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Abstracts

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Jahrestagung der Österreichischen Kardiologischen Gesellschaft 3. bis 6. Juni 2009, Salzburg

Abstracts

(in alphabetischer Reihenfolge nach Gruppen und Erstautoren)

Akutes Koronarsyndrom

Target Vessel Reopening by Guidewire Insertion in ST-Elevation Myocardial Infarction is a Predictor of Final TIMI Flow and Survival 015

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Background and Objective ST-elevation myocardial infarction (STEMI) results from acute thrombotic obstruction of a coronary artery. Percutaneous coronary intervention (PCI) is the treatment of choice to restore blood flow. Observational experience shows that guidewire insertion alone may lead to reopening of the infarct related coronary artery (IRA). The incidence of guidewire-induced target vessel reopening and its association with post procedural TIMI flow and long-term mortality were assessed.

Methods Angiograms of consecutive STEMI patients admitted to the catheter laboratory of the Medical University of Vienna between January 2003 and December 2005 were analyzed in a retrospective study. TIMI flow was graded prior to and after guidewire insertion to the distality of the IRA.

Results Initial TIMI 0 flow was present in 476 (47.0 %) of 1012 cases. TIMI flow after guidewire insertion was associated with better post procedural TIMI flow ($p < 0.001$) and target vessel reopening after guidewire insertion, defined as any flow > TIMI 0 flow, was associated with improved survival after a median of 914 (609–1238) days ($p = 0.001$). Reflow after guidewire insertion was an independent predictor of mortality (HR = 0.67; $p = 0.033$) in addition to postprocedural TIMI flow.

Conclusion Failure of target vessel reopening by guidewire insertion identifies a subset of high-risk STEMI patients, who may benefit from reperfusion-injury/myocardial regeneration treatments.

Welche intrahospitalen Faktoren beeinflussen die Door-to-balloon-Zeit bei der primären Koronarintervention im Rahmen eines ST-Hebungsinfarktes? 076

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Hintergrund In Anlehnung an die aktuellen ESC-Richtlinien sollte eine Zeitspanne von mehr als 90 Minuten zwischen erstem medizinischen Kontakt und Durchführung der Akut-Koronarintervention (Akut-PCI) nicht überschritten werden.

Anhand unserer Single-Center-Studie wurde überprüft, welche intrahospitalen Faktoren einen Einfluss auf den zeitlichen Ablauf haben.

Methodik Im Zeitraum von August 2008 bis Februar 2009 wurden alle Patienten, die an unserer Abteilung mit einem ST-Hebungsinfarkt einer Akut-PCI unterzogen wurden, bezüglich intrahospitaler Transportzeiten minutiös dokumentiert. Folgende Zeitintervalle wurden verglichen: Zeit vom Eintreffen des Patienten im Krankenhaus bis zur Aufnahme in der Überwachungsstation (t1), Zeit zwischen Überwachungsstation und Eintreffen des Patienten im Herzkatheterlabor (t2), Zeit zwischen Eintreffen im Herzkatheterlabor und Balloninflation (t3), sowie die Door-to-balloon-Zeit (t4 = t1 + t2 + t3). Bezüglich der Zeitintervalle wurde zwischen Tagdienst (7:00–15:00 Uhr) und Bereitschaftsdienst (15:00–7:00 Uhr) verglichen.

Ergebnisse Das Patientenkollektiv umfasste 60 konsekutive Patienten mit ST-Hebungsinfarkt. Im Tagdienst wurden 36 Patienten (60 %) und im Bereitschaftsdienst 24 Patienten (40 %) behandelt. Zwei Patienten waren bereits stationär und wurden deswegen von der Studie ausgeschlossen. Die demographischen Daten (Alter, Geschlecht, Infarktlokalisation, Einlieferung im kardiogenen Schock bzw. kreislaufstabil) hatten keinen statistisch signifikanten Einfluss auf die dokumentierten Zeiten. Die Erfolgsrate, definiert als TIMI-III-Fluss, lag bei 54 Patienten (90 %) vor. Eine perkutane koronare Intervention war bei 2 Patienten aufgrund der erhobenen Gefäßmorphologie nicht indiziert. Die Spitalsmortalität betrug 11,7 % und betraf ausschließlich Patienten mit kardiogenem Schock (7 von 11 Patienten).

Die Door-to-balloon-Zeit war während des Tagdienstes mit 37 ± 16 min statistisch signifikant kürzer als während des Bereitschaftsdienstes (56 ± 25 min; $p < 0{,}005$). Beim Vergleich der einzelnen Zeitintervalle zwischen Tag- und Bereitschaftsdienst zeigte sich kein signifikanter Unterschied bezüglich t1 (13 min ± 6/12 min ± 11) und t3 (17 min ± 7/18 min ± 8).

Die Zeitdauer zwischen Aufnahme in der Überwachungsstation und Eintreffen des Patienten im Katheterlabor (t2) war im Tagdienst (15 min ± 13) signifikant niedriger als im Bereitschaftsdienst (30 min ± 17; $p < 0{,}001$).

Schlussfolgerung Der festgestellte Zeitunterschied bezüglich der Door-to-balloon-Zeit zwischen Tag- und Bereitschaftsdienst ist durch das nicht anwesende bzw. verspätet einberufene Interventionsteam verursacht.

Eine Reduktion der Door-to-balloon-Zeiten könnte durch eine frühzeitige Abschätzung der nötigen Interventionen via prähospitalem Telemonitoring erfolgen.

Local Complement Activation Triggers Neutrophil Recruitment to the Site of Plaque Rupture in Acute Myocardial Infarction 037

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Background Atherosclerotic plaque rupture with subsequent mural thrombus formation is considered the main event compromising epicardial flow in acute myocardial infarction (AMI). However, the precise mechanisms underlying acute coronary occlusion are unknown.

Patients/Methods We compared the proteomic profiles of systemic plasma and plasma derived from the site of plaque rupture of patients with AMI by two-dimensional gel electrophoresis and ELISA.

Results We identified a local activation of the complement system, with selective accumulation of the complement activator C-reactive protein (CRP) and the downstream complement effectors C3a and C5a. CRP in coronary thrombus colocalized with C1q and C3 immunoreactivities, suggesting classical complement activation. In vitro, coronary thrombus derived plasma enhanced neutrophil chemotaxis in a C5a dependent fashion. In vivo, neutrophil accumulation at the site of plaque rupture paralleled the time delay after symptom onset, and was correlated with C5a and enzymatic infarct size.

Conclusions We present the first direct evidence for localized complement activation in acute coronary thrombi. Our data indicate that local complement effectors amplify the vascular occlusion process in AMI by enhanced neutrophil recruitment.

Multivessel Percutaneous Coronary Intervention is Associated with Higher In-Hospital Mortality in ST-Elevation Myocardial Infarction 087

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Introduction Multivessel coronary artery disease is associated with worse outcome after ST-elevation myocardial infarction. Revascularisation of the culprit lesion is the main goal in primary PCI. However, treatment strategy for patients with STEMI and multivessel coronary artery disease undergoing primary angioplasty is still controversial.

Aim We sought to evaluate multivessel PCI (MV-PCI) on in-hospital outcome in patients with STEMI undergoing primary PCI in Austria.

Methods and Results We analysed data of 3587 consecutive patients of the Austrian Acute PCI Registry undergoing primary PCI. Patients with cardiogenic shock (n = 371) were excluded. 8.2 % of the remaining 3216 patients underwent MV-PCI and 91.8 % patients received PCI of the infarct related (IRA) only. Patient characteristics, treatment delays and adjunctive antithrombotic pretreatment with ASS, clopidogrel, heparin and GPIIb/IIIa antagonists were not different in the two groups. Patients undergoing MV-PCI had a lower rate of TIMI III flow (5.3 % vs 9.7 %; p = 0.028) before, but a similar angiographic success rate after PCI (95.6 % vs 94.4 %; p = 0.543). In-hospital mortality was 4.5 % in MV-PCI and 1.6 % in IRA (p = 0.004). Reinfarction rate (1.2 % vs 1.2 %; p = 0.76) and bleeding rate (0.8 % vs 0.9 %; p = 1.0) were not different. In multivariate analysis including age, diabetes, angiographic success and prior myocardial infarction, MV-PCI remained an independent predictor of in-hospital mortality (OR 3.85; 95 %-CI: 1.59–9.34; p = 0.003).

Conclusion The higher in-hospital mortality after MV-PCI in ST-elevation myocardial infarction supports the concept that in hemodynamically stable patients, primary PCI should be restricted to the IRA. Whether specific subgroups in these high risk patients other than cardiogenic shock may benefit from MV-PCI remains to be established.

Influence of Stress Hyperglycemia on the Outcome of Patients with Acute Coronary Syndrome Undergoing Interventional Coronary Revascularization 151

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Introduction and Aim Stress hyperglycemia (SHG), which is defined as an admission glucose concentration of ≥ 126 mg%, has been shown to influence the outcome of patients with myocardial infarction. Furthermore, SHG shows a direct correlation to left ventricular function and the degree of myocardial damage. Interestingly, no relationship has been reported between SHG and the metabolic status of cardiovascular patients in general. We aimed to investigate the impact of admission glucose concentration on the clinical outcome of patients undergoing percutaneous coronary revascularization (PCI) presenting with an acute coronary syndrome (ACS).

Patients and Methods 416 patients admitted to the emergency department with the diagnosis of an acute coronary syndrome including non-ST-elevation myocardial infarction (NSTEMI; 51.2 %) and ST elevation myocardial infarction (STEMI; 48.8 %) who underwent acute PCI were included in the study. Patients were divided into those presenting with SHG or without SHG and followed for 19 ± 13 (mean ± SD) months.

Results The incidence of diabetes mellitus (DM) in our patient cohort was 20.1 % (n = 84). SHG occurred in 52.4 % (n = 218) of the studied patient cohort, while 47.5 % (n = 198) of patients exhibited normal admission glucose concentrations. Patients with SHG had significantly higher creatine phosphokinase (1101 ± 1363 vs 1600 ± 1808; p < 0.001) and CK-MB (178 ± 170 vs 233 ± 207; p = 0.01) levels as compared to non-SHG patients. All other clinical characteristics were comparable between groups. As expected, SHG occurred more frequently among diabetics compared to non-diabetics (89.3 % vs 43.1 %; p < 0.001). Most importantly, however, in both, univariate and multivariate Cox-regression analysis adjusted for age, gender, estimated glomerular filtration rate (eGFR), CK, CKMB, stent type (drug eluting or bare metal stent), and diabetes status, SHG was an independent predictor of survival (HR 3.48; CI: 1.22–9.91; p = 0.03).

Conclusion Although SHG occurs more frequently among patients suffering from DM it is a strong independent predictor of long-term mortality in medium-to high risk ACS-patients not only in diabetics but also in patients without underlying pathologic glucose metabolism.

Familial Combined Hyperlipidemia in Very Young Myocardial Infarction Survivors (≤ 40 Years of Age) 161

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Background Myocardial infarction (MI) in very young individuals is a rare disease associated with an unfavourable prognosis. Familial combined hyperlipidemia (FCHL) increases the risk for MI in individuals below 60 years, however, its role in very young MI patients below 40 years is not as well established. We investigated the prevalence and impact of FCHL in these very young MI patients.

Methods and Results We prospectively enrolled 102 consecutive MI survivors (≤ 40 years) from two high volume cardiac catheterization centres. Patients were frequency-matched for age, gender, and centre to 200 hospital controls free from coronary heart disease. MI patients were invited to send family members for FCHL screening. Overall, 37 families were screened. FCHL was diagnosed using a nomogram, which takes into account total cholesterol, triglycerides, and Apo B100 levels. Thirty-eight AMI patients (38 %) and five controls (2.5 %) displayed the FCHL phenotype, 21 of these MI patients sent family members for screening, and FCHL was confirmed in 16 families (76 %). The FCHL phenotype was associated with a 24-fold increased adjusted risk for MI (95 %-CI: 7.5–8.1;

p < 0.001). Of all lipid parameters, VLDL-cholesterol and non-HDL-cholesterol were most strongly associated with MI.

Conclusions The present study suggests that the FCHL phenotype seems to be a major risk factor for the occurrence of MI at a very young age. It remains to be determined whether this excessively increased risk can be favourably modified by therapeutic interventions.

Prognostic Value of ECG Pattern in Patients with Angiographically Proven Occlusion of the Left Circumflex Artery: ST-Elevation versus Non-ST-Elevation Acute Coronary Syndrome 109

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Purpose Myocardial infarction (MI) due to acute plaque rupture of the left circumflex artery (LCX) may present as ST-elevation MI (STEMI) but more likely as non ST-elevation acute coronary syndrome (NSTE-ACS). Therefore, recommended therapy options differ between immediate revascularisation in the first and a selective invasive approach in the latter. This observational study was performed at our university hospital to investigate the outcome of a consecutive series of patients (pts) suffering from ACS with occluded LCX and ECG signs of either STEMI or NSTE-ACS.

Methods Basic assessment consisted of physical examination, ECG, routine lab and assessment of individual cardiovascular risk preceding the qualifying event according to the risk score of the British Medical Association. All pts were followed by telephone calls, by checking the medical files and contacting their general practitioners. Predefined endpoints were death, re-MI, repeated revascularisation and hospitalisation due to vascular events.

Results In 2006 2519 pts underwent coronary angiography at our institution. 125 of these (76 % male; n = 95; mean age 67 ± 12 y) were qualified for inclusion by acutely occluded LCX. 20 pts (16 %) had STEMI, 105 (84 %) were enrolled in the NSTE-ACS group. 99 pts (79.2 %) underwent revascularisation. Time delay to PCI was significantly longer in the NSTE-ACS group. Individual cardiovascular risk at inclusion was higher in the NSTE-ACS compared to the STEMI pts (10.4 vs 6.9 % risk of death; p = 0.008). Mean follow up time was 14 ± 6 months.

Mortality was higher in the STEMI group, nonfatal events occurred more frequently with NSTE-ACS. However, multivariate analysis incorporating the preceding individual risk balanced the results. Therefore, the only significant determinant of outcome was individual risk at time of inclusion (p < 0.05).

Conclusions There is a tendency toward higher mortality in STEMI and higher morbidity in NSTE-ACS pts with occluded LCX, but preceding risk influences outcome most. Therefore, it should be strived for immediate PCI in both the STEMI but also the NSTE-ACS group.

Effects of High-Dose Atorvastatin on Mortality of Patients with Acute Coronary Syndrome Treated with Percutaneous Coronary Intervention and Stent Implantation 065

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Background The PROVE-IT TIMI 22 trial showed that high-dose of atorvastatin (80 mg/day) started median 7 days after acute coronary syndrome (ACS) significantly reduce mortality and major cardiovascular events compared to a standard-dose regimen. However, recent guidelines only support certain treatment aims with respect to LDL-cholesterol, recommend that these aims should be reached as fast as possible but do not recommend the early use of a high-dose potent statin, which might guarantee to reach this goal in short time. In the present study we investigated the effect of immediate high-dose atorvastatin started on admission versus standard therapy on all-cause mortality of patients with ACS in a "real-world" clinical setting.

Methods In total, 680 consecutive patients admitted to our department with the diagnosis of ACS (UA, NSTEMI, STEMI) who underwent PCI and stent implantation between January 1st, 2003 and December 31st, 2006 received either atorvastatin 80 mg/day on admission through 3 months followed by statin-treatment adopted to the aimed LDL-cholesterol level of 70 mg/dl (high-risk) to 100 mg/dl (medium- and low-risk) or standard statin-therapy. The median time of follow-up was 723 (390–1080) days. All-cause mortality was obtained from Statistics-Austria (STAT). To adjust for the potential bias inherent to the choice of either high-dose atorvastatin or standard-care, propensity score was calculated for each patient, which was included in the mulitvariate binary logistic regression analysis.

Results From the patient cohort, 40.4 % (n = 275) received high-dose atorvastatin, 50.1 % (n = 341) standard-statin-therapy and 9.4 % (n = 64) no statin at all. The clinical characteristics of patients with or without high-dose atorvastatin were significantly different with respect to age (60 y vs 62 y; p = 0.012), gender (female: 25.8 vs 36 %; p = 0.007), eGFR (95 ml/min vs 89 ml/min; p = 0.033), use of DES (34.5 vs 21.1 %; p < 0.001), betablockers (89.8 % vs 81.9 %; p = 0.009), existence of diabetes mellitus (15.3 vs 20.0 %; p = 0.035), and history of previous myocardial infarction (4.7 vs 12.3 %; p = 0.001), respectively. All-cause mortality rate of patients treated with high-dose atorvastatin was significantly lower compared to patients with standard-care (3.6 vs. 9.6 %; p = 0.004). In binary logistic regression analysis including treatment-groups and propensity score, high-dose atorvastatin was associated with significantly better outcome (OR: 2.22 [0.97–5.07]; p = 0.05).

Conclusion Our data suggest that high-dose atorvastatin treatment started in the acute phase of ACS and maintained for 3 months significantly reduces all-cause mortality in a "real-world" clinical setting and should be used more frequently.

Effect of Organized Network Formation on Time to Treatment and In-Hospital Mortality of Patients with ST-Elevation Myocardial Infarction (STEMI) 071

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Background and Aim Previously we could show that formation of a local network to optimize treatment of STEMI in Vienna dramatically reduced in-hospital and 1-year mortality. In this retrospective analysis we were interested whether pain-to-FMC, FMC-to-treatment and the total ischemic time (pain-to-treatment) changed between the first 18 months (January 1st, 2003–June 30th, 2004) and the second 18 months (July 1st, 2003–December 31st, 2005) of a functioning network.

Results The clinical characteristics of patients were not statistically different between the two time-periods. The median times from onset of pain-to-FMC decreased significantly (from 115 min to 88 min; p < 0.001). While in the first 18 months 58.4 % of patients contacted the network within 2 h after onset of pain, this value increased to 64.7 % during the second 18 months (p = 0.02). Median FMC-to-treatment also decreased significantly from 180 min to 120 min (p < 0.001). More importantly, the percentage of patients who received treatment within two hours of onset of pain increased from 22.3 to 41.8 % between the respective periods (p < 0.001). Accordingly, also total ischemia time decreased from 180 to 130 minutes (p < 0.001). The reduction of treatment delays was accompanied by a reduction of in-hospital mortality from 10.2 % to 6.4 % in the second time period (p = 0.02).

Conclusion Organization and permanent improvement of a local system of care leads to a significant reduction of delay times until treatment and is paralleled by a continuous reduction of in-hospital mortality.

Prediction of Cardiogenic Shock Using Plasma NT-proBNP Concentrations in ST-Elevation Myocardial Infarction: a Substudy of ASSENT IV-PCI 072

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Background Cardiogenic shock is one of the major causes of death in ST-elevation myocardial infarction (STEMI). We investigated in the present study, whether determination of NT-proBNP in the acute phase of STEMI could be used for identification of patients who develop cardiogenic shock.

Methods Plasma NT-proBNP was available in 1,014 STEMI patients when pts were randomized to primary PCI) or to full-dose tenecteplase prior to PCI (fPCI). The study endpoint for the present analysis was in-hospital cardiogenic shock defined as systolic blood pressure less than 90 mmHg for at least 30 min (or the need for supportive measures to maintain a systolic blood pressure of greater than 90 mmHg) in the presence of a heart rate of more than 60 bpm and in association with signs of hypoperfusion (cool extremities, or urinary output of less than 30 mL/h or mental confusion, or both); or (2) a cardiac index of less than 2.2 L/min/m^2 in the presence of a pulmonary capillary wedge pressure of more than 15 mm Hg. Optimal cut-off concentrations of NT-proBNP were calculated using classification and regression tree analysis (CHAID).

Results In addition to the 7 seven patients who were in cardiogenic shock at randomization, 59 (5.7 %) patients developed cardiogenic shock during index hospitalization and according to CHAID analysis, patients with NT-proBNP concentrations of > 694 pg/ml were at highest risk (12.18 % vs 4.22; $p < 0.001$) for shock irrespective of TIMI flow at diagnostic angiogram or time to reperfusion. In multivariate Cox-regression analysis, the systolic blood pressure lower than 100 mmHg at admission (0.27 [0.13–0.56]; $p < 0.001$), the patient's age > 65 y (2.34 [1.31–4.20]; $p = 0.004$) and admission NT-proBNP concentration (HR: 2.29 [1.30–4.03]; $p = 0.004$) were independent predictors of in-hospital cardiogenic shock.

Conclusion Early determination of plasma NT-proBNP concentrations in STEMI strongly predicts cardiogenic shock and might be used in addition to clinical characteristics to estimate the risk of STEMI patients to develop cardiogenic shock.

„Pseudo-NSTEMI": Anteil verschlossener Gefäße in NSTEMI-Patienten, die von rascher Reperfusion profitieren würden 172

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Hintergründe Die Behandlung der NSTEMI-Patienten sieht in der Mehrzahl der Fälle ein früh-invasives Vorgehen innerhalb von 24–72 h vor. Im Gegensatz dazu werden STEMI-Patienten bevorzugt einer primär-perkutanen Koronarintervention (PCI) zur raschest möglichen Reperfusion zugeführt. Über den Anteil verschlossener Gefäße unter den NSTEMIs in der täglichen Praxis gibt es wenig Information.

Methodik Es wurden Akut-Koronarangiographiebefunde unserer Abteilung aus den Jahren 2005–2008 analysiert. Wir untersuchten alle Patienten, die in unserer Datenbank nicht als STEMI klassifiziert wurden und identifizierten NSTEMI–Patienten anhand der Koronarangiographiebefunde, EKGs und einer Troponinerhöhung. Danach wurden die schuldigen Gefäße und der Anteil der präinterventionellen Gefäßverschlüsse (TIMI-Fluss 0–1) identifiziert.

Ergebnisse Es wurden 583 Akut-Koronarangiographien im Beobachtungszeitraum durchgeführt, davon waren 162 (27,8 %) NSTEMIs. Schuldige Gefäße konnten in 124 (76,5 %) identifiziert werden. In 61 Patienten (37.7 %) mit NSTEMI wurden akute Verschlüsse (TIMI 0–1) diagnostiziert (**Tabelle 1**).

Von den 36 RCA-Läsionen waren 11 im Bereich des R. posterolateralis (6,8 % der NSTEMIs), davon 7 verschlossen (11,5 % der Verschlüsse).

Verschlüsse im posterioren Stromgebiet (RCX und R. posterolateralis) machten 16,7 % aller NSTEMIs und 44,3 % (n = 27) aller Verschlüsse aus.

Schlussfolgerungen Akute Gefäßverschlüsse fanden sich in 38 % (n = 61) der NSTEMIs an unserer Abteilung. Sie verteilten sich gleichmäßig auf die 3 Hauptgefäße.

Dieser hohe Anteil weist darauf hin, dass viele NSTEMI-Patienten einer zeitgerechten Reperfusion entgehen und als Pseudo-NSTEMIs betrachtet werden können.

Routinemäßiges Aufzeichnen der EKG-Ableitungen V7–V9 sollte die Diagnostik der True-Posterior-STEMIs, bedingt durch RCX- und R. posterolateralis-Verschlüsse (44 % aller Verschlüsse in unserem Kollektiv), verbessern.

Der hohe Anteil an Verschlüssen in LAD (28 %) und RCA (33 %) trotz fehlender ST-Hebungen streicht die limitierte Sensitivität der EKG-Diagnostik heraus. Unsere Ergebnisse zeigen, dass viele NSTEMI-Patienten von einer früher als üblichen PCI profitieren würden.

Tabelle 1: F. Weidinger et al.

Schuldiges Gefäß	% aller NSTEMIs	n	% aller Gefäß-verschlüsse	n
RCX	25,3	41	32,8	20
RCA	22,2	36	32,8	20
LAD	24,7	40	27,9	17
R. intermedius	3,1	5	4,9	3
> 1 Gefäß	1,2	2	1,6	1
Nicht identifizierbar[1]	23,5	38	–	–
GESAMT	100	162	100	61

[1] Nicht identifizierbare Gefäße: vorbekannte Verschlüsse: 3,7 % (n = 6); signifikante Hauptstammstenosen: 5,6 % (n = 9); blande/nicht-signifikant veränderte Koronarien: 14,2 % (n = 23)

Basic Science

Loss of High Molecular Weight von Willebrand Multimeres in Aortic Stenosis Impairs Mainly Platelet Aggregation 122

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Background It has been shown that severe degenerative aortic valve stenosis is associated with low levels of the high-molecular-weight von Willebrand factor (VWF) multimeres, causing an increased risk of bleeding. We investigated if the deficiency of large VWF multimeres affects platelet adhesion, or aggregation, or both.

Patients and Methods We studied 57 patients with severe aortic stenosis before and 6 (median, 3–9 months) after valve replacement. VWF multimeres were separated on SDS-agarose low resolution gels (1.2 % agarose) and blotted on a PVDF membrane, platelet function was assessed under high shear stress conditions using the PFA-100 and the cone and plate analyzer Impact-R.

Results All patients had low levels of high-molecular-weight VWF multimeres before the operation and these VWF multimeres increased significantly thereafter ($p < 0.0001$). The PFA-1000 closure time of collagen-ADP cartridges was prolonged before the operation and improved significantly thereafter ($p < 0.0001$). In order to differentiate if the prolonged closure time was due to impaired

adhesion, impaired aggregation or both, we studied platelet adhesion and aggregation separately. Adherence and size of aggregates were slightly impaired before valve replacement and normalized thereafter. In vitro exposure of blood to ADP and subsequent application of high shear revealed reduced platelet aggregation before valve replacement that improved significantly thereafter ($p = 0.002$).

Conclusions The loss of high-molecular-weight VWF multimers in patients with aortic stenosis impairs platelet aggregation.

Aortic Valve Replacement in Patients with Severe Aortic Stenosis Corrects Only Partially the Formation of Platelet-Monocyte Heterotypic Aggregates 124

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Background It has been shown that severe aortic valve stenosis is associated with low levels of the high-molecular-weight Willebrand factor multimeres, rendering patients to an increased risk of bleeding. We were interested to evaluate if aortic valve replacement not only improves levels of high-molecular-weight Willebrand factor multimeres but also reduces the formation of platelet-monocyte heterotypic aggregates, which are considered to indicate platelet participation in inflammation.

Patients and Methods We studied 57 patients with severe aortic stenosis before and median 6 months (4–8 months) after valve replacement. VWF multimeres were separated on SDS-agarose low resolution gels (1.2 % agarose) and blotted on a PVDF membrane, platelet-monocyte heterotypic aggregates were determined by flow cytometry.

Results At the follow-up evaluation high-molecular-weight Willebrand factor multimers increased significantly ($p < 0.0001$ each). Platelet-monocyte heterotypic aggregates were above the normal range (< 36 %) in 52 patients before the operation. After valve replacement, still 40 patients had elevated levels of monocytes with adhering platelets. Indeed, in eleven patients the number of platelet monocyte aggregates was even higher after valve replacement than before surgery. Overall, we still noted a significant decrease of platelet-monocyte heterotypic aggregates ($p = 0.003$).

Conclusions These data indicate that aortic valve replacement induces normalization of high-molecular-weight Willebrand factor multimeres, but only partially corrects the increased inflammatory platelet response.

Interleukin-33 Increases Pro-Inflammatory Mediators in Human Endothelial Cells but Not in Smooth Muscle and Cardiac Cells 121

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Background Interleukin- (IL-) 33 is the most recently described member of the IL-1 family of cytokines and is a ligand of the ST2 receptor. IL-33 is produced as a 30 kD propeptide, and is cleaved by caspase-1 to generate a mature, secreted 18 kD form. Whereas IL-1β and IL-18 promote proinflammatory and T helper type 1 (Th1) lymphocytes-associated responses, IL-33 leads to the production of Th2-associated cytokines and increased serum immunoglobulin levels in mice. In addition to promoting Th2 responses, IL-33 exhibits pro-inflammatory potential by inducing pro-inflammatory cytokine production in human mast cells, eosinophils, and basophils. Influence of mature IL-33 on pro-inflammatory cytokine production, such as IL-6, IL-8, or monocyte chemoattractant protein-1 (MCP-1) in human cardiac and vascular cells was never studied before.

Methods Human coronary artery endothelial cells (HCAEC) or human coronary artery smooth muscle cells (HCASMC) were isolated from pieces of coronary arteries obtained from patients undergoing heart transplantation. Primary human adult cardiac myocytes (HACM) and human adult cardiac fibroblasts (HACF) were isolated from human hearts. Human umbilical vein endothelial cells (HUVEC) were isolated from fresh umbilical cords. Such cells were treated with recombinant human (rh) IL-33 at concentrations between 100 ng/mL and 1 ng/mL for time periods between 2 hours (h) and 48 h. IL-6, IL-8 and MCP-1 proteins were measured in cell culture supernatants using specific ELISAs (all from Bender MedSystems Diagnostics GmbH, Vienna, Austria). Specific mRNA level for IL-6, IL-8, MCP-1 and ST2 and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) mRNA expression were determined by real-time PCR.

Results We found that HCAEC, HUVEC, HCASMC, HACM and HACF expressed ST2 receptor on the level of specific mRNA. rhIL-33 significantly increased IL-6, IL-8 and MCP-1 protein production in both types of endothelial cells, but not in smooth muscle cells, cardiac myocytes or fibroblasts. IL-6 protein increased up to 20-fold in HCAEC and up to 4.5-fold in HUVEC; IL-8 production was up-regulated up to 3-fold in HCAEC and up to 2.3-fold in HUVEC; and MCP-1 protein increased up to 2.5-fold in HCAEC and up to 3.8-fold in HUVEC after incubation with 100 ng/mL of IL-33 for 48 h. The effect of IL-33 on pro-inflammatory protein production was dose-dependent. IL-33 up-regulated also IL-6, IL-8 and MCP-1 mRNA level in HCAEC and HUVEC between 2 h and 24 h of incubation, but not in HCASMC, HACM or HACF.

Conclusion We found that IL-33, a novel member of the IL-1 family of cytokines, is an inducer of IL-6, IL-8 and MCP-1 production in human endothelial cells from both coronary artery and umbilical vein, but not in smooth muscle or cardiac cells. Such differential effect of IL-33 on these pro-inflammatory cytokines production could be, at least in part, the explanation for previously described different roles of this novel cytokine during inflammatory, allergic, or cardiovascular pathologies.

A Novel Cytokine Interleukin-33 is Up-Regulated by Fluvastatin in Human Cardiac Fibroblasts: a New Mechanism for Cardioprotective Action of Hydroxymethylglutaryl-Coenzyme A Reductase Inhibitor? 123

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Background Interleukin- (IL-) 33 (described previously as nuclear factor-high endothelial venules [NFHEV]) is the most recently described member of the IL-1 family of cytokines and is a ligand of the ST2 receptor, which has a transmembrane ST2 (ST2L) and a soluble ST2 (sST2) isoform. Serum sST2 levels predict outcome in patients with myocardial infarction or heart failure. Recently, components of ST2/IL-33 system were shown to be expressed in rat neonatal cardiac fibroblasts [Sanada et al. J Clin Invest 2007], and in normal and pressure overloaded human myocardium [Bartunek et al. JACC 2008]. IL-33 was also shown to be cardioprotective via its anti-hypertrophic effects in vitro and in vivo [Sanada et al. J Clin Invest 2007]. Hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors or statins, an established class of drugs for the treatment of hypercholesterolemia, were found to attenuate myocardial hypertrophy both in vitro and in vivo. The aim of this study was to investigate the expression of IL-33, ST2L and sST2 in human adult cardiac fibroblasts, and the influence of fluvastatin on IL-33 production in these cells.

Methods Primary human adult cardiac fibroblasts (HACF) were isolated from human hearts obtained from patients undergoing heart transplantation. Such cells were treated with fluvastatin at the concentrations from 0.5 μM to 5 μM for different time periods. IL-33 protein in cell lysates and cell culture supernatants, and sST2 protein in cell culture supernatants were measured by specific ELISAs (both from R&D Systems, Minneapolis, MN). IL-33 mRNA, ST2 mRNA and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) mRNA expression were determined by real-time PCR.

Results We found that human cardiac fibroblasts constitutively expressed ST2 and IL-33 on the level of specific mRNA as shown by real-time PCR, and intracellular IL-33 on the protein level as measured by specific ELISA in total cell lysates. Fluvastatin, at concentrations from 1.25 μM to 5 μM, significantly increased intracellular IL-33 protein expression up to 3-fold after 48 hours of incubation. 0.5 μM fluvastatin also up-regulated specific IL-33 mRNA 9-fold in HACF after 72 hours of incubation. In cell culture supernatants of HACF, sST2 protein was undetectable both in untreated or fluvastatin-treated cells.

Conclusion We found that human cardiac fibroblasts constitutively express ST2 and IL-33 on the level of specific mRNA, and intracellular IL-33 on the protein level. Fluvastatin significantly increased IL-33 protein and mRNA expression in HACF. As IL-33 was previously shown to have cardioprotective effect in vitro and in vivo, one could speculate that such up-regulation of IL-33 expression could be a novel mechanism contributing to known cardioprotective effects of statins. The effects of different HMG-CoA reductase inhibitors on IL-33 and ST2 expression in vivo as well as a role of intracellular IL-33 need further investigations.

Differential Proteomic Profiling of Coronary Stent Thrombosis versus Atherothrombosis 038

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Purpose Coronary stent implantation is reducing the risk of major adverse cardiac events. However, the occurrence of stent thrombosis (ST) remains a severe complication that results in abrupt coronary artery closure and acute myocardial infarction (AMI). The underlying molecular and cellular mechanisms of ST are not fully understood.

Methods We compared thrombus aspirated from the site of plaque rupture of 34 patients with ST and 39 patients with AMI due to atherosclerotic occlusion within a native coronary artery (time from first medical contact to balloon inflation 89 ± 12 vs 81 ± 16 minutes) by proteomic profiling.

Results While leukocytes were low at the culprit site in ST (–0.48 ± 2.45 G/L), they accumulated at the site of atherosclerotic plaque rupture (1.71 ± 4.41 G/L; p = 0.019). In contrast to native thrombus, stent thrombus was characterized by high levels of von Willebrand factor, and platelet specific proteins e.g., Platelet glycoprotein I beta and Platelet glycoprotein IX and Platelet factor IV. Local complement activation was not detected in ST, with low levels of C-reactive protein, serum amyloid P, cell adhesion molecules, and low levels of other mediators of inflammation.

Conclusion Our results demonstrate different proteomic patterns in stent thrombus compared with native coronary artery thrombus, displaying proteins involved in platelet aggregation rather than inflammation.

Neutrophil Accumulation at the Site of Plaque Rupture is Associated with Enzymatic Infarct Size and N-Terminal pro B-natriuretic Peptide Levels 051

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Background The association of systemic inflammation with adverse outcome in acute myocardial infarction (AMI) has been shown. Our group has previously demonstrated an association between local neutrophil accumulation (LNA) at the site of plaque rupture and ST-segment resolution. The aim of the present study was to assess the effect of LNA on enzymatic infarct size and N-terminal pro B-natriuretic peptide (NT-proBNP) levels.

Patients/Methods In this prospective study we determined LNA of 153 patients admitted to the catheter laboratory in the setting of an acute myocardial infarction. Enzymatic infarct size (creatine phosphokinase maximum [CKmax]) was measured at the index hospitalization. At 6-month follow-up plasma NT-proBNP levels were determined. Primary study endpoint was the relationship between local neutrophil accumulation (i.e., ratio of culprit site/systemic leukocyte numbers) and CKmax.

Results The degree of LNA (detected in 75 patients) correlated significantly with CKmax (r = 0.176; p = 0.036). At 6 months (162 ± 98 days), patients with LNA had a significantly higher NT-proBNP level (4710 ± 8527 pg/ml) compared with patients without LNA (987 ± 2265 pg/ml; p = 0.046).

Conclusions The association between LNA with enzymatic infarct size reveals a pivotal role of culprit lesion neutrophils in final infarct size, and eventually, heart failure after myocardial infarction.

Values for Free Intracellular Myocardial Magnesium Differ Between Species and Depend on the Method of Assessment 054

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Intracellular free Mg is difficult to measure. Values differ according to method of measurement chosen. Hess, Metzger and Weingart measure an (Mg)i of 3.0 mM in ferret ventricular muscle. Using the same technique, we measured a free intracellular Mg in guinea-pig papillary muscle using ion-selective microelectrodes ETH 1117 of 2.74 + 0.16 mM (n = 7; + SEM). Using ETH 5214 in the same tissue, under the same experimental conditions, we assessed (Mg)i at 0.84 + 0.10 mM and, likewise, using ETH 7025 (Mg)i was 0.73 + 0.08 (n = 7; + SEM) in the same type of tissue. These values are similar to those assessed earlier in sheep Purkinje fibre by Gasser & Vaughan Jones and ferret papillary muscle by Blatter & McGuigan.

In order to look whether or not there are species differences of (Mg)i values we also have investigated (Mg)i resting levels in rat papillary muscle under the same experimental conditions and found it to be 0.53 + 0.06 (n = 7; + SEM). The values measured for (Mg)i amount to approximately the same values as those recommended as "within the normal range" in the serum (0.7–1.0 mM). Calculating from the Nernst equation, the equilibrium potential then would be around 0 mV, thus indicating equal distribution of Mg in both extracellular and intracellular space. For our experiments, it would be between +2 and +4 mV using ETH 5214 and ETH 7025. These findings would be in contrast with our measurements using ETH 1117, which would suggest an equilibrium potentia1 for Mg of –12.9 mV. In the present investigation, we show measurements of free intracellular Mg in two different tissues – rat and guinea-pig papillary muscle using the new Mg-selective neutral carrier ETH 7025 and find (Mg)i slightly lower (0.5 mM) in rat than in guinea-pig (0.7 mM). Both measurements indicate somewhat smaller values for (Mg)i than a mean value (1.4 + 0.2 mM) which we have calculated from 18 different publications using various techniques (references with the author). These results are in agreement with measurements of Gupta et al. who measured (Mg)i in guinea-pig muscle with 31p-NMR at 0.8 mM. Hu, using the same method, in rat found 0.5 mM. Interestingly, (Mg)i values of the same magnitude have already been calculated for rat myocardium by England et al as early as 1967 using the Mg-dependence of citrate/isocitrate, whereas later studies using Mg-efflux and microelectrodes found values between 3 and 4 mM. In summary, free intracellular Mg is difficult to detect and varies according to both the method and species used.

An Ion-Selective Microelectrode Study on the Effect of Acidification on Free Intracellular Magnesium Cardiac Guinea Pig Papillary Muscle 059

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It has been argued that a rise in free, unbound, intracellular magnesium (Mg2+i) could be beneficial during myocardial ischemia,

effecting the regulation of certain enzymes, the rectification of channels as wee as intracellular Na+ and Ca2+. Mg2+ is a co-factor of the Na/K-ATP-ase, competes with Ca2+ at the contractile apparatus etc. However, all of these properties are confined to the intracellular site. The present study investigates the effect of pH upon intracellular concentrations of Mg2+. Here we studied Mg2+i with Mg2+-selective microelectrodes (ETH 7025) in isolated guinea pig papillary muscle. Free intracellular Mg2+i in guinea-pig papillary muscle was 0.73 + 0.08 (n = 7; + SEM) in the same type of tissue. These values are similar to those assessed earlier in sheep Purkinje fibre and ferret papillary muscle.

In the present experiments we also changed extracellular pH from 7.4 to 6.4 and back to 7.4. In the same experiments, pHi has been measured using a pH-sensitive microelectrode in order to asses the change of pHi brought about by changing extracellular pH. This manoeuvre led to a change of pHi from a resting level of 7.19 + 0.03 (n = 7; +SEM) to 6.81 + 0.06 (n = 7; +SEM). These changes of pHi led to a small but consistent rise of intracellular Mg2+. In 7 experiments Mg2+i rose by 0.19 + 0.06 mM (+SEM) from an initial value of 0.73 + 0.21 mM. The small rise of Mg2+i is likely to result from ionised Mg2+ being liberated from the Mg-ATP-complex. Interestingly, despite pH had remained low, after about 7 minutes Mg2+i returned to normal levels. This observation indicates that intracellular regulation of Mg2+i is slow but operational at even very small changes of Mg2+i suggesting that Mg2+i levels are regulated within a very narrow band in order to guarantee its multifaceted intracellular biological activity.

Intracellular Magnesium during Simulated Ischemia in Isolated Guinea Pig Papillary Muscle 060

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Early animal studies and population based trials have shown that sufficient nutritional Mg supply is pivotal for myocardial function. Mg-free diet leads to myocardial necrosis and death of laboratory animals. Prospective clinical trials investigating possible benefits of supplemental administration of intravenous Mg in patients with ST-elevation myocardial infarction were controversial in outcome. Both intracellular Mg homeostasis and transmembrane Mg transport during myocardial ischemia have not been well understood as yet. Hence, the interpretation of the conflicting results from clinical trials remains difficult.

Here, we study free, unbound as well as total myocardial Mg during myocardial ischemia using different techniques. In guinea pig papillary muscle, using Mg-selective intracellular microelectrodes, we measure intracellular, free, unbound, biologically active Mg (Mg2+i) and, simultaneously, we assess free Mg2+ at the surface of the preparation (Mg2+s) during the same experiment, also using specific, Mg-selective microelectrodes pressed on the surface of the preparation.

In isolated guinea pig Langendorff perfused hearts, we use atomic absorption spectroscopy in order to measure total Mg (Mgtot) content of the left-ventricular myocardium after 28 minutes of hypoxia and metabolic inhibition with 2-deoxyglucose. In the same Langendorff-perfused hearts, Mg2+ is measured in the effluate (Mg2+e) using a Mg2+-selective macroelectrode (AVL) during hypoxia and metabolic inhibition.

In summary, we find that free intracellular Mg2+ (Mg2+i) rises during myocardial ischemia, while total Mg-content (Mgtot) of the ischemic tissue falls. Furthermore, we see a concomitant rise of Mg2+ concentrations at the surface (Mg2+s) of the preparation as well as in the effluate (Mg2+e) from the ischemic tissue. We conclude that, during hypoxia, simulated ischemia and metabolic inhibition, Mg2+ is liberated from intracellular binding sites and is extruded from the cell.

The Formation of Monocyte-Platelet Aggregates is Independent of On-Treatment Residual Agonists'-Inducible Platelet Reactivity 171

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Background Circulating monocyte-platelet aggregates (MPA) are a sensitive marker of in vivo platelet activation and patients with atherosclerotic vascular disease exhibit higher levels of MPA. Clopidogrel has been shown to reduce MPA formation in these patients to a greater extent than aspirin. However, response to clopidogrel and aspirin shows a wide variability, and patients with high on-treatment residual platelet reactivity are at an increased risk for adverse events after coronary stenting. We therefore investigated the association of MPA with on-treatment residual agonists´-inducible platelet aggregation in 125 patients on dual antiplatelet therapy after peripheral, coronary or carotid artery stenting.

Methods MPA were characterized by co-expression of monocyte marker CD14 and platelet-specific markers (CD42b and CD62P) by whole-blood flow cytometry. Platelet reactivity was determined by light transmission aggregometry, the VerifyNow P2Y12 and aspirin assays, and the vasodilator-stimulated phosphoprotein phosphorylation assay. Cut-off values for residual platelet reactivity were defined according to quartiles of each assay.

Results The extent of MPA formation showed no significant differences between patients without and with residual ADP-inducible platelet reactivity, and between individuals without and with residual arachidonic acid (AA)-inducible platelet reactivity. Even patients with combined on-treatment residual ADP- and AA-inducible platelet reactivity did not exhibit significantly higher levels of MPA than patients without any on-treatment residual platelet reactivity.

Conclusion The formation of MPA is independent of on-treatment residual ADP- and AA-inducible platelet reactivity.

Migration of Cardiac Injected Porcine Mesenchymal Stem Cells in Remote Healthy Organs: Comparison of Intracoronary and Intramyocardial Delivery 114

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Background Male porcine bone marrow-derived mesenchymal stem cells (MSC) were transiently transfected with luciferase (Luc) and green fluorescent protein (GFP) (Luc-GFP-MSC) for tracking cardiac delivery of MSCs to the myocardium and remote organs after intramyocardial or intracoronary delivery.

Methods Closed-chest, reperfused myocardial infarction (MI) was created in female domestic pigs. The male Luc-GFP-MSC (8.4 ± 1.3 × 10^6) were delivered either transendocardially in the infarct border zone or intracoronarilly in the open infarct-related artery 20 ± 3 days post-MI in female pigs. Tissue samples were collected 3 h, 24 h, and 7 days post-delivery from the myocardium and non-cardiac organs (lung, liver, spleen, lymphatic node, kidney, bone marrow). Tissue luciferase activity was measured in the homogenized tissues using dual-luciferase reporter assay. Quantitative TaqMan polymerase chain reaction (PCR) was performed in the female hearts and remote organs to detect the sex-mismatch MSC.

Results The highest luciferase activity was found in the intramyocardial injection sites at 3 h post delivery (528 ± 448 relative light units (RLU)/ per µg protein) and decreased to 382 ± 109 and 162 ±

58 RLU/µg protein at 24h and 7 days, respectively. Significantly less Luc-GFP-MSC was retained 3 h, 24 h and 7 days after intracoronary delivery (124 ± 8, 96 ± 46 and 76 ± 38 RLU/ per µg protein; p = 0.031, p = 0.021 and p = 0.048, respectively). On day 7, 0.5–2.7 % of totally injected Luc-GFP-MSC was found in all non-cardiac organs, with no difference between intramyocardial or intracoronary administration. PCR confirmed the presence of male Luc-GFP-MSC in female infarcted hearts 24 h post-injections by both delivery methods.

Conclusions Intramyocardial delivery of MSC is more effective in cell retention in the infarcted myocardium as compared to intracoronary delivery. Reporter gene method is a useful means to track the biodistribution of the transplanted cells quantitatively.

Myocardial Reperfusion Injury in Bone Marrow Chimeric PI3Kgamma Knock-Out Mice 006

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Introduction PI3Kγ functions within the immune compartment to promote inflammation in response to G-protein-coupled receptor agonists. PI3Kγ also acts within the heart itself as a negative regulator of cardiac contractility and as a pro-survival factor.

To directly test whether the in vivo effects of PI3Kγ during myocardial ischemia/reperfusion are due to its function in the immune system or in the myocardium, we generated bone marrow (BM) chimeras.

Methods Freshly isolated total host bone marrow cells were injected into the lateral tail vein of syngenic recipient mice 24 hours after irradiation. PI3Kγ–/–(KO) rodents carrying PI3Kγ+/+(WT) bone marrow and vice versa were then tested using our reversible coronary artery ligation model.

Results PI3Kγ mutant mice receiving PI3Kγ WT bone marrow exhibited severe infarction (WT-BM → KO: 1.02 ± 0.19 vs KO-BM → WT: 0.64 ± 0,19 mm²; p < 0.05; n = 7 per group) and markedly increased Troponin T release (WT-BM → KO: 3.27 ± 1.9 vs KO-BM → WT: 1.01 ± 0.31 ng/ml; p < 0.05; n = 7 per group) following ischemia/reperfusion injury compared to WT rodents with KO bone marrow. This greater extent of myocardial damage in the KO cohort was further confirmed by a greater loss of fractional shortening after 1 week of reperfusion.

PI3Kγ+/+ (WT-BM → WT) and PI3Kγ–/– (KO-BM → KO) controls confirmed that PI3Kγ is beneficial during ischemia/reperfusion injury. Western blotting and immunohistochemical analysis revealed Akt/PKB and ERK as crucial cardiac downstream targets of PI3Kγ in our experiments.

Conclusion We found that disrupting PI3Kγ function in the immune system using bone marrow chimeric mice had no protective effect on myocardial ischemia/reperfusion injury. PI3Kγ seems to be the key kinase that mediates activation of the pro-survival Akt/PKB and ERK pathway at the site of cardiac injury.

MKK7 Modulates the Cardiac Response to Chronic Pressure Overload 007

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Background Mitogen-activated protein kinase kinase 7 (MKK7) phosphorylates and thereby activates the crucial c-Jun N-terminal kinases (JNKs) in cardiomyocytes. This highly conserved pathway is suggested to be involved in a broad range of physiological functions, including cardiovascular homeostasis.

The precise in vivo cardiac role of MKK7 using muscle-restricted MKK7 knock-out (KO) rodents remaines unclear.

Methods Therefore, mice carrying a conditional MKK7 gene were generated. Crossbreeding with Mck-Cre positive rodents assured a muscle-restricted MKK7 KO model. We used cardiovascular magnetic resonance, echocardiography, and histological methods to characterize the transgenic phenotype. In addition, the transaortic constriction procedure facilitated the examination of mutagenic hearts upon cardiac stress.

Results At the age of 8 weeks, MKK7 KO hearts presented a markedly decreased contractility compared to WT mice (fractional shortening: KO 30.8 ± 2.1 vs WT 44.3 ± 3.0 %; p = 0.001; n = 9 per group). This was further combined with a significant left ventricular dilatation, independent of the cardiac cycle.

Upon 7 days of transaortic constriction, MKK7 KO mice but not WT rodents developed heart failure with a marked increase of the left ventricular systolic and diastolic diameter (LVESD: KO 3.1 ± 0.2 vs WT 1.4 ± 0.1 mm; p = 0.001; LVEDD: KO 4,2 ± 0.2 vs WT 2.8 ± 0.2 mm; p = 0,001; n = 7 per group). Whereas the WT cohort slightly gained contractility, the function of KO hearts further significantly deteriorated after constriction of the aorta.

Moreover, histological analysis revealed a dilated phenotype following 7 days of pressure overload.

Conclusion Our in vivo data demonstrate for the first time, that the muscle-restricted loss of MKK7 leads to a significant reduction of cardiac functions and heart failure upon cardiac pressure overload, respectively. This implies a distinct role of MKK7 in cardiac stress adaptation.

JTV 519 Attenuates Diastolic Sarcoplasmic Reticulum Calcium Leak Induced by Na Accumulation in Cardiomyocytes 143

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Diastolic calcium (Ca) leak from the sarcoplasmic reticulum (SR) Ca release channel (ryanodine receptor, RyR) promotes heart failure and arrhythmias. JTV519 has been shown to stabilize RyR and decrease Ca leak from the SR in conditions of protein kinase A- (PKA-) mediated hyperphosphorylation of the RyR ("leaky" RyR). However, arrhythmogenic Ca leak in cardiomyocytes is also observed in conditions of SR Ca overload following cytosolic Na ([Na]i) accumulation (mediated by the Na/Ca exchanger), as in heart failure, ischemia or digitalis toxicity. We investigated whether JTV519 attenuates RyR Ca leak independent of PKA-mediated effects on RyR gating.

Methods In electrically stimulated (1 Hz) murine cardiomyocytes, Ca transients, diastolic SR Ca leak (frequency of Ca sparks) and SR Ca content (Ca release during rapid caffein application, 30 mM) were measured using confocal microscopy (Ca-indicator Fluo4-AM). Na/K-pump inhibitor ouabain (OUAB, 100 µM) was used to increase intracellular Na as confirmed in parallel experiments using the Na indicator CoroNa (following calibration). Cells were studied in the absence (CTRL) and presence (JTV) of JTV519 (1 mM, > 1 h preincubation).

Results OUAB increased [Na]i from 13.5 ± 3.0 to 18.9 ± 2.8 mM (mean ± SE; p < 0.001). OUAB increased the systolic amplitude of the Ca transient (CaTsys, 5.1 ± 0.4 vs 3.4 ± 0.3 F/F0), diastolic spark frequency (132 ± 38*pL – 1*s – 1 in CTRL + OUAB vs 12 ± 7*pL – 1*s – 1 in CTRL) (both p < 0.05), and SR Ca content (8.0 ± 0.7 vs 6.4 ± 0.6 F/F0; p = 0.07) in CTRL. In JTV (without OUAB), spark frequency was lower than in CTRL (3.8 ± 2.9*pL – 1*s –1 ; p < 0.05). With ouabain (JTV + OUAB) spark frequency increased (20.4 ± 5.2*pL – 1*s – 1; p = 0.07), but remained significantly lower than in CTRL + OUAB. CaTsys (2.3 ± 0.3 F/F0) was significantly lower in JTV vs CTRL. In the presence of JTV, ouabain did not significantly change CaTsys (2.8 ± 0.2 F/F0 in JTV + OUAB; p = NS vs JTV) or SR Ca content (4.5 ± 0.4 in JTV + OUAB vs 4.8 ± 0.9 in JTV, F/F0); diastolic [Ca]i tended to be increased by OUAB.

Conclusion In summary, an increase in [Na]i leads to increased cytosolic [Ca] and diastolic Ca leak from the SR. In the presence of

JTV519, diastolic Ca leak from the SR is decreased. Our results suggest that the effect of JTV519 on SR Ca leak is independent of PKA-mediated effects on the RyR.

Kernhülle und nukleoplasmatisches Retikulum in Kardiomyozyten stellen einen funktionellen Kalziumspeicher zur lokalen Regulation der Kalziumkonzentration dar 070

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Hintergrund Die nukleoplasmatische Kalziumkonzentration ([Ca]) in Kardiomyozyten reguliert die Transkription und ist damit an zellulären Umbauprozessen (Remodelling) beteiligt, die in Hypertrophie und Herzinsuffizienz münden können. Wie genau die nukleoplasmatische [Ca] jedoch reguliert wird – möglicherweise unabhängig von der zytoplasmatischen [Ca] – ist bisher unklar. Wir charakterisierten daher die perinukleären Ca-Speicher und deren Bedeutung für die Regulation nukleoplasmatischer [Ca]-Transienten in Vorhof- und Ventrikelmyozyten aus dem Säugerherzen.

Methoden Perinukleäre Ca-Speicher wurden in isolierten Vorhof- und Ventrikelmyozyten aus Kaninchen- und Mausherzen mit Hilfe des hochaffinen Ca-Indikators Fluo-4/AM (8 μM, 30–60 min) oder der niederaffinen Ca-Indikatoren Mag-Fluo-4/AM (10 μM, 30–60 min) und Fluo-5N/AM (10 μM, 120–150 min) beladen und konfokalmikroskopisch dargestellt. Für die elektronenmikroskopische Darstellung des sarkoplasmatischen Retikulums (SR) und der Kernhülle wurden humane Vorhoftrabekel verwendet. Die perinukleäre Expression von IP3-Rezeptoren (IP3R), wurde mittels Immunogold-Färbung untersucht. Nukleoplasmatische und zytoplasmatische [Ca]-Transienten wurden mit Hilfe der schnellen, zweidimensionalen Konfokalmikroskopie aufgenommen in elektrisch-stimulierten Kaninchen-Vorhofmyozyten, die mit Fluo-4/AM (8 μM, 20 min) beladen waren.

Ergebnisse Vorhofmyozyten besaßen einen, Ventrikelmyozyten 2 Zellkerne (n > 150). In unstimulierten Myozyten wurde durch Färbung mit Fluo-4, Mag-Fluo-4 oder Fluo-5N eine Kernhülle sowie tubuläre Strukturen sichtbar, die in den Zellkern ragten oder diesen durchquerten (nukleoplasmatisches Retikulum). Kaninchen-Vorhofmyozyten (n = 11) besaßen Zellkerne mit einer Länge von 11,2 ± 0,7 μm, einer Breite von 4,1 ± 0,3 μm und 3,9 ± 0,4 Tubuli pro Kern. Für Maus-Ventrikelmyozyten (n = 53) betrugen die Werte 15,3 ± 0,4 μm (Länge), 5,0 ± 0,2 μm (Breite) und 4,9 ± 0,1 Tubuli pro Kern. Schnelle Gabe von Koffein (20 mM; n = 7) führte zu einer reversiblen Abnahme der Mag-Fluo-4-Fluoreszenz von Kernhülle und nukleoplasmatischem Retikulum. Elektronenmikroskopische Aufnahmen humaner Vorhoftrabekel (n = 5) zeigten direkte Verbindungen von SR und Kernhülle sowie Invaginationen der Kernhülle in den Zellkern. IP3R wurden sowohl in der Kernhülle als auch an den Invaginationen nachgewiesen. Dabei war die Dichte der IP3R an der Innenseite der Kernhülle signifikant größer als an der Außenseite (n = 3 Kerne; $p < 0.05$). In isolierten Kaninchen-Vorhofmyozyten führte Endothelin-1 (0,1 nM) über eine Aktivierung von IP3R zu einem selektiven Anstieg der [Ca]-Transienten im Zellkern (n = 6).

Schlussfolgerung Vorhof- und Ventrikelmyozyten aus Säugerherzen (Kaninchen, Maus, Mensch) enthalten eine Kernhülle mit einem nukleoplasmatischen Retikulum. Dieses System ist direkt mit dem sarkoplasmatischen Retikulum verbunden und fungiert als perinukleärer Ca-Speicher. Über IP3R in der Kernhülle und dem nukleoplasmatischen Retikulum kann die lokale Ca-Freisetzung ins Nukleoplasma kontrolliert werden. Dadurch können nukleoplasmatische [Ca]-Transienten unabhängig von zytoplasmatischen [Ca]-Transienten reguliert werden.

Calmodulin und Ca^{2+}/Calmodulin-abhängige Proteinkinasen tragen zur dehnungsinduzierten Kraftantwort im humanen Vorhofmyokard bei 144

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Hintergrund Dehnung ist ein wichtiger Regulator der Herzfunktion. Im Vorhof verändert Dehnung die Kontraktilität und trägt zur Entwicklung von Vorhofflimmern bei. Die Effekte von Dehnung auf die Kontraktilität können Ca2+-abhängig und Ca2+-unabhängig sein. Wir verfolgten die Hypothese, dass die Ca2+-abhängigen Effekte über Calmodulin und Ca2+/Calmodulin-abhängige Proteinkinasen vermittelt werden.

Methoden Humane Vorhoftrabekel (Muskelstreifen) wurden aus rechten Vorhofohrpräparaten isoliert, welche zuvor im Rahmen von herzchirurgischen Eingriffen Patienten aus operationstechnischen Gründen entnommen wurden. Die Trabekel (n = 35; Durchmesser < 0,8 mm) wurden mit Bikarbonat-gepufferter Tyrode-Lösung umspült (37 °C) und elektrisch stimuliert (Stimulationsfrequenz 1 Hz). Isometrische Kontraktionen wurden mittels eines Kraftaufnehmers gemessen. Die Trabekel wurden auf 88 % ihrer optimalen Länge vorgedehnt und 30 min auf diesem Dehnungsniveau belassen. Eine Lastzunahme wurde durch Dehnung der Muskelstreifen von 88 % (L88) auf 98 % (L98) ihrer optimalen Länge simuliert.

Ergebnisse Dehnung führte zu einer biphasischen Kraftzunahme: einer sofortigen Zunahme (Frank-Starling-Mechanismus, FSM) auf ca. 180 % der Kraft bei L88, gefolgt von einer zusätzlichen verzögerten Kraftzunahme (5–10 min; „slow force response", SFR) auf ca. 125 % des FSM. Gepaarte Dehnungsprotokolle zeigten, dass sowohl der FSM als auch die SFR reproduzierbar waren (n = 8). Eine Hemmung von Calmodulin (mittels 10 μM W-7) beeinflusste sowohl den FSM (Zunahme von 174,3 ± 10,2 auf 187,0 ± 10,7 %; n = 10; $p < 0,05$) als auch die SFR (Abnahme von 123,1 ± 1,9 auf 118,1 ± 1,7 %; n = 10; $p < 0,01$). Demzufolge hemmen Ca2+/Calmodulin-abhängige Prozesse den FSM und fördern die SFR. Eine Hemmung der Ca2+/Calmodulin-abhängigen Proteinkinase II (CaMKII, mittels 10 μM KN-93) bewirkte eine ähnliche Erhöhung des FSM (von 175,1 ± 10,2 auf 193,2 ± 7,4 %; n = 10; $p < 0,05$), hatte jedoch keinen Effekt auf die SFR (129,7 ± 4,8 vs. 131,1 ± 5,6 %; n = 10; p = n. s.). Anderseits ließ eine Hemmung der Ca2+/Calmodulin-abhängigen Myosin-Leichtketten-Kinase (MLCK, mittels 10 μM ML-7) den FSM unbeeinflusst (189,1 ± 13,9 vs. 182,3 ± 16,8 %; n = 7; p = n. s.), während die SFR von 129,4 ± 5,7 auf 118,5 ± 4,3 % reduziert wurde (n = 7; $p < 0,05$).

Schlussfolgerung Dehnung führt im Vorhof zu einer biphasischen Kraftzunahme: dem FSM und der SFR. Beide Phasen der Kraftantwort werden durch Calmodulin reguliert. Die Ca2+/Calmodulin-abhängige Aktivierung der CaMKII hemmt den FSM, während die Ca2+/Calmodulin-abhängige Aktivierung der MLCK maßgeblich zur Kraftzunahme während der SFR beiträgt.

Ryanodin-Rezeptor-Expression und -Phosphorylierung während Betaadrenozeptor-vermittelter Arrhythmogenese im humanen Vorhofmyokard 128

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Hintergrund Eine Fehlfunktion des kardialen Ryanodin-Rezeptors (RyR2), d. i. der Ca-Freisetzungskanal des sarkoplasmatischen Retikulums (SR), wird sowohl für erworbene als auch für angeborene Arrhythmien verantwortlich gemacht. Bei chronischem Vorhofflimmern wurde eine Proteinkinase A- (PKA-) abhängige Hyper-

phosphorylierung des RyR2 am Ser2809 beschrieben. Ob diese Hyperphosphorylierung ursächlich für die Entstehung und Progression des Vorhofflimmerns ist, ist jedoch bis heute unklar. Wir untersuchten daher die RyR2-Expression und -Phosphorylierung am Ser2809 während Betaadrenozeptor-vermittelter Arrhythmien in isoliertem humanem Vorhofmyokard.

Methode Trabekel („Muskelstreifen", Durchmesser < 0,8 mm) aus dem rechten Vorhofohr von Patienten, die sich einer Bypass- oder Klappenersatzoperation unterzogen, wurden im Organbad (Tyrode-Lösung, 37 °C) mit 1 Hz elektrisch stimuliert. Die isometrische Kraftentwicklung wurde vor und nach Gabe des Betaadrenozeptor-Agonisten Isoprenalin (ISO) gemessen. Arrhythmien wurden als Anzahl der arrhythmischen Extra-Kontraktionen (AEK) quantifiziert. Im Anschluss an die funktionellen Messungen wurden die Trabekel schockgefroren für molekularbiologische Untersuchungen. Die Proteinexpression and -phosphorylierung des RyR2 am Ser2809 wurde mittels Immunoblot, die mRNA-Expression von Betaadrenozeptoren und Ca-regulierenden Proteinen mittels RT-PCR bestimmt.

Ergebnisse ISO (n = 49; [ISO] = 1 nM – 10 μM) verursachte in humanen Vorhoftrabekeln einen konzentrationsabhängigen positiv-inotropen Effekt (EC_{50}: 22 nM) und AEK (EC_{50}: 28 nM). Unbehandelte Kontroll-Trabekel (n = 18) zeigten keine AEK. ISO (0,1 μM) hingegen induzierte AEK in 66 % (23/35) der untersuchten Trabekel mit einer Frequenz von 30,8 ± 5,2 min^{-1} (n = 35). Koffein (1 mM) erhöhte die AEK-Frequenz auf 56,0 ± 4,2 min^{-1} (n = 34; p < 0,05), wohingegen Ryanodin (1 μM; n = 6) die AEK vollkommen unterdrückte. H-89 (10 μM), ein Hemmstoff der PKA, reduzierte die ISO-induzierten AEK, konnte sie jedoch nicht vollständig unterdrücken (23 % [3/13] der Trabekel mit AEK; AEK-Frequenz: 17,2 ± 9,5 min^{-1}; n = 13; p < 0,05 vs. ISO allein). ISO verursachte auch einen konzentrationsabhängigen Anstieg der RyR2-Phosphorylierung am Ser2809 (Verhältnis des phosphorylierten RyR2 zum Gesamt-RyR2) von 0,52 ± 0,07 (Kontrolle; n = 12) auf 0,82 ± 0,10 bei 0,1 μM ISO (n = 23) und auf 1,27 ± 0,33 bei 1 μM ISO (n = 9; beide p < 0,05 vs. Kontrolle). H-89 (10 μM) reduzierte den ISO-induzierten Anstieg der RyR2-Phosphorylierung. Trabekel mit und ohne ISO-induzierte AEK zeigten keinerlei Unterschiede hinsichtlich der Expression und Phosphorylierung des RyR2 oder hinsichtlich der mRNA-Expression der Beta1- und Beta2-Adrenozeptoren, des RyR2, des FKBP12.6, der SR-Ca-ATPase (SERCA2a), des Phospholambans und des sarkolemmalen Na/Ca-Austauschers (NCX1).

Schlussfolgerung In humanem Vorhofmyokard verursacht beta-adrenerge Stimulation RyR2-vermittelte arrhythmische Extrakontraktionen und einen Anstieg der RyR2-Phosphorylierung am Ser2809 über einen PKA-abhängigen Mechanismus. Die PKA-abhängige Phosphorylierung des RyR2 am Ser2809 kann zur Arrhythmogenese beitragen, sie ist jedoch nicht ausreichend für die Auslösung der Betaadrenozeptor-vermittelten Arrhythmien.

SLC2A4 and its Regulator Gene SLC2A4RG is not Affected by Experimental Ischemia 055

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Myocardial ischemia increases glucose uptake through translocation of GLUT1 and GLUT4 from an intracellular compartment to the sarcolemma. This appears to be beneficial during ischemia and possibly recovery. Earlier experiments of our group have shown that myocardial GLUT4 mRNA expression is in fact decreased in arterial hypertension compared to normal controls indicating a genuine association of arterial hypertension with decreased GLUT4 expression. Both insulin and ischemia have additive effects to increase in vivo glucose utilisation and augment glucose transporter translocation. Delivery of glucose to the glycolytic pathway appears to be a major controlling site of glycolysis in low-flow ischemia. While many experimental studies suggest that an increase in glucose uptake and metabolism by the ischemic myocardium helps to protect myocardial cells from irreversible injury, little is known in this context about human cardiac trans-membrane glucose transport, SLC2A4-expression and its regulation.

In human cardiac tissue (right auricle), using microarray technique we first look at general changes in expression profiles during simulated myocardial ischemia, the behaviour of SLC2A4 (GLUT4, solute carrier family 2 facilitated glucose transporter, member 4) as well as its regulator gene SLC2A4RG. Then, using Real Time PCR (Light Cycler), we quantify GLUT4 mRNA expression changes in 8 single experiments under ischemic and control conditions.

Using the microarray technique, we find that both the expression of GLUT4 gene (SLC2A4) and its regulator gene remain practically unchanged. In Real Time PCR (Light Cycler), the mean ratio for GLUT4 gene expression compared to the house keeping gene G6PDH was under well oxygenated conditions –0.0052 + 0.0203 and under N2-simulated ischemia 0.0179 + 0.0196 (n = 8; + SEM). No statistically significant difference could be found between the two groups. Results show a trend to a slight increase in expression, however no statistical significance was evident.

No significant changes are seen in the expression of the GLUT4 gene as well as in its regulatory gene after 30 minutes of N2-mediated experimental ischemia. Similarly, biological processes (microarray) involved in glucose metabolism are not significantly de-regulated as are others. This, as well as a slight trend towards up-regulation, can be interpreted as an attempt of the myocyte to maintain energy metabolism also under hypoxic conditions.

NT-proBNP after Acute Myocardial Infarction. Relation with Acute and Chronical Infarct Size and Myocardial Function 158

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Aim of the Study We sought to assess the relation of N-terminal brain natriuretic peptide (NT-proBNP) determined on day 3 after onset of acute myocardial infarction (AMI) symptoms with acute and chronic infarct size and functional parameters assessed by cardiac magnetic resonance (CMR) imaging. Furthermore, we investigated its predictive value on recovery of global and regional myocardial function.

Methods CMR was performed in 49 consecutive patients (42 male; mean age 56 ± 11.2 years) within 6 days, 4 and 12 months after first acute ST-elevation AMI and successful primary angioplasty. (Infarct size was determined on delayed Gadolinium-enhanced phase-sensitive IR-SSFP CMR sequences and parameters of regional myocardial function were calculated from short-axis cine MR sequences.) NT-proBNP was collected in the subacute phase at 66 ± 8 hours after admission.

Results Log-transformed NT-proBNP (lgNT-proBNP) significantly correlated with infarct size in % of left ventricular myocardial mass (all r = 0.60; all p < 0.004), with ejection fraction (EF) (all r > –0.49; all p < 0.01) as well as with segmental wall thickening (SWT; mm) (all r > –0.41; all p < 0.01) at any time of assessment. Patients with NT-proBNP concentrations lower than the mean level of 1115 pg/ml significantly improved EF and SWT (p < 0.001 and p < 0.01, respectively) during study period, whereas patients with NT-proBNP above 1115 pg/ml did not show significant functional recovery.

Conclusion NT-proBNP on day 3 after admission correlates with acute and chronical infarct size and myocardial function after AMI. Global and regional myocardial function do not recover in patients with NT-proBNP above 1115 pg/ml early after AMI.

Evaluation of the Association of Genetic Variants on the Chromosomal Loci 9p21.3, 6q25.1, and 2q36.3 with Angiographically Characterized Coronary Artery Disease 101

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Background The chromosomal loci 9p21.3, 6q25.1, and 2q36.3, represented by their respective leading variants rs1333049, rs6922269 and rs2943634, have been linked with a history of coronary artery disease (CAD) by genome-wide association studies. Whereas the association of variant rs1333049 with CAD was analysed in several subsequent studies, replication studies of variants rs6922269 and rs2943634 are missing. Furthermore, no direct association with coronary atherosclerosis has been established. We therefore aimed at investigating the association of the above variants with coronary atherosclerosis.

Methods We performed genotyping in two large cohorts of consecutive Caucasian patients undergoing coronary angiography for the evaluation of suspected or established stable CAD, comprising 671 and 940 patients, respectively, with a total of 1611 subjects.

Results In models of dominant inheritance, variant rs1333049 conferred a significantly increased risk of significant coronary stenoses with lumen narrowing ≥ 50 % in both study cohorts, with adjusted odd ratios (OR) of 1.71 (1.15–2.52); p = 0.007 and 1.55 (1.10–2.18); p = 0.012, respectively. Variant rs6922269 in neither cohort was significantly associated with CAD. Although carriers of the A allele of variant rs2943634 were at an increased risk of significant coronary stenoses in the second cohort (OR = 1.41 [1.06–1.88]; p = 0.018), no such association was found for the first cohort nor for both cohorts combined.

Conclusions Our data from two populations show that variant rs1333049 is significantly associated with angiographically characterized CAD. In contrast, variant rs6922269 did not show any impact on coronary atherosclerosis. The association between variant rs2943634 and CAD warrants further investigation.

Der „Cardiac power output" korreliert eng mit der myokardialen Schlagarbeit über einer weiten Bereich myokardialer Inotropie 093

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Hintergrund Der „Cardiac power output" (CPO) wird bestimmt als das Produkt von Herzminutenvolumen (HMV, l/min) und mittlerem aortalen Druck (mAOD, mmHg) und ist ein Prädiktor der Mortalität im kardiogenen Schock. Die linksventrikuläre Schlagarbeit (LV-SA) entspricht dem Zeitintegral der Druckvolumenschleife und wird in derselben Einheit gemessen wie der CPO. Ob der CPO mit der LV-SA korreliert, ist bislang nicht untersucht worden.

Methode Daten aus einer laufenden Reanimationsstudie bei anästhesierten Schweinen (n = 13) wurden ausgewertet. CPO wurde über einen Swan-Ganz-Katheter und einen aortalen Druckkatheter bestimmt, und die LV-SA aus LV-Druck und Dimensionen errechnet (Konduktanzkatheter). Daten unter Kontrollbedingungen und nach 10 min, 1 h und 6 h nach Wiedereinsetzen eines spontanen Kreislaufs nach Kammerflimmern (5 min) und Defibrillation wurden analysiert.

Die Spanne der Daten betrug bei der Herzfrequenz 51–193/min, beim maximalen LV Druck 67–189 mmHg, beim mAOD 49–155 mmHg, beim HMV 2,1–10,7 l/min, und beim systemischen Widerstand 6,3–29,8 mmHg min/l.

Ergebnisse Wir fanden eine enge Korrelation zwischen LV-SA und CPO: CPO = 1,21 LV-SA – 17,3; $r^2 = 0,94$.

Schlussfolgerung Unter Bedingungen, die für kardiologische Intensivpatienten repräsentativ sind, ist der CPO ein exzellenter Parameter der tatsächlichen LV Schlagarbeit. Diese Daten unterstützen die Messung des CPO, um den Erfolg einer inotropen Therapie bei Patienten mit verminderter Herzfunktion zu überwachen.

Die Induktion der milden Hypothermie verhindert die Abnahme der myokardialen Kontraktilität nach Kammerflimmern und Wiederbelebung bei anästhesierten Schweinen 131

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Hintergrund Die Induktion einer milden Hypothermie (MH, 33 °C) vermindert den hypoxischen Hirnschaden nach Kammerflimmern und Wiederbelebung. Da die MH aber das Herzminutenvolumen absenkt, wird ihr Einsatz bei eingeschränkter Herzfunktion kritisch diskutiert.

Methode Anästhesierte Schweine (62 ± 5 kg) wurden nach Kammerflimmern (5 min) und Defibrillation einer normothermen (38 °C; n = 6; NT) oder hypothermen Gruppe (33 °C; n = 7; MH, intravaskulärer Kühlkatheter) zugeordnet. Die Zeitdauer bis zum Erreichen der MH betrug 130 ± 12 min ab Wiederkehr eines spontanen Kreislaufs (ROSC).

Ergebnisse Es werden Daten bei 6 h nach ROSC mit Kontrolle verglichen. Die Herzfrequenz (HF, 1/min) war bei NT unverändert (85 ± 4 vs. 87 ± 4) und bei MH verringert (61 ± 4 vs. 84 ± 6; p < 0,05). Der maximale linksventrikuläre (LV) Druck nahm in beiden Gruppen ab (NT: 86 ± 3 vs. 114 ± 7; MH: 94 ± 7 vs. 108 ± 4; beide p < 0,05). Das Herzminutenvolumen (HMV) war bei MH (3,6 ± 0,2 vs. 5,2 ± 0,4; p < 0,05) stärker reduziert als bei NT (4,6 ± 0,5 vs. 5,6 ± 0,5; p = n. s.). Die gemischt-venöse Sauerstoffsättigung (%) war bei NT reduziert (56 ± 3 vs. 64 ± 4; p < 0,05), bei MH (66 ± 2 vs. 64 ± 2) jedoch unverändert, da der Gesamtkörpersauerstoffverbrauch (GK-VO_2, ml/min) bei MH (169 ± 8 vs. 265 ± 17; p < 0,05), nicht jedoch bei NT (254 ± 17 vs. 273 ± 18; p = n. s.) vermindert war. Das LV dP/dtmax (mmHg/s) war bei NT reduziert (1200 ± 121 vs. 1767 ± 153; p < 0,05), bei MH jedoch erhalten (1609 ± 117 vs. 1601 ± 107). Aus LV-endsystolischen (ES) Druck-Volumen-Beziehungen (aortaler Ballonkatheter) wurde das ES-Volumen bei einem ES-Druck von 100 mmHg berechnet und auf Kontrolldaten normalisiert (LVV-Des100-%). LVV-Des100-% nahm während NT (138 ± 14 %), nicht jedoch während MH (93 ± 6 %; p < 0,05 vs NT) zu. MH verhinderte somit die Rechtsverschiebung der Druck-Volumenschleife nach Reanimation.

Schlussfolgerung Die Induktion der MH nach Kammerflimmern/Wiederbelebung verhindert die Abnahme der myokardialen Kontraktilität. Ein vermindertes HMV während MH wird durch einen verminderten GK-VO_2 ausgeglichen. Diese Daten deuten an, dass die Induktion der MH eine positiv inotrope Intervention darstellt.

A Role for PECAM-1 in Venous Thrombus Resolution 026

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Background Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by intraluminal thrombus organization and fibrous obliteration of pulmonary arteries, with concomitant endothelial dysfunction. Thrombi resolve by a process of organization and recanalization. Leukocyte recruitment and angiogenesis are key components of this process. Platelet endothelial cell adhesion molecule-1 (PECAM-1 or CD31) is a molecule expressed on all cells within the vascular compartment, and plays an important role in leukocyte-endothelial cell adhesion and transmigration. Thus, PECAM-1 represents a link between these two key components of thrombus resolution. We investigated the role of PECAM-1 in a murine model of stagnant flow venous thrombosis.

Methods Thrombosis was induced in the infrarenal vena cava of PECAM-1 –/– mice on an FVB/n background by creating a venous stenosis with a silk suture. Thrombi were harvested on days 3, 7, and 14 after surgery for analysis (n = 8 per time point). Wild-type mice served as controls.

Results Thrombus cross-sectional area analysis demonstrated a significant increase in thrombus area over time in PECAM-1 –/– animals compared with controls (t-Test; $p < 0.05$). Immunohistochemical staining using antibodies against F4/80 for detecting thrombus macrophages revealed a decreased number of macrophages in PECAM-1 –/– animals compared with controls (t-Test; $p < 0.05$). The number of Isolectin B4-positive micro vessels was significantly decreased on days 3 and 7 in PECAM-1 –/– mice (t-Test; $p < 0.05$).

Conclusion Deletion of PECAM-1 results in misguided thrombus resolution with a decrease of monocytes and micro vessels. PECAM-1 is critically involved in venous thrombus resolution.

Phospholipids in Misguided Thrombus Resolution after Splenectomy 095

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Purpose Splenectomy is associated with an increased risk of chronic thromboembolic pulmonary hypertension (CTEPH). CTEPH is a life-threatening condition characterized by single or recurrent pulmonary thromboemboli that obstruct or obliterate the pulmonary vascular bed. The aim of our study was to investigate the role of phospholipids in the pathogenesis of altered thrombus resolution after splenectomy.

Methods We utilized a mouse model of stagnant flow venous thrombosis to characterize venous thrombus resolution. Vena cava ligation was performed one month after splenectomy. At days 3, 7, 14 and 28 after vena cava ligation thrombi were harvested for histology and electrospray ionization - mass spectrometry analysis. Blood samples were collected for FACS.

Results Thrombus areas of splenectomized mice were significantly larger than those of controls at all time points (ANOVA; $n = 8$; $p < 0.03$). The composition of phospholipids enclosed in the thrombus was significantly different between thrombi of splenectomized mice and controls. In parallel, whole blood FACS revealed higher counts of CD41-platelet microparticles (day 14: 3216 vs 927 cells/µl; $p < 0.05$) and leukocyte/platelet aggregates (day 14: CD11b/CD41, 56.4 vs 38.7 %; $p < 0.05$).

Conclusion We suggest that an altered phospholipid profile in thrombus may derive from the loss of mechanical filtering function of the spleen permitting the accumulation of cell-derived phospholipids. Experiments are designed to examine which phospholipid components further thrombus persistence.

A Microarray Study on the Effect of Extracellular Magnesium Deprivation upon Expression Profiles of Molecular Pathways and Biological Processes in Isolated Human Atrial Myocardium 057

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While it is well understood that nutritional Mg2+-deprivation is lethal and causes numerous cellular dysfunctions ending up with myocardial cell necrosis, the effects of extracellular Mg2+-concentrations on molecular pathways and processes has not been studied as yet. Characterising these Mg2+-dependent intracellular molecular pathways may well constitute a further step towards understanding the effects of magnesium on myocardial function as well as protection.

Using molecular profiling technique, we look at more than 20,000 different gene expressions in the presence and absence of extracellular Mg2+, thus identifying the specific molecular signature of myocardial Mg2+-deprivation. This allows us to demonstrate its effects at the molecular level in resting human atrial myocardium. Using PANTHER software (Applied Biosystems) we assess up- and down-regulation of gene expression associated with biological processes and pathways.

Myocardial gene expression after exposure for 30 minutes to Mg2+-free solution is massively altered compared to control experiments. We find a complex de-regulation of gene expression secondary to Mg2+ deficiency. It can be seen that gene-expression associated with clusters of immunity- and defence-processes, protein metabolism and signal transduction as well as nucleoside, nucleotide and nucleic metabolism are significantly down-regulated. Similarly, biological processes involved in transcription, protein biosynthesis and cell communication, nucleoside, nucleotide and nucleic metabolism as well as signal transduction and protein metabolism are affected by up-regulation. Clusters of pathways down-regulated by Mg2+ deficiency are: various signalling pathways, T-cell activation, apoptosis and angiogenesis. Clusters of up-regulated pathways are mainly different groups of signalling.

In summary, experimental myocardial Mg2+-deprivation leads to complex changes in the expression profile of biological processes and molecular pathways. On the other hand, one can deduce from earlier observations that Mg2+i is well buffered and remains relatively uninfluenced by extracellular manoeuvres. The interdependence of intracellular and extracellular Mg2+, however, appears once more difficult to understand. Further studies are certainly needed in order to firmly establish the mechanisms of extracellular Mg2+ influencing intracellular processes and pathways.

Genetic Variant rs4355801 A > G is Associated with both Angiographically Determined Coronary Atherosclerosis and Reduced Bone Mineral Density 142

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Background A recent genome-wide association study found evidence for an association between bone mineral density (BMD) and variant rs4355801 on chromosome 8, near to the osteoprotegerin gene. Associations between bone mineral density (BMD) and atherosclerotic disease have been suggested. Potential links between variant rs4355801 and coronary artery disease (CAD) are not known.

Methods We performed genotyping of variant rs4355801 in a large cohort of 1593 consecutive Caucasian patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; significant CAD was diagnosed in the presence of significant coronary stenoses with lumen narrowing ≥ 50 %. BMD of lumbar spine and femur was by assessed by Dual Energy X-ray Absorptiometry (DXA) in a subset of 823 subjects.

Results The prevalence of significant CAD increased significantly from the AA over the AG to the GG genotype (55.0 %, 57.6 %, and 64.2 %, respectively; $p_{trend} = 0.011$). The odds ratio for homozygous carriers of the G allele vs carriers of the A allele was 1.37 [95 %-CI: 1.06–1.79] after adjustment for age and gender. Further, BMD scores increased significantly from the AA over the AG to the GG genotype (1.10 ± 0.20, 1.13 ± 0.20, and 1.16 ± 0.19; $p_{trend} < 0.001$ and 0.96 ± 0.18, 1.00 ± 0.15, and 1.02 ± 0.15; $p_{trend} < 0.001$, respectively).

Conclusions Genetic Variant rs4355801 A > G is associated with both angiographically determined coronary atherosclerosis and BMD, pointing to a pathophysiological link between CAD and bone mineralisation.

Cytosolic Na^+ Accumulation Triggers Arrhythmogenic Events in Murine Ventricular Myocytes Harbouring a Human CPVT Mutation ($RyR2^{R4496C+/-}$) 150

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Background and Aims Gain-of-function mutations in the cardiac ryanodine receptor (RyR2), the predominant Ca^{2+} release channel of the sarcoplasmic reticulum (SR), are linked with some forms of catecholaminergic polymorphic ventricular tachycardia (CPVT) that frequently lead to sudden cardiac death. CPVT is characterized by spontaneous diastolic SR Ca^{2+} release as a response to exercise-induced SR Ca^{2+} overload during beta-adrenergic activation. However, it remains elusive (1) whether an elevated SR Ca^{2+} content alone – in the absence of beta-adrenergic activation – triggers arrhythmogenic events and (2) whether JTV-519, a putative RyR2 stabilizer, prevents arrhythmogenic events due to an abnormal RyR2-mediated Ca^{2+} leak underlying CPVT.

Methods Isolated murine ventricular myocytes harbouring a human CPVT-linked RyR2 mutation ($RyR2^{R4496C+/-}$ knock-in mice) were investigated in the absence (control) and presence of 1 μM JTV-519 (≥ 1 h pre-incubation) followed by 100 μM ouabain intervention (Na^+/K^+-ATPase blocker) to increase cytosolic [Na^+] and SR Ca^{2+} load (mediated by altered Na^+/Ca^{2+} exchange). Changes in membrane potential and intracellular [Ca^{2+}] were monitored with whole-cell patch-clamping and confocal Ca^{2+} imaging (Fluo-4/AM), respectively.

Results At baseline (0.5 Hz stimulation), action potentials (APs), Ca^{2+} transients, SR Ca^{2+} content and fractional SR Ca^{2+} release did not differ between wild-type (WT) and $RyR2^{R4496C+/-}$ myocytes. In contrast, $RyR2^{R4496C+/-}$ cardiomyocytes showed significantly increased diastolic SR Ca^{2+} leak measured as Ca^{2+} spark frequency ($RyR2^{R4496C+/-}$ vs WT: 2.22 ± 0.2/pL·s; n = 68 vs 1.14 ± 0.1/pL·s; n = 46), amplitude (F/F_0: 1.70 ± 0.02; n = 192 vs 1.57 ± 0.02; n = 67) and duration (91.8 ± 3.4 ms; n = 183 vs 75.6 ± 4.3 ms; n = 65; all $p < 0.05$) in respect to WT cardiomyocytes. Ouabain evoked significant increases in diastolic [Ca^{2+}], peak systolic [Ca^{2+}], fractional SR Ca^{2+} release and SR Ca^{2+} content that were quantitatively comparable in both groups. Ouabain also induced arrhythmogenic events, i.e. spontaneous Ca^{2+} waves, delayed afterdepolarizations (DADs) and spontaneous APs in both groups. However, ouabain caused a significantly larger increase in the frequency of arrhythmogenic events in $RyR2^{R4496C+/-}$ as compared with WT cardiomyocytes (WT vs $RyR2^{R4496C+/-}$; Ca^{2+} waves: 0.09 ± 0.03/sec; n = 16 vs 0.19 ± 0.03/sec; n = 18; spont. APs: 10.3 ± 5.7/min; n = 12 vs 191.4 ± 58.1/min; n = 7; both $p \leq 0.05$). 1 μM JTV-519 significantly reduced the frequency of ouabain-induced spontaneous APs (7.8 ± 3.8/min; n = 8; $p \leq 0.05$) in current-clamped $RyR2^{R4496C+/-}$ cardiomyocytes.

Conclusions Na^+-mediated elevation of SR Ca^{2+} content increases the frequency of arrhythmogenic events in the absence of beta-adrenergic activation in $RyR2^{R4496C+/-}$ ventricular myocytes. Stabilization of RyR2 by JTV-519 effectively reduces these arrhythmogenic events.

The Role of MKK7 during Myocardial Ischemia/Reperfusion 022

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Background The highly conserved mitogen-activated protein kinases have proven to be of great importance regarding myocardial development, hypertrophy, and survival. Mitogen-activated protein kinase kinase 7 (MKK7) – JNK pathways demonstrated dichotomous properties during myocardial survival and remodelling.

The in vivo role of MKK7, using a muscle-specific knock-out strategy, in the setting of cardiac ischemia and reperfusion remained unclear.

Methods We therefore subjected muscle-specific MKK7 knock-out (KO) mice compared to MKK7 wild-type (WT) rodents to experimental myocardial ischemia and reperfusion. Cardiovascular magnetic resonance (CMR), echocardiography and histological methods were used to characterize the transgenic phenotype.

Results The extent of ischemia/reperfusion injury was significantly reduced in MKK7 KO compared to WT mice. Following 30 minutes of ischemia and 3 hours of reperfusion, MKK7 mutagenic rodents presented significantly reduced levels of troponin T (WT: 2.97 ± 0.39 vs KO: 1.78 ± 0.26 ng/ml; $p < 0.05$; n = 13 per group). This early decrement of troponin T in the transgenic cohort was followed by smaller areas of infarction after 1 week (WT: 3.58 ± 0.50 vs KO: 1.77 ± 0.30 mm²; $p < 0.05$; n = 14 per group; sum of 3 sections per heart). Concordantly, functional analysis after 1 week of reperfusion showed a greater reduction of contractility in MKK7 WT mice compared to the transgenic strain.

Conclusion Our data provide the first in vivo knock-out evidence for the critical role of MKK7 during myocardial ischemia/reperfusion injury. MKK7 deficient mice show a significantly better outcome concerning troponin T elevation, infarction area, and loss of contractility at all stages of reperfusion.

Frequenzabhängige Regulation des nukleoplasmatischen Kalziumtransienten in Ventrikelmyozyten: Ein zellulärer Mechanismus für Tachykardie-induziertes Remodelling? 127

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Hintergrund Die nukleoplasmatische Kalzium-Konzentration ([Ca]) spielt in Kardiomyozyten eine wichtige Rolle für die Regulation der Transkription und damit für zelluläre Umbauprozesse (Remodelling), die Hypertrophie und Herzinsuffizienz zugrunde liegen. Ob die nukleoplasmatische [Ca] unabhängig von der zytoplasmatischen [Ca] reguliert werden kann, ist jedoch unklar. Wir untersuchten daher die frequenzabhängige Regulation nukleoplasmatischer und zytoplasmatischer [Ca]-Transienten in isolierten Ventrikelmyozyten.

Methode Isolierte Maus-Ventrikelmyozyten wurden mit dem Ca-Indikator Fluo-4/AM (8 μM) beladen. Elektrisch-stimulierte [Ca]-Transienten wurden mit Hilfe der schnellen, zweidimensionalen Konfokalmikroskopie aufgenommen. Dies erlaubte die simultane Registrierung und Analyse zytoplasmatischer und nukleoplasmatischer [Ca]-Transienten. [Ca]-Änderungen wurden als Änderungen der normalisierten Fluo-4-Fluoreszenz (F/F0) quantifiziert. Dabei entsprach F0 der Fluo-4-Fluoreszenz unter Ruhebedingungen.

Ergebnisse In elektrisch-stimulierten Maus-Ventrikelmyozyten (n = 20) waren die nukleoplasmatischen [Ca]-Transienten deutlich langsamer und kleiner als die zytoplasmatischen [Ca]-Transienten. Bei einer Stimulationsfrequenz von 0,5 Hz betrug das Verhältnis aus systolischer nukleoplasmatischer zu zytoplasmatischer [Ca] 0,84 ± 0,02. Die Zeit bis zum Maximum des [Ca]-Transienten war im Zellkern mit 390 ± 25 ms deutlich länger als im Zytoplasma (108 ± 11 ms; $p < 0,01$ vs. Nukleoplasma). Ebenso war der Abfall des [Ca]-Transienten im Nukleoplasma erheblich langsamer als im Zytoplasma. Die Zeit vom Maximum bis zum 50 %igen Abfall des Transienten (RT50) betrug im Zellkern 275 ± 13 ms, im Zytoplasma hingegen nur 53 ± 3 ms ($p < 0,01$ vs. Nukleoplasma). Eine Erhöhung der Stimulationsfrequenz von 0,5 Hz auf 4,0 Hz führte zu einem Anstieg der diastolischen und systolischen [Ca] im Zytoplasma um 214 ± 16 % bzw. 67 ± 17 %. Im Zellkern waren diese frequenzabhängigen Anstiege mit 277 ± 23 % bzw. 92 ± 17 % signifikant größer (beide $p < 0.05$ vs. Zytoplasma). Die Zeit bis zum Maximum des Transienten blieb im Zytoplasma nahezu unverändert, nahm im Zellkern mit zunehmender Frequenz jedoch signifikant ab. Die Differenz zwi-

schen der maximalen [Ca] im Nukleoplasma und im Zytoplasma nahm dadurch von 55 ± 12 ms bei 0,5 Hz auf 8 ± 6 ms bei 4 Hz ab ($p < 0,05$). Die RT50 nahm mit zunehmender Frequenz um 67 ± 2 % im Zytoplasma und um 73 ± 4 % im Nukleoplasma ab.

Schlussfolgerung In Maus-Ventrikelmyozyten sind nukleoplasmatische [Ca]-Transienten durch eine distinkte Kinetik gekennzeichnet: sowohl der Anstieg als auch der Abfall ist im Zellkern deutlich langsamer als im Zytoplasma. Dadurch kommt es bei einer Erhöhung der Stimulationsfrequenz im Nukleoplasma zu einem stärkeren Anstieg der diastolischen und systolischen [Ca] als im Zytoplasma. Die Ergebnisse zeigen, dass nukleoplasmatische und zytoplasmatische [Ca]-Transienten in Kardiomyozyten differenziell reguliert werden können. Sie zeigen einen neuen zellulären Mechanismus auf, der Tachykardie-induziertem Remodelling im Myokard zugrunde liegen könnte.

Bildgebung

Influence of the Diagnosis of ARVD/C through Cardiac MRI on the Decision for Implantation of an AICD 058

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Background Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an uncommon, inherited cardiac disorder, characterized by progressive degeneration of the right ventricular myocardium, ventricular arrhythmias, fibrous-fatty replacement, and increased risk of sudden death. ARVD/C patients present either with symptoms of palpitations and syncope associated with ventricular tachycardia (VT) or with sudden cardiac death (SCD).

Methods and Results Within a period of 11 years, 452 patients (39.8 ± 16.7 yrs; 51 % males) with suspected clinical symptoms were referred to Cardiac MRI for morphologic verification of ARVD/C. Based on the tomographic criteria of the International Task Force, 18 patients (4.0 %) were diagnosed with ARVD/C. Within this group, five patients (1.1 %) received an automatic implantable cardioverter-defibrillator (AICD). One patient experienced syncope and the others presented with sustained VTs that were reproducible in electrophysiologic studies (EPS) with significant hemodynamic impairment. Moreover, 12 patients (3.3 %) who were screened but did not fulfill the criteria for the diagnosis of ARVD/C received an AICD. Within this group eight patients were SCD survivors, while the others experienced VTs. All together, AICD was implanted in 17 patients (3.8 %). All of them had severe clinical symptoms (syncope, SCD survivors) and/or experienced VTs that were reproducible in EPS. In none of the patients the decision for AICD implantation was established on the tomographic diagnosis of ARVD/C alone.

Summary In our patient population, the diagnosis of ARVD/C via cardiac MRI does not influence the decision for implantation of an AICD. Instead the decision was either based on prior severe clinical events or electrophysiologic testing.

NT-proBNP levels, Ejection Fraction and Global Longitudinal Strain in Alcohol Dependent Patients 010

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Introduction Alcohol plays an important role in the development of dilated cardiomyopathy. However, it is unclear whether patients with "acute" alcohol dependence exhibit left ventricular dysfunction and if this process is reversible after withdrawal. NT-proBNP and global longitudinal strain assessed by 2D speckle tracking echocardiography could allow the detection of early systolic left ventricular dysfunction in this patient population.

Methods A prospective study was performed in 49 alcohol dependent patients according to ICD-10 (mean age 49.5 ± 9 years; men/women 35/14) admitted for acute withdrawal therapy. These pts were compared to 18 asymptomatic healthy subjects (mean age 42.4 ± 14.8 years; male/female 13/5). All pts underwent transthoracic echocardiography (TTE) including LV longitudinal peak systolic strain analysis (GLPSS, EchoPAC 7.0, GE), EF (biplane Simpson) and measurements of plasma NT-proBNP. These tests were repeated after withdrawal (mean 23.6 ± 16.4 days).

Results Sixteen alcohol dependent patients (32.6 %) had elevated NT-proBNP levels (492 ± 558 pg/ml) at baseline (> 100 pg/ml) despite normal EF (61 ± 11 %). In this subset of pts GLPSS was lower compared to healthy subjects. However, this difference did not reach the level of significance (–14.4 ± 3.8 % vs –16.8 ± 3,8 %; p = n. s.). These pts also showed a significant decrease of NT-proBNP (492 ± 558 pg/ml vs 294 ± 329 pg/ml; p = 0.04), and a trend towards improvement of GLPSS (–14.4 ± 3.8 % vs –16.4 ± 4.3 %; p = n. s.) after withdrawal. The EF remained unchanged (61 ± 11 % vs 63 ± 10 %; n. s.). The 33 patients (67.4 %) with normal NT-proBNP (48.7 ± 29.5 pg/ml) did not differ in ejection fraction to those with an elevated NT-proBNP (66 ± 6 % vs 61 ± 11 %; n. s.) or to controls (67 ± 6 %). GLPSS was not different compared to healthy individuals (–17.4 ± 2.9 % vs –16.8 ± 3.8 %).

Conclusion Approximately 1/3 of patients with alcohol dependence exhibit elevated NT-proBNP levels. Alcohol withdrawal of approximately 3 weeks leads to a reduction of NT-proBNP values. The elevation of NT-proBNP can not be explained by a reduction in left ventricular ejection fraction. The role of longitudinal systolic function assessed by 2D strain analysis needs further investigations.

64-Zeiler Spiral-CT-Koronarangiographie im Vergleich mit konventioneller Koronarangiographie zur Evaluierung von Instent-Restenosen nach Stentrevaskularisation im Hauptstamm 048

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Hintergrund Im Gegensatz zur Detektion von Koronararterienstenosen hat die nicht-invasive Bildgebung in der Evaluierung von Koronarterienstents bislang keinen gesicherten Stellenwert. Durch hochauflösende Spiral-Computer-Tomographie („64-Zeiler", CT) ist jedoch auch eine Visualisierung des Lumens von gestenteten Koronararterienabschnitten möglich. Wir untersuchten die Aussagekraft der CT-Koronararterienangiographie (CT-CA) mittels 64-Zeiler-CT in der Evaluierung von Hauptstammstents (HS) im Vergleich zur konventionellen Koronararterienangiographie (K-CA) im Rahmen einer prospektiven Studie.

Methodik Bei allen Patienten (P), die von Jänner 2007 bis Dezember 2008 an unserer Abteilung einen HS erhielten, wurde 3–6 Monate nach der Stentimplantation eine CT-CA mittels 64-Zeiler-CT (Siemens „Somatom Sensation 64 Cardiac") sowie eine nachfolgende K-CA durchgeführt. Nicht eingeschlossen wurden lediglich Patienten mit einem Kreatininwert ab 2,0 mg/dl. Die technische Durchführung der CT-CA im Spiralmodus beinhaltete eine Rotationszeit von 370 ms und eine Kollimation von 64 × 0,6 mm bei einer intravenösen Injektion von 80 ml Kontrastmittel (Flussgeschwindigkeit 5 ml/s). Die Auswertung der CT-CA erfolgte über axiale Bilder sowie mittels multiplanarer und gekurvter planarer Reformation, die der K-CA erfolgte visuell durch 2 erfahrene Untersucher. Überprüft wurde die Detektion von signifikanten (> 70 %) Instent-Restenosen (ISR) mittels CT-CA im Vergleich zur K-CA.

Ergebnisse Insgesamt wurden 31 P (14 männlich; mittleres Alter 66 ± 19 Jahre) untersucht. Die Bildqualität der CT-CA erlaubte die Evaluierung von 25 HS (80 %). 5 HS (16 %) waren wegen Aufhärtungsartefakten infolge hochgradiger Verkalkungen im gestenteten Gefäß und 1 HS wegen Atemartefakte nicht beurteilbar.

Die K-CA fand insgesamt 2 ISR (6 %), von denen 1 ISR zuvor mittels CT-CA nicht erkannt worden war. Drei (10 %) in der K-CA als

nicht-signifikant eingestufte ISR wurden in der CT-CA überschätzt und als signifikant befundet.

Schlussfolgerung Die Evaluierung von ISR mittels CT-CA im Bereich des Hauptstamms ist häufig durch Gefäßkalk eingeschränkt. Trotz der durch die geringe Fallzahl eingeschränkten Aussagekraft unserer Untersuchung erscheint die CT-CA vorerst als alleinige Kontrollmethode von ISR bei Hauptstammstents nicht empfehlenswert.

Comparison of Heart Rate Reduction with Ivabradine versus Metoprolol before Coronary Computed Tomography Angiography 041

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Introduction Several studies have demonstrated the correlation of heart rate and image quality in coronary computed tomography angiography (CCTA). Beta-blocker administration prior to CCTA-scanning is crucial due to its hypotensive effect and, moreover, several contraindications need to be considered. Ivabradine is a selective heart rate-lowering agent that specifically inhibits the If-current on the sinoatrial node and has no effect on cardiac contractility or atrioventricular conduction.

Methods One hundred twenty patients were randomized to oral premedication with 50 mg metoprolol (a cardioselective beta-blocker) or 15 mg ivabradine. Heart rate and blood pressure were measured before administration of premedication and immediately before cardiac CT under the same conditions.

Results Mean time between premedication administration and follow-up were 116 ± 28 minutes for metoprolol and 108 ± 24 minutes for ivabradine (p = n. s.). When comparing groups, there were no significant differences in reduction of heart rate and diastolic blood pressure, whereas systolic blood pressure was found to decrease significantly less in patients who received ivabradine as compared to those in the beta-blocker group ($p < 0.001$). In the subgroup of patients who are on chronic beta-blocker therapy, we investigated significantly higher heart rate reduction in the ivabradine group (–13.19 vs –10.04 bpm; $p < 0.05$) while systolic blood pressure drop was found to be less (–2.00 vs –15.04 mmHg; $p < 0.05$).

Conclusion Ivabradine decreases heart rate prior to cardiac CT scans sufficiently, however, with a significantly less depression of systolic blood pressure as compared to metoprolol. Moreover, in patients with permanent beta-blocker medication ivabradine permits better heart rate control with less blood pressure reduction.

Two-Dimensional Speckle Tracking Strain Echocardiography in Heart Transplant Patients 025

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Background Longitudinal strain determined by 2 dimensional speckle tracking is a sensitive parameter to detect early systolic left ventricular dysfunction. However, it is unclear if heart transplant (HTX) patients exhibit reduced longitudinal strain compared to healthy individuals.

Methods Transthoracic echocardiography (TTE) and multidetector computed tomographic angiography (MDCT, dual source 2 × 32 × 0.6 mm, Siemens Definition) was performed in 31 HTX patients (126.8 ± 67.6 months [10.6 years] post transplantation) and in 42 asymptomatic healthy subjects. Grey-scale apical 2-, 3- and 4-chamber views were recorded and stored for automated offline speckle tracking for longitudinal strain analysis (EchoPAC 7.0, GE). The presence of coronary artery disease (CAD) and left ventricular ejection fraction (LVEF %) was assessed by MDCT.

Results Nine of the 31 transplant patients had significant allograft CAD. Mean global longitudinal peak systolic strain (GLPSS) was significantly lower in the transplant recipients than in the healthy population (–13.9 ± 4.2 % vs –17.4 ± 5.8 %, respectively; $p < 0.01$). This was still the case after excluding the 9 transplant patients with CAD (–14.1 ± 4.4 % vs –17.4 ± 5.8 %, respectively; $p < 0.02$). LVEF % was 60.7 ± 10.1 % in transplant recipients vs 64.8 ± 6.4 % in the healthy population (p = n. s.). There was no significant age difference within the two groups 62.9 ± 10.7 years vs 60.4 ± 11.6 years, respectively (p = n. s.).

Conclusion GLPSS is reduced in heart transplant recipients compared to healthy subjects despite equal LVEF %. This difference is independent of age. Longitudinal strain analysis could allow the early detection of subclinical left ventricular dysfunction in heart transplant recipients.

Murine Cardiac Examinations Using Routine Clinical 1.5 T MRI Scanners 024

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Background Mouse models are widely used in research of cardiac pathologies. Still, the acquisition of in vivo functional cardiac parameters in small rodents requires specialized equipment not widely available. Therefore, we tested the feasibility of a standard clinical 1.5 T MRI scanner on mice compared with echocardiography, and evaluated determination of infarct size by late gadolinium enhancement compared with histological methods.

Methods Mice subjected to ischemia/reperfusion procedure were randomized in groups of 0 min (n = 5), 30 min (n = 5) and 60 min (n = 5) of ischemia followed by Troponin T measurement. LGE using an adapted PSIR sequence (preoperative, 24 h and 1 week postoperative) facilitated the determination of in vivo infarct sizes, and compared to Troponin T values and histological sizes of infarction. In addition, fractional shortening (FS) measured with echocardiography was matched to fractional area change (FAC) assessed with CINE MRI: preoperative, 24 hours postoperative, and 1week postoperative.

Results In order to characterize interobserver variability, LGE determined infarctions were measured by three blinded investigators. Correlation analysis revealed a highly significant similarity among these observers (O) (O1:O2 r = 0.98; O1:O3 r = 0.97; O2:O3 r = 0.95; all $p < 0.001$). Infarct size measured through adapted PSIR sequence markedly correlated with histological infarct sizes (O1: r = 0.97; $p < 0.001$) and Troponin levels (O1: r = 0.93; $p < 0.001$). In addition, CINE imaging (FAC) and echocardiography (FS) correlated at all examinations significantly (preoperative r = 0.61; p = 0.036; 24 hours r = 0.61; p = 0.02; 1 week r = 0.07; p = 0.036). Impairment of left ventricular function measured by CINE MRI significantly associated with histological infarction size (1 W r = –0.94; $p < 0.001$), Troponin T levels (1 W r = –0.95; $p < 0.001$) and LGE measured infarct size (O1:1 W r = –0.093; $p < 0.001$).

Conclusion Here we demonstrate routine clinical MRI scanners (1.5 T) to enable accurate quantification of in vivo infarction areas in mice. Furthermore, CINE imaging greatly improves the quality of cardiac functional assessment in our mouse model providing exact measurements and detailed anatomical information.

Indikationen zur kardialen MRT: Single-center-Erfahrung einer kardiovaskulären Schwerpunktabteilung 162

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Hintergrund Die kardiale MRT hat sich zum Goldstandard in wichtigen Teilgebieten der Kardiologie entwickelt (z. B. Myokard-

Tabelle 2: P. Wexberg et al.

Indikationen	MCI	Chron. Ischämie	CMP	Vitien	Thrombus	Raumforderung	Myokarditis	Perikarderguss	Stressperfusion
Anzahl	6 (5,7 %)	37 (34,9 %)	23 (21,7 %)	4 (3,8 %)	3 (2,8 %)	4 (3,8 %)	23 (21,7 %)	1 (0,9 %)	4 (3,8 %)

Die häufigsten Untersuchungen erfolgten somit zur KHK-Diagnostik, gefolgt von Abklärung von Kardiomyopathien und Myokarditis.

vitalität, Myokarditis). Zur optimalen Nutzung der Möglichkeiten ist eine gemeinsame Untersuchung und Befundung durch Kardiologie und Radiologie wichtig. Wir beschreiben unsere Erfahrungen mit dem Aufbau einer interdisziplinären Arbeitsgruppe zur kardialen Schnittbildgebung.

Methodik und Ergebnisse In den letzten 12 Monaten wurden 106 Untersuchungen durchgeführt. Bei den Untersuchungen sind mindestens je ein/e Kardiologe/Kardiologin und ein/e Radiologe/Radiologin mit einer mindestens einjährigen Befundungserfahrung anwesend. Bei klar definierter Fragestellung liegt die Untersuchungsdauer zwischen 20 und 50 Minuten, die Auswertung benötigt ebenso viel Zeit. In diesem Zeitraum wurden insgesamt 98 PatientInnen (38 % Frauen, 62 % Männer; Durchschnittsalter 52,2 ± 16,7 Jahre) mit den in **Tabelle 2** angegebenen Indikationen untersucht.

Diskussion Die größte klinische Relevanz hat die kardiale MRT an unserem Zentrum wie auch international in der KHK- und CMP-Abklärung. Durch exakte Quantifizierung des vitalen Myokards können Revaskularisationsmaßnahmen optimal geplant werden. Die Myokarditis ist eine häufige klinische Verdachtsdiagnose und kann mit der kardialen MRT nicht-invasiv abgeklärt werden. Bei bestimmten Fragestellungen (z. B. Raumforderung, Thrombus) ergänzt die MRT-Untersuchung die nicht-invasiven Möglichkeiten jeder kardiologischen Schwerpunktabteilung durch eine höhere Sensitivität als die transthorakale Echokardiographie. Die ersten Erfahrungen mit Stress-MRT an unserem Zentrum zeigten vielversprechende Ergebnisse.

Reversed Left Ventricular Systolic Contraction Sequence during Right Ventricular Pacing: Assessment using Real-Time Three-Dimensional Echocardiography 080

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Background Chronic right ventricular apical (RVA) pacing has been associated with increased risk of heart failure and adverse outcome. RVA pacing induces abnormal electrical activation patterns of the left ventricle. However, few data exist on the acute effects of RVA pacing on three-dimensional ventricular function and mechanical dyssynchrony. We performed a three-dimensional (3D) echocardiographic study to assess global and regional left ventricular function during RVA pacing.

Methods 26 patients with implanted cardiac devices and normal intrinsic atrioventricular conduction were included in the study. Three-dimensional echocardiography was performed during intrinsic sinus rhythm and during RVA pacing. Three-dimensional datasets were acquired with a 4D matrix transducer. Quantification of global and regional left ventricular function was performed offline by time-volume analysis of 16 myocardial segments. Time to reach minimum regional volume was calculated for each segment as a percentage of the cardiac cycle. The systolic dyssynchrony index (SDI) was defined as the standard deviation (SD) of these time periods. Longitudinal function was assessed by time-volume analysis of apical, mid-ventricular and basal segments.

Results During RVA pacing, a reversed apical-to-basal longitudinal contraction sequence was observed in 58 % of all patients. RVA pacing was associated with increased LV dyssynchrony and reduced LV ejection fraction (LVEF). SDI increased from 4.4 ± 2.2 % to 6.3 ± 2.4 % ($p = 0.001$). Left ventricular ejection fraction (LVEF) declined from 53 ± 13 % to 47 ± 14 % ($p = 0.05$).

Conclusion RT3DE assessment of left ventricular function provides evidence that pacing from the RVA results in acute alterations in LV contraction sequence and increased LV dyssynchrony. Further studies are warranted to assess the potential of RT3DE to identify patients who might be at increased risk of pacing-induced heart failure or who might benefit from alternate-site or multisite pacing.

Chirurgie

Completely Endoscopic Removal of Dislocated Atrial Septal Closure Devices – Experience with 5 Patients 156

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Objectives Percutaneous closure of a patent foramen ovale or atrial septum defect is nowadays applied in the majority of the cases with acceptable results. Device displacement or incomplete closure of the interatrial communication may lead to residual shunt, hemolysis and recurrent neurological events. We report on our experience with 5 patients who underwent totally endoscopic removal of an insufficient atrial septal closure device at our institution.

Methods From May 2007 till December 2008 5 patients (3 males and 2 females; age: median (min/max) 40 [30/57]) with a displaced atrial septal closure device (Amplatzer Septal Occluder, AGA, Medical Plymouth, MN or PFO Star Occluder, Cardia Burnville, MI) were referred to our department. All patients were operated in a completely endoscopic fashion using the Da Vinci Telemanipulator (Intuitive Surgical, Sunnyvale CA), intraaortic balloon endooccclusion and remote access perfusion (ESTECH RAP, Danville, CA or Endo CPB System, Cardiovations, Redwood CA). Device removal was performed by means of Endo Catch 15 mm retrieval device Covidien (Norwalk, CT).

Results All 5 procedures were succesfully completed in a totally endoscopic fashion. The Amplatzer Septal Occluder and the PFO Star Occluder were removed in 3 and 2 cases respectively. Median size of the removed devices was 24 (22–26) mm. The entire procedure was completed in approximately 5 hours (median total operative time (min/max): 319 [288/369] min). Mean cardiopulmonary bypass time was 167 (137–238) min, mean cross clamp time was 108 (88–169) min. All but one defects were closed using a Dacron patch. There was no patient with rest shunt in the intraoperative transesophageal echocardiography, no interatrial communication was detected at the echocardiography before discharge. All patients had an uneventfull postoperative course and were discharged home on the 5th or 6th postoperative day. No residual shunt was detected in the follow up period (mean [min/max]: 9 [1/19] months).

Conclusions Removal of a dislocated atrial septal closure device can be successfully performed in a totally endoscopic approach using the robotic system and remote access perfusion with balloon endooccclusion. Operative times are acceptable and intermediate results are not compromized by the endoscopic technique.

Hybrid Coronary Revascularization Using Robotic Technology – an Appealing Concept for Minimally Invasive Treatment of Multivessel Disease 157

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Background Hybrid coronary revascularization is a combination of minimally invasive coronary surgery and percutaneous coronary intervention (PCI). It allows sternal preserving treatment of multivessel coronary artery disease and includes the longterm benefits of the internal mammary artery (IMA). In its classical version internal mammary artery bypass grafts were placed through minithoracotomy (MIDCAB). Most recently robotic technology has allowed completely endoscopic procedures (TECAB = totally endoscopic coronary artery bypass). We report on our experience with robotic techniques in hybrid coronary intervention.

Patients and Methods From 2001 to 2008 47 patients (41 male/6 female; age 58 [41–75] years) received hybrid coronary revascularization on an intention to treat basis. The daVinci™ telemanipulation system was used for performance of the following procedures: MIDCAB (endoscopic IMA harvesting) n = 2, TECAB single vessel arrested heart n = 35, TECAB single vessel beating heart n = 4, TECAB double vessel arrested heart n = 6. In 32 patients (68 %) robotic surgery was performed first, in 3 patients (6 %) PCI was performed first, in 12 patients (26 %) a simultaneous intervention was carried out.

Results Six conversions to larger thoracic incisions were necessary (13 %). In these cases the PCI target received an aortocoronary bypass graft. There was no hospital mortality, one patient required revision for bleeding. Ventilation time was 8 (1–132) h, ICU stay was 20 (16–240) d, hospital stay was 6 (4–20) d. In 16 patients who were asyptomatic during the early postoperative period after robotic surgery PCI was not carried out. There was no mortality on follow up. Overall freedom from angina was 97 % at two years, freedom from major adverse cardiac and cerebral events (MACCE) was 91 % at two years. No reinterventions were necessary on the internal mammary artery bypass grafts, two PCI targets required percutaneous reintervention.

Conclusion We conclude that robotic technology allows completely endoscopic placement of internal mammary artery bypass grafts in hybrid coronary revascularization. Single and double bypass grafts are feasible and simultaneous interventions can be performed. Conversion remains a challenge. Overall safety of the procedure seems to be adequate and perioperative clinical results are satisfactory. Intermediate term survival and freedom from angina are excellent.

Supra-Aortic Transposition for Combined Vascular and Endovascular Repair of Aortic Arch Pathology 152

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Background Supra-aortic transpositions to various extents followed by endovascular stent graft placement are now an established tool in the treatment of various pathologies affecting the aortic arch. Results remain to be determined.

Methods From 1996 through 2007, 73 patients (median age 71 years) presented with aortic arch pathology (atherosclerotic aneurysms, n = 42; type B dissections, n = 9; penetrating ulcers, n = 17; traumatic lesions, n = 2; aneurysms based on prior surgery for aortic coarctation, n = 3). Strategy for distal arch disease was subclavian-to-carotid transposition (n = 24) or autologous double-vessel transposition through upper hemisternotomy (n = 36). For entire arch disease, total supra-aortic rerouting with a reversed bifurcated prosthesis was applied (n = 13). Endovascular stent graft placement was performed metachronously.

Results In-hospital mortality was 6.8 % (n = 5). Persistent early type I and III endoleak rate was 9.6 %. Persistent late type I and III endoleak rate was 5.5 %. Overall actuarial survival was 90 %, 86 %, and 72 % at 1, 3, and 5 years. Mean follow-up is 37 months (range 1–120). Early and late endoleak formation was independently predicted by the number of prostheses (early odds ratio [OR] 0.210; p = 0.0003; late OR 0.216; p = 0.012), whereas logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation) reached borderline significance regarding late endoleaks (OR 2.1; p = 0.095). An earlier year of implantation reached borderline significance predicting survival (OR 1.9; p = 0.062). Furthermore, survival was independently predicted by higher logistic EuroSCORE levels (OR 1.8; p = 0.020). Interestingly, type of arch rerouting did not influence endoleak formation and survival (OR 0.9; p = 0.812).

Conclusions Results after supra-aortic transpositions to various extents followed by endovascular stent graft placement for the treatment of various pathologies affecting the aortic arch are promising. Endoleak formation is directly related to the number of prostheses and may be reduced by longer devices. Each type of arch rerouting, irrespective of extent, has turned out to be effective. Therefore, extended applications of these combined treatment strategies substantially augment the therapeutic options.

Novel Insights Into the Mechanisms and Treatment of Intramural Hematoma Affecting the Entire Thoracic Aorta 153

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

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

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

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

Pre- and Postoperative Multislice Computer Tomographic Evaluation of Patients Undergoing Total Endoscopic Coronary Surgery with Combined Percutaneous Interventions 020

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Purpose Robotically assisted coronary artery surgery, in particular total endoscopic bypass surgery (TECAB), is an innovative minimal invasive procedure requiring specific pre- and postoperative imaging to guide the surgical procedure and give proof of patency of grafts to compete with conventional bypass surgery. In addition this endoscopic approach may be combined with percutaneous coronary

interventions to achieve complete revascularization within an integrated minimal traumatic approach.

Methods In 15 patients with multivessel coronary disease (3-VD, n = 6; 2-VD, n = 9) planned for complete coronary revascularization combining TECAB surgery (15 arrested heart TECAB with LIMA to LAD or DG) and percutaneous interventions (14 RCA and 4 CX), preoperative MSCT angiography (MSCTA, Sensation 16 or Somatom 64, Siemens Medical Systems, Erlangen, Germany) of the coronaries as well as of the thoracic arteries was performed to identify the optimal distal bypass anastomotic site of the native target coronary artery in relation to the course of the internal mammary arteries used. Within 3 months after surgery, all patients underwent MSCTA and invasive coronary angiography (CA) follow up to evaluate graft and native vessel flow and patency.

Results Preoperative MSCT allowed to identify the distal mammary graft anastomotic target vessel site in all patients (100 %). Furthermore precise CT guided distance measurements between LIMA and native LAD course allowed avoidance of target vessel stenting with resulting TIMI III flow in 14/15 patients (93 %). One patient had to be converted to conventional sternotomy bypass surgery due to a distal graft anastomotic bleeding. Follow up MSCTA and/or invasive angiography were performed in 15 and 11 patients respectively. Patent grafts were found in all 15 patients by MSCTA, all confirmed by CA. PCI stented lesions were shown to be patent in 15 patients by MSCTA, in one patient CA revealed a restenotic lesion of the distal RCA, missed by MSCT and subsequently treated with a drug eluting stent. MSCTA image quality of proximal bypass anastomoses was judged excellent, scanning quality of distal anastomoses was of lower quality, but still sufficient to judge patency.

Conclusion The use of pre- and postoperative MSCT angiography in patients undergoing total endoscopic coronary surgery with combined percutaneous interventions allows a safe and precise performance of the surgery procedure as well as a good evaluation of the short term revascularization outcome.

A New Method for Motion Analysis of the Aortic Arch as a Risk Stratification after Supra-aortic Rerouting and Endovascular Stent-Graft Placement 154

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Background Total supra-aortic rerouting as well as double vessel transposition followed by endovascular stent graft placement are now an established tool for the treatment of various aortic arch pathologies. However, details about the motion of the aortic arch after this procedure remain unknown. Moreover, no perfectly fitting risk stratification score exists for outcome prediction of these specific patients.

Materials and Methods We applied a fully automated method to quantify the deformation patterns of the aortic arch in a gated CT sequence. The aorta is detected and segmented by an active surface approach, that accurately identifies the vessel wall in all frames. The correspondences of landmarks on the vessel wall are established by tracking the deformation during the cardiac cycle, resulting in a dynamic deformation model of the structure.

Results With help of this model, global and local deformation properties like stretching and bending were measured. After registering the models acquired pre-treatment, post-transposition, and post-stent-graft-placement we compared these local properties and were able to quantify the change caused to the aortic arch motion.

Conclusion This new method of automated computational motion analysis of the aortic arch may establish a risk stratification score for outcome prediction after supra-aortic rerouting followed by endovascular stent-graft placement.

Diverse

Die ärztliche Visite: Wie viel versteht der Patient davon? Der Stellenwert von Alter, Geschlecht und Migrationshintergrund 027

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Hintergrund Die Visite ist wesentlich für den Patienten hinsichtlich des Verstehens seiner Erkrankung, seiner Behandlung, wie auch weiterführender Maßnahmen. Die niedrige Compliance hinsichtlich Medikamenteneinnahme sowie auch von Lebensstilmaßnahmen ist zum Teil durch mangelndes Verstehen bedingt. Die vorliegende Studie untersucht daher die Zusammenhänge von Alter, Geschlecht und Sprachkenntnissen.

Methode Im Rahmen des stationären Aufklärungs- und Präventionsprogramms „Herzensbildung" wurden an einer kardiologischen Abteilung 30 Patienten befragt, wie viel sie selbst von den Inhalten, die mit ihnen während der Visite besprochen wurden, verstanden haben. Die Patienten gaben in Prozentzahlen an, wie viel sie verstehen. Geschlecht, Alter und Migrationshintergrund/Sprachkenntisse wurden evaluiert. Die Patienten wurden, je nach ihren Deutschkenntnissen, in 2 Gruppen aufgeteilt – Gruppe „native speaker" und Gruppe „non-native speaker". Mittels t-Test für ungleiche Varianzen wurde eruiert, ob „native speaker" im Mittel mehr verstehen als „non-native speaker". Mittels Korrelationsanalyse wurde der Zusammenhang von Verständnis und Alter evaluiert. Der t-Test für gleiche Varianzen wurde angewandt um herauszufinden, ob Männer oder Frauen bei der Visite mehr verstehen.

Resultate Im Gesamtkollektiv verstanden die Patienten 72,5 ± 30,3 %. Die „non-native speaker" verstanden 39,3 ± 39,0 %, die „native speaker" dagegen 82,6 ± 18,3 % ($p < 0{,}026$). Die Korrelation zwischen Alter und Verständnis fiel nicht signifikant aus ($p = 0{,}176$), auch der t-Test für gleiche Varianzen ($p = 0{,}374$), es kann also von keinem Zusammenhang des Verständnisses mit Alter/Geschlecht ausgegangen werden.

Zusammenfassung Männer und Frauen verstehen gleichermaßen viel von der Visite und ältere Patienten verstehen nicht weniger als jüngere. Unseren Daten zufolge verstehen „native speaker" mit durchschnittlich 80 % doppelt so viel wie „non-native speaker". Da das Verständnis vonseiten des Patienten wesentlich für seine Compliance und somit auch für seine Prognose ist, muss die Kommunikation zwischen visitierenden Ärzten und Patienten mit Migrationshintergrund verbessert werden. Dies sollte durch Hinzuziehen von Verwandten/Dolmetschern für die Visitenzeit bewerkstelligt werden.

Was unsere Patienten von uns Kardiologen wissen wollen: Die Top-5-Fragen aus Patientensicht 031

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Hintergrund Die ärztliche Spitalsvisite verläuft für unsere Patienten häufig nicht zufrieden stellend. Einerseits bezüglich der Dauer der Visite, andererseits bzgl. der Inhalte. Hier besteht eine Diskrepanz zwischen dem, was vom Arzt angesprochen wird, und dem, was der Patient als relevant ansieht. Bisher gibt es kaum Daten hinsichtlich der für die aus Patientensicht wesentlichen Inhalte. Ziel der vorliegenden Studie ist daher die Evaluierung der aus Patientensicht wesentlichsten Themen, die während einer Spitalsvisite besprochen werden sollten.

Methoden Im Rahmen des stationären Aufklärungs- und Präventionsprogramms „Herzensbildung" wurden an einer kardiologischen Abteilung in einer ersten Phase an 75 Patienten Fragebögen ausgeteilt. Fragestellung: „Nennen Sie uns die für Sie relevantesten Fragen, die im Rahmen der Visite beantwortet werden sollten."

Tabelle 3: S. Abayev et al.

	Frage	Phase 1 %	Phase 2 Mean/SD
F1	geplante Untersuchung	14,1 %	1,2 ± 0,4*
F8	Lebensstilmodifikation	8,7 %	1,42 ± 0,57*
F2	Art & Ursache der Erkrankung	7,6 %	1,3 ± 0,51*
F7	Heilungschancen	7,6 %	1,16 ± 0,37*
F5	Welche Medikamente	5,4 %	1,4 ± 0,64*

Insgesamt wurden 92 Fragen von den Patienten gestellt, wobei 60 Fragen mehrfach in ähnlicher Form vorkamen (65,2 %). Diese wurden zu 11 Fragen zusammengefasst. In einer 2. Phase wurde an 50 Patienten ein Fragebogen ausgeteilt, auf den die evaluierten 11 Fragen in 2 Blöcke aufgeteilt wurden:

1. Was will ich während meines Aufenthaltes wissen (F1–F6)?
2. Was ist mir nach meiner Entlassung aus dem Spital wichtig (F7–F11)?

Die von uns vorgegebenen Fragen wurden von den Patienten mit Noten von 1–4 bewertet: 1 = sehr wichtig, 2 = wichtig, 3 = weniger wichtig, 4 = unwichtig.

Es wurde auch verglichen, ob die Fragen zum Spitalsaufenthalt (F1–F6) besser bewertet worden sind (also als wichtiger angesehen werden), als Fragen (F7–F8) bzgl. nach dem Aufenthalt.

Resultate Von den 11 Fragen wurden 5 Fragen (**Tabelle 3**) von den Patienten sowohl in Phase 1 wie auch Phase 2 als besonders wichtig beurteilt (*p < 0,05). Davon betreffen 3 die Zeit während des Spitalsaufenthaltes und 2 Fragen beziehen sich auf die Zeit nach der Entlassung. Es konnte zwischen den 2 Frageblöcken kein signifikanter Unterschied festgestellt werden (p = 0,63).

Zusammenfassung Für den Patienten ist es während des Spitalsaufenthalts am Wichtigsten, genauestens über geplante Untersuchungen/Eingriffe, über Art und Ursache der Erkrankung und Medikation informiert zu werden. Für die Zeit nach dem Spitalsaufenthalt dagegen ist es eindeutig am Wichtigsten, über die Heilungsaussichten und Lebensstilmodifikation Bescheid zu wissen. Bei jeder Visite sollte man sich als visitierender Arzt auf die oben genannten 5 Fragen fokussieren. Aufgrund der zeitlich limitierten Ressourcen im Spitalsalltag ist eine effiziente und strukturierte Visite von wesentlicher Bedeutung, um das Patientenmanagement zu verbessern.

Wie viel weiß der kardiologische Patient über seine Erkrankung? Was bewirken Informationsveranstaltungen während des Krankenhausaufenthalts? 126

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Hintergrund Das Verständnis ihrer Erkrankung beeinflusst nachweisbar die Compliance von KHK-Patienten und steht daher in engem Zusammenhang mit einer erfolgreichen Therapie und somit einer besseren Prognose. Die vorliegende Studie zielt darauf ab, das Wissen über die eigene Erkrankung mittels Fragebogen an stationären kardiologischen Patienten zu evaluieren und den Einfluss einer Informationsveranstaltung darzustellen.

Methoden Im Rahmen des stationären Aufklärungs- und Präventionsprogramms „Herzensbildung" wurde an einer kardiologischen Abteilung mit 3 Bettenstationen eine prospektiv randomisierte Kohortenstudie („Usual care vs. Informationsgruppe"[INFO]) durchgeführt (n = 122). Die INFO-Gruppe nahm an einem ca. 60-minütigen Vortrag teil und erhielt anschließend den Patientenratgeber „Herzensbildung". Die Kontrollgruppe hingegen bezog ihre Informationen allein aus der ärztlichen Visite. Vor der Entlassung wurden die Überprüfungsbögen (mit 9 Fragen) an alle Patienten ausgeteilt. Ein Wissensscore wurde aus den Fragen 1–6 (single-choice mit 3 Möglichkeiten) und ein 2. Score aus den Fragen 7–9 (3 selbst zu nennende Antwortbeispiele) gebildet (**Tabelle 4**). Die Prozentangaben der beiden Scores beziehen sich auf den Anteil der Patienten, die alle Fragen richtig beantworten konnten.

Tabelle 4: B. Dutta-Függer et al.

		Gesamt (%)	Kontrolle (%)	INFO (%)	p
1	Eigenverantwortung	83,0	75,5	87,8	0,064
2	Lifestyle	74,3	50,9	89,2	< 0,001
3	Bewegung/Sport	66,7	42,3	81,9	< 0,001
4	Cholesterin	58,7	41,7	69,2	0,002
5	Blutdruck	73,3	64,2	79,5	0,052
6	LDL	45,7	39,6	50,0	0,024
	Score 1	**41,8**	**16,7**	**58,1**	**< 0,001**
7	Risikofaktoren	77,2	68,3	82,2	0,075
8	Gesundes Leben	64,3	47,5	73,6	0,004
9	Gesunde Ernährung	84,3	84,1	84,4	0,880
	Score 2	**61,5**	**41,7**	**74,3**	**0,001**

Resultate In der Kontrollgruppe erweist sich nur etwa die Hälfte der Patienten als ausreichend informiert (% der einzelnen Fragen). Wie aus der Tabelle erkennbar, zeigen sich sowohl in Score 1 als auch in Score 2 signifikante Verbesserungen des Patientenwissens in der INFO-Gruppe. Daraus ergibt sich im Gesamtkollektiv ein durchschnittliches Wissen von etwa 50 % (bezogen auf die % der einzelnen Fragen).

Zusammenfassung Je höher das Wissen um die eigene Erkrankung ist, desto höher ist auch die Compliance bezüglich medikamentöser Therapie und Lebensstiländerung. Wie unsere Daten zeigen, sind nur 50 % der kardiologischen Durchschnittspatienten ausreichend informiert. Die Abhaltung von Informationsveranstaltungen und das Angebot schriftlicher Unterlagen führten zu einem signifikanten Wissensanstieg, der mittel- bis längerfristig auch als sinnhafte, sekundärpräventive Maßnahme anzusehen ist.

Stationäres Präventionsprogramm „Herzensbildung": Wie nachhaltig sind Effekte auf das Patientenwissen? 173

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Hintergrund Die Abhaltung von Informationsveranstaltungen und das Angebot schriftlicher Unterlagen über Herz-Kreislauferkrankungen führen zu einem signifikanten Wissensanstieg bei stationären KHK-Patienten. Das bessere Krankheitsverständnis beeinflusst nachweisbar die Compliance von KHK-Patienten und steht daher in engem Zusammenhang mit einer besseren Prognose. Diese Studie hat sich zum Ziel gesetzt, die Nachhaltigkeit solcher Bildungsmaßnahmen mittels telefonischem Follow-up zu evaluieren.

Methoden Im Rahmen des stationären Aufklärungs- und Präventionsprogramms „Herzensbildung" wurde an einer kardiologischen Abteilung mit 3 Bettenstationen eine prospektiv randomisierte Kohortenstudie (Usual care vs. Informationsgruppe [INFO]) durchgeführt (n = 122). Die INFO-Gruppe nahm an einem ca. 60-minütigen Vortrag teil und erhielt anschließend den Patientenratgeber „Herzensbildung". Die Kontrollgruppe hingegen bezog ihre Informationen allein aus der ärztlichen Visite. Die in das stationäre Aufklärungs- und Präventionsprogramm „Herzensbildung" aufgenommenen Patienten wurden nach durchschnittlich 6 Monaten telefonisch kontaktiert und nochmals zu 4 Themen des Wissensscores (**Tabelle 5**) befragt. Die prozentuellen Angaben der Tabelle beziehen sich auf die einzelnen korrekt beantworteten Fragen, sowie zusätzlich auf jenen Patientenanteil, der alle 4 Fragenbereiche richtig beantworten konnte.

Resultate Sowohl am Ende ihres Krankenhausaufenthalts als auch nach durchschnittlich 6 Monaten zeigt sich die INFO-Gruppe signi-

Tabelle 5: B. Dutta-Függer et al.

	Gesamt (%)	Kontrolle (%)	INFO (%)	p
Stationär	n = 122			
Eigenverantwortung	84,1	78,0	87,8	0,137
Bewegung/Sport	66,7	40,8	81,9	< 0,001
Blutdruck	74,2	66,0	79,5	0,090
LDL	45,2	38,0	50,0	0,187
Alle 4	59,2	40,8	71,1	< 0,001
Follow-up	n = 74			
Eigenverantwortung	77,0	66,7	83,0	0,111
Bewegung/Sport	51,4	51,9	51,1	0,948
Blutdruck	64,9	51,9	72,3	0,078
LDL	29,7	11,1	40,4	0,008
Alle 4	35,1	22,2	42,6	0,010

fikant besser informiert. Fast doppelt so viele Patienten unseres Aufklärungsprogramms konnten im Follow-up alle 4 Fragen richtig beantworten – im Gegensatz zur routinemäßig betreuten Kontrollgruppe.

Zusammenfassung Zusätzlich in den stationären Alltag integrierte Patientenfortbildungen wie „Herzensbildung" führen nachhaltig zu einem signifikanten Wissensanstieg, der die Grundlage für eine verbesserte Compliance und konsequentere Lebensstiländerung darstellt.

Wie viel wissen unsere Patienten über ihre Medikamente? 112

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Einleitung Die Prognose einer Herz-Kreislauferkrankung hängt stark von den weiterführenden medikamentösen Maßnahmen und Lebensstiländerungen ab. Studien zeigen, dass medikamentöse Therapien nur zu 50 % beibehalten werden. Ein wesentlicher Prädiktor einer zufriedenstellenden Medikamenten-Adherence ist eine gute Aufklärung über die notwendige medikamentöse Therapie. Ziel der vorliegenden Studie ist die Evaluation des subjektiven und objektiven Medikamentenwissens kardiologischer Patienten und ihrer medikamentösen Adherence.

Methoden Im Rahmen des stationären Aufklärungs- und Präventionsprogramms „Herzensbildung" wurden Patienten (n = 135) mit koronarer Herzkrankheit, die stationär auf einer kardiologischen Abteilung aufgenommen waren, mittels Fragebogen über ihre medikamentöse Therapie befragt. In vier Fragen wurde das Wissen über die Wirkung der eingenommenen Medikamente geprüft. Eine Frage bezog sich auf die Namen der Medikamente und in zwei weiteren Fragen wurden die Patienten zu ihrer Medikamenten-Adherence befragt.

Ergebnisse 82 % aller Patienten glauben zu wissen, wofür sie welches Medikament einnehmen. Tatsächlich aber konnten nur 57 % alle 4 Fragen darüber richtig beantworten. Ihre Medikamente richtig benennen konnten überhaupt nur 24,2 % aller Patienten. 77,1 % der Patienten gaben an, ihre verordneten Medikamente täglich einzunehmen, wobei 18,3 % diese Frage nicht beantworten wollten. 78,4 % beabsichtigen, ihre Medikamente nach ihrer Entlassung regelmäßig einzunehmen, allerdings wollten sich 16,3 % der Patienten zu dieser Frage nicht äußern.

Zusammenfassung Unsere Daten zeigen, dass kardiologische Patienten sowohl eine unzureichende Adherence haben als auch zu wenig über ihre medikamentöse Therapie wissen. Eine verbesserte Aufklärung über die einzunehmenden Medikamente ist daher sinnvoll und notwendig, um die Medikamenten-Adherence zu erhöhen, und stellt eine wesentliche sekundärpräventive Maßnahme dar.

Adherence ist das Resultat einer erfolgreichen Kommunikation zwischen Arzt und Patient! Wie lange sprechen wir Kardiologen mit unseren Patienten bei der Visite? 113

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Einleitung Obwohl das Gespräch zwischen Arzt und Patient auch heute noch ein zentrales Instrument für die Diagnose und Therapie von Krankheiten ist, bleibt im Krankenhausalltag dafür oft nicht genug Zeit. Man schätzt, dass für eine erfolgreiche Aufklärung mindestens 90 Minuten Zeitaufwand notwendig sind. Eine gute Adherence resultiert aus einer erfolgreichen Aufklärung. Ziel dieser Studie ist es, die während der Visite effektive Aufklärungszeit und Gesamtgesprächsdauer zu bestimmen und somit das Ausmaß der ärztlichen Kommunikation im Spitalsalltag zu quantifizieren.

Methoden Im Rahmen des stationären Aufklärungs- und Präventionsprogramms „Herzensbildung" wurde an einer kardiologischen Bettenstation während 115 Arzt-Patienten-Gesprächen die effektive Gesprächsdauer im Rahmen der ärztlichen Visite geblindet gemessen. Die einzelnen Gespräche wurden in Aufklärungszeit, allgemeine Gesprächszeit und Gesamtdauer unterteilt.

Ergebnisse Die mittlere Gesprächsdauer betrug 3'12'' ± 2'40''. Davon wurden die Patienten im Schnitt 2'32'' ± 2'46'' aufgeklärt. Den Rest der Zeit (40'' ± 48'') wurde über allgemeine Themen gesprochen. KHK-Patienten im Speziellen wurden 2'14'' ± 2'22'' über ihre Krankheit aufgeklärt. Mit Frauen wurde signifikant länger als mit männlichen Patienten gesprochen (3'39'' ± 3'23'' vs. 2'54'' ± 2'02''; $p < 0,05$). Durchschnittlich dauerte das Gespräch mit weiblichen Patienten um 45 Sekunden länger.

Zusammenfassung Im stationären Setting einer kardiologischen Abteilung betrug die durchschnittliche Visitengesprächszeit knapp über 3 Minuten. In Anbetracht der Notwendigkeit von umfassenden Aufklärungsgesprächen erscheint die Visite als Instrument zur Aufklärung und Förderung der Adherence unzureichend.

Implementierung der therapeutischen Hypothermie nach Herzstillstand in Niederösterreich 075

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Hintergrund Patienten nach erfolgreicher Reanimation erleiden in vielen Fällen einen schweren hypoxischen Hirnschaden. Die bislang wirksamste Therapie zur Verbesserung des neurologischen Outcomes nach einem Herzstillstand ist die therapeutische Hypothermie für 12–24 Stunden. Diese Therapie wird seit 2005 auch in den Behandlungsrichtlinien des ERC und der AHA empfohlen. Unsere Studie hat die Implementierung der therapeutischen Hypothermie in Intensivstationen Niederösterreichs untersucht.

Methode Mittels eines schriftlichen Fragebogens wurden 25 Intensivstationen Niederösterreichs untersucht. Bei fehlender schriftlicher Rückmeldung wurde die betreffende Station telefonisch befragt, sodass ein kompletter Datensatz erhoben werden konnte. Der Fragebogen umfasste neben der grundsätzlichen Anwendung der Hypothermie nach Herzstillstand unter anderem die Art der Kühlung, die Begleittherapie, die Behandlungsdauer sowie gegebenenfalls die Gründe für die fehlende Anwendung der Methode.

Ergebnisse Von 25 Intensivstationen gaben 2 an, keine Patienten nach Herzstillstand zu betreuen. Von den übrigen 23 Stationen (im Folgenden 23 = 100 %) behandelten 10 (43 %) ihre reanimierten Patienten mit therapeutischer Hypothermie. Von diesen Stationen kühlten 9 (39 %) auf die empfohlene Temperatur von 32–34 °C und 1 Station (4 %) auf 34–35 °C ab. Die Kühlungsdauer betrug 24 Stunden (n = 8, 35 %), 24–48 Stunden (n = 1) und 48 Stunden (n = 1). Zur Induktion der Hypothermie wurden kalte Infusionen (n = 5; 22 %), Oberflächenkühlung (n = 7; 30 %) und endovaskuläre Kühlung (n = 6; 26 %) verwendet, wobei einige Stationen 2 Methoden kombinierten oder unabhängig voneinander einsetzten. Zur Aufrechterhaltung der Hypothermie wurden die oben genannten Methoden weiterge-

führt (Infusionen: n = 2; Oberflächenkühlung: n = 7; endovaskulär: n = 6). Die Gründe der Stationen, die keine Hypothermie einsetzten, waren vor allem fehlende Personalressourcen (n = 4; 17 %), zu hoher technischer Aufwand (n = 4; 17 %) und fehlende Information über die Methode (n = 3; 13 %).

Schlussfolgerung Die Implementierung der therapeutischen Hypothermie in Niederösterreich ist bislang nicht ausreichend erfolgt. Wenn die Methode eingesetzt wird, geschieht dies aber großteils entsprechend den Richtlinien. Die Ursachen der fehlenden Anwendung könnten durch Fortbildungsmaßnahmen wahrscheinlich leicht behoben werden.

Occult Myeloproliferative Disorder in Patients with Coronary Syndrome 107

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Polycythemia vera (PV) and essential thrombocythemia (ET) are clonal hematopoietic stem-cell diseases. A large number of patients with PV or ET have a somatic defect in JAK2 or MPL. The incidence rates are very low (1 to 10 patients per million people per year). The clinical image is dominated by a predisposition to arterial and venous thromboembolic complications. Patients with myeloproliferative disorders (MPD) are at risk of developing coronary disease due to atherothrombosis.

We hypothesized a high mutation frequency of JAK2 or MPL in a cohort of patients with coronary angiography due to coronary syndrome, because of the known that coronary disease is a complication of MPD´s. According to Tefferi et al. [Blood 2007; 110: 1092–7] all patients with elevated platelets e" 450 x 109/L were analyzed.

A total of 1009 patients with coronary angiography were investigated due to elevated red blood cells (hemoglobin > 18.5 g/dL in men and > 16.5 g/dL in women or other evidence of increased red cell volume) and/or thrombocytosis (platelets ≥ 450 × 109/L). Seven patients showed elevated red blood cells and eight patients had increased platelets. JAK2 mutation analysis (sequence-specific polymerase chain reaction) were realized. We identified two patients with occult JAK2 V617F mutation in the subgroup with elevated platelets (2/8; 25 %), whereas the platelet count of these patients were lower than 600 × 109/L. One patient, a 41 year old man, showed recurred coronary symptoms regardless of appropriate treatment and stop smoking.

As a result of our findings JAK2 mutation analysis should be considered in patients with recurrent unexplained coronary events, refractory to usual treatment and persistent elevation of blood count even though these might be modest. This approach can identify those patients with coronary syndrome and occult MPD. Due to diagnosis of occult MPD, these patients will be additionally concerned with cytoreductive therapy. The platelet count of ≥ 600 × 109/L as diagnostic criteria (WHO) for ET should be lowered to 450 × 109/L as proposed but not fixed in WHO recommendations. Patients with combined coronary disease and MPD need to be followed up carefully by a cardiologist and haematologist.

Hyperreninemia Secondary to ARB in a Young Hypertensive Patient 056

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Introduction The renin-angiotensin system plays a decisive role in the pathophysiology of hypertension. Renin release is regulated by a number of factors, including circulating angiotensin II (Ang II), the so-called short feedback loop. Both angiotensin-converting enzyme inhibitors and ATII receptor blockers show dose dependent effects on plasma renin activity. Renin-secreting tumors of both renal and non-renal origin have been known for a long time and cause a surgically curable form of hypertension. Hyperreninemia can derive from various sources and is thus involved in the pathophysiology of arterial hypertension. Hence, hyperreninemic hypertension in a patient certainly warrants special attention under the aspect of diagnosis and treatment.

Case A 28 year old man (75 kg/179 cm) presented with acute chest pain, dyspnoea and arterial hypertension of 240/120 at rest. He had arterial hypertension for 15 years and and a positive family history. At admission, he had already been under treatment with lercanidipin and candesartan.

Physical examination, chest x-ray, CT of head/brain, abdominal sonography, ocular fundus, EEG, CCDS of renal arteries, renal flow szintigraphy as well as renal MR angiography were normal. The initially very high BP was treated with intraveneous urapidil and, after 10 days, the patient could leave hospital with a multidrug antihypertensive therapy (lercanidipine 10 mg bid, candesartan 8 mg bid, hydrochlorothiazide 12.5 mg once a day, urapidil 60 mg bid, and rilmenidin 1 mg once a day. Routine laboratory: within the normal range. 24 h urine catecholamins were normal. Several months later, in order to exclude hyperaldosteronism, radio immune assay analysis of basal plama aldosteron had been performed. The latter was 5.0 ng/dl (normal: 3.0–15) and basal plasma renin (horizontal position of patient) was > 500 µU/ml (normal: 2.4–29 horizontal position, 3.3–41.0 vertical position). CT of the abdomen and retroperitoneum provided no evidence for a tumor. Under the assumption that hyperreninemia could possibly not be the cause of hypertension in this case, but be the effect of treatment, candesartan was discontinued for 1 month and basal renin returned to 30.8 µU/ml, while basal aldosteron was down at 2.7 ng/dl. Then, candesartan was again administered at a dose of 8 mg bid and within 3 weeks basal plasma renin rose to 213.3 µU/ml.

Conclusion Hyperreninemia can *per se* be the cause of hypertension and, especially in severe hypertension, one tends to a more complex investigation including measurement of basal plasma renin and aldosterone. We conclude that basal plasma renin activity and aldosterone should be measured in patients with severe hypertension, however, it is important to be viewed at in the context of ACE-inhibiton or ATII receptor blockade.

Einfluss von Nebivolol auf die Genexpression während experimenteller myokardialer Ischämie 061

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Betablocker werden seit über 30 Jahren zur antiischämischen Myokardprotektion verwendet. Zahlreiche klinische aber auch experimentelle Daten belegen den kardioprotektiven Effekt dieser Substanzen. Es ist bekannt, dass Betablocker wohl einerseits bestimmte Klasseneffekte haben, andererseits aber doch ein heterogenes Wirkungsprofil entfalten (vgl. z. B. Sotalol, Carvedilol und Nebivolol). Vor Kurzem entwickelte Messtechniken erlauben die Darstellung des Genexpressionsprofils (hier 23.000 Gene) während myokardialer Ischämie [J Clin Basic Cardiol 2006; 13–15] bzw. die Modifikation desselben durch Pharmaka (hier Betablocker). Über letztere ist noch wenig bekannt. Hier untersuchten wir die Wirkung von Nebivolol auf die Myokardischämie-spezifischen Genexpressionsmuster an humanem rechtsatrialen Myocard (Auriculum), welches bei herzchirurgischen Eingriffen anfällt.

Methodik 30 Minuten experimentelle Ischämie in Normal-Tyrode, simuliert durch 100 % N_2-Begasung. RNA Gewinnung: TRIZOL® Methode (Invitrogen Corporation, Carlsbad, CA, USA), RNeasy Mini Kit (QIAGEN Inc., Hilden, GERRNA); Qualitäts/Quantitätsanalyse: Spektrophotometrie und Agilent's Bioanalyzer 2100 System; In-vitro-Transkription: High Capacity cDNA Archive Kit (Applied Biosystems) und Thermocycler MyCyclerTM von Biorad. Microarrayuntersuchungen (Applied Biosystems) wurden mittels

AB 1700 Chemoluminescenz Array Reader gescannt und die Daten in einem MIAME-kompatiblen ORACLE dat. AB1700 Microarray Analyzer System gespeichert. Die Auswertung erfolgte mittels PANTHER-Software.

Ergebnisse Es zeigten sich mehrere biologische Prozesse, welche keine Veränderung unter experimenteller Ischämie zeigten, jedoch durch Einwirkung von Nebivolol (20 µmol/l) während Ischämie dann signifikant hochreguliert wurden. Darunter fanden sich vorwiegend apoptotische Prozesse sowie Prozesse des Ca-mediierten Signallings, der oxidativen Phosphorylierung, der mRNA-Transkription und Regulation, der Protein Biosynthese, der Zellproliferation und Differenzierung. Interessanterweise findet sich kein spezifischer biologischer Prozess, der unter Ischämie durch Nebivolol hinunterreguliert ist.

Aus der Beobachtung, dass Prozesse wie Zellproliferation und Proteinbiosynthese auf der einen Seite, andererseits der kontrollierte Zelltod betroffen sind, schließen wir, dass Betablocker (hier Nebivolol) eine aktive kardioprotektive Wirkung auf molekularer Ebene während Ischämie entfalten, was mit den klinischen Beobachtungen aus den großen Studien wie ISIS I in Übereinstimmung wäre.

Differential Effects of Atenolol and Nebivolol Inhibits the Activation of T-Cell Immunity During Experimental Ischemia in Human Myocardial Tissue 148

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

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

After 30 minutes of myocardial hypoxia we find that gene expression related to T-cell immunity is more than two-fold up-regulated compared to normoxic controls (25 of 185, 10.4 expected; $p \leq 0.00008$). In contrast, when 22,47 µmol nebivolol has been added to the solution, gene expression related to T-cell mediated immunity is significantly down-regulated (21 down of 249, 7.3 expected; $p \leq 0.0001$). Conversely, 15 of 21 genes down-regulated by nebivolol during experimental hypoxia have been neither up- nor down-regulated in the presence of an equipotent dose of atenolol during experimental hypoxia. Our observations are in accordance with published data indicating that nebivolol reduced the expression of pro-inflammatory genes in endothelial and vascular smooth muscle cells in vitro, whereas metoprolol did not. Similarly, carvedilol has recently been shown to attenuate inflammation.

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

Effects of Nebivolol in Patients with Arrhythmias and Arterial Hypertension: An Observational Small Cohort Study 149

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Betablockers are widely recommended in the treatment of arterial hypertension. Many clinical trials have investigated these drugs under various aspects of anti-hypertensive action and outcome. Despite their pharmacology being well understood, the exact mechanism by which their antihypertensive action is unfolded remains an open question.

Nebivolol is a rather new third generation beta-blocker with very pronounced cardioselectivity and additional features such as NO-dependent vasodilation. It has been used successfully in the treatment of patients with arterial hypertension. In an observational pilot trial, we here study the effects of nebivolol in a cohort of 62 hypertensive patients.

From the first visit, the arterial blood pressure fell from an initial value of 154.7 ± 2.8 mmHg after 11.7 ± 1.7 days to a value of 132.6 ± 2.8 mmHg ($p < 0.0001$), and stabilised at the third visit at 140.4 ± 2.5 mmHg after 67.1 ± 4.0 days. Compared to the initial measurements, the reduction was statistically significant ($p < 0.0001$). Diastolic blood pressure was elevated at the first visit with 85.7 ± 1.6 mmHg, fell at the second visit to 74.7 ± 1.6 mmHg ($p < 0.0001$) and remained stable at the third visit at 79.2 ± 1.6 mmHg ($p < 0.00015$) when compared to initial values. Compliance of all patients was good and the antihypertensive action of nebivolol was marked with 2.2 ± 0.1 by the physicians involved (scale from 1 [best] to 5). The mean heart rate of patients at the first visit was 77.4 ± 1.8 bpm, at the second visit 67.5 ± 1.3 bpm and at the third visit 69.4 ± 1.5 bpm, there was a significant fall in heart rate between the first and the second visit ($p < 0.0001$), however between the second and the third visit the heart rate did not change significantly anymore ($p < 0.14$). Nebivolol reduced symptoms of arrhythmias in hypertensive patients (**Figure 1**): at the first visit, 50 (81 %) of all patients showed palpitations, at the second visit 12 (19 %) showed palpitations and at the third visit 8 (13 %) reported palpitations. Symptoms of tachycardia were reported in 29 (47 %) of the patients at the first visit, 2 (3 %) had symptoms of tachycardia at the second visit and 2 (3 %) at the third. Similarly, dizziness seen in 35 (56 %) of the patients at the first visit, in 15 (24 %) at the second visit and in 10 (16 %) at the third. History of syncope was seen in the recent history of 6 (10 %) patients and re-occurred in 2 (3 %) of those, four remained without syncope after the administration of nebivolol. Adverse effects were minimal during the observation period. No noteworthy adverse effects have been seen.

Betablockers, in fact, have long been regarded as effective agents for supra-ventricular and ventricular arrhythmias. Betablockers as a class show multiple anti-arrhythmic mechanisms such as various membrane stabilising effects and they limit spontaneous depolarisa-

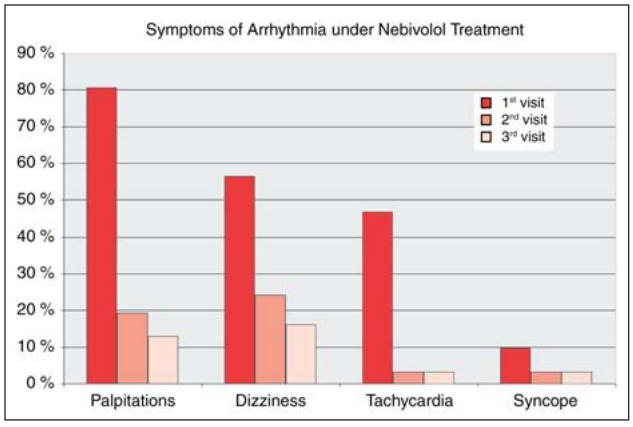

Figure 1: D. von Lewinski et al.

tion. Nebivolol too exhibits a remarkable anti-arrhythmic potential. However, there have been few attempts to explore and use it therapeutically. In this observational pilot study, we assess the anti-hypertensive effect of nebivolol in patients treated for arterial hypertension.

Despite the limitations of this study being non randomised and observational, we conclude that nebivolol exerts a satisfactory antihypertensive effect, is well tolerated and helps to reduce symptoms usually related to arrhythmias.

Cardiovascular Events during FIFA Soccer World Cup 2006 in Bavaria 138

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Objectives Recently, an increase in the incidence of cardiovascular events in Bavaria during FIFA Soccer World Cup 2006 (WC) has been reported. A significant pooling of cardiovascular events on days the German team played as well as on the day of the final game was shown. However, in this excellent report only a limited number of cardiac diagnoses were analyzed.

Methods In order to assess further acute cardiac disorders we requested data for the period of the WC (June 9–July 9, 2006) but also for control periods (May 1st–July 31st, 2003 and 2005; May 1st–June 8th, 2006 i.e. before WC and July 10th–31st, 2006 i.e. after WC) from the Bavarian Council for Statistics and Data Management on diagnoses. The following diagnoses were assessed: myocardial infarction (ICD-10; I 21); cardiac arrest (I 46); paroxysmal tachycardia (I 47); atrial fibrillation, atrial flutter (I 48); all remaining tachyarrhythmias (I 49).

Results Despite an increase in cardiac events among Bavarians on the days the German team played, there was no overall increase in events per day during the WC (31 days) compared to control periods (242 days): (I 21 myocardial infarction: 68 vs 68; I 46 cardiac arrest: 3 vs 3; I 47 paroxysmal tachycardia: 19 vs 20; I 48 atrial fibrillation and atrial flutter: 64 vs 65; I 49 other arrhythmias: 14 vs 18; all conditions above: 168 vs 174; p = 0.99).

Conclusion Whereas the original analysis by Wilbert-Lampen et al. urges organizers of large-scale events to be especially prepared on days on which local teams play, our data somewhat assure us that watching such enjoyable events does not lead to an overall increase in cardiac events beyond that seen during control periods. We rather hypothesize that emotional stress induced by watching soccer pools cardiovascular events to one specific moment i.e. a soccer game, but would have likely occurred anyway within the control period and thus within the very near future.

Effects of Pantoprazole and Esomeprazole on Platelet Inhibition by Clopidogrel 067

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Background Clopidogrel is activated by CYP2C19 which also metabolizes proton pump inhibitors (PPI). As proton pump inhibitors (PPI) are metabolized to varying degrees by CYP2C19, we hypothesized that the reported negative omeprazole-clopidogrel drug interaction may not be a class effect.

Methods Responsiveness to clopidogrel was assessed by the vasodilator stimulated phosphoprotein (VASP) phosphorylation assay and aggregometry (Multiplate Analyzer) in 300 patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI).

Results The mean platelet reactivity index (PRI, assessed by VASP assay) was nearly the same in patients with (n = 226; PRI = 51 %) or without PPI treatment (n = 74; PRI = 49 %; p = 0.724). Likewise, the ADP-induced platelet aggregation did not differ significantly between patients with or without PPI treatment (45 U vs 41 U; p = 0.619). Similarly, there was no difference in the PRI or the ADP-induced platelet aggregation between patients with pantoprazole (n = 152; PRI = 50 %; aggregation = 47 U), esomeprazole (n = 74; PRI = 54 %; aggregation = 42 U) or without PPI (n = 74; PRI = 49 %; aggregation = 41 U; p = 0.382).

Conclusion In contrast to the reported negative omeprazole-clopidogrel drug interaction, the intake of pantoprazole or esomeprazole is not associated with impaired response to clopidogrel. Therefore, the PPI-clopidogrel drug-drug interaction might not be a class effect.

Exercise Training on Top of Standard Medication Increases Endothelial Progenitor Cells and Decreases ADMA Levels in Patients with PAD 116

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Purpose We designed a prospective randomized controlled trial to study markers of angiogenesis 6-months after supervised exercise training compared to medical therapy alone.

Methods In 20 patients with intermittent claudication endothelial progenitor cells (EPC) were assessed by whole-blood flow cytometry (co-expression of CD34+CD133+KDR+) and cell culture assays (colony forming units/CFU and circulating angiogenic cells/CAC) at baseline and 6-months after training as well as 12-months after study begin. In addition, changes in maximum walking distance were recorded.

Results In the exercise group, EPC measured by flow cytometry increased significantly ($p < 0.05$) six months after training (EPC % pre: 0.0010 ± 0.0013 vs 6 mo: 0.0048 ± 0.0034) paralleled by a significant decrease of ADMA (asymmetric dimethylarginine µmol/l; pre: 1.13 ± 0.36 vs 6 mo: 0.69 ± 0.22), a major endogenous inhibitor of nitric oxide synthase. In parallel, the number of CFUs and CACs were significantly higher after 6-months compared to baseline upon exercise ($p < 0.05$). No differences were observed in the standard group in timecourse. However, 6-months after training cessation the number of EPC and ADMA levels were similar to baseline. Exercise training showed a delayed benefit on treadmill maximum walking distance with a significant increase at 12-months (training: baseline 104.9 ± 60 m vs 12-months 171.1 ± 68.9 m; p = 0.03; exercise: baseline 162.5 ± 145 m vs 12-months 126.6 ± 85.8 m; p = 0.17).

Conclusions The beneficial effect of exercise training in PAD patients might partly be due to EPC mobilization mediated by improved NO synthesis as we observed reduced ADMA levels.

Langzeittherapie mit Nebivolol verursacht keine Nitrattoleranz 004

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Kontinuierliche Langzeittherapie mit Nitraten kann zu Nitrattoleranz führen. Nebivolol ist ein hoch-selektiver Blocker von Beta-1-Rezeptoren mit zusätzlicher vasodilatierender Wirkung über den NO-Mechanismus. Es wurde jedoch noch nie untersucht, ob eine Langzeitgabe von Nebivolol zu Nitrattoleranz führt.

Im Rahmen einer eine randomisierten, überkreuzten Doppelblind-Studie erhielten daher 16 gesunde männliche Freiwillige in Abständen von 2 Wochen 5 mg Nebivolol oder Placebo *per os* 1× tägl. über jeweils 8 Tage. Der arterielle Fluss im Unterarm („forearm blood flow", FBF) wurde mittels Venenverschluss-Plethysmographie 3 Stunden nach Einnahme der jeweils letzten Einzeldosis gemessen, dann erhielten die Probanden 4 µg Nitroglyzerin/Minute/kg Körpergewicht intravenös für 5 Minuten, und der FBF wurde nochmals gemessen.

Nach 8 Tagen kontinuierlicher Einnahme von Placebo führte die intravenöse Gabe von Nitroglyzerin zu einem Anstieg des FBF von +54 % ($p < 0,05$), nach Einnahme von Nebivolol über die gleiche Zeit führte die gleiche Menge von Nitroglyzerin jedoch zu einem Anstieg des FBF von +96 % ($p < 0,05$). Dabei war die Wirkung von

Nitroglyzerin nach einer Woche Nebivolol sogar signifikant ausgeprägter (+78 %; p < 0,05) als nach einer Woche Placebo.

Diese Ergebnisse zeigen keinerlei Hinweis auf Nitrattoleranz bei Langzeitgabe von Nebivolol – ganz im Gegenteil scheint die vasodilatierende Wirkung von Nitraten nach Langzeitgabe von Nebivolol sogar noch weiter verstärkt.

Kein Hinweis auf Nitrattoleranz bei Langzeittherapie mit Nicorandil 005

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Kontinuierliche Langzeittherapie mit Nitraten kann zu Nitrattoleranz führen. Es wurde jedoch noch nie untersucht, ob eine Langzeitgabe von Nicorandil, einem NO-Donator mit zusätzlicher Wirkung auf den KATP-Kanal, Nitrattoleranz auslösen kann.

Im Rahmen einer randomisierten, überkreuzten Doppelblind-Studie erhielten daher 11 gesunde männliche Freiwillige in Abständen von 2 Wochen 20 mg Nicorandil oder Placebo *per os* 1× tägl. über jeweils 8 Tage. Der arterielle Fluss im Unterarm („forearm blood flow", FBF) wurde mittels Venenverschluss-Plethysmographie 3 Stunden nach Einnahme der jeweils letzten Einzeldosis gemessen, dann erhielten die Probanden 4 µg Nitroglyzerin/Minute/kg Körpergewicht intravenös für 5 Minuten, der FBF wurde nochmals gemessen.

Nach 8 Tagen kontinuierlicher Einnahme von Placebo führte die intravenöse Gabe von Nitroglyzerin zu einem Anstieg des FBF von +67 % (p < 0,05), nach Einnahme von Nicorandil über die gleiche Zeit zu einem Anstieg des FBF von +52 % (p < 0,05). Dabei fand sich zwischen diesen beiden Wirkungen kein signifikanter Unterschied.

Unsere Ergebnisse zeigen daher keinen Hinweis auf ein Auftreten von Nitrattoleranz bei Langzeitgabe von Nicorandil.

Patientennachbetreuung nach kardiologischer Rehabilitation mittels eines Patientenpasses und deren nachhaltiger Effekt auf das Cholesterin im Verlauf der letzten 8 Jahre 135

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Hintergrund Der positive Effekt eines 4-wöchigen stationären Rehabilitationsaufenthaltes auf kardiovaskuläre Risikofaktoren bei koronaren Patienten ist klar belegt. Der anhaltende Effekt konnte bisher noch nicht eindeutig gezeigt werden. Durch die Entwicklung einer Nachbetreuungsmöglichkeit mittels eines Patientenpasses („St. Radegunder Gesundheitspass") soll eine anhaltende Verbesserung der Risikofaktoren erreicht werden.

Methoden Im „St. Radegunder Gesundheitswegweiser" sind alle relevanten kardiovaskulären Risikofaktoren angeführt. Es werden die Aufnahmewerte erhoben, Ziele gemeinsam mit dem Patienten besprochen und die Werte am Ende des 4-wöchigen Aufenthaltes erhoben. Danach wird der Patient aufgefordert, dieselben Werte alle 3 Monate durch den Hausarzt kontrollieren zu lassen und nach 12 Monaten den Patientenpass zurückzuschicken. Nach Durchführung einer Pilotstudie zeigte sich, dass eine deutlich höhere Responderrate durch eine schriftliche Erinnerung der Patienten in 3-montigen Abständen erreicht werden konnte. Eingeschlossen wurden alle Patienten mit einer kardiovaskulären Erkrankung und ausreichenden kognitiven Fähigkeiten.

Ergebnisse Es liegen insgesamt 2643 vollständig ausgefüllte Patientenpässe aus den Jahren 2000–2007 vor. Innerhalb von 4 Wochen fand sich eine signifikante Absenkung des Gesamtcholesterins (173 ± 41 mg/dl vs. 154 ± 34 mg/dl) und des LDL-Cholesterins (112 ± 36 mg/dl vs. 93 ± 28 mg/dl), was einer Zielerreichungsquote bei Entlassung von 82,5 % bzw. 66,3 % entspricht. Nach 12 Monaten kam es zu einer Verschlechterung des Gesamtcholesterins (179 ± 37 mg/dl) und des LDL-Cholesterins (102 ± 31 mg/dl), wobei das LDL-Cholesterin weiterhin deutlich unter dem LDL-Aufnahmewert lag.

Im Verlauf der letzten 8 Jahre zeigte sich jedoch zu einer deutlichen Verbesserung der Lipidwerte sowohl bei Entlassung als auch nach 12 Monaten (**Tabelle 6**).

Konklusion Durch den Einsatz eines Patientenpasses wird die Motivation zur Durchführung regelmäßiger Kontrollen der kardiovaskulären Risikofaktoren gesteigert und ein anhaltender Erfolg der Rehabilitationsmaßnahmen gewährleistet. Zusätzlich zeigte sich eine stärkere Umsetzung der Cholesterin-Zielwerte im Verlauf der letzten 8 Jahre.

Herzinsuffizienz

Outcome of Chronic Heart Failure Patients after Device Implantation is Highly Dependent on Concomitant Medical Treatment Regimen 012

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Background Device implantation in chronic heart failure (CHF) for cardiac resynchronization therapy (CRT) with or without implantable cardioverter/defibrillator (ICD) is an established treatment option for symptomatic patients under medical baseline therapy. Although recommended, the need for optimization of medical therapy was never proven. As in "the real world", medical therapy is not always up-titrated to the desirable dosages, this provides the

Tabelle 6: M. Wonisch et al.

	2000 n = 161	2001 n = 368	2002 n = 383	2003 n = 425	2004 n = 361	2005 n = 349	2006 n = 376	2007 n = 220
				Gesamtcholesterin (mg/dl)				
Aufnahme	180 ± 42	178 ± 44	180 ± 42	178 ± 44	174 ± 40	166 ± 34	162 ±36	166 ± 37
Entlassung	164 ± 30	158 ± 35	162 ± 36	160 ± 36	157 ± 34	145 ± 30	142 ±28	140 ± 28
12 Monate	188 ± 36	187 ± 40	184 ± 37	181 ± 36	177 ± 33	171 ± 35	168 ±35	168 ± 33
				LDL-Cholesterin (mg/dl)				
Aufnahme	113 ± 37	115 ± 38	114 ± 36	112 ± 36	107 ± 33	104 ± 30	101 ±32	106 ± 32
Entlassung	98 ± 26	98 ± 30	98 ± 29	97 ± 30	91 ± 26	87 ± 28	85 ±25	84 ± 25
12 Monate	107 ± 31	110 ± 32	107 ± 32	104 ± 33	97 ± 28	96 ± 29	94 ±28	92 ± 27

opportunity to evaluate the impact of optimizing medical therapy in patients who had received a device therapy with proven effectiveness.

Aim This observational cohort study assessed the "real life"-effect of CRT compared to CRT/ICD therapy and the impact of concomitant pharmacotherapy on outcome.

Results Mean follow-up for the 205 CHF patients (95 CRT and 110 CRT/ICD) was 16.8 ± 12.4 months. In the total study cohort 83 (41 %) reached the combined primary endpoint of all-cause death or cardiac hospitalization (CRT group: 25 [26 %], CRT/ICD group: 58 [52.7 %]; $p < 0.001$). Cox regression analysis revealed non-optimized medical therapy at follow-up (HR = 2.080 [1.166–3.710]; $p = 0.013$) and CRT/ICD versus CRT (HR = 2.504 [1.550–4.045]; $p < 0.001$) as significant predictors of the primary endpoint.

Conclusion Our data stress the importance of professional monitoring and titration of pharmacotherapy not only in medically treated CHF patients but also in patients under device therapy by a heart failure unit or a specialized cardiologist.

Functional Exercise Capacity Affects the Response to CRT as Revealed by Submaximal Exercise Testing 145

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Introduction Despite high numbers of nonresponders to CRT there are some considerations to extend the inclusion criteria for CRT to NYHA class I patients. We evaluated the impact of functional exercise capacity as obtained by submaximal exercise testing to predict response to CRT.

Methods In 28 patients who underwent implantation of a CRT device (age 64 ± 10 years; LVEF < 35 %; NYHA class II–III; QRS 150 ± 24 msec) a submaximal cardiopulmonary treadmill exercise test was performed. As a measure of functional exercise capacity the oxygen uptake efficacy slope (OUES) was determined by breath-to-breath gas analysis. Response to CRT (> 10 % increase in cardiac output) was evaluated by bioimpedance cardiography.

Results Responders to CRT showed a significantly lower intrinsic (no pacing) functional capacity as compared to nonresponders (OUES 1200 ± 600 vs 2581 ± 681; $p < 0.01$). Responders to CRT showed a significant increase in OUES during biventricular pacing as compared to no pacing (deltaOUES 679 ± 185; $p < 0.05$) whereas nonresponders showed no significant effects (deltaOUES –387 ± 170; p = n. s.). The absolute increase in OUES during CRT was similar in both groups (1879 ± 863 vs 2194 ± 460; p = n. s.).

Conclusion Response to CRT is associated with the impairment of functional exercise capacity. Only patients with significantly decreased exercise capacity showed response to CRT. Therefore, estimation of OUES by submaximal exercise testing may help to identify responder to CRT.

Die nicht-invasive Darstellung der elektroanatomischen Aktivierung des Herzens ermöglicht die Identifikation von Respondern der kardialen Resynchronisationstherapie 146

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Hintergrund Eine etablierte Therapie der fortgeschrittenen Herzinsuffizienz ist die Implantation eines biventrikulären Schrittmacher/Defibrillators. Trotz Erfüllung aller Einschlusskriterien besteht immer noch das Problem des Nichtansprechens der kardialen Resynchronisationstherapie (CRT). Mithilfe einer neuen nicht-invasiven Darstellung der kardialen elektrischen Aktivierung (NICE) wird versucht, das Ansprechen der CRT darzustellen bzw. vorauszusagen.

Tabelle 7: T. Berger et al.

	Aktivierungsdauer der Ventrikel	RR-Intervall	QT-Intervall	Tpeak-Tend
Intrinsische Aktivierung	141 ms	466 ms	379 ms	123 ms
RV-Stimulation	99 ms	570 ms	372 ms	113 ms
Bivent-Stimulation	59 ms	570 ms	392 ms	65 ms

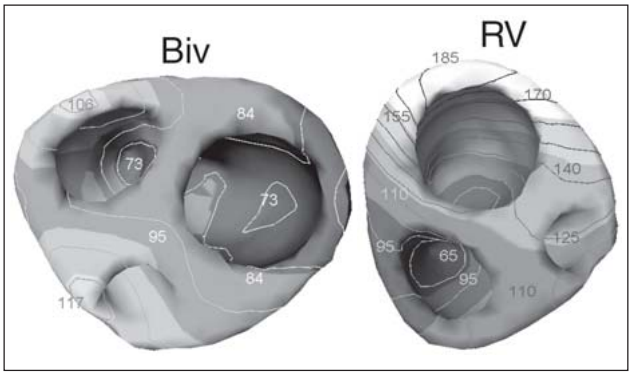

Abbildung 2: T. Berger et al.

Methode NICE benötigt zur nicht-invasiven Bestimmung der kardialen elektrischen Aktivierung eine MRI Darstellung des Torso. Damit wird ein individuelles Model des Herzens (inkl. evtl. Narbenareale und des Koronarvenensinus) erstellt. Zusätzlich wird mittels hochauflösendem Oberflächen-EKG (65 Elektroden) die epikardiale elektrische Aktivierung mittels inverser bidomainer Algorithmen berechnet. Anhand einer Fusionierung dieser Daten erfolgte die Darstellung der elektrischen Aktivierung (mittels Isochrone) am individuellen Patientenmodell. Die Berechnungen erfolgten jeweils vor Beginn der CRT bzw. während rechtsventrikulärer und biventrikulärer Stimulation.

Resultate Bei 4 Patienten erfolgte die Darstellung der elektroanatomischen ventrikulären Aktivierung für die intrinsische Aktivierung bzw. für unterschiedliche Stimulationsmodi. Dabei zeigt sich eine signifikante Abnahme der totalen ventrikulären Aktivierungszeit während biventrikulärer Stimulation im Vergleich zur rechtsventrikulären Stimulation bzw. zur intrinsischen Aktivierung (**Tabelle 7** und **Abbildung 2**: Totale ventrikuläre Aktivierungszeit für biventrikuläre [Biv] und rechtsventrikuläre [RV] Stimulation in Millisekunden).

Zusammenfassung Die nicht-invasive Darstellung der elektroanatomischen Aktivierung mittels NICE ermöglicht die genaue Lokalisation der Region der spätesten linksventrikulären Aktivierung am individuellen Patienten. In Kombination mit den MRI-Daten sollte in Zukunft bereits präoperativ die optimale Platzierung der linksventrikulären Elektrode (abhängig von evtl. Narbenarealen und der CS-Anatomie) planbar sein.

Sleep Apnea Syndrome in Patients with Stable Chronic Heart Failure: Results of an Austrian Pilot Study 029

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Purpose Treatment of congestive heart failure made remarkable progress over the last several years. Beside recommended medical and electrical therapy, new treatment strategies might contain non invasive ventilation in patients with Cheyne-Stokes respiration. Sleep laboratories, the gold standard of diagnosis of sleep apnea syndrome, are confronted with raising demand for examinations. Hence, patients access to supplemental non invasive ventilation therapy may be delayed. In case of adequate reliability, ambulant polygraphy

could provide a reasonable tool for compensating lack of polysomnographic monitoring units.

Methods We performed a pilot study to compare a portable monitoring device in reference to standardised polysomnography. All patients suffered from stable chronic heart failure with impaired left ventricular systolic function and levels of proBNP beyond 300 ng/ml.

Results A total of 20 patients (male 16; female 4) participated polysomnography and were examined with a portable overnight monitoring device. 11 patients (55.0 %) suffered from ischemic cardiomyopathy, and 9 (45.0 %) from nonischemic cardiomyopathy. Mean age was 65.7 years (minimum 51.0; maximum 82.4; SD 8.4). Median and quartiles of proBNP were 2237.0 ng/ml, 823.5 ng/ml and 4583.8 ng/ml, with a range from 420.4 ng/ml to 16,465.0 ng/ml, respectively. Standardised polysomnography detected a median apnea hypopnea index (AHI) of 9.1 per hour of sleep. Minimal AHI was 0.9 and maximal AHI was 38.0. Median average oxygen saturation was 92.0 %, and minimal oxygen saturation was 74.4 %. In 12 patients (60 %) polysomnography detected an AHI > 5, whereas 8 patients (40 %) had an AHI < 5. Examinations with a portable device disclosed a median AHI of 9.9 per hour of investigation with a minimal AHI of 0.7 and a maximal AHI of 50.7. Median average oxygen saturation was 92.0 %, and minimal oxygen saturation was 69.0 %. Ambulant polygraphy disclosed 16 patients (80 %) with an AHI > 5, whereas 4 patients (20 %) presented with an AHI < 5. For detection of sleep apnea sensitivity and specificity of ambulant polygraphy were 0.6, 0.6, respectively.

Conclusions Ambulant polygraphy might provide an accurate diagnostic tool for detecting sleep related breathing disorders with a substantial reduction of diagnostic procedures. Further investigations are needed to assess reliability and feasibility of portable monitoring devices.

Sequential Heart and Autologous Stem Cell Transplantation in a Patient with Cardiac Amyloidosis 120

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Background Systemic amyloidosis complicated by severe congestive heart failure is associated with high cardiovascular morbidity and mortality. In primary (AL) amyloidosis symptomatic cardiac involvement is associated with a particularly poor prognosis, the median survival time is 9 months. Patients suffering from severe cardiac amyloid infiltration are usually ineligible for the preferred treatment of chemotherapy followed by stem cell transplantation (SCT), because of the high risk for the treatment-related mortality. However, some rare cases have been reported, in which sequential heart and autologous SCT as a promising treatment option has been successful.

Patients and Methods A 47 years old woman with biopsy proven AL (primary) amyloidosis and signs of severe and therapy resistant progressive heart failure due to cardiac involvement was evaluated for heart transplantation (HTX) followed by high-dose chemotherapy and SCT.

Results The patient who had no former serious illness in prior medical history presented with signs of heart failure (NYHA class III-IV) and NT-proBNP levels of about 9000 pg/ml. Cardiac amyloidosis was proven by endomyocardial biopsy. An initial attempt to treat the underlying plasma-cell dyscrasia by chemotherapy only had to be abandoned because of worsening of heart failure. So the patient was evaluated and finally accepted for HTX combined with SCT. Before listing for HTX, CD34+ cells were collected for stem cell support. After two months on the acute waiting list the patient successfully underwent HTX. In order to remove all the diseased cardiac tissue a total HTX with resection of as much of the atria as possible was performed. The postoperative care was similar as for standard HTX patients. The immunsupression consisted of a triple drug regimen (Cyclosporine, MMF and steroids) with ATG antibody induction.

After a recovery period of 6 months the patient underwent high dose chemotherapy and autologous SCT. The patient currently has a normal exercise capacity and her cardiac function is normal on echocardiogram without wall thickening or myocardial texture changes.

Conclusion Cardiac transplantation followed by SCT provides a novel therapeutic option for cardiac amyloid patients who otherwise are faced with a malignant prognosis within few months. This is the first time in Austria that a female patient with plasma cell dyscrasia and cardiotropic amyloidosis underwent successful total HTX followed by SCT.

Entzündungsnachweis in der Endomyokardbiopsie und weibliches Geschlecht sind prognostisch bedeutsam bei Patienten mit hochgradig reduzierter Linksventrikelfunktion 008

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Hintergrund In den vergangenen Jahren gewann die Diagnostik und Therapie der viralen Herzerkrankung und inflammatorischen CMP zunehmend an Bedeutung. Ziel dieser Arbeit war es, die prognostische Bedeutung insbesondere des Entzündungs- und/oder Virusnachweises in der Endomyokardbiopsie (EMB) bei Patienten mit hochgradig reduzierter Linksventrikelfunktion zu untersuchen.

Methode Es wurden alle Patienten (n = 159; Alter 45 ± 13 Jahre) mit hochgradig reduzierter Linksventrikelfunktion (EF 28 ± 10 %), die zwischen März 2001 und März 2008 einer EMB an der Universitätsklinik für Innere Medizin III (Kardiologie) der Medizinischen Universität Innsbruck unterzogen wurden, eingeschlossen. Entsprechend dem Ergebnis der EMB wurden die Patienten in 4 Gruppen unterteilt: Gruppe 1: keine Entzündung, kein Virus (n = 79); Gruppe 2: Virusnachweis ohne Entzündung (n = 53); Gruppe 3: Virusnachweis mit Entzündung (n = 15); Gruppe 4: Entzündung, aber kein Virus (n = 12). Über einen Zeitraum von 24 Monaten wurden folgende Ereignisse dokumentiert: Tod, Assist Device Implantation und Herztransplantation.

Resultate Gruppe 3 (Virus- und Entzündungsnachweis) zeigte signifikant mehr Ereignisse im Vergleich zu den anderen Gruppen (9 % vs. 2 % vs. 40 % vs. 0 %; p < 0,001). Interessanterweise war der Virusnachweis kein Prädiktor für klinische Ereignisse (9 % vs. 12 %; n. s.), während ein Entzündungsnachweis mit einer signifikant höheren Ereignisrate assoziiert war (23 % vs. 8 %; p = 0,03). Auffallend war zudem, dass die Patientengruppe mit Entzündung doppelt so viel Frauen umfasste als die Gruppe ohne Entzündung (44 % vs. 22 %; p < 0,02). Weitere Analysen zeigten, dass Frauen mit Entzündung signifikant mehr Ereignisse hatten im Vergleich zu Frauen ohne Entzündung oder Männer mit/ohne Entzündung (42 % vs. 14 % vs. 5 % vs. 7 %; p < 0,001).

Schlussfolgerung Unsere Daten zeigen, dass nur der Entzündungsnachweis, nicht aber die Viruspersistenz mit einer ungünstigeren Prognose bei Patienten mit hochgradig reduzierter Linksventrikelfunktion assoziiert ist. Die größte Ereignisrate zeigt sich bei Frauen mit Entzündungsnachweis in der EMB. Studien an größeren Patientenpopulationen müssen die Unabhängigkeit dieser Parameter bestätigen.

Gibt es typische Patientencharakteristika bei inflammatorischer Kardiomyopathie? 009

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Hintergrund In den vergangenen Jahren gewann die Diagnostik und Therapie der viralen Herzerkrankung und inflammatorischen CMP zunehmend an Bedeutung. Ziel dieser Arbeit war es, Zusammenhänge zwischen klinischer Präsentation und verschiedenen Untersuchungsparametern mit Entzündungs- und Viruspersistenz in der Endomyokardbiopsie (EMB) zu erfassen.

Methode Es wurden alle Patienten (n = 159; Alter 45 ± 13 Jahre) mit hochgradig reduzierter Linksventrikelfunktion (EF 28 ± 10 %), die zwischen März 2001 und März 2008 einer EMB an der Universitätsklinik für Innere Medizin III (Kardiologie) der Medizinischen Universität Innsbruck unterzogen wurden, eingeschlossen. Dabei wurden die klinische Präsentation, Untersuchungsparameter wie EKG, Echokardiographie, Hämodynamik und Labor berücksichtigt. Entsprechend dem Ergebnis der EMB wurden die Patienten in 4 Gruppen unterteilt: Gruppe 1: keine Entzündung, kein Virus (n = 79); Gruppe 2: Virusnachweis ohne Entzündung (n = 53); Gruppe 3: Virusnachweis mit Entzündung (n = 15); Gruppe 4: Entzündung, aber kein Virus (n = 12).

Resultate Patienten mit Virusnachweis waren durchschnittlich 9 Jahre jünger als Patienten ohne Virusnachweis (40 vs. 49 Jahre; p < 0,001). Zudem hatten Patienten mit Virusnachweis eine tendenziell bessere EF und einen niedrigeren LVEDD im Vergleich zu Patienten ohne Virusnachweis (EF 30 vs. 27 %; p = 0,05; LVEDD 60 vs. 65 mm; p = 0,02). Bei Patienten mit Entzündungsnachweis waren hingegen CRP (3,3 vs. 0,9 mg/dl; p < 0,001), Leukozyten (8,2 vs. 6,9 g/l; p < 0,001), Troponin T (0,191 vs. 0,005 ng/ml; p < 0,001) und NTproBNP (6542 vs. 1863 pg/ml; p < 0,001) höher im Vergleich zu Patienten ohne Entzündungsnachweis. Hervorzuheben ist, dass 90 % der Patienten ein pathologisches EKG (Repolarisationsstörung oder Schenkelblock) aufwiesen. Keines der untersuchten Symptome (Dyspnoe, Thoraxschmerz oder Schwäche) zeigte eine Assoziation mit Virus- und/oder Entzündungsnachweis. In multivariaten Analysen bleiben nur das Alter mit dem Virusnachweis und die EF mit dem Entzündungsnachweis invers korreliert.

Schlussfolgerung Die Ergebnisse dieser Studie zeigen, dass bei jüngeren Patienten signifikant häufiger intramyokardial Viren nachgewiesen werden, während eine hochgradig eingeschränkte Linksventrikelfunktion häufiger mit myokardialer Entzündung assoziiert ist. Die klinischen Symptome hingegen weisen keinerlei Korrelation zum Ergebnis der EMB auf.

Prognose ambulanter Patienten mit Herzinsuffizienz an der Kardiologie Graz: Daten aus dem Herzinsuffizienz-Register 119

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Hintergrund Auch die Prognose ambulanter Patienten mit Herzinsuffizienz (HI) ist schlecht. Rezente Publikationen sprechen von einer 1-Jahres-Eventrate durch Tod/Rehospitalisierung/Transplantation von bis zu 49 % [Mullens, Am J Cardiol 2008]. Ziel der gegenständlichen Untersuchung war es, anhand der Daten aus dem Herzinsuffizienz-Register (HIR) der ÖKG Eventraten für die Population der an der Grazer Herzinsuffizienz-Ambulanz betreuten Patienten zu erheben.

Patienten und Methodik Aus dem Datenbestand des HIR wurden die Daten der Grazer PatientInnen herangezogen und hinsichtlich des kombinierten Endpunktes Tod oder Rehospitalisation im Zeitraum der ersten 360 Tage nach Registrierung untersucht. Es wurden mittels Kaplan-Meier Schätzung die Eventraten nach 90, 180 und 360 Tagen berechnet.

Ergebnisse Von 127 Patienten aus der HIR waren 1-Jahres-Follow-up-Daten bekannt (109 männlich, 18 weiblich; mittleres Alter 61 ± 13 Jahre). Von diesen hatten 35 Patienten (28 %) ein Event (30 männlich, 5 weiblich; mittleres Alter 65 ± 11 Jahre). Nach einem Mittel von 180 Tagen waren 24 Patienten (19 %) mit akuter Herzinsuffizienz rehospitalisiert worden, 2 mit akutem Koronarsyndrom, 1 aus rhythmogenen sowie 1 aus sonstigen Gründen. Die rehospitalisierten Patienten verbrachten durchschnittlich 29 Tage im Krankenhaus. 13 Patienten waren 1× wegen HI rehospitalisiert, 9 Patienten waren 2× sowie 2 Patienten waren 3× wegen HI rehospitalisiert. Nach einem Mittel von 221 Tagen waren 5 Patienten (4 %) verstorben, 3 wegen plötzlichem Herztod, 2 wegen progredienter Herzinsuffizienz. Die Eventraten nach 90, 180 und 360 Tagen betrugen 5 %, 11 % sowie 25 %.

Schlussfolgerung Patienten mit Herzinsuffizienz, die auch im Rahmen einer Herzinsuffizienz-Ambulanz betreut werden, haben eine geringere Rate an Tod oder Rehospitalisation als in der Literatur berichtet. Trotzdem müssen weitere Anstrengungen unternommen werden, um diese Rate weiter zu senken.

Telemonitoring Using Mobile Phones Reduces the Event Rate After Recent Acute Heart Failure. Results of the MOBIle TELemonitoring in Heart Failure Patients Study (MOBITEL) 147

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Purpose To test the influence of telemonitoring using mobile phones on the outcome of heart failure patients after an episode of acute heart failure (AHF).

Methods MOBITEL was a prospective, open, multi-centre study including patients with a recent episode of AHF-hospitalisation. They were randomly allocated to pharmacological treatment (control-group) or pharmacological treatment plus telemedical surveillance (tele-group) and followed for six months. Primary endpoint was hospitalisation for worsening heart failure or death from cardiovascular cause. After an initial individualised training tele-group patients sent vital parameters (blood-pressure, heart rate, body weight) and their daily dose of heart failure medication via the mobile phone. Study physicians had access to data on a secure website.

Results 120 patients were randomised (85 male, 35 female; median age 66 years [IQR 62–72]). During the initial training 12 tele-group patients emerged unable to begin transmission of data due to lack of technical understanding or visual impairment ("never beginners"). Therefore, the control-group comprised 54 patients (39 male, 15 female; median age 67 years [IQR 61–72]) and was compared with the tele-group including 54 patients (40 male, 14 female; median age 65 years [IQR 62–72]). Groups were well balanced at baseline.

Intention-to-treat analysis at study end indicated that 18 control-group patients (33 %) reached the primary endpoint (1 death, 17 hospitalisations) compared with 11 tele-group patients (0 death, 11 hospitalisations; 17 %; relative risk reduction 50 %; CI –3–74 %; p = 0.0577). Per-protocol analysis revealed 15 % of tele-group patients (0 death, 8 hospitalisations) reaching the primary endpoint (relative risk reduction: 54 %; CI: 7–79 %; p = 0.0397). NYHA-class improved by one class in tele-group patients only (p < 0.001 compared with control-group patients). Tele-group patients who were hospitalised for worsening heart failure during the study had a significantly shorter length of stay (median 6.5 days; IQR 5.5–8.3) compared with control-group patients (median 10.0 days; IQR 7.0–13.0; p = 0.038). The event rate of never-beginners was not higher than the event-rate of control-patients.

Conclusion In heart failure patients with a recent episode of acute heart failure telemonitoring using mobile phones as patient terminals has the potential to reduce frequency and duration of heart failure hospitalisations. Providing elderly patients with an adequate user

interface for daily data transfer remains a challenging part of this concept.

Combined Measurement of Cystatin C and N-terminal pro-B-type Natriuretic Peptide in Patients with Chronic Stable Heart Failure 073

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Background Plasma concentrations of Cystatin C are strongly related to outcome of patients with acute coronary syndromes, chronic renal failure and acute decompensated heart failure. In the present study we investigated the predictive value of Cystatin C in combination with plasma NT-proBNP concentrations in patients with chronic stable heart failure.

Methods We measured NT-proBNP and Cystatin C levels (Roche Diagnostics, Vienna, Austria) in 203 patients with chronic stable heart failure (NYHA II-III) who were admitted for control purposes to our outpatient clinic for heart failure. Patients were followed up for median of 1186 days (range: 2–1869). The endpoint of this study was all-cause mortality.

Results Median (IQ-range) Cystatin C concentrations were 1.27 mg/L (1.06–1.59) and showed significant positive correlation with age ($r = 0.4$; $p < 0.001$), plasma NT-proBNP levels ($r = 0.5$; $p < 0.001$) and LVEDD ($r = 0.22$; $p = 0.007$) and significant negative correlation with estimated GFR ($r = –0.64$; $p < 0.001$) and LVEF ($r = –0.27$; $p = 0.004$). Overall, 79 (38.9 %) patients died during the follow-up period. Plasma concentrations of Cystatin C were significantly higher in patients who died (1.47 mg/L [1.19–2.00]) compared to those who survived (1.16 mg/L [1.00–1.41]). In Cox regression analysis, Cystatin C was a significant predictor of survival (HR 2.28 [1.76–2.96]; $p < 0.001$), even among patients with no history of renal impairment HR 3.27 [1.66–6.46]; $p = 0.001$). In multivariate Cox regression analyses Cystatin C and NT-proBNP concentrations above the median were independent significant predictors of survival (Cystatin C: HR 2.69 [1.63–4.45]; $p < 0.001$; NT-proBNP: HR 2.87 [1.74–4.72]; $p < 0.001$; respectively). Patients with Cystatin C and NT-proBNP above the median had significantly worse outcome compared to patients with only one marker elevated ($p = 0.015$) or patients with both markers below the respective cut-offs ($p < 0.001$).

Conclusion Plasma concentrations of Cystatin C are predictors of survival in patients with chronic stable heart failure independent of plasma NT-proBNP concentrations. Our results suggest that combined measurements of these biomarkers could markedly improve risk stratification in advanced heart failure (**Figure 3**).

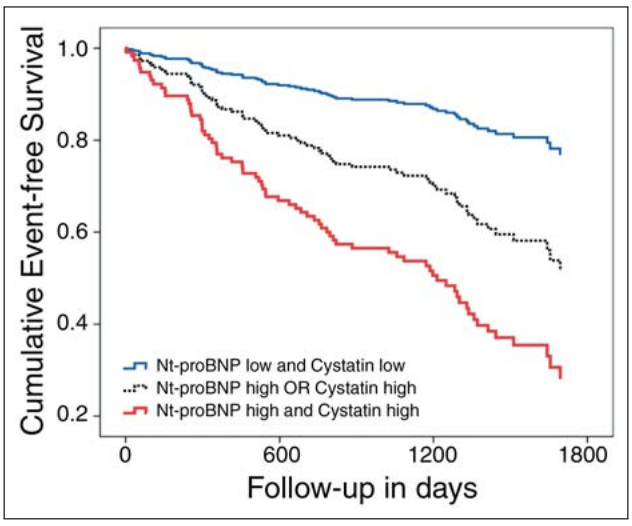

Figure 3: R. Jarai et al.

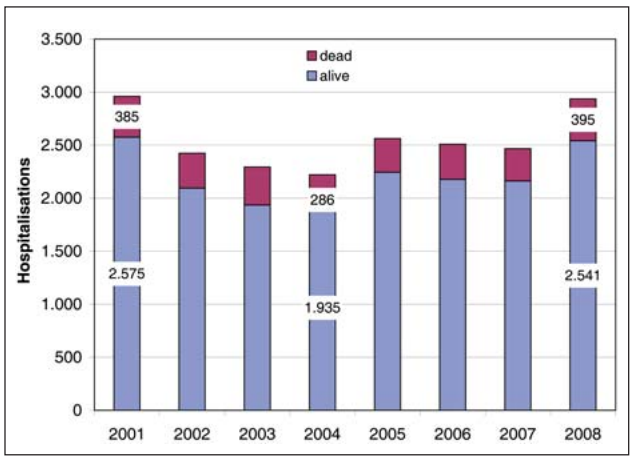

Figure 4: I. Kozanli et al.

Influence of Heart Failure Outpatient Units on the Prevalence of Hospitalisations Due to Congestive Heart Failure in Vienna 134

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Background and Aim Recurrent hospitalisations (hosps) due to congestive heart failure (CHF) represent a major public health problem and are associated with a significant reduction of quality of life and high mortality. Within the past years specialized heart failure (HF) outpatient units have been established and their influence of hospital admissions were investigated.

Methods Data acquired from the hospital database between 2001 and 2008 from pts admitted to a hospital in Vienna because of acutely decompensated HF (with the appropriate ICD-10 Code) frequency and in-hospital mortality were investigated. During this time span specific outpatient services for HF pts were implemented.

Results In the first year (2001) 2960 consecutive patients (pts) with CHF were registered and 385 pts (13 %) died in the hospital. The lowest number with 2221 hosps was registered in 2004. Finally in 2008, 2906 pts were admitted of whom 14 % died resulting in a small decrease of 2 % hospital admissions during this 8 years period (**Figure 4**).

Conclusions Although implementation of specialized HF outpatient units hospital admissions remained still high over the past 8 years. The remarkable decrease in hosps between 2002 and 2004 did not sustain over the following years obviously based on an increase of total number of HF pts. These data demonstrate that HF outpatient units alone are not powerful enough for the management of an increasing number of HF pts and a progressive disease with a high mortality and morbidity. Therefore the need of additional disease management programs and networks like home care projects and telemonitoring for the better management of this high risk/high cost individuals are mandatory.

Copeptin Predicts Outcome in Patients with Cardiogenic Shock 089

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Introduction Arginine vasopressin (AVP) is significantly increased in acute hemodynamic instability. As a stress hormone AVP is released in response to osmotic and hemodynamic changes in order to maintain fluid volume and vascular tone. Copeptin is a stable fragment of pre-pro-vasopressin which is synthesised and released in equimolar quantities as AVP. We assessed the hypothesis that an

elevation of copeptin serves as a predictor of adverse outcome in patients with cardiogenic shock.

Methods In a prospective observational study, consecutive patients with cardiogenic shock admitted to the Intensive Care Unit (ICU) of the Department of Cardiology/Medical University of Vienna between November 2004 and March 2006 were included. Blood samples for determination of routine laboratory tests and NT-proBNP and copeptin plasma levels were obtained in all patients on admission. Copeptin was assessed using an immunoassay in the chemiluminescence/coated tube format. Age, gender, presence of acute renal failure, mechanical ventilation, NT-proBNP and copeptin were analysed for prediction of ICU survival.

Results A total of 91 consecutive patients (66 male [72 %]; age 66.5 ± 11.4 years) presenting with cardiogenic shock were included. All patients were on intravenous inotropic support, 19 patients (21 %) were treated with an intraaortic balloon counterpulsation, 8 patients (8 %) were on extracorporeal membrane oxygenation and 1 patient (1 %) was on novacor support. A total of 56 patients (62 %) survived and 35 patients (38 %) died. Copeptin plasma levels were significantly higher in ICU non-survivors than in ICU survivers (164.4 ± 117.8 pg/ml vs 248.2 ± 256.6 pg/ml; p = 0.034). Using a logistic regression model, copeptin was the best predictor of ICU survival with only NT-proBNP providing independent additional information (copeptin odds ratio 1.002; p = 0.001 and NT-proBNP odds ratio 1.001; p = 0.05).

Conclusion Copeptin is a strong and independent predictor of adverse outcome in cardiogenic shock.

Neurohumoral Risk Stratification in Critically ill Cardiologic Patients – Comparison between Copeptin, MR-pro-adrenomedullin, MR-proANP and NT-proBNP 090

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Introduction Critical illness is associated with significant neurohumoral activation. The aim of this study was to assess the predictive value of CT-pro-vasopressin (copeptin) and MR-pro-adrenomedullin (MR-proADM) in critically ill cardiologic patients and to compare it to the known prognostic marker NT-proB-type natriuretic peptide (NT-proBNP) and to MR-pro-atrial natriuretic peptide (MR-proANP).

Methods This was a prospective observational study at a tertiary care cardiologic-medical Intensive Care Unit (ICU). Patients admitted to the ICU with a primary cardiac diagnosis during a 17 months study period were included. Plasma samples for determination of copeptin, MR-proADM, MR-pro-ANP and NT-proBNP were obtained in all patients on ICU admission.

Results A total of 235 cardiologic critically ill patients (156 male [66 %]; age 64 ± 14 years) were included. There were 192 ICU survivors at 28 days and 43 ICU non-survivors. ICU survivors had significantly lower levels of copeptin, MR-proADM, NT-proBNP and MR-proANP compared to ICU non-survivors (101.1 ± 99.5 pmol/l vs 220.6 ± 225.3 pmol/l; p < 0.0001 copeptin; 2.49 ± 2.27 nmol/l vs 4.66 ± 3.83 nmol/l; p < 0.0001 MR-proADM; 7682 ± 9776 pg/ml vs 17591 ± 13026 pg/ml; p < 0.0001 NT-proBNP; 467 ± 391 pmol/l vs 1002 ± 702 pmol/l; p < 0.0001 MR-proANP, respectively). In univariate regression analysis for prediction of ICU survival at 28 days, MR-proANP was the most potent predictor of ICU mortality within 28 days (Wald 39.790; p < 0.0001). Also, NT-proBNP, MR-proADM, and copeptin were strong predictors of ICU outcome (Wald 23.450; p < 0.0001 NT-proBNP; Wald 21.316; p < 0.0001 MR-proADM and Wald 18.593; p < 0.0001 copeptin, respectively). The area under the ROC curve for prediction of ICU survival was 0.774 for MR-proANP, 0.750 for NT-proBNP, 0.716 for MR-proADM and 0.702 for copeptin, respectively.

Conclusion Neurohumoral activation is a strong predictor of outcome in critically ill cardiologic patients. Increased levels of MR-proANP, NT-proBNP, MR-proADM as well as copeptin were linked to excess mortality, with MR-proANP being the most potent prognostic marker.

Comparison of Midregional Pro-atrial Natriuretic Peptide and B-type Natriuretic Peptides in Chronic Heart Failure: Influencing Factors, Detection of Left Ventricular Systolic Dysfunction, and Prediction of Death 110

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Objectives Midregional pro-atrial natriuretic peptide (MR-proANP) was assessed for the importance of influencing factors, the ability to detect left ventricular systolic dysfunction and the prognostic power compared to B-type natriuretic peptide (BNP) and aminoterminal pro-B-type natriuretic peptide (NT-proBNP) in chronic heart failure (CHF).

Background MR-proANP is a biologically stable natriuretic peptide measured by a recently developed assay with potential advantages over conventional natriuretic peptides like BNP and NT-proBNP.

Methods We measured MR-proANP, BNP and NT-proBNP in 797 patients with CHF.

Results All three natriuretic peptides were independently influenced by left ventricular ejection fraction (LVEF), glomerular filtration rate (GFR), and the presence of ankle edema. Area under receiver-operator characteristic curves for detection of an LVEF < 40 % were similar between MR-proANP (0.799 [0.753–0.844]) and BNP (0.803 [0.757–0.849]), and NT-proBNP (0.730 [0.681–0.778]). During a median observation time of 68 months, 492 (62 %) patients died. In multiple Cox regression analysis each natriuretic peptide was the strongest prognostic parameter among various clinical variables. Proportion of explained variation showed that NT-proANP (4.36 %) was a significantly stronger predictor of death than both NT-proBNP (2.47 %; p < 0.0001) and BNP (2.42 %; p < 0.0001).

Conclusions Despite similarities in influencing factors and detection of reduced LVEF, MR-proANP outperformed BNP and NT-proBNP in the prediction of death. A new assay technology and the high biological stability of MR-proANP are potential explanations for these findings.

Prognostic Value of Sequential Measurements of Amino-terminal Prohormone of B-type Natriuretic Peptide in Ambulatory Heart Failure Patients 111

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Background We evaluated the prognostic value of sequential NT-proBNP values in ambulatory heart failure patients after discharge, investigating whether the current value or the recent percent change is more important.

Methods and Results In 166 patients, NT-proBNP was measured at discharge from heart failure hospitalisation and three months later. The combined endpoint of death or heart failure rehospitalisation was evaluated after a maximum of 18 months or at follow-up closure. During a mean observation time of 14 ± 4 months, 63 patients (38 %) reached the endpoint. In multiple Cox analysis, NT-proBNP three months after discharge (NT-proBNP-3Mo) and NT-proBNP percent change (NT-proBNP-%change) were the only independent predictors of the endpoint among various clinical and laboratory variables. After definition of a high- (n = 83; 57 % endpoints) and a low-NT-proBNP patient subgroup (n = 83; 19 % endpoints) according to the median NT-proBNP-3Mo (1751 pg/ml), NT-proBNP-%change was the strongest predictor in the high-NT-

proBNP subgroup. In the low-NT-proBNP subgroup, NT-proBNP-3Mo was the only independent predictor.

Conclusions In ambulatory heart failure patients, the prognostic value of sequential NT-proBNP measurements depends on the magnitude of the current NT-proBNP value. Recent percent changes in NT-proBNP provide important prognostic information in patients with high NT-proBNP but not in patients with low NT-proBNP.

Effects of n3-Polyunsaturated Fatty Acids on Monocyte-Platelet Aggregate Formation in Patients with Advanced Chronic Heart Failure 117

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Introduction In chronic heart failure (HF), platelets are persistently activated as an expression of coagulation activation. N3-polyunsaturated fatty acids (n3-PUFA) have been shown to reduce monocyte-platelet aggregates (MPA) as a marker of platelet activation in healthy humans. We investigated the effects of n3-PUFA on MPA in severe chronic HF.

Methods Thirty patients with non-ischemic advanced chronic HF (LVEF < 35 %, NYHA class > 2) under optimized therapy were randomized to a daily dose of n3-polyunsaturated fatty acids (n3-PUFA) of 1 g, 4 g, or placebo for 3 months. Monocyte-platelet aggregates characterized by CD14+/CD42b+ coexpression were quantified by whole-blood flow cytometry. In addition, plasma levels of hs CRP, hs TNF-alpha, hs IL-6, MCP-1 and Galectin-3 were measured by immunoassay.

Results Mean baseline MPA was 22.7 ± 12.1 %. MPA was significantly reduced by 4 g/d (–9.5 ± 2.9 %; p = 0.011) and 1 g/d n3-PUFA (–5.3 ± 2.8; p = 0.049), but not in the placebo group (0.3 ± 4.3; p = 0.94), leading to a significantly lower MPA in treated (16.2 ± 6.1 %) vs untreated patients (22.1 ± 10.0 %; p = 0.047). However, no changes were observed for the aforementioned parameters of inflammation.

Conclusion N3-PUFA significantly reduced monocyte-platelet aggregate formation in patients with severe chronic HF in a dose-dependent manner. Although the underlying mechanisms and pathophysiological consequences are subject to further investigation, our data provide further insight into the potential beneficial effects of n3-PUFA in HF.

Subclinical Ebstein-Barr virus (EBV) Infection is Frequent in Long-Term Cardiac Transplant Recipients 016

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Introduction Viral infections account for substantial morbidity and mortality in solid organ transplantation. In heart transplant recipients viral infections have been associated with acute rejection, cardiac allograft vasculopathy (CAV), post-transplant lymphoproliferative disease (PTLD), and graft loss. The frequency of subclinical viral infections in the long-term course after heart transplantation (HTX) is unclear. It was the goal of our study to investigate the prevalence of various types of viral infections in stable heart transplant recipients.

Patients and Methods From June to December 2008 102 consecutive heart transplant recipients (21 % female) were tested for viral infection. All patients were on stable doses of immunosuppression and free from acute infection or rejection for at least 3 months before entry into the study. Mean patient age was 61 ± 11 years (range 23–81). Median time after HTX was 8 years (range 1–24). Patients were tested for cytomegalovirus (CMV), Ebstein-Barr virus (EBV), parvovirus B19 (PV B19), herpes simplex virus (HSV) 1/2, human herpes virus (HHV) 6/8, and hepatitis C using qualitative PCR in peripheral blood. In addition, serologic antibody screening was applied for all the above viruses including hepatitis A and B.

Results Reliable test results were available in 98 patients, of which 30 (30.9 %) were tested positive (EBV 26.3 %, HSV1/2 2.7 %, HHV6 2.6 %, HHV8 1.3 %, HVC 1.2 %). Co-infection with EBV and HSV1/2 was found in one patient. There was no difference between virus-positive and virus-negative patients with regard to age, gender, time after HTX, CMV- and gender-mismatch at time of transplantation, and type of immunosuppression. Of note, no differences were seen either in graft function and lab parameters such as ALT, AST, GGT, LDH, leucocytes, lymphocytes, monocytes and haemoglobin.

Conclusion Subclinical EBV infections are – unlike other viruses – frequent in stable heart transplant recipients. EBV infections were not correlated with donor a/o recipient related parameters and did not impact on blood count and liver function tests. Since the long-term consequences of subclinical EBV infections are unknown, effectiveness of routine viral testing in heart transplant recipients remains unclear and has to be addressed in a follow-up study.

Patients in Heart Failure Trails do not Represent Everyday Practice 136

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Objective Evidence-based medicine urges physicians to translate results from clinical trials to their patients. This, however, mandates that patients in clinical trials compare well with everyday patients. In order to find out if this holds true for heart failure research, we searched the literature for both clinical as well as epidemiological studies in Europe (European Survey on Heart Failure, ESHF) and Northern America (Framingham Heart Study, FHS).

Methods A MEDLINE search (MS) for "chronic heart failure" and "mortality" yielded 344 randomized trials in human adults. Once we stratified for "human adult patients with chronic heart failure", "heart failure" being the sole indication for inclusion in the study, "mortality" being the primary end point, and "drug" or "device" as possible intervention, 53 studies remained. Baseline characteristics of all 53 studies were entered into a database and compared with demographic data of ESHF and FHS.

Results Study participants (n = 103,183) significantly differed in age (MS: 64.2 ± 5.2; ESHF: 71 ± 3.5; FHS: 70 ± 10.8 years; p < 0.001), sex distribution (MS: 76.3 ± 10.3 % males vs 23.8 ± 10.3 % females; ESHF: 53 % males and vs 47 % females; FHS: 51 % males vs 49 % females; p < 0.001), BMI (MS: 27.7 ± 1.0; FHS: 27.2 ± 5.3; p < 0.001), NYHA class (MS: 2.7 ± 0.4; ESHF: 2.1 ± 1; p < 0.001), ischemic etiology (MS: 61.3 ± 25.7 %; ESHF: 68.0 ± 12.6 %; FHS: 53.5 %; p < 0.001), treatment with beta-blockers (MS: 44.6 ± 30.4 %; ESHF: 36.9 ± 8.8 %; p < 0.001), angiotensin converting enzyme-inhibitors (MS: 79.7 ± 27.2 %; ESHF: 61.8 ± 7.5 %; p < 0.001) and angiotensin receptor blockers (MS: 12.0 ± 7.5 %; ESHF: 4.5 ± 2.0 %; p < 0.001) as well as incidence of diabetes (MS: 25.9 ± 7.6 %; ESHF: 27.0 ± 8.8 %; FHS: 19 %; p < 0.001) and hypertension (MS: 46.4 ± 19.1 %; ESHF: 53.0 ± 11.42 %; FHS: 74.0 %; p < 0.001). Only 21 (39.6 %) of these studies reported ethnic background.

Conclusion Patients in clinical trials on chronic heart failure are not representatives of our everyday clinical patients. Thus, current evidence can only be translated to a minority but not the bulk of our patients. In order to improve treatment of patients with CHF, scientific evidence needs to be gained from populations that closer match real world patients.

Mismatch between Heart Failure Patients in Exercise Training Trials and the Real World 137

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Objective Physical exercise training in patients with chronic heart failure (CHF) was contraindicated until the early 1990ies, when clinical studies proved the opposite. Evidence-based medicine urges physicians to translate results from clinical trials to their patients. This, however, can only work, if real world patients are represented in clinical trials. We therefore searched the literature for clinical studies investigating exercise training in CHF and compared patient characteristics with epidemiological studies in Europe (Euro Heart Failure Survey, EHFS) and North America (Framingham Heart Study, FHS).

Methods We combined synonyms for heart failure with synonyms for physical exercise training and searched PubMed, MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, ISI Web of Knowledge und CINAHL for studies published before 2008. Patients' characteristics were compared with demographic data of CHF patients in Europe and North America.

Results 130 training studies (TS) were evaluated. Patients in TS were significantly younger than in EHFS (59.6 ± 6.4 vs 71.0 ± 3.5 years; $p < 0.001$) and FHS (59.6 ± 6.4 vs 70.0 ± 10.8 years; $p < 0.001$). Sex distribution between male and female patients was 53 % vs 47 % in EHFS, 51 % vs 49 % in FHS and 81.5 % vs 18.5 % in training studies ($p < 0.001$). Patients in EHFS were in NYHA functional class 2.01 ± 0.98 and in a significantly better clinical shape than patients in training studies (2.41 ± 0.32; $p < 0.001$). Ischemic cardiomyopathy was the primary cause of heart failure in 68.0 ± 12.6 % in EHFS, in 53.5 % in FHS and in 58.9 ± 24.6 % in TS (all $p < 0.001$). Comorbidities like diabetes (EHFS: 27.0 ± 8.8 %; FHS: 19 ± 8.8 %; TS: 12.4 ± 13.7 %; $p < 0.001$) and hypertension (EHFS: 53.0 ± 11.4 %; FHS: 74 ± 11.4 %; TS: 28.1 ± 30.5 %; $p < 0.001$) were underrepresented in training studies. ACE-inhibitors (87.4 ± 15 % vs 61.8 ± 7.5 %; $p < 0.001$), beta-blockers (54.0 ± 29.0 % vs 36.9 ± 8.8 %; $p < 0.001$) and angiotensin-receptor-blockers (17.8 ± 14.1 % vs 4.5 ± 2.0 %; $p < 0.001$) were more commonly used in EHFS than in TS.

Conclusion CHF patients in exercise training trials do not represent real world patients. In order to extrapolate data to the general population future exercise training trials need to include representative patients. Otherwise, knowledge gained can only be translated to a minority of our patients.

Onkologie und Herzinsuffizienz 175

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Fragestellung Herzinsuffizienz durch kardiotoxische Chemotherapie, Strahlentherapie? Wie viele Patienten sind betroffen?

Methode Erfassung durch Datenbank

In der Herzinsuffizienzambulanz des KFJ, eines Wiener Gemeindespitals mit ca. 700 Betten, wurden in den letzten 10 Jahren 566 herzinsuffiziente Patienten betreut. Nach der dilatativen und ischämischen Kardiomyopathie ist – aufgrund der räumlichen Nähe zur Onkologie des Hauses – die chemotherapieinduzierte Kardiomyopathie die drittgrößte Gruppe. Unter den 540 Patienten waren 34 onkologische Patienten – 29 Frauen und 5 Männer – 7 dieser Patienten (5 Frauen, 2 Männer) sind in diesem Zeitraum verstorben (2 Patienten an Herzinsuffizienz).

Die Patienten, die in den letzten 3 Jahre h. o. betreut wurden, werden mittels einer Datenbank erfasst. 8,1 % – 21 Frauen, 2 Männer – der Gesamtpatientenzahl (251) wurden in diesem Zeitraum wegen Herzinsuffizienz nach Chemotherapie betreut. Auf der h. o. onkologischen Abteilung wurden in diesem Zeitraum ca. 380 anthrayzyklinhältige Chemotherapien verabreicht (Doxorubicin, Epirubicin, Daunorubicin, Idarubicin). Bei einigen Patienten ist der Zusammenhang zwischen Chemotherapie und Herzinsuffizienz gesichert, da die Herzinsuffizienz und eine dramatische Verschlechterung der Linksventrikelfunktion unmittelbar nach bzw. während laufender Chemotherapie aufgetreten ist. Bei anderen wird die Diagnose nach Ausschluss anderer Möglichkeiten als wahrscheinlich angenommen. Bei diesen Patientinnen (keine Männer in dieser Gruppe) ist die HI zumeist 2–3 Jahre nach der CHT aufgetreten. Die Behandlung erfolgt wie bei allen anderen Formen der CMP. Die Verläufe sind sehr unterschiedlich, von nahezu vollständiger Rückbildung der LVF Verschlechterung und Symptomatik bis zu therapieresistentem letalem Ausgang.

Als weiteres Ergebnis der Erfassung mittels Datenbank zeigt sich, dass von allen Patienten der letzten 10 Jahre bisher 109 Patienten (81 Männer, 28 Frauen, 12 Patienten mit dil. CMP, 29 Ischäm, 7 CHt ind, restliche andere oder nicht bekannte Diagnose) verstorben sind, 9 davon gesichert an einer malignen Grunderkrankung (6 ohne kardiotoxische Chemotherapie, mit anderer CMP-Diagnose, 3 mit CHT ind.).

Mortality in Patients Treated with Device Therapy for Drug-Refractory Chronic Heart Failure 085

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Purpose Intermittent non-excitatory electrical stimulation delivered during absolute myocardial refractoriness results in cardiac contractility modulation (CCM) with improvement of impaired ventricular function. Thus, CCM became a therapeutic alternative in patients with drug-refractory chronic heart failure, especially in those not eligible for cardiac resynchronisation therapy (CRT). We aimed to compare mortality data of these two therapeutic options.

Methods Between November 2001 and December 2008, we implanted CCM devices in 36 patients with advanced drug-refractory chronic heart failure – i.e. NYHA-class III and left ventricular ejection fraction (LVEF) < 35 % – including 2 patients with heart transplantation and 2 patients non-responsive to CRT. Final analysis included 25 patients (all male; age at implantation: 64.1 ± 7.5 years) with daily stimulation only. 21 patients also had an implantable cardioverter-defibrillator (ICD). Mortality of this collective was compared with an historic group of 70 patients with CRT and ICD function (CRT-D).

Results Mean LVEF at the last follow-up did not differ significantly between patients with CCM and CRT-D (26 ± 11 % vs 29 ± 6 %; $p = 0.20$). Within a clinical follow-up period of 2.4 ± 2.0 years, all-cause mortality in patients with CCM was 40 % (10 of 25 patients), with a one-year mortality of 20 %. Causes were cardiogenic shock (3 patients), arrhythmic and non-cardiac death (2 patients respectively), while cause of death remained unknown in 3 patients. Compared to the 21 patients with combined CCM and ICD treatment, all-cause mortality (38 % vs 10 %; $p = 0.002$) and cardiac mortality (19 % vs 4 %; $p < 0.001$) were significantly lower in the historic CRT-D.

Conclusions Compared to patients with CRT-D, patients with combined CCM and ICD treatment showed a significantly higher cardiac and all-cause mortality. In this collective, a high mortality first reflects the end-stage character of the underlying heart failure.

Clinical Outcome of Cardiac Contractility Modulation in Patients with Drug-refractory Chronic Heart Failure 086

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Purpose Intermittent non-excitatory electrical stimulation delivered during absolute myocardial refractoriness results in cardiac contractility modulation (CCM) with improvement of impaired ventricular function. Thus, CCM became a therapeutic alternative in patients with drug-refractory chronic heart failure, especially in those not eligible for cardiac resynchronisation therapy (CRT). We analysed the clinical outcome of the use of CCM in this collective.

Methods Between November 2001 and December 2008, we implanted CCM devices in 36 patients with advanced drug-refractory chronic heart failure – i.e. NYHA-class III and left ventricular ejection fraction (LVEF) < 35 % – including 2 patients with heart transplantation and 2 patients non-responsive to CRT. Final analysis included 25 patients (all male; age at implantation: 64.1 ± 7.5 years) with daily stimulation only. 21 patients also had an implantable cardioverter-defibrillator (ICD).

Results Within a clinical follow-up period of 2.4 ± 2.0 years, mean NYHA-class improved slightly to 2.7 ± 0.8. Mean LVEF at the last follow-up was 26 ± 11 %. Incidence of device related complications was low: lead-reposition and infection of device loge in one patient respectively. All-cause mortality in patients with CCM was 40 % (10 of 25 patients), with a one-year mortality of 20 %. Causes were cardiogenic shock (3 patients), arrhythmic and non-cardiac death (2 patients respectively), while cause of death remained unknown in 3 patients.

Conclusions Cardiac contractility modulation is able to improve the symptoms of advanced drug-refractory chronic heart failure. In this collective, a high all-cause mortality first reflects the end-stage character of the underlying heart failure.

Interventionelle Kardiologie

Clinical Outcomes with Bivalirudin versus Heparin during Percutaneous Coronary Intervention 155

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Aims Bleeding and stent thrombosis are the major complications of percutaneous coronary interventions (PCIs). We analyzed the efficacy and safety of heparin versus bivalirudin in patients undergoing elective percutaneous coronary intervention (PCI).

Methods and Results A total of 89 patients with stable coronary heart disease were randomized to bivalirudin (n = 42) and heparin (n = 47) during PCI. Stent thrombosis was defined according to the time interval between implantation and the event as: early; 0–30, late > 30 days to 6 months. All major adverse coronary and cerebrovascular events (MACCEs) were recorded at 30 days and 6 months. Peri-interventional medical therapy was similar in both groups, with all patients being on stable dual antiplatelet treatment. Prior to PCI, patients were randomized to receive either unfractionated heparin (Heparin Immuno, Unterach, Austria, 65 U/kg as a bolus) or bivalirudin (Angiox, Nycomed, Vienna; 0.75 mg/kg followed by an infusion of 1.75 mg/kg per hour during PCI). Mean procedural ACTs was 246 ± 24. No stent thrombosis was observed. No bleeding occurred. Only a single patient in the heparin group had myocardial ischemia within 30 days after PCI (PCI in target vessel).

Conclusion In this small randomized trial, bivalirudin and heparin were equally safe during PCI (**Table 8**).

Table 8: R. Badr Eslam et al.

	Whole study population n = 89	Bivalirudin n = 42	Heparin n = 47	p-value
Mean serum creatinine level (mg/dl) post PCI		1.13	1.28	n. s.
30 day follow up, n (%)				
Early stent thrombosis (0–14 d)	0	0	0	–
Late stent thrombosis (0–30 d)	0	0	0	–
Ischemia (0–30 d)	1 (1.1 %)	0	1 (2.1 %)	1.00
6 month follow up, n (%)				
Patients rehospitalized (at least once/6 m)	38 (42.7 %)	18 (42.9 %)	20 (42.6 %)	0.98
Patients rehospitalized – cardiac events	35 (39.3 %)	16 (38.1 %)	19 (40.4 %)	0.82
Patients rehospitalized – non cardiac events	5 (5.6 %)	3 (7.1 %)	2 (4.3 %)	0.66
Follow-up-angiography	10 (11.2 %)	6 (14.3 %)	4 (8.5 %)	0.51
Target-vessel-revascularisation	5 (5.6 %)	2 (4.8 %)	3 (6.4 %)	1.00
Non-target-vessel-revascularisation	8 (9.0 %)	2 (4.8 %)	6 (12.8 %)	0.27
Bypass surgery	4 (4.5 %)	2 (4.8 %)	2 (4.3 %)	1.00
Death	3 (3.4 %)	1 (2.4 %)	2 (4.3 %)	1.00

Decrease of Neointimal Proliferation After Implantation of Activated Protein C- (Xigris) Coated Stent in Porcine Coronary Arteries 030

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Background Activated protein C (APC) is an endogenous protein that inhibits inflammation and thrombosis, promotes fibrinolysis and interrupts coagulation cascade. The aim of our study was to investigate the degree of neointimal hyperplasia after implantation of APC-coated stents in pig coronary arteries.

Methods Ten domestic pigs underwent general anaesthesia and coronary angiography after per os loading dose of aspirin (100 mg) and clopidogrel (300 mg) and intravenous heparin. 5 mg human recombinant APC (Drotrecogin alfa, Xigris, Eli Lilly) was prepared for 70 % alcohol solution, followed by direct (non-polymeric) coating of 10 Yucon Pearl stents using the Translumina stent coating machine (T-SCM 2003) (2.6 µg/mm^2 stent surface). The APC-coated and bare Yucon stents (BMS) were randomly implanted in the left anterior descending and circumflex arteries. During the 4-weeks follow-up (FUP), the animals were treated daily with dual antiplatelet therapy. After 1-month FUP, the development of neointimal hyperplasia was evaluated by coronary angiography and histomorphometry. Coronary arteries were stained with mouse anti-human P-selectin antibody with a known cross-reaction with porcine tissue to identifying activated endothelial cells at the injury site.

Results There was no procedural complication or allergic reaction. Fibrin deposition and adventitial inflammation were significantly decreased in pigs with APC-coated stents as compared with BMS. Endothelialization was complete in both groups. At the FUP, significantly smaller neointimal area (0.98 ± 0.92 mm^2 vs 1.44 ± 0.91 mm^2; p = 0.028) with higher lumen area (3.47 ± 0.94 mm^2 vs 3.06 ± 0.91 mm^2; p = 0.046) and lesser degree of area stenosis (22.2 ± 21.2 % vs 32.1 ± 20.1 %; p = 0.034) was measured in APC-coated stents as compared with the BMS stents. P-selectin immunostaining revealed significantly less prevalence of activated endothelial cells in the neointima in the APC-group (4.6 ± 1.9 mm^2 vs 11.6 ± 4.1/0.28 mm^2; p < 0.001).

Conclusions Coating of stent with hrAPC (non-toxic, non-cytostatic drug) reduces thrombo-inflammatory responses, neointimal proliferation, and in-stent restenosis and offers a promising therapy to improve clinical outcomes of coronary stenting.

Drug-eluting Balloon Aortic Valve Valvuloplasty to Prevent Restenosis in Experimental Aortic Stenosis: an Option for Patients Not Amenable for Aortic Valve Replacement 049

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Objectives Calcific aortic stenosis is characterized by extensive remodelling of the extracellular matrix due to active inflammatory processes, myofibroblast proliferation and release of proinflammatory cytokines. Balloon aortic valve valvuloplasty (BAV) is the choice of therapy, if aortic valve replacement (AVR) cannot be performed of any reason. This study investigated the effect of drug-eluting balloon (DEB) use for BAV on prevention of restenosis of the aortic valve.

Methods Rabbits have been fed with cholesterin-rich diet (0.5 %) with supplemental Vitamin D3 (50,000 IU/day) for 3 months. Under general anaesthesia, the peak aortic valve systolic pressure gradient was measured through the right carotid artery by placing the pressure wire (RADI) in the ventricle and aorta. The animals were randomized to group DEB-BAV (2 μg paclitaxel/1 mm^2 balloon surface) (n = 13) or group BAV (n = 12). The aortic valvuloplasty balloon (8 mm of diameter, 20 mm of length) was inflated 3 times for 10 sec. At 3 weeks follow-up (FUP) the right femoral artery was prepared and the aortic valve gradient was measured via pressure wire. Transthoracic echocardiography was performed at baseline and at the follow-up, and the left ventricular (LV) dimensions were measured. After follow-up examinations, euthanasia was performed and the aortic valve leaflets and the aortic root were prepared for histological examinations.

Results The mean serum cholesterol and calcium level was 23.6 ± 4.2 mM/L and 2.74 ± 0.21 mM/l, respectively. The tissue paclitaxel concentration of the aortic valve leaflet and aortic ring were 1.84 ± 2.19 μM/l and 0.07 ± 0.06 μM/l. Mild degree of aortic stenosis was measured in rabbits (7.2 ± 6.3 mmHg, by a mean systemic blood pressure of 52 ± 16 mmHg). At the FUP, a trend towards decrease in mean aortic stenosis gradient was observed in the group DEB-BAV as compared with the group BAV (3.0 ± 3.0 mmHg vs 4.6 ± 3.5 mmHg; p = 0.09). The end-diastolic volume of LV was smaller (8.61 ± 0.58 ml vs 9.16 ± 0.61 ml; p = 0.062) and the systolic volume higher (6.49 ± 1.0 ml vs 5.24 ± 1.58 ml; p = 0.056) in group DEB-BAV vs group BAV. Histology confirmed the smaller number of proliferating cells in the aortic valves and root in the group DEB-BAV.

Conclusions Use of paclitaxel-coated balloon for aortic stenosis valvuloplasty is safe, and results in less cell proliferation. DEB-BAV might be a choice for palliative aortic stenosis BAV with less restenosis offering a prolonged life-time and better quality of life in patients with severe aortic stenosis not amenable for AVR, or for extension of window of opportunity for AVR.

Biodistribution of Cardiac Injected Porcine Mesenchymal Stem Cells in Remote Healthy Organs: Comparison of Intracoronary and Intramyocardial Delivery 050

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Objectives Male porcine bone marrow-derived mesenchymal stem cells (MSC) were transiently transfected with luciferase (Luc) and green fluorescent protein (GFP) (Luc-GFP-MSC) for tracking cardiac delivery of MSCs to the myocardium and remote organs after intramyocardial or intracoronary delivery.

Methods Closed-chest, reperfused myocardial infarction (MI) was created in female domestic pigs. The male Luc-GFP-MSC (8.4 ± 1.3 × 106) were delivered either transendocardially in the infarct border zone or intracoronary in the open infarct-related artery 20 ± 3 days post-MI in female pigs. Tissue samples were collected 3 h, 24 h, and 7 days post-delivery from the myocardium and non-cardiac organs (lung, liver, spleen, lymphatic node, kidney, bone marrow). Tissue luciferase activity was measured in the homogenized tissues using dual-luciferase reporter assay, and expressed as relative light units (RLU) per μg protein. Quantitative real-time TaqMan polymerase chain reaction (PCR) was performed to detect a male genomic DNA sequence from the single copy gene "sex determining region Y" (SRY), which is specific for the porcine Y chromosome in the female hearts and remote organs to detect the sex-mismatch MSC.

Results The highest luciferase activity was found in the intramyocardial injection sites at 3 h post delivery (528 ± 448 RLU/μg protein) and decreased to 382 ± 109 RLU/μg and 162 ± 58 RLU/μg protein at 24 h and 7 days, respectively. Significantly less Luc-GFP-MSC was retained 3 h, 24 h and 7 days after intracoronary delivery (124 ± 8 RLU/μg, 96 ± 46 RLU/μg and 76 ± 38 RLU/per μg protein; p = 0.031, p = 0.021 and p = 0.048, respectively). At 7-day, 0.5–2.7 % of totally injected Luc-GFP-MSC was found in all non-cardiac organs, with no difference between intramyocardial or intracoronary administration. PCR confirmed the presence of male Luc-GFP-MSC in female infarcted hearts 24 h post-injections by both delivery methods.

Conclusions Intramyocardial delivery of MSC is more effective in cell retention in the infarcted myocardium as compared to intracoronary delivery. Reporter gene method is a useful means to track the biodistribution of the transplanted cells quantitatively.

One-year Clinical Outcomes of Treatment of Instent Restenosis with Dior Paclitaxel-eluting Balloon 088

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Objectives Implantation of drug-eluting stents (DES) for in-stent restenosis (ISR) is a promising treatment option, even if it may amplify the restenosis rate of the overlaying stents and the occurrence of late stent thrombosis. Drug-eluting balloon (DEB) can be an attractive treatment mode for coronary ISR avoiding the limitations of the stent-in stent. The aim of this prospective registry of treatment of in-stent restenosis with DEB was to evaluate the 1-year clinical outcomes of use of first generation Dior paclitaxel-eluting balloon for in-stent restenosis in "real-world" practice.

Methods Between July 2007 and August 2008 60 patients (60 ± 13 y; 78 % male) were treated by dilatation with Dior balloon of the significant ISR. All patients were clinically controlled 292 ± 144 days after stent implantation. Control coronary angiography was performed in 67 % of patients. Non-fatal acute myocardial infarction (AMI), stroke, cardiac death and target vessel revascularization (TVR) were considered as major adverse cardiac and cerebral events (MACCE) at 6-month and 1 year follow-up (FUP).

Results High prevalence of coronary risk factors (88 % hypertension, 38 % diabetes mellitus, 88 % hyperlipidaemia, 55 % smoking, 28 % positive family anamnesis for coronary artery disease) was documented. Bare-metal stent ISR was in 31 (52 %) and DES-ISR in 29 (48 %) patients. The indication for coronary intervention was UA/NSTEMI or STEMI in 27 % of patients. Forty-two percent of patients suffered from previous myocardial infarction and 23 % of patients underwent previous bypass operation. The Dior balloon size was 2.99 ± 0.37 mm, length of 22 ± 6 mm, balloon inflation pressure of 13 ± 3 atm and inflation time of 74 ± 38 sec. No intervention complication or short-term (within 30 days after stenting) MACCE occurred. No acute or subacute stent thrombosis was documented. During the 6-month FUP 3 AMI occurred, all of them had also TVR. One patient died due to non-cardiac reason (gastrointestinal cancer).

TVR was performed 9 patients (15 %). The composite 6-month MACCE was 15 %. At 1-year FUP, 1 patient with HIV infection died, 1 patient suffered from stroke. Between 6 and 12 months FUP, 11 additionally TVR was necessary. Thus, the composite 1-year MACCE was 35 %. Dior balloon angioplasty was repeated in 4 patients, while additional DES implantation was performed in 5 patients.

Conclusions This on-going registry reports the successful treatment of ISR with Dior DEB. The 1-year MACCE rate is between the reported MACCE rates of ISR treatment with BMS and DES, but the second generation of Dior DEB might have better results. The DEB use is justified in patients with severe concomitant disease or contraindication of use of DES of any reason.

Safety and Efficacy of the 2nd Generation of the Paclitaxel-eluting DIOR-Balloon in Porcine Coronary Arteries 096

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Purpose The aim of the present study was to investigate the safety and efficacy of the second generation of DIOR paclitaxel-eluting balloon (DEB) in a porcine coronary artery overstretch injury model (1.3:1 balloon/artery ratio).

Methods Nineteen domestic pigs were subjected to balloon dilatation with a 1.3:1 balloon to artery ratio overstretch injury. The use of DIOR was optimized by applying 15, 20, 30 and 45 sec inflation time, measuring the coronary arterial tissue concentration of paclitaxel and the remaining paclitaxel amount on the balloon surface post-inflation. Additionally, vessel injury and development of neointimal hyperplasia were compared using 2nd generation of Dior or conventional non-coated balloon at 2 weeks follow-up (FUP). Dior balloons and bare metal stents were coated with fluorescent paclitaxel-derivate (Oregon Green 488) to demonstrate the distribution of the paclitaxel in the vessel wall after use of DEB or DES.

Results Depending on balloon inflation time a 2-20-fold tissue drug concentration of the arterial wall could be reached, compared to the 1st generation of Dior with previous coating technique. The enhanced version of Dior DEB provided 29 ± 3, 52 ± 6, 196 ± 44 and 202 ± 36 µM/L paclitaxel to the vessel wall after 15, 20, 30 and 45 sec inflations. The remaining paclitaxel amount on the balloon surface was 182 ± 12, 144 ± 10, 131 ± 12 and 85 ± 4 µg after 15, 20, 30, 45 sec balloon inflations. Two weeks post-overstretch injury, the dilated arterial segment neointimal area (0.19 ± 0.04 vs 0.7 ± 0.66 mm²; p = 0.045) and maximal neointimal thickness (0.13 ± 0.06 vs 0.29 ± 0.19 mm; p = 0.039) were significantly smaller with Dior vs uncoated balloon use. Fluorescence paclitaxel derivative-coating of Dior showed a homogenous distribution of the drug onto the vessel, in contrast with the uneven dispersion caused by DES.

Conclusion The 2nd generation of the paclitaxel-eluting balloon DIOR is safe and effective in preclinical porcine model of coronary restenosis, providing a higher level of drug-delivery within the therapeutic range. The maximal antiproliferative effect can be achieved after 20 or 30 sec balloon inflation time, which is better tolerated than the usually recommended 1 min DEB inflation time.

A Case of Complicated Transcatheter Aortic Valve Implantation (TAVI) 167

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Background Surgical aortic valve replacement is the treatment of choice in severe aortic valve stenosis. However, TAVI is an emerging alternative in the elderly and in patients with limiting comorbidities. Although procedural risk might be lower with transcatheter approach, severe complications can occur anyway. We would like to present a case of TAVI complicated by cardiac arrest, which resulted in complete recovery of the patient.

Case Presentation

- 82-y-old female, symptomatic severe aortic valve stenosis (AVA 0.4 cm²)
- Several episodes of dizziness/day, progressive dyspnea NYHA III
- Patient was not accepted for surgical aortic valve replacement due to high risk, therefore transcatheter treatment was intended (CoreValve® prosthesis)

Setting of the Procedure

- Catheterisation laboratory
- Local anaesthesia and analgesic sedation, pat. breathing spontaneously
- Bifemoral percutaneous approach
- Balloon valvuloplasty under rapid pacing (175/min)

Uneventful procedure until balloon deflation: At this time aortic blood flow decreased rapidly. Patient experienced tonic muscle spasm due to lack of cerebral perfusion and lost muscle tone afterwards. Cardio-pulmonary resuscitation (CPR) was initiated immediately. Invasive ventilation was applied. A mechanical chest compression device (Lucas®, Medtronic) was attached and started. Coronary embolism was ruled out by a brief coronary angiography. Since coronary arteries were open, aortic root injection was performed to rule out aortic dissection or perforation. However, aortic root angiogram revealed severe aortic valve regurgitation resulting in functional cardiac arrest. Remaining left ventricular contraction was very poor. At this time we decided to insert the CoreValve® aortic valve prosthesis with ongoing CPR conditions.

- Insertion of the valve with a break of CPR (Lucas® removed for X-ray)
- Two episodes of ventricular fibrillation, terminated by a 200 J shock each
- Epinephrine 1.5 mg bolus and one more minute of CPR finally resulted in return of spontaneous circulation (duration of functional cardiac arrest: 20 min.)

Circulation stabilised and perfusion rates of vasopressors were reduced quickly. Procedure was completed and the patient transferred to the ICU.

- Vasopressors stopped and pacemaker removed after two days
- Ventilation for three days
- Discharge from ICU after five days
- Excellent function of valve prosthesis
- Patient recovered completely without any sequel

Conclusion Severe complications including cardiac arrest may occur in TAVI. Therefore, a mechanical chest compression device should be available to improve both, quality of chest compression and patients' clinical outcome.

Restenosis Rate and Late-Lumen-Loss: Angiographic Comparison of Paclitaxel-eluting Stents with Bare-metal Stents in Renal Artery Stenosis 163

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Purpose To compare the angiographically documented incidences of in-stent restenosis (ISR) in patients treated with either paclitaxel-eluting stents (PES) or bare-metal stents (BMS) for hemodynamically relevant renal artery stenosis (RAS).

Methods Ninety-five patients (55 women; mean age 71 ± 9 years) with 106 RAS (11 bilateral stenoses) were randomized to either the PES group (implantation of the Taxus stent in 49 [46 %] stenoses) or the BMS group (implantation of the Radix stent in 57 [54 %] lesions). All patients had uncontrolled hypertension, defined by (1) recurrent hypertensive crises despite optimized medical therapy and (2) angiographic findings of unilateral or bilateral significant RAS (≥ 50 %). Angiographic follow-up was performed at 6 months, and all angiographic data were evaluated by 2 blinded reviewers using a semi-automated quantitative acquisition technique. Significant

ISR was defined as ≥ 50 % diameter stenosis on follow-up-angiography.

Results Stent-implantation was successful in all stenoses. Mean stent diameter was 5.4 ± 0.9 (BMS) vs 4.7 ± 0.7 mm (PES; $p < 0.05$) with a mean stent-length of 14.4 ± 2.5 (BMS) vs 15.2 ± 3.7 mm (PES; $p > 0.05$). Angiographic follow-up was performed in 45 (79 %) of the BMS-group and in 36 (73 %) of the PES group. In total, the late lumen loss was 1.5 ± 1.1 mm in the BMS patients vs 0.7 ± 0.7 mm in the PES cohort ($p = 0.0006$). There were 7 (6.6 %) ISRs observed in the BMS group versus 2 (1.9 %; p = n. s.) in the PES group.

Conclusion Stent-implantation in RAS shows effective long-term results with either BMS or PES insofar as luminal diameter is concerned. Compared to BMS, PES had less intimal hyperplasia and a reduced late lumen loss. The rate of significant restenosis in the PES group was lowered by two third despite a significantly smaller stent diameter compared to the BMS group. However, as a result of the lower sample size, this difference did not reach statistical significance.

Optische Kohärenz-Tomographie (OCT) nach Stentthrombose 165

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Einleitung Ein 45-jähriger Patient mit kardialem Risikoprofil (Hypertonie, Hyperlipidämie, Diabetes mellitus Typ II, Nikotinabusus sowie positive Familienanamnese) und bekannter koronarer Herzkrankheit wurde unter dem Bild eines akuten Hinterwandinfarkts zur primären PCI aufgelegt.

Anamnestisch bestand eine Zweigefäßerkrankung mit Zustand nach Hinterwandinfarkt 2003 und zweimalig frustranem Wiedereröffnungsversuch eines chronischen RCA-Verschlusses. Ein proximaler CX-Verschluss war vor drei Monaten wiedereröffnet und mit einem Taxus liberté- (3,5/32 mm-) Stent erfolgreich versorgt worden.

Es zeigte sich eine akute Stentthrombose des CX-Stents, der mittels Thrombektomie und PTCA erfolgreich behandelt wurde.

Methode Zur Evaluierung der Stentanatomie wurde eine Optische Kohärenz-Tomographie (OCT) durchgeführt. OCT ist ein bildgebendes Verfahren, das sich aufgrund seines hohen Auflösungsvermögens (10–15 μm) gut zur Analyse komplexer Stentprobleme eignet.

Resultate Die OCT-Untersuchung zeigte im proximalen Segment der CX eine Malapposition des Taxus liberté-Stents. Insgesamt waren 154 Stentstruts (15 % bezogen auf die Gesamtzahl) über eine Länge von etwa 10 mm unterexpandiert, wobei der maximale Abstand von der Intima 0,56 mm betrug. Frakturierte Stentstruts wurden nicht gesehen. Um der Malapposition entgegenzuwirken, wurde mit einem Quantum-4,5/8 mm-Ballon und 20 Atmosphären nachdilatiert, wobei eine Rest-Unterexpansion von 0,34 mm im proximalen Stentsegment zurückblieb.

In der Kontroll-Herzkatheteruntersuchung 6 Monate nach Intervention wurde neben dem bekannten RCA-Verschluss ein zufriedenstellendes Langzeitergebnis des CX-Stents dokumentiert.

Schlussfolgerung Malapposition ist ein Risikofaktor für Stentthrombose. Die Optische Kohärenz-Tomographie erlaubt eine mögliche Malapposition früh zu erkennen, um diese sofort zu korrigieren.

Case report: „Black Hole"-Phänomen bei Optical Coherence Tomography (OCT) 168

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Einleitung Eine 68-jährige Patientin mit Hypertonie, Hyperlipidämie und bekannter koronarer Herzkrankheit wurde zur elektiven Kontroll-Herzkatheteruntersuchung bei subjektiver Beschwerdefreiheit aufgenommen.

Anamnestisch bestand ein Zustand nach Hinterwandinfarkt 2006, welcher mittels PCI behandelt wurde. Es wurde im Rahmen der Intervention ein DES- (Taxus liberté- [3,0/28 mm-] Stent implantiert. Fünf Monate postinterventionell ereignete sich eine akute Stentthrombose, welche mittels Thrombus-Aspiration und mehrfacher PTCA erfolgreich behandelt wurde. Im Rahmen einer Kontroll-Herzkatheteruntersuchung nach 6 Monaten zeigte sich eine Pressure Wire verifizierte proximale LAD-Stenose, weshalb ein DES (Xience 3,0/15 mm) implantiert wurde.

Methode Zur Beurteilung des Endothelialisierungsgrades der Stents wurde im Rahmen der Kontroll-Herzkatheteruntersuchung eine OCT (Optical Coherence Tomography) durchgeführt.

Resultate Im Xience-Stent in der LAD zeigte sich eine intimale Hyperplasie zwischen 0,06 und 0,22 mm ohne relevante Stenose mit einem Endothelialisierungsanteil von 96 % der Stentstruts. In der RCA konnte im Bereich des Taxus liberté-Stents eine intimale Hyperplasie zwischen 0,05 und 0,8 mm mit einem Stenosegrad von 46 % festgestellt werden. Der Endothelialisierungsanteil betrug 97 %. Auffallend waren hypodense Areale im Bereich der Stentstruts, welche als „Black Holes" bezeichnet werden.

Schlussfolgerung Als mögliche Ursache für „Black Holes" im Rahmen von DES-Implantationen werden neben positivem Remodelling andere Ursachen wie die Entstehung freier Proteoglykane bzw. matrixarmer Zellen diskutiert.

Clinical and Angiographic Outcomes of Xience Stent Implantation: a Single Center Prospective Registry 159

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Background First-generation drug-eluting stents (DES) have brought major improvements in results of percutaneous coronary intervention (PCI). However, there is currently debate on the safety of first-generation DES, given the potential for late stent thrombosis, especially after discontinuation of dual antiplatelet therapy. Second-generation DES, such as everolimus-eluting stents (Xience V), have recently become available in the USA and Europe. The recently published SPIRIT III trial on single de novo coronary lesions reported a 2.9 % target vessel failure after 1 year. The aim of our prospective registry was to evaluate the clinical and angiographic outcomes after implantation of Xience stents in a real world clinical setting.

Methods Between December 2006 and January 2008, 71 patients with 82 lesions (64 ± 12 y; 68 % male) with symptomatic coronary artery disease (CAD) have been prospectively included in the registry. Clinical control was performed in all patients 210 ± 68 days post-PCI, with 62.5 % control angiography rate at 6 month. The primary clinical endpoint of the study was the composite of major adverse cardiac and cerebrovascular events (MACCE, defined as non-fatal AMI, all-cause mortality, stroke and target vessel revascularization/TVR/). Baseline and follow-up (FUP) quantitative angiographic (QCA) parameters of in-stent and in-lesion (defined as lesion within 5 mm proximal or distal from stent edge) were measured. Acute lumen gain (ALG), and in-stent and in-lesion late lumen loss (LLL) were calculated.

Results Totally 112 Xience stents were implanted. The procedural success was 100 %, with no intervention complication. The stent/patient ratio was 1.6 ± 0.9. The rate of acute, subacute and late thrombosis was 0 %, 1.4 % and 0 %, respectively. Two patients (2.8 %) developed complication during the first month (1.4 % AMI, 1.4 % cardiac death). Between 1 and 6-month FUP, 1 death (1.4 %) and 1 TVR (1.4 %) occurred, resulting in a composite MACCE of 5.6 %. The binary restenosis rate of the angiographically controlled lesions (56 % of all lesion) was 1.5 %. QCA resulted in an in-stent LLL of –0.09 ± 0.12 mm, and proximal and distal in-lesion LLL of –0.32 ± 0.14 mm and –0.18 ± 1.33 mm, respectively.

Conclusions Implantation of Everolimus-eluting stent (Xience) proved to be safe and effective in patients with symptomatic CAD

with low rates of target vessel failure and excellent quantitative angiographic results.

From Feasibility to Durability: 30-day and One-year Outcomes after Percutaneous Aortic Valve Replacement 160

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Background Percutaneous aortic valve replacement (PAVR) is an emerging alternative treatment option for patients with symptomatic severe aortic stenosis (AS) and high risk for operative valve replacement. Beyond feasibility and acute success of the procedure itself, durability of hemodynamic results and mid-term clinical follow-up are of major interest.

Patients and Methods In our institution, 56 patients (20 male, 36 female; mean age 80 ± 6 years) with symptomatic severe AS and a logistic EuroSCORE > 20 % underwent PAVR between May 2007 and February 2009. The procedure was performed in the catheterization laboratory via a bifemoral percutaneous approach under local anesthesia and analgesic sedation without surgical cut-down and hemodynamic support. After balloon valvuloplasty, the self-expanding CoreValve prosthesis (diameter 26 mm, n = 32; 29 mm, n = 23) was implanted using the current 18 French delivery catheter system. All patients were scheduled for clinical evaluation and echocardiographic follow-up at 30 days as well as three, six and twelve months after PAVR.

Results Acute procedural success rate was 98 %. In one patient the prosthesis could not be safely positioned and had to be removed before complete deployment. Echocardiography 30 days after device implantation revealed a significant reduction of peak aortic transvalvular pressure gradient (PPG: 99 ± 28 vs 20 ± 6 mmHg; $p < 0.0001$) and mean aortic transvalvular pressure gradient (MPG: 59 ± 16 vs 11 ± 3 mmHg; $p < 0.0001$), and a significant increase of calculated aortic valve area (AVA: 0.5 ± 0.1 vs 1.4 ± 0.2 cm²; $p < 0.0001$). Aortic regurgitation was trivial or mild in 49 patients and moderate in seven patients. Permanent pacemaker implantation was necessary in five patients (8.9 %) due to complete atrioventricular block. Major complications were myocardial infarction (n = 1), stroke (n = 2) and pericardial tamponade (n = 2). Six patients (10.7 %) died within the first 30 days, another eight patients (14.3 %) deceased up to twelve months after PAVR. There was no device-related mortality. 14 patients completed the one-year follow-up period so far. All of them had an uneventful postprocedural course with marked clinical amelioration and sustained hemodynamic improvement. At one-year follow-up, reduction of transvalvular pressure gradients and increase of valve area were maintained and not significantly different from 30-day results (PPG 18 ± 7 mmHg, MPG 10 ± 4 mmHg, and AVA 1.5 ± 0.4 cm²).

Conclusion PAVR with the self-expanding CoreValve bioprosthesis is an emerging alternative therapy for high-risk patients with symptomatic severe AS. Complication rate is acceptable and mortality rate lower than predicted by risk calculation. Favourable hemodynamic features of the prosthesis yield a beneficial clinical course and remain unchanged at least up to one year after PAVR.

Comparison of Angiographic Outcome of Cypher and Taxus Stents Implanted in the same Patients 166

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Background Cypher (sirolimus-eluting stent) and Taxus (paclitaxel-eluting stent) have been approved for use in percutaneous coronary intervention. Both of the stents have shown superiority over bare metal stents in reducing major adverse cardiac events, restenosis rates and target vessel revascularisation. Results of clinical trials with head-to-head comparison of Taxus and Cypher stents in patients with significant coronary lesion reported similar clinical but somewhat worse angiographic outcome of Taxus stent implantation favouring using of Cypher stent. The results of these clinical trial hampered by the fact, that there are differences (even not significant) in the patient population receiving either Cypher or Taxus stents. Therefore the aim of the present study was to compare the angiographic outcome of patients receiving both Cypher or Taxus stents during the same procedure.

Methods Twenty-four patients (65 ± 12 y; 71 % male) with significant coronary artery disease underwent both Cypher (13 LAD, 4 LCx and 7 RCA lesions) and Taxus (10 LAD, 4 Lcx and 10 RCA lesions) stent implantations. The 1-year clinical outcome of the patients was recorded. Baseline and follow-up (FUP) quantitative angiographic (QCA) parameters of in-stent and in-lesion (defined as lesion within 5 mm proximal or distal from stent edge) were measured. Acute lumen gain (ALG), and in-stent and in-lesion late lumen loss (LLL) were calculated.

Results Hypertension was recorded in 71 %, diabetes mellitus in 50 %, hyperlipidaemia in 79 %, smoking 33 % of patients. Nine patients (38 %) suffered from previous myocardial infarction and 2 patients had previous bypass operation. The size and length of the implanted Cypher (3.0 ± 0.3 and 21.2 ± 6.8 mm, respectively) and Taxus (3.1 ± 0.4 and 17.2 ± 6.3 mm, respectively) stent, the stent balloon inflation pressure and time were similar. During the 6-month FUP, 1 patient died after heart valve replacement due to multiorgan failure. One patient underwent target vessel revascuarization of the Taxus stent. The acute lumen gain (1.21 ± 0.88 vs 1.4 ± 0.61 mm; $p = 0.226$) similar in both stents. No significant differences were observed between the Cypher and Taxus stents in the same patient, as in-stent LLL was 0.37 ± 0.59 mm vs 0.28 ± 0.26 mm ($p = 0.288$), the proximal im-lesion LLL was 0.17 ± 1.07 mm vs 0.13 ± 0.87 mm ($p = 0.459$) and the distal in-lesion LLL was 0.52 ± 0.67 mm vs 0.31 ± 0.36 mm ($p = 0.132$) in Cypher stents vs Taxus stents.

Conclusions Head-to head comparison of Cypher and Taxus stents in the same patients revealed no differences between the two drug-eluting stents during the first 1 year follow-up.

Kontrolle des Endothelialisierungsgrades von Paclitaxel-, Sirolimus- und Everolimus-eluting Stents 6–8 Monate nach deren Implantation mittels Optischer Kohärenz-Tomographie (OCT) 083

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Einleitung Die inkomplette Endothelialisierung von Drug-eluting Stents (DES) wird als mögliche Ursache für die späte Stentthrombose diskutiert.

Methode Aufgrund ihres hohen Auflösungsvermögens (10–15 µm) stellt die Optische Kohärenz-Tomographie (OCT) derzeit die Methode der Wahl zur Abschätzung der Endothelialisierung von Stentstruts dar. Im Rahmen von Kontroll-Herzkatheteruntersuchungen (6–8 Monate post PCI) wurden bei 39 Patienten OCT-Untersuchungen durchgeführt. Die endothelialisierten und die freiliegenden Stentstruts wurden in jedem einzelnen Frame aller OCT-Aufnahmen ermittelt. Der Endothelialisierungsgrad wurde als prozentueller Anteil der endothelialisierten Struts an der Gesamtzahl der gezählten Struts definiert.

Resultate 19 Patienten mit Paclitaxel-eluting Stents (PES), 7 Patienten mit Sirolimus-eluting Stents (SES) und 13 Patienten mit Everolimus-eluting Stents (EES) wurden analysiert.

Der Endothelialisierungsgrad betrug 97 % (± 4 %) bei den Paclitaxel-eluting Stents, 98 % (± 2 %) bei den Sirolimus-eluting Stents und 97 % (± 3 %) bei den Everolimus-eluting Stents.

Eine komplette Endothelialisierung zeigte sich nur bei 3 der 39 untersuchten Patienten (2 Patienten mit SES und 1 Patient mit EES).

Zusammenfassung Der Endothelialisierungsgrad der mit Paclitaxel-, Sirolimus-, und Everolimus-eluting Stents versorgten Patienten betrug 6–8 Monate nach deren Implantation 97–98 % und

war bei den 3 untersuchten Drug-eluting Stents vergleichbar. Eine komplette Endothelialisierung nach 6–8 Monaten fand sich nur bei 8 % der Patienten.

Comparison of Platelet Aggregometry and the VASP Assay for the Prediction of Stent Thrombosis 066

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Background and Aim An insufficient platelet inhibition by clopidogrel can result in stent thrombosis leading to severe clinical complications. The aim of our study was to investigate which of the two common tests assessing the antiplatelet effect of clopidogrel, the very specific VASP assay or a functional platelet aggregometry has a better predictive value for stent thrombosis.

Methods Responsiveness to clopidogrel was assessed by the vasodilator-stimulated phosphoprotein (VASP) phosphorylation assay and ADP+PG-induced platelet aggregometry (Multiplate Analyzer) in 416 patients with coronary artery disease undergoing percutaneous coronary intervention. The rate of stent thrombosis was recorded during a 6-month follow-up.

Results Stent thrombosis occurred in three patients (0.7 %): two patients suffered from an acute and one from a late stent thrombosis. Area under the ROC curve was higher in platelet aggregometry (c-index = 0.92; 95 % CI = 0.85–0.99; p = 0.012) than in the VASP assay (c-index = 0.60; 95 % CI = 0.40–0.80; p = 0.55), indicating a very good predictive performance of aggregometry. In platelet aggregometry, the cut-off value of 54 U resulted in 100 % sensitivity and 87 % specificity. In the VASP assay, the cut-off value of 42 % platelet reactivity index resulted in 100 % sensitivity but low specificity (37 %). The probability to predict the occurrence of stent thrombosis (positive predictive value) was higher for platelet aggregometry than for the VASP assay: 61 % vs 25 %. The probability to predict the absence of stent thrombosis (negative predictive value) was 100 % for both tests.

Conclusions The assessment of the antiplatelet effect of clopidogrel by platelet aggregometry was more predictive for stent thrombosis than the VASP assay. This could indicate that the overall platelet activation might be a better estimate for risk of stent thrombosis than the assessment of the clopidogrel effect on its target, the P2Y12 receptor.

Long-term Outcome after Drug-eluting Stent Implantation in Chronic Total Occlusions in Comparison with Bare-metal Stents: a Single Centre Experience 002

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Purpose Aim of our study was to evaluate the effect of use of drug-eluting stents (DES) in successfully reopened chronic total occlusions (CTOs) compared with bare metal stents (BMS) on all-cause mortality and target vessel revascularization (TVR) in a "real world" clinical setting.

Methods 113 consecutive patients, who underwent PCI and stent implantation for CTO, were included in a prospective registry from January 2003 until December 2007. Patients were subdivided retrospectively into two groups, those who had received a DES and those who had received a BMS on discretion of the interventionalist. All-cause mortality, TVR and the combined endpoint of death or TVR was evaluated during a mean follow-up period of 22.92 ± 11.9 months (range 6–52 months).

Results 69 patients (61.1 %) received BMS, while 44 patients (38.9 %) received DES. Gender, age, arterial hypertension, hyperlipidemia, heart failure, history of MI, PCI, CABG, cerebral insult, smoking, chronic renal failure and PAOD were not different between groups. Significant difference was found for diabetes mellitus (DES: 40.9 % vs BMS: 18.8 %; p = 0.01). Furthermore, angiographic parameters like location of CTO (LAD, ACX or RCA) and diameter of the stents used was not different between DES and BMS. Significant difference was obtained for the stent length (DES: 27.08 ± 5.81 mm vs BMS: 19.54 ± 5.24 mm; p < 0.001).

In total 11 Patients (9.7 %) needed TVR, 11 (9.7 %) died and 20 (17.7 %) reached the combined endpoint (all-cause death or TVR). 10 patients (2.3 %) of the BMS group and 1 patient of the DES group died during the follow up (p = 0.1). 8 patients (11.6 %) of the BMS group but only 3 (6.8 %) patients of the DES group had a TVR (p = 0.4).

With respect to the combined endpoint 9.1 % of patients with DES and 23.2 % with BMS (p = 0.1) had an event during the follow up.

Conclusion Our results obtained in a "real world" clinical setting showed in general a low event rate after PCI and DES implantation of CTOs but a much higher rate for the use of BMS in this indication with no statistical difference between groups most obviously based on the low number of patients investigated. Nevertheless, the data demonstrate that DES should be favoured after recanalization of CTOs.

Theoretical Considerations on Medina 0.0.1. – Mission Impossible? 091

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Background Ostial side branch (SB) stenoses (Medina 0.0.1) without involvement of the main branch (MB) constitute a major challenge for the interventionist. "*Primum nihil nocere*" is quite difficult to predict in that situation. Stenting of the SB is hampered by deficiencies in scaffolding of SB-ostium or stent protrusion into MB thereby obstructing the MB with all possible catastrophic sequelae.

Methods To get a deeper understanding of this dilemma, we studied the influence of various bifurcational angulations in engineering drawings true to scale (30, 45 and 75 degree angled 3.0 mm MB and 3.0 mm SB). We compared the influence of positioning of the SB-stent on minimal lumen diameter (MLD) of MB and on deficiencies in scaffolding of SB-ostium (GAP). 3 stent positions were studied: a) perfect SB (complete scuffolding of the SB-ostium) or b) perfect MB (no stent-protrusion into MB) or c) a compromised deployment with reducing MB-MLD ≤ 0.5 mm.

Results

Angle 30° 45° 75°				
Perfect SB	MB-MLD (mm)	0.40	0.85	2.10
Perfect SB	SB-GAP (mm)	0.00	0.00	0.00
Perfect MB	MB-MLD (mm)	3.00	3.00	3.00
Perfect MB	SB-GAP (mm)	4.70	3.00	0.80
Compromise	MB-MLD (mm)	2.50	2.50	2.50
Compromise	SB-GAP (mm)	4.10	2.30	0.30

Conclusions Stenting in Medina 0.0.1 is unlikely to result in a satisfying result in with acute angles ≤ 30 degrees. Both, stent protrusion into the MB with MLD of 0.40 mm in a 3 mm vessel and failing scuffolding of the very proximal SB with gaps up to 4,70 mm have to be considered as major limitation. In more obtuse angles of ≥ 45 degrees acceptable results will be obtained.

The Dogbone Technique: A Novel Approach to Standardize and Optimize Stent Deployment in Side-branch Lesions Medina 0.0.1 and T-stenting 092

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Background Stenting of the SB in Medina 0.0.1 is hampered by deficiencies in scaffolding of SB-ostium (GAP) or stent protrusion into MB thereby obstructing the MB with all possible catastrophic sequelae. The use of an inflated MB ballon while retracting the SB-stent has been advocated. However, using a ballon/vessel ratio of 1:1 will result in endothelial damage of the MB and smaller ballons are unable to stop SB-stent retraction at a predefined point.

Table 9: S. Winkler et al.

MB & SB 3,00 mm – Angle/Ballon-Size	30°/2.25	45°/2.00	75°/2.0
MB-MLD (mm)	2.50	2.50	2.70
SB-GAP (mm)	4.40	2.30	0.45
Difference: MB-Diameter to MB-Ballon	0.75	1.00	1.00
MB & SB 3,50 mm – Angle/Ballon-Size	**30°/2.75**	**45°/2.50**	**75°/2.50**
MB-MLD (mm)	2.8	2.9	3.1
SB-GAP (mm)	4.6	3.0	0.5
Difference: MB-Diameter to MB-Ballon	0.75	1.00	1.00

Methods Inflating Taxus Liberté-stents (Boston Scientific) with low pressures of 2.5 atm results in reproducible inflation of the stent ballon at the stent-edges, creating an dogbone appearance. This allows the use of MB-ballons with a ratio < 1:1. We studied different ballon sizes (Maverick, Boston Scientific) in a 3 and 3.5 mm bifurcational silicon model with angulations of 30°, 45° and 70° in MB and SB. MB-ballon was inflated to the desired diameter. Stent was placed in the SB and positioned some mm distally to the bifurcation and inflated with 2.5 atm and then gently retracted proximally till the MB-ballon stopped that maneuvre. Stent was implanted with nominal pressure. MB ballon was then deflated followed by deflation of the stent-ballon. GAP was measured and minimal lumen diameter (MLD) of the MB was determind by use of a nozzle gage.

Results In a pilot phase different ballon-sizes were tested (results not shown) to allow stent deployment with only minimale protrusion into the MB and acceptable scaffolding of SB-ostium. In final series the optimal ballon for the appropriate angle and vessel diameter was used (**Table 9**).

Conclusions The dogbone technique allows predictable stent-apposition in Medina 0.0.1 and T-stenting. In 45° and 75°, ballons 1 mm smaller than MB-vessel and in 30° ballons 0.75 mm smaller showed best results. However, stenting in with acute angles ≤ 30° is unlikely to result in a satisfying result.

Strahlendosis und Kontrastmittelverbauch: Rotationsangiographie versus konventionelle Koronarangiographie 174

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Einleitung Die Rotationsangiographie stellt ein neues Verfahren zur Darstellung der Koronarien dar. Dabei erfolgt die Darstellung der Koronarien während einer definierten Rotationsbewegung der Röntgenröhre über ca. 4 Sekunden: für die Darstellung der rechten Kranzarterie Rotation von LAO 70 bis RAO 30 Grad, für die Darstellung der linken Kranzarterie LAO 90 Grad bis RAO 30 Grad. Während der Rotationsbewegung wird eine konstante Kippung von 10 Grad kranial beibehalten. Durch die Rotationsangiographie wird die Zahl der nötigen Projektionen verringert. Unsere Hypothese war, dass dadurch auch die Strahlendosis und die Kontrastmittelmenge verringert werden können.

Methoden und Resultate 100 zur Koronarangiographie zugewiesene Patienten wurden mittels konventioneller Angiographie (n = 50) oder Rotationsangiographie (n = 50) untersucht. Durchleuchtungsdauer (Sek), Strahlendosis (Gycm^2) und Kontrastmittelmenge (ml) wurden während der Koronarangiographie gemessen. Der Vergleich beider Gruppen erfolgte durch einen 2-seitigen T-Test (SPSS-Programm). Im Vergleich Rotationsangiographie vs. konventionelle Angiographie betrug die Strahlendosis 18 ± 9 vs. 25 ± 15 Gycm^2 (p = 0,013), die Durchleuchtungsdauer 116 ± 50 vs. 121 ± 77 Sek (p = 0,7) und die Kontrastmittelmenge 67 ± 21 vs. 76 ±15 ml (p = 0,013).

Konklusion Die vorliegende Untersuchung ergibt einen Hinweis für eine signifikant geringere Strahlendosis und Kontrastmittelmenge der Rotationsangiographie.

First-in-Man-Nachweis einer Einheilung eines Drug-eluting Stent mit resorbierbarem Polymer nach 3 Monaten mittels OCT 023

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Hintergrund Bis zu ihrer vollständigen Endothelialisierung erfordern Drug-eluting Stents heute eine duale Antiaggregationstherapie von 6–12 Monaten und teilweise mehr. Wir stellen die Ergebnisse bezüglich der Endothelialisierung nach 3 Monaten bei einem neuen Drug-eluting Stent mit bioresorbierbarem Polymer (Nobori-Stent) vor.

Im Vergleich zum derzeitigen Goldstandard, dem intravaskulären Ultraschall (IVUS), weist die OCT-Untersuchung 2 wesentliche Unterschiede auf. Zum einen ist die Auflösung der OCT-Bilder um den Faktor 10 höher (10 µm anstelle von 100–150 µm), zum anderen basiert die Bildherstellung auf den optischen Eigenschaften des Gewebes und nicht den akustischen [1, 2]. In einer rezenten Studie zeigten OCT-Bilder eine weit überlegene Darstellung der Gefäßwand im direkten Vergleich mit IVUS und korrelierten signifikant besser mit dem histologischen Präparat [3].

Methode Wir untersuchten 5 Nobori-Stents nach elektiver PCI bei NSTEMI-Patienten mittels OCT nach 3 Monaten (max. 3 Monate und 20 Tage). Alle Patienten waren mit Aspirin 500 mg i.v. und Plavix 600 mg oral vorbehandelt worden und erhielten Bivalirudin i.v. während der PCI. Nach Entlassung erhielten alle Patienten 100 mg Aspirin tägl. sowie Plavix 75 mg tägl. Außerdem erhielten alle Patienten Atorvastatin 80 mg tägl., Tritace 2,5 mg 2× tägl., Nevibolol 5 mg tägl. sowie Lansoprazol oder Esomeprazol tägl.

Ergebnisse OCT-Bilder aller 5 Patienten zeigten eine komplette Beschichtung sämtlicher Stent-Struts nach 3 Monaten (max. 3 Monaten + 20 Tage). Es zeigten sich keine Stellen mit Malapposition oder unbeschichtete Struts. In einer ähnlichen Studie zeigte sich nach 2 Monaten ein 88 %-Beschichtung des untersuchten DES und eine 95 %-Beschichtung des untersuchten BMS [4].

Diskussion Die komplette Beschichtung aller Struts dieses neuen Drug-eluting Stents mit bioresorbierbarem Polymer lässt evtl. eine Verkürzung der dualen Antiaggregationstherapie zu. Dadurch verkürzt sich zum Beispiel das Intervall zwischen PCI und chirurgischem Eingriff. Der Unterschied zur Dauer der dualen Antiaggregationstherapie bei BMS wäre auch nicht mehr signifikant. Zu diesem Zeitpunkt empfehlen wir jedoch weitere Untersuchungen mit einer größeren Anzahl von Patienten bevor eine eindeutige Empfehlung abgegeben werden kann.

Literatur beim Verfasser

Pulmonale Hypertension

Impact of Thrombus Borne Active Endothelin on the Vasoconstrictive Capacity of Thrombi from Patients with Chronic Thromboembolic Pulmonary Hypertension 013

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Background Chronic thromboembolic pulmonary hypertension (CTEPH) can occur after acute pulmonary embolism. Surgical pulmonary endarterectomy (PEA) is the treatment of choice for CTEPH. Recently, medical treatment with endothelin- (ET) receptor antagonists has been attempted as a treatment option for inoperable patients. However, the pathophysiologic basis of this treatment effect in a disease where mechanical obstruction is thought to play the major role in impairing hemodynamics is unclear.

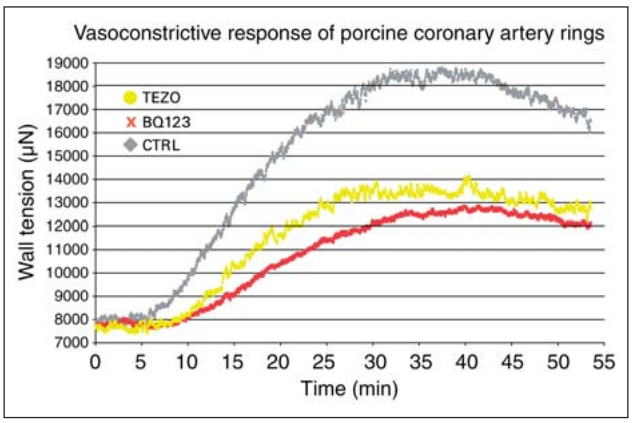

Figure 5: C. Adlbrecht et al.

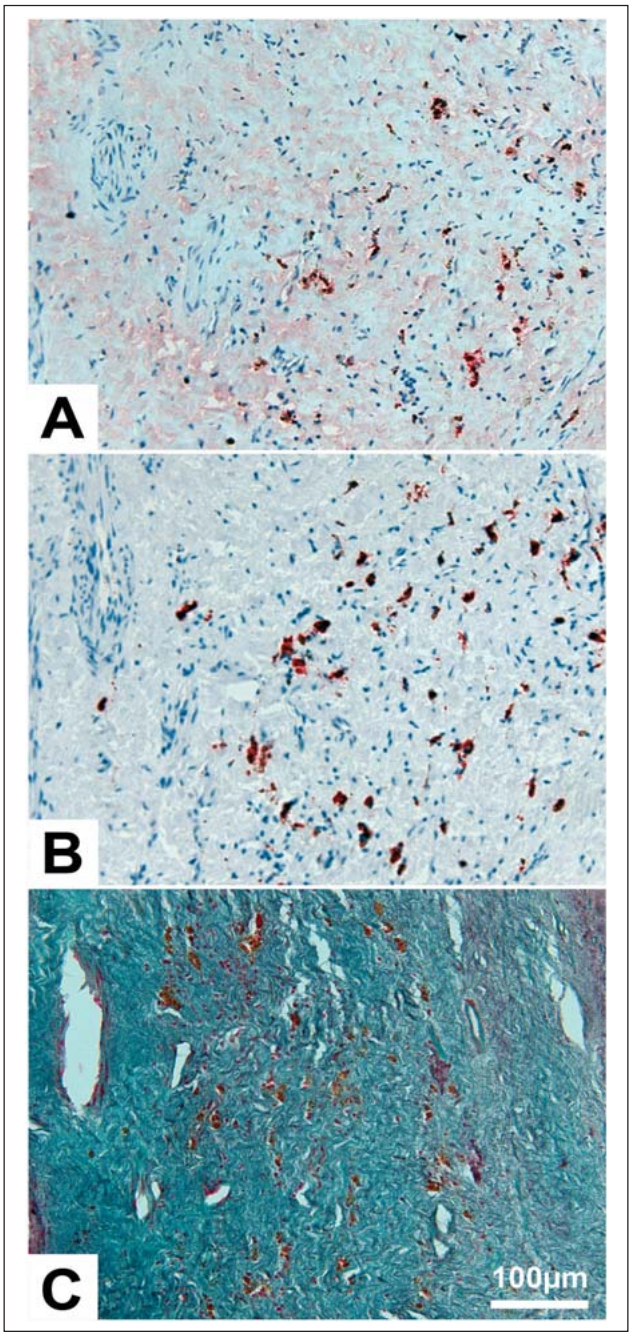

Figure 6: C. Adlbrecht et al.

We hypothesized that in CTEPH, thrombus-associated ET mediates vasoconstriction in the distal vascular bed, impairing pulmonary capillary flow and furthering adverse remodelling.

Aim The aim of the present study was to investigate the role of thrombus borne ET in CTEPH.

Methods 19 surgical thrombus samples from patients with CTEPH undergoing PEA were homogenized and subjected to in-vitro vasoconstriction experiments on porcine artery rings evaluating dual and selective ET-A receptor antagonism. Thrombus ET synthesis was analyzed in an animal model of CTEPH.

Results CTEPH thrombi exerted pronounced vasoconstrictive properties in 17 of 19 (90 %) samples. Pre-incubation with a dual ET antagonist inhibited thrombus-induced constriction by 30.4 (18.6–62.9) % of the crossover self control (**Figure 5**). Immunohistological evaluation revealed colocalization of ET-1 positivity (**Figure 6, Panel A**) with CD-68 positive macrophages (**Figure 6, Panel B**) within the thrombi (**Figure 6, Panel C**).

Conclusion The vasoconstrictive capacity of CTEPH thrombi is caused by thrombus borne ET to a major extent. Our data may explain the effect of ET receptor antagonists in some CTEPH patients and may represent a link between failed thrombus resolution and ET mediated microvascular remodelling.

Exercise Capacity and Pulmonary Artery Pressure – Flow Relations in Patients After Successful Pulmonary Endarterectomy 034

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Background Pulmonary endarterectomy (PEA) provides potential cure for patients with chronic thromboembolic pulmonary hypertension (CTEPH). Successfully operated patients have been shown to normalize hemodynamic parameters in long-term studies. The aim of the present study was to assess exercise capacity, and to test the hemodynamic response to exercise at least one year after successful PEA.

Methods 13 successfully operated CTEPH patients and 14 healthy volunteers underwent cardiopulmonary exercise testing (CPET). In addition, patients and 10 age-matched controls without precapillary pulmonary hypertension underwent right heart catheterization at rest and after 10 minutes of submaximal supine bicycle-exercise. Between-group differences were analyzed utilizing the unpaired t-test, ANOVA or the Fisher's exact test. P-values < 0.05 were considered statistically significant.

Results Peak work rate (110.5 ± 50.9 Watt) and O_2 uptake at maximum exercise (1.8 ± 0.7 l/min) were reduced as compared to healthy volunteers (166.9 ± 49.2 Watt; p = 0.01 and 2.3 ± 0.6 l/min; p = 0.03).

There were no differences between patients and controls with respect to resting hemodynamic parameters. After 10 minutes of exercise, CTEPH patients displayed significantly higher levels of pulmonary vascular resistance than controls with a steeper pressure-flow gradient (p = 0.005).

Conclusions The decline in PVR that occurs as a physiological reaction to exercise in healthy individuals is reduced in successfully operated CTEPH patients. This abnormal hemodynamic response to physical stress is associated with a limited exercise capacity of CTEPH patients after PEA.

A Simple Non-Invasive Diagnostic Algorithm for Pulmonary Hypertension 035

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Background Current guidelines for the diagnosis of precapillary pulmonary hypertension (PH) recommend right heart catheterization (RHC) in symptomatic patients or patients at risk with echocardiographic systolic pulmonary pressures (sPAP) ≥ 36 mmHg. The growing awareness for PH, a high prevalence of postcapillary PH and the inability to discern between pre- and postcapillary PH by transthoracic echocardiography (TTE), have led to unnecessary RHCs. The aim of the present study was to test the ability of standard non-invasive diagnostic procedures to discriminate between pre- and postcapillary PH in a selected patient population with clinical and echocardiographic suspicion of PH.

Methods In a first step, data from 251 patients with sPAP ≥ 36 mmHg by echocardiography were retrospectively analyzed in a tertiary referral center for PH. The diagnostic value of clinical parameters, blood gas analyses, serum N-terminal brain natriuretic peptide (NT-proBNP) and ECG was assessed. Parameters with independent discriminative abilities derived from logistic regression were used to construct a diagnostic decision tree. In a second step, overoptimistic estimations of the decision tree were corrected by internal and temporal validation. For the latter, data from 121 prospectively recruited consecutive patients were used.

Results NT-proBNP (OR [95 % CI] 2.01 [1.21–3.33]; p = 0.007) and electrocardiographic right ventricular strain (RVS) (OR [95 % CI] 52.931 [17.27–162.18]; p < 0.001) were predictors of precapillary PH. A diagnostic decision tree was derived that stratified patients into a group with and a group without RVS. The latter were further stratified by serum NT-proBNP levels below and above 80 pg/ml. In the diagnostic pathway of precapillary PH, integration of the decision tree subsequent to TTE may increase specificity from 0 % to internally validated 17.3 % or prospectively temporally validated 26.3 %. The validated sensitivity remains high at 97.9 % or 100 %, respectively.

Conclusion The incorporation of ECG and NT-proBNP into the work-up of PH provides incremental diagnostic value and may reduce the number of invasive hemodynamic assessments.

Rhythmologie

Surface ECG based AV Optimization for Cardiac Resynchronization Therapy 105

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Introduction There are many techniques for optimizing AV-delays (AVD) during CRT. A simple method is the adjustment of the AVD based on surface-ECG. The purpose of this abstract is the retrospective comparison of the surface ECG-algorithm with the echo based algorithm for optimizing mitral inflow (Ritter-method). The optimum AVD is given if at the end of left atrial contraction the mitral valve is closed by the ventricular pressure increase (onset of isovolumetric contraction time, ICT).

Methods The atrial conduction time can be defined from atrial stimulus, or beginning of P-wave to the end of P-wave (EP). Beginning of ICT corresponds to the peak/nadir of the paced QRS-complex. The time from EP to the peak/nadir of the R-wave was measured in 100 normal individuals. An age-related average value of 100 ms was determined, which serves as a physiologic reference. The approximated optimum AVD is given if the delay from EP to the ICT amounts to 100 ms. Thus, the optimum AVD for sensed and paced P waves can be calculated: [AVDopt = AVDprog +100 – T] AVDopt = optimized-AVD; AVDprog = programmed-AVD at baseline; T = interval EP to peak/nadir of paced-QRS; 100 ms physiologic reference. 83 patients (69 ± 9 y, 57, (QRS 129 ± 18 ms, LVEF 36 ± 11 %, LVEDD 59 ± 8 mm) with implanted CRT devices underwent AVD-optimization (Ritter method) during each follow up. 12-lead-ECG from all patients were retrospectively analysed, by measuring the distance from EP to peak/nadir of the paced QRS-complex.

Results Echocardiography optimized-AVD compared with the surface ECG-AVD method showed a statistically significant correlation (p < 0.01). Mean interval from EP to peak/nadir of the paced QRS complex were found to be 103 ± 7 ms.

Conclusion The approximate AVD adjustment with the surface ECG appears to be a viable technique.

Invasive Validation of a Modified Myocardial Performance Index (TEI Index) which is Applicable to Heart Failure Patients with Atrial Fibrillation, Left Bundle Brunch Block or AV-Conduction Disorders 104

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Background Congestive heart failure is related to contraction and relaxation abnormalities of the ventricle. A combined myocardial performance index (MPI, isovolumetric contraction time [ICT] plus isovolumetric relaxation time [IRT] divided by ejection time [ET], Tei Index) can be used to analyze an overall assessment of the ventricular function. The MPI has the disadvantage that it can not be used in patients with AV-conduction disorders (AV-block, bundle branch block, atrial fibrillation). Therefore we propose the calculation of a modified MPI and postulate that the closure of the mitral valve and the beginning of the ICT correlate with the peak of the QRS-complex of the surface ECG.

Purpose The purpose of this prospective study is the invasive validation of the modified MPI and to prove its applicability.

Methods Thirty-two subjects (mean age 67.1 years; 20 male; 12 female), were included in a consecutive manner. Twenty-seven patients had sinus rhythm and five patients were in atrial fibrillation. All patients had an indication for a coronary angiography, and underwent left heart catheterization. A dual lumen pigtail catheter was used for the invasive measurement of the left ventricular- and aortic pressure onset. The ICT was calculated from the beginning of the ventricular pressure rise to the onset of the aortic pressure. Echo-Doppler methods were used to measure ICT, ET and IRT. The MPI was obtained by subtracting ET from the interval between peak (nadir) of the QRS complex (ECG) and the onset of the mitral flow. The echocardiopgraphic measured modified ICT was compared with the invasively measured ICT.

Results The modified echocardiographic measured MPI was easily obtained in all subjects. Mean values of the ICT were found to be 74 ± 18 ms, from the ET 262 ± 32 ms and from the IRT 137 ± 31 ms. For the invasively measured ICT the mean values were 73 ± 16 ms and from the ET 263 ± 44 ms. There is a good correlation between the invasively measured ICT and the echocardiographically measured modified ICT (r = 0.94; p < 0.0001), also in the group of patients who had atrial fibrillation (r = 0.96; p = 0.01).

Conclusion The modified echocardiographic MPI shows a good correlation with the invasively measured data and may be used in the work-up of CRT patients. The modified MPI has the advantage to also include patients with atrial fibrillation and AV-conduction problems.

Ablation of Left Accessory Pathways Guided by Double Cannulation of the Coronary Sinus 044

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Introduction The signals recorded by the coronary sinus (CS) catheter are the main guide for localization of left-sided accessory

pathways (AP). In general, a single multipolar CS catheter is used during the electrophysiological study (EPS) to diagnose the presence or absence of a left AP. We hypothesized, that the introduction of a second CS catheter might be helpful for detailed mapping of the distinct pathway insertion.

Patients and Methods This retrospective analysis comprised 9 pts (8 men) with a mean age of 39 yrs (range 21–58 yrs) who underwent EPS and ablation of pathway-mediated re-entrant tachycardia. In two patients a repeat procedure was performed due to recovery of conduction. The CS was cannulated with two different catheters which were inserted from above and below the heart. According to our standard we introduced fixed-shaped decapolar catheters from the right internal jugular vein and deflectable quadri-, hexa-, or decapolar catheters from the femoral vein.

Results A concealed WPW was diagnosed in 6 pts, whereas an overt WPW syndrome was present in 3 pts. The AP was localized left anterolateral (n = 5), left lateral (n = 3), and in one patient in both the left-anterolateral and posteroseptal region. The exact localization of the AP was determined after introduction of a second CS catheter from inferior with help of adequate signal bracketing in 7 pts. In one case, distal CS cannulation from superior failed due to an anatomical obstacle (valve of Vieussens) that could be negotiated from inferior. In another case, the presence of a persistent left superior caval vein required circumferential mapping of the enlarged distal CS with two catheters. In 6 patients we were able to record double potentials along the CS with retrograde conduction during ventricular overdrive pacing. Using this method the AP was eliminated sucessfully with a single burn in 5 pts and with 2 to 6 ablations in 4 pts. No complications occurred related to these procedures.

Conclusion In selected cases, introduction of two multipolar CS catheters from superior and inferior may be helpful for the exact localization of left-sided APs and improve ablational outcome. Bracketting of very distal pathway insertion was the main reason for using this technique. Moreover, simultaneous recordings of signals from the roof and floor of the CS provide additional insights from the musculature of this variable venous structure.

Predictive Value of NT-proBNP Levels and Body Mass Index for Recurrence of Atrial Fibrillation after Successful Cardioversion 017

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Background The pathogenesis of atrial fibrillation (AF) is multifactorial and includes inflammatory processes as well as myocyte degeneration, hypertrophic and fibrotic changes in the atria, respectively. Plasma concentrations of B-type natriuretic peptides are influenced both by inflammatory cytokines as well as by pathological alterations of cardiomyocytes. Adipose tissue is a major source of pro-inflammatory cytokines and hormones, which might also contribute to the increased cardiovascular risk of obese patients. In the present study we investigated whether plasma NT-proBNP concentrations and body mass index (BMI) could be used to predict the recurrence of atrial fibrillation after successful restoration of sinus rhythm.

Design and Methods In this observational study, plasma levels of NT-proBNP were determined in 94 patients before cardioversion (CV), immediately after CV, and 24 hours thereafter. The endpoint of the study was the recurrence of AF within 1 year after successful restoration of sinus rhythm.

Results 45 patients had recurrence of AF during the follow-up period, while 49 patients remained event free. Median concentrations of NT-proBNP prior (1031 vs 724 pg/ml; p = 0.418) and 24 hours after CV (322 vs 359 pg/ml; p = 0.199) were not significantly different between patients with or without recurrence of AF. The amount of decrease of plasma NT-proBNP concentrations during the first day after CV (% change with respect to the initial level; 45 vs 47 %; p = 0.458) was also not statistically different with respect to outcome. However, patients with BMI values of > 25 had a significantly higher risk of relapse of AF (HR 3.26; p = 0.013).

Conclusion Although, successful cardioversion significantly decreased NT-proBNP levels, changes in plasma concentrations of this biomarker after successful CV could not be used for prediction of recurrence of AF. The novel finding of our study that obese patients are at higher risk of recurrent AF deserves further intensive research.

Cryoballoon Pulmonary Vein Isolation with Real Time Recordings From the Pulmonary Veins – Time to Isolation Predicts Sustained Conduction Block 077

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Background Cryoballoon (CB) ablation (Arctic Front, Cryocath) represents a novel technology for pulmonary vein isolation (PVI) to treat atrial fibrillation, lacking, however, real time visualization of PV conduction during the freezing period. We investigated feasibility and safety of CB PVI utilizing a novel spiral catheter (SC), and evaluated real time PV potential registration.

Methods Following double transseptal puncture, a lasso catheter (Biosense Webster) and the 28 mm CB inserted via a steerable sheath (12F, Flexcath, Cryocath) were positioned within the left atrium (LA). Baseline PV angiograms and ostial lasso recordings were obtained from all PVs. A novel SC with a soft distal shaft originally designed for ultrasound balloon ablation (0.9 mm diameter, 6 electrodes, Promap, Prorhythm) was inserted through the central lumen of the CB serving as a (1) guide wire and (2) allowing real time visualization of PV conduction during the freezing period (duration: 300 sec). Time to PV conduction block was analysed if PVI occurred during the first freeze. Sustained PV conduction block was defined as PVI > 30 min after initial PV conduction block. If no stable balloon position was obtained, the SC was exchanged for a regular guide wire (stiff wire, Amplatz) and PV conduction was assessed after each freeze using the lasso catheter.

Results Among 18 patients (14 males; age: 62 ± 8 years; LA: 41 ± 5; 72 PVs), 39 PVs (54 %) were successfully isolated using the CB in conjunction with the SC. The remaining 33 PVs (46 %) were isolated switching to the regular guide wire. Time to PV conduction block was assessed in 32/72 (44 %) PVs. Time to PV conduction block was significantly shorter in PVs in which sustained PVI was achieved as compared to PVs in which PV conduction recovered (33 ± 21 s vs 99 ± 65 s; p = 0.002). In the remaining 40 PVs, time to PV conduction block was not obtained because: (1) PVI was not achieved during the initial cryo-energy application (4 PVs); (2) no PV spike was recorded due to a distal position of the SC (4 PVs); or (3) the regular guide wire was used (32 PVs). No procedural complications occurred.

Conclusion Visualization of real time PV conduction during CB PVI is safe, feasible and allows accurate timing of PVI onset in a subset of PVs. Time to PV conduction block predicts sustained PVI. However, mechanical properties of the SC need to be improved to further simplify CB PVI.

Circumferential Pulmonary Vein Isolation Performed by Pure Anatomical Approach – Dream or Reality? 078

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Introduction Pulmonary veins (PV) can be circumferentially isolated using continuous circular lesions (CCLs) around the ipsilateral PVs. However, it is unknown whether PV isolation can be performed without guidance of a Lasso catheter within the PV.

Methods Fifty patients with symptomatic atrial fibrillation (43 paroxysmal, 7 persistent) underwent ablation of CCLs around the right-sided and subsequently the left-sided ipsilateral PVs guided

only by 3-D mapping (CARTO, Biosense Webster). One or two Lasso catheters (Biosense Webster) placed within the PVs were disconnected from the EP system during ablation. After anatomical completion of the CCLs, PV activation or isolation was confirmed by reconnection of the Lasso catheters. In case of ongoing PV conduction, complete PV isolation was achieved by additional ablation of remaining conduction gaps in the previous CCLs guided by the Lasso catheters.

Results In 21 out of 50 patients (42 %), total PV isolation was achieved after purely anatomical ablation around the right and left ipsilateral PVs. PV isolation was achieved in 43 patients (86 %) in the right-sided PVs and in 21 patients (42 %) in the left-sided PVs. In the patients with ongoing PV conduction, there were 8 conduction gaps in the right CCLs and 40 conduction gaps in the left CCLs. The mean number of conduction gaps was 1.1 ± 0.4 for the right-sided PVs, and 1.4 ± 0.6 for the left-sided PVs. On the left CCLs, conduction gaps were found at the ridge between the PV ostia and the left atrial appendage in 27 out of 40 gaps (68 %). One or two additional irrigated RF applications abolished all conduction gaps.

Conclusions Complete PV isolation is difficult to achieve without a continuous recording of PV activation during ablation. The PV activation sequence recorded by the Lasso catheter can facilitate location of conduction gaps within the CCLs.

Vorhofflimmern bei Patienten mit primärprophylaktischem Kardioverter-Defibrillator – Erfahrungen aus einem Langzeitkollektiv 118

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Einleitung Vorhofflimmern (AF) ist die häufigste Arrhythmie in der klinischen Praxis und bedingt eine erhöhte kardiovaskuläre Morbidität und Mortalität. Bei Patienten mit implantiertem Kardioverter-Defibrillator (ICD) kann durch tachyarrhythmisch übergeleitetes AF die adäquate Diskriminierung des Aggregats zwischen supraventrikulären und ventrikulären Arrhythmieereignissen erschwert werden. Daten über einen längeren Beobachtungszeitraum von Patienten mit primärprophylaktischer ICD Indikation zum Stellenwert von AF liegen nicht vor. Ziel dieser retrospektiven Untersuchung war die Beurteilung adäquater und inadäquater Therapien bei Patienten mit Vorhofflimmern im Vergleich zu Patienten mit permanentem Sinusrhythmus.

Methoden Alle Patienten in unserer ICD-Ambulanz, die in dem Zeitraum zwischen 07/2000 und 07/2008 primärprophylaktisch einen ICD erhielten, wurden erfasst, vollständige Datensätze mit einer Nachsorgezeitraum > 3 Monate wurden inkludiert. Das Kollektiv wurde retrospektiv stratifiziert in Patienten mit durchgehend Sinusrhythmus (SR) und Patienten mit Dokumentation einer Vorhofflimmerarrhythmie (AF, paroxysmal oder persistierend) in zumindest einer der Nachsorgeuntersuchungen. Die Subkollektive wurden in Hinblick auf die Medikation, linksventrikuläre (LV) Ejektionsfraktion (LVEF), Inzidenz von ICD-Therapie und Komplikationsrate charakterisiert.

Ergebnisse Zwischen 2000 und 2008 wurde bei 182 Patienten ein ICD aus primärprophylaktischer Indikation implantiert (26 % aller implantierten ICD), es konnten 159 Datensätze in die Auswertung eingeschlossen werden. Bei 67,4 % der Patienten bestand bei Indikationsstellung SR. Bei 25,8 % dieser Patienten wurde im Nachsorgeintervall AF dokumentiert. Der mittlere Beobachtungszeitraum betrug 23,8 ± 1,6 Monate (Mittelwert ± SE: 14,5 % ≥ 48 Monate) ohne signifikanten Unterschied zwischen SR (22,7 ± 1,7) und AF (25,6 ± 2,9). Es fand sich eine hohe Prävalenz einer Betablockertherapie (96,9 % der Pat. in SR, 92,3 % in AF; p = n. s., deutlich mehr Patienten in AF erhielten Amiodaron (27,7 % vs. 7,3 % in SR; p = 0.001). Es ergab sich kein Unterschied bzgl. der LVEF bei Indikationsstellung (26,9 ± 1,1 % vs. 26,5 ± 1,1 %) oder der minimalen LVEF im Beobachtungszeitraum (25,8 ± 1,5 % vs. 25,3 ± 1,6 %) zwischen SR und AF. Während die Inzidenz adäquater ICD-Therapie in beiden Gruppen gleich war (SR: 0,46 ± 0,08 vs. AF: 0,42 ± 0,12 Nachsorgen mit Ereignis/Jahr/Patient), kam es bei signifikant mehr Patienten mit AF zu inadäquater ICD-Therapie (AF: 27,7 %; SR: 11,3 %) und inadäquaten ICD-Schocks (AF: 16,9 % vs. SR: 4,1 %) (jeweils p < 0,05). Die Komplikationsrate während der Nachsorge (SR: 0,69 ± 0,12 vs. AF: 0,79 ± 0,21 Nachsorgen mit Ereignis/ Patient/Jahr) sowie die Hospitalisationen aufgrund von Komplikationen (SR: 0,14 ± 0,06 vs. AF: 0,23 ± 0,08 Hospitalisationen/ Patient/Jahr) unterschieden sich nicht signifikant.

Zusammenfassung In diesem monozentrischen Kollektiv mit primärprophylaktischer ICD-Implantation waren Patienten mit AF gegenüber Patienten mit SR in Bezug auf therapiebedürftige ventrikuläre Tachyarrhythmien, LV Funktion, Komplikationen und Hospitalisationen nicht zusätzlich beeinträchtigt, die Inzidenz inadäquater ICD-Therapie war in AF allerdings höher als im SR.

Continuous Reduction of N-terminal Pro-brain Natriuretic Peptide Levels after Successful Catheter Ablation in Patients with Paroxysmal or Short Persistent Atrial Fibrillation 021

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

Methods In 71 patients (mean age of 62 ± 8 years) undergoing successful PVI for drug-resistant highly symptomatic paroxysmal or shortly persistent AF, BNP levels were analysed the day before, 30 days after, three months after and one year after the procedure, respectively. Based on a personal log of duration and frequency of symptoms and repetitive 24 h-ECG recordings, patients were divided into two groups: 50 patients had clinical success, and 21 patients had clinical failure. Clinical demographic and procedural data were similar in both groups. Of note, all patients had lone AF without any clinical signs of congestive heart failure.

Results Baseline BNP levels were similar in both groups (387 ± 550 pg/ml vs. 492 ± 513 pg/ml; p = 0.6). After 30 days, patients who had a clinical successful procedure showed a significant decrease of BNP levels compared to those patients with clinical failure (315 ± 430 pg/ml vs 754 ± 888 pg/ml; p = 0.02). After three months, a further reduction of BNP levels could be observed in clinical successful treated patients compared to patients with clinical failure, in whom no significant change compared to baseline could be detected (214 ± 213 pg/ml vs. 673 ± 907 pg/ml; p = 0.01). After one year of successful PVI a repeated reduction of BNP in patients with clinical success could be observed (173 ± 198 pg/ml vs 448 ± 628 pg/ml; p = n. s.), but due to the small sample size the difference did not reach statistic significance.

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

Acute Results of Pulmonary Vein Isolation Using a Single Combined Mapping and Ablation Catheter and Conventional Fluoroscopy Only 069

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Introduction Catheter-based isolation of pulmonary veins (PVs) has emerged as established therapy to treat patients with paroxysmal atrial fibrillation. We attempted to simplify the interventional procedure by using a single novel multipolar catheter for mapping and ablation, guided by fluoroscopy only.

Methods and Results Forty-eight patients with paroxysmal atrial fibrillation scheduled for PV isolation were screened by cardiac computed tomography for anatomical suitability to undergo a simplified procedure with the High Density (HD) Mesh Ablator Catheter as the only left atrial device. The procedure was finally performed in 26 patients (12 males, mean age 61 years) matching the criteria of 4 clearly separated PVs with an ostial diameter of 15–25 mm. The remaining 22 patients served as control group and were treated by a three-dimensional mapping system guided ablation using a decapolar spiral catheter for mapping and a conventional irrigated tip catheter for ablation.

In all 26 patients, all four PVs could be accessed and mapped with the HD Mesh Ablator Catheter. Electrical isolation could be achieved in 99/102 (97 %) PVs revealing potentials. Mean total procedure time and fluoroscopy time were 187 ± 36 and 35 ± 10 min, and were significantly shorter compared to the control group of conventionally treated patients (232 ± 31 and 41 ± 10; $p < 0.00005$ and $p < 0.05$, respectively).

Preliminary follow up data using 48-hours ECG recording and clinical history did not reveal a statistically significant difference between the two different ablation strategies after 3 months: Eleven out of 18 patients vs 11 out of 17 patients were classified as event-free. The remaining patients are within the "blanking period" of 2 months.

Conclusion The single catheter approach using the HD Mesh Ablator Catheter for mapping and ablation reveals a high acute success rate despite the reduced complexity of the procedure. Long-term data on clinical success are needed to justify this simplified approach.

Sudden Cardiac Death – Prävention bei vorübergehender Kontraindikation für eine ICD-Implantation 045

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Hintergrund Aktuelle Leitlinien empfehlen, Patienten mit Kammerflimmern ≥ 48 Stunden nach akutem Myokardinfarkt einen ICD zu implantieren. Ist eine rasche Implantation aber nicht möglich, scheint eine kontinuierliche Überwachung indiziert, weil rezente Daten zeigen, dass das Risiko für den plötzlichen Herztod in den ersten 30 Tagen nach Myokardinfarkt am höchsten ist (VALIANT, NEJM 2005). Neben einer ständigen Überwachung auf einer Intermediate Care Unit und der Telemetrie ist die LifeVest WCD 3100® (**Abbildung 7**) eine kostengünstige Alternative.

Methode Ein 39-jähriger Patient erleidet 6 Tage nach erfolgreicher Primär-PCI bei Vorderwandinfarkt am Entlassungstag zu Hause ohne ein neuerliches Schmerzereignis Kammerflimmern und wird erfolgreich reanimiert. Eine rasche ICD-Implantation ist aufgrund einer schweren urogenitalen Infektion nicht möglich. Wir entschließen uns, den Patienten nach 18 Tagen Intensivaufenthalt mit der LifeVest WCD 3100® zu versorgen.

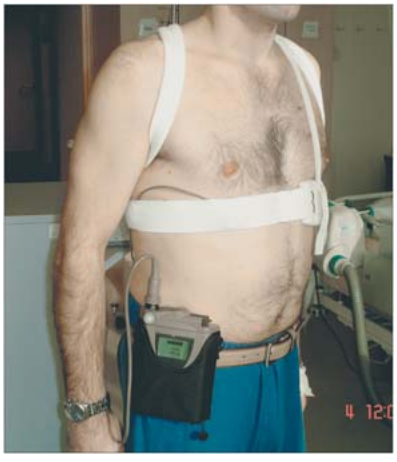

Abbildung 7: H. Keller et al.

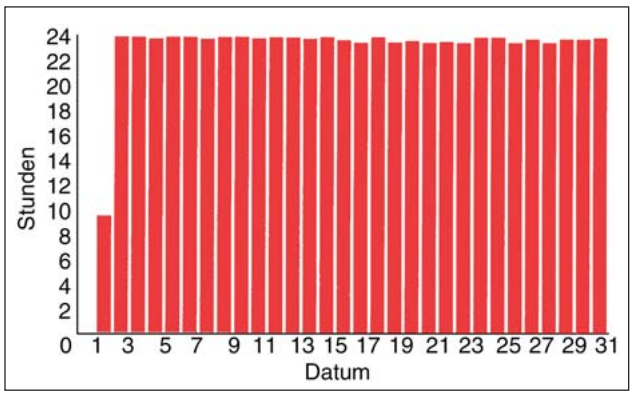

Abbildung 8: H. Keller et al.

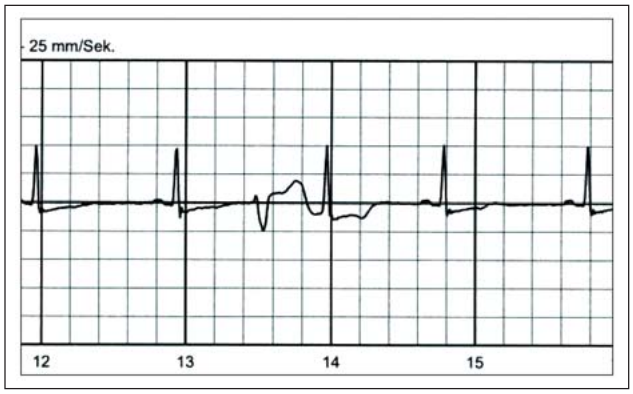

Abbildung 9: H. Keller et al.

Funktion der Weste: Über trockene, nicht klebende Elektroden wird ein kontinuierliches EKG abgenommen. Bei Detektion einer lebensbedrohlichen Arrhythmie wird der Patient über einen akustischen und visuellen Alarm informiert und er kann die Schockabgabe durch das gleichzeitige Drücken zweier Tasten unterbinden, solange er bei Bewusstsein ist. Vor einer notwendigen Defibrillation (mit 150 J) wird automatisch Kontaktgel auf die trockenen Defibrillationselektroden appliziert.

Der Patient tritt nach genauer Instruktion mit der Weste die Rehabilitation an. Aus dem Rehabilitationszentrum sendet er mehrmals einen Report der Tragedauer und qualitativ hochwertige EKGs per FAX an eine Zentrale nach Deutschland. Alle Daten sind für uns über eine Internetplattform abrufbar (**Abbildung 8 und 9**). Ein Infektrezidiv und die noch ausständige dringende Sanierung beherdeter Zähne veranlassen uns, die Anwendung der LifeVest zu prolongieren.

Schlussfolgerung Im Falle einer vorübergehenden Kontraindikation für eine ICD-Implantation bietet die Defibrillatorweste LifeVest 3100® eine Alternative zu einer deutlich kostenintensiveren permanenten stationären Überwachung (Intermediate Care oder Telemetrie). Die Weste wird ausgezeichnet toleriert, die Handhabung ist einfach. Der Patient bleibt über eine Internetplattform unter Observation des betreuenden Zentrums.

Drastische Zeiteinsparungen und äußerst positives Patientenfeedback durch telemedizinische Nachkontrollen von ICD-Patienten im Langzeitverlauf 125

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Hintergrund Die sich ausweitenden Indikationen und die verstärkte Umsetzung der Guidelines und die damit einhergehende steigende Zahl an Patienten mit implantierbaren Kardioverter Defibrillatoren (ICDs) machen neue Ansätze in der Durchführung von Nachkontrollen (FU) von ICD-Patienten nötig.

Telemedizinische Nachkontrollen könnten helfen, Zeit einzusparen, aber das Ausmaß sowie die Reaktion der Patienten im Langzeitverlauf sind noch nicht ausreichend bekannt.

Ziel dieser prospektiven Untersuchung war es, Durchführbarkeit, Zeiteinsparungen und Patientenakzeptanz eines neuen telemedizinischen Systems (Medtronic CareLink Network) in der Routine-Nachsorge von ICD Patienten über einen Zeitraum von einem Jahr zu evaluieren.

Methoden Konsekutive Patienten von ICD-Ambulanzen zweier Zentren wurden im Rahmen einer normalen Routinekontrolle eingeschlossen. Nach entsprechender Einschulung führten die Patienten alle drei Monate die Geräteabfrage mittels eines speziellen Monitors selbständig zu Hause durch und übertrugen die Daten mittels einer Standard-Telefonleitung. Der Arzt wertete anschließend die Daten über einer gesicherten Webseite aus. Die Datensammlung erfolgte bei Einschluss und der Einjahreskontrolle in der Klinik sowie bei jedem telemedizinischen FU. Die Machbarkeit und die Patientenakzeptanz wurden mittels eines Fragebogens nach drei Monaten und nach einem Jahr erfasst.

Ergebnisse 142 konsekutive Patienten (mittleres Alter 66 ± 12 Jahre) wurden vollständig erfasst (113 ICD, 29 CRT-D). Während einer FU-Periode von 12 Monaten wurden 825 FUs durchgeführt (61,5 % telemedizinische FUs). Es gab keine falschen oder inkorrekten Übertragungen. Die Auswertung der Patientenfragebögen zeigte, dass die Datenübertragung für 99 % der Patienten einfach war. 67 % der Patienten gaben an, sie hätten einen größeres Gefühl der Sicherheit, 32 % keine Änderung und nur 1 % fühlte sich weniger sicher. 94 % aller Patienten würden die telemedizinische Nachkontrolle der konventionellen Nachsorge vorziehen.

Verglichen mit FUs im Krankenhaus benötigen telemedizinische FUs signifikant weniger Zeit für Patienten (10 ± 6 vs. 172 ± 67 min; $p < 0,001$) und Ärzte (5 ± 4 vs. 36 ± 19 min; $p < 0,001$).

Zusammenfassung Dieses neue telemedizinische System ist eine praktikable und sichere Methode für Routine FUs von ICD-Patienten. Die Patientenakzeptanz ist außerordentlich hoch. Die Zeiteinsparungen sind sowohl für den Patienten als auch für den Arzt und damit das Gesundheitssystem drastisch. Wir gehen davon aus, dass diese Zeiteinsparungen dem Arzt Möglichkeiten für andere relevante Tätigkeiten eröffnen könnten.

Inzidenz adäquater und inadäquater Therapien in einem Langzeitkollektiv von Patienten mit primärprophylaktisch implantiertem Kardioverter-Defibrillator 129

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Hintergrund Patienten mit höhergradig reduzierter Linksventrikelfunktion (EF) haben ein erhöhtes Risiko, am plötzlichen Herztod (SCD) zu versterben. Der Kardioverter-Defibrillator (ICD) ist die Therapie der Wahl in der Prävention des SCD. Über die Inzidenz adäquater und inadäquater ICD-Therapien im Langzeitverlauf sind jedoch nur wenige Daten bekannt.

Methoden In dieser retrospektiven monozentrischen Untersuchung wurden alle Patienten, denen im Zeitraum von 2000 bis 2008 an unserer Abteilung ein primärprophylaktischer ICD implantiert wurde, aufgenommen. Die Inzidenz adäquater und inadäquater ICD-Therapien wurde als Anzahl der Nachsorgen mit Ereignis pro Patient pro Jahr bestimmt.

Ergebnisse Im Beobachtungszeitraum wurden insgesamt 699 ICD-Implantationen durchgeführt, davon 182 (26 %; Alter 63 ± 12 Jahre) aus primärprophylaktischer Indikation. Der mittlere Nachbeobachtungszeitraum war 22 Monate (Spanne 5–93 Monate). Die Ätiologie der Kardiomyopathie war ischämisch (ICM) in 55 % (99 Patienten), nicht-ischämisch (DCM) in 38 % (7 % andere). Die Inzidenz adäquater ICD-Therapie war vergleichbar bei Patienten mit ischämischer und nicht-ischämischer Kardiomyopathie (0,47 ± 0,82 vs. 0,39 ± 0,86; p = n. s.). Ein verbreiterter QRS-Komplex im EKG (> 120 ms vor Implantation) war bei 120 Patienten (66 %) vorhanden, war aber nicht mit einer erhöhten Inzidenz appropriater ICD-Therapien verbunden (0,42 ± 0,88 vs. 0,45 ± 0,83 bei Patienten mit schmalem QRS-Komplex). Die Rate inappropriater ICD-Therapien war 0,20 ± 0,68 pro Patient und Jahr (Schocks 0,10 ± 0,47; ATP 0,17 ± 0,60). In einer Subgruppe von Patienten (n = 24) mit einem Beobachtungszeitraum von mehr als 48 Monaten (mittleres FU 63, Spanne 48–93 Monate) war die Inzidenz appropriater ICD-Therapie 0,50 ± 0,61.

Zusammenfassung In unserem Kollektiv von konsekutiven Patienten, die seit 2000 einen ICD aufgrund einer primärprophylaktischen Indikation erhielten, beobachteten wir eine vergleichbar hohe Inzidenz behandlungsbedürftiger ventrikulärer Arrhythmien. Adäquate Therapien waren 2–3-mal häufiger als inadäquate Therapien. Ein verbreiterter QRS-Komplex war nicht mit einer erhöhten Inzidenz appropriater Therapieabgaben vergesellschaftet. Selbst bei Patienten mit einer Nachbeobachtung von mehr als 4 Jahren blieb die Inzidenz adäquater ICD-Therapien unverändert hoch.

Inzidenz monomorpher Kammertachykardien bei Patienten mit implantiertem Kardioverter-Defibrillator – wie viele Patienten wären potenzielle Kandidaten einer Katheterablation? 130

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Hintergrund Die Inzidenz ventrikulärer Arrhythmien beträgt je nach Untersuchung und Indikation (Primärprävention, Sekundärprävention) bis zu 50 % innerhalb der nächsten 2 Jahre nach erfolgter Implantation eines Kardioverter-Defibrillators (ICD). Die dadurch bedingten Synkopen bzw. Schockabgaben beeinträchtigen die Lebensqualität der Patienten beträchtlich. Neueste Untersuchungen zeigen einen positiven Effekt einer prophylaktischen Katheterablation mit signifikanter Reduktion der ICD Schocks und verbesserter Lebensqualität.

Ziel der Untersuchung war die Beurteilung der Häufigkeit und Charakteristik von Kammertachykardien (VT) sowie die Häufigkeit einer ATP- und Schocktherapie bei Patienten mit implantiertem ICD im Hinblick auf eine mögliche ablative Therapiemaßnahme.

Methoden Alle Patienten, denen im Zeitraum von 2005 bis 2008 an unserer Abteilung aus primär- oder sekundärprophylaktischer Indikation ein ICD-Aggregat implantiert wurde, sind für die retrospektive Untersuchung herangezogen worden. Die Arrhythmien wurden anhand des intrakardialen EKGs als monomorphe oder polymorphe Kammertachykardien und Kammerflimmern klassifiziert und der Therapieerfolg hinsichtlich Effektivität, Ineffektivität und Akzeleration beurteilt.

Ergebnisse Insgesamt wurden 342 ICD-Implantationen durchgeführt, davon 191 (55,8 %) aus primärprophylaktischer Indikation. Der mittlere Nachbeobachtungszeitraum war 23 ± 14 Monate (Spanne 2–50 Monate). 26 Patienten verstarben im Langzeitverlauf, von den restlichen Patienten hatten 114 (36 %) adäquate ICD-Therapien, davon 40 Patienten Episoden von Kammerflimmern. Bei 39 Patienten (Alter 63 ± 17) wurden mehr als 3 monomorphe VT-Episoden pro Follow-up-Jahr aufgezeichnet. 11 dieser Patienten (28 %) hatten eine KHK, 18 (46 %) eine dilatative Kardiomyopathie (26 % andere), eine primärprophylaktische ICD-Indikation lag bei 15 (38 %) vor. Die mittlere Tachykardiezykluslänge betrug 327 ± 39 ms. Die mittlere VT-Anzahl pro Jahr betrug 41 (Spanne 6–227/Jahr), 7 Patienten hatten mehr als 100 VT-Episoden pro Jahr.

Zusammenfassung In unserem Kollektiv hatten ein Drittel aller Patienten mit implantiertem ICD mehr als 3 monomorphe VT-Episoden pro Follow-up-Jahr. In knapp der Hälfte der Patienten lag eine dilatative Kardiomyopathie vor. Durch ablative Therapiemaßnahmen könnten bei diesen Patienten der VT-Burden sowie ICD-Schockabgaben reduziert werden.

Development of a Risk Score for Predicting Esophageal Injury during Atrial Fibrillation Ablation 018

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Background Atrio-esophageal fistula is a rare but potentially lethal complication of atrial fibrillation (AF) ablation. The purpose of this study was to develop a risk score for the appearance of esophageal ulcerations (ESUL).

Methods Out of a randomized study protocol including 175 patients (pts) published in JCE 2009 (Martinek M et al.) we developed a risk score and prospectively tested this scoring system on another 50 consecutive pts. All 225 pts underwent AF ablation and esophagoscopy 24 hours thereafter to screen for ESUL.

Results In total we found 2.6 % of pts (6/225) presenting ESUL. We identified (1) maximum energy delivered on posterior wall, (2) usage of a nasogastric tube to visualize the esophageal course in general anesthesia pts, and (3) additional left atrial lines as discriminating parameters for ESUL creation. Discriminant analysis reached sensitivity as high as 88.0 % to positively predict ESUL creation. Pts with a score higher than 6 were at increased risk for ESUL. This could also be confirmed in the next 50 pts (1 ESUL; 2 %).

Conclusions With a power limitation to a maximum of 25 W at the posterior wall and avoidance of esophageal visualization by nasogastric tubes only pts with more than 2 additional linear ablations (roofline, left atrial isthmus, coronary sinus line, inferior line) are at increased risk for ESUL (3/32; 9.4 %). We were able to determine risk factors to predict esophageal injury and identify pts at highest risk for ESUL which should be examined by esophagogastroscopy after AF ablation.

Development of Gastroesophageal Reflux after Catheter Ablation of Atrial Fibrillation 019

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Background Rise of esophageal acidity may have an impact on the progression of esophageal injury after radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF). We assessed the acute effect of RFCA on esophageal acidity using pH-metry capsules.

Methods We investigated 27 patients (pts; 22 male, 15 paroxysmal) with AF who underwent RFCA and esophagoscopy 24 hours before and after ablation to assess esophageal lesions. A pH-metry capsule was initially inserted into the lower esophagus to assess pH changes, number and duration of refluxes, and the Demeester-score (a standardized measure of acidity and reflux). No pt was taking proton pump inhibitors within 2 weeks before and 24 hours after ablation. We used a 4 mm irrigated-tip catheter with 43 °C and 25 W power limitation on the posterior wall. General anesthesia was applied in 6 pts, other pts had conscious sedation performed.

Results None of our patients had esophageal lesions before or after ablation as documented by esophagoscopy. 4 pts (14.8 %) demonstrated significant pathologic increase in the Demeester-score after ablation. Duration of pH < 4 and refluxes were significantly prolonged in these patients after RFCA ($p = 0.012$ and $p = 0.001$). There were no statistical differences in baseline parameters, method of sedation, and the total energy delivered on the posterior wall between those with and without pathologic Demeester-scores.

Conclusions In our initial series, we found significant rise in the Demeester score after RFCA of AF in 14.8 % of pts. No correlation was found with morphologic esophageal changes as assessed by esophagoscopy. This finding may explain a potential mechanism for the progression of esophageal lesions to atrio-esophageal fistulae in a subgroup of pts undergoing RFCA of AF.

Primärprophylaktische Implantation eines Kardioverter-Defibrillators bei Patienten über 70 Jahre 132

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Hintergrund Die primärprophylaktische Implantation eines Kardioverter-Defibrillators (ICD) ist nunmehr Standardtherapie bei Patienten mit hochgradig reduzierter Linksventrikelfunktion (LVEF). In den meisten Untersuchungen ist jedoch das mittlere Alter der Studienpatienten zwischen 58 und 65 Jahren. Über die Inzidenz adäquater und inadäquater Therapien sowie die Komplikationsrate bei Patienten über 70 Jahre im Vergleich zu jüngeren Patienten sind nur wenige Daten bekannt.

Methoden In diese retrospektive Untersuchung wurden alle Patienten, denen im Zeitraum von 2000 bis 2008 an unserer Abteilung ein primärprophylaktischer ICD implantiert wurde, aufgenommen. Die Inzidenz appropriater und inappropriater ICD-Therapie sowie die Komplikationsrate wurden bestimmt und als Anzahl der Nachsorgen mit Ereignis pro Patient und Jahr angegeben.

Ergebnisse Im Beobachtungszeitraum wurden insgesamt 699 ICD-Implantationen durchgeführt, davon 182 (26 %) aus primärprophylaktischer Indikation (ischämische CMP 55 %, nicht-ischämische CMP 38 %, andere 7 %). 49 Patienten hatten ein Alter ≥ 70 Jahre (Gruppe I; mittleres Alter 75 ± 3 Jahre), in Gruppe 2 (Alter < 70 Jahre) waren 133 Patienten (mittleres Alter 57 ± 10 Jahre). Die mittlere Follow-up-Dauer (21,6 vs. 24,7 Monate) und die LVEF (24,9 ± 6 % vs. 25,4 ± 7 %) waren in beiden Gruppen vergleichbar. Die QRS-Breite war in Gruppe I signifikant höher (159 ± 30 ms vs. 140 ± 27 ms; $p < 0{,}001$). Es gab keinen Gruppenunterschied in der Rate appropriater (0,30 ± 0,14 vs. 0,50 ± 0,08; $p = 0{,}2$) und inappropriater (0,20 ± 0,13 vs. 0,20 ± 0,05; $p = 0{,}9$) ICD-Therapien bzw. inadäquater ICD-Schocks (0,13 ± 0,09 vs. 0,09 ± 0,04; $p = 0{,}6$). Bei Patienten über 70 Jahre war die Komplikationsrate (Implantation, FU) signifikant höher (1,58 ± 0,35 vs. 0,82 ± 0,12; $p = 0{,}0093$), die Rehospitalisierungsrate wegen Komplikationen ebenfalls, jedoch nicht signifikant höher (0,33 ± 0,12 vs. 0,12 ± 0,05; $p = 0{,}05$). Perioperative Komplikationsrate und Dauer des stationären Aufenthaltes (9 ± 1 vs. 10 ± 1 Tage; p = n. s.) waren vergleichbar.

Zusammenfassung In unserem Kollektiv von Patienten mit primärprophylaktischer ICD-Implantation seit 2000 hatten Patienten über 70 Jahre im Vergleich zu jüngeren Patienten eine signifikant höhere Gesamtkomplikationsrate, vor allem bedingt durch peri- und postoperative Komplikationen. Die Rate an adäquater und inadäquater ICD-Therapien war hingegen nicht unterschiedlich.

Telemedizinische Kontrolle von Herzschrittmachern und ICDs 094

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Hintergrund Steigende Implantationszahlen führten in den vergangenen Jahren zu einer deutlichen Zunahme an Routinekontrollen von Herzschrittmachern (PM) und Implantierten Kardioverter-Defibrillatoren (ICD). Um auch in Zukunft eine effiziente und sichere Betreuung dieser Patienten zu gewähren, werden telemedizinische Systeme an zunehmender Bedeutung gewinnen. Im Rahmen einer randomisierten, kontrollierten Studie wird die Sicherheit und Praktikabilität des Home-Monitoring-Systems zur Fernüberwachung von kardialen Implantaten an 150 ICD- und 400 PM-Patienten evaluiert: im Folgenden werden die Zwischenergebnisse nach 2 Jahren präsentiert.

Methoden 108 PM- (65 Männer) und 29 ICD- Patienten (27 Männer) wurden bis dato in die Studie eingeschlossen: Das mittlere Alter der PM-Patienten betrug 75 ± 9 Jahre, das der ICD-Patienten 63 ± 9 Jahre. 55 PM-Patienten wurden zur telemedizinischen Überwachung mittels Home-Monitoring-System randomisiert (HM-ON); 53 PM-Patienten verblieben im Routine-Follow-up mit jährlichen Kontrollen (HM-OFF). In der ICD-Gruppe wurden 14 Patienten in die HM-

ON-Gruppe mit jährlicher ambulanter Kontrolle und 15 Patienten in die HM-OFF-Gruppe mit 3- bis 6-monatiger ambulanter Nachsorge randomisiert.

Ergebnisse In der PM HM-ON-Gruppe wurden von 15 Patienten (35 %) Ereignisnachrichten (ER) erhalten, welchen 5 ambulante Nachsorgen folgten. Weitere 9 ambulante Kontrollen wurden aufgrund subjektiver Beschwerden oder interner Überweisungen durchgeführt. Bei diesen 14 Kontrollen erfolgten 10 Umprogrammierungen. In der PM-HM-OFF-Gruppe erhielten 9 Patienten aufgrund von subjektiven Beschwerden oder internen Überweisungen eine außertourliche ambulante Kontrolle; hier erfolgte bei 4 Patienten eine Umprogrammierung.

In der ICD-HM-ON-Gruppe wurden von 11 Patienten ER gesendet, wovon 2 Patienten ambulant kontrolliert werden mussten, bei einem resultierte eine rechtsventrikuläre Sondenrevision. In der ICD-HM-OFF-Gruppe erfolgten 4 außertourliche Kontrollen aufgrund subjektiver Symptome; auch hier folgte eine rechtsventrikuläre Sondenrevision.

Schlussfolgerung Die telemedizinische Überwachung mittels Home-Monitoring-System ist eine sichere und brauchbare Alternative zur routinemäßigen ambulanten PM- und ICD-Kontrolle. Dysfunktionen können rasch erkannt und ambulante Kontrollen auf jene reduziert werden, bei denen eine Umprogrammierung indiziert ist.

Long-term Results of Remote-Controlled Magnetic Navigation for Pulmonary Vein Isolation and Differences Compared to Hand-Navigated Ablation of Atrial Fibrillation 047

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Purpose Radiofrequency ablation (RF) for atrial fibrillation (AF) demands prolonged procedure and fluoroscopy times. Remote-controlled magnetic navigation (RMN) claims to represent a novel approach towards improving pulmonary vein isolation (PVI).

Methods PVI was performed in 80 consecutive patients with paroxysmal or persistent AF. Forty patients underwent RF with RMN (NIOBE II, Stereotaxis, Inc., St. Louis, Missouri) and 40 underwent RF using a conventional hand navigated catheter. In all patients a combined wide area circumferential RF and segmental PVI was performed. The procedural end point was PV entrance block.

Results There was no difference in age, type of AF, left ventricular systolic function and atrial size between the groups. Mean mapping time in the RMN group was 59 ± 30 minutes versus 26 ± 13 minutes in the conventional group ($p < 0.001$). Maps were more detailed in the RMN group (mapping points: 111 ± 41 vs 81 ± 25; $p = 0.033$ and map volume cm^3: 111 ± 37 vs 98 ± 46; $p = 0{,}048$). The punctual RMN ablation approach differed from the more linear ablation approach in the conventional group resulting in unequal RF counts (148 ± 52 vs 53 ± 30; $p < 0.001$). Mean procedure time was 248 ± 55 minutes in the RMN group vs 225 ± 65 minutes in the conventional group ($p = 0.057$). Mean fluoroscopy time was 46.6 ± 18.2 minutes in the RMN group versus 99.6 ± 39.3 in the conventional group ($p < 0.001$). A close follow-up in the RMN group with daily transmission of external ECG and 24-h Holter recordings was performed. At 1, 3, 6, and 9 months of follow-up there were 55, 60, 68 and 73 % of patients in the RMN group free of AF.

Conclusions Ablation of AF with RMN is feasible and leads to long-term success rates up to 73 %. Compared to hand-navigated ablation, RMN ablation results in approximately similar procedure times but significantly decreased fluoroscopy times.

Die Induktion der milden Hypothermie beschleunigt die Wiederkehr des parasympathischen Anteils der Herzfrequenzvariabilität nach Kammerflimmern und Wiederbelebung bei anästhesierten Schweinen 106

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Hintergrund Die Induktion der milden Hypothermie (MH, 33 °C) ist Leitlinientherapie zur Prävention des hypoxischen Hirnschadens nach Kammerflimmern und Wiederbelebung. Bei wachen Patienten führt ein Auskühlen zum Muskelzittern und zur Aktivierung des sympathischen Nervensystems. Ob dies auch für die Induktion der MH nach Reanimation während Narkose und Relaxation zutrifft, ist nicht bekannt.

Methode Bei anästhesierten und relaxierten Schweinen (62 ± 5 kg) wurde ein Kammerflimmern (5 min) elektrisch induziert. Nach Herzdruckmassage und Defibrillation wurden die Tiere einer normothermen (38 °C; n = 6; NT) oder hypothermen Gruppe (33 °C; n = 7; MH, intravaskulärer Kühlkatheter) zugeordnet und ein intrakardiales EKG über eine Sonde im linken Ventrikel hochauflösend (1 kHz) aufgezeichnet. Die Zeitdauer bis zum Erreichen der MH betrug 130 ± 12 min ab Wiederkehr eines spontanen Kreislaufs (ROSC). Unter Kontrollbedingungen und ab 10 min, 2 h und 6 h nach ROSC wurde das Spektrum eines 15 min Intervalls des aufgezeichneten EKGs analysiert. Der hochfrequente Anteil der Herzfrequenzvariabilität (HF; 0,07–0,5 Hz; arbiträre Einheit) in der Spektralanalyse diente als Parameter der parasympathischen Aktivität, der Quotient aus HF und niederfrequentem Anteil (NF; 0,01–0,07 Hz) als Parameter der sympatischen Aktivität.

Ergebnisse Bei ROSC 10 min war HF in beiden Gruppen gegenüber Kontrolle vermindert (NT: 31 ± 4 vs. 61 ± 10; $p < 0.05$; MH: 38 ± 6 vs. 66 ± 9; $p < 0{,}05$). 2 h nach ROSC war HF während MH bereits höher als während NT (75 ± 4 vs. 44 ± 9; $p < 0{,}05$); 6 h nach ROSC war HF in beiden Gruppen nicht mehr von Kontrolle verschieden. Ebenso war LF/HF bei 2 h nach ROSC während MH bereits niedriger als während NT (0,52 ± 0,14 vs. 1,87 ± 0,59; $p < 0{,}05$). 6 h nach ROSC war LF/HF in beiden Gruppen nicht mehr von Kontrolle verschieden.

Schlussfolgerung Nach Kammerflimmern und Wiederbelebung ist der Sympathikotonus vorübergehend erhöht. Die Induktion der MH nach Kammerflimmern und Wiederbelebung führt zu einem rascheren Absinken des Sympathikotonus. Diesem Effekt der MH könnte eine protektive Rolle bei der Erholung der Herzfunktion nach Reanimation zukommen.

Biochemical Markers Reflecting Cardiac Repair Predict Left Atrial Structural Changes and Clinical Outcome after Ablation of Atrial Fibrillation 133

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Purpose Radiofrequency (RF) ablation of atrial fibrillation (AF) creates left atrial (LA) tissue damage initiating a cardiac repair process. We sought to prospectively monitor this repair process by biochemical markers and to evaluate its clinical relevance.

Methods 30 consecutive patients (57.2 ± 9 yrs; 63 % males) with paroxysmal AF underwent AF ablation comprising CARTO-guided LA antrum ablation, Lasso-guided segmental pulmonary vein isolation and ablation of complex fractionated potentials. Matrix metalloproteinase 9 antigen (MMP-9), transforming growth factor-β 1 (TGF-β1), both key regulators of tissue repair, and the aminoterminal propeptide of type III procollagen (PIIINP), representing collagen III turnover, were determined in venous blood samples before and 6 hours, 1, 2, 7, 30, 90 and 180 days after ablation.

Results At 6 months of follow-up including 7-day-Holter-monitoring, 60 % of patients were AF-free after a single procedure. All markers showed a significant ablation-induced up-regulation (maxi-

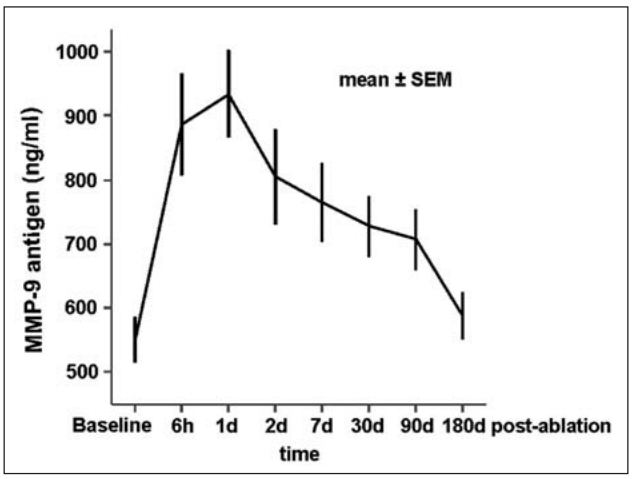

Figure 10: B. Richter et al.

mum vs baseline: MMP-9: 2.2 ± 0.1-fold (mean ± SEM), TGF-β1: 3.3 ± 0.4-fold; PIIINP: 1.4 ± 0.1-fold). The markers remained significantly elevated until day 90 (MMP-9), day 7 (PIIINP) and day 2 (TGF-β1) after ablation. The area under the curve (AUC) of MMP-9 and TGF-β1 significantly correlated with the ablation-induced reduction of LA volume measured by echocardiography before and 6 months after ablation (MMP-9: R = –0.56; $p < 0.05$; TGF-β1: R = –0.57; $p < 0.05$). The AUC of PIIINP predicted an adverse ablation outcome ($p < 0.05$).

Conclusions Markers of tissue healing show a significant up-regulation after AF ablation detectable for up to 3 months. A more pronounced up-regulation of TGF-β1 or MMP-9 levels is associated with a stronger reduction of LA size. High PIIINP predicts a poor ablation outcome (**Figure 10**).

The Time Course of Inflammatory Markers after Ablation of Atrial Fibrillation and their Relation to Energy Delivery, Outcome and Structural Changes 169

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Purpose Radiofrequency (RF) ablation of atrial fibrillation (AF) creates left atrial (LA) tissue damage with an associated inflammatory response. This prospective clinical study was performed to evaluate the time course and clinical relevance of this inflammatory reaction.

Methods 30 consecutive patients (57.2 ± 9 yrs; 63 % males) with paroxysmal AF underwent AF ablation comprising CARTO-guided LA antrum ablation, Lasso-guided segmental pulmonary vein isolation and ablation of complex fractionated potentials. High-sensitivity C-Reactive Protein (hsCRP) and Interleukin-6 (IL-6) were determined in venous blood samples before and 6 hours, 1, 2, 7, 30, 90 and 180 days after ablation.

Results At 6 months of follow-up including 7-day-Holter-monitoring, 60 % of patients were AF-free after a single procedure. Both markers showed a significant ablation-induced up-regulation (maximum vs. baseline: hsCRP: 41.2 ± 43.9-fold, IL-6: 5 ± 3.9-fold). IL-6 peaked at day 1, hsCRP at day 2 after ablation and remained significantly elevated until day 2 and day 7, respectively. A significant association between the up-regulation of hsCRP and IL-6 could be detected (R = 0.74; $p < 0.001$). The increase in hsCRP and IL-6 levels significantly correlated with the amount of RF-energy applied during the procedure (hsCRP: R = 0.55; $p = 0.002$; IL-6: R = 0.39; $p = 0.034$). However, the magnitude of the observed up-regulation did not significantly predict ablation outcome ($p > 0.05$) or the ablation-induced reduction of LA volume measured by echocardiography ($p > 0.05$).

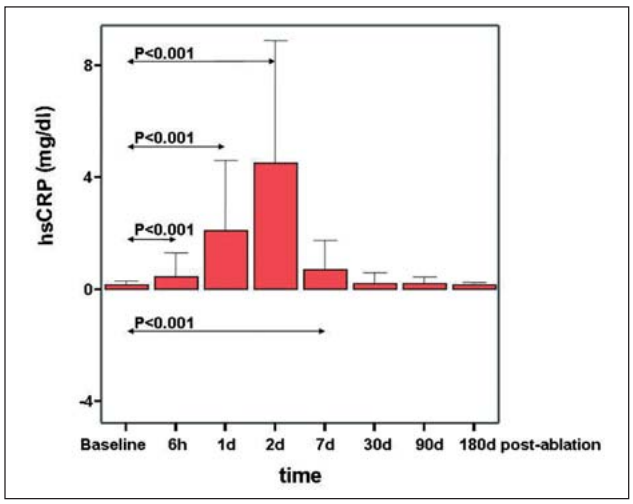

Figure 11: B. Richter et al.

Conclusions Inflammatory markers showed a significant up-regulation after AF ablation which is confined to the first post-ablation week. Its magnitude is associated with the amount of RF-energy delivered, but not with the ablation-induced structural LA changes or the ablation outcome (**Figure 11**).

Clinical Outcome in Patients with Hypertrophic Cardiomyopathy and Implantable Cardioverter Defibrillator Therapy 063

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Purpose Hypertrophic cardiomyopathy (HCM) is associated with an increased risk of sudden cardiac death (SCD) or syncope caused by ventricular tachyarrhythmia. Thus, implantable cardioverter defibrillators (ICD) became the main therapeutic option for high risk patients with HCM. The purpose was to investigate the outcome of ICD therapy in this collective.

Methods We followed overall 264 patients with HCM during the last 18 years. In this collective, 28 patients (17 male [60 %]; age at implantation: 41.6 ± 16.0 years; 15 with outflow tract obstruction [53 %]; 10 with atrial fibrillation or atrial flutter [36 %]) were treated with an ICD for at least one major risk factor: SCD survival, documented ventricular tachycardia (VT), unexplained syncope, or family history of SCD. In case of severe left ventricular hypertrophy (thickness of septal wall > 30 mm), patients initially were treated with percutaneous alcohol septal ablation. Previous to availability of guidelines, electrophysiological studies were performed for risk stratification in 9 patients.

Results Indications for ICD implantation were SCD survival (50 %), documented VT (18 %), family history (14 %), inducible VT (11 %), and syncope (7 %). Mean ICD follow-up period was 62.3 ± 55.8 months. Appropriate defibrillation was documented in 2 patients (7 %), and appropriate anti-tachycardic pacing (ATP) in 3 further patients (11 %). There was no predominant risk factor for ventricular tachyarrhythmia, and no difference was found between obstructive and non-obstructive HCM. Inappropriate shocks were found in 8 patients (29 %), two of them also had inappropriate ATP. Causes of inappropriate ICD therapies were atrial fibrillation (62.5 %), T-wave oversensing (25 %), and lead dysfunction (12.5 %). Finally, all-cause mortality was 14 %: causes of death were acute heart failure in 2 patients, as well as stroke and hospital-acquired pneumonia in one patient, respectively.

Conclusions Patients with HCM do benefit from ICD implantation, but less frequently than anticipated. The problem of inappropriate ICD therapies with further risk for arrhythmia induction is still of major concern, with atrial fibrillation being the major cause.

Esmolol zur periinterventionellen Induktion von ventrikulären Extrasystolen bei geplanter Hochfrequenzkatheterablation 164

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Hintergrund Symptomatische ventrikuläre Extrasystolen (VES) aus dem rechtsventrikulären Ausflusstrakt (RVOT) stellen eine Indikation zur Hochfrequenzkatheterablation dar. Wenn der Patient die VES während der elektrophysiologischen Studie (EPS) im Katheterlabor nicht spontan bietet, kann das Target für die Ablation nicht identifiziert werden. Provokationsmanöver zur VES-Induktion werden vorwiegend mit Katecholaminen wie Orciprenalin durchgeführt. Bei VES, die vor allem in Ruhe bei niedriger Herzfrequenz auftreten, ist diese Methode wenig effektiv.

Methode Wir berichten über eine 36-jährige Patientin, die seit der Schwangerschaft vor 7 Jahren an symptomatischen VES leidet. Magnetresonanztomographisch stellen sich sowohl der linke als auch der rechte Ventrikel gering vergrößert dar, die linksventrikuläre Funktion ist mit einer Auswurffraktion von 53 % geringgradig reduziert, die rechtsventrikuläre mit 58 % im Normbereich. Im 24-Stunden-EKG werden insgesamt 18.690 vorwiegend monomorphe VES dokumentiert, deren Morphologie im Oberflächen-EKG auf einen Ursprung aus dem anteroseptalen RVOT hinweist. Eine zweite komplett differente Morphologie wird ganz vereinzelt nachgewiesen. Der überwiegende Anteil der VES tritt nachts in Ruhe auf, wo die Patientin bradykard bis minimal 46/min ist. Zu Untersuchungsbeginn der EPS ist die Patientin verhältnismäßig tachykard (90/min) bei Sinusrhythmus ohne Auftreten ihrer typischen VES. Nach langsamer Infusion von insgesamt 50 mg Esmolol als Kurzinfusion sinkt die Sinusfrequenz unter 60/min, und die im Oberflächen-EKG dokumentierten VES treten mit identischer Morphologie auf. In der rechtsventrikulären Angiographie zeigen sich keine anatomischen Auffälligkeiten. Anschließend wird der Focus der Zielextrasystole mittels Pacemapping anteroseptal im RVOT aufgesucht und mit zwei Energieabgaben über den Ablationskatheter erfolgreich abliert. Danach kann die Zielextrasystole auch nach nochmaliger Provokation mit 50 mg Esmolol i. v. nicht mehr nachgewiesen werden. Dieses Ergebnis bestätigt sich auch in einer 24-Stunden-EKG-Kontrolle 5 Wochen nach der Ablation, die Patientin ist komplett beschwerdefrei.

Konklusion Bei Patienten mit VES, die unter Belastung auftreten, ist eine periinterventionelle Provokation mit Katecholaminen vor geplanter Ablation sinnvoll. Bei Auftreten von VES vorwiegend im Ruhezustand bei niedriger Sinusfrequenz stellt die intravenöse Gabe von Esmolol im Katheterlabor eine gute Alternative dar, um den erhöhten Sympathikotonus des Patienten in der Situation der Ablation zu antagonisieren und das Auftreten der Zielextrasystole zu induzieren.

CT-Evaluierung der Pulmonalvenen-Ostien vor und 6 Monate nach Ablation mit dem Mesh Ablator®-Katheter 039

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Hintergrund Der Mesh Ablator®-Katheter (Bard Inc., Lowell, USA) ist ein neues Device zur Durchführung von Pulmonalvenen-(PV-) Isolationen bei paroxysmalem Vorhofflimmern. Er besteht aus einem zirkulären Drahtgeflecht, über das sowohl hochauflösendes bipolares Mapping als auch Radiofrequenzstrom-Ablationen durchgeführt werden können. Der Katheter hat in entfaltetem Zustand die Form eines Diskus, der im Bereich des Antrums der einzelnen PV platziert wird und dort die Erstellung zirkumferentieller Läsionen ermöglicht.

Die prozedurale Effektivität und Sicherheit des Katheters wurde bereits in mehreren Studien nachgewiesen. Daten zur klinischen Langzeitsicherheit, vor allem in Hinblick auf die Auswirkungen der zirkumferentiellen Ablation auf die PV-Ostien fehlen noch. Ziel unserer prospektiven Studie war es, die PV-Ostien vor und mindestens 6 Monate nach der Isolation mit dem Mesh Ablator®-Katheter mittels hochauflösender Spiral-Computer-Tomographie (64-Zeiler, CT) zu untersuchen.

Methodik Es wurden nur Patienten (P) mit paroxysmalem Vorhofflimmern eingeschlossen. Bei allen P wurde vor und mindestens 6 Monate nach der Ablation eine CT des linken Vorhofs inklusive der PV-Ostien durchgeführt. Von einem gegenüber den Patientendaten verblindeten Untersucher wurden mittels multiplanarer Rekonstruktionen in zwei Ebenen (parallel und orthogonal zum Verlauf der PV unmittelbar vor der Mündung in den Vorhof) die kurzen und lange Achsen der PV-Ostien vermessen. Die Fläche der PV-Ostien wurde mittels der beiden Halbachsen als Ellipse berechnet. Die Veränderungen der Achsen und der Fläche der PV-Ostien zwischen Basis und Kontrolle wurden für alle PV ermittelt und in Beziehung zur während der Ablation dokumentierten Dauer der Energieabgabe pro PV gesetzt.

Ergebnisse Wir untersuchten 92 PV-Ostien bei 23 P (12 männlich; mittleres Alter = 61 ± 9 Jahre) vor der PV-Isolation und nach 9 ± 4 Monaten. Vor der Ablation betrugen die langen und kurzen Achsen (cm) sowie die Fläche (cm^2) der PV-Ostien der links-superioren PV (LSPV): 1,9 ± 0,2; 1,5 ± 0,3; 2,2 ± 0,6, der links-inferioren PV (LIPV): 1,6 ± 0,2; 1,3 ± 0,2; 1,6 ± 4, der rechts-superioren PV (RSPV): 1,9 ± 0,2; 1,7 ± 0,3; 2,5 ± 0,6, und der rechts-inferioren PV (RIPV): 1,7 ± 0,3; 1,5 ± 0,2; 2,1 ± 0,6. Als einzige signifikante Veränderung fand sich bei der Kontrolle eine Abnahme der mittleren langen Achse der LSPV (von 1,9 ± 0,2 cm auf 1,4 ± 0,3 cm; p = 0,03) und damit der rechnerisch ermittelten Fläche des Ostiums der LSPV (von 2,2 ± 0,6 cm^2 auf 2,1 ± 0,6 cm^2; p = 0,02). Die LSPV war die PV mit der längsten mittleren Energieabgabedauer aller PV (724 ± 192 sek) und unterschied sich darin nicht signifikant von der LIPV (713 ± 185 sek; p = 0,43) und der RSPV (646 ± 193 sek; p = 0.09), sowie signifikant von der RIPV (609 ± 210 sek; p = 0,03).

Der Stenosegrad der PV-Ostien, berechnet als Quotient der Flächen bei Basis und Kontrolle, betrug bei 15 PV (16 % der PV) mehr als 10 %, jedoch bei keiner PV mehr als 30 % (mittlerer Stenosegrad LSPV: 5 ± 1 %; LIPV: –2 ± 1 %; RSPV: 2 ± 1 %; PIPV: –2 ± 2 %).

Schlussfolgerung PV-Isolationen mit dem Mesh Ablator®-Katheter waren in unserer Serie nicht durch die Entstehung von signifikanten Stenosen der PV-Ostien kompliziert. Eine signifikante Reduktion der Größe des PV-Ostiums konnte nur für die LSPV nachgewiesen werden, die allerdings auch die PV mit der längsten mittleren Energieabgabedauer war.

Cryoballon-Ablation bei paroxysmalem VH-Flimmern: erste österreichische Erfahrungen 043

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Einleitung Ektope Aktivität aus den Pulmonalvenen (PV) ist der wichtigste Trigger für paroxysmales Vorhofflimmern (PAF). Die Isolation der PV durch eine Ablationsbehandlung stellt die wirksamste nicht-medikamentöse Behandlung von Patienten mit PAF dar und kann die Frequenz von symptomatischen Episoden von PAF signifikant reduzieren. Im Gegensatz zu der am häufigsten angewandten Ablationstechnik mit Radiofrequenzkathetern ist die neuartige Cryoballon-Ablation (CBA) in ersten präklinischen und klinischen Studien eine weniger komplexe Prozedur, bei der komplette, kontinuierliche Läsionen um die PV erzeugt werden können. Wir berichten über die ersten österreichischen Erfahrungen mit der (CBA) bei Patienten mit PAF.

Methoden Zwischen Mai 2008 und Februar 2009 wurden an unserem Zentrum 25 Patienten (4 w, 21 m) mit symptomatischem PAF ohne zugrundeliegende strukturelle Herzerkrankung mit CBA behandelt, deren Arrhythmien refraktär auf mindestens ein Antiarrhythmikum waren. Die Prozedur wurde mit einem Cryoballon-Katheter (28 mm, Arctic Front, Cryocath) und einer steuerbaren Schleuse (Flexcath, Cryocath) durchgeführt. Die Navigation des

Katheters wurde durch Röntgendurchleuchtung und intrakardiale Echokardiographie (ICE; AccuNav, Biosense Webster) gesteuert. Am Ende der Untersuchung wurde die PV-Isolation jeweils mit einem Lasso-Katheter überprüft. Der klinische Erfolg der Ablation wurde in Follow-ups nach 3, 6, 9 und 12 Monaten nach der Intervention beurteilt.

Resultate Insgesamt erfolgten 219 CBA in 102 PV (im Mittel 3,1 Cryoablationen/PV). Die Okklusion der PV mit dem Cryoballon wurde bei 5 Patienten nur mit Injektion von Kontrastmittel in die Vene bei inflatiertem Ballon, und bei 20 Patienten zusätzlich mit ICE überprüft. Durch die Ablationsbehandlung konnten alle 102 PV isoliert werden, allerdings waren bei 4 Patienten zur Vervollständigung der Isolation auch lineare Läsionen mit einem Cryo-Katheter (Freezor Max, CryoCath; im Mittel 5,75 Ablationen) notwendig. Bei 2 Patienten trat während der Behandlung der rechten oberen PV eine Phrenikus-Parese auf, die allerdings keine Auswirkung auf die Lungenfunktion der Patienten hatte. Perikard-Tamponaden oder neurologische Komplikationen wurden nicht beobachtet. Die PV-Isolation führte bei allen Patienten zu einer Verbesserung der Symptomatik (mittlere Frequenz der Episoden 15,0 auf 3,7/Woche), bei 11/25 Patienten trat seit der Prozedur (mittleres Follow-up 5,1 Monate) ohne antiarrhythmische Therapie keine einzige symptomatische Episode von Vorhof-Flimmern mehr auf.

Zusammenfassung In unserer Kohorte konnten alle Pulmonalvenen durch eine linksatriale CBA erfolgreich isoliert werden. Die Prozedur erwies sich als sicher und führte nach relativ kurzem Follow-up zu einer deutlichen Verringerung der symptomatischen Vorhofflimmerepisoden.

Pulmonary Vein Isolation with Remote Robotic Navigation: Safety, Feasibility and Efficacy 042

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Introduction Assessing the feasibility and efficacy of a novel robotic catheter navigation system; RNS, Hansen Medical Inc, CA, USA; for circumferential pulmonary vein isolation (CPVI).

Methods Using the RNS in conjunction with different 3D mapping systems, CPVI was performed for paroxysmal (n = 43) or persistent (n = 22) AF in 65 patients (pts). The ablation catheter used for left LA mapping and ablation and a transseptal sheath for a spiral mapping catheter were advanced into the left atrium (LA). PV ostia were determined by selective angiography. Ablation consisted of wide area CPVI until electrical isolation of all PVs.

Ablation catheter stability was assessed at each quadrant of the ipsilateral PVs and classified as good (no catheter dislodgement during RF delivery), moderate or poor (1 or > 1 interrupted RF application, respectively).

Results Complete PVI, exclusively using the RNS, was achieved in 62/65 pts (95 %) using the CARTO (n = 42) or the NavX system (n = 23). In 2 pts isolation of the left PVs had to be finalized manually, in 1 pt access to the LA could not be achieved due to a technical malfunction of the RNS. Procedure time was 195 ± 40 min. Fluoroscopy time was 17 ± 7 min including 6 ± 4 min using the RNS without exposure to the operator.

Three complications occurred: Transient ST segment elevation (n = 1), cardiac tamponade following right atrial perforation by the RNS (n = 1), and an oesophageal ulcer demonstrated by endoscopy that resolved within two weeks (n = 1).

Catheter stability at the superior and inferior aspect of both PVs was good in > 90 %, poor in 0 %. Catheter stability was more challenging at the posterior wall (right PVs: good in 74 %, poor in 4 %, left PVs good in 71 %, poor in 6 %) and anterior wall (right PVs: good in 81 %, poor in 2 %, left PVs: good in 54 %, poor in 12 %). 47/65 pts (73 %) remained in SR after a single procedure during a median FU period of 239 (184–314) days.

Conclusions The initial experience of CPVI using RNS in conjunction with different 3D mapping systems is feasible and effective. Using RNS, 1/3 of fluoroscopy time is used during remote navigation. Achieving catheter stability at the anterior left PV ostium remains challenging.

Simplified Mapping Approach for Circumferential Pulmonary Vein Isolation Based on the NavX Technology 062

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Introduction Isolation of the pulmonary veins (PV) has been proven to be the standard treatment for catheter ablation in patients with paroxysmal atrial fibrillation (AF). Different methods for 3D mapping have been described. The limitations of all these techniques are that they are time consuming also because they involve the mapping of the entire left atrium (LA).

The purpose of this study was to perform complete PV isolation by continuous circular lesions around the ipsilateral PVs using a new mapping strategy which includes only NavX mapping of the left atrial appendage (LAA) proximal PVs and the adjacent LA tissue but not the entire LA.

Methods 20 patients (Ptn; 15 male; age 55 ± 9 years; LA diameter 41 ± 7 mm) underwent catheter ablation for drug refractory symptomatic paroxysmal AF (mean AF duration 83 ± 64 month). Complete PV isolation by continuous circular lesions around the ipsilateral PVs was performed using a reduced and simplified 3D reconstruction of the cardiac geometry. Only the LAA, the proximal PVs and the adjacent atrial tissue (but not the entire LA) were reconstructed. The PV ostia determined by angiography were marked in the 3D image with the ablation catheter by using 3D labels. For better orientation in the geometry, red labels were used for the posterior aspect of the ostia, and white labels were used for the anterior aspect. Procedural end point was defined as complete PV isolation 30 minutes after the last radiofrequency application was applied.

Results In all 20 Ptn all PVs could be isolated with a mean of 15 ± 5 (septal PVs) and 14 ± 4 (lateral PVs) radiofrequency applications. Procedure time was 173 ± 38 minutes, fluoroscopy time was 21 ± 11 minutes. 1, 3, 6 month after ablation a holter ECG was performed. During a mean follow up of 67 ± 88 days 13/20 Ptn (65 %) remained in sinus rhythm without antiarrhythmic drugs after a single ablation procedure. There was no procedure related complication in all Ptn.

Conclusion Simplified reconstruction only of the left atrial appendage, the proximal PVs and a small part of the atrial tissue adjacent to the PVs is sufficient to perform complete PV isolation by continuous circular lesions around the ipsilateral PVs. This strategy helps to reduce fluoroscopy time and procedure time by mapping only the essential of the left atrium needed to perform ablation. The clinical outcome (AF recurrence rate) appears to be similar to the outcome using other 3D mapping strategies where the entire LA is mapped.

Safety, Outcome and Patient Satisfaction Following Outpatient Radiofrequency Catheter Ablation Procedures in a University Hospital Setting 081

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Background Catheter ablation has been shown to be an effective and safe treatment for various arrhythmic disorders. Patients are typically admitted overnight after the ablation procedure to monitor for possible post-procedure complications or a recurrence of the arrhythmia. The aim of this study was to assess safety, clinical outcomes, and patient satisfaction following catheter ablation on an outpatient basis in a university hospital setting.

Methods 243 consecutive patients (129 male, 53 %; mean age 49 ± 17 years) underwent electrophysiology study and radiofrequency catheter ablation either on an outpatient basis or an hospital-

ization which included at least an overnight hospital stay (inpatient) at the University Hospital of Zürich. All patients were asked to complete a specially-designed questionnaire that addressed questions about the outcome of the ablation at 6 months, procedure-related complications, time to return to work and patient satisfaction.

Results The procedure was performed on an outpatient basis in 119 patients (49 %). The long-term procedural success rate was 99 %. Overall, 90 % of the patients were satisfied with the ablation procedure and with 6-month outcomes. There were no significant differences between the outpatient and inpatient groups with respect to ablation outcome and patient satisfaction. Patients in the outpatient group returned to work after 2.8 ± 1.9 days as compared to 3.9 ± 2.2 days in the in-hospital group (p = 0.001).

Conclusion Catheter ablation procedures performed on an outpatient basis are feasible and safe. The success rates and the overall patient satisfaction are comparable for both outpatient and inpatient ablations. However, patients who undergo ablation procedures on an outpatient basis can return to work earlier. Therefore, outpatient catheter ablation may be considered for selected patients without significant comorbidities.

Stabile Koronare Herzkrankheit

N-terminales pro B-Typ natriuretisches Peptid, C-reaktives Protein und Gamma-Glutamyltransferase sind unabhängige Risikomarker bei Patienten mit stabiler koronarer Herzerkrankung 001

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Hintergrund Biomarker werden zunehmend zur Risikostratifizierung auch bei Patienten mit stabiler koronarer Herzerkrankung (KHK) verwendet, wobei der Stellenwert der einzelnen vorgeschlagenen Marker in Zusammenschau mehrerer Biomarker und der klassischen Risikofaktoren noch weiter evaluiert werden muss. Dies wurde in der vorliegenden Studie durchgeführt.

Methodik Wir untersuchten 525 konsekutive Patienten mit stabiler KHK, die im Zeitraum März 2004–Ende Februar 2005 zur Herzkatheterdiagnostik an unsere Abteilung zugewiesen wurden. Patienten mit akutem Koronarsyndrom, Vitium, nach Herztransplantation oder ohne angiographische Zeichen einer KHK wurden ausgeschlossen. N-terminales pro B-Typ natriuretisches Peptid (NT-proBNP), high sensitivity C-reaktives Protein (hs-CRP), Gamma-Glutamyltransferase (γGT) wurden im Rahmen der Routinelabordiagnostik vor der Koronarangiographie (CAG) bestimmt. Der Schweregrad der KHK wurde nach angiographischen Kriterien erhoben und die Ventrikelfunktion bestimmt. Die Mortalität und klinische Endpunkte (Revaskularisationsnotwendigkeit, Herzinfarktrate, stationäre Wiederaufnahmen wegen kardialer Ereignisse, Insultrate) wurden anhand von Analyse der Todesfallmeldedaten und Krankengeschichten bzw. mittels Telefoninterview erhoben. Von den 525 Pat. konnten 394 (75 %) nachverfolgt werden, die anderen konnten telefonisch nicht erreicht werden bzw. lehnte eine Befragung ab. T-Test, Mann-Whitney-U-Test und Chi-Quadrat-Test wurden für die Gruppenvergleiche verwendet. Der prognostische Wert der Variablen wurde univariat mittels Kaplan-Meier-Überlebensanalyse und multivariat mittels Cox-Regressionsanalyse untersucht. P-Werte von < 0,05 wurden für statistisch signifikant angesehen.

Ergebnisse Die nachverfolgten 394 Patienten unterschieden sich in ihren klinischen, angiographischen Charakteristika und Laborwerten nicht signifikant von der ursprünglichen Population der 525 Pat. mit stabiler KHK. Der durchschnittliche Nachbeobachtungszeitraum war 1177 Tage (1001–1328 Tage). Die Mortalitätsrate betrug 10,2 %, die Rate des kombinierten Endpunktes (Tod oder klinisches Ereignis) 31 %. In der univariaten Analyse waren bis auf Diabetes mellitus und erhöhte Kreatininwerte die klassischen Risikofaktoren zum Zeitpunkt der CAG für den weiteren Verlauf von keiner prognostischen Relevanz bezüglich Mortalität und kombinierten Endpunkt. Der Schweregrad der KHK und ein Zustand nach Bypasschirurgie bzw. Stentimplantation und die Ventrikelfunktion waren prognostisch relevant. NT-proBNP, hs-CRP und γGT waren signifikante univariate Prädiktoren der Mortalität, nur NT-proBNP war ein signifikanter Marker für den kombinierten Endpunkt. In der alters- und geschlechtsadjustierten multivariaten Analyse war NT-proBNP der stärkste Prädiktor des kombinierten Endpunktes (Odd-Ratio 2,92). Alle 3 Laborparameter blieben unabhängige Risikomarker der Mortalität in der multivariaten Analyse, wobei NT-proBNP die höchste Odd-Ratio zeigte (5,23).

Schlussfolgerungen Im Vergleich mit anderen Biomarkern und klassischen Risikofaktoren zeigte NT-proBNP die stärkste prognostische Relevanz bei Patienten mit stabiler KHK und ist ein vielversprechender Risikomarker, jedoch müssen unmittelbare therapeutische Konsequenzen erst durch zukünftige Interventionsstudien belegt werden.

Comparison of Methods to Evaluate Clopidogrel-mediated Platelet Inhibition after Percutaneous Intervention with Stent Implantation 170

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Objectives High on-treatment residual ADP-inducible platelet reactivity in light transmission aggregometry (LTA) has been associated with an increased risk of adverse outcomes after percutaneous coronary intervention. However, LTA is weakly standardized and results obtained in one laboratory may not be comparable to those obtained in another one. We therefore sought to determine the test correlating best with LTA to estimate clopidogrel-mediated platelet inhibition in 80 patients on dual antiplatelet therapy after elective percutaneous intervention with stent implantation.

Methods We selected four whole blood assays for comparison with LTA based on their commercial availability, and either feasibility of performance (VerifyNow P2Y12 assay), or similarity to LTA (VerifyNow P2Y12 assay; Multiple electrode platelet aggregometry), specificity for the assessment of the ADP receptor blockage (VASP assay), or use of high shear (Impact-R). Cut-off values for residual ADP-inducible platelet reactivity were defined according to quartiles of each assay. Sensitivities and specificities of the different platelet function tests were based on the results from LTA.

Results The results from all four assays correlated significantly with those from LTA. The VerifyNow P2Y12 assay revealed the strongest correlation (r = 0.61; p < 0.001). Sensitivities and specificities ranged from 35 to 55 %, and from 78.3 to 85 %, respectively.

Conclusions Although all assays correlated significantly with LTA, they need to be improved to become clinically used diagnostic tests. Further, it may be too early to define the gold standard method for assessing residual ADP-inducible platelet reactivity and generally acceptable cut-off values.

Effects of Proton-Pump Inhibitors on Outcome of Patients Discharged on Dual-Antiplatelet Therapy after Percutaneous Coronary Intervention and Stent Implantation 064

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Background Recently, the CREDO trial showed a significantly higher risk of major gastrointestinal bleedings associated with dual antiplatelet therapy after coronary intervention. Therefore, routine prescription of proton-pump-inhibitors (PPI) in addition to clopidogrel and aspirin might be essential for prevention of gastrointestinal

complications. However, it has been suggested that PPI might reduce the effect of clopidogrel and increase the risk of adverse thrombembolic events.

Methods In this retrospective analysis we investigated the effect of concomitant PPI and dual antiplatelet therapy on all-cause mortality and in-stent restenosis in 1506 consecutive patients who underwent PCI and stent implantation between the 1st of January 2003 and 31st of December 2006 in our hospital. The patients were followed-up for median 723 (390–1080) days.

Results Dual antiplatelet therapy with concomitant PPI therapy was associated with significantly higher proportion of female patients (33.6 % vs 27.4 %; p = 0.015), significantly more patients with drug eluting stent (35.1 % vs 28.4 %; p = 0.01), significantly more patients discharged on statins (87.4 % vs 80.3 %; p < 0.001) and significantly less patients with diabetes mellitus (19.5 % vs 26.6 %; p = 0.002) compared to those who had no PPI at discharge. Clinical characteristics of patients with or without PPI therapy were not significantly different. All-cause mortality and in-stent restenose did not differ significantly with respect to use or non-use of PPI-therapy (7.4 % vs 7.6 %; p = 0.87). Even in different subgroups of patients e.g. acute vs elective, BMS vs. DES, diabetics vs. no diabetics, had concomitant PPI-therapy no significant influence on outcome.

Conclusion Our data suggest that the combination of dual antiplatelet therapy with proton-pump inhibitors obviously does not significantly influence thrombembolic events.

Gender Differences in 7819 Consecutive Patients Undergoing Elective Coronary Angiography 108

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Background The management and presentation of acute coronary syndromes is known to be partially gender dependent. Whether gender differences can also be found in consecutive, stable patients undergoing elective coronary angiography (CA) for the evaluation of coronary artery disease (CAD) is still a matter of investigation.

Methods 7819 consecutive patients (33.7 % women) were analysed. Cardiovascular risk factors were assessed by standardised questionnaire and routine blood chemistry. CAD was graded by visual estimation of lumen diameter stenosis. Significant stenoses were defined as lumen diameter reduction ≥ 70 % in at least one major coronary artery. Coronary angiograms were graded as non-significant CAD, 1-, 2- or 3-vessel disease or as non-CAD.

Results Women were older than men (65 ± 11 vs 63 ± 11 years; p < 0.001) and suffered more often from atypical thoracic pain (6.0 vs 4.1 %; p = 0.001), whereas the rate of stable (40.9 vs 38.8 %; p = 0.22) and unstable AP (17.3 vs 16.7 %; p = 0.73) prior to CA was not different between gender. Prior myocardial infarctions (6.1 vs 10.4 %; p < 0.001) as well as prior revascularisation procedures (16.5 vs 27.1 %; p < 0.001) were found more often in men. Women had a higher prevalence of positive family history for premature cardiovascular disease (26.4 vs 20.5 %; p < 0.001) and men were more often smokers (14.4 vs. 20.1 %; p < 0.001), whereas the prevalence of hypertension, diabetes and hypercholesterolemia was similar. Furthermore, HDL cholesterol was found to be higher in women (62 ± 18 vs 51 ± 15 mg/dl; p < 0.001), whereas C-reactive protein (0.77 ± 1.89 vs 0.89 ± 2.15 mg/dl; p < 0.001) and triglyceride levels (135 ± 83 vs 161 ± 135 mg/dl; p < 0.001) were lower in women. LDL-cholesterol was not different between gender (125 ± 38 vs 121 ± 37 mg/dl; p = 0.11). No CAD was more common in women (39.8 vs 18.6 %; p < 0.001), whereas women more often had non-significant CAD (20.4 vs 16.6 %; p < 0.001). In patients with any CAD, conservative treatment was more often decided in women (52.9 vs 42.7 %; p < 0.001). However, among patients with significant CAD (i.e. stenosis ≥ 70 %) conservative treatment was similar between gender (32.7 vs 30.0 %; p = 0.08). In multivariate analysis, including variables being different between gender in univariate analyses, female gender remained independently associated with older age, the absence of CAD, conservative treatment, higher HDL cholesterol, lower C-reactive protein, less prior myocardial infarctions and family history.

Conclusion In the contemporary management of patients with suspected CAD, women are more likely to have no CAD or to present with non-significant CAD probably due to a more favourable risk factor profile. Furthermore, among patients with significant CAD, the rate of PCI is not different between gender.

Long-term Outcome of Treatment with Angiotensin II Type-1 Receptor Blocker (ARB) in Comparison with ACE-inhibitors (ACEI) after PCI and Stent Implantation: a Single Centre Experience 079

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Purpose Aim of our study was to evaluate the effect of treatment of angiotensin II type-1 receptor blocker (ARB) after PCI and stent implantation compared with ACE inhibitors (ACEI) on all-cause mortality and target vessel revascularization (TVR) in a "real world" clinical setting.

Methods 891 consecutive patients, who underwent PCI and stent implantation and treated with ACEI or ARB in addition to standard therapy (ASS+Clopidogrel), were included in a prospective registry from January 2003 until December 2006. Patients were subdivided retrospectively into two groups, those who were treated with ACEI and those who were treated with ARB, which were only used when ACEI therapy was contraindicated due to side effects. All-cause mortality, TVR and the combined endpoint of death or TVR was evaluated during a mean follow-up period of 24,56 ± 12,5 months (range 6–52 months). As the two groups showed significant differences in some clinical aspects we calculated propensity score in attempt to eliminate this selection bias.

Results 736 patients (82.6 %) were treated with ACEI, while 155 patients (17.4 %) were treated with ARB. Clinical characteristics like hyperlipidemia, history of MI, PCI, cerebral insult, diabetes mellitus and 3-vessel disease were not different between groups. Significant difference was found for age (ACEI: 63.81 ± 12.15 vs ARB: 68.03 ± 10.83; p < 0.001), gender (males in the ACEI group: 71.2 % vs ARB: 61.9 %; p = 0.023), chronic renal failure (ACEI: 22 % vs ARB: 34.8 %; p = 0.001) history of CABG (ACEI: 4.5 % vs ARB: 10.3 %; p = 0.04), heart failure (ACEI: 4.6 % vs ARB: 11 %; p = 0.002), presence of acute coronary syndrome (ACS) during the intervention(ACEI: 53 % vs ARB: 37.4 %; p < 0.001), and use of drug-eluting stent (ACEI: 29.2 % vs ARB: 38.1 %; p = 0.03), respectively.

In total 87 patients (9.8 %) needed TVR, 63 (7.1 %) died and 146 (16.4 %) reached the combined endpoint (all-cause death or TVR) during the follow up. Fifty patients (6.8 %) of the ACEI group and 13 patients (8.4 %) of the ARB group died during the follow up (p = 0.7), while 75 patients (10.2 %) of the ACEI group and 12 (7.7 %) patients of the ARB group had a TVR (p = 0.4). With respect to the combined endpoint 121 patients (16.4 %) with ACEI and 25 patients (16.1 %) with ARB (p = 0.4) had an event during the follow up. The stent type or the presence of ACS had no effect on outcome between ACEI or ARB-treated patients.

Conclusion Our results generated in a "real world" clinical setting confirmed a similar long-term outcome for patients treated with ACEI during secondary prevention as compared with ARB. Accordingly, there is no need to prescribe ARB in favor of ACEI in patients after coronary interventions.

Gamma Glutamyl Transferase Levels, Coronary Artery Disease Prevalence and Severity in Consecutive, Stable Patients Undergoing Elective Coronary Angiography 040

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Background Gamma glutamyl transferase (gGT) levels are predictive for cardiovascular (CV) events in cohort studies and gGT-like proteins are localized in atherosclerotic plaques. Whether gGT concentrations also reflect coronary artery disease (CAD) prevalence and/or severity independently from traditional CV risk factors is still unclear.

Methods 7819 consecutive patients undergoing elective coronary angiography for the evaluation of CAD were analysed. CV risk factors were assessed by standardised questionnaire and routine blood chemistry. gGT levels were measured with enzymatical colour assay. CAD was graded by visual estimation of lumen diameter stenosis (significant stenoses were defined as lumen diameter reduction ≥ 70 %) into non-significant CAD, 1-, 2- or 3-vessel disease or as non-CAD.

Results Given the numerous reasons for unspecific gGT elevations only patients with gGT levels within the 2.5th and 97.5th percentiles of normal range were used for final analyses (n = 5967, 32.3 % women). Women with non-CAD (40.1 %) had lower gGT levels compared to women with any kind of CAD (21.3 ± 8.4 vs 22.8 ± 8.7 U/L; p = 0.0003), whereas in men gGT levels were not associated with the prevalence of CAD (82.6 %). At univariate analyses, gGT concentrations increased with increasing severity of CAD in women (ANOVA p = 0.001), but not in men (ANOVA p = 0.88). Furthermore, gGT levels were associated with the number of traditional CV risk factors (hypertension, diabetes, smoking, hypercholesterolemia, positive family history for premature CAD) in women and in men (**Figure 12**) How ever, at multivariate analyses including risk factors significant different at univariate analyses, gGT levels lost their independent association with both CAD prevalence and severity in women.

Conclusion In this large consecutive cohort of stable patients undergoing elective coronary angiography, gGT levels within the normal range were neither independently associated with CAD prevalence nor severity, but increased with the number of CV risk factors in both gender, suggesting that gGT levels may reflect CV risk factor burden.

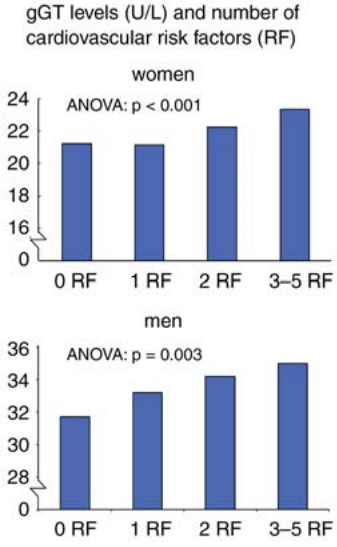

Figure 12: M. Wanitschek et al.

Table 10: Wanitschek et al.

	Odds ratio 95 %-CI	p-value
Age (per year)	1.067 (1.060–1.074)	p < 0.001
Gender	3.074 (2.677–3.530)	p < 0.001
Calcium-phosphate product (per mmol2/L2)	1.145 (1.026–1.278)	p < 0.03
Smoking status	1.736 (1.441–2.090)	p < 0.001
Hypertension	1.786 (1.515–2.105)	p < 0.001
Diabetes	1.804 (1.485–2.191)	p < 0.001
CRP (per log-unit)	1.266 (1.105–1.451)	p < 0.03
HDL cholesterol (per mg/dL)	0.980 (0.976–0.985)	p < 0.001

Calcium-Phosphate Product Levels are Associated With Coronary Artery Disease Prevalence and Severity in 7819 Consecutive Patients Undergoing Elective Coronary Angiography 115

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Background Calcium-phosphate (Ca-P) product levels, linked to vascular dysfunction, predict future cardiovascular events. Whether Ca-P product levels are also associated with the prevalence and severity of coronary artery disease (CAD) has not been studied extensively so far.

Methods 7819 consecutive patients undergoing elective coronary angiography for the evaluation of CAD were analysed. CV risk factors as well as serum calcium and phosphate levels were assessed by standardised questionnaire and routine blood chemistry. CAD was graded by visual estimation of lumen diameter stenosis (significant stenoses were defined as lumen diameter reduction ≥ 70 %) into non-significant CAD, 1-, 2- or 3-vessel disease or as non-CAD (no lumen irregularities).

Results Ca-P product levels were higher in non-CAD (n = 1816) compared to CAD (n = 5360) patients (2.44 ± 0.60 vs 2.39 ± 0.63 mmol^2/L^2; p = 0.004). At univariate analyses, Ca-P product levels decreased with increasing severity of CAD (ANOVA p = 0.009). In multinomial logistic regression analyses including all traditional cardiovascular risk factors, C-reactive protein and HDL cholesterol, Ca-P product levels remained ndependently associated with both the prevalence (**Table 10**) and the severity of CAD.

Conclusion In this large consecutive cohort of stable patients undergoing elective coronary angiography, calcium-phosphate product levels as potentially modifiable risk factors were independently associated with the prevalence of CAD.

Stoffwechsel

NT-proBNP is Decreased in Severe Gestational Diabetes mellitus 014

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Objectives NT-proBNP is elevated in gestational hypertension and preeclampsia but no data exist in gestational diabetes mellitus (GDM) patients, who are at risk to develop these complications.

Methods We have measured NT-proBNP in otherwise healthy women between gestational week 24 and 32 referred to the outpatient diabetes unit in a cross-sectional study. Inclusion criteria comprised age ≥ 18 years and single pregnancy. Exclusion criteria were

presence of a clinically relevant disease other than GDM and intake of concomitant medication.

37 control subjects, 41 patients with indication for medical nutrition therapy (mild GDM) and 78 patients who required additional insulin therapy (severe GDM) were included.

To compare outcome parameters between groups, an analysis of variance or the Kruskal-Wallis test was applied for parametric and non-parametric datasets, respectively.

Results None of the 156 included pregnant women developed (pre-) eclampsia or gestational hypertension. Groups of women were comparable regarding age and gestational week. Body mass index (BMI) before pregnancy and at blood draw was significantly higher in subjects with severe GDM compared to mild GDM.

NT-proBNP and serum creatinine were significantly lower in patients with severe GDM (35 ± 26 pg/ml and 0.6 ± 0.1 mg/dl) as compared to those with mild GDM (45 ± 41 pg/ml and 0.7 ± 0.1 mg/dl) and controls (55 ± 45 pg/ml and 0.7 ± 0.1 mg/dl).

Conclusions NT-proBNP is not elevated in women with GDM and upper cut-off values may therefore also be applied to this group of patients. Differences in BMI, changes in glomerular filtration rate and haemodynamics may explain lower NT-proBNP concentrations in severe GDM. A false negative interpretation needs to be considered in these women. The interpretation of our study findings is limited by the fact that women with concomitant diseases were excluded. Further investigation on this issue should be performed.

Incidence of Diabetes Mellitus and Stress Hyperglycemia in Patients with Stable and Acute Coronary Artery Disease 046

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Background and Aim To estimate the real prevalence of diabetes mellitus (DM) among patients undergoing percutaneous coronary angioplasty (PCI), we screened 199 consecutive patients admitted with acute coronary syndromes (ACS; n = 141) or chronic stable coronary artery disease (CAD; n = 58) to our department. As diagnostic tools for detection of DM either a history of DM, an increased fasting blood sugar, or a positive standardized oral glucose tolerance test (OGTT) were used. An impaired glucose tolerance (IGT) was described when post-load glucose levels were > 140 mg%. Furthermore we aimed to investigate the relationship between stress hyperglycemia (SHG) and the metabolic state in our patients.

Results A pathologic glucose metabolism indicative for DM was diagnosed in 19 % of patients according to the patient's medical history alone, and in 23.1 % based on fasting glucose concentrations. However, by use of a standardized OGTT, DM could be detected in 41.2 % of the patients' cohort, while another 22.1 % exhibited an impaired glucose tolerance. Patients with a DM or IGT had significant higher HbAc1 concentrations (DM: 6.35 ± 0.99; IGT: 5.73 ± 0.36 %) than patients with NGT (5.5 ± 0.36; p = 0.023 for both comparisons). These patients had a significant higher incidence of multivessel disease compared to those with normal glucose tolerance (NGT) (DM and IGT: 22 % and 13.6 % vs. NGT: 9.6 %; p = 0.018). There was no difference in the incidence of SHG when comparing patients with DM, IGT, or NGT based on OGTT (DM 43.3 %; IGT: 27.2 %; NGT: 30.9 %; p = 0.28).

Conclusion When the metabolic state is tested by means of OGTT, pathologic glucose metabolism was present in almost two thirds of patients with CAD referred for angiography and PCI. SHG could be detected with a higher tendency in patients with DM than in those with NGT or IGT but reached nearly 30 % also in these groups. Exact diagnosis of DM and IGT as well as of stress hyperglycemia might have important predictive value for further clinical course and lead to more intensive therapeutic measures in these patients.

Glukosetransporter im menschlichen ventrikulären Gewebe 028

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Insulin vermittelt funktionelle, trophische und metabolische Effekte im menschlichen Myokard. Positiv inotrope Effekte (PIE) sind teilweise Ca2+-abhängig und zu anderen Teilen Ca2+-unabhängig. Letzterer Mechanismus ist potenziell Glukose-abhängig. Im Gegensatz zu den meisten Tierspezies exprimiert das Myokard des Menschen neben den herkömmlichen Glukosetransportern GLUT1 und GLUT4 (glucose-transporters-1 and -4) große Mengen des Membran-ständigen sodium-glucose-transporter-1 (SGLT-1). Wir haben die Hypothese getestet, dass die Glukosetransporter direkt in die Vermittlung funktioneller Effekte eingebunden sind.

Die Experimente wurden an isolierten multizellulären Streifenpräparaten aus 61 terminal insuffizienten menschlichen Herzen, sowie aus 13 menschlichen Spenderherzen durchgeführt. Die funktionellen Effekte von Insulin wurden mit und ohne Blockade der PI3-Kinase (Wortmannin), der GLUT4-Translokation (Latrunculin B) oder des SGLT-1 (Phlorizin, T-1095A) getestet. Die mRNA-Expression der Glukosetransporter wurde in gesunden und insuffizienten Herzen gemessen.

Insulin (0,02 µmol/L) führte zu einem PIE von 122 ± 7,4 % in gesundem Myokard, 121,7 ± 2,7 % in Myokard von Patienten mit dilatativer CMP und 134,9 ± 6,1 % bei Patienten mit ischämischer CMP ($p < 0,05$ vs. DCM). Der Effekt war unabhängig von Alter oder Geschlecht der Patienten. Im insuffizienten Myokard war der PIE teilweise hemmbar durch Blockade der PI-3-Kinase, von GLUT4 bzw. SGLT1. Die kombinierte Hemmung von PI3-Kinase und eines der Glukosetransporter führte zu einer kompletten Aufhebung des PIE; die kombinierte Hemmung beider Glukosetransporter hatte keinen additiven Effekt. Die mRNA-Expression unterschied sich nicht signifikant zwischen den getesteten Gruppen (Gesund, ICM, DCM).

Der Ca2+-unabhängige PIE von Insulin am menschlichen Myokard wird über die Aktivierung der Glukosetransporter GLUT4 und SGLT1 vermittelt. Dies beschreibt zu ersten Mal einen funktionellen Effekt von SGLT1 an myokardialem Gewebe. Der PIE von Insulin ist bei ischämischer CMP stärker ausgeprägt als bei DCM und könnte den therapeutischen Nutzen von Glukose-Insulin-Kalium-Infusionen begünstigen.

Significant Impact of Chromosomal Locus 1p13.3 on Serum LDL Cholesterol and on Angiographically Characterized Coronary Atherosclerosis 097

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Background Recently, a significant impact of a new locus on chromosome 1p13.3 on serum LDL cholesterol and clinical events of coronary artery disease (CAD) was described. Potential associations between variants on this locus and angiographically characterized coronary atherosclerosis are unknown. We therefore aimed at investigating the association of variants of locus 1p13.3 with coronary atherosclerosis.

Methods We performed genotyping of variants rs599839, rs646776, and rs4970834 on chromosome 1p13.3 in a large cohort of 1610 consecutive Caucasian patients undergoing coronary angiography, where lesions of 50 % or more were classified as significant.

Results Compared to the homozygous common allele the rare alleles of variants rs599839, rs646776, and rs4970834 were significantly associated with decreased serum LDL cholesterol (132 ± 40 vs 125 ± 36 mg/dl; p = 0.003, 132 ± 40 vs 124 ± 36 mg/dl; p < 0.001, and 131 ± 40 vs 125 ± 37 mg/dl; p = 0.005, respectively). Further, carriers of the rare alleles of variants rs599839 and rs646776 were at a significantly lower risk of significant coronary stenoses than sub-

jects who were homozygous for the frequent allele, with odds ratios (OR) of 0.78 [0.63–0.96]; p = 0.019 and 0.74 [0.60–0.91]; p = 0.004, respectively. After multivariate adjustment including LDL cholesterol, the protective effect of the rare allele of variant rs646776, but not of variant rs599839, on CAD risk remained significant (OR = 0.77 [0.61–0.98]; p = 0.034).

Conclusion We conclude that chromosomal locus 1p13.3 is significantly associated with both, serum LDL cholesterol and coronary atherosclerotic lesions.

Type 2 Diabetes and the Coronary Angiographic State are Mutually Independent Predictors of Future Vascular Events Among Angiographied Coronary Patients 098

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Background Type 2 diabetes (T2DM) in cross-sectional studies is associated with coronary artery disease (CAD) and prospectively confers a strongly increased risk of vascular events. It is not certain to what extent the baseline CAD state accounts for the increased vascular risk of diabetic patients in prospective studies because angiography usually is not performed.

Methods We therefore enrolled 750 consecutive patients undergoing coronary angiography for the evaluation of stable CAD. At angiography, CAD was diagnosed in the presence of any irregularities of the vessel wall. Stenoses ≥ 50 % were considered significant, and the extent of CAD was defined as the number of significant stenoses in a patient. Vascular events were recorded over 8 years.

Results The prevalence of CAD (87.8 % vs 80.4 %; p = 0.029) and of significant stenoses (69.5 % vs 58.4 %; p = 0.010) as well as the extent of CAD (1.7 ± 1.5 vs 1.4 ± 1.5; p = 0.014) were significantly higher in patients with T2DM (n = 164) than in nondiabetic subjects (n = 586). Prospectively, vascular events occurred in 257 patients (34.3 % of the study population). T2DM after multivariate adjustment strongly predicted vascular events (adjusted hazard ratio [HR] = 1.55 [1.17–2.05]; p = 0.002). Also, the presence of CAD (HR = 3.59 [2.11–6.13]; p < 0.001), the presence of significant stenoses (HR = 2.29 [1.70–3.09]; p < 0.001) and the extent of CAD (standardized adjusted HR = 1.40 [1.25–1.56]; p < 0.001) significantly predicted vascular events. These angiographic characteristics still predicted vascular events after additional adjustment for T2DM (HR = 3.46 [2.03–5.91]; p < 0.001; 2.24 [1.66–3.02]; p < 0.001; and 1.38 [1.24–1.54]; p < 0.001, respectively). Conversely, T2DM remained strongly and significantly predictive of future vascular events after adjustment for the presence and extent of CAD (HR = 1.41 [1.07–1.87]; p = 0.016).

Conclusions Among angiographied coronary patients, the presence and the extent of CAD are higher in patients with T2DM than in nondiabetic individuals. Prospectively, T2DM and the baseline CAD state are mutually independent predictors of future vascular events.

Gamma-Glutamyl-Transferase, Glutamate-Pyruvate-Transaminase, and the Glutamate-Pyruvate-Transaminase/Glutamate-Oxalacetate Transaminase Ratio are Significantly Reduced by Eight Weeks of Eccentric Endurance Exercise 099

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Background Elevated serum gamma-glutamyl-transferase (GGT) and glutamate-pyruvate-transaminase (GPT) as well as an elevated glutamate-pyruvate-transaminase/glutamate-oxalacetate transaminase (GPT/GOT) ratio are associated with the metabolic syndrome and, in some studies, with an increased cardiovascular risk. We hypothesised that eccentric endurance exercise lowers these parameters of liver function.

Methods Over a training period of 8 weeks, 51 healthy non-diabetic subjects (16 men and 35 women, mean age 50.3 years) 3 to 5 times per week performed eccentric endurance exercise by hiking downhill a path in the Austrian alps covering a difference in altitude of 540 meters; for the upward way a cable car was used, where compliance was recorded electronically.

Results GGT (from 51 ± 90 at baseline to 41 ± 60 mg/dl after 8 weeks of eccentric endurance exercise; p = 0.001), GPT (from 35 ± 30 to 30 ± 17 mg/dl; p = 0.006) and, most strongly, the GPT/GOT ratio (from 1.18 ± 0.39 to 1.00 ± 0.32; p < 0.001) were significantly decreased with 8 weeks of eccentric endurance exercise.

Conclusion GGT, GPT, and the GPT/GOT ratio even in apparently healthy individuals are significantly reduced by 8 weeks of eccentric endurance exercise. This modestly strenuous exercise modality therefore may me represent a promising treatment option for metabolic syndrome related non-alcoholic fatty liver disease.

Postprandial Triglycerides and Postprandial Inflammation are Significantly Reduced by Eight Weeks of Eccentric Endurance Exercise 100

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Background Postprandial triglyceridemia is considered to be a substantial risk factor for cardiovascular disease. The atherogenicity of postprandial hypertriglyceridemia may in part be driven by inflammatory mechanisms. We hypothesised that eccentric endurance exercise lowers both, postprandial triglyceride excursions and the postprandial inflammatory response.

Methods Over a training period of 8 weeks, 51 healthy non-diabetic subjects (16 men and 35 women, mean age 51 years) 3 to 5 times per week performed eccentric endurance exercise by hiking downhill a path in the Austrian alps covering a difference in altitude of 540 meters; for the upward way a cable car was used, where compliance was measured electronically. The area under the triglyceride curve according to Patsch was measured after a standardized oral fat load; together with postprandial trigylcerides also postprandial leukocytes were measured.

Results Both postprandial triglyceridemia (from 1762 ± 880 mg * dl – 1 h – 1 at baseline to 1417 ± 664 mg * dl – 1 h – 1; p < 0.001) and postprandial leukocytes (from 68.8 ± 11.6 G * L – 1 h – 1 to 66.5 ± 13.6 G * L – 1 h – 1; p = 0.031) were reduced significantly with 8 weeks of eccentric endurance exercise.

Conclusions Eight weeks of modestly strenuous eccentric endurance exercise significantly reduce postprandial triglyceridemia and postprandial inflammation.

Type 2 Diabetes Significantly Modulates the Impact of TCF7L2 rs7903146 Variant on the Risk of Coronary Atherosclerosis 102

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Background Variations in the transcription factor 7-like 2 (TCF7L2) gene, particularly rs7903146, increase the risk of type 2 diabetes (T2DM). Coronary artery disease (CAD) is the most frequent cause of death in T2DM patients, and CAD shares common risk factors with T2DM. Potential associations between TCF7L2 variant rs7903146 and coronary atherosclerosis are unknown.

Methods We addressed the association between rs7903146 and CAD in a large cohort of 1595 consecutive Caucasian patients undergoing coronary angiography for the evaluation of stable CAD. An additive model of inheritance was used; significant CAD was diagnosed in the presence of coronary stenoses ≥ 50 %.

Results The prevalence of T2DM significantly increased from homozygous carriers of the frequent allele over heterozygous subjects to those who were homozygous for the rare allele (20.3 %, 24.9 %, and 31.3 %; p-trend = 0.001). In the total study cohort, variant rs7903146 was significantly associated with the presence of significant CAD (adjusted odds ratio (OR) 1.27 [1.06–1.51]; p = 0.008). Importantly, subgroup analyses with respect to the presence of T2DM showed a strong and significant association between variant rs7903146 and significant CAD in T2DM patients (n = 373; OR = 1.84 [1.27–2.68]; p = 0.001), whereas in non-diabetic subjects (n = 1222), variant rs7903146 was not associated with significant CAD (OR = 1.08 [0.88–1.32]; p = 0.446). An interaction term T2DM × rs7903146 was significant (p = 0.004), indicating that this variant had a significantly stronger impact on CAD in patients with T2DM than in non-diabetic individuals.

Conclusion We conclude that T2DM significantly modulates the impact of TCF7L2 rs7903146 variant on angiographically characterized coronary atherosclerosis.

Key Role of Low HDL Cholesterol for the Association of the Metabolic Syndrome With Inflammation 103

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Purpose The association of the metabolic syndrome (MetS) and of the individual MetS stigmata with inflammation in patients undergoing coronary angiography has not been investigated yet.

Methods We enrolled 1010 consecutive patients who were referred to coronary angiography. According to National Cholesterol Education Programme Adult Treatment Panel III criteria, the MetS was defined in the presence of at least 3 out of the 5 quantitatively defined criteria large waist circumference, low HDL cholesterol, high triglycerides, high blood pressure, and elevated fasting glucose.

Results In univariate analyses, hsCRP was higher in patients with the MetS (n = 459) than in those who did not have the MetS (0.46 ± 0.62 vs 0.35 ± 0.49 mg/dl; p < 0.001), and also was higher in patients who fulfilled the large waist (0.44 ± 0.58 vs 0.36 ± 0.53 mg/dl; p < 0.001), the low HDL (0.62 ± 0.80 vs 0.35 ± 0.46 mg/dl; p < 0.001), the blood pressure criterion (0.41 ± 0.57 vs 0.33 ± 0.43 mg/dl; p = 0.016) and the fasting glucose (0.44 ± 0.58 vs 0.35 ± 0.52 mg/dl; p < 0.001) criteria than in those who did not. Importantly however, when all MetS traits were entered simultaneously into one ANCOVA model, only the low HDL cholesterol (F = 26.47; p < 0.001) proved independently associated with hsCRP by means of analysis of covariance after adjustment for age, gender, smoking and LDL cholesterol.

Conclusions We conclude that among angiographied coronary patients, low HDL cholesterol drives the association between the MetS and subclinical inflammation. This observation is well in line with the paramount role of low HDL cholesterol as a marker of cardiovascular risk in this important patient population.

Risk Profile of Statin-Treated Austrian Patients with Cardiovascular Disease 139

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Background and Aim Patients with established cardiovascular disease (CVD) are at a high risk for future cardiovascular events, therefore it is crucial to minimize risk factors in these patients. The cross-sectional Dyslipidemia International Study (DYSIS) aimed at examining persistent lipid abnormalities and other risk factors in patients under statin therapy. Austria participated among 12 countries (Europe, Canada).

Methods Data on consecutive statin-treated Austrian patients were recorded by their treating physicians (GPs and internists) after at least 3 months of statin-therapy. This is an analysis of a subset of patients with CVD defined as coronary heart disease, cerebrovascular disease, heart failure and peripheral artery disease).

Results In this sample of 561 statin treated patients with CVD (mean age 68 years; 64 % male), 72 % of the patients had total cholesterol < 200 mg/dl and 54 % had LDL-cholesterol < 100 mg/dl. HDL-cholesterol > 40 (men)/> 50 (women) mg/dl was not achieved by 70 % of the patients, and 55 % did not reach a triglyceride level of < 150 mg/dl. Among other risk factors the most common were hypertension (86 %) and diabetes mellitus (41 %). The mean BMI was 28 kg/m², 15 % were current smokers, and 51 % had a sedentary lifestyle.

Conclusion Large proportions of patients with CVD in this study showed abnormal lipid values and also a high prevalence of other risk factors despite statin therapy. The results show the need of a more intense lipid management and of increased efforts to reduce other risk factors in these high risk patients.

Genetic Variant rs1051730 C > T in the Nicotinic Acetylcholine Receptor Gene Cluster on Chromosome 15q24 Significantly Predicts Smoking Severity in Coronary Artery Disease Patients 140

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Background Smoking is a major cause of preventable premature death, mainly due to its strong and dose-dependent impact on coronary artery disease (CAD). Recently, genetic determinants of nicotine dependence (which correlates with the amount of smoked cigarettes rather than with the smoker status per se) have been suggested. No data are available for patients already affected by CAD.

Methods We genotyped variant rs1051730 C > T in the nicotinic acetylcholine receptor gene cluster on chromosome 15q24 in a large cohort of 1303 consecutive Caucasian patients with angiographically proven CAD.

Results From our patients, 62.1 % had a history of smoking (n = 809; 226 current and 581 past smokers). Genotype distributions of variant rs1051730 were not significantly different between patients with a history of smoking and those who had never smoked (p_{trend} across genotypes = 0.471). However, the variant among smokers proved strongly predictive for the average amount of cigarettes smoked per day (24/d, 23/d, and 30/d for subjects with the AA, the AT, and the TT genotypes; p < 0.001 for those with the TT genotype vs. carriers of the A allele). This association remained significant after adjustment for age and gender (F = 12.4; p < 0.001).

Conclusions Genetic variant rs1051730 C > T in the nicotinic acetylcholine receptor gene cluster significantly predicts smoking severity in patients with angiographically proven CAD.

Low Serum LDL Cholesterol in Patients with Type 2 Diabetes: An Analysis on Two Different Patient Populations 141

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Background Patients with type 2 diabetes (T2DM) typically exhibit a pattern of dyslipidemia with high triglycerides, low HDL cholesterol, and small LDL particles. We aimed at investigating whether also LDL cholesterol levels are altered in diabetic patients.

Methods Lipid panels were obtained in a consecutive series of angiographied coronary patients (n = 750), and in a large sample of hypertensive outpatients (n = 5949).

Results T2DM patients in the cohort of coronary patients (n = 164; 21.9 %) had significantly higher triglycerides (203 ± 138 vs 153 ± 91 mg/dl; p < 0.001), lower HDL cholesterol (44 ± 14 vs 50 ± 14 mg/dl; p < 0.001), lower apolipoprotein A1 (140 ± 28 vs 148 ± 28 mg/dl; p = 0.002), lower total cholesterol (211 ± 48 vs 220 ±

42 mg/dl; p = 0.006) and, importantly, lower LDL cholesterol (122 ± 38 vs 134 ± 35 mg/dl; p < 0.001) than non-diabetic subjects. Whereas apolipoprotein B was similar in T2DM patients as in non-diabetic subjects (113 ± 26 vs 114 ± 25 mg/dl; p = 0.648), the LDL cholesterol/apolipoprotein B ratio was significantly lower (1.08 ± 0.24 vs 1.18 ± 0.21; p < 0.001) and LDL particles were significantly smaller (257 ± 7 vs 259 ± 6; p < 0.001) in T2DM patients. Also among the hypertensive subjects, diabetic patients (n = 1632; 27.3 %) besides higher triglycerides (173 ± 70 vs 151 ± 65 mg/dl; p < 0.001) and lower HDL cholesterol (53 ± 17 vs 57 ± 19 mg/dl; p < 0.001) exhibited lower total cholesterol (216 ± 44 vs 222 ± 41 mg/dl; p < 0.001) and lower LDL cholesterol (127 ± 40 vs 136 ± 37 mg/dl; p < 0.001) than non-diabetic subjects.

Conclusion Both among angiographied coronary patients and hypertensive outpatients, LDL cholesterol is significantly lower in T2DM patients than in non-diabetic individuals.

Postprandiale Hyperglykämie ist prädiktiv für zukünftige kardiovaskuläre Ereignisse bei angiographierten Koronarpatienten 074

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Hintergrund Die Prävalenz von Glukosestoffwechselstörungen bei Patienten mit KHK ist hoch. Bisher ist unklar, ob postprandiale Hyperglykämie mit einem erhöhten Risiko für zukünftige kardiovaskuläre Ereignisse in diesem Patientenkollektiv assoziiert ist.

Methoden und Resultate Wir untersuchten 1040 Patienten, die einer elektiven Koronarangiographie bei Verdacht auf KHK unterzogen wurden. Bei Patienten ohne vorbestehenden Diabetes mellitus wurde ein oraler Glukosetoleranztest (oGTT) durchgeführt. Prospektiv wurden kardiovaskuläre Ereignisse über im Mittel 3,8 Jahre registriert.

394 Patienten hatten eine normale Glukosetoleranz, 280 eine postprandiale (Postbelastungs-) Hyperglykämie (gestörte Glukosetoleranz und Diabetes mellitus Typ II anhand des oGTT) und 366 einen konventionellen Diabetes mellitus Typ II.

Die Inzidenz vaskulärer Ereignisse war signifikant höher bei Patienten mit postprandialer Hyperglykämie und bei Patienten mit konventionellem Diabetes mellitus im Vergleich zu Patienten mit normaler Glukosetoleranz (23,6 % und 29,5 % vs. 18,5 %; p = 0.013 bzw. p < 0.001). Die korrigierten Hazard Ratios waren 1,50 ([95 %-CI: 1,06–2,15]; p = 0.022) für Patienten mit postprandialer Hyperglykämie und 1,81 [1,3–2,48]; p < 0.001) für Patienten mit konventionellem Diabetes mellitus.

Schlussfolgerung Postprandiale Hyperglykämie ist signifikant prädiktiv für zukünftige kardiovaskuläre Ereignisse bei angiographierten Koronarpatienten. Ein oGTT bei diesen Hochrisikopatienten ist sinnvoll, um jene Patienten mit besonders ungünstiger Prognose zu identifizieren.

Insulin Resistance is Associated with Metabolic Syndrome but not with Angiographically Determined Coronary Artery Disease 082

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Objectives Insulin resistance (IR) is the key feature of the metabolic syndrome (MetS) and in prospective studies predicts atherothrombotic events. Its association with directly visualised coronary atherosclerosis is unclear. We hypothesised that IR is associated with both angiographically determined coronary artery disease (CAD) and with the MetS.

Methods We enrolled 986 consecutive patients undergoing coronary angiography for the evaluation of suspected or established stable CAD; significant CAD was diagnosed in the presence of significant coronary stenoses with lumen narrowing ≥ 50 %. IR was determined by the HOMA index; the MetS was defined according to ATPIII criteria.

Results HOMA IR scores were significantly higher in MetS patients than in subjects without the MetS (6.4 ± 2.1 vs 2.2 ± 2.0; p < 0.001). In contrast HOMA-IR did not differ significantly between patients with significant CAD and those who did not have significant CAD 4.3 ± 18 vs 3.2 ± 4; p = 0.141). When both, the presence of MetS and of significant CAD were considered, HOMA-IR was significantly higher in patients with the MetS both among those who had significant CAD (7.2 ± 28 vs 2.3 ± 2.1; p < 0.001) and among those who did not have significant CAD (5.3 ± 5.7 vs 2.1 ± 1.4; p < 0.001) whereas it did not differ significantly between patients with significant CAD and subjects without significant CAD in patients with the MetS (7.2 ± 28 vs 5.3 ± 5.7; p = 0.679) nor in those without MetS (2.1 ± 1.4 vs 2.3 ± 2.1; p = 0.411). Similar results were obtained with the IDF definition of the metabolic syndrome.

Conclusion IR is significantly associated with the MetS but not with angiographically determined coronary atherosclerosis.

Eccentric Endurance Exercise Significantly Improves Fasting Glucose and Glucose Tolerance in Non-Diabetic Subjects 084

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Background Eccentric exercise (i.e. active resistance to muscle stretching, e.g. with hiking downwards) is less strenuous than concentric exercise; its metabolic effects are largely unknown. We aimed at investigating whether eccentric endurance exercise improves glucose tolerance in healthy subjects without diabetes.

Methods Over a training period of 8 weeks, 51 healthy non-diabetic subjects (16 men and 35 women; mean age 50.3 years) 3–5 times per week performed eccentric endurance exercise by hiking downhill a path in the Austrian alps covering a difference in altitude of 540 meters; for the upward way a cable car was used, where compliance was recorded electronically. An oral glucose tolerance test (OGTT) was obtained at baseline and after 8 weeks of eccentric exercise.

Results The eccentric exercise intervention significantly decreased fasting plasma glucose (from 97 ± 6 at baseline to 94 ± 9 mg/dl after 8 weeks of eccentric endurance exercise; p = 0.027). Further, glucose tolerance (which was quantified as the incremental area under the glucose curve) was significantly improved by 9.8 %; p < 0.001.

Conclusions Eccentric endurance exercise even in non-diabetic subjects significantly improves fasting glucose and glucose tolerance. Because elevated fasting and postchallenge glucose values indicate an increased risk of diabetes, eccentric endurance exercise may help to prevent diabetes.

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Long-term Outcome of Patients with Tetralogy of Fallot – A Single Center Experience 052

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Introduction Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease (CHD) with an incidence approaching 10 % of all CHD. The lesion comprises a non-restrictive ventricular septal defect (VSD), an overriding aorta, right ventricular outflow (RVOT) obstruction, and subsequent right ventricular hypertrophy.

Results Of 122 patients (mean age 32.7 ± 10.0 yrs; 79 males), with TOF who were followed-up at the Adult Congenital Heart Disease Center (age > 18 years) at the Vienna General Hospital, 121 patients had an initial repair operation at the median age of 4.0 (2.7; 6.3) years. Forty-two patients (35 %; 26 males) underwent a re-operation 16.5 (10.5; 22.9) years after the initial surgery. By far the most frequent cause of re-operation was the implantation of a homograft in pulmonary position due to pulmonary insufficiency (n = 33) and pulmonary stenosis (n = 5). Within this group 16 patients received the homograft alone, whereas the other 22 patients had accompanying corrections: Reconstruction of the tricuspid valve (n = 11); VSD closure (n = 7); RVOT enlargement (n = 5) and aortic valve replacement (n = 3). Compared to patients who did not require a pulmonary homograft, re-operated patients had prior to implantation a significantly lower left ventricular ejection fraction (EF), 48.9 ± 6.6 vs 52.5 ± 6.0 %; $p < 0.02$; lower right ventricular EF 42.2 ± 10.8 vs 46.3 ± 7.0 %; $p < 0.03$ and a higher regurgitation fraction over the pulmonary valve 45.0 ± 14.1 vs 25.0 ± 14.3 %; $p < 0.001$. Four patients who received no homograft were re-operated because of closure of the VSD. Beside, pacemakers were implanted in two patients due to high grade conduction blocks and one patient who survived a sudden cardiac death received an intra-cardiac defibrillator.

Summary In this single-center collective the long term outcome of patients with surgically corrected TOF was excellent. However a relatively high percentage (35 %) of patients who underwent initial repair operation needed a re-operation, mainly for correction of the pulmonary valve.

1-Jahres-Überlebensrate der Patienten ≥ 80 Jahre nach biologischem Aortenklappenersatz und aortokoronarem Bypass 003

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Hintergrund Die Zunahme des perkutanen Aortenklappenersatzes berechtigt die Notwendigkeit zur Evaluation der Überlebensrate nach operativem biologischem Aortenklappenersatz mit und ohne zusätzlichen aortokoronaren Bypass bei Patienten über 80 Jahren. In dieser Studie wurden Risikofaktoren, die die 1-Jahres-Mortalität beeinflussen, untersucht.

Methodik Retrospektiv wurden im Zeitraum von Jänner 2005–Dezember 2007 154 Patienten (102 w, 52 m) mit einem medianen Alter von 82,9 ± 2,5 Jahren (80–92 Jahre), einem biologischen Aortenklappenersatz mit (n = 80) oder ohne (n = 74) aortokoronarem Bypass unterzogen. Mittels Chi-Quadrat- und Mann-Whitney-Test wurden die Einflussfaktoren auf die Überlebensrate untersucht.

Ergebnisse Das 1-Jahres-Follow-up zeigte eine Überlebensrate von 81,8 %. Nach isoliertem Aortenklappenersatz sind 12 Patienten (7,8 %) und nach einem Kombinationseingriff mit koronarem Bypass 16 Patienten (10,4 %) verstorben. Die präoperativen Risikofaktoren in Bezug auf Mortalität, wie renale Insuffizienz (38,1 % vs. 39,3 %; p = 0,44), COPD (49,2 % vs. 60,7 %; p = 0,45), Diabetes mellitus II (27,8 % vs. 32,1 %; p = 0,82), CAVK (15,9 % vs. 14,3 %; p = 0,94), PAVK (7,9 % vs. 21,4 %; p = 0,07), logistischer EURO-Score (median 12,3 vs. 13,0; p = 0,64) und Kombinationseingriff (50,8 % vs. 57,1 %; p = 0,69) wurden evaluiert. Die einzelnen Risikofaktoren zeigten keinen signifikanten Einfluss auf die Mortalitätsrate bei Patienten ≥ 80 Jahren.

Conclusio Die vorliegenden Daten zeigen gute Ergebnisse der Überlebensraten nach operativem Aortenklappenersatz bei Patienten über 80 Jahren in einem Beobachtungszeitraum von einem Jahr.

Device Closure of Secundum-type Atrial Septal Defect in Adults – Safety and Efficacy 068

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Background Atrial septal defects (ASD) are among the most common congenital heart defects and are frequently not diagnosed before adulthood. If the defect is diagnosed at an early age, the best treatment is to close it electively at age of 3 to 5 years. Volume and pressure-related changes are completely reversible at this time, resulting in normal life expectancy. The aim of the present study was to evaluate the safety and efficacy of catheter interventional ASD closure using the ASO in a single center experience with a large number of adult patients. In particular we sought to investigate whether adult patients with ASD still benefit from late ASD closure and to compare the results of different age groups.

Methods 237 consecutive patients with a mean age of 49 years (SD 17.9; 15–82), who underwent device closure of a secundum-type ASD at the Vienna General Hospital from June 1998 until September 2006 were included. Patient's date of birth, sex, size, weight and dates of interventions were collected in a retrospective database. Interventional data, including stretched ASD diameter, defect rims, device size, intervention time, fluoroscopy time, closure rate and complications were recorded. Examinations were made after 1 day, 1 week, 3–6 months, 12 month and then each year after the implantation, including medical histories, clinical status, electrocardiography (ECG) and transthoracic echocardiography (TTE).

Results There was a significant ($p < 0.05$) decrease of size of the right ventricle (RV) (21.9 % on average) and of the right ventricular pressure (RVP) (17.4 % on average) after device closure. RV and RVP changes were significant in all age groups. We also found a clear improvement in exercise tolerance in all age groups.

Conclusion Due to a very high success rate and a very low complication rate, device closure of secundum-type ASDs using the Amplatzer Septal Occluder is safe and effective in all age groups, even in adult patients. Patients at all ages benefit from ASD closure, including a decrease of RV size and pressure and of dyspnea. When patients get older, their RVP increases. After device closure, there is a decrease of RVP even in older patients, but their RVPs remain at an elevated level. Patients should undergo ASD-closure as soon as the diagnosis is confirmed, even if asymptomatic.

Mitral and Tricuspid Valve Disease in a Patient with Takayashu Arteriitis 053

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Takayashu arteriitis constitutes a rare form of arteriitis ($1/10^{-6}$), usually occurring in young women and associated with a multitude of organ manifestations. In the literature aortic aneurysm, and dissection as well as aortic insufficiency have been associated with this type of vasculitis. Valvular disease other than aortic regurgitation has been rarely described. Three cases of mitral insufficiency have been reported in 1983 and 1993 secondary to severe aortic regurgitation and no case of associated tricuspid valve insufficiency has been publishes as yet.

A 62 years old women with long standing Takayashu disease reported to our department of cardiology with congestive heart failure and signs of cardiac decompensation (NYHA III–IV, ankle oedema, rales, NTproBNP was 23.908 pg/ml), hyponatremia (127 mmol/l) and atrial fibrillation. Echocardiographic evaluation showed mild aortic, severe mitral and moderate tricuspid insufficiency, LVEF was 50 % and, PAP was 80 mmHg assessed from the tricuspid reflow jet. Both arterial and pulmonary hypertension are clinical features reported earlier in Takayashu disease, the combined triple valve insufficiency, however, has not been reported so far. Furthermore, the patient suffered from occlusion of the A. subclavia dextra, multiple smaller and larger aneurisms of the large arteries including

the aorta, dilation of the ascendant aorta with massive calcifications, kinking and aneurysm of the descending infrarenal part of the aorta, 80 % stenosis of the superior mesenteric artery and truncus coeliacus, arteria renalis sinistra, and occlusion of the right renal artery with collaterals from the lumbal arteries, minimal renal insufficiency and coronary heart disease MR showed multiple cerebral white matter lesions and complex degenerative alterations with leucencephalopathy, clinically presenting with progressive dementia and depression (including attempted suicide). In addition, the patient had suffered from Hashimoto Thyroiditis earlier.

The patient was treated with IV furosemide, low dose oral spironolactone, hydrochloriothiazide and candesartan for three days and the signs of cardiac decompensation resolved, NTproBNP returned to 11.281 pg/ml. Sodium has been substituted intravenously. The patient has been discharged with NYHA II–III. Mitral valve repair has been rejected because of progressive dementia and the successful pharmacological treatment. The patient is seen at regular intervals in our out patient clinic and has presented in a stable cardiac condition so far.

In summary, here we present a complex case of Takayashu disease with triple valve disease. Because of co-morbidity pharmacological treatment has been preferred to the surgical option and has proven successful.

The Role of Myeloid Dendritic Cells for Progression of Calcific Aortic Stenosis 036

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Background The degree of valvular calcification predicts disease progression in calcific aortic stenosis (CAS). Recently, dendritic cells (DCs) that ingress from circulating blood have been identified in aortic valves explanted from patients with CAS. We hypothesized that the number of circulating DCs is increased in affected individuals and correlates with disease progression.

Methods Venous blood and aortic valve tissue were obtained from 39 otherwise healthy patients undergoing valve replacement surgery for CAS. 24 healthy individuals served as controls. Circulating myeloid DCs (mDCs) defined as CD14-CD16-CD85+CD33+, plasmacytoid DCs (pDCs) defined as CD14-CD16-CD85+CD123+ and respective cytokines, such as interleukin-1, interleukin-2 and tumor necrosis factor α (TNFα) were analyzed using 5-color flow cytometry. The progression of stenosis is reflected by the echocardiographically assessed mean gradient within one year (mmHg/year).

Results Compared with controls, CAS patients displayed higher numbers of circulating mDCs with increased levels of corresponding cells-bound cytokine TNFα. There was a strong correlation between the number of peripheral blood mDCs and progression of aortic valve disease ($\rho = 0.784$; $p = 0.012$) and a correlation between mDCs and increased levels of TNFα ($\rho = 0.271$; $p = 0.033$)

Conclusion The number of circulating mDCs and cell-bound TNFα, important for differentiation and maturation of dendritic cells are increased in CAS and may serve as biomarkers to predict disease progression in affected patients.

Severe Pulmonary Hypertension and Significant Tricuspid Regurgitation in Patients with Aortic Stenosis – Prevalence and Impact on Surgical Outcome 011

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Background Prevalence and prognostic implications of severe pulmonary hypertension (PHT) and significant tricuspid regurgitation (TR) in patients undergoing valve replacement for severe aortic stenosis (AS) have not been well defined.

Methods In 361 consecutive patients referred for aortic valve replacement for severe AS (age 69.5 ± 10.2 years; 54 % female) prevalence of PHT as defined by a Doppler estimated systolic pulmonary artery pressure (sPAP) ≥ 60 mmHg and of moderate to severe TR were analyzed. The relation of their presence to operative and late mortality was studied. Pre-op. and serial post-op. echocardiographic and clinical examinations were performed.

Results PHT was present in only 24 patients (6.7 %) and moderate to severe TR in only 14 patients (3.9 %), 3 patients had both. Although patients with PHT more frequently had previous valve surgery (27 % vs 6 %; $p = 0.02$) and reduced left ventricular function (24 % vs 5 %; $p = 0.001$) they did neither significantly differ from patients without PHT in operative mortality (8.0 vs 8.2 %) nor in late survival rates (1-, 3-, and 5-year survival rates of 92 %, 87 % and 73 % in patients with PHT vs 91 %, 86 % and 80 % in patients without PHT; $p = 0.5$; Cox regression hazard ratio 1.35). However, of those 10 patients with PHT by echo who eventually underwent invasive measurement, only 6 had sPAP > 50 mmHg and only 2 had a pulmonary vascular resistance (PVR) > 3 Wood units. One of these with a PVR of 5 Wood units died perioperatively.

Patients with significant TR had a higher EURO Score (8.2 ± 2.9 vs 6.2 ± 2.4; $p = 0.004$) and higher rates of previous valve surgery (23 % vs 3 %; $p = 0.0001$) and hypertension (100 % vs 67 %; $p = 0.013$). 1-, 3-, and 5-year survival rates were significantly worse than in patients without TR (77 %, 68 %, and 68 % vs 91 %, 87 % and 80 %; $p = 0.029$; Cox regression hazard ratio 2.65).

Conclusions Severe PHT and significant TR are rare conditions in patients with isolated AS referred for surgery. While moderate to severe TR predicts a poor outcome, PHT by echo may not influence operative and late mortalities. However, these patients frequently do not have severe PHT by invasive assessment and actual pulmonary vascular disease, which must indeed be assumed to raise mortality, is extremely rare.

Mitral Valve Surgery in Current Clinical Practice: Outcome of Valve Repair Compared to Modern Valve Replacement 032

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Background Rate of mitral valve repair (MVRep) has substantially increased over the years, but still a considerable percentage of patients receive mitral valve prostheses (MVP). How much they really lose by not having repair is controversial since studies favoring repair mostly compared to historical series of MVP.

Methods 195 consecutive pts (age, 61 ± 13 years; 51 % female; 53 % degenerative regurgitation (MR); 42 % rheumatic disease; 13 % redo) referred for mitral valve surgery by our outpatient clinic between 1998 and 2007 were included. Type of surgery was assessed and related to operative and late mortality as well as postoperative functional status.

Results Overall, 131 pts had MVP and 64 MVRep. MVP pts did not differ from MVRep pts in age ($p = 0.69$) but were more frequently female ($p = 0.048$). Furthermore, MVP pts had more severe symptoms ($p = 0.01$), a higher Euro SCORE (6.1 vs 5.6; $p = 0.009$) and additional valve surgery was more frequent (52 % vs 23 %; $p < 0.0001$). Operative mortality was higher in the MVP group (6.1 % vs 0 %; $p = 0.044$).

Patients were followed for 3.5 ± 2.4 years (up to 8.7 years). 1-, 3-, and 5-year survival was 93 %, 93 %, 84 % in MVP vs 100 %, 100 %, 100 % in MVRep patients ($p = 0.0015$). By multivariate logistic regression the probability of receiving a mitral prosthesis instead of having repair (propensity score) was calculated. The relationship between type of surgery and survival was evaluated with Cox regression, adjusted for propensity score, propensity score^2 and age. In contrast to age, propensity score, propensity score^2, and MVP were no significant predictors of death ($p = 0.30, 0.34, 0.09$).

When studying unfavorable functional outcome defined as postoperative NYHA class > 2, type of surgery was again not a predictor.

Conclusions Although MVRep is superior to MVP concerning the need for long-term anticoagulation, modern MVP with the pres-

ervation of chordae has less impact on operative mortality, long-term survival and functional outcome than generally thought. The most important determinators of outcome seem to be baseline patient characteristics.

Analysis of Gender Differences Regarding the Size and Type of Aortic Valve Prostheses 033

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Background Whether there are gender differences in the size and type of aortic prostheses irrespective of patients' height and weight has not been assessed so far. We aimed to assess the factors, which influence the choice of prosthesis and to evaluate potential gender specific differences.

Methods 361 consecutive patients who underwent aortic valve replacement for isolated severe aortic stenosis were prospectively analysed. Effective orifice areas (EOA) of aortic prostheses were determined according to the literature. The impact of age, sex, weight, height and type of prosthesis (biological vs mechanical) on EOA were assessed.

Results Male patients on average received larger valves than females ($p = 0.003$) and this difference was present even for men and women of equal height. As a consequence, the presence of patient-prosthesis mismatch was substantially more frequent in female patients (63 % vs 41 %; $p < 0.0001$). The observed decrease of prosthetic size with age ($p < 0.0001$) could be explained by an increasing use of biological valves with smaller EOAs in older patients. However, females under the age of 71 were significantly more often provided with bioprostheses ($p = 0.020$).

A significant increase in prosthetic size with increasing height was only observed in male patients ($p = 0.032$) but not in females. On the other hand, an influence of weight on prosthetic size was only shown in the subgroup of female patients who received mechanical valves ($p = 0.0098$) but not in male patients and females provided with bioprostheses.

Conclusion In this study we observed that irrespective of height, male patients on average are provided with larger aortic valve prostheses than women. In addition, prosthetic size significantly increased with increasing height in men while it did not in women. Although females have a longer mean life expectancy of about 8 years, younger women were significantly more often provided with bioprostheses. The reasons for these differences are unclear. Whether these phenomena can be shown in other institutions as well has to be determined.

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