor which showed similar efficacy as warfarin for stroke prevention yet a lower bleeding rate in patients with atrial fibrillation (AF) in the RELY study. The serum concentration of dabigatran is influenced by renal function as well as the P-glycoprotein-(P-gp)-system. The aim of this cross-sectional study was to assess renal function and prescription frequency of P-gp-affecting drugs in hospitalized AF patients.

Methods P-gp-affecting drugs were searched from the literature. Consecutive patients with AF hospitalized between December 2009 and January 2010 were included. The $CHADS_2$-score was assessed, the medication was registered and screened for P-gp-affecting drugs. The glomerular filtration rate (GFR) was calculated by the "modification of diet in renal disease" formula.

Results In 100 patients (47 females, mean age 74 ± 12 y), the mean $CHADS_2$-score was 2.4 ± 1.4. GFR was < 30 ml/min/1.73 m^2 in 9 patients, 30–45 in 12 patients, 46–59 in 21 patients, 60–89 in 42 patients and ≥ 90 ml/min/1.73 m^2 in 16 patients. Forty-two patients took at least one, and 4 patients 2 P-gp-affecting drugs: Simvastatin (n = 22), amiodarone (n = 8), vitamin E (n = 8), carvedilol (n = 4), diltiazem (n = 2), dipyridamole (n = 1), propranolol (n = 1), verapamil (n = 1). P-gp-affecting drugs were prescribed to 3 patients with GFR < 30 ml/min/1.73 m^2, 4 patients with GFR 30–45, 9 patients with GFR 60–89, 18 patients with GFR 60–89 and 7 patients with GFR ≥ 90. Only 9 patients had a normal renal function as well as no prescription of P-gp-affecting drugs.

Conclusion Normal renal function was present in only 16% of hospitalized AF-patients. P-gp-affecting drugs were prescribed to 42% of hospitalized AF patients. Only 9% of hospitalized AF patients have a normal renal function and do not receive P-gp-affecting drugs. More information about the relevance of impaired renal function and drug interactions is warranted before dabigatran may be widely used for stroke prevention.

Significant Reduction of Procedure Time and Fluroscopy Exposure Using the Achieve Mapping Wire for Pulmonary Vein Isolation with the Cryocath Ballon XVII – 4

S. Hönig, C. Steinwender, A. Kypta, K. Saleh, T. Lambert, F. Leisch
I. Medizinische Abteilung mit Kardiologie, Allgemeines Krankenhaus, Linz

Purpose The aim of our examination was to figure out whether there was an advantage in using the novel mapping wire (Achieve, Medtronic) performing pulmonary vein isolation (PVI) in combination with the Cryocath Ballon (Medtronic) in a paroxysmal atrial fibrillation (AF) population.

Methods We performed PVI with the Cryo-Ballon in a total population of 105 patients. In the first group a conventional mapping catheter (Lasso, St. Jude) was used to check pulmonary vein isolation after application of Cryo-energy. In the second group the new Achieve mapping wire was used for mapping the PV-potentials during Cryo-ablation. Procedure time, fluoroscopy time and clinical follow-up were analysed in a retrospective manner. Clinical follow-up consisted of repetitive 48-hr-Holter-ECGs and a personal log of duration and frequency of symptoms in terms of palpitations at 1 month, 3 months and 12 months after PVI. Clinical success was proven by freedom of atrial arrhythmias longer than 30 sec.

Results Significant reduction of procedure time (conventional group: mean 180,7 min vs 146,8 min in the Achieve-group, $p > 0.01$) and fluoroscopy exposure (conventional group: mean 35.3 min. vs 30.9 min Achieve-group, $p > 0.001$) were reached by using the new achieve mapping wire. These differences showed high significance already after a small cohort of patients suggesting avoidance of a learning curve as supposed for every new technique. No safety issues appeared and efficacy was shown as high as in the conventional group with a trend towards the Achieve group (free of AF: 75% in the conventional and 81% in the Achieve-group, p = n. s.) with a mean follow-up of 16 months (3–24 months).

Conclusion Using the Achieve during Cryo-Ablation for paroxysmal AF showed significant reduction in procedure and fluoroscopy time with the same efficacy as the standard approach and without decrease in safety profile. The Achieve may be a tool for increasing the number of ablations by making the intervention easier and faster, but further studies are needed to prove this hypothesis.

Voltagegeführte Katheterablation der Pulmonalvenen (PV) bei Vorhofflimmern XVII – 7

E. Gatterer, M. Wurm, H. Keller, Ch. Steger, F. Weidinger
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien; St. Jude Medical

Einleitung Die antrale Pulmonalvenenisolation (PVI) hat sich in den vergangenen Jahren als die effektivste Ablationsmethode von paroxysmalem Vorhofflimmern herausgestellt. 3D-Mapping-Systeme werden zur Darstellung des linken Atriums und der Lungenvenen und zur Markierung der Ablationsläsionen verwendet. Mit dem Ensite NavX Velocity System von St. Jude Medical kann simultan mit dem anatomischen Map ein sogenanntes Voltage-Map (VM) erstellt werden. Aber nur wenige Zentren nutzen die Möglichkeit der farblichen Darstellung der Voltage. Die voltagegeführte Ablationsstrategie wird anhand von zwei Beispielen demonstriert.

Methode Unsere Methode der PVI umfasst das gleichzeitige Erstellen einer anatomischen 3D-Karte und des VM (automatische

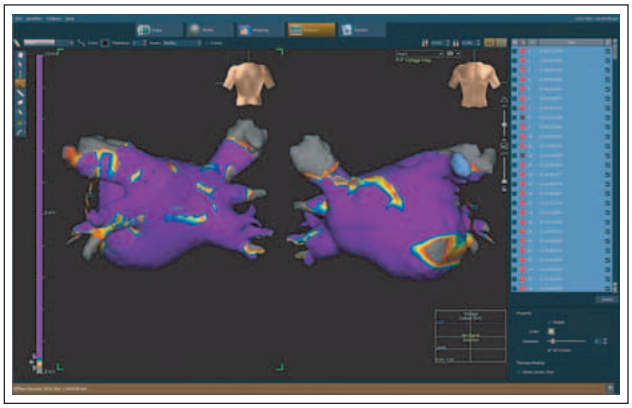


Abbildung 45: E. Gatterer et al. Voltage-Map vor Energieabgaben

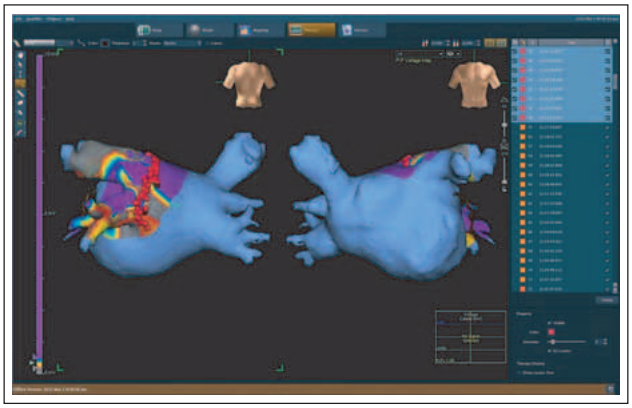


Abbildung 46: E. Gatterer et al. Voltage-Map nach der posterioren Linie. Die Energieabgabe erfolgt nur mit 15–20 Watt, weil es wiederholt zu Alarmen der Ösophagustemperatursonde kommt.

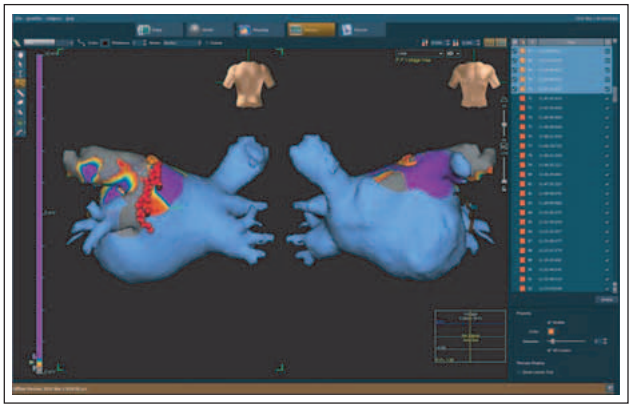


Abbildung 47: E. Gatterer et al. Signifikante Änderung der Voltage posterior nach Energieabgaben am Dach der Vene (LSPV)

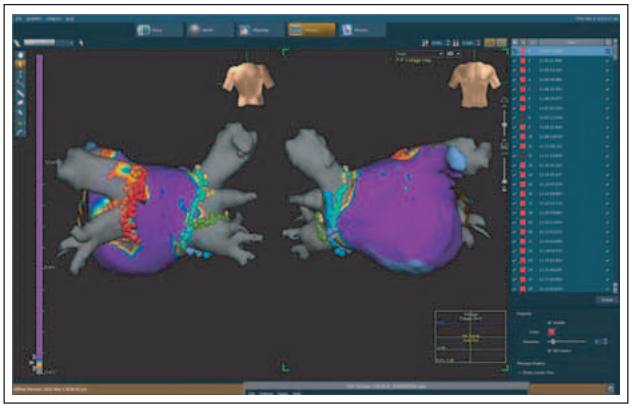


Abbildung 48: E. Gatterer et al. Voltage-Map nach Isolation aller Venen (anterior posterior)

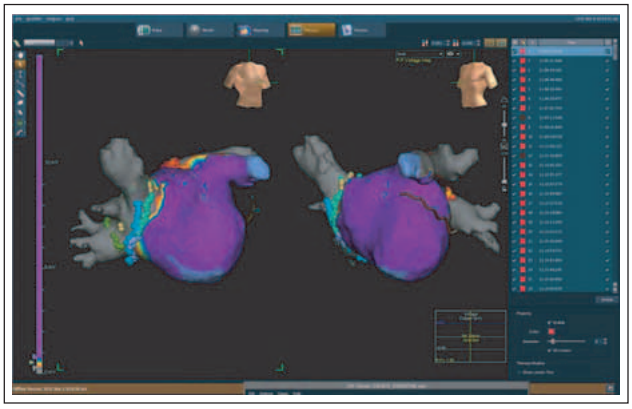


Abbildung 49: E. Gatterer et al. Voltage-Map nach Isolation aller Venen (LAO-Projektion)

Quantifizierung der elektrischen Potenziale und Farbkodierung: Signalgröße > 0,5 mV violett, < 0,2 mV grau, dazwischen Farbspektrum blau bis rot), die Darstellung der akuten Veränderungen der Voltage während der Ablation, Erstellen eines neuen Maps nach Fertigstellung einer Linie bzw. nach Umkreisen eines Venenpaares, Lokalisation von Gaps im Ablationsring (AR) und abschließende Darstellung der Voltage des übrigen Vorhofs nach Isolation aller Venen. Am Ende der Prozedur muss der Bereich innerhalb der ARe (Venen und Antrum) grau sein. Abschließend wird der graue Bereich mit dem Ablationskatheter abgetastet und es wird mit 20 Volt stimuliert. Bei Capture des Sinus Coronarius wird Energie appliziert bis kein Capture mehr vorliegt.

Abkürzungen:

LSPV: linke oberen PV; LIPV: linke unteren PV; RSPV: rechte obere PV; RIPV: rechte untere PV

Beispiel 1 70-jähriger Mann mit paroxysmalem Vorhofflimmern. **Abbildung 45** zeigt das VM vor den Energieabgaben und man sieht, wie weit erregbares Gewebe in die großen Lungenvenen hineinreicht. **Abbildung 46** zeigt den nur geringen Effekt der ersten posterioren Linie links auf die Voltage, **Abbildung 47** die signifikante Änderung der Voltage nach den Energieabgaben am Dach der Vene (orange Punkte). Zu diesem Zeitpunkt finden sich bereits deutlich gesplittete Signale auf dem Spiralkatheter (atriales Farfield und Venensignal). Die Ablationslinie wird nun am Unterrand der LIPV in Richtung Ridge fortgesetzt, danach erfolgt die Ablation anterior vom Dach nach inferior. Die Isolation der LSPV gelingt im anterioren Zwickel der sog. Carina zwischen den linken Venen, die Isolation der linken unteren Vene in einer Lücke am posterioren Unterrand der LIPV. Analoges Vorgehen bei Ablation der rechten Venen. **Abbildungen 48 und 49** zeigen das VM nach Isolation aller Venen.

Beispiel 2 Redo-Prozedur: 55-jähriger Mann, primär erfolgreiche PV-Isolation im September 2011. **Abbildung 50** zeigt das Ausgangs-VM im Sinusrhythmus. Die LSPV und die LIPV sind antral anhaltend isoliert. Die RSPV ist nicht mehr isoliert, auch die posteriore Linie, vorbei an der akzessor. Vene ist nicht dicht. Die RIPV ist anhaltend isoliert. Es erfolgt eine ringförmige Ablation um die RSPV und eine zweite um die kleine akzessor. Vene. Die Isolationsstelle der RSPV (gelber Punkt) liegt im Bereich der posterioren Carina **(Abbildung 51)**.

Schlussfolgerung Die Voltagegeführte PVI ist eine elegante Methode, um die akuten Veränderungen im leitfähigen Gewebe und den Fortschritt der Prozedur zu zeigen. Die Methode ist besonders hilf-

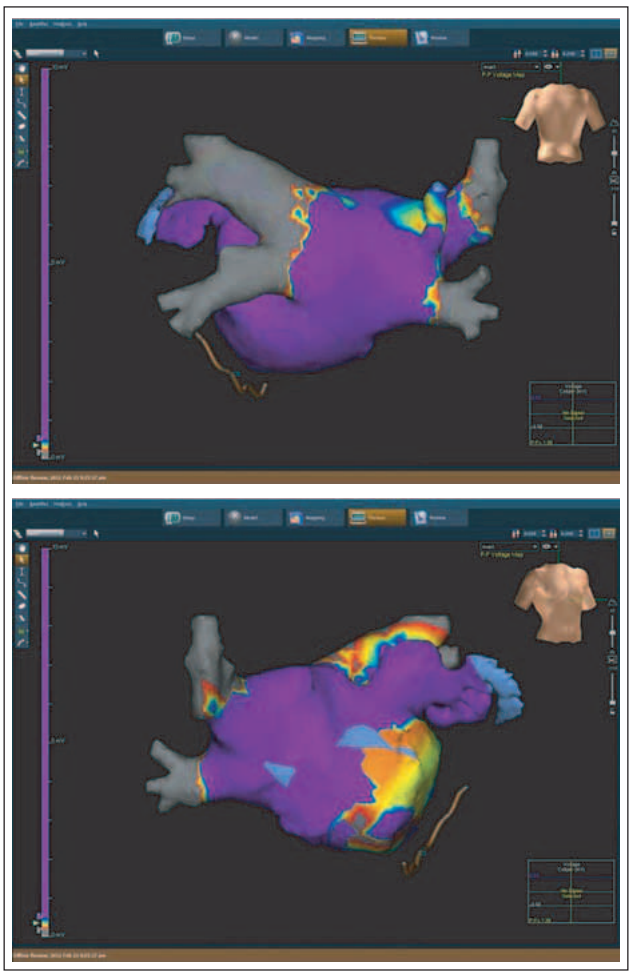


Abbildung 50: E. Gatterer et al. Voltage-Map zu Beginn der Untersuchung (oben posteriore, unten anteriore Ansicht). Die linken Venen sind anhaltend isoliert, die rechte obere und die kleine akzessorische Vene rechts nicht.

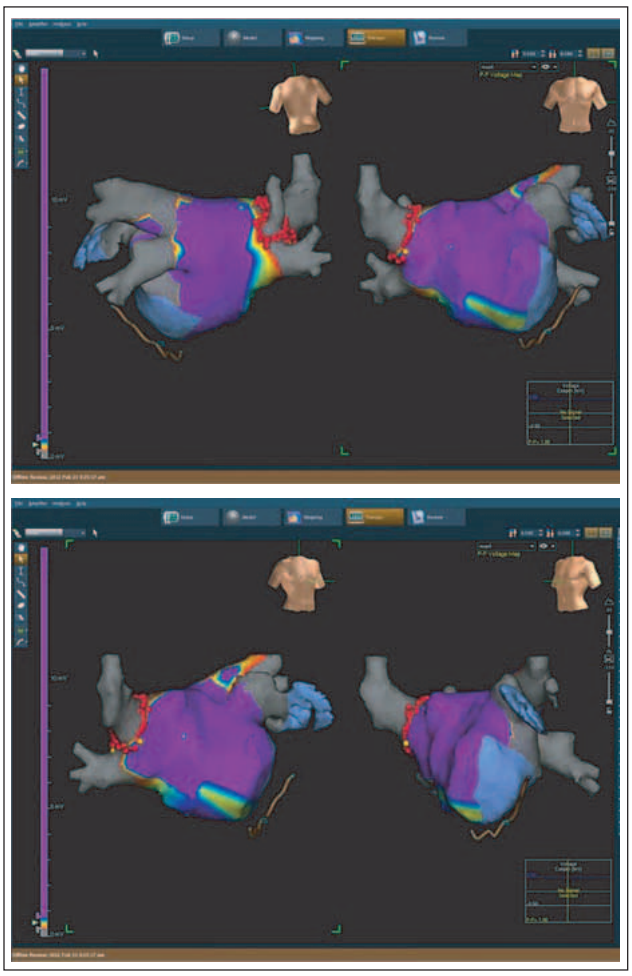


Abbildung 51: E. Gatterer et al. Reisolation der RSPV durch komplette Ablation um die Vene (Isolation anterior, siehe gelber Punkt) sowie Re-Isolation der kleinen akzessorischen rechten Vene durch zirkumferentielle Ablation um die Vene (gelber Punkt in der Carina).

reich bei Redo-Prozeduren, weil die Ablationslinien der vorangehenden Prozedur ohne zusätzlichen Zeitaufwand dargestellt werden und sich sofort eine klare Ablationsstrategie ableiten lässt.

M. Wurm: techn. Unterstützung von der Fa. St. Jude Medical (SJM)

Das posturale orthostatische Tachykardiesyndrom (POTS) bei Patienten mit Synkope und Präsynkope VIII – 5

H. Keller, Ch. Steger, E. Gatterer
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Einleitung POTS (posturales orthostatisches Tachykardiesyndrom) ist definiert durch Symptome einer orthostatischen Intoleranz, verbunden mit einem Frequenzanstieg von >30 Schlägen oder einem Anstieg der Herzfrequenz (HF) auf > 120 Schläge/min innerhalb von 10 Minuten in Orthostase (**Abbildung 52**). Bei 30 % der Patienten kommt es zu Synkopen. Die Pathogenese ist ungeklärt. Möglicherweise liegt eine Störung der sympathischen Vasokonstriktion mit venösem Pooling vor. Die Prävalenz wird mit 0,2 % angenommen. Neben allgemeinen Maßnahmen wie Volumenzufuhr, Salzen der Nahrung, Tragen von Stützstrümpfen und Ausdauertraining werden auch Medikamente wie Fludrocortison, α-Rezeptoragonisten und Betablocker eingesetzt.

Die Kipptischuntersuchung ist die einzig etablierte Methode, POTS zu diagnostizieren. Ziel der retrospektiven Untersuchung war es, den Anteil von POTS bei Pat., die zur Kipptischuntersuchung zugewiesen wurden, festzustellen, die Behandlung auszuwerten und das Ansprechen auf die Therapie zu analysieren.

Methodik Von 1/2010 bis 12/2011 führten wir bei 84 Patienten mit ungeklärten Synkopen und Präsynkopen eine Kipptischuntersuchung durch. Es wurde der Task Force Monitor von CNSystems verwendet, die Dauer der Orthostase (60°) betrug 30 Minuten. Das Follow-up erfolgte telefonisch, teilweise ambulant.

Ergebnisse Kriterien für POTS erfüllten 16/84 (19,0 %) Pat. Frauen waren häufiger betroffen (9:7), das Durchschnittsalter betrug 33,3 Jahre (17–70 Jahre) für Frauen und 37,6 Jahre (22–65 Jahre) für Männer. 14/16 Pat. hatten insgesamt 69 Synkopen (durchschn. 4,1) vor der Untersuchung (10 Pat. mit 1–4 Synkopen, 4 Pat. mit ≥ 5 Synkopen), 2/16 Patienten hatten Präsynkopen.

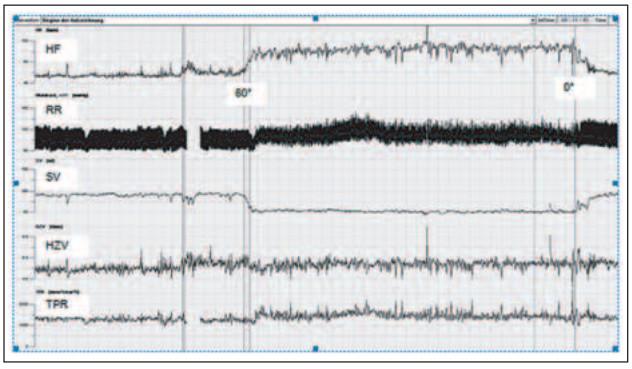


Abbildung 52: H. Keller et al. POTS bei der Kipptischuntersuchung.

Bei der Untersuchung stieg die HF von 70 (50–109) auf 109 (81–146) an; Bei 15/16 Pat. erfolgte der HF-Anstieg < 3 Minuten. 3 Pat. entwickelten eine orthostatische Hypotonie, 4 Pat. eine vasovagale Synkope, 1 Pat. eine Präsynkope. Die Barorezeptorsensitivität war bei 11/16 Pat. reduziert (BRS < 7 ms/mm Hg).

Als Therapie wurden Volumenzufuhr, Stützstrümpfe, Salzen, Counter-Manöver bei Symptomen, Stehtraining sowie ein Ausdauertraining empfohlen. 3 Patienten erhielten Betablocker, 1 Patientin Midodrin, 1 Pat. einen Loop-Recorder implantiert, 1 Pat. erhielt in einem anderen Zentrum einen Schrittmacher implantiert.

Bei 15/16 Pat. erfolgte ein Follow-up von 54 Wochen (9–107, median 51). 47/64 Therapieempfehlungen wurden übernommen (73 %). Während die Volumenzufuhr (15/15), Salzen (7/9), Ausdauertraining (12/14; Æ 2,3 Std./Woche), Counter-Manöver (5/7) und Stehtraining (3/4) häufig umgesetzt wurden, haben nur 5/15 Patienten Stützstrümpfe getragen.

Insgesamt traten 15 Synkopen im Follow-up auf (78 % Reduktion). Bei 3/4 Pat. mit ≥ 5 Synkopen kam es nur mehr 1× zu einer Synkope, auch bei 10 Pat. mit 1–4 Synkopen trat nur mehr 1 Synkope auf. Die Zahl reduzierte sich von 4,1 auf 1,0 pro Pat. Nur 2 Pat. hatten nach der Kipptischuntersuchung mehr Synkopen. Die Lebensqualität (1 für sehr gut, 10 für sehr schlecht) wurde mit 3,6 vor und 2,3 nach der Kipptischuntersuchung angegeben.

Diskussion Die Prävalenz von POTS betrug 19 %. Die Compliance der Pat. war gut (73 %). Die Synkopenhäufigkeit konnte durch die Diagnosestellung, Aufklärung und Therapievorschläge reduziert und die Lebensqualität verbessert werden. Neben einer ausführlichen Aufklärung sind die nicht-medikamentösen Therapieformen als „First-line"-Therapie angezeigt und effektiv, ebenso wie ein moderates Ausdauertraining.

Autonome und kardiovaskuläre Effekte von Licht VIII – 1

S. Kohl, U. Bauer, M. Schmitt, M. Edlinger, A. Süssenbacher, O. Pachinger, M. Stühlinger
Universitätsklinik für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck

Einleitung Licht ist ein bedeutender Einflussfaktor auf den menschlichen Körper, über autonome und kardiovaskuläre Auswirkungen bestimmter Lichtszenarien ist allerdings wenig bekannt. Während rotes Licht als vorwiegend adrenerg aktivierender Trigger wirkt, führt blaues Licht eher zu Entspannung und Aktivierung des Parasympathikus. Wir überprüften daher die Hypothese, dass eine kontrollierte und spezifische Licht-Exposition für 3 Stunden zur Beeinflussung der Herzfrequenz-Variabilität (HRV) und in weiterer Folge zu Veränderungen des Blutdruck-Verhaltens, der Endothelfunktion und der Entwicklung von Arrhythmien führt.

Methode Zusammen mit der Bartenbach Lichtlabor GmbH entwickelten wir eine spezielle Lichtkabine, in der sich Probanden für jeweils 4 Stunden aufhielten und verschiedenen Lichtszenarien ausgesetzt wurden. Während der Lichtszenarios wurde als Maß für die Aktivierung des autonomen Nervensystems die HRV bestimmt, zusätzlich wurden zur Analyse von kardiovaskulären Auswirkungen des Lichts Holter-EKGs, Langzeit-Blutdruck-Messungen durchgeführt und zusätzlich die Endothelfunktion (EF; Endopat®, Itimar) gemessen. Die Untersuchungen wurden nach 30 min Neutrallicht (NL) jeweils während einem roten (RL) und einem blauen Lichtszenario (BL) bei 10 trainierten Probanden (TP), 10 Patienten nach Katheterablation einer akzessorischen Bahn (WPW) und bei 10 Patienten mit ischämischer Kardiomyopathie (CMP) durchgeführt.

Resultate Im Vergleich zu NL führte das rote Lichtszenario (RL) zu einer signifikanten und konkordanten Verbesserung der HRV nach 60 min (SDNN –35,2; RMSSD –19,9; SD-1 –14,1; p < 0,05) und 120 min (SDNN –25,7; RMSSD –19,3; SD-1 –13,7; p < 0,05) Lichtexposition, während blaues Licht (BL) keine signifikanten Veränderungen hervorrief. Der Anstieg der HRV war in der Gruppe der Sportler (TP) besonders stark ausgeprägt. Parallel zu diesen autonomen Veränderungen beeinflusste die Lichtexposition die Endothelfunktion (Enopat Index –0.35 RL vs. NL; p < 0,001). Auch hier wurden die stärksten Veränderungen in der TP-Gruppe beobachtet. Die Auswirkungen des RL-Lichtszenarios für 3 Stunden führte allerdings nicht zu Veränderungen des Blutdruck-Verhaltens während oder 24 Stunden nach der Exposition. Auch Messungen der Herzfrequenz und der Häufigkeit von ventrikulären oder supraventrikulären Extrasystolen wurden durch die Lichtszenarien nicht beeinflusst (alle p = n. s.).

Zusammenfassung Durch eine Lichtexposition über 2 Stunden mit rotem, aber nicht mit blauem Licht kann unter kontrollierten Bedingungen die Herzfrequenz-Variabilität und die Endothelfunktion signifikant beeinflusst werden. Diese kurzfristigen Effekte führen aber nicht zur Veränderung von Blutdruck-Verhalten oder Neigung zu ventrikulären oder supraventrikulären Arrhythmien.

Asymptomatic Cerebral Lesions in Pulmonary Vein Isolation Under Therapeutic Anticoagulation BAI

M. Martinek, E. Sigmund, Ch. Lemes, M. Derndorfer, H.-J. Nesser, H. Pürerfellner
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Left atrial radiofrequency ablation has been shown to carry a risk of asymptomatic cerebral lesions. No data exists in patients under full anticoagulation throughout the ablation procedure. The aim of this study was to quantify the amount of silent cerebral lesions assessed by preprocedural and postprocedural MRI in these patients and to identify clinical or procedural parameters that increase the risk

Methods A total of 80 consecutive patients undergoing catheter ablation for paroxysmal (n = 53; 66.3%) or persistent (n = 27; 33.8%) atrial fibrillation were included in the study. Pulmonary vein antrum isolation, roofline, mitral isthmus line, and CFAE ablation using 3.5 mm open-irrigated tip catheters were performed, as

Table 15: M. Martinek et al. Clinical and procedural parameters in univariate analysis

	Patients with silent cerebral lesion	Patients without silent cerebral lesion	p
No. of patients	13	67	
(Congestive) Heart failure	0	4 (6)	0,606
Hypertension	9 (69)	39 (58)	0,547
Mean age, y	62,6 ± 7,8	58,9 ± 8,5	0,167
Diabetes mellitus	1 (8)	3 (5)	0,515
Previous stroke or TIA	2 (15)	6 (9)	0,610
Coronary heart disease	2 (15)	3 (16)	0,926
Male gender	9 (69)	44 (66)	0,804
Dyslipidemia	8 (61)	32 (48)	0,363
CHADS-VASc score	1,9 ± 1,0	1,3 ± 1,2	0,099
Type of AF			
Paroxysmal	5 (39)	48 (72)	0,021
Persistent	8 (61)	19 (28)	
Left ventricular ejection fraction, %	53 ± 3	53 ± 4	0,755
Left atrial parasternal diameter, mm	42 ± 4	40 ± 5	0,271
Mean ACT value during procedure, s	330 ± 52	343 ± 36	0,282
INR at the day of ablation procedure	2,2 ± 0,5	2,4 ± 0,6	0,322
Type of procedure			
PV isolation (only)	4 (31)	48 (72)	0,009
Linear lesions	7 (54)	19 (28)	0,073
CFAE	4 (31)	6 (9)	0,052
Linear lesions + CFAE	2 (15)	6 (9)	0,610
Radiofrequency time, min	54 ± 16	50 ± 18	0,516
Total energy delivered, Ws	84,013 ± 31,365	79,195 ± 28,453	0,612
Electrical cardioversion	9 (69)	19 (28)	0,009

needed. All patients underwent preprocedural and postprocedural cerebral MRI.

Results Postprocedural MRI revealed new embolic lesions in 13 patients (16.3%), all of them asymptomatic. The only clinical parameter showing a significant correlation with cerebral embolism was the type of atrial fibrillation (5/53 paroxysmal – 9.4% vs 8/27 persistent – 29.6%; p = 0.021). Procedural parameters contributing to an increased risk were electrical cardioversion (p = 0.009) and additional linear (p = 0.07) or CFAE lesions (p = 0.05). The only factor showing a trend to significance in multivariate analysis remained electrical cardioversion with an increased risk of 3.98 (95%-CI: 0.83–19; p = 0.08).

Conclusion Radiofrequency ablation in patients under therapeutic anticoagulation is associated with a substantial risk of silent embolism detected by cerebral MRI. Risk factors for cerebral lesions are the type of atrial fibrillation, additional linear of CFAE lesions and, in particular, electrical cardioversion during the ablation procedure **(Table 15)**.

Impact of a New Contact Force Sensing Catheter on Procedural Parameters in Radiofrequency Ablation of Atrial Fibrillation IX – 2

M. Martinek, Ch. Lemes, E. Sigmund, M. Derndorfer, H.-J. Nesser, H. Pürerfellner
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Left atrial radiofrequency ablation has been established for the treatment of atrial fibrillation. New catheter material with the unique opportunity to directly visualize catheter contact force and direction as well as integration of this information into a 3D electro-anatomic System (CARTO 3) have recently been released. The aim of this study was to assess the impact of this new technique on procedural parameters.

Methods A total of 29 consecutive patients (65% male, 59.6 ± 10.5 years) undergoing catheter ablation for paroxysmal atrial fibrillation were included in the study. Pulmonary vein antrum isolation with documented entry and exit block was performed using either the standard NaviStar® ThermoCool® catheter (n = 17) or the new ThermoCool® SmartTouch™ (n = 12) contact force sensing catheter (both Biosense Webster). Both catheters are mounted with equal 3.5 mm open-irrigated tips. A maximum of 25 W was delivered at the left atrial posterior wall, 30 W were used in other positions with an irrigation flow rate of 2 ml/min at baseline and 20 ml/min during radiofrequency application.

Results Procedural data showed a remarkable decline in ablation time (radiofrequency time needed to isolate all pulmonary veins) from 56.2 ± 16.1 to 40.9 ± 9.5 minutes (p = 0.007) with a reduction in overall procedure time of 25.5 ± 11.8 minutes (p = 0.003). In parallel the total energy delivered could be significantly reduced from 78,051 ± 18,239 to 63,421 ± 13,511 Ws (p = 0.026).

Conclusion The use of novel contact force sensing technology was able to significantly reduce ablation and procedure times in atrial fibrillation ablation in this small pilot study. Energy delivery was substantially reduced by avoiding radiofrequency ablation in positions with insufficient surface contact.

CHA_2DS_2-VASc als Risikomarker für Vorhofflimmern VIII – 2

R. Riedlbauer, M. Gruber, H. Forstner, F. M. Fruhwald, K. Horvath, T. Pieber, B. Pieske, F. R. Heinzel
Klinische Abteilung für Kardiologie; Klinische Abteilung für Endokrinologie, Medizinische Universität Graz

Einleitung Die CHA_2DS_2-VASc-Score wurde 2010 aktualisiert, um das Risiko von Thromboembolien bei bestehendem Vorhofflimmern (VHF) besser beurteilen zu können. Die Diagnose VHF erfordert gewöhnlich die EKG-Dokumentation und ist bei asymptomatischem paroxysmalem VHF erschwert. Die meisten der in der CHA_2DS_2-VASc-Score zusammengefassten Begleitfaktoren (chronische Herzinsuffizienz, Hypertonus, fortgeschrittenes Alter, Diabetes, stattgehabter Schlaganfall, Gefäßerkrankungen) begünstigen

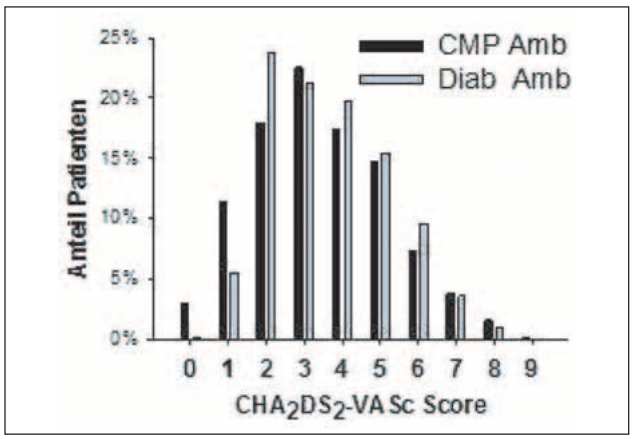


Abbildung 53: R. Riedlbauer et al.

für sich das erstmalige Auftreten von VHF. CHA_2DS_2-VASc könnte daher geeignet sein, das Risiko für das Auftreten von VHF mit thromboembolischen Komplikationen insgesamt zu beurteilen. Wir untersuchten den Zusammenhang zwischen der CHA_2DS_2-VASc-Score und der Prävalenz von VHF in einem kardiologisch engmaschig überwachten Patientenkollektiv.

Methoden Wir verglichen die Prävalenz von VHF in diesem Kollektiv mit einer Patientenkohorte einer nicht-kardiologischen Ambulanz. Es wurden fortlaufend 501 Patienten der Kardiomyopathie-Ambulanz (CMP-Amb) und 473 Patienten der diabetischen Ambulanz (Diab-Amb) unserer Klinik retrospektiv eingeschlossen und die Patientendaten bzgl. der CHA_2DS_2-VASc-Risikofaktoren, der Prävalenz der Diagnose VHF und zusätzlicher Begleiterkrankungen und medikamentösen Therapie analysiert.

Ergebnisse Bei den Patienten mit engmaschiger kardiologischer Kontrolle (CMP-Amb) fand sich eine signifikante positive Korrelation zwischen CHA_2DS_2-VASc-Score und der Prävalenz von VHF ($p < 0,05$; Chi-Quadrat). Beim Vergleich von DM-Amb und CMP-Amb reflektierten Unterschiede in der Häufigkeit von Herzinsuffizienz (2 % in DM-Amb vs. 61 % in CMP-Amb) und Diabetes (99 % vs. 29 %) die Auswahl der Kollektive. Das Diab-Amb-Kollektiv umfasste mehr Frauen (38 % vs. 28 %; $p < 0,001$). Patienten aus der Diab-Amb litten häufiger an Hypertonus (83 % vs. 68 %), seltener an vaskulären Manifestationen (41 % vs. 57 %) und Niereninsuffizienz (21 % vs. 29 %; für alle $p < 0,01$).

Die Verteilung der CHA_2DS_2-VASc-Scores war in beiden Patientenkollektiven vergleichbar (**Abbildung 53**). Der Anteil der Patienten mit bekanntem VHF war in der Diab-Amb signifikant geringer als in der CMP-Amb (8 % vs. 32 %; $p < 0,001$). Der Anteil der Patienten mit zerebrovaskulärem Ereignis war jedoch nicht unterschiedlich (15 % in Diab-Amb vs. 12 % in CMP-Amb). Der Anteil der Patienten mit sehr hoher CHA_2DS_2-VASc-Score (≥ 5) ohne orale Antikoagulation (unabh. von dem Vorliegen von VHF) war signifikant höher in der DM-Amb (77 % vs. 60 %).

Diskussion Das Risiko für das Vorliegen von VHF korreliert mit der CHA_2DS_2-VASc-Score. Die geringe Prävalenz der Diagnose VHF bei gleicher CHADS-VASc-Score und gleicher Schlaganfalls-Prävalenz in dem nicht-engmaschig kardiologisch kontrollierten Kollektiv könnte auf eine höhere Prävalenz von klinisch nicht-apparentem VHF bei diesen Patienten zurückzuführen sein.

Circumferential Pulmonary Vein Ablation with One or Two Eyes Opened: A Retrospective Comparison of Single vs Double Transseptal Approach VIII – 3

R. Schönbauer, B. Dinov, L. Fiedler, P. Sommer, T. Gaspar, Ch. Piorkowski, G. Hindricks, A. Arya
Abteilung Rhythmologie, Herzzentrum Leipzig, Deutschland

Introduction Pulmonary vein isolation is the cornerstone of catheter ablation of atrial fibrillation. The perfect method to achieve this goal is still under debate. For this reason we analyzed whether the

concomitant or alternating use of circular mapping catheter and ablation catheter is the better approach.

Methods 95 consecutive patients with atrial fibrillation (38% male, 42% paroxysmal, age 61 ± 10 years) were analyzed retrospectively. In all patients complete bidirectional circumferential pulmonary vein isolation was the endpoint. Patients were divided into two groups. In single transseptal group (STSP) (n = 48) one transseptal puncture was performed with alternating use of ablation catheter and circular mapping catheter. In the double transseptal group (DTSP) (n = 47) 2 transseptal punctures were performed, allowing the use of circular mapping catheter during ablation.

Results Baseline patients' characteristics were comparable between the 2 groups. Comparing procedure related data there was no significant difference in procedure time, radiation time and radiation dose, but there was a trend towards longer ablation time in the STSP-group (37,8 vs 32,0 minutes; p = 0.07). Severe procedure related complications occurred in two patient in the DTSP-group and in no patient in the STSP-group (p = n. s.). After a median follow-up of 9.8 months 34 (70.8%) patients in the STSP-group and 37 (78.7%) patients in the DTSP-group were free of recurrence of atrial fibrillation and/or atrial flutter (p = 0.259).

Conclusion DTSP and concomitant use of circular mapping and ablation catheter does not lead to superior ablation success however, there is a trend toward shorter ablation time compared to STSP-Group. Further randomized studies are warranted to clarify this issue.

Left Atrial Flutter in Absence of Previous Left Atrial Ablation or Heart Surgery: Mapping, Ablation and One-Year Follow-up VIII – 4

R. Schönbauer, B. Dinov, L. Fiedler, G. Hindricks, Ch. Piorkowski, A. Bollmann
Abteilung für Rhythmologie, Herzzentrum Leipzig, Deutschland

Background In days of routinely performed left atrial ablation procedures (mainly for atrial fibrillation) the incidence of left atrial flutter has strongly increased. Savety and feasibility of ablation of these, obviously iatrogenic induced arrhythmias is well known and described in detail before.

Objective In this present retrospective study we describe the arrhythmia-findings, -management and ablation results of patients presenting with highly symptomatic left atrial flutter but in absence of previous left atrial ablation or heart surgery.

Methods From 01/2009 to 12/2010, 30 patients (18 male) with recurrent highly symptomatic left atrial flutter without previous left atrial ablation or heart surgery presented for catheter ablation. 24 patients also had documented episodes of atrial fibrillation. The diagnose of left atrial flutter was based on body surface ecg and additionally required characteristic findings in biatrial entrainment maneuvers. Using a nonfluoroscopic electroanatomic mapping system (CARTO [n = 6] or NavX [n = 24]) the left atrium was reconstructed and integrated in its previously acquired computer tomography image. Then the documented arrhythmia was mapped by entrainment- and/or activation-mapping. Additionally pulmonary vein isolation was performed. Bidirectional block of ablation lesions and non-inducibility of any tachycardias were procedure endpoints. The primary study endpoint was cumulative freedom from any arrhythmia 6 and 12 months after a single ablation procedure.

Results In 30 patients a total of 54 tachycardias was documented (1–4/patient). 39 tachycardias (72%) could be mapped and ablated successfully. 13 patients (43.3%) reached the study endpoint at 6 months and 9 (30.0%) at 12 months post ablation procedure. In 9 patients a second ablation procedure was done.

Conclusion Ablation of atypical left atrial tachycardias without previous left atrial ablation are challenging procedures with an eventually poor outcome. So these arrhythmias might be a sign of a an already more diseased left atrium with multiple possibilities of reentry circuits.

Outcome of Left Atrial Radiofrequency Catheter Ablation in Patients with Paroxysmal and Persistent Atrial Fibrillation IX – 8

A. Schratter, R. Achleitner, St. Oblin, St. Fritsch, M. Brunner
4. Medizinische Abteilung mit Kardiologie, Krankenhaus Hietzing, Wien

Background Atrial fibrillation (AF) is the most common arrhythmia and may lead to substantial symptoms and loss of quality of life. Left atrial radiofrequency catheter ablation is a therapeutic alternative when antiarrhythmic drugs fail in maintaining stable sinus rhythm (SR). At our department, catheter ablation is used since 2009 in patients with symptomatic AF (either paroxysmal or persistent) that can not be controlled by antiarrhythmic drugs. We wanted to evaluate the efficacy of catheter ablation of AF in this new centre.

Methods We conducted follow-ups at 3, 12 and 24 months after left atrial radiofrequency catheter ablation performed since 2009 in 71 patients suffering from symptomatic AF. Catheter ablation was performed as follows: after anatomical and electrical 3D-reconstruction of the left atrium, either only pulmonary veins were isolated by circumferential lesions (first procedure), or pulmonary vein isolation was combined with roofline and anterior line lesions placed in the left atrium (second procedure). In addition, in patients where pulmonary veins were shown to be isolated in the second procedure, we looked for complex fractionated electrograms (CFE) and ablated at the site of their appearance, if appropriate.

At each follow-up, ECG at rest as well as holter-ECG-recordings (48 hours) were analyzed; furthermore, symptoms and current medications were assessed. Patients presenting with relapse of AF at follow-up received a second procedure, if appropriate.

Results 71 patients were followed up, 32 women and 39 men. Mean age was 60 years. 58 patients presented with paroxysmal and 13 with persistent AF (i. e. 82% and 18%, respectively). 3-month follow-up was conducted in 71, 12-month follow-up in 40 and 24-month follow-up in 15 patients. At 3 months, 54 patients presented with SR (76%) and 27 with AF (24%). 81% of patients with formerly paroxysmal AF and 54% of patients with formerly persistent AF showed SR at follow-up. At 12 months, 35 patients showed SR (87.5%; 88% of formerly paroxysmal and 83% of persistent AF) and 5 showed AF (12.5%). At 24 months, 14 patients presented with SR (93%; 93% of formerly paroxysmal and 100% of persistent AF) and 1 with AF (7%). All patients with SR were without any further arrhythmia-related symptoms.

13 patients (18%) underwent a second procedure due to recurrent AF, which results in an average of 1.2 procedures per patient. After the second procedure, 11 patients showed stable SR (85%) and 2 patients presented with AF (15%).

Procedure-related complications occurred in 5 out of 71 patients (7%): 3 aneurysma spuria and 2 pericardial tamponades, all of them non fatal.

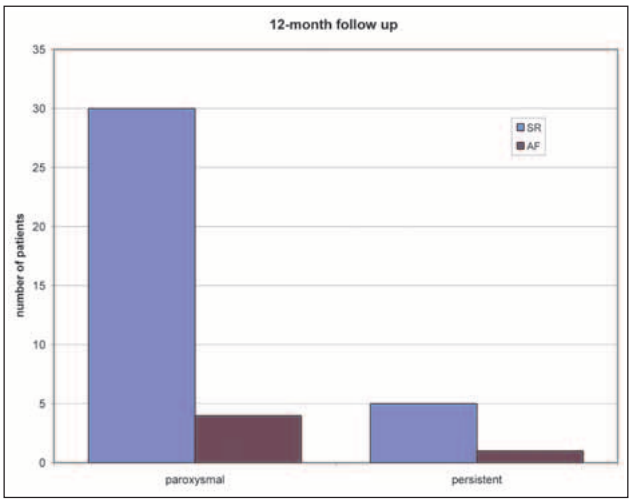


Figure 54: A. Schratter et al.

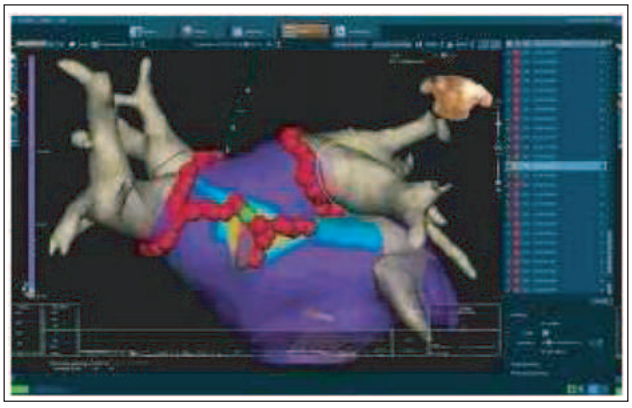


Figure 55: A. Schratter et al.

Conclusion In a collective of 71 patients treated by catheter ablation for AF in a newly implemented centre, 13 patients (18%) presented with AF at follow-up and received a second procedure. Non fatal complications occurred in 5 patients (7%). Catheter ablation showed to be a feasible and efficient method in our centre for patients suffering from symptomatic AF when drug therapy failed **(Figures 54, 55)**.

Vernakalant: Medikamentöse Kardioversion bei Vorhofflimmern – Erfahrungen am eigenen Patientengut XVII – 5

E. Sigmund, M. Martinek, M. Derndorfer, H.-J. Nesser, H. Pürerfellner
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Einleitung Seit Jänner 2011 ist Vernakalant (Brinavess®, Fa. MSD), welches zur Substanzgruppe ARDA („atrial repolarization-delaying agents“) angehört, in Österreich erhältlich und wird bei Vorhofflimmern von kurzer Dauer (< 7 Tage) eingesetzt. Wir berichten über unsere Erfahrungen im Rahmen des klinischen Routinebetriebs bei individuell körpergewichtsadaptierter Zubereitung als intravenöse Infusion unter stationären Bedingungen bei adäquater Hydrierung.

Methodik 25 Patienten (Pat.) (12 weiblich/13 männlich) im Alter von 66,3 ± 14,7 Jahren wurden bislang behandelt. Die Arrhythmiedauer lag bei 18 Pat. (72 %) < 12 Stunden, bei 3 Pat. (12 %) < 24 Stunden und bei 4 Pat. (16 %) bei < 48 Stunden.

Resultate Die Gesamtkonversionsrate lag bei 14 Pat. (56 %), davon konvertierten 11 Pat. (78,6 %) bereits nach der Initialdosis in den Sinusrhythmus, bei 3 Pat. (21 %) war die Gabe einer 2. Dosis erforderlich. Die Konversionszeit lag zwischen 10 und 35 Minuten nach Beginn der Infusion.

An unerwünschten Wirkungen (UAW) waren Hustenanfall mit Niesen (17,4 %), Dysgeusie (13 %), Hitzegefühl (13 %), Flush-Symptomatik (4,3 %) sowie einmalig VES in Salvenform (4,3 %) zu dokumentieren. Alle UAW waren nach wenigen Minuten selbstlimitierend.

Entgegen der in den klinischen Studien berichteten Hypotonie-Neigung konnten wir eher die Tendenz einer Blutdrucksteigerung von 10–30 mmHg systolisch im Rahmen der Anwendung mit Vernakalant verzeichnen (8 Patienten; 32 %). Relevante Hypotensionen wurden (bei adäquater Hydrierung) nicht beobachtet.

Diskussion Vernakalant konnte bislang seine Effizienz im Ausmaß der in den klinischen Studien beobachteten Konversionsrate von knapp über 50 % bestätigen. Auch die Sicherheit konnte bezüglich maligner ventrikulärer Arrhythmien bzw. Hypotonien verifiziert werden. Somit kommt diesem Medikament bei der Auswahl des adäquaten Patientengutes und unter Einhaltung einer ausreichenden Hydrierung durchaus ein Stellenwert zur medikamentösen Kardioversion von Vorhofflimmern in der klinischen Routine zu.

Robotic Navigation for Catheter Ablation of Paroxysmal and Persistent Atrial Fibrillation: A Single-Center Experience After 165 Cases XVII – 2

C. Steinwender, S. Hönig, T. Lambert, A. Kypta, F. Leisch
I. Medizinische Abteilung mit Kardiologie, Allgemeines Krankenhaus, Linz

Introduction Remote navigation systems represent a novel method for catheter ablation of atrial fibrillation (AF). The Sensei robotic navigation system (Hansen Medical, Mountain View, USA) enables remote catheter navigation via a robotic steerable sheath (Artisan™, Hansen Medical). The aim of this study is to report the first Austrian experience with the Sensei™ system for the treatment of patients (P) with paroxysmal and persistent AF.

Materials and Methods Between November 2009 and September 2011, 165 P (59 ± 7 years, 109 males) underwent robotic circumferential pulmonary vein isolation (PVI) for paroxysmal AF (87 P, 53%) or robotic circumferential PVI plus robotic creation of a left atrial roof line for persistent AF (78 P, 47%). The EnSite NavX™ system (St. Jude Medical, Minneapolis, USA) was used for 3-dimensional mapping. For ablation, a 3.5 mm open-irrigated cooled-tip ablation catheter (Therapy Cool Path ns™, St. Jude Medical) was used. PVI was confirmed by a multipolar spiral catheter (Optima™, St. Jude Medical) as second left atrial catheter. Completeness of block along the roof line was confirmed by appropriate left atrial pacing maneuvers. All procedures were performed during deep sedo-analgesia after left atrial thrombi had been excluded by transesophageal echochardiography.

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

Results PVI of all pulmonary veins was achieved in 158 P (96%). In 7 P (4%), one pulmonary vein could not be isolated, respectively. Block along the roof line could be achieved in all cases. The mean procedure time was 229 ± 47 minutes (224 ± 48 minutes in paroxysmal AF versus 239 ± 35 minutes in persistent AF, p = n. s.). The mean fluoroscopic time was 24 ± 8 minutes (23 ± 9 minutes in paroxysmal AF versus 24 ± 8 minutes in persistent AF, p = n. s.). The mean operator's fluoroscopy exposure was 12 ± 8 minutes. As complications, two groin hematoma requiring transfusion and two pericardial tamponades requiring pericardiocentesis occurred, respectively.

After a median follow-up of 16 months (range 5–28 months), the success rate after a single procedure was 66% for P with paroxysmal AF and 51% for P with persistent AF, respectively.

Success rates increased to 79% in paroxysmal AF and 72% in persistent AF, respectively, after a second procedure (in 29% of P with paroxysmal and in 42% of P with persistent AF).

Discussion Remote navigation with the Sensei™ robotic system is effective, safe and requires limited fluoroscopy. For the first 165 P, mid-term success rates for P with paroxysmal and persistent AF were comparable to other technologies.

Evaluierung eines zirkulären Kryoablationskatheters zur Isolation von Pulmonalvenen im Schweinemodell IX – 1

M. Stöger, M. Stühlinger, K. Spuller, D. Pehböck, G. Klima, H. Rabl, C. N. Nowak, G. Fischer, F. Hintringer
Abteilung für Kardiologie, Universitätsklinik für Innere Medizin III; Universitätsklinik für Anästhesie und Intensivmedizin; Department für Anatomie, Histologie und Embryologie, Medizinische Universität Innsbruck; AFreeze GmbH Innsbruck; UMIT – Private Universität für Gesundheitswissenschaften; Medizinische Informatik und Technik, Institut für Elektrotechnik und Biomedizinische Technik, Hall in Tirol

Einleitung Die Isolation der Pulmonalvenen (PVs) ist eine etablierte Strategie der Behandlung von Vorhofflimmern (VHF) mittels Katheterablation. Rezidive durch elektrische Rekonnektion sind aber häufig. Zudem können durch alleinige Isolation der PVs nicht alle für das VHF verantwortlichen Mechanismen behandelt werden. Daher wurde

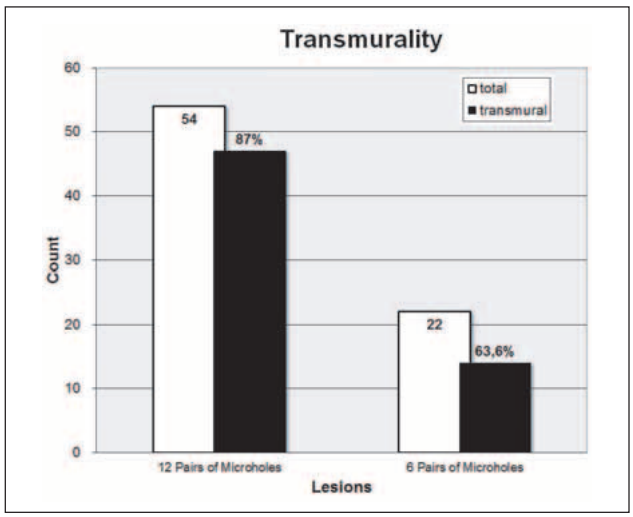


Abbildung 56: M. Stöger et al.

ein neuartiger zirkulärer Kryoablationskatheter für die Erzeugung periostialer linearer Läsionen entwickelt und im Tierversuch validiert.

Material und Methoden Der Prototyp eines zirkulären Kryoablationskatheters (CoolLoop; AFreeze GmbH, Österreich) wurde entwickelt und im Tiermodell getestet. Nach Einführung des Katheters in die Vorhöfe wurde am Antrum der PVs und am Ostium der oberen Hohlvene (SVC) von insgesamt 14 Hausschweinen (50–70 kg) eine Kryoablation durchgeführt. Nach einer Woche wurden die Tiere sakrifiziert, die Atria entnommen und die mit Azan gefärbten Läsionen hinsichtlich Größe, Tiefe und Transmuralität untersucht.

Ergebnisse Während der Analyse der insgesamt 76 Läsionen an PVs und SVC stellte sich heraus, dass die mit dem Prototyp erzeugten Läsionen kaum transmural bzw. kontinuierlich waren. Deshalb wurde unter anderem die Anzahl der Mikrolochpaare zur Emission des Kühlmittels in die Siedekammer von 6 auf 12 erhöht, was zu einer verbesserten effektiven Kühlleistung bei gleich bleibendem Kühlmittelfluss führte. Nach diesen Anpassungen konnten 7,65 ± 5,15 mm lange durchgehende Läsionen mit einer mittleren Tiefe von 1,4 ± 0,62 mm erzeugt werden. Dabei waren 87 % der Läsionen transmural.

Diskussion Nach Optimierung der Siedekammer können mit unserem neuen Kryoablationskatheter im Tierversuch lange, lineare, transmurale Läsionen erzeugt werden (**Abbildung 56**).

Implantable Loop Recorders are Useful to Eventually Indicate Antiarrhythmic Devices in Myotonic Dystrophy 1 IX – 3

C. Stöllberger, Ch. Steger, W.-B. Winkler, J. Finsterer, F. Weidinger
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Since implantable cardioverters/defibrillators and pacemakers prevent fatal outcomes of arrhythmias in myotonic dystrophy1, the proper selection is crucial. Implantable loop-recorders are developed to detect arrhythmias. Seven patients with myotonic dystrophy1, aged 34–64 years, with inconclusive findings on 24-hour-Holter recording, received implantable loop recorders. Implantable loop-recorders detected arrhythmias which resulted in implantation of pacemakers in 3 and of cardioverter/defibrillator in 1 patient. Only 1 of these patients reported symptoms suggestive of arrhythmias. In a further patient with symptoms suggestive of arrhythmia, implantable loop-recorder disclosed no rhythm disturbance. We conclude that implantable loop-recorders are useful in detecting arrhythmias in myotonic dystrophy1 patients.

Isolation of the Entire Substrate: A Novel Ablation Strategy for Treatment of Multiple Ventricular Tachycardias After Anterior Wall Myocardial Infarction IX – 5

R. Tilz, A. Rillig, Y. Yoshiga, A. Metzner, E. Wissner, K.-H. Kuck, F. Ouyang
Abteilung für Kardiologie, Asklepios Klinik St. Georg, Hamburg, Deutschland

Background Ventricular tachycardia (VT) with multiple morphologies originating in the anterior wall may occur after anterior wall myocardial infarction. At present time, there is no consensus about the best ablation strategy. We report about three patients in whom isolation oft the entire substrate was performed.

Methods Three patients (pts, 66 ± 5 years, 3 male, LVEF 29 ± 14%) with ischaemic cardiomyopathy after anterior wall myocardial infarction underwent catheter ablation for sustained VT. All pts had recurrent ICD shocks (VT storm in 2) despite amiodarone and beta-blocker therapy. Mean VT Cl was CL 440 ± 127 ms and demonstrated a right-bundle-branch morphology.

During electrophysiological study, 4 ± 2 VTs were induced. Clinical VT occurred spontaneously in 1 pt and was inducible in 2 pts. CARTO mapping of the left ventricle (LV) was performed in SR (n = 2) or during RV pacing (n = 1) and revealed a low voltage (< 1.5 mV) area with fractionated electrograms and late potentials in the antero-apical LV (mean area of 90 ± 34 cm^2). Perfect pace map of the clinical VTs was obtained in this area. The entire low voltage area was isolated with a circumferential isolation line along the low voltage area border-zone with a mean of 30 ± 9 RF applications. No RF application was applied within the area. Isolation of the areas was defined as absence of all potentials within the isolated area demonstrated by detailed point-by-point mapping. Automaticity was demonstrated in 2/3 pts.

Procedure and fluoroscopy time was 155 ± 22 min and 10.3 ± 0.7 min, respectively. At the end oft the procedure, there was no (n = 2) or one fast non-clinical VT (n = 1) inducible. No complications occurred. No clinical VT occurred during a follow-up of 5 ± 7 months.

Conclusion Isolation of the entire substrate appears to be feasible in patients with antero-apical wall myocardial infarction.

Persistierendes Vorhofflimmern: Nicht-invasive Evaluierung der mittleren linksatrialen Zykluslänge und Vergleich mit EPU-Daten XVII – 6

S. Winter, H. Pürerfellner, M. Martinek, J. Aichinger
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Einleitung Bei Patienten mit persistierendem Vorhofflimmern ist die mittlere atriale Zykluslänge des linken Herzohres (LAACL) nach den Arbeiten von Haïsaguerre und seiner Arbeitsgruppe aus Bordeaux eine wichtige Determinante für die Erfolgswahrscheinlichkeit einer Ablationsprozedur mit kurativer Intention. Eine LAACL unter 130 Millisekunden gilt dabei als Prädiktor für besonders schlechte Erfolgsraten. Diese LAACL wurde in den Originalarbeiten aus Bordeaux invasiv im Rahmen der elektrophysiologischen Prozedur im Katheterlabor bestimmt. Unsere Intention war es hingegen, auch eine nicht-invasive Möglichkeit zur Bestimmung dieses Messwertes zu finden – der Vorteil einer derartigen Methode wäre darin zu sehen, dass diese Kenngröße mit prognostischer Implikation schon in der Vorfelddiagnostik im Rahmen der Therapiestratifizierung zur Verfügung stehen würde. Dies wäre eine zusätzliche potenzielle Möglichkeit, um damit Patienten mit persistierendem Vorhofflimmern und besonders schlechten Erfolgsaussichten hinsichtlich der Ablationstherapie schon frühzeitig identifizieren zu können. Da in unserer Institution vor jeder Vorhof-Flimmer-Prozedur standardmäßig eine transösophageale Echokardiographie (TEE) durchgeführt wird, bot sich dieses bildgebende Verfahren an, um damit nicht-invasive Daten über die linksatriale Zykluslänge zu gewinnen und diese mit den intraprozeduralen und somit invasiv gewonnenen intrakardialen EKG-Daten zu vergleichen.

Material und Methode Untersucht wurden 11 Patienten mit persistierendem Vorhofflimmern bzw. 3 Pt. mit atypischem Vorhof-

flattern und geplanter linksatrialer Ablationsprozedur. Mittels transösophagealer Echokardiographie wurde das linke Herzohr dargestellt und das Sample-Volume des gepulsten Dopplers im Bereich des Herzohr-Ostiums positioniert. Aufgezeichnet wurde der zeitliche Verlauf der Blutflussgeschwindigkeit des Herzohres mit einem zeitlichen Maßstab von zumindest 100 mm/sec: 10 konsekutive „mechanische" atriale Zykluslängen des linken Herzohres wurden vermessen und als Mittelwert dokumentiert. Die elektrischen Daten hingegen wurden invasiv im Rahmen der Ablationsprozedur gewonnen. Ein zirkulärer Multipolar-Katheter („Lasso") wurde in das Herzohr positioniert und ein intrakardiales EKG mit 100 mm/sec aufgezeichnet. Auch in diesem Falle wurden 10 konsekutive „elektrische" atriale Zykluslängen vermessen und als Mittelwert dokumentiert. Die Messwerte beider Methoden wurden gegenübergestellt und die Korrelation bzw. die Signifikanz berechnet.

Ergebnisse Die Pearson-Korrelation zwischen den mittels TEE gemessenen linksatrialen Zykluslängen und den entsprechenden intraprozedural gewonnenen elektrischen Daten beträgt 0,837 auf einem Signifikanzniveau von $p < 0,01$. Die entsprechende lineare Regressionsgleichung lautet: Zykluslänge_EPU = (Zykluslänge_TEE × 0,845) + 27,6 [ms].

Diskussion Unsere vorläufigen Daten zeigen, dass bei persistierenden Flimmerarrhythmien das TEE potenziell eine Methode ist, mit der die LAACL nicht-invasiv gemessen werden kann. Die Anzahl der gemittelten atrialen Zyklen muss bei Einsatz von Echokardiographie aus Praktikabilitätsgründen auf etwa 10 limitiert werden. Potenzielle Fehlerquellen der Echomessungen sind Dropouts der Dopplerkurve bei niedrigen Flussgeschwindigkeiten bzw. suboptimale Schallbedingungen bei der Einstellung des linken Herzohres.

Safety of RFID Gates at Ski Resorts for Patients with Implanted Cardioverter-Defibrillators XVII – 3

T. Wolber, I. Fauchere, A. Moini, L. Haegeli, F. Duru
Universitätsspital Zürich, Schweiz

Background Recently published in vitro tests with radiofrequency identification readers (RFID) revealed clinically significant electromagnetic interference with implantable pacemakers and implantable cardioverter-defibrillators (ICDs). Incidents in patients with pacemakers and ICDs have not been reported yet. The aim of this clinical study was to evaluate the risk of electromagnetic interference (EMI) during use of RFID-based access control systems used in ski resorts in patients with ICDs and cardiac resynchronization therapy-defibrillators CRT-Ds).

Methods 34 patients implanted with an ICD or CRT-D were included in the study. Tests were performed using two commercially available RFID access control systems (gates) used at ski resorts operating on different frequencies of 125 kHz and 13 mHz. After initial device interrogation, patients were standing upright within each gate for a minimum of 30 seconds both at a random position as well as with the ICD positioned at the closest possible distance from the RF source, simulating a worst case scenario. Electrocardiographic and telemetric real-time monitoring of devices and patients' heart rhythm was performed throughout the study.

Results ECG monitoring by body surface ECG demonstrated RF artifacts in all patients. However, real-time telemetry of intracardiac electrograms did not show artifacts or evidence of EMI causing inappropriate pacing, changes in pacing rate, or delivery of antitachycardia pacing. Interrogation of devices after the test revealed no inappropriate tachycardia detection, programming changes, oversensing or ICD malfunction during all tests in all patients.

Conclusion Although in vitro test demonstrated the ability of RFID systems to interfere with the function of ICDs, this clinical study showed no evidence of EMI during use of RFID-based access-control systems used in ski resorts simulating a real-world setting. Therefore, the use of these access-control systems seems to be safe for patients implanted with an ICD or CRT-D. However, patients should be advised to avoid prolonged standing in close proximity to RFID antennas.

Risikofaktoren – Stoffwechsel – Lipide/ Risk Factors – Metabolism – Lipids

Myokardinfarkt als Auswirkung der angeborenen Stoffwechselstörung Kearns-Sayre-Syndrom XVIII – 2

S. Gasser, B. Gissing, H. Mächler, H. Brussee
Abteilung für Kardiologie; Abteilung für Experimentelle Kardiologie, LKH Graz; MEDUK Kardiologie, Graz

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: 43-jähriger Patient in stark reduziertem Allgemeinzustand, wach, orientiert. Größe: 182 cm, Gewicht: 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 V3, 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 von einander 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 46-jährigen Patienten eine noch nicht beschriebene Facette des Kearns-Sayre-Syndroms sein könnte.

Welche Bedeutung besitzen Von-Willebrand-Faktor, Faktor VIII, PAI-1 und t-PA als Prädiktoren der kardiovaskulären Mortalität? Ergebnisse der Ludwigshafen Risk and Cardiovascular Health Study XVIII – 4

M. E. Kleber, R. Siekmeier, T. B. Grammer, B. R. Winkelmann, B. O. Boehm, W. März
Abteilung Medizinprodukte, Bundesinstitut für Arzneimittel und Medizinprodukte, Bonn; Institute of Public Health, Social and Preventive Medicine, Medical Faculty of Mannheim, Universität Heidelberg; Cardiology Group, Frankfurt-Sachsenhausen, Frankfurt/Main; Division of Endocrinology, Department of Medicine, University Hospital, Ulm, Deutschland

Fragestellung In den Industrieländern stellen kardiovaskuläre Erkrankungen eine wesentliche Ursache der Morbidität und Mortalität dar. Neben den Plasmalipiden sind auch Faktoren der Blutgerinnung als Risikofaktoren dieser Erkrankung von Bedeutung. In der vorliegenden Studie wurde die Rolle von Von-Willebrand-Faktor (vWF-AG), Faktor VIII, PAI-1-Antigen (AG) und t-PA-Antigen (AG) als Prädiktoren der Gesamtmortalität und der kardiovaskulären Mortalität bei zur Koronarangiographie vorgestellten Patienten der Ludwigshafen Risk and Cardiovascular Health Study (LURIC) untersucht.

Methoden Bei insgesamt 3286 Patienten mit Indikation zur Koronarangiographie, die in der Ludwigshafen Risk and Cardiovascular Health Study eingeschlossen waren, erfolgte eine Bestimmung der Plasmakonzentrationen bzw. -aktivitäten von Von-Willebrand-Faktor (vWF-AG), Faktor VIII, PAI-1-Antigen und t-PA-Antigen. Während des medianen Beobachtungszeitraums von 10 Jahren verstarben 982 Patienten.

Ergebnisse Die Analysen erfolgten nach Aufteilung in Quartile (vWF-AG: Q1: ≤ 120 U/dl, Q2: 121–158 U/dl, Q3: 159–202 U/dl und Q4: > 203 U/dl; Faktor VIII: Q1: ≤ 128 U/dl, Q2: 129–168 U/dl, Q3: 169–215 U/dl und Q4: > 216 U/dl; PAI–1: Q1: ≤ 15,8 µg/l, Q2: 15,81–24,7 µg/l, Q3: 24,71–36,9 µg/l und Q4: > 36,91 µg/l; t-PA: Q1: ≤ 9,4 µg/l, Q2: 9,41–11,9 µg/l, Q3: 11,91–15,4 µg/l und Q4: >15,41 µg/l). Es fand sich ein Anstieg der Gesamtmortalität mit zunehmender Konzentration bzw. Aktivität von vWF-AG, Faktor VIII und t-PA (jeweils p for Trend: p ≤ 0,001) sowie PAI-1 (p for Trend: p = 0,005) **(Tabelle 16)**. Vergleichbare Werte von HR und 95 %-CI fanden sich auch für die kardiovaskuläre Mortalität vor Adjustierung auf Alter und Geschlecht. Eine zusätzliche Adjustierung auf die Parameter Alter und Geschlecht führte zu keiner relevanten Änderung der erhaltenen Ergebnisse.

Schlussfolgerungen Die gewonnenen Daten zeigen, dass vor allem die Parameter vWF-AG, Faktor VIII und t-PA-Antigen bei Patienten mit koronararterieller Erkrankung als Prädiktoren zur Abschätzung des individuellen Risikos für Gesamtmortalität und kardiovaskuläre Mortalität geeignet sind. Demgegenüber weist PAI-1 im Vergleich zu diesen Parametern eine etwas geringere Bedeutung auf. Eine Bestimmung der genannten Parameter sollte daher ergänzend zur Bestimmung der Plasmalipide (einschließlich Lp[a]) und weiterer Prädiktoren (z. B. Homocystein) sowie persönlicher Faktoren (Rauchen, Lebensstil) erfolgen, um eine möglichst genaue Abschätzung des individuellen Risikos zu erhalten.

Tabelle 16: M. E. Kleber et al.

	Gesamtmortalität	Kardiovaskuläre Mortalität	
	HR (95 %-CI) Q4 vs. Q1	unadjustiert HR (95 %-CI) Q4 vs. Q1	adjustiert HR (95 %-CI) Q4 vs. Q1
vWF-AG	3,20 (2,65–3,86)	3,36 (2,64–4,29)	2,19 (1,71–2,81)
Faktor VIII	2,68 (2,22–3.13)	2,89 (2,29–3,65)	2,08 (1,64–2,65)
PAI-1-AG	1,36 (1,14–1,63)	1,45 (1,15–1,83)	1,57 (1,24–1,98)
t-PA-AG	2,38 (1,98–2,87)	2,21 (1,76–2,79)	1,64 (1,30–2,07)

Die Pulswellenanalyse im Rahmen der ambulanten Blutdruckmessung korreliert mit der linksventrikulären Muskelmasse XVIII – 5

C. Kos, K. Ablasser, T. Weber, A. Schmidt, B. Pieske, R. Zweiker
Abteilung für Kardiologie, Landeskrankenhaus, Medizinische Universität Graz; Paracelsus Medizinische Privatuniversität Salzburg

Hintergrund In der Diagnostik und Therapie der arteriellen Hypertonie nimmt die ambulante 24-Stunden-Blutdruckmessung die zentrale Stellung ein. Die Gefäßsteifigkeit, die durch die Pulswellenanalyse bestimmt werden kann, ist ein unabhängiger Risikofaktor für das Auftreten von kardiovaskulären Ereignissen. Die neuesten Generationen der ambulanten Blutdruckmonitorgeräte ermöglichen neben den oszillographischen Blutdruckmessungen auch die Pulswellengeschwindigkeitsanalysen mit Bestimmung der arteriellen Gefäßsteifigkeit. Für die Abschätzung des gesamten kardiovaskulären Risikos ist zusätzlich die Bestimmung der linksventrikulären Hypertrophie erforderlich, da die linksventrikuläre Muskelmasse (LVMM) ein wichtiger Prädiktor für kardiovaskuläre Ereignisse bei Hypertonikern ist.

Hypothese Die linksventrikuläre Muskelmasse (LVMM) korreliert mit der ambulanten Pulswellengeschwindigkeitsanalyse aus der 24-Stunden-Blutdruckmessung.

Methodik Bei 32 Probanden ohne antihypertensive Therapie wurde echokardiographisch die linksventrikuläre Muskelmasse aus dem M-Mode nach der Penn-Cube-Methode (LVMM) bestimmt, sowie eine ambulante 24-Stunden-Blutdruckmessung mit Bestimmung des Mittelwertes des systolischen und diastolischen Blutdrucks, des zentralen aortalen Blutdrucks, der Pulswellengeschwindigkeit, des Augmentationsindex, des peripheren Widerstandes, des Reflexionsindex und des Pulsdrucks durchgeführt. Statistisch wurde eine multiple Regressionsanalyse durchgeführt, wobei ein p < 0,05 als signifikant angesehen wurde.

Ergebnisse Sowohl die Pulswellengeschwindigkeit (p = 0,024) als auch der Augmentationsindex (p = 0,049) korrelieren unabhängig vom gemessenen Blutdruck hochsignifikant mit der LVMM. Für den mittleren systolischen und diastolischen Blutdruck konnte in dieser Studie keine Signifikanz erreicht werden.

Beurteilung Die Pulswellengeschwindigkeit und der Augmentationsindex aus der ambulanten 24-Stunden-Blutdruckmessung korrelieren hochsignifikant mit der LVMM bei Patienten ohne antihypertensive Therapie. Daher bietet die ambulante Pulswellengeschwindigkeitsanalyse zusätzliche Information zur 24-Stunden-Blutdruckmessung für die Diagnostik und Therapie der arteriellen Hypertonie.

Oxygen Administration Improves Peripheral Endothelial Function in Young Healthy Adults XVIII – 6

L. Leitner, J. Doerler, C. Trost, M. Wanitschek, H. F. Alber, Ch. Kaehler, O. Pachinger, M. Frick, A. Suessenbacher
Universitätsklinik für Innere Medizin III/Kardiologie, Medizinische Universität Innsbruck

Background Long term oxygen treatment decreases cardiovascular risk in patients with severe chronic obstructive pulmonary disease (COPD). Peripheral endothelial dysfunction is associated with COPD. In patients with atherosclerotic disease an improvement in peripheral endothelial function was related to a decrease in cardiovascular risk. Whether oxygen administration reduces cardiovascular risk by an improvement in peripheral endothelial function is unknown. The aim of the present project was to test the short-term effect of oxygen inhalation in young healthy adults as a feasibility and pilot study before investigating this issue in patients with COPD.

Methods In 32 young healthy adults (14 women, mean age 27.5 ± 5.1 years) peripheral endothelial function was measured using the EndoPAT™ device: a plethysmographic record of the finger arterial pulse wave amplitude (PWA) was captured for 5 minutes at rest, followed by 5 minutes occlusion of the right upper arm using a sphygmomanometer cuff inflated to suprasystolic levels. After de-

flation reactive hyperaemia was measured for 5 minutes. Endothelial function was calculated using the reactive hyperaemia peripheral arterial tonometry (RH-PAT) index as the ratio between the magnitude of the average post occlusive PWA and an average of 5 minutes of the preocclusion PWA. RH-PAT index was assessed at baseline and after 30 minutes of 4 liters/minute oxygen administration via a non-rebreather oxygen mask. Arterial partial pressure of oxygen (PaO_2) was obtained by arterialized earlobe capillary sampling before and after oxygen administration.

Results Cardiovascular risk factors: smoking (n = 10), positive family history for premature cardiovascular disease (n = 4), hypercholesterolemia (n = 3), arterial hypertension (n = 3). Oxygen administration increased the mean PaO_2 from 90 ± 15 to 158 ± 25 mmHg ($p < 0.001$). After oxygen administration the mean RH-PAT index increased from 2.21 ± 0.54 to 2.54 ± 0.52 ($p < 0.001$). A bivariate correlation was found between the absolute increase of RH-PAT index and the absolute PaO_2 increase ($r = 0.537$; $p = 0.026$). Additionally, a correlation was found between HDL cholesterol and the absolute increase of RH-PAT index ($r = 0.663$; $p = 0.01$).

Conclusion Endothelial function measurement during oxygen inhalation is feasible. Short term oxygen administration improves peripheral endothelial function in young healthy individuals. Whether the reduction of cardiovascular risk by oxygen treatment, in patients with COPD can be explained by an improvement in peripheral endothelial function, will be investigated in further studies.

Regulation L-Arginine-Glycine Amidotransferase in Normoxia and Hypoxia XVIII – 7

S. Pätzold, E. Holzwart, D. von Lewinski, H. Mächler
Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin, Medizinische Universität Graz

Many genes and pathways have been screened in myocardial tissue of patients with congestive heart failure (CHF) and ischemia in order to provide insight into mechanisms of recovery brought about pharmacologically. In a recent paper, Cullen and co-workers (Circulation 2006) have shown that myocardial arginine-glycine amidotransferase (AGAT) gene expression showed a significant decrease during improvement of heart failure under beta-blockade. This was an unexpected finding, as AGAT is the rate-limiting enzyme that catalyzes formation of guanidinoacetate (GAA), the immediate precursor of creatine. It has been suggested that the return of AGAT expression from its elevated level to normal levels in remodelling may be a consequence of beta-blocker therapy that the patients in this study have undergone. The authors could verify that there is indeed creatine synthesis in myocardial tissue, whereas until then it has been thought that creatine be mainly produced only in liver and kidney. Its myocardial expression seems to be increased in CHF and ischemia as an attempt to preserve contractile integrity, as a result of the number of functional myocytes being decreased in CHF or ischemia.

We found that, without the influence of beta-blockers, there is no significant regulation of AGATM-expression during myocardial ischemia. There is, however a significant difference between the expression of AGATM during myocardial ischemia in the presence of atenolol (1546 ± 0.05) and nebivolol (1.10 ± 0.04; +SEM; $p < 0.05$).

Table 17: S. Pätzold et al. AGAT is more than 3 times down-regulated in nebivolol under hypoxia as well as under normoxia, with atenolol less than 2 times

	N_2-Hypoxia	
	Nebivolol : Control	**Atenolol : Control**
AGAT	0,33	0,65
	O_2-Normoxia	
	Nebivolol : Control	**Atenolol : Control**
AGAT	0,30	0,91

In the microarray preliminary **(Table 17)** analyses, we found that the gene expression of AGATM is down-regulated by both nebivolol and atenolol. This regulation seemingly constitutes a class effect of beta-blockers.

Using real-time PCR, we could confirm the above data. While there is just a trend of down-regulation under atenolol in ischemia, there is a strong, statistically significant down-regulation of AGATM gene expression in the nebivolol group during experimental ischemia.

In fact, the excessive adrenergic drive both in untreated heart failure and likewise in ischemic heart failure as well as the increase in cellular Ca levels and creatine production ultimately lead the heart into a vicious circle resulting in progressive heart failure. Research of the last two decades tells us that beta-blockers not only are excellent antihypertensive drugs but also successfully counteract this deleterious spiral in CHF and ischemia. As to myocardial ischemia, O_2-consumption correlates with the amount of cytoplasmic creatine available. The synthesis of high energy phosphate and thus oxygen consumption will be decreased in myocardial tissue prone to a lesser creatine synthesis. Thus, down-regulation of myocardial AGATM by beta-blockers will certainly be beneficial in myocardial protection of hypertensive patients at risk for ischemic heart disease an CHF.

Coronary Artery Disease as a Risk for Developing Type-2 Diabetes Mellitus X – 3

Ch. H. Saely, A. Vonbank, P. Rein, St. Beer, H. Drexel
Abteilung für Innere Medizin, Landeskrankenhaus, Feldkirch

Background Diabetes mellitus is a major risk factor for coronary artery disease (CAD); whether conversely CAD confers an increased risk for diabetes has not been studied so far.

Methods We prospectively recorded incident diabetes over 7.5 years in 506 consecutive non-diabetic Caucasian patients undergoing coronary angiography for the evaluation of stable CAD, covering 3795 patient years.

Results During follow-up, diabetes was newly diagnosed in 107 patients, i. e. in 21.1% of the study population or in 2.8% per year. Patients with significant CAD (n = 293) when compared to subjects who did not have significant CAD at the baseline angiography were at a 33% ($p = 0.027$) increased diabetes risk. However, the relationship between CAD and incident diabetes was attenuated and no longer statistically significant after adjustment for potential confounders including metabolic syndrome (MetS) status. The MetS as diagnosed according to the current consensus definition in turn was strongly predictive of diabetes, in particular when the more selective NCEP-ATP-III waist cut-off values were applied for its diagnosis (OR = 2.91 [1.83–4.64]; $p < 0.001$).

Conclusion We conclude that albeit apparently not causally related to diabetes incidence, the presence of CAD indicates a strongly increased risk for incident diabetes. Repeated diabetes screening of coronary patients and targeted programs to prevent diabetes in these high-risk patients are warranted.

Serum Omentin is Neither Associated with the Metabolic Syndrome Nor with Angiographically Determined Coronary Artery Disease X – 4

Ch. H. Saely, A. Muendlein, A. Vonbank, K. Geiger, P. Rein, H. Drexel
VIVIT-Institute, Landeskrankenhaus, Feldkirch

Background Some recent small studies have described associations of the new adipocytokine omentin with the metabolic syndrome (MetS) and with cardiovascular disease. However, data still are very scarce.

Methods We therefore measured serum omentin in 395 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; the MetS was defined according to NCEP-ATPIII criteria; significant CAD was diagnosed when coronary stenoses ≥ 50% were present.

Results Omentin was positively correlated with age ($r = 0.170$; $p < 0.001$) but did not show significant correlations with waist cir-

cumference, fasting glucose, HDL cholesterol, triglycerides, systolic blood pressure, or diastolic blood pressure; it was similar in MetS patients (n = 118) as in subjects without the MetS (15 ± 21 vs 14 ± 15 ng/ml; p = 0.460). Omentin also did not differ significantly between patients with significant CAD (n = 190) and those without significant CAD (14 ± 19 vs 15 ± 15 ng/ml; p = 0.233). When both, MetS and CAD status were considered, chemerin similar in MetS patients as in subjects without the MetS both among those who had significant CAD (15 ± 13 vs 15 ± 13 ng/ml; p = 0.482) and among those who did not have significant CAD (16 ± 30 vs 14 ± 15 ng/ml; p = 0.876); it further did not differ significantly between patients with significant CAD and subjects without significant CAD among MetS patients (p = 0.321) nor among subjects without MetS (p = 0.452).

Conclusion We conclude that omentin is neither associated with the MetS nor with angiographically determined CAD. Omentin therefore does not appear to be a useful marker of cardiometabolic disease.

Influence of Age and Smoking on Venous Endostatin Levels: Gender Aspects X – 6

M. Sponder, St. Kampf, M. Priglinger, Ch. Reuter, A.-M. Braas, J. Voitl, M. Mittlböck, R. Marculescu, M. Fritzer-Szekeres, A. Zimmermann, J. Strametz-Juranek
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna, Austria; Medical University Heidelberg, Germany

Background Endostatin inhibits proliferation and migration of endothelial cells and therefore is an important angiostatic factor. Additionally, it stimulates endothelial nitric oxide synthase (e-NOS). Smoking impairs e-NOS, induces endothelial dysfunction, inflammation and subsequent atherosclerosis. Aging is associated with impaired endothelium-derived NO release and alterates angiogenesis by structural and hormonal reasons. Therefore, the aim of the study was to investigate the impact of gender, age and smoking on venous endostatin levels.

Material and Methods Venous endostatin levels were measured (ng/ml) at rest in 165 healthy individuals without concomitant medication divided into 4 groups: 43 elderly smoker (es; mean age: 51.81 ± 6.61 yrs), 45 elderly non-smoker (ens; mean age: 54.02 ± 7.04 yrs), 38 young smoker (ys; mean age: 24.82 ± 3.79 yrs) and 39 young-non-smoker (yns; mean age: 23.10 ± 3.88 yrs).

Results The yns-group showed the lowest endostatin levels (91.28 ± 15.11) followed by the ens-group (114.21 ± 20.68) with no gender-specific difference in non of these both groups. Female ys (94.30 ± 19.23) showed similar amounts of endostatin as yns but male ys (157.25 ± 33.04) had significantly higher levels than all other groups. In contrary, in the es-group female es (136.31 ± 34.44) had significantly higher levels (p = 0.001) than male es (103.32 ± 16.45).

Conclusion

1. In non-smoking individuals aging is associated with a significant increase in resting venous endostatin (p < 0.001).

2. Moreover, smoking increases significantly the endostatin release in female (but not in male) elderly smoker (p = 0.001) and vice versa in young smoker (p = 0.001).

3. Future studies are warranted to investigate the influence of sex-steroid on endostatin release.

Influence of Gliptins on Endostatin and Intima Media Thickness in 35 NIDDM Patients X – 7

M. Sponder, D. Dangl, A. Sabri, L. Kosi, A. Kautzky-Willer, St. Kampf, A. Hammer, M. Fritzer-Szekeres, B. Litschauer, J. Strametz-Juranek
Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

Background Gliptins are complete inhibitors of dipeptidyl-peptidase-4 (DPP4) and therefore increase the blood levels and bioavailability of glucagon-like peptide 1 (GLP-1). Consequently, the insulin production and release rises, glucagon release decreases and blood glucose level recede. Endostatin, a potent angiostatic factor, inhibits endothelial cell proliferation and migration and stimulates endothelial nitric oxide synthase (e-NOS).

Table 18: M. Sponder et al.

	preTH	postTH	p-value
BMI	30.74 ± 5.00	30.37 ± 5.02	0.175
Performance	65.03 ± 14.67	67.62 ± 12.98	0.644
Endostatin	126.15 ± 35.43	145.71 ± 54.67	0.044
Glucose	140.00 ± 18.78	113.47 ± 25.26	< 0.001
HbA_{1c}	7.70 ± 1.06	6.53 ± 0.73	< 0.001
IMT left	0.069 ± 0.01	0.068 ± 0.01	0.115
IMT right	0.070 ± 0.01	0.070 ± 0.001	0.914

Material and Methods The study population consisted of 35 NIDDM-patients (15 female, mean age: 60.13 ± 10.80; 20 male, mean age: 58.10 ± 7.32) who could not reach a HbA_{1c} < 7% by a metformin monotherapy. The patients obtained 50 mg Vildagliptin + 1000 mg Metforminhydrochlorid 2x/d (1-0-1) in tablet-form for 6 months. BMI (kg/m^2), blood glucose (mg/dl), HbA_{1c} (%), endostatin (ng/ml), intima media thickness (IMT; cm) and physical performance (by ergometry; %) were measured before and after treatment for 6 months.

Results Gliptin treatment was associated with significant decrease in glucose (p < 0.01) and HbA_{1c} (p < 0.01). HbA_{1c} decreased from 7.70 ± 1.06 to 6.53 ± 0.73% resp. glucose from 140.00 ± 18.78 to 113.47 ± 25.26 mg/dl. Endostatin levels increased significantly from 126.15 ± 35.43 to 145.71 ± 54.67 ng/ml (p < 0.04).

Conclusion A 6-month gliptin treatment is associated with a significant increase in venous endostatin levels in patients suffering from NIDDM. If this gliptin-mediated endostatin up-regulation can be interpreted as an additional vasoprotective property it should be elucidated more closely **(Table 18)**.

Influence of High-Dose Highly Efficient Statins (Atorvastatin and Rosuvastatin) on Long-Term Clinical Outcome in Patients Undergoing Percutaneous Coronary Interventions plus Coronary Stenting XVIII – 1

I. Tentzeris, M. Rohla, R. Jarai, S. Farhan, M. Freynhofer, E. Samaha, E. Wessely, A. Geppert, M. Nürnberg, G. Unger, J. Wojta, K. Huber
3rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital Vienna; Division of Cardiology, Department of Internal Medicine II, Medical University Vienna

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

Methods In a retrospective analysis medical therapy, cardiovascular risk factors, co-morbidities and coronary morphology were evaluated in 2,405 prospectively registered patients undergoing PCI and coronary stenting at our institution between January 2003 and March 2009. Basal circulating lipid variables (total cholesterol (T-C); LDL-cholesterol (LDL-C); were measured. Moreover, all-cause mortality after a mean follow-up period of 52.27 ± 22.82 months was evaluated. Results were compared between patients receiving high-dose, highly effective statins, normal-dose statins and in patients without lipid-lowering therapy.

Results From 2,405 unadjusted patients undergoing PCI plus coronary stenting, 858 (35.7%) received high-dose atorvastatin or rosuvastatin, 1,240 (51.6%) received other (normal) statin therapy and 307 (12.8%) patients were not on statins at discharge. Their

mean plasma levels of lipid variables were for T-C: High-dose statin:193 ± 60 mg/dl; low-dose statin: 172 ± 42 mg/dl; p-value for high-dose versus low-dose = 0.056; no statin: 191 ± 43 mg/dl; p-value for high-dose versus no statin = 0.4. The mean plasma levels of lipid variables were for LDL-C: High-dose statin: 118 ± 55 mg/dl; low-dose statin: 96 ± 34; p-value for high-dose versus low-dose = 0.005; no statin 114 ± 37 mg/dl; p-value for high-dose versus no statin = 0.2.

Clinical characteristics in terms of current smoking ($p < 0.001$) diabetes ($p = 0.028$), hypertension ($p = 0.026$), cerebrovascular disease ($p = 0.002$), peripheral vascular disease ($p < 0.001$), previous PCI ($p < 0.001$), previous MCI ($p < 0.001$), previous CABG ($p < 0.001$) and atrial fibrillation ($p < 0.001$) were significantly different between the study groups.

Eighty-one (9.4%) patients under high-dose statin therapy, 164 (13.2%) patients on low-dose statins (p-value for high-dose versus low-dose = 0.06), and 71 (23.1%) patients without statins at discharge died during the follow-up (p-value for high-dose versus no statin < 0.001).

After adjustment with propensity score no significant reduction in mortality could be seen: HR for high-dose versus low-dose 0.94, 95%-CI: 0.66–1.34; $p = 0.73$, HR for high-dose versus no statin 0.72, 95%-CI: 0.44–1.16, $p = 0.2$.

Conclusion In this small single-center series of 2,405 "real world" patients undergoing PCI and coronary stenting no significant reduction in long-term all-cause mortality was seen in patients under high dose, highly-efficient statins compared to patients receiving normal-dose statins or no lipid lowering therapy at all. Accordingly, risk factors and co-morbidities and not the dose and selection of statins at discharge influenced mortality. A potential influence of the duration of high-dose statin therapy on these results cannot be excluded.

Plasma Renin and Cardiovascular Mortality in Patients with Type 2 Diabetes: A 10-Year Cohort Study XVIII – 3

A. Tomaschitz, K. Kienreich, St. Pilz, E. Ritz, T. Grammer, B. Pieske, B. O. Boehm, W. März
Klinische Abteilung für Kardiologie; Klinische Abteilung für Endokrinologie und Stoffwechsel, Medizinische Universität Graz; Abteilung für Nephrology, Universität Heidelberg; Mannheim Institute of Public Health, Ruperto Carola University Heidelberg; Medical Faculty Mannheim; Division of Endocrinology, Diabetes and Metabolism, Graduate School of Molecular Diabetology and Endocrinology, Ulm University; Synlab Centre of Laboratory Diagnostics, Heidelberg, Germany

Introduction Diabetes mellitus is a major risk factor for cardiovascular disease (CVD) mortality worldwide and is strongly linked to the activation of renin-angiotensin systems. Insight into the corresponding impact of circulating renin on cardiovascular-related mortality in patients with diabetes is however lacking. This study sought to evaluate the association between plasma renin concentration (PRC) and CVD mortality in patients with type-2 diabetes after long-term follow-up of almost 10 years.

Material and Methods We studied participants with type-2 diabetes of the Ludwigshafen RIsk and Cardiovascular health (LURIC) study (29.6% females).

Results PRC (median: 12.6 [6.0–27.0] pg/mL) was measured in 1319 patients (mean age: 64.0 ± 9.8 years) referred to coronary angiography. After a median follow-up of 9.9 years, 372 participants (28.1%) with PRC measurement at baseline had died due to fatal cardiovascular events. Multivariable adjusted Cox analysis revealed that compared to subjects in the lowest PRC quartile, those in the highest quartile were at increased risk of cardiovascular mortality (Hazard ratio: 1.71, 95%-CI: 1.19–2.46; $p = 0.004$). Analyses of specific causes of cardiovascular death showed that for each SD increase in log-PRC there was a 47% ($p < 0.001$) increase in risk of death due to heart failure. The relationship between PRC and cardiovascular mortality remained stable after adjustment for established cardiovascular risk factors, ongoing antihypertensive, antidiabetic medication and angiotensin II levels.

Discussion High PRC is a strong and independent predictor of fatal cardiovascular events and death due to heart failure in a stable population of patients with diabetes. Our results indicate that PRC represents a promising cardiovascular risk marker in a broad range of high CVD risk patients with type 2 diabetes.

The Metabolic Syndrome Significantly Affects the Association Between Resting Heart Rate and All Cause as Well as Cardiovascular Mortality X – 5

A. Vonbank, F. Schmid, P. Rein, Ch. H. Saely, H. Drexel
VIVIT-Institute, Landeskrankenhaus, Feldkirch

Background Epidemiological studies suggest that the resting heart rate (RHR) is an independent predictor of cardiovascular and all cause mortality. However, the power of the RHR to predict cardiovascular events in patients with the metabolic syndrome (MetS) is not known.

Methods We prospectively investigated the relationship between RHR and cardiovascular events in 756 consecutive patients undergoing coronary angiography for the evaluation of coronary artery disease (CAD) over a follow-up period of 7.1 ± 0.1 years. The MetS was defined according to NCEP-ATPIII criteria.

Results In the total study population, both all cause and cardiovascular mortality were increased with an increasing RHR (standardized adjusted HRs 1.03 [1.01–1.04]; $p = 0.001$ and 1.15 [1.03–1.47]; $p = 0.001$, respectively). From our patients, 357 (47.2%) had the MetS and 399 did not have the MetS. Among patients without the MetS, a higher baseline RHR indicated a significantly higher risk of total mortality (HR = 1.14 [111–1.16], $p = 0.001$) and cardiovascular mortality (HR = 1.13 [1.12–1.16], $p = 0.001$) after multivariate adjustment. However, the RHR did not significantly affect total mortality ($p = 0.120$) or cardiovascular mortality ($p = 0.244$) in patients with the MetS. Interaction terms RHRxMetS were significant for both total and cardiovascular mortality ($p = 0.027$ and $p = 0.037$, respectively), indicating that the respective risks conferred by a high RHR were significantly higher in patients without the MetS than in patients with MetS.

Conclusion We conclude that among angiographically characterized coronary patients, the metabolic syndrome status significantly affects the association of the RHR with total and cardiovascular mortality: RHR is a strong predictor of both total and cardiovascular mortality among subjects without the MetS, but not among MetS patients.

Adipose Tissue Pro-Inflammatory Gene Expression is Associated with Cardiovascular Disease X – 1

T. Weiss, I. Seljeflot, H. Arnesen
3rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna, Austria; Oslo University Hospital, Ulleval, Oslo, Norway

Background Obese patients are at high risk of developing cardiovascular disease. Several studies suggest obesity as an independent risk factor. Adipose tissue is now accepted as an endocrine organ that produces and secretes a variety of cytokines, hormones and other metabolic players involved in the pathogenesis of atherosclerosis. Among this versatile group of mediators and effectors of inflammation and atherothrombosis, we have studied the expression of matrix metalloproteinase-9 (MMP-9), tissue inhibitor of metalloproteinase-1 (TIMP-1), plasminogen activator inhibitor-1 (PAI-1), interleukin-18 (IL-18) and interleukin-6 (IL-6). All these markers have in their circulatory form been associated with cardiovascular disease. However, there is not much data available on their expression in adipose tissue in human subjects with and without cardiovascular disease.

Material and Methods We successfully isolated RNA from subcutaneous fat biopsies of 61 patients with or without cardiovascular disease. We then measured the RNA expression of MMP-9, TIMP-1, PAI-1, IL-18 and IL-6 with Real-Time PCR, using relative quantification.

Results Albeit not statistically significant, all inflammatory mediators – except IL-18 – were higher expressed in patients with car-

diovascular disease (n = 16) compared to those without (n = 45). Pooling the gene expression data, trying to capture the overall inflammatory activity in adipose tissue in a score system, we observed a highly significant association with CVD.

Conclusions Trying to capture the overall inflammatory activity, in addition to the mass of adipose tissue, could provide useful hints towards a pathogenetic link between obesity and presence of cardiovascular disease.

Components of the Interleukin-6 Transsignalling System are Associated with the Metabolic Syndrome, Endothelial Dysfunction and Arterial Stiffness X – 2

T. Weiss, H. Arnesen, I. Seljeflot
3rd Med. Department of Internal Medicine, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna, Austria; Oslo University Hospital, Ulleval, Oslo, Norway

Introduction The metabolic syndrome (MetS) is an increasing epidemiologic challenge and cardiovascular risk factor. Interleukin-6 (IL-6) is a cytokine that exerts its biological function via a complex orchestration of soluble and membrane bound receptors. We have investigated associations between IL-6 and its soluble receptors, soluble IL-6 receptor (sIL-6r) and soluble glycoprotein 130 (sGP130) and the metabolic syndrome. Furthermore, we have investigated possible associations with endothelial dysfunction and arterial stiffness.

Methods A total of 563 subjects were included in this study. Adult treatment panel III criteria of the national cholesterol education program were used for the definition of MetS. We used commercially available ELISA to analyze circulating levels of the markers. Pulse wave propagation time (PWP) was determined to assess arterial stiffness.

Results The criteria for having MetS were filled by 221 subjects. sGP130, sIL-6r and IL-6 levels were elevated in subjects with MetS ($p < 0.05$ for all markers), and are associated with increasing components of MetS. Particularly hypertriglyceridaemia, hypertension and fasting plasma glucose (FPG) seem to carry this association. sGP130 ($p < 0.01$), IL-6 ($p < 0.05$) and partially sIL-6r ($p < 0.05$) correlated with markers of endothelial function (E-selectin, I-CAM-1, V-CAM-1) and inversely with PWP after adjustment for relevant covariates.

Discussion sGP130, sIL-6r and IL-6 were significantly elevated in subjects with MetS. In addition, sGP130, IL-6 and partially sIL-6r were associated with markers of endothelial function and arterial stiffness. This finding sheds new light on the role of these inflammatory cytokines in subjects with MetS and the development and progression of clinically silent atherosclerosis.

Vitien/Cardiac Defects

Implementation of TAVI Procedures as a Team Approach. The Innsbruck Experience of Using a New Generation Mobile c-Arm in the Cardiac OR XIX – 4

N. Bonaros, S. Müller, G. Feuchtner, N. Fischler, A. Heinz, F. Plank, T. Schachner, G. Friedrich, M. Grimm, L. Müller, T. Bartel
Abteilung für Herzchirurgie, Medizinische Universität Innsbruck

The implementation of a TAVI (Trancsatheter Aortic Valve Intervention) program in an interdisciplinary fashion has been recommended by several scientific societies. However the number of centers with multidisciplinary TAVI programs seems to be very limited. The aim of the study was to evaluate the need of a close cooperation between interventional cardiologists, cardiac surgeons, echocardiographers and radiologists in an institutional TAVI program.

Between February 2008 and March 2012 93 patients received TAVI at the University Hospital Innsbruck. Transapical (n = 43, %), transfemoral (n = 42, %), transaxillary (n = 5, %), and transaortic (n = 3, %) implantations were performed on an intend to treat basis. The decision for intervention, preoperative planning, procedure conduction and postoperative management were performed in consensus of the responsible team consisting of interventional cardiologists, echocardiographers, cardiac surgeons, and radiologists. The vast majority of the patients (n = 85, %) were treated in the cardiac OR using a new generation mobile c-arm (Ziehm RFD, OEC 9800, Phillips Veradius).

The observed success rate of implantation was 96%. There were 6 conversions to larger thoracic incisions, 2 of them as a result of apical bleeding, and two conversions from the transfemoral to the transapical approach. One patient underwent minimally invasive aortic valve replacement after a non-reversible c-arm crash (old generation) before the beginning of the procedure and one patient had redo aortic valve replacement (AVR) because of valve embolization. There were three bail-out conversions from surgical to TAVI because of intraoperative contraindications. Cardiopulmonary bypass was used in 6 patients (7%). The majority of the transfemoral cases (27/42, 65%) required an extensive reconstruction of the femoral vessels. In two cases an endoluminal treatment was needed. In 42 patients (45%) a low volume contrast agent technique was applied after combining diagnostic information gathered by preoperative CT scan, and intracardiac echocardiography. As a result 61/93 patients have a substantial profit from the implementation of an interdisciplinary approach.

Conclusions Two thirds of the patients treated in an interdisciplinary model of TAVI have profited from the approach. The expertise provided by different disciplines can offers significant advantages for the preoperative planning as well as the intra and postoperative treatment.

Transaortic Catheter Valve Implantation: The Solution for Intraoperative Contraindications for Conventional Surgery? XIX – 7

N. Bonaros, S. Müller, G. Feuchtner, A. Heinz, N. Fischler, F. Plank, G. Friedrich, T. Schachner, M. Grimm, L. Müller, T. Bartel
Abteilung für Herzchirurgie, Medizinische Universität Innsbruck

Transcatheter valve implantation (TAVI) via transaortic approach has been previously described for patients in whom a transfemoral or transapical approach is not desirable or possible. We describe our experience in three patients with intraoperatively diagnosed contraindications to conventional aortic valve replacement, who underwent transaortic TAVI as a bail-out procedure.

A 68-year-old patient, out of vessels and with previous history of kidney transplantation and peripheral vascular disease, assigned for aortic valve replacement due to severe aortic stenosis ($\Delta P_{max} = 85$ mmHg) decompensated during anesthesia induction and required a high dose vasoconstrictor therapy. Because of the high risk for conventional surgery a transaortic approach to allow central cannulation for extracorporeal circulation was performed. A 26 mm Edwards Sapien prosthesis crimped upside-down was successfully implanted without the use of extracorporeal circulation. The patient had a prolonged recovery period after early extubation, mainly because of pneumonia complicated by acute renal failure, but left the hospital 3 weeks after the procedure in a good condition.

A 77-year-old male with isolated aortic stenosis ($\Delta P_{max} = 79$ mmHg) was assigned for minimally invasive aortic valve replacement via upper partial sternotomy. A severe calcification of the proximal ascending aorta and the aortic root not affecting the distal part of the aorta was found intraoperatively. Because of the high risk conventional surgery, the strategy was changed to TAVR via transaortic access. A 26 mm Edwards Sapien prosthesis was implanted after echocardiographic evaluation of the aortic annulus without the use of extracorporeal circulation. The patient had an uneventful postoperative course and was discharged home 6 days after the procedure.

The third patient had severely calcified regurgitant aortic root prosthesis, who underwent open TAVI via aortotomy in cardiopulmonary bypass and cardioplegic arrest.

All procedures were monitored by transesophageal echocardiography and fluoroscopy using a new generation mobile C-arm.

This access allows external marking of the coronary ostia in order to avoid coronary obstruction, as well as immediate repair of complica-

tions during the procedure. Closing of the aortic entry site is a very common procedure in cardiac surgery, which can be easily managed.

In conclusion, transaortic TAVR can be performed as a minimally invasive bail-out procedure in unexpectedly inoperable patients without alternative peripheral access.

Minimally Invasive Double Valve Surgery: 5-Year Experience XIX – 5

J. Dumfarth, A. Heinz, H. Hangler, J. Kilo, S. Semsroth, M. Grimm, L. Müller
Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck

Introduction Minimally invasive techniques for valve surgery have emerged as a safe and efficient approach in many institutions. Based on data and growing experience of minimally invasive mitral valve procedures, the technique was extended to double valve surgery. Aim of this study was to evaluate immediate and mid-term outcome in patients receiving minimally invasive double valve surgery.

Methods After implementation of a minimally invasive valve program and the first 54 successful isolated mitral valves, double valve surgery was started through this approach. Additional tricuspid annuloplasty was indicated for severe tricuspid regurgitation or tricuspid annular dilatation > 40 mm. Intraoperative and follow-up data of all patients undergoing double valve surgery from 2006 to 2011 were analyzed.

Results From 2006 to 2011, a total of 93 patients underwent minimally invasive double valve surgery through a mini-thoracotomy. Mean patients age was 67.5 years (range 38–86), 52% were female. In 76 patients (81%) mitral valve repair could be performed, all patients received tricuspid valve repair. Intraoperative conversion to full sternotomy was necessary in two cases (2%) due to pleural adhesion and bleeding. In hospital mortality was 2%. During a mean follow-up of 26 ± 12 months reoperation was performed in two patients due to endocarditis and significant tricuspid regurgitation.

Conclusion Minimally invasive tricuspid valve repair indicated for severe tricuspid regurgitation can be added safely to mitral valve surgery. Neither mortality nor major complications related to the combined procedures were increased. Follow-up data show convincing results.

Experience with the Mitraclip System in Patients with Significant Mitral Regurgitation, Distinct Impairment of LV-Function and Multiple Co-Morbidities XIX – 2

Ch. Ebner, T. Sturmberger, W. Tkalec, J. Aichinger, R. Steringer-Mascherbauer, V. Eder, G. Kabicher, J. Niel, H.-J. Nesser
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

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

Methods and Results So far we treated 32 patients as the first department in Austria, starting in August 2009. Indication for percutaneous catheter-based mitral valve repair with the MitraClip system was significant MR ≥ grade 3. 31/32 patients were refused by cardiac surgeons, 1 had failed surgical mitral repair. 22 patients (68.8%) presented with functional MR, 4 patients (12.5%) with degenerative disease and 6 patients (18.8%) had a mixed pathology. Patients median age was 72.5 years (IQR; 59–80) and 50% were male. The EuroScore of the total group was 21.62 ± 12.5% and increased in the group with a LVEF ≤ 35% up to 23.3 ± 13.6%. 14/32 patients had a LVEF ≤ 35% and 9 further patients (28.1%) of even ≤ 25%. A single clip was successfully implanted in 25 patients (78.1%), 5 patients (15.6%) received two clips and 1 patient received 3 clips. In one patient the clip could not be positioned successfully and in another patient we had a partial leaflet detachment of the second clip. The mean device implantation time was 109 ± 56 minutes. Only one patient developed cardiac tamponade treated successfully by conservative means, all the other procedures were uncomplicated. In-hospital and 30 days mortality was zero. ICU median duration was 2 days and total hospitalization was 11.2 ± 6.8 days (median 9, 7–11,75 days). In the very high surgical risk group (LVEF ≤ 35%) including multiple co-morbidities the 12 month mortality was 23.1%. In the 31/32 successful treated patients NTproBNP levels could be reduced from mean 7614 ± 8107 to 4767 ± 4835 pg/ml and mitral regurgitation intensity from grade 3.6 ± 0.3 to grade 1.56 ± 0.54.

Conclusion Mitral valve repair using the MitraClip system was shown to be feasible with high success rate in patients with significant mitral regurgitation. Particularly patients with distinct impaired LV-function in combination with multiple co-morbidities have a low periinterventional risk and may improve but have to be selected very carefully.

Evaluation of Changes in Geriatric Symptoms and MRI- or CT-Determined Cerebral Embolic Lesions Among Patients Undergoing Transcatheter Aortic Valve Implantation Before and After Procedure XIX – 1

V. Eder, Ch. Ebner, H. Koller, T. Schickmaier, T. Sturmberger, J. Aichinger, W. Tkalec, R. Steringer-Mascherbauer, H.-J. Nesser
Abteilung für Kardiologie, Krankenhaus der Elisabethinen, Linz

Background Transcatheter aortic valve implantation (TAVI) is an alternative treatment option in elderly patients with symptomatic severe aortic valve stenosis who are not eligible for conventional aortic valve replacement. A geriatric assessment is a multidisciplinary diagnostic approach designed to collect data on the medical, psychosocial and functional capabilities and limitations of elderly patients. Goal of this study was to assess changes in geriatric assessment parameters and MRI or CT determined cerebral embolic lesions after TAVI procedure and its correlation with changes of B-Type natriuretic peptide (BNP) levels and peak systolic gradient.

Methods and Results Between October 2007 and December 2011, 87 patients underwent TAVI with the CoreValve system for severe symptomatic aortic valve stenosis in our institution. In 12 consecutive patients (83.8 ± 2.9 years, 4 men and 8 women, mean aortic valve area 0.64 ± 0.16 cm^2, mean peak systolic gradient of 98.8 ± 21.15 mmHg, mean LVEF 50.4 ± 8.9%) with a logistic EuroScore of 23.7 ± 9.6% and NT pro BNP of 1137 pg/ml (IQR 605–2521), a comprehensive geriatric assessment as well as a cerebral diffusion weighted MRI or CT scan was performed before and within one year after TAVI. Geriatric assessment included the MNA©, ADLs, IADLs, GDS, Timed Get up&Go, Chair Rising Test, the Mini Cog©, Frieds Frailty criteria and the Carlson Morbidity score. Based on the geriatric assessment patients were stratified into functional performance categories defined as healthy/'GoGo' (n = 3), vulnerable/'SlowGo' (n = 7) or Frail/'NoGo' (n = 2).

After a follow-up period of 12 ± 5 months, 10 of our 12 patients showed no changes in functional performance category or other geriatric assessment parameters (e. g. frailty), while 1 patient deteriorated and 1 patient improved to a better functional performance category. New (clinically silent) perfusion deficits, presumably due to atherothrombotic emboli, occurred in 2 patients, but these findings were not associated with deteriorations in geriatric performance category. No patient suffered a clinical cerebral stroke. Overall, BNP levels and peak systolic aortic gradients decreased after TAVI (2040 ± 2370 vs 789 ± 704 pg/ml; p = 0.055; 89.7 ± 21.5 vs 22.5 ± 6.6 mmHg; p < 0.0001)

Conclusion and Discussion Our preliminary results of 12 patients undergoing TAVI indicate that successful TAVI, illustrated by a significant reduction of peak systolic aortic gradient and lower BNP levels after the procedure, is not associated with improvements in geriatric outcome parameters e. g. functional performance categories. There was no correlation between new cerebral embolic lesions and geriatric assessment status. Although in previous studies TAVI demonstrates better clinical outcomes than standard medical treatment, our report does not support improvements in typical geriatric categories.

Root Replacement for Excavating Aortic Valve Endocarditis With the Freestyle® Xenograft XIX – 10

A. Heinz, J. Dumfarth. M. Grimm, L. Müller
Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck

Introduction The choice of the optimum conduit for aortic root replacement in destructive endocarditis depends on technical considerations, resistance to infection and longevity of the graft. Since 1998 we systematically used the Freestyle® xenograft instead of homografts.

Material and Methods Patients requiring left ventricular outflow tract (LVOT) and/or aortic root replacement for severe, excavating native or prosthetic valve endocarditis (NVE or PVE) who received a xenograft full root from 1998 to 2012 were studied. Outcome analysis was performed for perioperative complications, mortality and technical success of the operation.

Results In 31 patients a Freestyle® porcine aortic root (21–29 mm) was implanted. 17 patients had additional procedures: CABG (n = 9), mitral valve repair or replacement (n = 3), tricuspid valve repair (n = 1), LVOT patch repair (n = 6), ascending aorta replacement (n = 2) and ascending aorta reduction plasty (n = 4). 22 patients were operated for PVE with annulus destruction. 30 days and hospital mortality was 6 (19.4%). There were no instances of technical failure requiring reoperation for bleeding or replacement of the xenograft by a different conduit. 3 patients needed postoperative mechanical circulatory support, 3 patients had a pacemaker implantation for new heart block, and 7 patients required hemofiltration for acute renal failure. Median ICU stay was 5 days (1–136), median intubation time 2 days (1–115). Hospital stay was 26 days (8–36).

Conclusion The Freestyle® aortic root xenograft can be used technically successful instead of a homograft in the most severe cases of excavating aortic valve endocarditis.

Impact of Tricuspid Regurgitation Late After Left-Heart Valve Surgery XIX – 3

A. Kammerlander, B. Marzluf, D. Bonderman, M. Nikfardjam, A. Bachmann, A. Graf, G. Maurer, J. Mascherbauer
Department of Cardiology; Department of Medical Statistics, Medical University Vienna

Background Significant tricuspid regurgitation (TR) occurring late after left-heart surgery is frequent and associated with decreased exercise tolerance and quality of life. Reoperative tricuspid valve (TV) surgery has been reported to result in early mortality rates as high as 10–25%.

The aim of the study was to evaluate whether significant TR late after left-heart valve surgery impacts on prognosis.

Methods 647 consecutive patients who were seen in our outpatient clinic of valvular heart disease at least 6 months after successful surgery of the aortic or/and the mitral valve were prospectively followed. The severity of TR was assessed by echocardiography. Significant TR was defined as TR ≥ moderate. Multivariable logistic and Cox regression models were used to determine the impact of TR on survival.

Results From 647 patients, 399 (61.7%) presented with prior aortic valve replacement (AVR); 138 (21.3%) patients had previous surgery of the mitral valve (MV) (78 (12.1%) MV replacement; 60 (9.3%) MV repair). 63 (9.7%) patients had both AVR and MV surgery. 47 (7.3%) had previous tricuspid surgery in addition to left-sided procedure. Significant TR was present in 161 (24.9%) patients.

Patients with significant TR were predominantly female (68% vs 45%; $p < 0.001$), had a higher EuroSCORE at the time of last surgery (8.2 ± 3.1 vs 5.5 ± 2.4: $p < 0.001$); and a higher number of previous cardiac surgeries (1.2 ± 0.5 vs 1.1 ± 0.3; $p = 0.007$). They presented with a higher frequency of atrial fibrillation (52% vs 17%; $p < 0.001$), diabetes (20% vs 13%; $p = 0.030$), and pulmonary hypertension (31% vs 13%; $p < 0.001$); and were more symptomatic (NYHA functional class 1.97 ± 0.75 vs 1.47 ± 0.62; $p < 0.001$). They furthermore had more dilated right ventricles (37.5 ± 7.9 mm vs

32.7 ± 5.0 mm; p < 0.001), more dilated left and right atria (both p < 0.001) and presented with worse left ventricular function (LVEF < 50% 20,5% vs 11,1%; p = 0.005).

Patients were followed for 698 ± 124 days (TR ≥ 2: 681 ± 147 days vs TR < 2: 703 ± 116 days; p = 0.08).

In total, 54 patients died during follow-up (13,7% of patients with TR ≥ 2 vs 6,6% patients with TR < 2, p = 0.034). By Kaplan-Meier analysis, survival rates were significantly worse in patients with significant TR (1- and 2-year survival rates 92.6% and 87.6% in significant TR versus 96.1% and 93.4% in non-significant TR; log rank p = 0.005).

By multivariable Cox regression analysis, significant TR (p = 0.002), atrial fibrillation (p = 0.001), and age (p < 0.001) were found to independently predict mortality.

Conclusion Significant TR late after left-sided heart valve surgery is frequent and predicts outcome in addition to age and atrial fibrillation.

A New Concept for Aortic Valve Repair XIX – 9

L. Müller, A. Heinz, J. Dumfarth, S. Semsroth, M. Grimm
Universitätsklinik für Herzchirurgie, Medizinische Universität Innsbruck

Background Repair of the aortic valve for severe regurgitation is still a matter of debate since results are equivocal. Introduction of a systematic approach to aortic valve repair similar to the proven concept of mitral valve repair, however, made results much more predictable. The new concept addresses simultaneously all three components of the aortic root: the annulus, the cusps and the sino-tubular junction, since alteration of each of them influences form and function of the other two components.

Materials and Methods Since December 2011, 9 patients with severe aortic valve regurgitation have been operated with the intention to repair the valve. Indication for valve surgery was derived from clinical symptoms, progressive ventricular dilatation or reduction of ejection fraction. Valve analysis included anatomical classification (tricuspid, biscuspid, quadricuspid), geometrical height and effective height of the cusps as well as diameter of the aorto-ventricular and the sino-tubular junction. Repair aimed at correction of cusp prolaps by plication of the free margin, subvalvular annuloplasty and corresponding reconstruction of the sino-tubular junction.

Results Median age of the patients was 33 (21–53 years), 7 patients were male. Valve morphology included bicuspid AV Type I L-R in 5, Type 0 in 1, tricuspid AV in 2 and quadricuspid AV in 1 patient. In 1 patient the intraoperative decision was for AV plus ascending aorta replacement due to unfavorable anatomy in 1 and the valve had to be replaced for an unsatisfactory repair result in 1 other patient. 7 valves were repaired successfully. Subvalvular suture annuloplasty was performed in 5 patients, 2 received reconstruction of the sino-tubular junction. Echo control before discharge revealed no regurgitation (grade 0) in 3 and trace to mild (grade I) in 4 patients.

Conclusion Implementation of a new concept of aortic valve repair for severe aortic regurgitation which addresses all components of the aortic root has led to very satisfying short term results promising long lasting freedom from valve replacement in this young cohort of patients.

Perkutaner Aortenklappenersatz (TAVI) bei Patienten mit inoperabler Aortenklappenstenose XIX – 6

E. Zeindlhofer, K. Höllinger, A. Winter, Ch. Steiner, M. Schmid, D. Kiblböck, L. Pilgerstorfer, F. Rausch, J. Reisinger, P. Siostrzonek
Interne II/Kardiologie, Krankenhaus der Barmherzigen Schwestern, Linz

Einleitung Der perkutane Aortenklappenersatz (TAVI) hat sich in den vergangenen Jahren als neue erfolgversprechende Behandlungsmöglichkeit bei inoperablen Patienten mit Aortenklappenstenose (AS) etabliert. Wir führen die TAVI seit Februar 2011 in multidisziplinärer Kooperation durch und berichten über unsere Ergebnisse.

Material und Methode Bisher wurden 52 Patienten (32 Männern, 20 Frauen; Alter: 82,0 ± 5,4 Jahre) mit inoperabler AS behandelt. Bei allen Patienten lag eine signifikante symptomatische AS (Mittlerer Gradient: 58,6 ± 17,9 mm, NYHA III: 45 Pat., NYHA IV: 7 Pat.) vor, der logistische EuroSCORE betrug 28,2 ± 11,3. Bei 9 Patienten lag eine linksventrikuläre Auswurffraktion < 40 % vor. 20 Pat. hatten eine koronare Herzkrankheit, bei 14 war eine koronare Intervention vorangegangen.

Ergebnisse Die Klappenimplantation wurde durchwegs transfemoral unter Verwendung des CorValve-Systems (Medtronic, Minneapolis, MN, USA) durchgeführt. Die Implantation erfolgte perkutan unter Sedoanalgesie, nur bei 2 Pat. mit vorbestehender Lungenstauung wurde eine Intubationsnarkose vorgenommen. Die Einbringung der Klappe war in allen Fällen erfolgreich, bei einem Pat. mit Aorteninsuffizienz musste eine zweite Klappe (Valve in Valve) implantiert werden. Die Gesamtdauer des Eingriffs betrug 80 ± 28 min, die Durchleuchtungsdauer 23 ± 9 min. Bei keinem Pat. musste eine Konversion zur Herzchirurgie vorgenommen werden. Nach Implantation reduzierte sich der mittlere Gradient auf 10,2 ± 5,8 mm (p < 0,001), die Aorteninsuffizienz nach Implantation wurde bei 36 Pat. als gering (Grad 0/I) und bei 6 Pat. als mäßig (Grad II) eingeschätzt.

Bei 10 (19 %) Pat. trat nach Schleusenentfernung eine periphere Gefäßkomplikation auf, die bei 8 Pat. (15,2 %) gefäßchirurgisch versorgt werden musste. Drei Pat. (5,7 %) erlitten ein reversibles neurologisches Defizit. Bei 14 Pat. (26,9 %) musste ein permanenter Schrittmacher implantiert werden. Die Aufenthaltsdauer auf der Intensivstation betrug 4,8 ± 3,6 Tage, die Krankenhausaufenthaltsdauer 16,3 ± 6,5 Tage.

Ein Monat nach TAVI hatte sich das NYHA-Stadium bei allen bis auf einen Pat. verbessert (NYHA I: 4 Pat., NYHA II: 35 Pat. und NYHA III: 2 Pat.). Das BNP war von 1347 ± 929 auf 745 ± 541 gesunken (p < 0,001). Die 30-Tage-Mortalität betrug 2/52 (3,8 %), die Mortalität nach einem Jahr 4/24 (16,7 %).

Diskussion Unsere Ergebnisse sind in Anbetracht der Multimorbidität der behandelten Patienten ermutigend und durchaus mit den Ergebnissen aus größeren Studien und Registern vergleichbar.

Vergleich von 2 femoralen Verschlusssystemen nach perkutanem Aortenklappenersatz XIX – 8

E. Zeindlhofer, K. Höllinger, A. Winter, Ch. Steiner, A. Gierlinger, M. Schmid, D. Kiblböck, F. Rausch, J. Reisinger, P. Siostrzonek
Interne II/Kardiologie, Krankenhaus der Barmherzigen Schwestern, Linz

Einleitung Der perkutane Aortenklappenersatz (TAVI) hat sich in den vergangenen Jahren als erfolgversprechende Behandlungsmöglichkeit bei inoperablen Patienten mit Aortenklappenstenose (AS) etabliert. Gefäßkomplikationen an der femoralen Punktionsstelle stellen eine typische Komplikation nach TAVI dar. Wir berichten über die Ergebnisse bei Verwendung von zwei unterschiedlichen perkutanen Verschlusssystemen.

Material und Methode Bei 51 Pat. (Alter: 82 ± 5,4 Jahre, 32 Frauen, 20 Männer, logistischer EuroSCORE: 28,2 ± 11,3) wurde in perkutaner Technik erfolgreich eine CoreValve-Klappe (Medtronic, Minneapolis, MN, USA) über einen femoralen Zugang implantiert. Der Gefäßverschluss nach Entfernung der 18F-Schleuse erfolgte bei den ersten 31 Pat. mit dem Prostar-XL- (PS-) System (Abbott Vascular, Redwood, California, USA) und bei den weiteren 20 Pat. unter Verwendung von 2 ProGlide- (PG-) Systemen (Abbott Vascular, Redwood, California, USA). Patientenalter, Geschlechtsverteilung und logistischer EuroSCORE waren in beiden Gruppen vergleichbar. Der präinterventionelle Gefäßdurchmesser an der Punktionsstelle betrug in der PS-Gruppe 7,9 ± 0,7 mm und in der PG-Gruppe 8,1 ± 1,2 mm (p = n. s.).

Ergebnisse Der residuale Stenosegrad an der Verschlussstelle betrug nach PS 26,5 ± 11,6 % und nach PG 15,5 ± 10,9 % (p < 0,005). Bei 10 (19 %) Pat. trat nach Schleusenentfernung eine periphere Gefäßkomplikation auf, die bei 8 Pat. (15,2 %) gefäßchirurgisch und bei 2 Pat. (2,8 %) interventionell versorgt werden musste. Gefäßchirurgische Revisionen an der 18F-Insertionsstelle waren bei 6/31 Pat. (19,4 %) nach PS und bei 0/20 Pat. (0 %) nach PG notwen-

dig (p = 0,041). Erythrozytenkonzentrate waren nach PS bei 9/31 Pat. (29 %) und nach PG bei 2/20 Pat. (10 %) erforderlich (p = 0,09). Ein Pat. mit PS verstarb am Tag 20 nach einer chirurgischen Revision wegen einer Nachblutung. Die 30-Tage-Mortalität (PS: 3.2 %, PG: 0 %) und die Aufenthaltsdauer auf der Intensivstation (PS: 4,8 ± 4,0 Tage, PG: 4,7 ± 2,2 Tage) waren nicht-signifikant unterschiedlich.

Diskussion Der Verschluss der femoralen Punktionsstelle mittels PG anstelle von PS geht nach unserer Erfahrung mit weniger Blutungskomplikationen, einer reduzierten Notwendigkeit einer gefäßchirurgischen Korrektur und mit einer geringeren residualen Gefäßstenose einher.

Severe Asymptomatic Aortic Stenosis in an Elderly Population BAI

R. Zilberszac, H. Gabriel, G. Maurer, R. Rosenhek
Klinische Abteilung für Kardiologie, Universitätsklinik für Innere Medizin, Medizinische Universität Wien

Background The aim of the present study was to assess the natural history of severe asymptomatic AS in a large cohort of elderly patients older than 70 years. As life expectancy in the western world climbs, calcific aortic stenosis (AS) has become more frequent since its prevalence continuously increases with age. This results in large numbers of elderly patients receiving aortic valve interventions. However, these patients are underrepresented in most natural history studies on AS where the average age of patients is between 60 and 70 years.

Methods 103 consecutive elderly patients (51 female, age 77 ± 5 yrs) with asymptomatic severe AS defined by a peak aortic jet velocity (V_{max}) ≥ 4.0 m/s (average peak V_{max} 4.75 ± 0.57 m/s, mean gradient 58 ± 17 mmHg, valve area 0.70 ± 0.20 cm^2) were included and followed at regular intervals. Patients with other significant valve lesions or concomitant aortic regurgitation were excluded. Outcome was assessed and event-free survival with events defined as development of criteria warranting aortic valve replacement or cardiac death was determined. All of the patients in this series had moderately-to-severely calcified aortic valves.

Results During a mean follow-up of 19.4 (IQR 9.8–36.4) months, 82 patients developed criteria warranting aortic valve replacement and 15 patients died. Event-free survival rates after 1, 2, 3 and 4 years were 72%, 44%, 23%, and 16% respectively and were not significantly different for patients younger or older than 80 years. Event-free survival was significantly worse for patients with an AV-Vel ≥ 5.0 m/s with respective event-free survival rates of 51 ± 8%, 21 ± 6%, 12 ± 5% and 3 ± 3% at 1, 2, 3 and 4 years respectively, as compared to 83 ± 5%, 55 ± 6%, 37 ± 6% and 23 ± 8% for patients with an AV-Vel < 5.0 m/s. 7 cardiac deaths (2 myocardial infarction and 5 cardiac decompensation) occurred after a mean of 6.3 ± 5.1 months after the last follow-up visit where the patients were reportedly asymptomatic. 3 of these pts had a restricted mobility due to comorbidities. There were five perioperative deaths among 72 patients who underwent aortic valve replacement, while 10 patients refused surgery. Postoperative survival rates were 89%, 81%, 77% and 66% after 1, 2, 3 and 4 years respectively.

Conclusion In elderly asymptomatic patients with severe aortic stenosis, a very high event rate can be expected. Symptomatic status is often difficult to assess due to comorbidities and patients are at high risk of rapid deterioration and death. Surgical outcomes are good and risk stratification based on peak aortic jet velocity may also be helpful in elderly patients with severe AS.

Nachträglich erhalten

Multiple Arterial Revascularization in CABG Surgery – Investigation of Long-Term Benefit in a Consecutive Cohort of 3129 Patients BAII

E. Ruttmann, H. Ulmer, A. Sakic, N. Fischler, H. Alber, M. Wanitschek, O. Pachinger, R. Schistek, M. Grimm, O. Chevtchik
Department of Cardiac Surgery; Department of Cardiology, Innsbruck Medical University, Department of Medical Statistic, Informatics, and Health Economy Innsbruck

Objective Lacking utilization of accompanying arterial grafts to a left internal thoracic artery (LITA) in CABG surgery appear to be based on the lack of conviction regarding any long-term benefit.

Aim of our study was to investigate whether multiple arterial revascularization (MAR) has an impact on survival after CABG.

Methods A consecutive series of 3129 patients undergoing first, isolated, non-emergent multivessel CABG procedure receiving at least 2 arterial grafts from 2001 to 2010 was investigated. MAR was performed in 1068 patients (34.1%) using radial artery in 791 patients (25.3%) and a second ITA graft in 344 patients (11%). The remaining 2061 patients received single ITA and concomitant SVG (conCABG group). Proportional hazard model was performed to estimate independent predictors for survival.

Results Median follow up was 56.9 months in the MAR group and 44.5 months in the conCABG group (p < 0.001). Baseline characteristics were different regarding age, gender, smoking, cerebro- and peripheral vascular (all < 0.001), and pulmonary disease (p = 0.04). Actuarial survival at 1, 3, and 5 years was 98.3%, 97.7%, and 96.5% in the MAR group compared to 97.1%, 93,1%, and 92.1% in the conCABG group.

MAR remained a strong independent predictor for long term survival (Hazard Ratio HR: 0.65; 0.45–0.95; p = 0.02). Additionally cerebro-vascular events (HR: 2.1; 1.3–3.5; p = 0.003) and peripheral arterial disease (HR:2.5; 1.9–3.5; p < 0.001) revealed significant factors for survival beside age (3.2% increase/year; 1.01–1.05; p < 0.001). Multivariate analysis revealed an absolute mortality reduction of MAR of 2.5% and 4% at 5 and 8 years after CABG.

Conclusion The result of our study implies that MAR should be the standard-of-care and survival benefit seems to widen over time.

Spontaneous Gross Hematuria During Dabigatran Therapy for Secondary Stroke Prevention IX-4

C. Stöllberger, St. Rakusan, E. Sehnal, F. Wimpissinger, J. Finsterer
2. Medizinische Abteilung, Krankenanstalt Rudolfstiftung, Wien

Background Dabigatran is an oral thrombin inhibitor, approved in several countries for prevention of stroke/embolism in atrial fibrillation as an alternative to vitamin-K-antagonists (VKAs) although important issues have not been clarified, as illustrated by the following case.

Case Report An 85-year old man with gross hematuria had a history of hypertension, atrial fibrillation, chronic obstructive pulmonary disease, renal failure, metastatic prostate cancer and non-disabling stroke. Despite well-controlled VKA-therapy, two further non-disabling ischemic strokes occurred, and anticoagulation therapy was switched from phenprocoumon to dabigatran assuming that dabigatran would be indicated in a case of "VKA-failure". Since the glomerular filtration rate was 38 ml/min/1.73 m^2 dabigatran 110 mg/bid was prescribed.

Following antibiotic therapy of an urinary tract infection, the patient suffered from diarrhea and loperamide 2 mg bid for 2 days was prescribed. Two days later gross hematuria started. Dabigatran was stopped after the patient had taken the last dose in the morning of day 1. Hematuria persisted, necessitating 2 blood transfusions. On cystoscopy no bleeding source was identified. The thrombin time was 75 sec even 31 hours after intake of the last dabigatran dose. To stop bleeding, 4 units of fresh frozen plasma were given. On day 3, hematuria ceased and eventually the patient was discharged with enoxaparin-therapy.

Conclusion Dabigatran in patients with carcinoma and P-gp-affecting drugs may cause major bleeding. There is a need for monitoring tools of the anticoagulant status of patients receiving dabigatran in bleeding situations, an antidote and research about drug-drug interactions and urological side effects.

Autorenindex

(nur Erstautoren)

Mitteilungen aus der Redaktion

Besuchen Sie unsere Rubrik

☑ Medizintechnik-Produkte

Neues CRT-D Implantat
Intica 7 HF-T QP von Biotronik

Artis pheno
Siemens Healthcare Diagnostics GmbH

Philips Azurion:
Innovative Bildgebungslösung

Aspirator 3
Labotect GmbH

InControl 1050
Labotect GmbH

e-Journal-Abo

Beziehen Sie die elektronischen Ausgaben dieser Zeitschrift hier.

Die Lieferung umfasst 4–5 Ausgaben pro Jahr zzgl. allfälliger Sonderhefte.

Unsere e-Journale stehen als PDF-Datei zur Verfügung und sind auf den meisten der marktüblichen e-Book-Readern, Tablets sowie auf iPad funktionsfähig.

☑ Bestellung e-Journal-Abo