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Jahrestagung der Österreichischen Kardiologischen Gesellschaft 1. bis 4. Juni 2005, Salzburg

Abstracts

VORTRÄGE

Donnerstag, 2. Juni 2005, 14–15.30 Uhr

Freie Vorträge I – Best Abstracts

TpTe-Interval and Autonomic Tone 103

P. Smetana[1], A. Schmidt[1], V. Batchvarov[2], K. Hnatkova[2], K. Huber[1], M. Malik[2]
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Objective The interval from the peak to the end of the T wave (TpTe) has been proposed to reflect the heterogeneity of action potential durations within the ventricular wall. A prolonged TpTe interval has been suggested to indicate arrhythmic risk. Prolongation of QT interval due to increased parasympathetic tone occurs at night. It is not known to which extent TpTe is influenced by autonomic tone and thus independent of other risk markers.

Methods During 24-hours recordings (SEER MC) in 52 healthy young volunteers (27 f), a 10-second 12-lead ECG was obtained every 30 seconds. Recordings were repeated after 1, 7, and 30 days and results in each subject were pooled together and grouped for day (9 am–8 pm) and night (12 pm–5 am). The QT and QTpeak (QTp) intervals were obtained automatically using QT Guard software (Marquette) and TpTe was computed as the difference between QT and QTp. In each subject values for day and night were averaged over 10 ms RR interval bands from 550 to 1150 ms.

Results (Figure 1) Both QT and QTp interval showed marked prolongation during the night (filled circles) at all investigated RR intervals (900–910 ms day vs. night: QT 390 ± 16 vs. 409 ± 19, $p = 4 \times 10^{-7}$; QTp 289 ± 18 vs. 308 ± 19; $p = 1 \times 10^{-6}$). However, TpTe intervals did not show any difference between day and night (900–910 ms day vs. night: 101 ± 6 vs. 101 ± 9; p = 0.5).

Conclusion Unlike QT and QTp intervals the TpTe interval is not prolonged during the night. This suggests that the TpTe interval is less influenced by autonomic tone. TpTe is therefore likely to provide assessment of arrhythmic risk independent of other markers as heart rate variability.

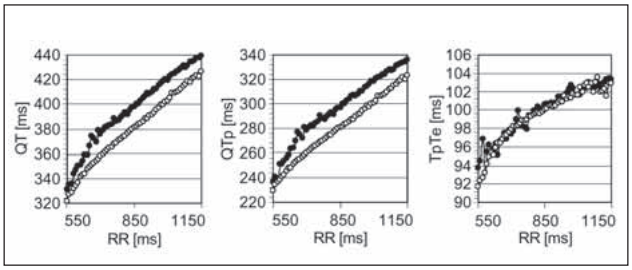

Figure 1: P. Smetana et al.

Datenanalyse der physiologischen Schrittmacherstimulation (AAI-Modus, DDD-Modus) im Langzeitverlauf von 20 Jahren bei Patienten mit Sick Sinus Syndrom 117

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Einleitung Die physiologische Stimulation hat sich in randomisierten Studien in der Behandlung des Sick Sinus Syndroms (SSS) als überlegen erwiesen. Randomisierte Studien, die AAI- mit DDD-Stimulation vergleichen, sind noch nicht abgeschlossen. Wir untersuchten retrospektiv die Mortalität unseres Patientengutes seit 1985.

Patienten und Methodik Bei 692 SSS-Patienten (♂ = 295; 43 %, ♀ = 397; 57 %) wurden Schrittmacher (VVI n = 98, 14,1 %; AAI n = 118, 17,02 %; DDD n = 476, 68,68 %) implantiert und bezüglich des Erstimplantationsalters, der Mortalität sowie der Schrittmacher-Tragzeit bis zum Tod analysiert. VVI-Schrittmacher wurden vorwiegend in den 1980er Jahren implantiert und stellen hier ein historisches Vergleichskollektiv dar.
Kriterien für die Implantationen eines AAI-Schrittmachers waren: normale AV-Leitung, kein Schenkelblock, kein faszikulärer Block, intraoperativer Wenkebach-Punkt > 120/Min. Die Daten der Mortalität beziehen sich auf telefonische Kontakte von Angehörigen/Hausarzt, Meldeamt, Städtische Bestattung.

Ergebnisse Wie aus **Tabelle 1** hervorgeht, ergab sich beim Vergleich der Mortalitätsraten der zwei physiologisch stimulierten Schrittmacher, AAI- und DDD-Modus, eine hoch signifikant (p < 0,001) niedrigere Mortalitätsrate für AAI-Schrittmacher im Vergleich zu den DDD-Generatoren. Auch die Tragedauer bis zum Tod war im Schnitt um 13 Monate länger (n. s.).

Diskussion Unsere retrospektive Analyse ergibt eine deutlich niedrigere Mortalitätsrate beim AAI-Modus mit einer längeren

Tabelle 1: L. Pachinger et al.

	Anzahl der Patienten n (%)	Alter bei Implantation	Mortalität	PM-Tragezeit in Monaten bis zum Tod
SSS-Patienten				
gesamt	692 (100 %)	76,1 ± 9,8	31,09 % (n = 220)	44,7 ± 43,4
DDD	476 (68,6 %)	75,5 ± 9,6	**29,83% (n = 142)***	39,7 ± 35,2
AAI	118 (17,0 %)	76,7 ± 9,8	**11,86% (n = 14)***	52,8 ± 54,3
VVI	98 (14,1 %)	78,3 ± 10,4	65,3% (n = 64)	53,5 ± 55,7

*p < 0,0001

Tragedauer bis zum Tod. Die EKG-Kriterien bei Erstimplantation scheinen ein „gesünderes" Patientengut zu selektionieren. Andererseits weiß man, daß die unnötige und unphysiologische Ventrikelstimulation im DDD-Modus zu einer erhöhten Inzidenz von Vorhofflimmern und einer Reduktion der Pumpfunktion führt.

Schlußfolgerung Die AAI-Stimulation ist im nichtrandomisierten retrospektiven Vergleich der DDD-Stimulation in der Behandlung des SSS überlegen. Man sollte Schrittmacherkandidaten mit SSS diese Therapie nicht vorenthalten. In Zeiten der Gesundheitsökonomie kann zusätzlich eine erhebliche Kostenreduktion (50 %) erzielt werden. 2003 wurden in ganz Österreich bei Patienten mit SSS nur 3 % AAI-Schrittmacher implantiert, an unserem Zentrum 30 %.

Non-invasive Assessment of Hemodynamic Response to Moderate Physical Activity in Patients Undergoing Resynchronisation Therapy 090

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Background Most studies concerning cardiac resynchronisation therapy were performed during resting conditions and there is little information about its effects during moderate physical activity. The aim of our study was to evaluate the immediate effects of biventricular pacing during submaximal exercise on hemodynamic and respiratory parameters.

Methods Eleven patients (4 ♀; age 69 ± 5 y; NYHA II–III; LVEF < 30 %; sinus rhythm, QRS > 130 msec; biventricular DDDR pacemaker implantation > 3 months) underwent a treadmill exercise test using the modified Bruce protocol (2.7 km/h; 9 % elevation; 4.6 METS). Heart rate (HR), mean blood pressure (RR_{mean}), cardiac output (CO) and total peripheral resistance (TPRI) were evaluated noninvasively with the TaskForceMonitor™ (CNSystems). The ventilatory equivalent ($\dot{V}_E/\dot{V}O_2$) and the respiratory exchange ratio (RER) were performed using a V_{max}Spectra System (Viasys). Measurements were performed during a 3-minute exercise period followed by a 10-minute resting period for biventricular pacing (VDD30) as well as during sinus rhythm (VVI30) in each patient. Physical recovery in-between the different modes was proven by measurement of blood lactate levels.

Results Biventricular pacing exhibits an increase in CO (108 ± 14 % vs. 100 %; $p < 0.05$) and a consecutive decrease in RER (0.76 ± 0.04 vs. 0.81 ± 0.07; $p < 0.05$) as compared to sinus rhythm during exercise. RR_{mean} was increased during biventricular pacing by 17 ± 2 % ($p < 0.05$). Furthermore, responders to biventricular pacing (n = 6, defined as a > 10 % increase in CO) had significant lower basal CO (88 ± 22 % vs. 103 ± 3 %; $p < 0.05$) and simultaneous higher $\dot{V}_E/\dot{V}O_{2max}$ (37.6 ± 6.9 vs. 30.0 ± 4.9; $p < 0.05$) levels as compared to non-responders. HR, TPRI and blood lactate levels did not show any changes as compared to sinus rhythm.

Conclusion Biventricular and left ventricular pacing significantly increase CO, RR_{mean} and oxygen uptake in patients with congestive heart failure during rest as well as during physical exercise. The beneficial effect of CRT is augmented during moderate physical activity. Responders to biventricular pacing may be identified by measuring basal CO and $\dot{V}_E/\dot{V}O_2$.

Sex Differences in Regional Repolarisation Heterogeneity 105

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Objective The so-called T-wave residuum (TWR – non-dipolar components of the 12-lead ECG T-wave) was shown to reflect regional heterogeneity of ventricular repolarisation and to provide independent prognostic information on long-term survival in cardiovascular disease patients. TWR was also found larger in women than in men reflecting higher female propensity to Torsades de Pointes. Since significant sex differences between the ascending and descending part of the T-wave were also described, we hypothesised that regional heterogeneities differ during early and late ventricular repolarisation.

Table 2: P. Smetana et al.

TWR_d/TWR_a	Young	Old	p-value
Women	0.36 ± 0.10 %	0.25 ± 0.05 %	0.0004
Men	0.49 ± 0.19 %	0.35 ± 0.12 %	0.0123
p-value	**0.0138**	**0.0033**	

Methods During 24-hours recordings (SEER MC) in 60 healthy volunteers (30 f) of two age groups (A: 25–35 y, B: > 60 y), a 10-second 12-lead ECG was obtained every 10 seconds for 20 minutes combining supine and standing positions. Using custom written software package, the non-dipolar contents of the 12-lead ECG T-wave (that is the signal beyond the 3-dimensional T-wave vector), were obtained for the entire T wave (TWR_t) and for the ascending (TWR_a) and descending T wave limb (TWR_d). Results were compared between age groups and between women and men.

Results As described before TWR_t in women was significantly larger in both age groups (A: 7.3×10^{-4} vs. 3.1×10^{-4}; $p < 0.05$; B: 7.3×10^{-4} vs. 5.0×10^{-4}; $p < 0.05$). However, while TWR_a also was significantly larger in women in both age groups (3.7×10^{-4} vs. 1.6×10^{-4}; $p < 0.05$; B: 4.9×10^{-4} vs. 2.7×10^{-4}; $p < 0.05$), it was the exact opposite for TWR_d (1.2×10^{-4} vs. 6.2×10^{-5}; $p < 0.05$; 1.1×10^{-4} vs. 9.2×10^{-5}; $p = 0.25$). This was especially reflected in the relation of TWR_d/TWR_a which differed not only significantly between women and men but also between old and young.

Conclusion Women and men not only differ significantly in absolute repolarisation heterogeneity but also in its distribution. While women have a more heterogeneous ascending part of repolarisation, their terminal parts of T wave are more homogeneous. Considering that voltage gradients on both sides of the M-region are responsible for the inscription of the ECG T-wave, our findings suggest significant sex differences in electrophysiologic properties across the ventricular wall that also appear to change with age **(Table 2).**

Aortic Valve Calcification Assessed by Multislice Computed Tomography Predicts Short-Term Clinical Outcome in Patients with Asymptomatic Aortic Stenosis 75

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Background The rate of progression in patients with asymptomatic aortic stenosis (AS) varies significantly. The degree of aortic valve calcification diagnosed by echocardiography is a risk factor for poor clinical outcome. However, precise echocardiographic quantification of aortic valve calcification may be unreliable. This work was performed to prospectively analyse the clinical value of aortic valve calcification (AVC) measured by multidetector computed tomography (MDCT).

Methods Possible risk factors for adverse short-term clinical outcome were prospectively tested in 25 patients with asymptomatic moderate to severe AS. These included (1) Agatston calcification score of the aortic valve as assessed by unenhanced MDCT (16 × 1.5 mm, 0.42 sec, TF = 3.5 mm, Sensation 16, Siemens), (2) echocardiographic parameters (aortic valve area calculated by continuity equation, mean and maximal pressure gradients, enddiastolic diameter of the septal wall), (3) laboratory tests (NT-proBNP, CRP).

Results Within 12 months of follow-up, 6 out of 25 patients developed a major adverse clinical event (MACE). All six patients suf-

Table 3: W. Dichtl et al.

Parameter	Unit	MACE (n = 6)	SD	No MACE (n = 19)	SD	p-Value
AVC		6377	2282	2323	982	< 0.01
P_{mean}	mmHg	36	9	27	9	0.05
P_{max}	mmHg	56	12	44	13	0.06
AVA	cm^2	0.75	0.14	0.88	0.251	0.23
EDD Sept	mm	13.8	2.1	12.9	1.9	0.40
NT-proBNP	ng/L	1268	1328	544	1066	0.07
CRP	mg/dL	0.89	1.07	0.45	0.60	0.12

fered from onset of symptoms accompanied by hemodynamic progression. Four underwent aortic valve replacement, one patient so far denied operation, and another individual was not accepted for surgery and died of sudden death soon afterwards. Baseline characteristics of the patients with and without MACE are presented in **Table 3.**

Conclusions AVC is a strong predictor of hemodynamic progression of aortic stenosis and onset of symptoms requiring valve replacement within 12 months. In these patients, close follow-up examinations are mandatory and early elective surgery may be considered even in the absence of symptoms.

Characterisation of Coronary Soft-Tissue Plaques Using 16-Slice Multidetector Computed Tomography (16-MDCT) 080

T. Postel[1], M. Frick[1], G. Feuchtner[2], H. F. Alber[1], R. Zwick[1], G. Friedrich[1], O. Pachinger[1], D. zur Nedden[2], F. Weidinger[1]
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Background In addition to the detection of coronary artery stenoses, the new generation of Multidetector Computed Tomography (16-MDCT) is now being explored for the assessment of plaque morphology. Although a good correlation between MDCT and intracoronary ultrasound (ICUS) was found for detecting calcified plaques, data on soft-tissue plaque characterisation by MDCT are controversial. The aim of our study was to compare the efficacy of MDCT in the characterisation of non-calcified coronary artery plaques with ICUS.

Methods Eighteen patients (age 60 ± 9 years) undergoing selective coronary angiography (CA) were included. All patients underwent MDCT-angiography (Siemens, Sensation 16, Forchheim, Germany) on the day before CA. ICUS (Boston Scientific, 40 MHz, automatic pullback of 0.5 mm/sec) was performed in all patients following CA. Overall 42 coronary segments in 19 vessels (according to AHA classification) were assessed. The mean HU (Hounsfield unit) of soft-tissue components were measured using MDCT. According to ICUS the soft tissue components were divided into two groups: (1) hypodense (plaque area composed of tissue producing echoes with an echogenicity less than that of the adventitia) and (2) hyperdense (plaque area composed of tissue producing echoes with an echogenicity as bright or brighter than that of the adventitia, but with no acoustic shadows) lesions.

Results Using MDCT 34 of 42 coronary segments were eligible for evaluation. Overall 28 plaques were identified. Out of 21 soft-tissue components, we found 8 hypodense and 13 hyperdense lesions according to ICUS criteria. The corresponding mean HU in MDCT between hypodense and hyperdense lesions were significant different (48 ± 24 vs. 122 ± 48 HU; p = 0.002).

Conclusion In sonographically hypodense and hyperdense coronary lesions, HU are significantly different on MDCT images, suggesting a good correlation with the gold standard (ICUS) for coronary plaque characterisation. The use of MDCT for detection of soft-tissue plaques in coronary arteries is attractive due to its non-invasiveness and its role in this needs to be explored in prospective studies.

Freie Vorträge II – Best Abstracts

Incidence of Thrombus Formation on Patent Foramen Ovale and Atrial Septal Defect Closure Devices 056

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Background Device closure of patent foramen ovale (PFO) or small atrial septal defects (ASD) is a suitable therapy for well selected patients after an embolic event. The procedure itself is safe and effective, however, a few potential complications have to be kept in mind. Amongst them, thrombus formation on the closure device is of major importance. In the literature there is ongoing controversy, whether differences exist between various devices regarding the risk of thrombus formation. Therefore, we reviewed our own patient registry (TACET = The Austrian Paradoxical Cerebral Embolism Trial) with respect to this particular question.

Patients and Methods In our institution, 112 patients [53 male (47 %); mean age 43 ± 11 years, age range 15–63 years] underwent PFO and/or ASD transcatheter closure between October 2002 and July 2004. All patients had suffered a cerebral embolic event and were considered for PFO/ASD closure because of a spontaneous or provokable right-to-left shunt during contrast transesophageal echocardiography (TEE). We used an Amplatzer occluder in 48 (43 %), a CardioSeal in 28 (25 %), a CardiaStar in 22 (19.5 %), and a StarFlex in 14 (12.5 %) patients. Device deployment was performed with TEE-guiding. All patients had a transthoracic echocardiogram (TTE) the day after the procedure, and a thorough TEE follow-up six months later. Periprocedurally, enoxaparin (1mg/kg subcutaneously bid) was administered to each patient. In addition, 5,000 IU of unfractionated heparin were injected intravenously in the cath lab. Antiplatelet therapy, started with the embolic event, was maintained for at least six months after the procedure.

Results The postprocedural TTE study was unremarkable in all patients. In two cases (1.8 %), six-month TEE follow-up revealed a small thrombus (1 × 1 mm) on the left atrial side of the device. Both patients had received an Amplatzer occluder. Antiplatelet therapy was maintained for another six months in both patients. None of them suffered a recurrent embolic event, and no more thrombus could be detected by repeated TEE.

Conclusions With current anticoagulation regimen the incidence of thrombus formation on PFO and ASD closure devices is low. In contrast to reports in the literature, thrombi may occur on Amplatzer devices as well. A period of six months of antiplatelet therapy seems to be adequate in most patients, however, thorough TEE evaluation is mandatory before termination.

Mobilfunkgesteuertes Telemonitoring von Patienten mit chronischer Herzinsuffizienz nach akuter kardialer Dekompensation: erste Daten der MOBITEL-Studie

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Hintergrund Chronische Herzinsuffizienz ist eine progrediente Erkrankung mit einer hohen Hospitalisierungsrate. In der prospektiv randomisierten, multizentrischen MOBITEL-Studie wird untersucht, ob mittels telemedizinischer Überwachung durch einen Studienarzt unter Zuhilfenahme eines internetbasierenden, mobilfunkgestützten Home-Monitoringsystems eine kardiale Dekompensation frühzeitig erkannt und somit die Rehospitalisierungsrate und Mortalität reduziert werden können.

Patienten und Methodik Patienten mit chronischer Herzinsuffizienz werden nach Hospitalisierung wegen kardialer Dekompen-

sation in die Kontrollgruppe (mit medikamentöser Therapie) oder in die Telemonitoring-Gruppe (mit medikamentöser Therapie plus telemedizinischem Home-Monitoring) randomisiert. Die Patienten der Telemonitoring-Gruppe werden mit einer Personenwaage, einem Blutdruckmeßgerät und einem Mobiltelefon ausgerüstet und senden während der Studiendauer von 6 Monaten ihre Vitalparameter täglich via Mobiltelefon an die Monitoring-Zentrale.

Resultate In 6 Studienzentren wurden bisher 71 Patienten (50 ♂, 21 ♀, Alter 64 ± 10) randomisiert, davon haben 57 Patienten die Studie bereits beendet. Telemonitoring-Gruppe: 28 Patienten (20 ♂, 8 ♀; Alter 63 ± 10); NYHA-Klasse (nicht primärer Endpunkt) bei Studieneinschluß: I (1 Patient), II (3), III (20), IV (4) (Mean 2,93 ± 0,58); NYHA-Klasse bei Studienende: I (9), II (8), III (7) und IV (4) (Mean 2,37 ± 1,07; p = 0,004). Kontrollgruppe: 29 Patienten (20 ♂, 9 ♀, Alter 64 ± 10); NYHA-Klasse bei Studieneinschluß: II (6), III (17), IV (6) (Mean 3,10 ± 0,65); NYHA-Klasse bei Studienende: I (2), II (11), III (11) und IV (5) (Mean 2,90 ± 0,87; p = 0,376). Während bei Studieneinschluß in bezug auf die NYHA-Klasse kein Unterschied zwischen der Telemonitoring-Gruppe und der Kontrollgruppe (2,93 ± 0.58 vs. 3.10 ± 0.65; p = 0,583) bestand, zeigte sich bei Studienende ein signifikanter Unterschied zugunsten der Telemonitoring-Gruppe (2,37 ± 1,07 vs. 2,90 ± 0,87; p = 0,020). Im Mittel übertrug jeder Patient 149mal seine Vitalparameter, eingenommene Medikation und Wohlbefinden. In 969 Fällen kam es zu einer Verletzung der bei Studienbeginn individuell festgesetzten Grenzwerte, was zu einer automatischen E-Mail-Benachrichtigung des Studienarztes führte. Daraus resultierten 93 Patientenkontakte und 25 Therapieänderungen.

Zusammenfassung Die Zwischenergebnisse der MOBITEL-Studie geben einen klaren Hinweis darauf, daß durch telemedizinische Überwachung von Patienten mit chronischer Herzinsuffizienz nach akuter Dekompensation die Therapie optimiert und in der Folge die körperliche Leistungsfähigkeit signifikant verbessert werden kann.

Prediction of Neurological Outcome after Cardiac Arrest by Serial Determination of Serum Neuron-Specific Enolase – Final Report on 177 Patients 019

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Abstract Neuron-specific enolase (NSE) is increasingly used as a marker of hypoxic brain damage. The purpose of this prospective study was to evaluate the prognostic value of NSE to predict persistent coma after cardiopulmonary resuscitation.

Methods We examined 227 consecutive patients (pts) (143 men, 84 women, age 16 to 93 years, mean 65) who returned to spontaneous circulation after cardiac arrest (ventricular fibrillation in 119, asystole in 47, and pulseless electrical activity in 61) but were unconscious and mechanically ventilated on admission to the intensive care unit. Serum NSE concentrations (Cobas Core NSE EIA, Roche, normal range 0–15 ng/mL) were serially determined on admission (day 0) and on the following 4 days. Hemolytic samples were discarded. Pts were classified according to the "best-ever achieved" Glasgow-Pittsburgh cerebral performance categories (CPC, 1 to 4) of the Utstein recommendations. 16 of the 227 pts were excluded from the study due to incomplete NSE data and 34 because they died under analgesia/sedation, leaving 177 pts for analysis. To avoid any false positive predictions of persistent coma (CPC 4), sensitivity, positive and negative predictive value and accuracy of the test were calculated for the lowest peak NSE concentration that resulted in a specificity of 100 % in our study population.

Results Until discharge from hospital a total of 118 pts (67 %) regained consciousness, with good cerebral performance (CPC 1) in 46 pts (26 %), moderately impaired cerebral performance (CPC 2) in 37 pts (21 %), and severely impaired cerebral performance (CPC 3) in 35 pts (20 %), whereas 59 pts (33 %) remained comatose (CPC 4). In-hospital mortality was 15 % for pts with CPC 1–3 and 93 % for pts with CPC 4. None of the surviving comatose pts regained consciousness at 6 months follow-up after cardiac arrest. At a specificity of 100 %, a peak NSE concentration of more than 80 ng/mL during the first 4 days after cardiopulmonary resuscitation predicted persistent coma (CPC 4) with a sensitivity of 63 %, a positive predictive value of 100 %, a negative predictive value of 84 % and an accuracy of 88 %.

Conclusion Serial determinations of serum NSE concentration after cardiac arrest are highly predictive of neurological outcome.

Ist BNP ein Prädiktor bei Low-flow-Aortenstenose? Wiener Ergebnisse der TOPAS-Multicenter-Studie 002

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Hintergrund Bei Patienten mit chronischer Herzinsuffizienz stellt das B-Typ-natriuretische Peptid (BNP) einen wichtigen Prognoseparameter dar. BNP wurde als Prädiktor auch bei der Aortenstenose (AS) untersucht, bisher wurden keine Daten für die Untergruppe der Patienten mit Low-flow/low-gradient-AS erhoben.

Methodik Plasma-BNP-Spiegel wurden prospektiv bei 16 konsekutiven Patienten mit Low-flow-AS (effektive Öffnungsfläche < 0,6 cm²/m², mittlerer Gradient < 40 mmHg und LV-Auswurffraktion [EF] ≤ 0,40) bestimmt und Dobutamin-Streßechokardiographie (DSE) durchgeführt. Die Patienten wurden über 2 Jahre beobachtet.

Ergebnisse Das mittlere BNP war zu Studienbeginn deutlich erhöht (729 ± 394 pg/ml), wobei bei keinem Patienten BNP < 100 pg/ml lag (106 bis 1710 pg/ml). Operiert wurden 5 von 16 Patienten (BNP-operierte Patienten vs. nichtoperierte, p = n. s.). Patienten, welche im Verlauf verstarben (alle BNP > 500 pg/ml), wiesen zu Studienbeginn im Mittel höhere BNP-Plasmaspiegel auf als Patienten, welche überlebten (6 Patienten verstorben, 955 ± 389 vs. 10 Patienten überlebt, 596 ± 348 pg/ml; p = 0,05). Postoperativ verstarben 2 Patienten (nach 1 bzw. 12 Monaten; BNP n. s. vs. operierte überlebende Patienten). Von 11 Patienten, welche nur medikamentös behandelt wurden, verstarben 4 Patienten, diese wiesen signifikant höhere BNP-Werte zu Studienbeginn auf (4 verstorben, 1083 ± 418 vs. 7 überlebt, 493 ± 291 pg/ml, p = 0,022). Darüber hinaus zeigten Patienten, welche überlebten, signifikant niedrigere BNP-Verlaufswerte als solche, die verstarben (10 Patienten überlebt, 260 ± 197 vs. 6 Patienten verstorben, 956 ± 384 pg/ml, p < 0,01). Postoperativ fand sich bei den 3 Patienten, welche im Verlauf überlebten, eine deutliche Abnahme der BNP-Werte (präoperativ 833 ± 414, postoperativ 154 ± 85 pg/ml). Patienten, welche im Verlauf ohne Operation klinisch stabil blieben, zeigten häufiger eine Abnahme oder kein weiteres Ansteigen der BNP-Werte. BNP korrelierte invers mit der basalen EF (p < 0,01, t = 0,475). Die EF war nicht signifikant unterschiedlich zwischen überlebenden und verstorbenen Patienten (0,39 ± 0,09 vs. 0,36 ± 0,08, n. s.).

Zusammenfassung BNP ist bei Patienten mit Low-flow-Aortenstenose deutlich erhöht, wobei Patienten mit anhaltend hohen BNP-Werten > 500 pg/ml eine besonders ungünstige Prognose hinsichtlich des Überlebens aufweisen. Postoperativ nimmt BNP bei günstigem Verlauf deutlich ab.

Ischemic Preconditioning Promotes Initial Recruitment of Coronary Collateralisation in Porcine Coronary Occlusion-Reperfusion 001

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Background and Aim Proposed mechanisms for "warm-up" after angina pectoris include ischemic preconditioning and collateral recruitment. Fractional flow reserve (FFR) of > 0.3 measured by pressure wire distal to chronic coronary occlusion discriminates patients

protected by collateral circulation. The aim of this study was to investigate the effect of brief repetitive ischemia on collateral development in porcine coronary occlusion-reperfusion model.

Methods Sixteen pigs underwent 90 min coronary occlusion followed by 60 min reperfusion under general anaesthesia. Preconditioning was obtained in 8 of 16 pigs by 2 cycles of 5 min of percutaneous balloon occlusion of LAD with 2 cycles of 5 min interval of reperfusion before 90 min occlusions. The coronary pressure was measured with pressure wire placed distal to occluding balloon. FFR was calculated as the ratio between the coronary pressure distal to occlusion and the proximal part of the artery. Area at risk and myocardial infarct was determined by blue dye injection and triphenyl tetrazolium chloride staining.

Results The myocardial infarct size, expressed as percentage of area at risk, was reduced in the preconditioning group (17.2 ± 4.3 vs. 23.3 ± 4.7 %, $p < 0.05$). FFR increased gradually during the 90 min occlusion from 0.09 ± 0.1 (occlusion start) to 0.27 ± 0.21 (90 min occlusion) in preconditioning group, and was significantly higher ($p < 0.05$) than the FFR of non-preconditioning group (0.06 ± 0.08) **(Figure 2).** Preconditioning induced significantly higher hyperemic response at the first 10 min after reperfusion (FFR: 1.08 ± 0.11 vs. 0.98 ± 0.06, $p < 0.05$).

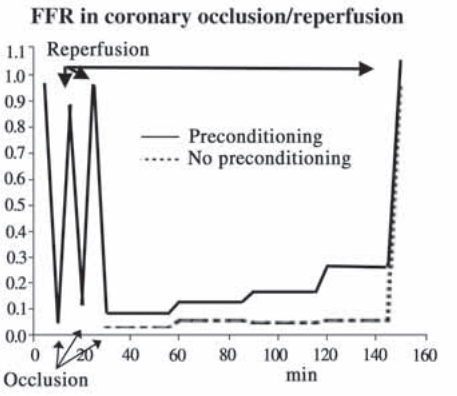

Figure 2:
N. Pavo et al.

Conclusion Brief repetitive episodes of ischemia induce initial collateralisation to the ischemic myocardium paired with reactive hyperemia after reperfusion.

The Complement Component C5a Regulates Matrix Metalloproteinases and Their Inhibitors in Human Macrophages 37

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Background Activation of complement may occur in atherosclerotic lesions. The anaphylotoxin C5a formed during activation of the complement cascade exerts chemotactic and proinflammatory effects. Macrophages may be involved in destabilisation of atherosclerotic plaques by production of matrix metalloproteinases. We examined the effect of C5a on the production of matrix metalloproteinases (MMPs) and their tissue inhibitors of MMPs (TIMPs) in human monocyte derived macrophages (MDM).

Methods and Results rhC5a increased MMP-1 and MMP-9 mRNA levels as detected by RealTime-PCR up to 6-fold, respectively. MMP-2 mRNA was not regulated by C5a whereas mRNA of MMP-3 was not detectable. These results were confirmed on antigen level by ELISA. MMP-1 and MMP-9 activity also increased as detected by a specific activity assay. Levels of TIMP-1 and TIMP-2 mRNA and antigen was up-regulated up to 2-fold, respectively. Pertussis toxin or anti-C5a receptor antibodies, completely abolished the effect of rhC5a on MMP-1 production. Co-incubation with catalase showed no effect, suggesting that the C5a-induced up-regulation of MMP-1 and MMP-9 was not mediated by oxidative burst. Nuclear shift assay revealed that rhC5a stimulated activator protein-1 (AP-1) and NF-κB DNA binding.

Conclusion C5a induce the expression of MMP-1 and MMP-9 in human macrophages in vitro. If this effect is also present in vivo it may play a role in destabilisation of atherosclerotic plaques.

POSTERDISKUSSION A

Donnerstag, 2. Juni 2005; 13–14.00 Uhr

Sitzung 1 – Allgemein I

1-I **096**

Is Watchful Waiting Safe in Severe but Asymptomatic Mitral Regurgitation?

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Department of Cardiology, Medical University Vienna

Background The management of severe but asymptomatic organic (degenerative) mitral regurgitation (MR) remains controversial. The aim of this study was to evaluate a relatively conservative strategy referring patients for surgery when symptoms occur or when asymptomatic patients develop left ventricular (LV) enlargement (endsystolic diameter ≥ 45 mm), impairment of LV-function (EF < 60 %), pulmonary hypertension (PHT, systolic pressure > 50 mmHg) and/or new onset atrial fibrillation.

Methods 132 consecutive asymptomatic patients (age 55 ± 15 yrs, 49 female) with severe degenerative MR who were referred to our outpatient clinic between 1995 and 2002, were prospectively followed until July 2004 (mean follow-up 62 ± 26 months). Patients underwent serial clinical and echocardiographic examinations and were referred for surgery when the criteria mentioned above were fulfilled.

Results 32 of 132 patients eventually underwent mitral valve surgery. Reasons for surgery were development of symptoms (21), LV size or function (10), PHT (10), atrial fibrillation (7). 15 patients fulfilled more than 1 criterion. 4 pts died before surgery (1 sudden death in an 80 year-old man, 3 unrelated to MR). 2 deaths occurred in patients who had refused surgery (1 unknown, 1 cancer). There was no operative mortality. Postoperative outcome was good with regard to survival (no MR-related deaths, 2 deaths following stroke and myocardial infarction, respectively) and symptomatic status (NYHA functional class I in 24 pts, class II in 8 pts). At last follow-up, left ventricular function was normal in 28 of 32 patients. 4 pts with LV-dysfunction had either additional bypass-surgery or required mitral valve replacement (repair unsuccessful). Overall survival for the entire patient group was 99 ± 1 % at 2 yrs, 96 ± 2 % at 4, 91 ± 3 % at 6 and 91 ± 3 % at 8 yrs.

Conclusion Asymptomatic patients with severe organic mitral regurgitation can be safely followed conservatively until either symptoms occur or currently recommended cutoff values for LV size, LV function or PHT are reached. This management strategy is associated with good pre-, peri- and postoperative outcome but requires careful follow-up with serial echocardiographic examinations.

1-II **095**

Pulmonary Hypertension in Atrial Septal Defect: Natural History and Effect on Interventional Outcome in Adults

R. Rosenhek, H. Gabriel, F. Rader, N. Loho, M. Heger, T. Binder, G. Maurer, P. Probst, H. Baumgartner
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Background The natural history of pulmonary hypertension in atrial septal defect (ASD) during adult life and its effect on outcome after late ASD closure has insufficiently been studied.

Methods 190 patients (136 female, 50 ± 18 yrs, range 16–83 yrs) who presented with unrepaired ASD during adult life were included. The relation between pulmonary artery pressure (PAP) and age, defect size, right ventricular (RV) enlargement, and symptoms at presentation was studied. Furthermore, the effect of late ASD closure on PAP and the relation between initial PAP and postinterventional outcome was evaluated.

Results Only 4 of 190 pts presented with severe pulmonary vascular disease (pulmonary vascular resistance > 5 Wood units). All 4 were younger than 30 yrs at presentation and two of them had Eisenmenger physiology. In the remaining 186 pts, PAP was not significantly related to ASD size but correlated closely with age ($r = 0.6$; $p < 0.0001$). Mean syst. PAP was 33 ± 9 mmHg in pts presenting in their 4th decade and increased to 40 ± 12 and 60 ± 17 in those presenting in their 6th and 8th decade, respectively. PAP was strongly related to symptoms and to RV size at presentation. All 186 pts underwent ASD closure. PAP and RV size decreased and symptoms improved in general. However, 11 % of the patients remained symptomatic, PAP remained elevated (> 35 mmHg) in 34 % and RV enlarged (> 40 mm) in 19 %. PAP was again closely related to age ($r = 0.6$; $p < 0.0001$).
By univariate analysis, age, PAP, RV size, and symptoms at presentation but not ASD size were related to postprocedural outcome with regard to symptoms, PAP and RV size. By multivariate analysis postinterventional PAP and RV size were strongly related to their respective preinterventional values. Furthermore, in multivariate analysis, PAP at presentation was the strongest predictor of postprocedural symptoms.

Conclusion Severe pulmonary vascular disease is very rare in ASD and occurs in general during early adulthood. PAP however, continuously increases with age. With rising PAP, the likelihood of an unfavorable outcome after ASD closure with regard to symptoms and persisting elevated PAP increases. Therefore, ASD should be closed as soon as possible even in pts presenting during advanced age.

1-III **030**

Neurohormones Predict Outcome in Asymptomatic Severe Mitral Regurgitation

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Abstract The management of asymptomatic severe mitral regurgitation (MR) remains controversial. This study sought to evaluate whether plasma levels of neurohormones can predict short-term development of symptoms or left ventricular (LV) dysfunction and, therefore, improve timing of surgery.

Methods 78 asymptomatic pts (age 57 ± 15 yrs; 27 female) with severe MR, normal LV function (LVEF > 60 % [64 ± 5 %], LVESD < 45 mm [33 ± 5mm]) and no severe pulmonary hypertension (systolic pulmonary artery pressure [PAP] 36 ± 9 mmHg) were followed for 465 ± 221 days (range 41–811). Clinical and echocardiographic evaluation as well as determination of plasma levels of B-type natriuretic peptide (BNP) and N-terminal BNP (NtBNP) were repeated every 6 months. Endpoints were defined as development of symptoms or of LV dysfunction (LVEF ≤ 60 %, LVESD ≥ 45 mm).

Results 18 of 78 pts became symptomatic during FU whereas no pt developed LV dysfunction. Pts who developed symptoms within the following 6 months had higher BNP and NtBNP levels and higher PAP at their previous visit than those who remained asymptomatic.
By univariate analysis, BNP, NtBNP, and PAP were significant predictors of symptom development whereas LV size and EF were not. ROC-analysis yielded c-values of 0.874, 0.839 and 0.824 for BNP, NtBNP and PAP.

By multivariate analysis, neither BNP nor NtBNP nor PAP reached statistical significance as an independent predictor of symptom development.
A BNP value ≥ 65 pg/mL had a sensitivity of 84 % and specificity of 77 % for symptom development within 6 months. Sensitivity/specificity were 82 %/76 % for NtBNP ≥ 234 pg/mL and 80 %/60 % for PAP ≥ 37 mmHg. Pts with BNP < 47 pg/mL, NtBNP < 182 pg/mL or PAP < 33 mmHg had a very low likelihood to become symptomatic (sensitivity for values beyond these cut-offs 95 %) whereas those with BNP > 93 pg/mL, NtBNP > 510 pg/mL or PAP > 44 mmHg were very likely to develop symptoms during the following 6 months (specificity for values beyond these cut-offs 90 %).

Conclusion BNP and NtBNP are together with PAP predictors of outcome in asymptomatic severe MR. Their serial measurement (every 6 months) appears to allow stratification of these pts into a group likely to benefit from elective surgery, a group that may savely be followed conservatively and an intermediate group that requires further evaluation.

1-IV **32**

Duale Endothelin-Rezeptor-Blockade mit Tezosentan bei akuter pulmonaler Hypertension im experimentell induzierten Lungenschaden

R. Geiger[1], A. Löckinger[2], A. Kleinsasser[2], J. Stein[1], W. Pajk[2], S. Maier[2]
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Hintergrund Die akute pulmonale Hypertension im Rahmen akuten Lungenversagens erschwert den Krankheitsverlauf und verschlechtert die Prognose. Der erhöhte Umsatz endogenen Endothelins-1 spielt bei pulmonaler Hypertension verschiedenster Ursachen nachgewiesenermaßen eine erhebliche Rolle. Wir untersuchten die Wirkung des intravenös verabreichten dualen Endothelin-Rezeptor-Antagonisten Tezosentan bei Mekonium-induzierter, akuter Lungenschädigung im Tiermodell.

Methodik Bei 12 anästhesierten und installierten Schweinen wurde eine akute pulmonale Hypertension durch intratracheale Instilliation einer 20 %igen Mekonium-Lösung induziert. Hämodynamik und pulmonale Gasaustausch-Parameter wurden alle 30 Minuten registriert. Sechs Tiere erhielten 5 mg/kg Tezosentan im Abstand von 90 Minuten, sechs Tiere dienten als Kontrolle.

Ergebnis Tezosentan führte zu einer raschen und anhaltenden Senkung des pulmonal-arteriellen Druckes und Widerstandes (von 33,4 ± 4,0 mmHg auf 24,7 ± 2,1 mmHg [p = 0,001] und von 7,85 ± 1,44 mmHg × L^{-1} × min × m^2 auf 5,25 ± 0,75 mmHg × L^{-1} × min × m^2 [p = 0,0003]). Alle Tezosentan-behandelten Tiere überlebten bis zum Ende der Versuchsdauer, während vier der Kontrolltiere vorzeitig an Rechtsherzversagen starben (p = 0,03).

Schlußfolgerung Die duale Endothelin-Rezeptor-Blockade mit Tezosentan erwies sich als erfolgreicher Therapieansatz bei Mekonium-induzierter pulmonaler Hypertension.

1-V **35**

Effect of Competitive Marathon Cycling on Plasma N-Terminal Pro-Brain Natriuretie Peptide and Cardiac Troponin T in Healthy Cyclists

G. Neumayr[1], R. Pfister[1], G. Mitterbauer[1], G. Eibl[2] , H. Hoertnagl[1]
[1] Institute of Sports & Cardiovascular Medicine, University Clinics of Innsbruck; [2]Department of Biostatistics, University of Innsbruck

N-terminal pro-brain natriuretic peptide (NT-proBNP) and cardiac troponin T (cTnT) are today's preferred humoral marker for heart failure and myocardial injury. Prolonged strenuous exercise may cause cardiac fatigue characterized by transient impaired cardiac function. For a further depiction of exercise-induced cardiac dysfunction we measured NT-proBNP and cTnT in recreational marathon cyclists (n = 29) during the "Ötztal Radmarathon" 2004.

NT-proBNP and cTnT were assessed by standard methods the day before, immediately after, 24 hours and one week after the competition. The workload of the race (total distance: 230 km; altitude difference: 5500 m) is comparable to that of the hardest mountain stages of the Tour de France. In all subjects levels of NT-proBNP rose significantly immediately after race from 27.9 ± 21.1 to 278.4 ± 151.5 ng/L (p < 0.001), fell again on the following day and returned to baseline values one week later **(Figure 3).** The mean percentage increase in NT-proBNP was calculated to be 1128 ± 803 %. There was no correlation between NT-proBNP and baseline features or the markers investigated including cTnT × cTnT, negative in all subjects before, rose transiently in 8 athletes (27.5 %) with levels ranging between 0.043–0.224 µg/L. A day after competition cTnT had normalized again in all athletes **(Figure 4).** Athletes with and without exercise-induced cTnT elevation did not differ in their baseline features, such as age, race time, training-km in 2004, etc.

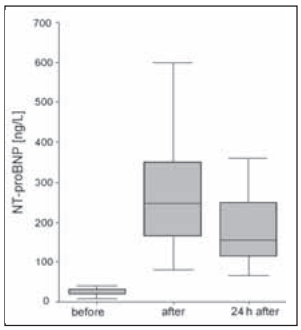

Figure 3: G. Neumayr et al.

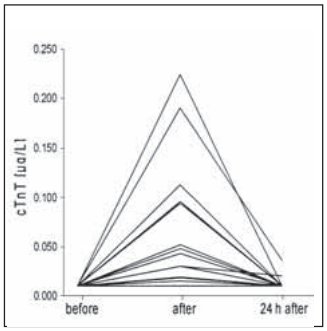

Figure 4: G. Neumayr et al.

Owing to the general physiological effects of BNP and the release kinetics observed we consider the deflection of NT-proBNP to be the adequate volume-regulatory response of a haemodynamically stressed myocardium to cardio-renal distress. The observed kinetics of cTnT substantiates a release from the free cytoplasmatic pool due to the half-life of cytosolic cTnT (6 h). As the underlying mechanism we suppose an exercise-induced overload of free radicals by the oxidative long-term stress which causes a hasty cardiomyocyte-membrane leakage with some egress of cytosolic cTnT into circulation. In healthy cyclists transient increases in NT-proBNP and cTnT are more likely to reflect reversible cardiac fatigue than irreversible cardiac injury or dysfunction in respect of the typical release kinetics of the indicators.

1-VI **097**

Predictors of Outcome in Severe but Asymptomatic Mitral Regurgitation

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Department of Cardiology, Medical University Vienna

Background Current guidelines for surgical intervention in valvular mitral regurgitation (MR) include: onset of symptoms, left ventricular (LV) endsystolic diameter ≥ 45 mm, ejection fraction < 60 %, pulmonary hypertension (systolic pressure > 50 mmHg) and new onset atrial fibrillation. The aim of this study was to identify predictors allowing risk stratification among patients having not yet fulfilled these criteria.

Methods The study population comprises 132 consecutive asymptomatic pts (age 55 ± 15 yrs, 49 female) with severe degenerative MR who were referred to our outpatient clinic between 1995 and 2002 and prospectively followed until July 2004. Patients underwent serial clinical and echocardiographic examinations. The following potential predictors for development of above mentioned criteria for surgery were studied: systolic and diastolic LV diameter, presence of hyperdynamic ventricular function, pulmonary artery pressure and clinical risk factors.

Results Kaplan-Meier event-free survival for the entire pt group, with endpoints defined as indication for MV surgery according to guidelines (n = 35) or death related to MR (n = 1) was 92 ± 2 % at 2 yrs, 77 ± 4 % at 4, 63 ± 5 % at 6, and 54 ± 6 % at 8 yrs. Left ventricular enddiastolic diameter (LVEDD) was the strongest predictor

of outcome: Event-free survival for patients with a LVEDD < 60 mm was 95 ± 2 % at 2 yrs, 83 ± 4 % at 4, 74 ± 5 % at 6, and 64 ± 7 % at 8 yrs versus 84 ± 6 %, 61 ± 9 %, 31 ± 11 %, and 23 ± 11 % for patients with a LVEDD ≥ 60 mm (p = 0.0001). Furthermore patients with systolic pulmonary artery pressures > 40 mmHg and patients with hyperdynamic ventricular function were more likely to require surgery during follow-up (p = 0.02 and p = 0.03, respectively). There was a trend towards higher event-rates among patients with left ventricular endsystolic diameter greater than 37 mm (p = 0.07).

Conclusion Among patients with asymptomatic severe MR who have not yet reached indications for surgery according to current guidelines, the strongest predictor of outcome is LVEDD. Patients having a LVEDD of less than 60 mm can be expected to have a good outcome with less than 5 % requiring surgery per year. These patients are particularly unlikely to benefit from early elective surgery.

1-VII **14**

Die Psychodynamik von Angst und Depression in der ambulanten kardialen Rehabilitation

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[2]Ludwig-Boltzmann-Institut für Rehabilitation interner Erkrankungen, Saalfelden

Einleitung Umfangreiche Studien belegen die Bedeutung von Angst und Depressivität für den Verlauf der koronaren Herzkrankheit. Besonders die Kombination von negativem Affekt, hoher subjektiver Belastung und sozialer Inhibition weist auf eine schlechte Prognose hin. Der Einfluß psychosozialer Unterstützung auf diese psychodynamischen Prozesse wurde bisher wenig untersucht.

Methodik In eine Längsschnittuntersuchung wurden Patienten einbezogen, die nach einem kardialen Ereignis an einem einjährigen ambulanten Rehabilitationsprogramm teilnahmen. Dieses umfaßte neben körperlichem Training edukative Betreuung in somatischer und psychischer Hinsicht. Neben somatischen Daten wurden mit zwei Selbstbeurteilungsfragebögen Angst- und Depressionswerte (HADS-D) sowie kognitive und affektive Anteile des Realitätsbezugs (FAPK) erhoben und somit psychodynamische Veränderungen während der Rehabilitation erfaßt.

Ergebnisse Das Gesamtkollektiv umfaßte 343 Patienten, davon 75 % ♂. Das mittlere Alter betrug 59 ± 9 Jahre. Der mittlere Angstscore (A) fiel bis Rehabilitationsende von 6,4 ± 4,1 auf 5,3 ± 3,7 (p < 0,0001), der mittlere Depressionswert (D) von 4,6 ± 3,7 auf 3,7 ± 3,5 (p < 0,0001). Die Zahl der Patienten mit auffälligem A sank von 13,5 % auf 9,7 %, jener mit auffälligem D von 11,6 % auf 9 % (p < 0,001). Eine anhaltend schwere ängstliche oder depressive Symptomatik zeigte sich bei jeweils 5 % der Patienten, die individuelle Änderung von A und D folgte keinem linearen Trend. Es ergaben sich Zusammenhänge mit eigener Krankheitseinschätzung, psychosozialen Faktoren und der Compliance. Die Werte für emotionale Beziehungsleere, soziale Anpassung und Aggression sanken (p < 0,001). Hohe A und D korrelierten mit verminderter Realitätsbewältigung, Zentrierung der Wahrnehmung nach innen, Abwehr von Kontakt und Gefühlen und einer negativ antizipierten Zukunft (p < 0,001).

Schlußfolgerung Anhaltend hohe A und D im Sinne einer eigenständigen Co-Morbidität erschweren das Erreichen des Rehabilitationsziels, jedoch bei ängstlich-depressiver Krankheitsverarbeitung werden die emotionalen Risikofaktoren durch das Rehabilitationsangebot günstig beeinflußt.

1-VIII **022**

Dokumentation und Ergebnisse der ambulanten kardiologischen Phase-III-Rehabilitation in Österreich

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Einleitung Verlaufskontrollen und Ergebnisanalysen sind in der ambulanten kardiologischen Rehabilitation (AKR) zum Erreichen des Rehabilitationszieles und zur Sicherung des langfristigen Therapieeffektes von großer klinischer Bedeutung. Die Arbeitsgemeinschaft für ambulante kardiologische Rehabilitation (AGAKAR) entwickelte ein internetfähiges Programm, das klinisch bedeutsame Daten von AKR-Patienten erfassen und auswerten kann.

Patienten und Methodik Die ersten 8 von derzeit insgesamt 15 an die Datenbank angeschlossenen AKR-Instituten geben ihre Daten ein. Diese werden monatlich ausgewertet und statistisch aufgearbeitet. Zur Zeit verfügt das Auswertezentrum über Aufnahmedatensätze von 267 und über Ergebnisanalysen von 64 Patienten. Die Mittelwerte von Alter, Geschlecht, Diagnose, Risikofaktoren und Medikation vor AKR stimmen gut mit den Daten anderer großer Register überein.

Ergebnisse 84 % Männer und 16 % Frauen werden in Österreich derzeit in ein AKR-Phase-III-Programm aufgenommen. Die häufigste Indikation ist Z. n. AMI (26 %), gefolgt von Z. n. PTCA (14 %) und Z. n. ACBP (12 %). Zum Zeitpunkt des Eintritts in die AKR waren 85 % der Patienten auf ASS und/oder Clopidogrel, 68 % auf Betablocker und 67 % auf ein Statin eingestellt. Die ersten Ergebnisanalysen der AKR-Phase-III-Programme zeigen eine signifikante Reduktion des Risikofaktors Rauchen (von 21 auf 3 % der Patienten); Cholesterin (von 211 ± 60 auf 182 ± 52 mg/dl, p < 0,02) und LDL-C (von 126 ± 45 auf 103 ± 39 mg/dl, p < 0,02). Die Patienten erreichten im Verlauf der Programme eine signifikante Zunahme der körperlichen Leistungsfähigkeit (von 149 ± 41 auf 172 ± 40 Watt, p < 0,02).

Schlußfolgerung Die ersten Erfahrungen mit der AGAKAR-Internetdatenbank beweisen, daß dieses Medium zur Verlaufskontrolle und Ergebnisanalyse der AKR geeignet ist. Die Aufnahmedaten stimmen gut mit den Ergebnissen aus anderen großen Registern überein. Dies zeigt die Homogenität des Patientengutes und rechtfertigt standardisierte Therapieprogramme. Erste Ergebnisse deuten darauf hin, daß die derzeit in den AKR-Instituten angebotenen Phase-III-Programme zur Reduktion von Risikofaktoren und zur Verbesserung der körperlichen Leistungsfähigkeit geeignet sind.

Sitzung 2 – Allgemein II

2-I **5**

Salzburger Herzinfarktregister 2004: Single-Center-Daten einer unselektierten Kohorte aus einer Abteilung mit „Rund-um-die-Uhr-Katheterbereitschaft" – Patientencharakteristika, Management, Outcome

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Einleitung Kardiologische Fachabteilungen mit einem Herzkathetermeßplatz und der Verfügbarkeit eines Rund-um-die-Uhr-Akut-PTCA-Teams stellen eine wesentliche Voraussetzung zur Umsetzung einer optimalen Herzinfarkttherapie dar. Mittels retrospektiver Datenanalyse wurden im Salzburger Herzinfarktregister alle Patienten erfaßt, die mit der ICD-10-Diagnose Myokardinfarkt auf die kardiologische Fachabteilung des LKH Salzburg im Jahre 2004 zugewiesen und stationär behandelt wurden.

Patientencharakteristika n = 499 Patienten, davon 69,2 % Männer (64,5 Jahre ± 13, 1) und 30,8 % Frauen (71,4 Jahre ± 11,7), 23,2 % Diabetiker. 57,3 % STEMI (inklusive LSB), 42,7 % als NSTEMI. Kardiogene Schocks lagen in 6,6 % vor. In 17 % waren die Patienten bereits prähospital oder durch die zuweisenden Spitäler analysiert. Die Untergruppenanalyse ergab 36 % akute Myokardinfarkte (davon STEMI 78,7 %; NSTEMI 21,3 %) und in 64 % subakute Myokardinfarkte (davon STEMI 46,3 %, NSTEMI 54,7 %).

Management Die Mehrzahl der Patienten (87,7 %) wurde einer Koronarangiographie zugeführt, eine Minderheit (12,2 %) der Patienten wurde aufgrund des hohen Alters oder schwerer Co-Morbiditäten primär konservativ behandelt. Bei 78,1 % der angiographier-

ten Patienten wurde eine koronare Intervention vorgenommen, davon in 179 Fällen (54,6 %) in Form einer Akut-PTCA. Bei 66 Patienten (14,6 %) wurde entweder im Gefolge der invasiven Diagnostik nicht interveniert (keine PTCA möglich oder indiziert) oder eine chirurgische Revaskularisation durchgeführt.

Outcome Die In-Hospitalmortalität des Gesamtkollektivs betrug 8,8 %. Bei Exklusion der Schockpatienten reduziert sich die Mortalität auf 4,7 %. Die Mortalität im kardiogenen Schock betrug 66,6 %. Die Mortalität der Patienten, welche mittels Akutintervention behandelt und im Anschluß daran auf der kardiologischen Fachabteilung versorgt wurden, betrug 0,6 %. Die Mortalität der im Subakutstadium versorgten Patienten betrug 6,9 %.

Schlußfolgerung Erfahrungen aus einzelnen Zentren mit der Erfassung von Real-World-Daten dienen dem jeweiligen Zentrum als Qualitätskontrolle. Die Sinnhaftigkeit einer konsequent durchgeführten 24 h/365 Tage/Jahr Akut-PTCA-Bereitschaft für den Myokardinfarkt ist anhand der niedrigen Mortalitätsdaten insbesondere der Akut-PTCA-Patienten dokumentiert.

2-II **031**

Relation of High-Sensitivity C-Reactive Protein to Coronary Artery Disease Severity and Risk Factor Burden

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Background Inflammation is an inherent process in coronary artery disease (CAD) measurable by levels of high-sensitivity C-reactive protein (hsCRP). HsCRP may be used for risk stratification in primary and secondary prevention. Whether CRP is actively involved in atherogenesis, reflects risk factor burden and/or functions as a marker for the presence of CAD is still debated. The aim of this study was to investigate the correlation of hsCRP levels with the severity of CAD and risk factors in consecutive patients undergoing coronary angiography.

Methods 2000 consecutive patients undergoing coronary angiography were prospectively analysed. Patients with valvular or congenital heart disease and patients with acute coronary syndromes were excluded. Cardiovascular risk factors were assessed by routine laboratory and questionnaire. HsCRP was determined by Latex agglutination assay. Severity of CAD was graded by visual estimation of lumen diameter stenosis. Significant stenoses were defined as lumen diameter reductions ≥ 50 % in at least one major coronary vessel. Coronary angiograms were graded as 1-, 2- or 3-vessel disease (VD) or as non-CAD.

Results HsCRP levels were higher in patients with CAD (n = 1528) compared to non-CAD patients (n = 472) (1.32 ± 2.63 vs. 0.78 ± 1.97 mg/dL; $p < 0.0001$), but were not different between 1-VD (n = 850), 2-VD (n = 335), and 3-VD (n = 343). CAD patients were older (65.1 ± 10.4 vs. 61.2 ± 10.5 years; $p < 0.0001$), more often had diabetes (18.4 vs. 10.8 %; $p = 0.001$) and hypertension (76.1 vs. 63.2 %; $p = 0.001$), had lower LDL cholesterol (123.3 ± 37.9 vs. 127.7 ± 38.9 mg/dL; $p < 0.05$) and HDL cholesterol (49.6 ± 14.0 vs. 59.2 ± 18.1 mg/dL; $p < 0.0001$) and higher triglycerides (154.5 ± 110.0 vs. 136.5 ± 93.3 mg/dL; $p < 0.005$). Prior statin use (44.4 vs. 31.8 %; $p < 0.001$) was more common in CAD compared to non-CAD patients. Overall, hsCRP was higher in diabetics vs. non-diabetics (1.48 ± 2.96 vs. 1.11 ± 2.34 mg/dL; $p < 0.0001$) and in smokers vs. non-smokers (1.53 ± 2.90 vs. 1.10 ± 2.35; $p < 0.001$), but was not different in hypertensive vs. non-hypertensive patients and between patients with and without prior statin therapy. The total number of risk factors was not associated with hsCRP levels.

Conclusion In this large consecutive patient cohort, hsCRP is higher in CAD than in non-CAD patients, but is not related to severity of CAD or total number of risk factors. This data suggest that hsCRP is a marker for the presence of CAD, but seems not to reflect total risk factor burden.

Tabelle 4: A. Jezl et al.

Patienten mit ACS (n = 32)	IA (n = 9)	NSTEMI (n = 14)	STEMI (n = 9)
Alter (Jahre)	81 ± 7	79 ± 12	73 ± 16
Keine AP-Symptomatik bei Aufnahme (n)	4	8	3
Typische AP < 6 h (n)	4	1	2
Chron. Immobilität (bei Aufn./Ent.) (%)	22,2/33,3	35,7/44,4	44,4/40,0
Reanimation (prähospital) (n)	2	0	1
Respiratorische Insuffizienz bei Aufnahme (n)	2	5	1
Akute Dekompensation/Arrhythmie (n)	0	3/1	3/1
Rezenter Insult (n)	0	0	2
Koronarintervention (n)	3	3	2
Lyse (n)	0	0	3
Tod (n)	0	5	4

2-III **115**

ACS in einem großstädtischen Versorgungsspital – Patientencharakteristik und Prognose

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In den den Guidelines zur Therapie des akuten Koronarsyndroms (ACS) zugrundeliegenden Studien mit Fibrinolyse und Koronarintervention wird die 30-Tages-Mortalität mit 6–7 % (STEMI) angegeben; die Letalität der nicht im Protokoll inkludierten Patienten dieser kardiologischen Zentren liegt bei 16,8–19,7 %.

Wir erhoben den Krankheitsverlauf und die Anwendbarkeit der ACS-Therapieempfehlungen für ein konsekutives Patientengut (I/II 2005), bei dem in einem von kardiologischen Spezialzentren umgebenen großstädtischen Versorgungsspital ein ACS diagnostiziert wurde: n = 32; ♀ = 9; ♂ = 23; Alter: 78 ± 12 Jahre; Hypertonie (78,13 %); Diabetes-mellitus-Therapie (43,75 %); Status post MCI/Status post Koronarintervention (31,25 %) **(Tabelle 4)**.

Patienten mit Koronarintervention waren deutlich jünger (65 ± 11 J.) im Vergleich zu Patienten, bei denen eine Kontraindikation gegen eine Intervention bestand (83 ± 8 J.).

Die ACS-Patienten in unserem nichtkoronarintervenierenden Versorgungskrankenhaus sind überwiegend hochbetagt und weisen zumeist bei längerer Anamnese inital keine typische AP-Symptomatik auf. Die Gesamtmortalität von 28,13 % ist durch die prähospitale Vorselektionierung, die Co-Morbiditäten und die Limitationen in der Umsetzbarkeit der Guidelines bei diesem Patientengut erklärbar.

2-IV **10**

Wochentags- und Monatsverteilung der akuten Herzinfarkte in Wien 2002

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Einleitung Wetterbedingte (Winter) und psychische Belastungen (Weihnachten, Wochenbeginn?) führen zum vermehrten Auftreten von AMI. Anhand der im Jahr 2002 aus den Spitälern des Wr. Krankenanstaltenverbundes entlassenen Pat. mit AMI (ICD-10 121) wurde die Monats- und Wochentagsverteilung der AMI unter Berücksichtigung des Geschlechtes, der Morbidität (MOB) und der Spitals-Letalität (LET) analysiert.

Ergebnisse Unter 1520 PatientInnen (62 % ♂, 48 % ♀) im Alter von 68 J (25–99 Jahren), die 1–5 × (insgesamt 1.844 ×) mit AMI stationär aufgenommen wurden, waren die Monate Dezember (9,76 % aller 2002-AMI) und Jänner (9,6 %) die stärksten Aufnahmemonate, wohingegen im Ferienmonat August nur 6,13 % der jährl. AMI anfielen. Das Verhältnis ♂ zu ♀ schwankte nur gering, ist im

März mit 60 % ♂ am höchsten und im August bei absolut niedrigster AMI-Anzahl auch rel. mit 33 % am geringsten. Die monatliche LET ist naturgemäß im Dezember und im Jänner mit 18,89 % und 18,64 % weitaus am höchsten und im Juni bzw. im Oktober am niedrigsten (10 % bzw. 10,7 %). Bei geschlechtsspezifischer Betrachtung sterben ♀ mit AMI im Jänner, Dezember und im August am meisten, die ♂ vor allem im Mai, August und Dezember. Hinsichtlich der Wochentage treten die meisten AMI zum Wochenbeginn (16,76 % am Mo) auf, die wenigsten zum Wochenende (Sa 11,44; So 11,06 %). Am Mo ist der Anteil der ♂ mit 17,5 % gegenüber dem der ♀ deutlich höher, wohingegen ♀ am Sa gegenüber den ♂ einen höheren AMI-Anteil aufweisen. Die Tage mit der höchsten AMI-LET sind der Sa (17,4 %) und der Mi (17,1 %). Die niedrigste LET findet sich am Fr (11,7 %) und Mo (12,5 %). Bei geschlechtsspezifischer Betrachtung versterben ♂ gleich häufig am Sa und Mi (je 17,6 %), wohingegen bei ♀ die LET am Fr signifikant niedriger ist (7,4 %), zum Wochenende aber auch zur Wochenmitte wieder ansteigt (17,2 % bzw. 16,4 % am Mi).

Schlußfolgerung Die AMI-MOB zeigt ein Hoch zum Jahreswechsel und ein Tief zu „Ferragosta", wobei dann, verglichen mit den anderen Monaten, eine hohe LET auftritt. Machen die Patienten einen AMI vor allem zum Wochenbeginn durch, so versterben sie zum Wochenende und zur Wochenmitte.

2-V **9**

Geschlechts- und altersabhängige Morbidität (MOB) und Letalität (LET) der akuten Herzinfarkte (AMI) in Wien

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Einleitung Außer den Berichten der Gesundheitsstatistik liegen für die Regionen Österreichs keine detaillierten Registerdaten o. ä. vor, die Rückschlüsse auf MOB und LET beim AMI ermöglichen. Es wurden daher alle im Jahr 2002 aus den Spitälern des Wr. Krankenanstaltenverbundes entlassenen Patienten mit AMI (ICD-10 121) hinsichtlich des Geschlechts, des Alters, des Wohnortes und der Spitals-LET analysiert.

Ergebnisse 1520 PatientInnen (62 % ♂, 48 % ♀) im Alter von 68 J (25–99 J) wurden 1–5 × mit AMI stationär aufgenommen. ♀ waren mit 74 J um 10 Jahre älter als ♂ ($p < 0{,}002$). Die LET war mit 14,3 % unter dem österr. Durchschnitt (16 %), ebenso bei den ♀ mit 10,6 % und ♀ mit 20,4 %. Die meisten AMI-Patienten wohnten in Favoriten (13,3 %, n = 223), gefolgt vom 21. und 22. Bezirk (6,7 % und 5,9 %). Bezogen auf die Einwohnerzahlen (EW) der Bezirke fand sich die höchste Inzidenz (AMI/100.000 EW) ebenfalls im 10. Bezirk (148,04), gefolgt vom 1. (128,99) und 12. (116,27) Bezirk. Der niedrigste AMI-Anteil an der Bevölkerung fand sich im 8. (44,3), 17. und 9. Bezirk. Die LET war bei Patienten aus Hietzing mit 30 % am höchsten, gefolgt von Währing (22,86 %) und Mariahilf (21,21 %). Bei geschlechtsspezifischer Betrachtung starben die meisten ♂ in Hietzing (31,03 %) gefolgt von Döbling, die meisten ♀ in Mariahilf (35 %) gefolgt vom 13. Bezirk (28,6 %). Die niedrigsten LET fanden sich gesamt im 16. Bez. (6,82 %), in Liesing mit 5,26 % bei ♂ und ebendort mit 13,6 % bei den ♀. Es besteht eine signifikante Korrelation zwischen LET und dem durchschnittlichen Alter der AMI-Patienten in den Bezirken ($p < 0{,}01$).

Schlußfolgerung Bei Detailanalyse lassen sich MOB und LET von AMI-Patienten regional aufschlüsseln und sind Basis der Gesundheitsplanung (**Abbildung 5).**

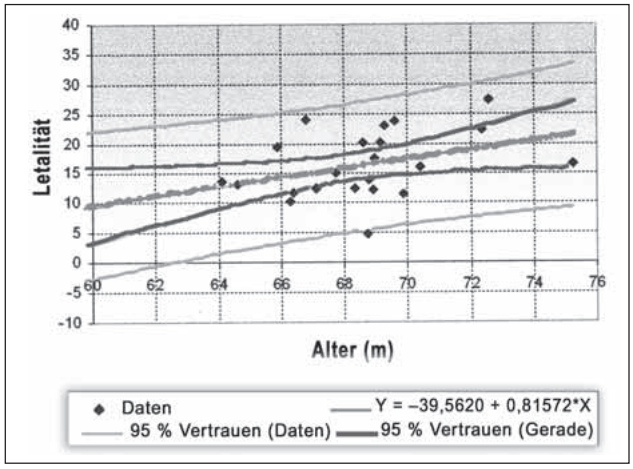

Abbildung 5: H. Weber et al.

2-VI **021**

Tako-Tsubo-Phänomen

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Hintergrund In den letzten Jahren wurde verstärkt Augenmerk auf streßbedingte Auslöser einer Myokardischämie gelegt. Ein unter dem Begriff Tako-Tsubo-Phänomen (japan. Tintenfischfänger) oder apical ballooning zusammengefaßtes Krankheitsbild betrifft vorwiegend Frauen im Alter > 60 Jahre. Häufig ist emotionaler Streß Auslöser einer linksventrikulären Dysfunktion, die mit einer regionalen Wandbewegungsstörung (WBS) der Vorderwand und des Apex sowie einer Hyperkontraktilität der basalen Abschnitte einhergeht. Es besteht ein Mißverhältnis zwischen der ausgeprägten WBS und dem nur mäßigen Anstieg der myokardialen Nekrosemarker. Entscheidend ist der angiographische Ausschluß einer obstruktiv wirksamen KHK und die Normalisierung der Linksventrikelfunktion innerhalb von Wochen.

Fallbericht Eine 63jährige Patientin präsentierte sich mit typischem Thoraxschmerz seit 4 Stunden. Im EKG trat eine ST-Hebung in I, II, aVL und V3–6 auf. Echokardiographisch zeigte sich eine Dyskinesie der distalen Vorderwand und des Apex bei hyperkontraktilen basalen Abschnitten. Labordiagnostisch kam es zu einem diskreten Anstieg der CK auf 151 U/l (Normbereich bis 140 U/l) und des Troponin T auf 0,63 ng/ml (Normbereich bis 0,030 ng/ml). Angiographisch wurde eine KHK ausgeschlossen. Unter konservativer Therapie kam es in der Kontrolle 6 Wochen nach dem Ereignis zu einer Normalisierung der Linksventrikelfunktion.
Anamnestisch waren der Tod des Ehemanns wenige Tage vor der Aufnahme und Suizidgedanken der Patientin am Aufnahmetag (24. Dezember) zu erheben.

Zusammenfassung Der beschriebene Fall reiht sich in eine zunehmende Zahl von Berichten von europäischen Patienten mit einer durch emotionalen Streß bedingten LV-Dysfunktion, die sich klinisch wie ein Myokardinfarkt präsentieren. Obwohl die Patienten in der Regel eine gute Prognose aufweisen, ist noch viel zu wenig bekannt über den Zusammenhang zwischen Streß und myokardialer Schädigung, über Prävention und Therapie

2-VII **6**

Gibt es den „Risikofaktor Frau" bei ST-Hebungsinfarkten (STEMI)?

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Hintergrund Studien haben gezeigt, daß Frauen mit STEMI eine schlechtere Prognose haben als Männer. Ziel ist es, geschlechtsspezifische Unterschiede bei Patienten mit STEMI aufzuzeigen.

Patienten 220 Patienten (168/76 % ♂ und 52/24 % ♀) wurden zwischen 1.3.2003 und 8.12.2004 mit STEMI registriert. Zeitparameter konnten bei 198/90 % Patienten (154/92 % ♂, 44/85 % ♀) erfaßt werden.

Resultate Frauen (♀) waren im Durchschnitt 8 Jahre älter als Männer (♂) (67 ± 15,2 vs. 59 ± 12,4 J), ($p < 0{,}05$). Zeit vom Schmerzbeginn bis zur Einlieferung in das Akutspital: < 6 Std. 146/74 % Patienten (112/73 % ♂, 34/77 % ♀); 6–12 Std. 19/10 % Patienten (15/10 % ♂, 4/9 % ♀); > 12 Std. 33/17 % Patienten (27/18 % ♂, 6/14 % ♀). Während 43/26 % ♂ eine kardiale Anamnese (prior AMI, PCI,

ACBG) angaben, hatten nur 10/19 % ♀ eine kardiale Vorgeschichte aufzuweisen. Infarkt-Lokalisation: ♂ erlitten häufiger einen Hinterwandinfarkt als ♀ (88/54 % vs. 20/39 %), während ♀ häufiger mit Vorderwandinfarkt diagnostiziert wurden (31/60 % vs. 79/47 %). Als Primärtherapie erhielten ♂ in 17/10 % Fällen eine Thrombolyse (TL) und in 151/90 % Fällen eine PCI. Während 50/96 % ♀ eine primäre PCI (PPCI) erhielten, wurde nur 1/2 % ♀ einer TL unterzogen. Eine ♀ lehnte jegliche Therapieform ab. Die „Door to Catheter Time" (DCT) bei PPCI betrug bei 111/74 % ♂ bzw. 40/80 % ♀ weniger als 2 Std. 33/15 % Patienten waren initial im kardiogenen Schock (KS) (21/13 % ♂ vs. 12/23 % ♀). Von diesen 33 Personen verstarben 14/42 % im KS, wobei es sich hier um 4/19 % ♂ und 10/83 % ♀ handelte. Mortalität: Insgesamt verstarben 22/10 % Patienten während des Krankenhausaufenthaltes (8/5 % ♂ vs. 14/27 % ♀, $p < 0{,}01$).

Schlußfolgerung Es zeigte sich, daß Frauen bei höherem Durchschnittsalter seltener eine kardiale Anamnese, jedoch bei gleichem Delay und ähnlicher DCT eine höhere Spitalsletalität insbesondere im KS aufwiesen.

2-VIII **029**

Routine-Koronarangiographie bei Patienten mit perkutaner Karotisintervention: hohe Inzidenz einer signifikanten koronaren Herzkrankheit

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Hintergrund Die Koinzidenz von Schlaganfall bei Patienten (Pat.) mit koronarer Herzkrankheit (KHK) und *vice versa* Myokardinfarkt bei Patienten mit Stenose der Arteria carotis interna (ACI) ist bekannt. Über die Koronarmorphologie bei Pat., die einer perkutanen ACI-Intervention unterzogen werden, gibt es keine systematischen Daten. Ziel der Studie war, die Häufigkeit, Morphologie und klinische Symptomatik einer KHK bei Pat., die einer interventionellen Therapie einer ACI-Stenose unterzogen wurden, festzustellen.

Methodik In einer prospektiven Beobachtungsstudie wurde bei 420 von 444 konsekutiven Pat., die einer elektiven Stentimplantation einer ACI-Stenose unterzogen wurden, eine angiographische Darstellung der Koronararterien durchgeführt. 24 Pat. wurden wegen fehlender Compliance, chronischer Niereninsuffizienz oder Komplikationen bei der Gefäßpunktion von der Untersuchung ausgeschlossen. Bei 390 Pat. erfolgte die Koronarangiographie in einer Sitzung mit der ACI-Intervention, bei 30 Pat. lag eine rezente Koronarangiographie vor. Die Vermessung der Koronarstenosen erfolgte semiautomatisch (Hicor®, Siemens®), Stenosen ≥ 70 % (im Hauptstamm ≥ 50 %) wurden als signifikant definiert. Die klinische Symptomatik wurde entsprechend der Canadian Cardiovascular Society (CCS) eingeteilt. Sämtliche Daten wurden prospektiv erhoben.

Ergebnisse Ein-, Zwei-, Dreigefäßerkrankungen und Hauptstammstenosen wurden bei 70 (17 %), 64 (15 %), 93 (22 %) und 31 (7 %) Pat. festgestellt. 93 dieser 258 Pat. mit signifikanter Koronarstenose hatten eine bekannte KHK, bei 165 Pat. wurde die KHK im Rahmen der Koronarangiographie neu entdeckt. 157 Pat. (61 %) hatten keine klinischen Symptome einer KHK. Bei Patienten mit CCS-III-Angina lagen signifikant häufiger Hauptstammstenosen vor ($p < 0{,}01$), davon abgesehen war der Gefäßbefall statistisch nicht signifikant unterschiedlich verteilt. Die Lokalisation und Morphologie der ACI-Stenose war bei Patienten mit und ohne KHK nicht unterschiedlich. Hypertonie, Herzinsuffizienz, periphere arterielle Verschlußkrankheit und Hypercholesterinämie fanden sich statistisch signifikant häufiger bei Pat. mit KHK. 105 Pat. (61 %) mit einer oder mehreren signifikanten Stenosen wurden interventionell behandelt, davon 82 in der gleichen Sitzung mit der ACI-Stentimplantation, 18 Pat. (7 %) wurden elektiv bypassoperiert, die anderen konservativ behandelt.

Schlußfolgerungen Die routinemäßig durchgeführte Koronarangiographie bei Pat. mit ACI-Intervention ergibt eine hohe Koinzidenz einer signifikanten KHK. Aufgrund des hohen Prozentsatzes koronar asymptomatischer Patienten ist diese einfach in einer Sitzung mit der ACI-Intervention durchzuführende Untersuchung eine sinnvolle Methode zur Diagnostik einer Erkrankung mit hoher klinischer Implikation.

Sitzung 3 – Bildgebung I

3-I **76**

Aortic Valve Area Planimetry Assessed by Multislice Computed Tomography in Patients with Aortic Stenosis

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Purpose To evaluate planimetry of aortic valve area (AVA) in aortic valve stenosis with multidetector computed tomography (MDCT) in comparison to accepted diagnostic standard transthoracic echocardiography (TTE). Retrospective ECG-gating allows an image reconstruction during systole, subsequently a display of aortic valve orifice may be feasible.

Material and Methods 21 patients with asymptomatic mild, moderate and severe aortic valve stenosis were examined prospectively with contrast enhanced MDCT (Somatom Sensation 16, Siemens Medical Systems, Germany) (16 × 0.75 mm; gantry rotation time 0.5 sec, inc. 0.6). 120 mL contrast agent (Visipaque, Amersham) with a concentration of 320 mg was injected intravenously with a flow rate of 3 mL/sec. Scan delay = 30 m/sec. FOV = 21 cm, 120 kV, 250 niAs. Retrospective ECG-gating was performed with mid-late systolic image reconstruction. Images were reconstructed 3-dimensionally with multiplanar reformation (MPR) technique.

Results Planimetry of aortic valve area (AVA) with MDCT was feasible in all patients (n = 21) with a significant correlation to TTE (r = 0.50, p = 0.01, Pearson). Bland-Altman plot shows a good intermodality agreement. Interobserver variability was mean ± 0.03 cm^2.

Conclusions MDCT may provide an accurate new imaging modality for planimetry of aortic valve area (AVA) in aortic valve stenosis.

3-II **079**

Role of 16-Slice Multidetector Computed Tomography in the Assessment of Coronary Artery Stenosis in Everyday Practice: Comparison with Selective Coronary Angiography

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Background Recent studies demonstrated a high sensitivity of 16-Slice Multidetector Computed Tomography (16-MDCT) for the detection of significant coronary artery stenoses. Whether these results are applicable to clinical practice is unclear. The aim of our study was to compare 16-MDCT angiography with selective coronary angiography (CA) regarding the detection of significant coronary artery stenosis in a consecutive series of patients.

Method 93 consecutive patients (mean age: 59 ± 9 years), in whom CA was performed due to stable angina pectoris underwent 16-MDCT angiography (ECG-gated, 16-channel, contrast enhanced MDCT, 16 × 0.75 mm; TF = 6.5 mm/sec; rot.time 0.42 sec – Siemens Sensation 16, Forchheim, Germany) on the day before CA. Patients with diabetes mellitus, serum creatinine > 1.5 mg/dL and/or acute coronary syndromes were excluded. Two observers blinded to CA results evaluated MDCT-angiogram according to standard criteria. Segment-based (13 segments per patient) and patient-based analyses (at least 1 stenosis > 50 % lumen diameter reduction) were performed.

Results In total 1209 segments were analysed. 173 segments (14 %) were excluded due to poor image quality or massive calcification. In 86 segments CA revealed a significant coronary artery stenosis. On segment-based analysis, 16-MDCT revealed 47 stenoses (sensitivity 55 %, specificity 97 %, positive predictive value 64 %; negative

predictive value 96 %). On a patient-based analysis, sensitivity increased to 85 %, whereas specificity remained high (88 %).

Conclusion In this evaluation of consecutive patients, sensitivity of 16-MDCT for the detection of significant coronary artery stenosis was moderate on a segment-based analysis, but increased on a patient-based analysis. Specificity was high in both analyses supporting the usefulness of 16-MDCT for exclusion of significant coronary artery stenosis. Further enhancement of spatial and temporal resolution in MDCT technology will likely lead to a lower exclusion rate and higher sensitivity.

3-III **78**

Multislice Computer Tomographic Angiography for Evaluation of Coronary Artery Lesion Morphology and Relation to Clinical Presentation

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Purpose Multislice Computer Tomographic Angiography (MSCTA) of native coronary arteries has proven to be a reliable imaging modality to detect significant stenotic lesions. Furthermore first data show possible differentiation between soft and calcified coronary plaques. We sought to investigate the potential of MSCTA to detect various types of coronary lesions and to relate these findings to the clinical presentation of patients.

Methods ECG-gated contrast enhanced 16-row MSCTA (Siemens™, Forchheim, Germany) was performed in 29 consecutive patients with symptomatic coronary artery disease referred to invasive coronary angiography. Clinical presentation of patients ranged from atypical to stable and unstable angina symptoms. Furthermore acute coronary syndromes (ACS; Non-STEMI) or STEMI events were included. MSCTA coronary plaque findings (based on CT density expressed by Hounsfield units) were compared to the respective clinical presentation of the patients. MSCT contrast flow rate was 3 mL/sec, scan delay 26 sec, slice collineation 0.75 mm, table feed 6.7 cm/sec and rotation time 0.42 sec. Images were reviewed in axial planes and volume rendering technique.

Results A total of 29 coronary lesions were investigated. A typical or stable angina (n = 19) patients presented a MSCT mixed plaque configuration with dominant calcified plaque (17/19). Only 2 stable patients had an excess of soft plaque morphology. Unstable angina, ACS and STEMI patients (n = 10) had mixed or only soft tissue MSCT lesion pathology.

Conclusion ECG-gated CTA with 16-row MSCT offers a reliable non-invasive imaging technique for the differentiation of coronary lesion pathology. These findings may be related to the individual clinical presentation of the patients.

3-IV **77**

Multislice Computer Tomographic Coronary Angiography for Evaluation of Patients Undergoing Liver Transplantation

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Purpose Multislice Computer Tomographic Coronary Calcium Scoring (CCS) combined with angiography (MSCTA) of native coronary arteries has proven to be a reliable non-invasive imaging modality to detect coronary artery disease (CAD). Patients (pts) with endstage liver disease scheduled for transplantation often present with a higher bleeding risk during invasive coronary angiography (CA) and are not suitable for stress testing. We sought to investigate the potential of MSCTA to evaluate CAD in these pts, compared to CA.

Methods ECG-gated contrast enhanced 16-row MSCTA (Siemens™, Forchheim, Germany) with CCS were performed in 20 pts scheduled for liver transplantation. All pts presented without any angina symptoms and had normal echocardiographic reports. Only 7 pts were suitable for stress tests with 100 % negative results. Pts with a very low CCS (< 30) and normal MSCTA were not referred to CA. CCS > 30, in combination or not with pathologic MSCTA (stenotic plaques), as well as low CCS patients with pathologic MSCTA were compared to CA.

Results A total of 20 pts were investigated: 9 pts had CCS < 30 with negative MSCTA and were considered low risk cardiac candidates for liver transplantation without CA. 11 pts had pathologic CCS and/or MSCTA and were referred to CA. Compared to CA, pts with pathologic MSCTA and/or high CCS (15–1519) had diffuse CAD without significant stenotic lesions (9/11). Two pts presented a severe LAD stenosis: one with need for angioplasty/stenting, the other was referred to bypass surgery. Both lesions were correctly detected by MSCTA.

Conclusion MSCTA combined with CCS offers a reliable non-invasive imaging technique for the assessment of CAD in pts undergoing liver transplantation. CA may be reserved to pts with severe coronary pathology with additional therapeutical interventional options. Peri- and postoperative transplant results will allow additional information about preoperative patient evaluation.

3-V **081**

Diminished Neo-Aortic Elastic Properties Following the Ross Operation

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Introduction In young patients with severe anomaly of the aortic valve and/or left ventricular outflow tract obstraction the Ross operation is an established surgical option. The main concern of this procedure is dilatation of the neo-aortic root leading to progression of aortic regurgitation. In order to quantify the potential for pulmonary autograft dilatation, we determined neo-aortic and abdominal aortic elastic properties non-invasively.

Methods In 6 patients aged 9 to 16 years (mean 12.3 ± 2.9 years) who underwent a Ross procedure for severe valvular aortic stenosis and insufficiency diameter measurements were obtained at the sinuses of Valsalva, the ascending (neo-)aortic and descending abdominal aorta out of M-mode echocardiographic images by a special autocontour finding software developed by our institutions. Investigations were done one day postoperatively to 3.4 years (mean 1.3 years) post surgery. Six age and sex matched healthy persons served as controls. After simultaneous oscillometric blood pressure determination several aortic elastic parameters were calculated automatically.

Results Patients showed larger mean enddiastolic neo-aortic diameters (29 ± 3 vs. 19 ± 1 mm, $p < 0.001$) than controls. Neo-aortic distensibility was more than 50 % decreased in patients (28 vs. 62 kPa $- 1 \times 10–3$; $p < 0.05$) paralleled by a reduction of maximum systolic area increase (MSAI, 24 vs. 53 %/100 ms; $p = 0.001$), wall stiffness index of patients was markedly increased (10,1 vs. 3,7; $p < 0.05$). Descending aortic elastic properties tended to be reduced in patients, but differences were not statistically significant. Early postoperative measurements and measurements obtained at follow-up investigations years after operation did not differ significantly.

Conclusions Our preliminary results show, that the reduction of neo-aortic elasticity can be accurately quantified out of M-mode echocardiographic images in young patients after Ross operation. Correlation of neo-aortic diameter and elasticity changes during follow-up investigations in a larger patient population may help to estimate the potential for neo-aortic dilatation and arterial hypertension, and perhaps gives hints to optimize surgical details of the Ross procedure.

3-VI **74**

Sensitivity of Cardiac Magnetic Resonance Imaging in the Diagnosis of Left Ventricular Hypertrabeculation/Non-compaction and its Dependency on Neuromuscular Disorders

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Study objectives Left ventricular hypertrabeculation/non-compaction (LVHT) is a cardiac abnormality mainly diagnosed by echocardiography and frequently associated with neuromuscular disorders (NTMD). Aim of the study was to assess if and with which sensitivity LVHT can be diagnosed by cardiac magnetic resonance imaging (CMRI) and if the sensitivity of CMRI to detect LVHT is dependent on the presence of NMD.

Design, Setting CMRI images of patients with echocardiographically diagnosed LVHT were re-evaluated. LVHT was diagnosed by CMRI if > 3 prominent trabeculations with the same signal intensity like the myocardium in one imaging plane, protruding from the left ventricular wall apically to the papillary muscles, and communication of the intertrabecular spaces with the left ventricular cavity were visible. All patients underwent a cardiological investigation and were invited for a neurological investigation.

Results CMRI images of 19 patients were re-evaluated (10 female, 14–67 years). LVHT was diagnosed by CMRI in 9 cases. Patients in whom CMRI diagnosed LVHT were more often female (67 vs. 40 %), had more often heart failure (100 vs. 50 %), a left ventricular enddiastolic diameter > 57 mm (67 vs. 40 %), a left ventricular fractional shortening < 25 % (89 vs. 40 %) and a larger extension of LVHT than patients in whom CMRI did not diagnose LVHT. The sensitivity of CMRI was not dependent on the presence of NMD, which were diagnosed in 87 %.

Conclusions The sensitivity of CMRI to diagnose LVHT is only 47 %. When looking for LVHT by CMRI left ventricular size, function and location of LVHT as assessed by echocardiography have to be considered.

3-VII **082**

Feasibility of 64-Row Multislice Computed Tomography to Evaluate Coronary Lesions in Patients with Stable Angina

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Methods We studied prospectively 20 consecutive patients (9 male, 11 female, mean age 66 ± 13.4 years) with presumed coronary artery disease by MSCT (CT Sensation 64, Siemens) after i. v. injection of 50 mL contrast agent and by invasive coronary angiography 20 ± 5 days later. The coronary arteries were evaluated in both methods as without pathology, stenosis < or > 50 % or occluded by the first two authors separately and blinded. The coronary arteries were subdivided in left main, proximal, mid- and distal segments of LAD, LCX, and RCA (200 segments in all patients). Statistical analysis with respect to sensitivity, specificity, positive and negative predictive value were calculated. Invasive coronary angiography (CA) was regarded as reference method.

Results A total of 193 segments (96 %) in MSCT showed diagnostic image quality. Seven segments were regarded as false negative for statistic evaluation. In CA out of 200 segments 19 revealed stenotic lesions > 50 %, no occlusion. Whereas in MSCT 26 segments revealed stenotic lesions > 50 % (7 false positive). The comparison of both methods revealed for MSCT a sensitivity, specificity, positive and negative predictive value of 73 %, 96 %, 73 %, and 96 % respectively.

Conclusion 64-MSCT accurately detects significant coronary stenosis and can be reliably used to exclude coronary artery disease and that way excludes patients from unnecessary (diagnostic) CA.

3-VIII **18**

Cardiologic and Neurologic Findings in Left Ventricular Hypertrabeculation/Non-compaction Related to Wall Thickness, Size and Systolic Function

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Left ventricular hypertrabeculation/non-compaction (LVHT) is a rare cardiac abnormality, diagnosed echocardiographically when > 3 left ventricular trabeculations are visible in one image plane apically to the papillary muscles and intertrabecular spaces are perfused from the ventricular cavity. In the majority of the cases, LVHT is associated with neuromuscular disorders (NMD). LVHT occurs in dilated as well as in normally sized ventricles, with or without systolic dysfunction and wall thickening. Aim of the study was to assess whether cardiologic and neurologic findings differ between patients, according to echocardiographically determined left ventricular size, systolic function and wall thickness.

In 77 patients (19 ♀, mean age 52 years) LVHT was diagnosed. LVHT was assessed as "dilative" (enddiastolic diameter ≥ 60 mm and fractional shortening ≤ 25 %) in 43 cases, in 18 patients as "hypertrophic" (interventricular septum and posterior wall ≥ 12 mm and fractional shortening ≥ 26 %) and in the remaining 16 patients as "normally-dimensioned". Dilative LVHT patients were older than hypertrophic or normally-dimensioned LVHT patients. The prevalence of NMD was 63 % in dilative LVHT, 67 % in hypertrophic LVHT, and 56 % in normally-dimensioned LVHT.

LVHT is more frequently found in dilated than hypertrophic ventricles. NMD is equally frequent in dilative, hypertrophic and normally-dimensioned LVHT. Cardiac abnormalities may progress with age.

Sitzung 4 – Grundlagen I

4-I **11**

Endurance Training Reduces Circulating Asymmetric Dimethylarginine (ADMA) and Myeloperoxidase (MPO) Levels in Persons at Risk of Coronary Events

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Background The enzymes asymmetric dimethylarginine (ADMA), myeloperoxidase (MPO) and paraoxonase 1 (PON1) are directly involved in the pathogenesis of atherosclerosis by modulation of oxidative stress and/or nitric oxide (NO) bioavailability. We wanted to assess whether endurance exercise which is known to be cardioprotective could beneficially affect these novel risk markers in a prospective controlled trial.

Methods and Results Thirty-two subjects (31–68 yrs, 56 % males) with elevated cardiovascular risk including ten patients with coronary artery disease volunteered for a supervised twelve-week endurance training (196 ± 15 min/week). Their fitness evaluated by 2 km test runs improved significantly after training (pre: 17.3 ± 0.8 min vs. post: 15.7 ± 0.9 min (mean ± SEM), $p < 0.001$). ADMA (pre: 0.94 ± 0.03 μmol/L^{-1} vs. post: 0.75 ± 0.04 μmol/L^{-1}) and MPO (pre: 296.8 ± 22.2 ng/mL^{-1} vs. post: 185.7 ± 19.5 ng/mL^{-1}) serum levels decreased significantly by 17.6 ± 4.6 % and 28.5 ± 7.5 %, respectively, in response to training (both $p < 0.001$). PON1 activity towards phenylacetate was not significantly influenced by training

(pre: 133 ± 6 µmol/mL^{-1} × min^{-1} vs. post: 130 ± 5 µmol/mL^{-1} × min^{-1}, p = 0.375). In a matched inactive control group (n = 16) ADMA, MPO and PON1 activity did not change over time. ADMA- and MPO-changes were significantly different between participants and controls (both p < 0.05).

Conclusion Regular endurance exercise was successful in reducing the circulating levels of two promising cardiovascular risk markers, ADMA and MPO, in persons prone to cardiac events. These changes may result in numerous antiatherosclerotic effects such as improvement of NO bioavailability, reduction of oxidative stress, and lipid peroxidation. As MPO represents vascular inflammation its reduction may also reflect an anti-inflammatory effect of exercise.

4-II **33**

Rolle des endogenen NOS-Antagonisten ADMA in einem Mausmodell für myokardiale Ischämie/Reperfusion

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Einleitung Eine der ersten und wichtigsten Veränderungen nach Reperfusion eines ischämischen Myokards ist eine ausgeprägte endotheliale Dysfunktion, charakterisiert durch den Verlust von endothelialem Stickstoffmonoxid (Nitric Oxide, NO). Die Reduktion der NO-Bioverfügbarkeit führt zu einer Reihe von pathophysiologischen Veränderungen in der frühen Phase der myokardialen Reperfusionsschädigung, wie z. B. Adhärenz von Leukozyten an das reperfundierte Koronarendothel, Migration von Monozyten und in weiterer Folge Gewebsnekrose im reperfundierten Myokard. Wir konnten zuletzt zeigen, daß die NO-Synthese in Atherosklerose-Modellen durch den endogenen NOS-Antagonisten asymmetrisches Dimethylarginin (ADMA) gehemmt werden kann. Wir stellten uns daher die Frage, ob ADMA auch in einem etablierten Mausmodell für myokardiale Ischämie/Reperfusion (mI/R) von Bedeutung ist.

Methoden 8 Wochen alte, anästhesierte C57-bI6-Mäuse wurden einer myokardialen Ischämiephase von exakt 30 min, gefolgt von 0, 2, 4, 8, 12, 24 und 72 Std. Reperfusion unterzogen. Dafür wurde die LAD der Mäuseherzen nach einer in unserem Labor validierten Methode ligiert und wiedereröffnet. Nach der Operation wurde der linke Ventrikel der Mäuseherzen homogenisiert und Proteine, Aminosäuren und NO-Metabolite (NOx) wurden für die Analyse von Determinanten des NOS-Reaktionswegs isoliert. Weiters wurden C57-bI6-Wildtypes mit DDAH-überexprimierenden Mäusen (mit niedrigen ADMA-Plasma- und -Gewebskonzentrationen) auf Gewebsschaden und Nekrosegröße nach 30 min Ischämie und 4 Std. Reperfusion verglichen.

Resultate NOx-Gewebs-Konzentrationen fielen signifikant auf minimal 4,1 µmol nach 4–8 Std. Reperfusion verglichen mit sham-operierten Kontrollen (6,9 µmol). Allerdings wurden keine Veränderungen der Protein-Expression der konstitutiven NOS-Isoformen (eNOS und nNOS) gefunden, sodaß die NO-Verfügbarkeit in diesem Modell der mI/R durch eine Reduktion der NOS-Aktivität hervorgerufen werden muß. Als Erklärung für diesen Mechanismus fanden sich bis zu 3fache Erhöhungen von Gewebs-ADMA nach 2 Std. (238 µmol), 4 Std. (276 µmol) und nach 8 Std. (199 µmol) mI/R verglichen mit sham-operierten Kontroll-Mäusen (86 µmol). Die Erhöhungen von ADMA und eine konsekutive Reduktion der NOS-Aktivität waren mit signifikanten Anstiegen der P-Selectin- und ICAM-I-Expression mit einem Maximum bei 4 Std. Reperfusion assoziiert. Schließlich führte die Reduktion von ADMA durch DDAH-Über-Expression in einer transgenen Mauskolonie zur deutlichen Reduktion des Reperfusionsschadens, gemessen mit Serum-Troponin T (0,47 vs. 0,68 ng/ml) und histologischer Infarktgröße (beide p < 0,05).

Zusammenfassung Wir konnten eine signifikante Reduktion der myokardialen NO-Konzentrationen, vergesellschaftet mit einer Erhöhung von ADMA in unserem Maus-Modell für myokardiale Ischämie und Reperfusion feststellen, die den beobachteten Anstieg in NO-abhängigen Selektinen erklären. Weiters konnte gezeigt werden, daß eine Reduktion von ADMA durch genetische Modifikation in diesem Modell den Reperfusionsschaden signifikant absenkt. Unsere Resultate weisen auf eine wichtige Rolle von ADMA in dieser Situation hin und erlauben Spekulationen auf eine potentielle neue Therapiemöglichkeit des Myokardinfarkts.

4-III **17**

EGF-like Domain of Tenascin-C is Proapoptotic for Cultured Smooth Muscle Cells

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Objektive Based on our previous observations on the expression of Tensascin-C (Tn-C) in human atherosclerotic plaques and its colocalisation with macrophages, we explored whether Tn-C undergoes fragmentation and the potential pathobiological significance of this fragmentation.

Methods and Results Using cultured human smooth muscle cells (SMCs), we found that Tn-C upregulates expression of matrix metalloproteinases (MMPs). Western blot analysis revealed that Tn-C substrate is fragmented and most of the cleavage products have fibronectin-like and epidermal growth factor-like (EGF-like) domains of Tn-C. One fragment containing an EGF-like domain was found in some human atherosclerotic plaques. Cell culture studies revealed that the recombinant EGF-like domain inhibits growth, induces apoptosis of SMCs in a dose-dependent, time-dependent, and caspase-dependent manner, and activates caspase-3 before SMC detachment. Conversely, the caspase inhibitor z-YVAD.cmk, serum, and protease inhibitors blocked cell apoptosis conferred by the EGF-like domain. In addition, these inhibitors blocked EGF-like domain-induced caspase-3 activation. In contrast to this EGF-like domain, intact Tn-C, its fibronectin-like, and its fibrinogen-like were inactive.

Conclusions Together with our previous observations, our data suggest that Tn-C upregulates MMP expression that cleaves Tn-C into fragments containing the EGF-like domain. This domain has proapoptotic activity for SMC's.

4-IV **038**

Interferon-Gamma Activates Inducible Nitric Oxide Synthase in Human Adult Cardiac Myocytes and Coronary Artery Smooth Muscle Cells In Vitro

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Abstract The regulation and sources of inducible nitric oxide synthase (iNOS) in the human heart are controversial. We examined the regulation of iNOS expression by different pro-inflammatory cytokines and endotoxin in human adult cardiac myocytes (HACM) and human coronary artery smooth muscle cells (HCASMC) *in vitro*.

Methods Primary cultures of HACM were established from ventricular tissue and HCASMC were isolated from pieces of coronary arteries obtained from hearts from patients undergoing heart transplantation. The cells were incubated with interferon (IFN) gamma 500 U/mL, lipopolysaccharide (LPS) 10 µg/mL, tumor necrosis factor (TNF) alpha 500 U/mL, interleukin (IL) 1-alpha 200 U/mL alone or with a mixture of these cytokines and LPS for time periods between 6 hours (h) and 24 h. Total RNA was prepared from cell lysates of such treated cells with Gentra Purescript RNA Purification Kit. Specific RNA levels for iNOS were determined by RT-PCR using LightCycler-RNA Master SYBR Green I. PCR-products were visualized by agarose gels electrophoresis.

Results IFN-gamma alone up-regulated iNOS RNA in both HACM and HCASMC between 6 h and 24 h of incubation. In contrast there was no detectable iNOS RNA expression if human cardiac myocytes were treated with LPS alone or combination of TNF-alpha and IL-1alpha. The most potent activation of iNOS RNA expression was achieved with a mixture of all three cytokines and LPS in both HACM and HCASMC.

Conclusion IFN-gamma is a potent activator of iNOS in human adult cardiac myocytes and human coronary artery smooth muscle cells *in vitro*.

4-V **036**

Complement Component C5a Predicts Future Cardiovascular Events in Patients with Advanced Atherosclerosis

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Aims Complement activation occurs in atherosclerotic lesions, and particularly complement component C5a exerts potent chemotactic and proinflammatory effects. However, it is yet unknown, whether plasma levels of C5a may predict cardiovascular risk. The aim of this study was to examine whether plasma levels of the complement component C5a may predict cardiovascular risk in patients with advanced atherosclerosis.

Methods and Results We studied 173 patients with symptomatic peripheral artery disease (median age 72, 82 male). Cardiovascular risk profile, levels of complement factor C5a and other non-specific inflammatory parameters (high sensitivity CRP [hs-CRP], serum amyloid A [SAA], fibrinogen) were obtained at baseline, and patients were followed for median 22 months (interquartile range 13–27) for the occurrence of major adverse cardiovascular events (MACE: myocardial infarction, percutaneous coronary interventions, coronary artery bypass graft, carotid revascularisation, stroke, and death). We observed 65 MACE in 49 patients (28 %). Cumulative event rates (95 % confidence interval) within quartiles of C5a at 24 months were 16 % (5–27), 26 % (13–39), 36 % (21–51), and 37 % (23–51), respectively ($p = 0.0077$). Adjusted hazard ratios for the occurrence of MACE according to increasing quartiles of C5a were 1.93 ($p = 0.20$), 2.53 ($p = 0.050$), and 2.88 ($p = 0.023$), respectively, as compared to the lowest quartile, irrespective of the level of other inflammatory parameters.

Conclusion Complement activation, indicated by elevation of C5a, seems to contribute to the cardiovascular risk of patients with advanced atherosclerosis. Clinically, determination of C5a may add to the predictive value of other non-specific inflammatory parameters.

4-VI **044**

Vascular Endothelial Growth Factor is Increased by Inflammatory Cytokines Interleukin-6 and Oncostatin M in Human Adipose Tissue-Derived Stem Cells

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Background Adipose tissue is increasingly recognised for its angiogenic properties and recent studies suggest a role for adipose tissue-derived stem cells in therapeutic angiogenesis. Using stem cells derived from adipose tissue for treatment of cardiovascular ischemia, it is of major interest how these cells respond to environmental conditions after cell delivery. Although several reports indicate that vascular endothelial growth factor (VEGF) accounts for most of the angiogenic activity of adipose tissue, its regulation has been poorly examined. Elevated levels of the glycoprotein 130 (GP130) ligand interleukin-6 (IL-6) are found after myocardial infarction and in patients with peripheral artery disease. The aim of our study was to investigate the impact of the GP130 ligands IL-6 and oncostatin M (OSM) on VEGF expression in human adipose tissue-derived stem cells.

Methods Stromal-vascular fraction (SVF) cells were prepared by collagenase digestion of human subcutaneous and omental adipose tissue and characterized by flow cytometry. $CD34^+$ cells were isolated by magnetic microbeads from SVF cells. $CD34^+$ cells were treated with IL-6 (100 ng/mL) and OSM (100 ng/mL), respectively, for 48 h. VEGF antigen in supernatants was quantified by ELISA, mRNA levels were determined by RealTime-PCR.

Results The freshly harvested SVF of human subcutaneous and omental adipose tissue contained large numbers of $CD34^+$ cells. 75 % of the subcutaneous SVF cells were $CD34^+$ and 78 % of the omental SVF cells expressed CD34. IL-6 significantly up-regulated VEGF production in $CD34^+$ cells of subcutaneous and omental adipose tissue up to 3-fold and 4-fold, respectively. In subcutaneous and omental $CD34^+$ cells OSM also significantly increased VEGF production up to 4-fold and 6-fold, respectively. These results were confirmed by RT-PCR on the level of specific mRNA expression.

Conclusion We could show that selected GP130 ligands significantly upregulate VEGF expression in $CD34^+$ cells of human adipose tissue. If these effects are also operative in vivo one could hypothesize that elevated levels of GP130 ligands such as IL-6 seen after myocardial infarction could promote neovascularisation through upregulation of VEGF in adipose tissue-derived stem cells after cell transplantation.

4-VII **45**

Inflammatory Cytokines Interleukin-6 and Oncostatin M Increase Vascular Endothelial Growth Factor in Human Adipose Tissue

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Background Obesity is characterised by an increased adipose tissue mass with increased size and number of mature adipocytes. Recent studies suggest that adipose tissue mass could be regulated through the vasculature, and differentiation of preadipocytes into adipocytes is angiogenesis-dependent. Vascular endothelial growth factor (VEGF), a key agonist of angiogenesis is expressed and secreted by adipose tissue, but its regulation has been poorly examined. Elevated levels of the glycoprotein 130 (GP130) ligand interleukin-6 (IL-6) are found in obese patients. The aim of our study was to investigate whether the GP130 ligands IL-6, oncostatin M (OSM), leukemia inhibitory factor (LIF) and cardiotrophin-1 (CT-1) regulate VEGF expression in human visceral and subcutaneous adipose tissue *in vitro* and *ex vivo*.

Methods Primary human preadipocytes were prepared from visceral and subcutaneous adipose tissue. Differentiation to adipocytes was induced by hormone-supplementation. Explants of adipose tissue, preadipocytes and adipocytes were treated with IL-6 (100 ng/ml), OSM (100 ng/mL), LIF (104 U/mL), and CT-1 (100 ng/mL), respectively, for 48 h. VEGF antigen in supernatants was quantified by ELISA, mRNA levels were determined by RealTime-PCR.

Results IL-6 and OSM significantly upregulate VEGF production in both visceral and subcutaneous adipose tissue explants up to 2.5-fold (IL-6) and up to 9-fold and 6.5-fold (OSM), respectively. VEGF production is significantly upregulated in both preadipocytes and adipocytes up to 3-fold and 3.5-fold by IL-6, up to 7-fold and 15-fold by OSM and up to 3-fold and 1.5-fold by LIF. CT-1 upregulates VEGF only in visceral adipocytes (up to 3-fold). These results were confirmed on the level of mRNA expression.

Conclusion We could show that selected GP130 ligands significantly upregulate VEGF expression in human adipose tissue explants and in cultured human preadipocytes and adipocytes. We postulate that GP130 ligands participate in the modulation of VEGF synthesis in adipose tissue and we hypothesize, that high levels of circulating GP130 ligands such as IL-6 found in obese patients could promote angiogenesis in adipose tissue.

4-VIII **102**

GLUT4 mRNA Expression in Human Myocardium does not Correlate with Coronary Heart Disease

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Cellular metabolism depends on the insulin-responsive GLUT4 isoform of the transmembrane glucose transport molecule. At the level of gene expression, GLUT 4 regulation is achieved by modulating transcription rates as well as mRNA stability. Changes in cellular GLUT4 density and hence its mRNA expression have been suspected as one of the mechanisms involved in the pathophysiology of diabetes and coronary heart disease (CHD). Probes (60–150 mg of right atrial auricle from 43 consecutive patients subjected to cardiac surgery; 28 male, 15 female) were snap frozen in liquid nitrogen and stored at –70 °C until homogenisation. Total RNA was isolated using guanidium thiocyanate, phenol chloroform extraction and alcohol precipitation (for further meth. see our earlier paper e.g. [Mol Cell Biol 1988: 2394–400]. Total RNA was hybridized with 32p-labelled human GLUT4 cDNA and rehybridized with a human GAPDH cDNA probe to correct for equal amounts of RNA. Quantification was performed by scanning densitometry of the autoradiograms using a laser scanner.

Our results represent the first measurements of GLUT4 mRNA expression in human myocardial tissue. Thirtyone patients suffered from coronary heart disease and underwent bypass surgery, 12 served as controls (valve replacement, reconstruction or ASD) without coronary heart disease. In male patients, GLUT 4 mRNA was 64.7 ± 13.9 (n = 7) in the controls and 53.9 ± 16.7 (n = 21) in the CHD group (p = 0.13; ± SEM). There was no statistical significant difference between subgroups like male and female, diabetics or other.

In summary, our results show that myocardial mRNA expression of the insulin responsive GLUT4 isoform is unchanged in CHD and diabetic patients. This suggests that, unlike expected, altered cellular GLUT4 expression may play little or no role in the pathophysiology of CHD and possibly diabetes mellitus.

4-IX **100**

Effect of Intracellular Acidification on Free Intracellular Mg^{2+}: An ETH 7025-Mg^{2+}-Ionselective Microelectrode Study on Guinea Pig Papillary Muscle

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The assessment of free, ionised, intracellular Mg^{2+} ($[Mg^{2+}]_i$) in myocardial tissue is problematic and its metabolism has not been well understood as yet. This, for example, makes the design of trials on therapeutic use of Mg (e.g. Limit II and ISIS 4) difficult and the interpretation of conflicting results almost impossible.

Here, we assess the effect of changing intracellular pH (pH_i; measured with pH selective microelectrodes) on cytoplasmatic $(Mg^{2+})_i$ using a newly designed Mg^{2+} selective microelectrode with the neutral carrier ETH 7025 and measure $(Mg^{2+})_i$ in isolated resting guinea pig papillary muscle (Tyrode, pH 7.4, 36 °C; for details of method see our earlier work [J Physiol 1990; 431: 713–41; Pflugers Arch 1993; 423: 338–42].

We found that changing extracellular pH for 15 minutes from 7.4 to 6.4 leads to a change of intracellular pH from 7.19 ± 0.03 to 6.81 ± 0.006 (n = 7; ± SEM for all exp.). This change of pHi leads to a small, but detectable rise in $(Mg^{2+})_i$ by a maximum amount of 0.19 ± 0.06 mM from an initial value of 0.73 ± 0.08 mM after approximately 7 minutes, followed by a slow decrease of $(Mg^{2+})_i$ to almost normal. This would amount to a liberation of 1.5 % of the cells total Mg content, assuming that $(Mg^{2+})_i$ constitutes 1/17 of the cells total Mg [J Physiol 1972; 224: 121–39].

In summary, we found that intracellular acidification liberates $(Mg^{2+})_i$ from intracellular binding sites. The transient nature of the observed $(Mg^{2+})_i$ rise further suggests, that the levels of cytoplasmatic $(Mg^{2+})_i$ are well regulated and even small changes in $(Mg^{2+})_i$ are adjusted within short time.

Sitzung 5: Interventionelle Kardiologie I

5-I **47**

Comparison of Intracoronary Beta-Radiation Brachytherapy with the Implantation of Paclitaxel-Eluting Stents for the Prevention of Recurrent Diffuse In-Stent Restenosis – Primary Results of the Randomized COBRA Trial

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Background Intracoronary brachytherapy was the primary therapeutic option for the prevention of recurrent in-stent restenosis (ISR) during the last years. Especially for the treatment of diffuse ISR (lesions > 10 mm, according to Mehran classification), beta-source brachytherapy was significantly superior to singular balloon angioplasty. On the other hand, despite of lacking clinical data base, the implantation of drug eluting stents became a common procedure for the treatment of ISR during the last two years.

Objective Our randomized trial aimed to compare the efficacy of beta-brachytherapy (Beta-Cath, Novoste) and paclitaxel-eluting stent-implantation (Taxus, Boston Scientific) for the prevention of recurrent diffuse ISR.

Methods Until february 2005, 40 patients with diffuse ISR were randomly assigned to Beta-Cath (19 patients) or Taxus (21 patients). Six-month clinical follow-up was available for 27 of 29 patients until march 2005.

Results Target lesion revascularisation for recurrent ISR was needed in two of 13 patients treated with Beta-Cath (15 %), whereas none occurred in 14 patients treated with Taxus (p = 0.14). No further major adverse cardiac events (myocardial infarction, death) were found in both groups. Stent-implantation was not only the faster (mean difference 25 minutes, including intravascular ultrasound control) but also the more cost effective procedure.

Conclusion These primary results showed comparable efficacy of paclitaxel-eluting stent-implantation and beta-brachytherapy in the prevention of recurrent diffuse ISR.

5-II **NEU-110**

Preliminary results of the Austrian Taxus Multivessel Registry

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Aim The aim of the on-going Austrian Taxus Multivessel Registry is to investigate the frequency of MACE in patients with multivessel coronary artery disease treated percutaneously with multiple drug-eluting stent implantations in the „real world" stenting.

Methods Totally, 227 patients have been included in the Registry. Until March 2005, 56 of them so far have been clinically controlled (40 of them angiographically too) for 6 months. The occurrence of major adverse cardiac events (MACE as cardiac death, non-fatal myocardial infarction, target vessel revascularisation) and the target vessel failure were recorded for all patients, and the minimal lumen (MLD), reference diameter (RD), % diameter stenosis (% DS) and the follow-up (FUP) in-stent and in-lesion (10 mm proximal and distal from stent end). MLD, RD, % DS and late lumen loss (LLL) were measured.

Results The mean age of the patients is 65 ± 12 y, with 62 % male. Diabetes mellitus is present in 29 %, hypertension in 81 %, hypercholesterolemia in 72 %, smoking in 24 %. The stent/patient ratio is 3.2 ± 1.8. Additional 3-vessel stenting occurred in 35.1 % of patients, 4-vessel stenting in 12.1 %. One patient with unstable angina

Table 5: M. Gyöngyösi et al.

Baseline	Pre-stenting	Post-stenting
MLD (mm)	0.94 ± 0.5	2.31 ± 0.25
RD (mm)	2.49 ± 0.4	2.78 ± 0.28
% DS (%)	62.3 ± 19.1	16.5 ± 6.6
Follow-up (FUP) (n = 95 lesions of 40 patients)	**FUP In-stent**	**FUP In-lesion**
MLD (mm)	2.08 ± 0.76	1.72 ± 0.61
RD (mm)	2.59 ± 0.54	2.41 ± 0.58
% DS (%)	21.7 ± 24.0	30.8 ± 23.6
LLL (mm)	0.283 ± 0.127	0.67 ± 0.319

and left main stenosis died during bail-out multiple stenting procedure with open arteries but due to cardiac failure, side branch occlusion occurred in 1 patient. Among the controlled 56 patients, no further death or myocardial infarction occurred; target lesion revascularisation was necessary in 25 % of the clinically checked patients (included 1 patient with bypass operation). The binary in-stent restenosis of the angiographically controlled 95 lesions of 40 patients was 8.4 % (8 patients), the binary in-lesion restenosis 10.5 % (10 patients). The quantitative angiographic results are listed in **Table 5.**

Conclusion The patient characteristics in the Austrian Taxus Multivessel registry are comparable to the ARTS II study (Cypher stent implantation in multivessel de novo lesions). The preliminary results of our Registry indicate that drug-eluting stent implantation in patients with multivessel disease is safe. Further follow-up records will provide data about the efficacy and economic impact of the percutaneous treatment of multivessel disease with multiple implantations of Paclitaxel-eluting stents.

5-III **84**

Effect of Percutaneous Coronary Intervention on Heart Rate and QRS Complex Duration in Patients with Acute Myocardial Infarction or Acute Coronary Syndrome

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Background The QRS duration is known to be an independent predictor of mortality in acute myocardial infarction (AMI) and acute coronary syndrome (ACS). The short term effect of acute percutaneous coronary intervention (PCI) on heart rate and QRS duration may be of interest as simple markers for the general outcome of patients (pts) with critical coronary artery disease.

Methods The surface ECGs (paper speed 25 mm/sec) of 233 pts (173 men, 60 female; mean age 63 ± 12.1 years) who were enrolled at our center in the Austrian Acute PCI-Registry, have been retrospectively reviewed with respect to heart rate and QRS duration at admission and discharge. After exclusion of pts with preexistent bundle branch block, of pts with an unsuccessful revascularisation procedure and of those with incomplete data a total of 216 pts remained valid for final data analysis.

Results The ECG at admission, obtained either at the ambulance or the emergency department, showed sinus rhythm in 198 pts, atrial fibrillation in 15 pts, junctional rhythm in 2 pts and ventricular tachycardia in one. Mean heart rate at admission was 79 ± 1.4 bpm and at discharge 74 ± 1.2 bpm (p = 0.001). The mean QRS duration prior to PCI was 105 ± 1.5 ms and 983 ± 1.3 ms at discharge (p < 0,0001). PCI had no influence on bundle branch block in 15 pts, however normalization of the QRS complex was noted in 6 pts. Death occurred in 15 pts (7 %) following PCI despite achievement of TIMI II or III flow in the infarct related artery. At admission the mean heart rate of these pts was 85 ± 6.2 bpm. The mean QRS complex was 118 ± 7.7 ms, which was significantly larger than in patients with good outcome (p = 0.02). Pts with ST-Elevation Myocardial Infarctions (STEMI; n = 164) had a significantly higher heart rate at admission compared to those with a Non-ST-Elevation Myocardial Infarction (NSTEMI; n = 52) – 81 ± 1.6 bpm vs. 74 ± 2.4 bpm (p = 0.03). There was no difference in the QRS duration at admission and at discharge between STEMI and NSTEMI pts.

Conclusion Successful PCI for AMI or ACS is associated with a significant reduction of heart rate and shortening of the QRS complex duration as measured on surface ECG. Pts with STEMI presented with a higher heart rate compared to pts with NSTEMI. Pts with in-hospital death despite PCI on emergency showed significantly broader QRS complexes at admission than pts with favourable outcome.

5-IV **049**

Comparison of the Follow-up Angiographic Results after Cypher and Taxus Stent Implantations for In-Stent Restenosis

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Background The major and most frequent complication of coronary stent implantation is the in-stent restenosis. The brachytherapy, as the standard therapy for in-stent restenosis led to better short- and mid-term follow-up results, but longitudinal studies revealed an increased late stent thrombosis. The introduction of drug-eluting stents into the clinical practice for the treatment of stent restenosis might result a better long-term outcome. Therefore the aim of our prospective 2-center Austrian Registry was to investigate the clinical and angiographic outcomes of the two most frequently used drug-eluting stents after stenting of the in-stent restenosis.

Methods Cypher stent was implanted in 32 patients and Taxus stent in 38 patients with in-stent restenosis. Until March 2005 14 patients with Cypher (86 % male, 62 ± 11 y) and 26 patients with Taxus (85 % male, 61 ± 11 y) were controlled clinically and angiographically 7 ± 2 months after stent implantation. The baseline clinical (coronary risk factors, previous myocardial infarction, unstable angina at clinical presentation), and qualitative angiographic parameters (location of lesion, stent size and length) and the baseline and follow-up quantitative angiographic parameters [pre-, post and follow-up in-stent and in-lesion minimal lumen diameter (MLD), reference diameter (RD) and % diameter stenosis (% DS)] were recorded for each patient. Target lesion in-stent restenosis and peri-stent restenosis and reintervention, occurrence of major adverse cardiac events (MACE, as non-fatal myocardial infarction, death, revascularisation) were documented.

Results There were no significant differences between the Groups Cypher and Taxus as regards the baseline clinical and angiographic parameters. No differences were found between the groups regarding the follow-up in-stent and in-lesion parameters **(Table 6)**. The

Table 6: Badr Eslam et al.

Follow-up	In-stent			In-lesion		
	MLD (mm)	RD (mm)	% DS (%)	MLD (mm)	RD (mm)	% DS (%)
Cypher (n = 14)	2.06 ± 0.77	2.79 ± 0.31	15.3 ± 27.7	2.14 ± 0.38	2.66 ± 0.33	17.2 ± 13.7
Taxus (n = 26)	2.08 ± 0.41	2.57 ± 0.37	19.8 ± 13.7	1.95 ± 0.37	2.66 ± 0.54	24.6 ± 14.4

MLD = minimal lumen diameter, RD = reference diameter, % DS = % diameter stenosis, no significant differences between the groups

follow-up in-stent late lumen loss (LLL) was non-significantly higher in Cypher group as compared with Taxus (0.42 ± 0.61 vs. 0.19 ± 0.39 mm, respectively), the in-lesion LLL was similar. The binary in-stent restenosis was 7 % vs. 0 % in Cypher vs. Taxus Groups, while the in-lesion binary restenosis was 4 % in Taxus and 0 % in Cypher patients (non-significant). No death or myocardial infarction occurred during the follow-up. According to the restenosis rate, the MACE was 7 % in Cypher and 4 % in Taxus groups.

Conclusion Our preliminary study on Cypher and Taxus stent implantation in patients with in-stent restenosis shows a low incidence of in-stent and peri-stent restenosis and occurrence of MACE, indicating a successful treatment of in-stent restenosis with drug-eluting stents.

5-V **053**

Langzeitverlauf nach Verlust von Koronarstents – eine retrospektive Analyse

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Abstract Der Verlust des Koronarstents vom Ballon stellt eine seltene Komplikation von Koronarinterventionen dar. Über den Langzeitverlauf nach dieser Komplikation existieren keine systemischen Daten.

Patienten und Methodik In einer retrospektiven Analyse wurden jene 36 Patienten nachuntersucht, bei denen seit Beginn der Stentimplantation an unserer Abteilung Koronarstents verloren wurden. Als bildgebende Maßnahme wurde eine 16-Zeiler-Nativ-Computertomographie-Untersuchung des Beckens und der Beine (Sensation; Fa. Siemens) sowie eine Femoralis-Dopplersonographie durchgeführt.

Ergebnisse An unserer Abteilung wurden von 01/1994 bis 01/2005 7139 Sitzungen mit koronarer Stentimplantation durchgeführt. In insgesamt 36 Fällen (0,6 %) kam es zum Verlust eines Stents vom Trägerballon und konsekutiv zu einer Dislokation ins Gefäßsystem. 29 Patienten waren männlich (81 %), das Durchschnittsalter lag zum Interventionszeitpunkt bei 66,9 ± 9,3 Jahren.
Bei 6 Patienten konnte noch während der Prozedur der verlorene Stent interventionell geborgen werden. Bei zwei weiteren Patienten wurde ein chirurgisches Vorgehen notwendig: Einmal kam der Stent im Bereich der Punktionsstelle der A. femoralis nach einem Bergungsversuch hämodynamisch wirksam zu liegen, bei einem weiteren Patienten mußte eine semielektive aortokoronare Bypassoperation vorgenommen werden, da der verlorene Stent hämodynamisch wirksam im Ostium des Ramus interventricularis anterior zu liegen kam.
Von den restlichen 28 Patienten wurden 26 beschwerdefrei aus der Spitalspflege entlassen. Zwei Patienten verstarben im Rahmen des Aufenthalts an den Folgen ihrer kardialen Grunderkrankung, jedoch nicht infolge des Stentverlusts.
Nach im Mittel 59,5 ± 29,6 Monaten wurden die Patienten zu einer ambulanten Nachuntersuchung einberufen. 3 weitere Patienten waren zu diesem Zeitpunkt bereits verstorben. 2 Patienten konnten nicht zur Untersuchung eingeladen werden („lost of follow up"). Bei den restlichen 21 Patienten fanden sich in den von uns durchgeführten Untersuchungen bei 5 Patienten in der Peripherie keine den Stents entsprechende Strukturen, wobei ausgeprägte Nativverkalkungen der peripheren Gefäße die Auffindung im Computertomogramm unmöglich machten.
Von den 16 detektierten Stents zeigten sich 12 (75 %) in Seitenästen der A. femoralis profunda, 2 (13 %) in der A. iliaca externa, 1 (6 %) im Bereich der A. femoralis communis und 1 (6 %) im Truncus tibiofibularis. Eine hämodynamische Wirksamkeit der Stents konnte mittels Femoralis-Dopplersonographie in keinem der Fälle nachgewiesen werden.

Schlußfolgerung Verluste von Koronarstents sind seltene Komplikationen. Sofern es zu keinem Auftreten akuter Komplikationen im Sinne von koronaren oder peripheren Ischämien, die einer akuten chirurgischen Intervention bedürfen, kommt, verlaufen die Verluste asymptomatisch.

5-VI **098**

Einfluß von kontinuierlicher Applikation von Paclitaxel nach Implantation eines konventionellen Stents mittels eines perforierten Stentballons: Angiographie, intravaskulärer Ultraschall sowie histomorphometrische Ergebnisse 1 Monat nach Implantation in Schweinekoronarien

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Hintergrund Drug-eluting Stents haben ein großes Potential, die Entwicklung der Instent-Restenose zu reduzieren, die Auswirkungen eines lebenslang zurückbleibenden Trägerpolymers können jedoch noch nicht abgeschätzt werden. Die Hypothese dieser Studie war es, durch Applikation von Paclitaxel nach der Stentimplantation mittels eines perforierten Stentballons die Entwicklung der neointimalen Hyperplasie zu reduzieren.

Methodik Unter Allgemeinanästhesie wurde, nach Vorbehandlung mit Aspirin und Ticlopidin, je ein konventioneller Stent (3.0/9 mm) in die LAD und LCX von 9 Hausschweinen (18–30 kg) mittels Judkinstechnik implantiert. Bei einem der beiden Gefäße (Gruppe PAC) (jeweils abwechselnd) wurde eine kontinuierliche (2–atm, 127 ± 47 sek.) Applikation von Paclitaxel (0,9 mg gemischt mit 3 ml Kochsalzlösung, 3 ml Kontrastmittel und 3 ml Blut) mittels eines perforierten Ballons durchgeführt, beim anderen Gefäß nicht (Gruppe BARE). Nach der Prozedur wurde die verwendete rechte Femoralarterie ligiert. Kontrollangiographie und IVUS wurden nach einem Monat durchgeführt. Nach Aufzeichnung der angiographischen und sonographischen Daten wurden die Tiere euthanasiert, um die histologische und histomorphometrische Analyse der gestenteten Arterien (Einbettung in Technovit 9100, Schnitt mittels eines Leica Hartmetallmesser-Mikrotoms und Färbung mit Hämatoxylin-Eosin) zu ermöglichen.

Ergebnisse Es kam zu keinen interventionellen Komplikationen, alle Tiere konnten wohlauf in ihre Stallungen zurückgebracht werden. Während des 1-Monats-Follow-ups starb eines der Tiere, wobei ein Vorderwandinfarkt in der Obduktion festgestellt wurde. Bei diesem Tier wurde die Paclitaxelinfusion an der LCX durchgeführt, die Lateralwand zeigte keine pathologischen Veränderungen. Bei den übrigen 8 Schweinen konnte nach 4 Wochen eine Kontrollangiographie und IVUS durchgeführt werden, wobei sich in der Angiographie keine Unterschiede zwischen den beiden Gruppen zeigten (PAC vs. BARE: MLD 2,62 ± 0,42 vs. 2,77 ± 0,20 mm, RD 3,0 ± 0,08 vs. 3,08 ± 0,09 mm, % Diameter-Stenose 12,8 ± 13,1 vs. 9,7 ± 7,1 %). Auch die 3D-IVUS Rekonstruktion konnte keine signifikanten Unterschiede zwischen den Gruppen feststellen (PAC vs. BARE: Lumenvolumen 42,4 ± 11,5 vs. 44,2 ± 9,7 mm^3, intimales Volumen 22,1 ± 7,4 vs. 22,4 ± 8,0 mm^3, Gefäßvolumen 86,3 ± 9,1 vs. 86,0 ± 3,7 mm^3). Die qualitative histologische Analyse konnte ebenfalls, mit Ausnahme leicht erhöhter Entzündungszellen in der PAC-Gruppe, keine Unterschiede (Injury Score, Fibrose, Endothelialisierung) feststellen. In der Histomorphometrie allerdings zeigten sich grenzwertig signifikante ($p > 0,05$) Trends von geringerer neointimaler Fläche (PAC 1,78 ± 0,65 vs. BARE 1,53 ± 0,7 mm^2) sowie geringerer maximaler neointimaler Dicke in den Stents der PAC-Gruppe (PAC 0,37 ± 0,18 vs. BARE 0,45 ± 0,3 mm).

Zusammenfassung Die lokale Applikation von Paclitaxel nach Implantation von konventionellen Stents kann sicher durchgeführt werden. Die geringe Effektivität im Vergleich zur unbehandelten Kontrollgruppe könnte durch die vergleichsweise geringe Fallzahl erklärt werden. Für zukünftige Experimente könnte auch eine Adaptierung der Paclitaxelmenge und Infusionsdauer zu erhöhter Wirksamkeit dieser Methode führen.

5-VII **50**

Gute Ergebnisse von „Drug-eluting Stents" in der Behandlung von Instent-Restenosen

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Einleitung Neuere Studien haben gezeigt, daß „Drug-eluting Stents" (DES) in der Lage sind, die Restenoserate deutlich zu senken. Ziel unserer Untersuchung war es, den angiographischen und klinischen Verlauf nach Implantation eines DES zur Behandlung von Instent-Restenosen zu untersuchen.

Methoden und Ergebnisse Bei 214 konsekutiven Patienten (Pat.), (60 ♀, 154 ♀, mittleres Alter 66 [43–83]) mit Instent-Restenosen, mittlerer Stenosegrad 71 ± 21 %, mittlerer Durchmesser der Stenose (MLD) 0,7 ± 0,5 mm, wurde eine erfolgreiche Stent-in-Stentimplantation durchgeführt. Bei 115 (53 %) Pat. wurde der R. interventricularis anterior interveniert, bei 21 (10 %) die A. circumflexa, bei 72 (33 %) die A. coronaria dextra und bei 7 (4 %) eine Hauptstammstenose. Es wurde pro Instent-Restenose jeweils ein Stent implantiert. Es konnten 66 (31 %) Stenosen primär mit einem Stent versorgt werden, bei den restlichen 148 (69 %) wurde der Stent nach Ballonvordehnung implantiert. Die Stentlängen betrugen im Mittel 20,7 ± 8,9 mm bei einem mittleren Durchmesser von 2,7 ± 0,2 mm. Der Restenosegrad nach Stentimplantation betrug im Mittel 7,4 ± 10 % bei einem MLD von 2,3 ± 0,7 mm. Klinische Kontrollen wurden nach 3 Monaten, eine angiographische Kontrolle nach 6 Monaten vorgesehen. Drei (1,4 %) Pat. verstarben im Beobachtungszeitraum. Bei einem dieser Pat. kam es zum Auftreten einer akuten Stentthrombose 2 Tage nach der Intervention, welche erfolgreich erneut revaskularisiert werden konnte. Der Pat. verstarb jedoch 7 Tage nach der zweiten Intervention am Pumpversagen. Die beiden anderen Pat. verstarben 2 bzw. 4 Monate nach Intervention im Pumpversagen bei Kardiomyopathie. Bis jetzt konnten 147 (68 %) Pat. angiographisch und 64 klinisch nachkontrolliert werden. Von diesen hatten 30 die 6 Monate nach Intervention noch nicht erreicht. Die übrigen 34 waren bei der 6-Monats-Kontrolle beschwerdefrei und wollten nicht nochmals angiographiert werden.
Der MLD betrug nach 6 Monaten 2,3 ± 0,8 mm bei einem Restenosegrad von 8,6 ± 9 %. Der „late luminal loss" betrug 0,15 ± 0,8 mm. Bei 17 (7,9 %) der kontrollangiographierten Pat. kam es zum Auftreten einer neuerlichen Restenose (> 50 %), wobei 15 Pat. symptomatisch waren. Die MACE-Rate nach 30 Tagen betrug 0,5 % und nach 6 Monaten 8,4 %.

Schlußfolgerung Diese kleine Serie demonstriert den Nutzen von DES in der Behandlung der Instent-Restenose.

5-VIII **054**

„Crushinterventionen" bei Bifurkationsstenosen im Hauptstamm – eine neue interventionelle Therapieoption

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Abstract Bifurkationsstenosen des Hauptstammes der linken Koronararterie waren bislang eine Domäne der Herzchirurgie. Wir berichten über 10 Fälle einer interventionellen Sanierung mittels Drug-eluting Stents (DES) in der Crushtechnik.

Patienten und Methodik 10 Patienten (Pat.) mit einer Bifurkationsstenose des Hauptstammes der linken Koronararterie wurden mittels perkutaner transluminaler Angioplastie in Crushtechnik therapiert. Gemäß der beschriebenen „Crushtechnik" wurde zuerst der sekundären Ast gestentet (in 7 Fällen der R. circumflexus, in 3 Fällen der R. interventricularis anterior) und nachfolgend der Stent im Hauptast so implantiert, daß der im Hauptstamm liegende Anteil des Stents im Nebenast an die Wand des Hauptstamms gedrückt („gecrushed") wurde. Ein angiographischer Follow-up 3 Monate nach Intervention wurde vorgesehen.

Ergebnisse Insgesamt wurden 10 Pat. (6 davon männlich) mit einem Durchschnittsalter von 77,5 ± 4,6 Jahren mittels Crushintervention an der Bifurkation des Hauptstammes der linken Koronararterie therapiert. Bei 2 Pat. lag ein „geschützter" Hauptstamm bei Z. n. aortokoronarer Bypassoperation (CABG) vor. 5 Pat. präsentierten sich klinisch mit dem Bild eines akuten Koronarsyndroms, bei den restlichen bestand ein NYHA-Stadium III. Bei 8 Pat. lag eine koronare Drei-Gefäß-Erkrankung vor. In allen Fällen konnte die Stentimplantation erfolgreich durchgeführt werden. Bei 7 Pat. wurde nach Stentimplantation mit der Kissing-Balloon-Methode nachdilatiert.
Der Stenosegrad konnte im Hauptgefäß von 75 ± 12 % auf 7 ± 5 % und im Nebengefäß von 68 ± 19 % auf 7 ± 6 % gesenkt werden. Der MLD konnte von 0,68 ± 0,27 % auf 2,46 ± 0,5 8% im Hauptgefäß sowie von 0,52 ± 0,29 % auf 1,8 ± 0,49 % im Nebengefäß angehoben werden.
Während des stationären Aufenthalts traten keine Komplikationen, definiert als Tod, Q-wave- und Non-Q-Wave-Myokardinfarkt sowie Akut-CABG auf. Einmal kam es im Anschluß an die Versorgung der Punktionsstelle mit einem Angio-Seal-Verschluß zu einer Nachblutung im Bereich der rechten Leiste, welche chirurgisch saniert werden mußte.
Im Nachbeobachtungszeitraum von derzeit im Mittel 6,5 ± 4,2 Monaten wurden keine Komplikationen verzeichnet. 5 Pat. wurden bislang nachangiographiert. Die angiographische Restenose betrug 8 ± 8 % im Hauptgefäß sowie 26 ± 25 % im Nebengefäß. Lediglich bei einem Pat. kam es zu einer angiographisch signifikanten 66%igen Abgangsrestenose des Nebengefäßes, welche jedoch bei klinisch fehlender Angina pectoris nicht interventiert wurde.

Schlußfolgerung Die interventionelle Behandlung von Bifurkationsstenosen des Hauptstammes der linken Koronararterie mittels „Crushtechnik" ist technisch durchführbar und scheint in der Hand erfahrener Kardiologen sicher zu sein. Ob die Langzeitergebnisse die Methode rechtfertigen, müssen entsprechende Beobachtungen zeigen.

Sitzung 6 – Rhythmologie I

6-I **092**

„Smooth conduction curve" bei Patienten mit AV-nodaler Reentrytachykardie und AV-Block I – Kein erhöhtes Risiko von AV-Blockierungen nach Modifikation des „slow pathway"

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Hintergrund Als Therapie der Wahl bei Patienten (Pat.) mit AV-nodaler Reentrytachykardie (AVNRT) ist die kathetervermittelte Modifikation des „slow pathway" (SP) mit einem lediglich geringen Risiko der Induktion eines persistierenden totalen AV-Blocks behaftet. Rezente Studien belegen die Sicherheit der Methode auch bei vorbestehendem AV-Block I° (AV I), definiert durch eine PQ-Zeit (PQZ) von über 200 Millisekunden (ms), wobei diese Pat. im Follow-up jedoch häufiger kurze AV-Blockierungen II° aufweisen. Pat. mit AV I und AVNRT können gemäß der Leitung über den AV-Knoten während der programmierten atrialen Stimulation in 2 Gruppen unterteilt werden: Während bei den einen ein AH-Sprung (AHS) als Hinweis für das Vorhandensein eines noch leitenden „fast pathways" (FP) auftritt, fehlt dieser bei den anderen („Smooth conduction curve", SCC). Bei Pat. mit SCC ist somit theoretisch von einem nicht mehr ausreichend funktionierenden FP und einem damit verbundenen erhöhten Risiko der Entwicklung von AV-Blokkierungen auszugehen. Ziel dieser Untersuchung war es, zu klären, ob periprozedural oder im Follow-up Unterschiede in der Häufigkeit von AV-Blockierungen zwischen Pat. mit AV I und vorhandenem AHS sowie Pat. mit AV I und SCC bestehen.

Patienten und Methodik Bei 23 Pat. mit AVNRT und AV I wurde eine Modifikation des SP (inferio-posterior des AV-Knotens) durchgeführt. Das Durchschnittsalter betrug 61 + 12 Jahre, 16 Pat. (69 %) waren weiblich, 5 Pat. (22 %) hatten kardiovaskuläre Begleiterkrankungen. Als AHS wurde eine Zunahme der AH-Zeit um > 40 ms

bei Verkürzung des Kopplungsintervalls um 10 ms definiert. Bei allen Pat. wurde im Intervall eine ambulante klinische Kontrolle mit EKG und eine Langzeit-EKG-Aufzeichnung (LZ-EKG) über 24 Stunden durchgeführt.

Ergebnisse Es fanden sich 14 Pat. mit AHS (61 %, Gruppe I, G I) und 9 Pat. mit SCC (39 %, Gruppe II, G II). Demographisch und bezüglich der PQZ bestanden zwischen G I und G II keine signifikanten Unterschiede. Die primäre interventionelle Erfolgsrate betrug 100 %, wobei die mittlere PQZ mit der SP-Modifikation nicht zunahm (G I vor: 248 + 28 ms, nach: 249 + 32 ms, G II vor: 251 + 26 ms, nach: 247 + 30 ms; jeweils p = n. s.). In beiden Gruppen kam es periprozedural zu keinem Auftreten von AV-Blockierungen. Bei einem Follow-up von 24 + 8 Monaten wurden weder Rezidive der AVNRT noch Synkopen oder symptomatische Bradykardien erhoben. Die mittlere PQZ war mit 244 + 35 ms in G I und 247 + 56 in G II unverändert, in den LZ-EKGs wurden in 3 Fällen in G I (21 %) und in 2 Fällen in G II (22 %) kurzzeitige, nächtliche AV-Blockierungen II° (Typ Wenckebach) dokumentiert. Diese 5 Pat. unterschieden sich in sämtlichen erhobenen Parametern nicht von den übrigen 18 Pat.

Schlußfolgerung Die Modifikation des „slow pathways" zur Behandlung einer AV-nodalen Reentrytachykardie bei Patienten mit AV-Block I° ist sowohl bei vorhandenem AH-Sprung als auch bei „smooth conduction curves" in der programmierten atrialen Stimulation effektiv und sicher.

6-II **104**

TpTe-Interval does not Change with Age

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Objective Evidence from experimental studies suggests that ion channel properties and consequently transmural action potential duration heterogeneity are age dependent. The interval from the peak to the end of the T wave (TpTe) has been proposed to reflect this heterogeneity within the ventricular wall. A prolonged TpTe interval is consequently considered to indicate larger transmural gradients and higher arrhythmic risk. At the same time, there is some evidence contradicting the link between the TpTe interval and intramyocardial heterogeneity. We therefore tested the concept of TpTe interval by studying its age dependence and hypothesised that if it truly reflects the heterogeneity, it would be longer in the elderly compared to young subjects.

Methods During 24-hours recordings (SEER MC) in 60 healthy volunteers (30 ♀) of two age groups (A: 25–35 y, B: > 60 y), a 10-second 12-lead ECG was obtained every 10 seconds for 20 minutes combining supine and standing positions. The QT and QTpeak (QTp) intervals were obtained automatically by a previously verified extension of the QT Guard package (GE Medical). TpTe was computed as the difference between QT and QTp and averaged in leads V4–V6. Both QT and TpTe were heart-rate corrected using Fridericia formula.

Results In accordance with prior studies, both QT_c as well as $TpTe_c$ intervals differed between women and men in both age groups. While there was a significant prolongation of QT_c intervals with age in men, the prolongation in women was not statistically significant (men: 392.05 ± 11.64 ms vs. 402.24 ± 12.10 ms; p = 0.026; women: 409.67 ± 12.34 ms vs. 413.20 ± 9.48 ms; p = 0.254). However, $TpTe_c$ intervals showed age dependent differences neither in women nor in men (men: 88.42 ± 6.60 ms vs. 87.25 ± 7.11 ms; p = 0.389; women: 85.24 ± 7.27 ms vs. 84.58 ± 5.67 ms, p = 0.360). Similar lack of age differences were found for the heart-rate uncorrected TpTe interval **(Table 7)**.

Table 7: A. Schmidt et al.

QT_c	Young	Old	p-value
Women	409.67 ± 12.34 ms	413.20 ± 9.48ms	0.254
Men	392.05 ± 11.64 ms	402.24 ± 12.10ms	< 0.05
p-value	< 0.05	< 0.05	
$TpTe_c$	**Young**	**Old**	**p-value**
Women	85.24 ± 7.27 ms	84.58 ± 5.67 ms	0.360
Men	88.42 ± 6.60 ms	87.25 ± 7.11 ms	0.389
p-value	0.158	0.162	

Conclusion Despite sufficient experimental evidence that transmural heterogeneity of action potential duration increases with age, there was no age-related difference in TpTe and $TpTe_c$ intervals in both women and men. This further contributes to serious doubts about TpTe interval used as an index of transmural repolarisation heterogeneity in human hearts *in situ*.

6-III **106**

Repolarisation Synchrony is Decreased in the Elderly

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Objective Number of repolarisation gradients exist within the myocardium because of regional differences in action potential duration. These heterogeneities are physiologic and considered partly protective. Although experimental studies suggest that ion channel properties and thus action potential duration heterogeneity are age dependent, little is known on the age influence of physiologic repolarisation gradients. The angle between overall repolarisation and depolarisation dipoles (expressed by its cosine – TCRT) and the length of the T wave loop (TLL) have been shown to reflect global repolarisation homogeneity and to provide independent information on cardiac risk. While both very small (–1) and very large (+1) TCRT values reflect deviations from a physiologic repolarisation pattern (either a very large or a very small angle between repolarisation and depolarisation wavefront) large values of TLL indicate that more cells repolarise at the same time. Consequently, we hypothesised that age-related changes in global repolarisation patterns lead to differences in these two parameters between old and young subjects.

Methods During 24-hours recordings (SEER MC) in 60 healthy volunteers (30 ♀) of two age groups (A: 25–35 y, B: > 60 y), a 10-second 12-lead ECG was obtained every 10 seconds for 20 minutes combining supine and standing positions. Using custom-written software, TCRT and TLL values were obtained for each 10-second ECG. In both age groups, results in women and men were considered separately.

Results While TLL values in women were significantly smaller than in men reflecting smaller T waves in women (1546 ± 513 vs. 2305 ± 810; p < 0.05), there was also a significant decrease in TLL in both sexes with ageing (women A vs. B: 1546 ± 513 vs. 1201 ± 264; p < 0.05; men A vs. B: 2305 ± 810 vs. 1690 ± 534; p < 0.05). This was confirmed by a non-significant trend in TCRT with larger values in the elderly reflecting smaller angles and thus larger global differences in action potential duration (women: 0.45 ± 0.32 vs. 0.58 ± 0.23; men: 0.47 ± 0.34 vs. 0.64 ± 0.31).

Conclusion Using two descriptors of ventricular repolarisation dynamics, we found global repolarisation to be less synchronised in the elderly as compared to young subjects. This is likely to contribute to the increased arrhythmic risk at advanced age **(Figure 6)**.

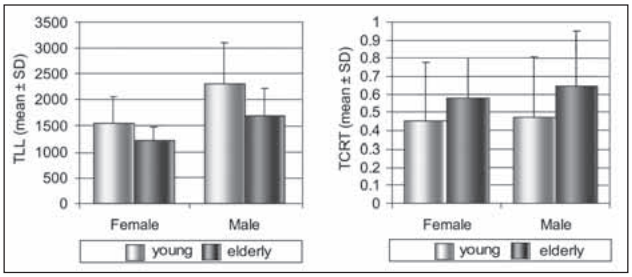

Figure 6: P. Smetana et al.

6-IV **089**

QTc Interval Predicts Risk of Future Adverse Cardiac Events in Patients Undergoing Percutaneous Coronary Intervention

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Background QTc interval prolongation is a predictor of cardiovascular morbidity and mortality in the general population. Currently, knowledge is limited about the association with outcome in patients undergoing percutaneous coronary interventions (PCI). We aimed to study the predictive value of heart rate-corrected QT interval (QTc) for major adverse cardiovascular events (MACE) in patients undergoing PCI.

Methods and Results We carried out a prospective study with 376 patients (age 64.8 ± 11 years) with stable or unstable coronary artery disease (CAD) undergoing PCI. Several clinical, laboratory, and ECG variables were recorded at baseline. QT was manually determined and the QT interval was corrected for heart rate using the method described by Bazett. MACE were defined as death from any cause, myocardial infarction, or restenosis assessed by clinically driven repeated angiography. After a median follow-up of 22 months (range, 17 to 25 months), 81 MACE were observed. QTc was 378.3 ± 61.7 and 363.8 ± 50.1 ms1/2, respectively ($p = 0.02$). QTc interval was 400 ms 1/2 in 30.9 % and 18.6 % of patients with and without MACE, respectively ($p < 0.05$). QTc 400 ms1/2 was a predictor of MACE, with an adjusted hazard ratio of 1.7 (95 %-CI, 1.1 to 3.8). Other factors significantly associated with MACE were older age, the presence of lower left ventricular ejection fraction at baseline, higher heart rate, higher hs-CRP, and more severe CAD at baseline.

Conclusions QTc interval is a predictor of future MACE in patients undergoing PCI. Intervention studies are needed to assess whether this factor could be modified.

6-V **088**

Postoperative White Blood Cell Count predicts Atrial Fibrillation after Cardiac Surgery

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Background Postoperative atrial fibrillation (AF) occurs in up to 50 % of cardiac surgery patients and represents the most common postoperative arrhythmic complication. The etiology of AF after open-heart surgery is incompletely understood and its prevention remains suboptimal. Currently, the role of inflammation and oxidative stress on electrical remodelling is under investigation and recent studies have demonstrated that CRP levels are elevated in atrial fibrillation. The aim of the present study was to investigate the correlation between the postoperative white blood cell (WBC) count as a marker of inflammation and the development of postoperative AF after cardiac surgery.

Methods and Results Patients undergoing elective cardiac surgery in the absence of significant left ventricular dysfunction (n = 253; average age 65 ± 11 years) were recruited to the present prospective study. 99 patients (39.1 %) of the total study population developed AF during the postoperative period. WBC was prospectively assessed in all patients to determine the predictive value of baseline and postoperative WBC count on development of postoperative AF. Baseline and postoperative peak WBC count was 6.8 ± 1.9 K/µL and 6.8 ± 2.2 K/µL ($p = 0.95$), and 16.3 ± 6.5 K/µL and 15 ± 4.2 K/µL ($p = 0.048$) in patients with and without postoperative AF, respectively. However, neither baseline nor peak monocyte count differed significantly between patients with and without postoperative AF (0.43 ± 0.15 K/µL and 0.46 ± 0.46 K/µL [$p = 0.5$], and 0.91 ± 0.3 K/µL and 0.93 ± 0.4 K/µL [$p = 0.8$], respectively). In addition to elevated peak WBC count (above versus below median [odds ratio (OR) = 1.8; 95 %-CI, 1.1 to 2.7; $p < 0.05$]), increasing age (above versus below median [OR = 2.6; CI, 1.2 to 3.9; $p < 0.01$]), surgery for valvular heart disease (versus coronay artery bypass grafting [OR = 2.8; CI, 1.1 to 3.5; $p < 0.01$]), development of postoperative complications (stroke, infections, unstable hemodynamics [OR = 1.9; CI, 1.0 to 7.5; $p < 0.05$]), and perioperative nonuse of beta-adrenergic blockers (OR = 1.7; CI, 1.1 to 4.9; $p < 0.05$) were identified as independent predictors of postoperative AF by multivariate logistic regression analysis.

Conclusions Cardiac surgery is associated with elevated postoperative WBC count that represents a common marker of inflammation. A more pronounced increase in postoperative WBC counts independently predicts development of postoperative AF. These data provide additional evidence supporting the association between inflammatory response and postoperative AF.

6-VI **091**

Katheterablation akzessorischer Leitungsbahnen mit Hilfe des LocaLisa®-Mapping-Systems – Erhöhung der Effektivität bei vereinfachter Prozedur und Reduktion der Strahlenbelastung

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Hintergrund Das LocaLisa®- (LL) Mapping-System (Medtronic Inc., Minneapolis, USA) erleichtert durch eine nichtfluoroskopische dreidimensionale Darstellung von Katheterpositionen und -bewegungen das Führen und Plazieren von diagnostischen und Ablationskathetern. Mit Hilfe eines niedrigenergetischen Spannungsfeldes erfolgt rechnergesteuert eine virtuelle Echtzeit-Darstellung auf einem zusätzlichen Bildschirm, wodurch ein genaueres Manövrieren bei gleichzeitiger Reduktion der Strahlenbelastung gewährleistet werden soll. Dies konnte bereits bei technisch einfachen, aber durchleuchtungsintensiven Prozeduren wie der cavotrikuspidalen Isthmusablation bei typischem Vorhofflattern gezeigt werden. Ziel unserer Untersuchung war es, den theoretischen Vorteil dieser bildgebenden Methode nun auch bei der Ablation komplexerer Substrate, im gegebenen Fall akzessorischer Leitungsbahnen (ALB), zu evaluieren.

Patienten und Methodik Das LL-System ist seit April 2002 an unserer Abteilung regelmäßig bei jeder Katherablation in Verwendung. In einem 2jährigen Beobachtungszeitraum bis April 2004 wurde bei 32 Patienten (Pat.) unter LL-Unterstützung eine Ablation einer ALB durchgeführt (Gruppe I, G I). Sämtliche klinische und prozedurale Daten wurden nun mit denen der 33 Pat. verglichen, bei denen in den 2 Jahren zuvor ALB ohne LL-Unterstützung abladiert wurden (Gruppe II, G II). Als primärer Ablationserfolg wurde die Eliminierung der Leitungseigenschaften der ALB definiert. Bei linksseitig gelegenen ALB wurde primär ein retrograder transaortaler Zugang gewählt, erst bei fehlendem Ablationserfolg wurde in gleicher oder 2. Sitzung eine transseptale Punktion (TSP) durchgeführt.

Ergebnisse Die primäre Erfolgsrate in G I betrug 97 % (31 von 32 Pat., 1 Pat. mit 2 ALB), verglichen mit 85 % (28 von 33 Pat., 1 Pat. mit ALB und AVNRT) in G II ($p = 0,09$), wobei in beiden G je 1 Rezidiv (3 %) sowie 1 kleiner postinterventioneller Insult (G I) und 1 Perikardtamponade (G II, nach TSP) auftraten. In beiden G fand sich eine vergleichbare Anzahl linksseitiger ALB (G I: 27, G II: 26; p = n. s.), wobei zur erfolgreichen Ablation in G I 6 TSP (22 %) und in G II 12 TSP (46 %) erforderlich waren ($p < 0,05$). Die mittlere Durchleuchtungszeit betrug insgesamt in G I 31,9 + 29,1 (7–113) Minuten (min) und in G II 46,1 + 27,1 (7–108) min ($p < 0,05$). Diese Ersparnis war vor allem bei linksseitigen ALB durch die signifikante Reduktion der Anzahl von TSP und die gute virtuelle Steuerbarkeit des Ablationskatheters entlang des Mitralklappenanulus (ebenfalls virtuell durch den Koronarsinuskatheter dargestellt) ausgeprägt (G I: 29,1 + 27,1 min, G II: 47,6 + 26,3 min; $p = 0,02$).

Schlußfolgerung Durch den routinemäßigen Einsatz des LocaLisa®-Mapping-Systems bei der Ablation akzessorischer Leitungsbahnen kann ohne Lernkurve die Strahlenbelastung für Patient und Untersucher signifikant reduziert werden. Besonders bei der Behandlung linksseitiger ALB können durch die Möglichkeit des genaueren Führens des Ablationskatheters bei höherer Effektivität und niedrigerer Notwendigkeit transseptaler Punktionen Durchleuchtungs- und Prozedurzeit eingespart werden.

6-VII **12**

Underdetection of Atrial Flutter in Patients with Cardiac Resynchronisation Devices

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Background Atrial fibrillation (AF) and atrial flutter (AFL) are frequently observed in pts with congestive heart failure. Cardiac resynchronisation therapy (CRT) may help reducing AF/AFL by improving global hemodynamic output and decreasing mitral regurgitation. However, occurrence of AF/AFL requires immediate mode-switch (MS) to a non-atrial tracking mode.

Methods Seven pts (6 ♂, 1 ♀; age 60 ± 11 y) with CRT devices were admitted to our hospital as emergencies. The automatic MS feature was programmed on in all pts. Underlying heart disease was ischemic (n = 3) and idiopathic cardiomyopathy (n = 4). Mean LVEF was 25 ± 8 %. Four pts had a history of AF. All pts were on optimal treatment including ACE inhibitors and beta-blockers, 4 pts were on digitalis and amiodarone.

Results In all 7 pts cardiac decompensation was caused by rapid ventricular rates during AFL. Surface ECG showed paced QRS complexes at a mean rate of 123 ± 9 ppm and sensed ventricular beats in the pts with CRT-D. Device interrogation revealed AFL (CL 246 ± 18 ms, range 220–280 ms) on the bipolar atrial electrogram. MS failure was noted in all pts with CRT-P due to coincidence of every second flutter wave with atrial blanking (PVAB 143 ± 34 ms, range 80–180 ms). The 2:1 lock-in response occurred, as the sum of AV interval and PVAB was longer than the atrial cycle length, and as the AV interval plus PVARP was shorter than two atrial cycles. In addition, the MS detection rate and maximum tracking rate were both higher than half the AFL rate. Shortening of PVAB was required for interruption of 2:1 atrial sensing and restoration of MS. AFL was managed by cardioversion in 4 pts, overdrive stimulation and flutter ablation in the other pts.

Conclusion Underdetection of AFL may result in sustained rapid ventricular pacing and deterioration of NYHA functional classes in pts with CRT. The interplay between pacemaker refractory/blanking periods and the flutter cycle length provides the substrate for malrecognition (2:1 lock-in phenomenon). Pts presenting with intolerance to biventricular pacing should undergo immediate device interrogation for potential MS failure.

POSTERDISKUSSION B

Donnerstag, 2. Juni 2005, 17–18.30 Uhr

Sitzung 1 – Allgemein III

1-I **028**

Evidence for Elevated Triglycerides and Low HDL Cholesterol as the Main Lipid Risk Factors for Diabetic Atherosclerosis

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Background There is a paucity of longitudinal data on the impact of serum lipids on the future incidence of vascular events among the high risk cohort of coronary patients with diabetes.

Methods We therefore enrolled 750 consecutive patients undergoing coronary angiography for the evaluation of coronary artery disease (CAD). At baseline, serum lipids were measured, and the incidence of fatal and non-fatal vascular events was recorded over 4 years. The following endpoints were recorded: coronary death, fatal ischemic stroke, non-fatal myocardial infarction, non-fatal stroke, and need for coronary artery bypass grafting, percutaneous coronary intervention, or non-coronary revascularisation.

Results From our coronary patients, 272 (36.2 %) had normal fasting glucose < 5.6 mmol/L (NFG), 314 (41.9 %) impaired fasting glucose ≥ 5.6 mmol/L (IFG), and 164 (21.9 %) type 2 diabetes (T2DM). The incidence of vascular events significantly ($p < 0.001$) increased from subjects with NFG (14.7 % [40 of 272 patients]) over patients with IFG (19.4 % [61 of 314 patients]) to patients with T2DM (30.5 % [50 of 164 patients]). Factor analysis revealed two factors in the lipid profiles of our patients: triglycerides, HDL cholesterol, apolipoprotein A1, and LDL particle diameter loaded high on a HDL-related factor; and total cholesterol, LDL cholesterol, and apolipoprotein B loaded high on a LDL-related factor. The HDL-related factor ($p < 0.001$) but not the LDL-related factor increased significantly from subjects with NFG over patients with IFG to patients with T2DM. In patients with T2DM, the HDL-related factor (OR 0.707 [0.514–0.971]; $p = 0.032$), but not the LDL-related factor (OR 1.159 [0.896–1.498]; $p = 0.261$) proved significantly predictive for vascular events.

Conclusions The low HDL/high triglyceride pattern is associated with the degree of hyperglycemia and significantly predicts the future incidence of vascular events among coronary patients with T2DM. This characteristic diabetic dyslipidemia is thus the main lipid risk factor for vascular events in our diabetic coronary patients.

1-II **119**

PAI-1 Plasma Levels are Elevated in Insulin Resistant Women with a History of Gestational Diabetes mellitus

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Background Elevated plasma concentrations of plasminogen activator inhibitor (PAI-1) have been demonstrated in patients with type 2 diabetes and are independent risk factors for cardiovascular events.

Methods and Results We investigated plasma levels of PAI-1 in women with a history of gestational diabetes (p-GDM) (n = 50) 4–6 months postpartum. Mathematical model analysis of data derived from frequently sampled intravenous glucose tolerance tests showed that 58 % of the pGDM subjects had normal insulin sensitivity (NIS) and 42 % impaired insulin sensitivity (IIS). Women with IIS had significantly higher body mass index ($p < 0.001$), waist to hip ratio ($p < 0.001$), body fat mass ($p < 0.001$), fasting and stimulated plasma insulin, proinsulin and C-peptide ($p < 0.001$) but lower HDL-cholesterol (HDL-c) ($p < 0.05$) as compared to women with NIS. IIS women had significantly higher tPA plasma levels compared to NIS and controls. Mean PAI-1 was 70 % higher in women with IIS when compared to NIS and healthy subjects ($p < 0.001$). PAI-1 significantly correlated with BMI, fasting and stimulated insulin and proinsulin and was inversely related with the insulin sensitivity index (S_I). In addition, obese women with IIS had higher PAI-1 levels ($p < 0.001$) than normal weighted women with IIS and NIS as well as obese NIS. The ratio PAI-1/S_I was elevated in women with IIS compared to NIS and control subjects independently of their glucose tolerance status ($p < 0.001$).

Conclusion Elevated PAI-1, and PAI-1/S_I were observed in p-GDM patients with IIS and might contribute to an increased cardiovascular risk.

1-III **020**

Creatinine Clearance Independently Predicts Extent and Severity of Coronary Atherosclerosis in Patients with Stable Coronary Artery Disease

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Background Although there is accumulating evidence that renal insufficiency is associated with an increased risk for cardiovascular events in patients with coronary artery disease (CAD), it is not known whether creatinine clearance rates at the time of hospital admission are associated with the extent and severity of coronary atherosclerosis assessed angiographically.

Patients and Methods We studied 1062 consecutive white subjects (336 ♀ and 726 ♂; mean age 65.6 ± 18.8 years) undergoing coronary angiography for stable CAD at a single referral center. In addition to conventional risk factors and clinical characteristics as predictors of extent and severity of coronary atherosclerosis, we assessed creatinine clearance rates at the time of admission. Two experienced cardiologists blinded to the clinical and laboratory data reviewed the angiographic films and defined severity of CAD on the basis of the sum of three scoring systems, whose total score could range from 0 to 27: (1) a vessel score with one point for each of the three main coronary arteries with a diameter stenosis > 30 %; (2) a segment score with each coronary artery being divided into three segments (proximal, mid, distal); and (3) a stenosis score with 0, 1, 2 or 3 points being given for no, 30–50 %, 51–75 %, and > 75 % diameter stenosis.

Results Patients were devided into three groups according to CAD severity score. Creatinine clearance rates were 67.5 +12.8, 60.1 + 15.9, and 57 + 18.3 mL/min for group I (410 patients; CAD score 0–3), group II (316 patients; CAD score 4–8), and group III (336 patients; CAD score > 8), respectively ($p < 0,05$). Significant renal dysfunction, as defined by the National Kidney Foundation in the Kidney Disease Outcomes Quality Initiative classification of kidney function as an estimated glomerular filtration rate of < 60 mL/min/1.73 m^2, was significantly more common in groups II and III compared to group I ($p < 0.01$). When grouped according to levels of creatinine clearance (group A: > 75 mL/min; group B: < 75 to > 68; group C: < 68 to > 58; group 4: < 58), scores of the angiographic severity of CAD were 5.0 + 3.7, 5.64 + 3.6, 6.63 + 4.1, and 7.35 + 4.0, respectively (p for trend < 0.0001). After adjustment for baseline characteristics including age, gender, and CAD risk factors, patients in groups C and D had significantly higher scores of CAD severity as compared to group A and B patients ($p < 0.01$).

Conclusion Creatinine clearance on admission independently predicts extent and severity of coronary atherosclerosis in patients with stable CAD. Thus, increased serum creatinine may be a marker for non-traditional proatherogenic factors.

1-IV **108**

NT-proBNP-Spiegel und Mortalität im kardiogenen Schock

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Fragestellung Das N-terminal B-type natriuretic peptide (NT-proBNP) ist ein natriuretisches Peptid, dessen Plasmawerte bei Druck- oder Volumenbelastung des Herzmuskels ansteigen. Rezente Studien zeigten, daß erhöhte BNP-Spiegel bei akutem Koronarsyndrom sowie bei kritisch kranken Patienten auf Intensivstationen mit einer schlechten Prognose assoziiert sind. Wir untersuchten die prognostische Relevanz erhöhter NT-proBNP-Spiegel bei Patienten im kardiogenen Schock.

Methoden Retrospektive Analyse der NT-proBNP-Spiegel bei 48 Patienten mit einem kardiogenen Schock zum Zeitpunkt der Aufnahme auf der CCU/ICU. Korrelation mit Mortalität und Organversagen.

Ergebnisse Ursachen für den kardiogenen Schock waren (1) akute Ischämie ± mechanische Komplikationen (n = 36), (2) dilatative Kardiomyopathie (n = 5) und (3) Schock als Folge eines dekompensierten Klappenvitiums (n = 7). Im Median wurden die Plasmaproben 16 Stunden nach Schockbeginn gewonnen. Der durchschnittliche Vasopressorenbedarf (kombinierte Noradrenalin- und Adrenalindosis) zu diesem Zeitpunkt betrug 0,39 ± 0,66 mg/kg/min. Im Median (25., 75. Perzentile) betrug der NT-proBNP-Spiegel bei Aufnahme 12.580 (5634–23.449) pg/ml. 8 Patienten zeigten NT-proBNP-Spiegel bei Aufnahme von > 35.000 pg/ml. Schockpatienten mit unterschiedlichen kardialen Grunderkrankungen unterschieden sich nicht signifikant in ihren initialen NT-proBNP-Werten. Die NT-proBNP-Spiegel waren bei Patienten mit vorbekannter reduzierter Linksventrikelfunktion (LVEF) vergleichbar wie bei Patienten ohne vorbekannte Einschränkung der LVEF. Es fand sich keine Korrelation zwischen dem Vasopressorenbedarf und der Höhe der NT-proBNP-Spiegel ($r = –0,02$, $p > 0,8$). Patienten mit Multiorganversagen (n = 17, definiert nach SOFA-Score) hatten vergleichbar hohe initiale NT-proBNP-Spiegel wie Patienten mit 1-Organversagen (n = 20) oder Patienten ohne Organversagen (n = 11; p = 0,99 mittels ANOVA). Auch Patienten mit einem akuten Nierenversagen (n = 22) hatten keine höheren NT-proBNP-Spiegel als Patienten, mit normaler oder eingeschränkter Nierenfunktion (n = 26) (17.026 ± 11.824 vs. 14.527 ± 10.970; p = 0,45). Patienten, die innerhalb der ersten 30 Tage verstarben, zeigten jedoch signifikant höhere NT-proBNP-Spiegel als Patienten die nach 30 Tagen überlebten (18.910 ± 11.864 vs. 9771 ± 7424, p = 0,002). In einer ROC-Analyse (p = 0,01) war ein NT-proBNP-Spiegel von > 27.000 pg/ml mit einer 100%igen 30-Tage-Mortalität assoziiert (Sensitivität jedoch nur 30 %). Ein NT-proBNP-Spiegel von > 13.000 pg/ml war mit einer 30-Tage-Mortalität von 82 % (bei einer Sensitivität von 62 %) assoziiert.

Zusammenfassung Die initialen NT-proBNP-Spiegel bei Patienten im kardiogenen Schock korrelieren mit der 30-Tage-Überlebensrate, unabhängig von der kardialen Grunderkrankung, der vorbekannten LVEF, dem Katecholaminbedarf und dem Schweregrad des Schockzustandes.

1-V **027**

High Triglycerides, Low HDL Cholesterol, and Small LDL Particles Predict Incident Type 2 Diabetes in Non-Diabetic Coronary Patients

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Background and Hypothesis Patients with type 2 diabetes mellitus (T2DM) exhibit a typical pattern of dyslipidemia with high triglycerides, low HDL cholesterol, and small LDL particles, which is also frequently observed in pre-diabetic patients. We therefore hypothesized that high triglycerides, low HDL cholesterol, and a small LDL particle diameter are predictive of incident T2DM among non-diabetic individuals.

Methods We enrolled 362 non-diabetic patients undergoing coronary angiography for the evaluation of CAD. Diabetes was diagnosed according to ADA criteria; thus at baseline all patients had a fasting plasma glucose (FPG) ≤ 125 mg/dL and no patient was receiving antidiabetic medication. The incidence of T2DM (FPG ≥ 126 mmol/L, or intake of antidiabetic medication) was recorded after a follow-up period of 4 years.

Results From our non-diabetic coronary patients, 172 had normal fasting glucose (NFG) < 100 mg/dL, and 190 had impaired fasting glucose (IFG) ≥ 100 mg/dL at baseline. After 4 years, T2DM was

newly diagnosed in 15 patients. IFG was associated with a strongly increased risk of T2DM (adjusted HR = 5.559 [1.230–25.136] p = 0.026). Whereas serum values of total cholesterol, LDL cholesterol, and apolipoprotein B were not associated with the incidence of T2DM, triglycerides (standardized adjusted HR = 2.123 [1.351–3.337]; p = 0.001), and, inversely, HDL cholesterol (HR = 0.315 [0.124–0.801]; p = 0.015) as well as the LDL particle diameter (HR = 0.062 [0.008–0.492]; p = 0.008) proved significantly predictive of incident T2DM in our cohort of coronary patients.

Conclusions From our data we conclude that among patients undergoing coronary angiography IFG is strongly predictive of incident T2DM. Importantly, high triglycerides, low HDL cholesterol, and a small LDL particle diameter also are significant predictors of the 4-year incidence of T2DM among non-diabetic coronary patients.

1-VI **026**

Lipoprotein(a) in Coronary Patients with Type 2 Diabetes is Low and Not Predictive of Vascular Events

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Background Lipoprotein(a) [Lp(a)] is an important cardiovascular risk factor in the general population. However, prospective data on Lp(a) as a cardiovascular risk factor in patients with type 2 diabetes (T2DM) are scarce and controversial.

Methods We therefore measured serum levels of Lp(a) in 587 consecutive patients undergoing coronary angiography for the evaluation of coronary artery disease (CAD). Over a median [interquartile range] follow-up period of 4.0 [3.6–4.2] years the incidence of vascular endpoints was recorded.

Results From the total cohort, 136 patients (23.2 %) had T2DM, and 451 patients did not have diabetes. At baseline, Lp(a) was significantly lower in patients with T2DM than in non-diabetic patients (11 [0–30] mg/dL vs. 16 [0–51] mg/dL; p = 0.025). Whereas Lp(a) was strongly and significantly predictive for the presence of CAD at angiography for non-diabetic patients (standardized adjusted HR = 1.437 [1.137–1.815]; p = 0.002), it was not associated with CAD in patients with T2DM (1.335 [0.721–2.469]; p = 0.358). Consistently, in the prospective part of the study Lp(a) proved independently predictive for vascular events among non-diabetic patients (HR = 1.316 [1.094–1.582]; p = 0.004), but not among patients with T2DM (HR = 0.656 [0.380–1.133]; p = 0.130). An interaction term T2DM × Lp(a) was significant (p = 0.023), indicating that Lp(a) was a significantly stronger predictor of vascular events among non-diabetic patients than among patients with T2DM.

Conclusions Among coronary patients with T2DM, Lp(a) is low and neither associated with the presence of CAD at angiography nor with the future incidence of vascular events.

1-VII **025**

Type 2 Diabetes Mellitus is Not a Coronary Artery Disease Risk Equivalent

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Background An equally high risk to die from a myocardial infarction (MI) has been described for patients with type 2 diabetes mellitus (T2DM) without a history of MI as for non-diabetic patients with a prior MI by one study from Finland, but other studies have not confirmed T2DM as a coronary artery disease (CAD) risk equivalent. Cardiovascular risk among diabetic patients may vary considerably if coronary atherosclerosis is present or absent.

Methods We therefore assigned 750 consecutive patients according to their coronary angiograms to one of four groups: DM–/CAD– (patients with neither T2DM nor CAD at angiography, n = 244), DM+/CAD– (patients with T2DM but without CAD, n = 50), T2DM–/CAD+ (patients without T2DM but with CAD, n = 342), and DM+/CAD+ (patients with both T2DM and CAD, n = 114). The incidence of fatal and non-fatal vascular events was recorded over 4 years.

Results The incidence of vascular events averaged 20.1 % in the 750 patients and was strongly affected by the angiographic state but not by the diabetic state: the proportion of patients with vascular events was similar in DM–/CAD– (8.9 %) and DM+/CAD– (10.0 %) patients (p = 0.739), but higher in DM–/CAD+ (23.8 %, p < 0.001) and DM+/CAD+ patients (40.2 %, p < 0.001) when compared to DM–/CAD–. Also, the incidence of vascular events was significantly higher in DM+/CAD+ than in DM+/CAD– (p < 0.001) or DM–/CAD+ (p < 0.001). Most importantly, patients with T2DM only (DM+/CAD–) had a significantly lower event rate than non-diabetic coronary patients (DM–/CAD+, p = 0.034).

Conclusions Our 4-year prospective study provides strong evidence that T2DM is not a CAD risk equivalent: patients with T2DM and normal coronary angiography face only half the risk of non-diabetic CAD patients to develop an atherosclerotic event.

1-VIII **34**

Stroke in Diabetic and Non-Diabetic Patients: Course and Prognostic Value of Admission Serum Glucose

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Background, Aims Whether diabetes mellitus affects the prognosis of stroke patients, and whether admission hyperglycemia influences prognosis similarly in diabetic and non-diabetic patients is assessed controversially. Aim of the study was to (1) compare the course of diabetic and non-diabetic acute stroke patients and (2) assess the influence of admission serum glucose levels on mortality.

Methods In 57 Austrian medical departments the hospital course of consecutive stroke patients was documented prospectively between June 1999 and October 2000.

Results 296 (30 %) of 992 patients had a history of diabetes mellitus. Intracerebral hemorrhage was more frequent in non-diabetic patients than diabetic (13 vs. 5 %, p = 0.0001). Coronary heart disease was more frequent in diabetic than in non-diabetic patients (25 versus 24 %, p = 0.0003). The mortality was 18 % among non-diabetic und 16 % among diabetic patients (p = 0.3559). Among patients who were discharged alive, the Barthel Index increased from 50 to 90 in non-diabetic and from 45 to 75 in diabetic patients (p = 0.0403). In non-diabetic patients, admission serum glucose > 9.2 mmol/L was associated with a more than 4-fold increased mortality, compared with patients with serum glucose < 5.7 mmol/L (p < 0.0001).

Conclusions Diabetic stroke patients need special care since they tend to have a poorer recovery than non-diabetic patients. Admission hyperglycemia in non-diabetic acute stroke patients predicts a poor prognosis.

Sitzung 2 – Chirurgie

2-I **071**

Die MAZE-Operation zur Behandlung des chronischen Vorhofflimmerns im Langzeitverlauf: 3-Jahres-Ergebnisse

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Grundlagen Die MAZE-Operation mittels Ablation mit Mikrowelle oder Radiofrequenz ist ein etabliertes Verfahren zur Behandlung des chronischen Vorhofflimmerns. Diese Studie untersucht die Langzeitergebnisse nach 36 Monaten.

Methodik Zwischen 2/2001 und 12/2002 wurden 42 Patienten mit chronischem Vorhofflimmern > 6 Monate (64,5 ± 2,2 Jahre, 9 Männer) und zusätzlicher teils kombinierter Klappenerkrankung mittels Mitralklappenersatz/-rekonstruktion ± Trikuspidalklappenrekonstruktion (n = 30), Aortenklappenersatz ± Trikuspidalklappenrekonstruktion (n = 6) und Mitralklappen- und Aortenklappenersatz/-rekonstruktion ± Trikuspidalklappenrekonstruktion (n = 6) und MAZE operiert. Die mittlere Dauer des Vorhofflimmerns lag bei 63 ± 29 Monaten (7–384 Monate). Bei der MAZE-Operation wurden, dem Cox-III-Konzept folgend, in beiden Vorhöfen lineare Läsionen mit Mikrowellen- bzw. Radiofrequenzablation gesetzt.

Ergebnisse Die MAZE-Operation führte zu 23 ± 2 Minuten zusätzlicher Aortenklemmzeit (total: 89 ± 3 min). Aufgrund eines SIRS war bei einem Patienten der Intensivaufenthalt verlängert. Bei den restlichen Patienten war die Intubationsdauer 18,3 ± 6,7 Stunden, der Intensivaufenthalt 1,7 ± 0,6 Tage. 54 % wurden mit Sedacoron behandelt, 64 % kardiovertiert. 25 % Patienten benötigten wegen eines AV-Blockes bzw. eines Sick-Sinus-Syndroms einen Schrittmacher. Nach 12 Monaten waren 80 % frei von Vorhofflimmern. Beim letzten Nachuntersuchungszeitpunkt (36 ± 8 Monate) waren 78 % frei von Vorhofflimmern: 60 % SR, 4 % Knotenrythmus, 16 % PM, 20 % Vorhofflimmern bzw. -flattern.

Schlußfolgerungen Die MAZE-Operation mittels Mikrowellen bzw. Radiofrequenzablation dem Cox-III-MAZE-Konzept folgend erhöht das chirurgische Risiko nur gering. Die Freiheit von Vorhofflimmern ist nach 1 und 3 Jahren praktisch gleich. Es ist also auch langfristig möglich, Patienten mit chronischem Vorhofflimmern einen stabilen Sinusrhythmus zu gewährleisten.

2-II **66**

Totally Endoscopic Coronary Artery Bypass-Grafting – Feasibility, Safety, Perioperative and Intermediate Term Results

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Background Robotic technology has enabled completely endoscopic procedures in heart surgery and totally endoscopic coronary artery bypass grafting (TECAB) has become a reality. We report on our experience with TECAB performed on the arrested heart (AH-TECAB).

Methods From 10/2001 to 3/2005 48 patients underwent AH-TECAB at our institution. Median age was 59 (38–70) years, 33 patients were male (69 %), median EuroSCORE was 1 (0–4). The following endoscopic procedures were carried out: Left internal mammary artery (LIMA) bypass to the left anterior descending artery (LAD) system: n = 44, right internal mammary artery (RIMA) bypass to the right coronary artery (RCA): n = 1, double bypass grafting (RIMA to LAD, LIMA to obtuse marginal branch/OM): n = 3. All interventions were performed using the daVinci™ telemanipulation system (Intuitive Surgical) and the ESTECH Remote Access Perfusion (RAP™) system, which was installed through the femoral vessels. 3 or 4 thoracic ports were used.

Results There were 5 conversions to larger thoracic incisions (15 %) and 5 grafts had to be revised on table (10 %). Aortic occlusion time, cardiopulmonary bypass time, and procedure time including intraoperative angiography were 79 (37–223) min, 115 (72–368) min, 371 (260–724) min, respectively. Patients were extubated 8 (0–278) h, postoperatively and discharged from the ICU after 21 (11–389) h. Maximum CK was 660 (71–7672) U/L, maximum CKM13 was 23 (7–137) U/L. There was no hospital mortality. Freedom from angina was 100 % at 6 months and 93 % at 36 months.

Conclusion AH-TECAB can be performed with acceptable safety. Long procedure times and high conversion rates are a fact, at least during the implementation phase. Besides single LIMA to LAD grafting totally endoscopic double bypass procedures have become feasible. Intermediate term clinical results are satisfactory.

2-III **122**

The Efficacy of Perioperative Beta-Blockers in the Prevention of Surgery Related Mortality and Morbidity: A Cochrane Review of Randomised Clinical Trials*

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Background Cardiovascular mortality and morbidity are prevalent and costly in patients undergoing cardiac and non-cardiac surgery. The prevention of early postoperative complications remains a major issue in these interventions. Surgery for acquired cardiac disease has a mortality rate of up to 3 %, up to 6 % perioperative myocardial infarction and overall complication rates of 15 % to 24 %, depending on the kind of operation and patients' comorbidity. Even in non-cardiac surgery an estimated 4 % of the patients will have a perioperative cardiac complication and 0.5 % will suffer a myocardial infarction.

Objectives The objective of this review was to systematically analyse the evidence of the effect of perioperatively administered beta-adrenoceptor blocking agents for the prevention of surgery related mortality and morbidity. Study participants are individuals 18 years or older undergoing any type of surgery. We looked at some of the most debilitating surgery related complications. The main outcome of our study was all cause mortality (up to 30 days postoperatively).

Methods Databases were searched from the time period when they started to cover the literature up until march 2005. We identified trials by searching CENTRAL (The Cochrane Library issue 3 2003), the Cochrane Anaesthesia Group Specialized Register, MEDLINE (inception:1966), EMBASE (inception: 1980), Biological Abstracts (BIOSIS), CAB Health, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Derwent Drug File, Science Citation Index/Current Contents. A highly sensitive search strategy (Dickersin 1994) identified by the Cochrane Collaboration was used for the identification of RCT's.

Results From the initial database search we retrieved 3672 titles and their respective abstracts. All titles were screened by two reviewers independently. Of all trials 3509 were judged to be irrelevant for our review. We obtained and reviewed the full-text versions of the remaining 163 studies. Of these 62 trials were found to meet the preset inclusion criteria. In our analysis we found that beta-blocker reduce all cause mortality (OR: 0.43; p-value: 0.008), they reduce the occurrence of myocardial ischemia (OR: 0.35; p-value: < 0.001), lower the rate of ventricular arrhythmias (OR: 0.31; p-value: < 0.001), and prevent atrial fibrillation (OR: 0.62; p-value: < 0.001). Furthermore, these drugs can shorten the length of hospital stay by 0.8 days per patient (p-value: 0.02). Interestingly, beta-blockers failed to reduce the rate of perioperative myocardial infarction (OR: 0.75; p-value: 0.24).

Conclusion This is the most extensive review on the topic carried out to date. We could demonstrate that beta-blockers can reduce many life-threatening conditions, as well as length of hospital stay. Most of their beneficial effects derive from their antiarrhythmic properties. They do not seem to have any effect on the occurrence of acute coronary syndromes. Beta-blockers should be used more extensively in patients at risk for cardiac events undergoing surgery.

* This study is the topic of an upcoming Cochrane review. A peer-reviewed research protocol was published in August 2003.

2-IV **072**

Minimal-invasive Koronarchirurgie bei Patienten mit reduzierter LV-Funktion – erste Ergebnisse einer prospektiv-randomisierten Single-Center-Studie

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Hintergrund Obwohl gezeigt werden konnte, daß die Koronarchirurgie am schlagenden Herzen zu einer Reduktion der Morbidität und Mortalität führt, bestehen keine Richtlinien, welche Patienten

von dieser Methode am meisten profitieren. Ziel dieser laufenden, prospektiv-randomisierten Studie ist es, die postoperativen Ergebnisse von OFF- und ON-Pump-Patienten mit niedriger Auswurffraktion (EF) zu vergleichen.

Methode Zwischen Dezember 2003 und Februar 2005 wurden 34 Patienten randomisiert und erhielten entweder eine Revaskularisation mit oder ohne Herz-Lungen-Maschine (HLM). Einschlußkriterien waren eine EF kleiner 35 % und das Vorliegen einer Mehrgefäßerkrankung, Ausschlußkriterien waren instabile AP und Notoperationen. Die Endpunkte der Studie waren die Zeit bis zur Extubation sowie die Spitalsmorbidität und -mortalität (MW ± Stabw).

Ergebnisse Die EF lag in der OFF-Pump-Gruppe bei 26 ± 4 %, in der ON-Pump-Gruppe bei 25 ± 4 %, der EuroScore bei 8 ± 1 und 7 ± 1. Insgesamt erhielten 17 Patienten (70 ± 6 Jahre) durchschnittlich 3 ± 1 Grafts ohne HLM, 17 Patienten (71 ± 5 Jahre) 3,2 ± 1 Grafts mit HLM. Die Zeit bis zur Extubation war in der Gruppe ohne HLM 12 ± 2,3, mit HLM 16,1 ± 2,1 Stunden ($p < 0,05$). Die CK-MB war zu den Zeitpunkten 4, 12 und 24 Stunden in der OFF-Pump-Gruppe 20 ± 5, 21 ± 7 und 22 ± 9 ng/ml verglichen mit der ON-Pump-Gruppe 36 ± 7, 48 ± 6 und 60 ± 9 ng/ml und somit immer niedriger ($p < 0,05$). Kein Patient verstarb während des Aufenthaltes, 3 Patienten in der ON-Pump-Gruppe jedoch während der Nachbeobachtungszeit (2 Patienten kardial nach 2 und 12 Monaten; 1 Patient nichtkardial nach 6 Monaten).

Schlußfolgerung Die vorläufigen Ergebnisse legen den Schluß nahe, daß Patienten mit schlechter Auswurffraktion sowohl postoperativ als auch im Langzeitverlauf von einer Operation ohne HLM profitieren.

2-V **069**

Risk Factors of Postoperative Atrial Fibrillation after Cardiac Surgery

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Background Postoperative atrial fibrillation (AF) occurs in up to 50 % of cardiac surgery patients and represents the most common postoperative arrhythmic complication. The etiology of AF after open-heart surgery is incompletely understood and its prevention remains suboptimal. Identification of patients vulnerable for postoperative AF would allow targeting of those most likely to benefit from aggressive prophylactic intervention. The aim of the present study was to evaluate clinical predictors of postoperative AF.

Methods and Results Patients undergoing elective cardiac surgery in the absence of significant left ventricular dysfunction (n = 253; average age 65 ± 11 years) were recruited to the present prospective study. 99 patients (39.1 %) of the total study population developed AF during the postoperative period. The median age for patients with postoperative AF was 69 years compared with 64 years for patients without ($p < 0.001$). In addition to advanced age, AF patients were more likely to have surgery for valvular heart disease and less likely to have preoperative beta-adrenergic blockers than patients without AF. Multivariate logistic regression analysis (odds ratio, ± 95 %-CI, p-value) was used to identify the following independent clinical predictors of postoperative AF: increasing age (above versus below median [OR = 2.6; CI, 1.2 to 3.9; $p < 0.01$]), and surgery for valvular heart disease (versus coronary artery bypass grafting [OR 2.8; CI, 1.1 to 3.5; $p < 0.01$]). Additionally, postoperative complications (stroke, infections, unstable hemodynamics [OR = 1.9; CI, 1.0 to 7.5; $p < 0.05$]), and preoperative non-use of beta-adrenergic blockers (OR = 1.7; CI, 1.1 to 4.9; $p < 0.05$) were associated with increased risk for postoperative AF. Both, patients with and without AF had similar Body Mass Index, preoperative heart rate, preoperative blood pressure, and duration of surgery. Male sex did not identify patients at high risk for development of AF after cardiac surgery.

Conclusions Postoperative AF remains the most common complication after cardiac surgery. A combination of advanced age and type of surgery identifies patients at high risk for development of AF after cardiac surgery.

2-VI **65**

Prä- und perioperatives Management von Aortendissektionen (Typ-A) bei herzoperierten Patienten

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Thorakale Aortendissektionen (AD) stellen eine potentiell lebensbedrohliche Situation dar. Die Inzidenz einer AD in Folge oder als Komplikation von herzchirurgischen Eingriffen beträgt 10–13 %. Klinik und Management unterscheiden sich jedoch grundlegend von primären AD und beeinflussen die Prognose. Aus den Aneurysmadateien der Universitätskliniken für Herzchirurgie Graz, Innsbruck und Salzburg wurden retrospektiv alle Fälle von AD nach herzchirurgischen Eingriffen identifiziert. Die Kasuistiken wurden analysiert und die Ergebnisse mit rezent publizierten Daten anderer Zentren verglichen.

Seit Januar 1990 wurden insgesamt 27 Fälle (19 ♂, 8 ♀, Alter 64,7 ± 8,6 Jahre) von AD (Typ A; 15 akut, 12 chronisch) nach herzchirurgischen Eingriffen (10 × AKE, 3 × AKE + CABG, 2 × DKE, 1 × MKE + CABG, 11 × CABG) identifiziert, davon alleine 12 Fälle seit 2000. Das Intervall seit dem Ersteingriff betrug 4,0 ± 5,6 (Mean). Die Operationen wurden als Ascendens-Ersatz (n = 15), Bentall (n = 6), Ascendens-Ersatz mit Hermiarch (n = 3), Cabrol (n = 1), AKE (n = 1) oder mit direkter Naht (n = 1) durchgeführt. 13 der 27 Patienten (48 %) verstarben während des Spitalsaufenthaltes (6 × MCI, 3 × LCO, 2 × MOF, 2 × Blutung). In mindestens 14 Fällen konnte der Dissektionseintritt an vorangegangenen Manipulationsstellen der Aorta identifiziert werden. Eine präoperative Angiographie wurde nur fünfmal durchgeführt. Rezente Daten anderer Zentren berichten von höheren Angiographierate (bis 64 %), häufigeren zusätzlichen Bypassversorgungen (bis 87 %) und einer Mortalität von nur 6 % (Akutfälle 12 %).

Die Inzidenz von AD nach herzchirurgischen Eingriffen wird weiter zunehmen. Ein typisches Intervall gibt es nicht. Mindestens die Hälfte der Fälle nimmt ihren Ausgang an früheren chirurgischen Manipulationsstellen. Eine vergleichsweise hohe Mortalität ließe sich durch den vermehrten Einsatz der präoperativen Angiographie risikolos senken.

Sitzung 3 – Grundlagen II

3-I **16**

Influence of Myocardial I/R on Telomere-length

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Background Ischemia/reperfusion (I/R) injury in the myocardium is mainly caused by generation of ROS, Ca^{2+} overload and loss of membrane phospholipids, leading to necrosis and apoptosis. In this study we tried to determine what impact I/R injury has on telomere length and what type of senescence is forced on cells within the area-at-risk (AAR).

Methods 31 C57b1/6 mice underwent 1 hour of ischemia followed by either 24, 48 or 168 hours of reperfusion. Telomere length was measured by quantitative PCR. p161NK4a, p21WAV1, p27Kip1 gene expression, infarction size and Troponin T concentrations were assessed.

Results There was a significant reduction of telomere length in the 48 h and 168 h group, compared to the 24 h group (0.87 ± 0.069 vs. 0.37 ± 0.052; $p < 0,0001$ and 0.87 ± 0.069 vs. 0.39 ± 0.059; $p < 0.0001$). Troponin T was highest at 24 hours followed by 48 hours and not detectable at 168 hours reperfusion, correlating with infarction size. Normal tissue (NT) compared to the infarctioned tissue (IF) showed significant up-regulation of p161NK4a, p21WAV1 and p27Kip1 in a stress or aberrant signalling-induced senescence (STASIS) like manner (IF vs. NT at 168 h: $p < 0, 01$).

Conclusions I/R injury leads to different types of cell damage within the AAR. Necrosis and apoptosis are well known consequences but the fate of the remaining probably I/R damage triggered senescent cells has not yet been investigated. It was assumed that this third population consists of unharmed, dedifferentiated and/or pre-apoptotic cells. As the old concept of the postmitotic cardiac cells is obsolete and stem cell activity has been shown, the question of the regeneration capabilities of still viable myocardium is imminent. Our results point out that these capabilities must be diminished, as a form of ROS induced cellular senescence has occurred. Shortening of telomeres and up-regulation of p161NK4a, p27Kip1 and p21WAV1 indicate STASIS. Mouse telomerase reverse transcriptase (mTERT) up-regulation and simultaneous telomere shortening to a new mean length is shown inside the infarction. Apart from the loss of possible capabilities for regeneration the resulting limited function of senescent cells could be a reason for prolongation of the known phenomena stunned and hibernating myocardium.

3-II **042**

Coronary Stents Cause Turbulent Flow Acceleration and Reduction of Flow in Jailed Branches: An In Vitro Study Using Laser-Doppler Amenometry

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Background Despite the increasing number of stents deployed not much is known whether these prosthesis cause any change in flow behavior. Since it is well established that flow has an important impact on endothelial cell function, this study sought to assess flow within stents and in branches jailed by the stents.

Methods and Results To enable detailed measurement of flow changes within a stent, an *in vitro* model of a coronary tree was manufactured using silicone-rubber, showing elastic behavior comparable to coronary arteries. The model was connected to a flow pump, providing pulsatile flow identical to coronary flow waves and perfusion pressure. The perfusion fluid consisted of dimethylsulfoxide/polyacrylamide water mixture with particles simulating erythrocytes and had the same consistency and temperature as blood. The perfused models were brought into a laserdoppleramenometer (2 plane laser field resolution measuring cross-sectional flow at 49 positions/cross-section, m/sec) after an appropriately sized stent was deployed into each model, jailing a coronary side branch. Mean cross-sectional flow in stented segments was 0.53 ± 0.15 m/sec, but was significantly reduced in segments distal to the stent (0.44 ± 0.05 m/sec; $p < 0.01$) as well as in jailed branches (0.02 ± 0 m/sec; $p < 0.01$). When no stent was implanted, flow was comparable between segments (0.21 ± 0.02 vs. 0.20 ± 0.02 vs. 0.25 ± 0.04 m/sec; NS).

Conclusion These data show that intracoronary stents indeed cause important flow changes potentially resulting in cell function disturbance. Stents also cause permanent flow reduction in jailed branches which should be taken into consideration when selecting a coronary segment for stent treatment.

3-III **046**

Vitronectin Receptor Antagonist as a New Substance for Drug-Eluting Stent Systems?

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Background In an effort to reduce restenosis, several substances for stent coating with different antiproliferative, antithrombotic and cytostatic properties have been tested. Recently, the use of the alpha-v-beta-3 integrin (vitronectin) receptor antagonist (VRA) has been shown to limit neointimal hyperplasia in small animal models of restenosis, including the rabbit and hamster carotid angioplasty model. Furthermore the guanylate cyclase enhancer (GCE) has been shown to exert an antithrombotic/cytoprotective influence in the vessel wall. The aim of this experimental study was to investigate the antiproliferative effect of two new DES systems (VRA, GCE).

Table 8: J. Matiasek et al., FUP-results

	Angiography		3D-IVUS		Histomorphometry	
	MLD (mm)	DS (%)	NV (mm³)	NVO (%)	MNT (mm)	MNA (mm²)
BARE	2.09 ± 1.14	32.1 ± 36.5	34.3 ± 20.55	33.65 ± 21.6	0.33 ± 0.26	1.26 ± 0.93
GCE	1.44 ± 0.65**	52.5 ± 21.9**	57.2 ± 16.5**	55.7 ± 14.4**	0.38 ± 0.24**	1.75 ± 0.97**
VRA	2.53 ± 0.67 *	16.8 ± 20.7*	26.2 ± 14.6*	28.0 ± 18.4*	0.26 ± 0.17*	1.08 ± 0.74 *

NV (Neointimal Volume), NVO (Neointimal Volume Obstruction), MNT (Max. Neointimal Thickness), MNA (Max. Neointimal Area); * $p < 0,05$; ** $p > 0,05$

Methods 18 stents (mean diameter of 2.98 ± 0.07 mm, length of 15 mm, 6 of each type) were implanted in 10 domestic crossbred pigs (30 seconds inflation time, 6–12 atm pressure, to achieve a stent : artery ratio 1.1 : 1), into the left anterior descending and left circumflex coronary artery under general anaesthesia and after administration of 200 IU of heparin per kg. One day before coronary stent implantation, a loading dose of acetylsalicylic acid (ASA, 250 mg) and 500 mg ticlopidine were administered per os, during the follow-up period the pigs received a daily dose of 100 mg ASA and 250 mg ticlopidine per os. After four weeks control coronary angiography and intravascular ultrasound (IVUS) were performed. Subsequently the animals were euthanized and the stented arteries were prepared for histomorphometry. Angiographic, IVUS and histologic results of a bare stent, VRA coated and GCE coated stents were compared.

Results Coating the stents with VRA decreased formation of neointimal hyperplasia as an obvious trend to smaller neointima was observed as compared with bare stents, assessed by angiography, IVUS and histomorphometry **(Table 8).** GCE resulted in macroscopic worst outcome, with high degree of in-stent stenosis as compared with the bare stents. The best histopathological result was archieved by implanting the VRA-coated stent, showing high degree of endothelialisation and the lowest inflammation.

Conclusions Vitronectin receptor antagonist-coated stents seem to be promising as a new drug-eluting stent system.

3-IV **113**

Oxidized Phospholipids Induce Neoangiogenesis In Vitro and In Vivo – A Role in Plaque Instability?

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Purpose Pathological neovascularisation is a consistent feature of atherosclerotic lesion formation and may play a role in plaque rupture by promoting inflammatory cell recruitment and intraplaque hemorrhage. Microvessel density has been shown to be increased in lipid-rich and ruptured plaques when compared with fibrocalcific lesions. We hypothesized that lipid oxidation products, such as oxidized phospholipids (OxPL), may stimulate neoangiogenesis. Thus, we investigated effects of OxPL on angiogenesis *in vitro* and *in vivo*.

Methods, Results In endothelial sprouting assays OxPL stimulated formation of sprouts by human umbilical vein endothelial cells (HUVEC) in a time- and concentration-dependent manner. Furthermore, OxPL promoted microvessel growth in Matrigel plug assays in mice in vivo. To investigate which angiogenic factors might be involved in this effect we used DNA microarrays as well as quantitative real-time polymerase chain reaction, demonstrating that OxPL stimulate expression of VEGF, COX-2 and IL-8 in HUVEC. Low molecular weight inhibitors of VEGF receptors and COX-2, as well as blocking antibodies to IL-8 suppressed angiogenic effects of OxPL in endothelial sprouting assays. Finally, application of OxPL to the adventitia of murine carotid arteries *in vivo* resulted in upregulation of VEGF, COX-2 and KC/IL-8 mRNA in the artery wall.

Conclusions We demonstrate that OxPL, known to accumulate in atherosclerotic lesions, exhibit angiogenic properties *in vitro* and *in vivo*. The underlying mechanisms involve VEGF, IL-8 and COX-2,

all of which can be induced by OxPL in the adventitia of murine arteries. Thus, we suggest OxPL as important mediators of neoangiogenesis in complex lesions. Interventions targeted at OxPL may slow plaque progression and improve plaque stability.

3-V **039**

Mobilisation of Bone Marrow Derived Mesenchymal Stem Cells in Response to Coronary Occlusion/ Reperfusion

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Background and Aim Neoangiogenesis in response to brief repetitive ischemia called preconditioning may represent an additional potent mechanism leading to survival of the ischemic tissue during infarction. Additionally, no data exist about the myogenesis induced by differentiation of pluripotent mesenchymal stem cells with triggered activity by profound myocardial ischemia, reperfusion and ischemic preconditioning. The aim of the present study was to investigate the mobilisation of bone marrow derived hematopoietic and mesenchymal stem cells in response to myocardial ischemia/ reperfusion injury in porcine during temporarily and constant percutaneous coronary occlusion.

Methods Eight pigs underwent 90 min catheter-based LAD occlusion followed by 60 min reperfusion under general anaesthesia. Preconditioning was obtained in 4 of 8 pigs by 2 cycles of 5 min of balloon occlusion of LAD with 2 cycles of 5 min interval of reperfusion before 90 min occlusions. Two-dimensional echocardiography were performed on each pig at baseline and at the end of the final reperfusion. The ejection fraction was calculated from the end-diastolic and end-systolic volumes calculated from the area-length method of echocardiography. The size of area at risk and myocardial infarction was measured by blue dye injection and triphenyl tetrazolium chloride staining. Bone marrow derived hematopoietic and mesenchymal stem cells were characterized by coexpression of CD31+, CD90+, and CD44+, measured by whole blood flow cytometry from venous blood taken at baseline and at the end of the reperfusion.

Results The global left ventricular function was decreased in pigs without vs. with preconditioning (ejection fraction: 34 ± 12 % vs. 41 ± 11 %) and the myocardial infarct size, expressed as precentage of area at risk, was larger (22.8 ± 5.6 % vs. 16.1 ± 5.8 %, respectively). No change in hematopoietic progenitor cell peripheral concentration was observed in groups with or without preconditioning. Relative increase (ratio of post-final reperfusion and baseline values) of the bone marrow derived mesenchymal stem cells (CD90+ and CD44+) (131 ± 0.34 % vs. 81 ± 26 %, p = 0.093) was found in peripheral venous blood in pigs with larger myocardial infarction and worse ventricular function (pigs without preconditioning). The relative increase of mesenchymal stem cells correlated negatively with the global ejection fraction (r = 0.686, p = 0.076), indicating a stronger stimulus for stem cell mobilisation caused by constant coronary occlusion.

Conclusion Profound myocardial ischemia resulting deep myocardial damage without „warm-up" protective preconditioning, induces mobilisation of bone marrow derived mesenchymal stem cells, which cells were observed to might differentiate into cardiomyocytes.

3-VI **41**

The Regulation of the Placenta Growth Factor (PlGF) in Human Cardiac Myocytes and Fibroblasts

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Objective The Placenta Growth Factor (PlGF) is a member of the Vascular Endothelial Growth Factor (VEGF) family of growth factors. It occurs in 4 different isoforms due to alternative splicing and binds specifically to VEGF-receptor1, neuropilin1 and neuropilin2. PlGF has been found to act synergistically with VEGF by affecting smooth muscle cells, recruiting inflammatory cells and mobilizing vascular and progenitor cells. In mice the expression of PlGF is increased after myocardial infarction. The regulation of PlGF in the human heart is still unknown. We investigated the expression of PlGF in human adult cardiac myocytes (HACM) and human adult cardiac fibroblasts (HACF) under normoxic (21 % O_2) and anoxic (< 1 % O_2) conditions and the regulation of PlGF by inflammatory mediators and glycoprotein (gp) 130 ligands.

Methods HACM and HACF were isolated from myocardial tissue and treated with the inflammatory mediators Interleukin-1α (IL-1α), Tumor Necrosis Factor α (TNF-α) and the gp130 ligands Oncostatin M (OSM), Cardiotrophin-1 (CT-1), Leukemia Inhibitory Factor (LIF) and IL-6. Additional HACM and HACF were cultivated under anoxic conditions (< 1 %) using the Anaerocult® IS system. The PlGF protein in the conditioned media was determined by a specific ELISA and RT-PCR was used to determine mRNA levels of PlGF employing specific primers.

Results OSM down-regulates PlGF in HACM and HACF significantly (up to 50 %). A down-regulation of the PlGF protein secretion by IL-1α and TNF-α by 30 % could only be detected in HACM. This results could also be confirmed on the level of specific mRNA. On the other hand we detected a 7-fold up-regulation of PlGF on the mRNA level by anoxia.

Conclusion We could show PlGF expression for the first time in human adult cardiac myocytes and fibroblasts, which indicates that PlGF might be involved in repair processes in the injured heart. Based on our observation that OSM down-regulates PlGF, but up-regulates VEGF in cardiac myocytes, which we have shown recently [Weiss et al., 2003], we provide evidence that VEGF and PlGF might be differentially regulated under inflammatory conditions in the heart. In contrast anoxia – similar to its effect on VEGF expression – also up-regulates PlGF in cardiac cells.

3-VII **040**

Cardiac Myocytes and Cardiac Fibroblasts Are Actively Involved in the Recruitment of Monocytes

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Objective Monocytes play an active role in angiogenesis after myocardial infarction. They are an important source of cytokines involved in angiogenesis and repair. Monocytes also contribute directly to compensatory neovascularisation via monocyte/macrophage drilled tunnels. The main attractant for monocytes is monocyte chemotactic protein 1 (MCP-1), which is present in the infarcted heart. We asked if human adult cardiac myocytes (HACM) and human adult cardiac fibroblasts (HACF) contribute to the recruiting process of monocytes by producing MCP-1 under inflammatory or hypoxic conditions.

Methods HACM and HACF were isolated from myocardial tissue. They were treated with IL-1α and TNF-α to stimulate inflammatory conditions. Hypoxia was achieved using a hypoxic chamber which was flushed with 100 % N_2 (O_2 content was monitored and kept below 1 %) and controlled by measuring VEGF using a specific ELISA, which is known to be stimulated under hypoxic conditions. MCP-1 protein was detected by a specific ELISA and RT-PCR employing specific primers for MCP-1 was used to measure mRNA levels. To test the biological activity of the secreted MCP-1 a Boyden Chamber assay for chemoattraction using the monocytic cell line U937 was done.

Results IL-1α and TNF-α both increased MCP-1 protein secretion in HACM and HACF significantly. Under hypoxic conditions basal MCP-1 expression was reduced by 50 %. Stimulation with IL-1α and TNF-α under hypoxia increased MCP-1 but the values only reached basal normoxia expression values. The value for VEGF was increased 2 fold under hypoxic conditions. These results were confirmed on the level of specific mRNA expression. In the chemo-attractant assay approximately 50 % more U937 cells migrated to the conditioned medium of TNF-α treated HACM than to

conditioned medium of untreated HACM. Chemo-attraction could be reduced to basal level when a specific neutralizing antibody for MCP-1 was added to the conditioned medium of TNF-α treated HACM.

Conclusions Our *in vitro* data suggest that cardiac myocytes and cardiac fibroblast might play an active role in the recruitment process of monocytes to the infarcted myocardium. Whereas under inflammatory conditions they secrete MCP-1, hypoxia alone is down-regulating the expression of MCP-1 in these cells and the effect of inflammatory cytokines is reduced. If also operated in vivo our results suggest that recruitment of monocytes to the injured heart might be differentially regulated under inflammatory conditions and hypoxia.

3-VIII **3**

Effect of Various Forms of Body Weight Reduction on the Endothelial Function of Patients with Visceral Obesity

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Aim To determine to what extent the endothelial function of healthy men with "apple" type of obesity is impaired, and further, what changes various types of weight reduction cause in endothelial function, in C-reactive protein (CRP) levels and in lipids.

Patients and Methods 60 males were enrolled into the study. Endothelial dysfunction was evaluated by Celermajer's method of flow-mediated dilatation (FMD). BMI, WHR, CRP and metabolic parameters were measured in the probands. The inclusion criteria were: 30 kg/m^2 < BMI < 40 kg/m^2, waist > 102 cm, waist/hip ratio > 1, triglyceride < 4 mmol/L, glucose < 6.1 mmol/L, LDL-cholesterol < 4.1 mmol/L, no acute or chronic diseases, no medication, age between 20 and 40 years. Patients were randomised into 3 therapeutic groups (A, B and C). All groups were put on a diet with 1.200 kcal a day, group B underwent dynamic training 150 minutes a week, group C were put on 120 mg of orlistat a day in addition to the diet. Measured parameters were controlled after 3 months time.

Results Pathologic FMD values were found in 54 of the 60 enrolled patients thus the data of 3 × 18 patients in the groups A, B and C were processed. Body weight was reduced significantly after 3 months of treatment in all groups. A: 32 ± 1 vs. 28.6 ± 0.9 kg/m^2, B: 33 ± 1.8 vs. 27.8 ± 1.1 kg/m^2, C: 32 ± 1.2 vs. 27.6 ± 0.9 kg/m^2; $p < 0.01$. Endothelial function improved highly significant in group B (4.2 ± 0.63 vs. 5.9 ± 0,79 %; $p < 0.001$) and significantly in group C (6.4 ± 1.3 vs. 4.9 ± 1.1 %; $p < 0.05$). CRP lowered significantly in groups B (6.7 ± 1.9 mg/L vs. 4.1 ± 1.21 mg/L; $p < 0.01$) and C (6.4 ± 1.3 vs. 4.9 ± 1.1 mg/L; $p < 0.05$). Regarding lipid parameters, triglyceride lowered significantly in all three groups, the most significant lowering was found in group C.

Conclusions Visceral obesity caused endothelial dysfunction, increased CRP and serum triglyceride levels in 90 % of the young, otherwise healthy probands. Significant body weight reduction gained by diet only was not followed by the impairment of the endothelial function, nor by that of CRP levels. The completion of diet with regular dynamic training showing anti-inflammatory effect is necessary. That more beneficial effect of orlistat alone than diet was probably linked to the effect of orlistat on lipid metabolism.

3-IX **43**

Coronary Stents do not Worsen Coronary Flow when Implanted into Coronary Arteries with Pre-existing Stenosis: An In Vitro Study Using Laser-Doppler Amenometry in a Coronary Stenosis Model

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Background In clinical practice it is frequently unavoidable to deploy stents into coronaries with pre-existing proximal disease. It is not known so far whether this results in aggravation of flow disturbance or loss in flow velocity. Therefore we performed a study in coronary models with stenosis at clinically typical topographical situations.

Methods and Results To enable detailed measurement of flow changes within a stent, an in vitro model of a coronary tree was manufactured using silicone-rubber, showing elastic behavior identical to coronary arteries. At selected topographical sections synthetic plaques were molded using the same material. The plaques resembled a 40–50 % stenosis comparable to the clinical situation, when stents are deployed into an already diseased vessel. Three different models were investigated paralleling 3 different "plaque situations". The model was connected to a flow pump, providing pulsatile flow identical to coronary flow waves and perfusion pressure. The perfusion fluid consisted of dimethylsulfoxide/polyacrylamide water mixture with particles simulating erythrocytes and had the same consistency and temperature as blood. The perfused models were brought into a laserdoppleramenometer (2 plane laser field resolution measuring cross-sectional flow at 49 positions/cross-section, m/sec) after an appropriately sized stent was deployed into each model. Measurements were performed in all models before and after stenting to compare the respective stent-effect. In Model 1 mean cross-sectional flow was 0.0286 (min.) m/sec and 0.4288 (max.) m/sec before stenting and 0.0188 (min.) m/sec and 0.4367 (max) m/sec after stenting. Model 2 revealed a mean cross-sectional flow of –0.0408 (min.) m/sec and 0.3319 (max.) m/sec before stenting and showed a min. flow of –0.0270 m/sec as well as a max. flow of 0.3540 m/sec after stenting. Cross-sectional flow in model 3 was –0.0005 (min.) m/sec and 0.3020 (max.) m/sec before stenting and demonstrated after stenting a min. flow of –0.0647 m/sec and a max. flow of 0.4253 m/sec.

Conclusion These data demonstrate that flow is not worsened after stent implantation in prediseased arteries in a coronary stenosis model.

Sitzung 4 – Herzinsuffizienz

4-I **063**

FMD Predicts Outcome in CHF Independent of the Etiology of the Disease

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Objective This study evaluated if the predictive value of flow-mediated vasodilation (FMD) in patients with chronic heart failure (CHF) depends on the etiology of the disease.

Background Endothelium-mediated vasodilation is similarly impaired in patients with dilated cardiomyopathy (DCMP) and ischemic cardiomyopathy (ICMP). Moreover, impaired FMD is a strong independent predictor of adverse outcome in CHF. It is unknown whether FMD differs between event-free survivors and patients with adverse outcome in ICMP and DCMP.

Methods FMD was assessed in 75 CHF patients. 35 patients presented with DCMP whereas 40 patients presented with ICMP, respectively. Diagnosis of DCMP was made by angiographic exclusion of a > 75 % stenosis of a major epicardial coronary artery. FMD measurements were performed according to the guidelines for the ultrasound assessment of FMD in the brachial artery.

Results Up to three years, 44 patients survived and 31 patients reached the combined endpoint death/urgent heart transplantation (HTx). 19 of 35 patients with DCMP (61 %) and 12 of 40 patients with ICMP (39 %) reached the combined endpoint. In the Kaplan-Meier blot, significantly more patients with a FMD < 6.8 % (median) reached the combined endpoint compared to patients with a FMD > 6.8 % ($p = 0.0007$). FMD differed in the subgroup of DCMP patients (11.6–8.0 % vs. 6.1–4.8 %; $p = 0.02$) and in the subgroup of ICMP

patients (11.6–7.4 % vs. 5.7–4.9 %; p < 0.01) between the event-free survivors and the patients who reached the combined endpoint.

Conclusion FMD is a strong independent predictor of outcome in CHF patients independent of the etiology of the disease. Our data demonstrated that FMD differs similarly in ICMP as well as DCMP patients between event-free survivors and patients who died or underwent HTx.

4-II **58**

Einfluß von Carvedilol auf die Basis- und Begleittherapie der Herzinsuffizienz bei älteren Patienten: Daten aus dem Österreichischen COLA-II-Kollektiv

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Hintergrund Trotz eindeutiger Empfehlungen ist der Einsatz von Betablockern gerade bei älteren Patienten mit Herzinsuffizienz (HI) oft von Bedenken hinsichtlich Tolerabilität überschattet. In der zweiten „Carvedilol Open Label Assessment"-Studie (COLA-II) konnte gezeigt werden, daß diese Bedenken unbegründet sind: Ältere HI-Patienten sind zu 80 % in der Lage, Carvedilol in einer Tagesdosis von mindestens 12,5 mg einzunehmen. Das Ziel der vorliegenden Analyse des österreichischen COLA-II-Kollektives war es, den Einfluß von Carvedilol auf die Basis- und Begleittherapie für Herzinsuffizienz zu untersuchen.

Patienten und Methodik In der multinationalen COLA-II-Studie wurden 1030 Patienten untersucht, davon waren 531 aus Österreich. Die Ausgangs- sowie die Enddaten dieses Kollektivs wurden hinsichtlich Vitalparameter, NYHA-Klasse und Basis-/Begleittherapie vor Beginn der Carvedilol-Therapie und am Ende der Studie untersucht, wobei die Dosen von ACE-Hemmern, Angiotensin-Rezeptor-Blockern (ARB) sowie von Spironolacton in bezug zur empfohlenen Tagesdosis (ESC-Guidelines 2001) gesetzt wurden.

Ergebnisse Das österreichische COLA-II-Kollektiv bestand aus 269 männlichen und 262 weiblichen Patienten mit einem mittleren Alter von 77 ± 6 Jahren. Der Blutdruck zu Beginn der Studie betrug 142 ± 22/82 ± 12 mmHg, die mittlere Herzfrequenz 80 ± 15/min. 36 Patienten befanden sich in NYHA-Klasse I, 249 in NYHA II, 225 in NYHA III und 21 in NYHA IV. Die Basistherapie bestand aus ACE-Hemmern (n = 363; 95 % der von der ESC empfohlenen Tagesdosis), ARB (n = 92; 71 % ESC), Furosemid (n = 272; mittlere Tagesdosis: 47 mg) und Spironolacton (n = 98; 105 % ESC). Die mittlere Carvedilol-Dosis betrug am Ende des Follow-up 39 ± 14 mg/Tag. Von 458 Patienten liegen Follow-up-Daten vor (229 ♂, 229 ♀). Der mittlere Blutdruck betrug bei der Abschlußuntersuchung 128 ± 16/76 ± 9 mmHg, die mittlere Herzfrequenz 69 ± 10/min (p < 0,001 im Vergleich mit dem Beginn). Zuletzt waren 174 Patienten in NYHA I, 242 in NYHA II, 38 in NYHA III und 4 in NYHA IV. Die Therapie bestand zuletzt aus ACE-Hemmern (n = 311; 103 % ESC), ARB (n = 88; 70 % ESC), Furosemid (n = 222; mittlere Tagesdosis: 42 mg) und Spironolacton (n = 97; 103 % ESC).

Schlußfolgerung Trotz signifikanter Reduktion von Blutdruck und Puls im österreichischen COLA-II-Kollektiv durch die Therapie mit Carvedilol bestand offensichtlich kein Grund, die Basis-/Begleittherapie zu reduzieren. Es zeigte sich durch die zusätzliche Betablockertherapie zudem eine deutliche Verbesserung der NYHA-Klasse, sodaß Carvedilol als sichere Therapie bei älteren Patienten mit Herzinsuffizienz betrachtet werden kann.

4-III **062**

Combination of FMD and BNP is a Strong Predictor of Outcome in CHF

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Objective The aim of the study was to assess whether a combination of flow-mediated vasodilation (FMD) and brain-natriuretic peptide (BNP) improves predictive potency in CHF patients.

Background We recently demonstrated that FMD and BNP are strong independent predictors of outcome in patients with chronic heart failure (CHF).

Methods Seventy-five CHF patients with a left ventricular ejection fraction < 30 % despite optimized medical therapy were evaluated. FMD of the brachial artery was assessed using high resolution ultrasound. BNP levels were measured using commercially available kits. FMD and BNP were combined to a prognostic factor by stratifying patients according to the median of FMD and BNP and combining these parameters to one factor (group A: FMD > 6.8 %, BNP < 208 pg/mL – n = 17; group B: FMD < 6.8 %, BNP < 208 pg/mL – n = 21; group C: FMD > 6.8 %, BNP > 208 pg/mL – n = 20; group D: FMD < 6.8 %, BNP > 208 pg/mL – n = 17).

Results Up to three years, 44 patients survived, 14 patients died, and 17 patients underwent heart transplantation. Univariate indicators for the combined endpoint were the combined factor FMD/BNP (x2 = 24.7992; p = 0.0001), FMD (x2 = 8.0910; p = 0.0044), logBNP (x2 = 7.4685; p = 0.0063), NYHA class (x2 = 6.7397; p = 0.0094), furosemide therapy (x2 = 6.5831; p = 0.0103), mean blood pressure (x2 = 5.5777; p = 0.0182), and beta-blocker therapy (x2 = 4.0984; p = 0.0429). In the multivariate analysis, the combined factor FMD/BNP was the only independent predictor of the combined endpoint. No patient in group A, 9 patients in group B (43 %), 7 patients in group C (35 %), and 15 patients in group D (88 %) reached the combined endpoint resulting in a highly significant difference between groups (except for group B and C) in the Kaplan-Meier analysis.

Conclusion The combination of FMD and BNP improves risk stratification in patients with CHF.

4-IV **061**

Heart Transplantation Provides Long-Term Survival Benefit in Stable Outpatients with Heart Failure

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Background We recently demonstrated that in heart transplantation (HTx) candidates who tolerate uptitration of ACE-inhibitors and β-blockers, HTx does not seem to provide additional survival benefit in the short term (2 years). The aim of this study was to compare the outcome of these HTx candidates (treated with combined ACE-I and β-blockers) with patients post HTx in the long term.

Methods 318 patients (NYHA class III or IV, LVEF 16 ± 7 %, cardiac index 2.2 L/min × m^2 at time of referral) were treated with digitalis, loop diuretics, maximally uptitrated RAAS-antagonists, β-blockers (as tolerated), and intravenous support (if needed). Patients were retrospectively stratified according to their medical therapy 3 months after referral into those receiving β-blockers plus ACE-I (Group A, n = 126), ACE-I (Group B, n = 135), and ACE-I plus intravenous support (Group C, n = 57). Patients who underwent HTx within 3 years after study-start formed Group D (n = 70). During an observation period of six to nine years outcome was documented.

Results 115 patients (36 %) survived without HTx, 89 patients (28 %) underwent HTx, and 114 patients (36 %) died. In Group A 65 patients (52 %) survived without HTx, 18 patients (14 %) underwent HTx, and 43 patients (34 %) died. In Group D 17 patients (21 %) died after HTx. Using the endpoint death or HTx in Group A and death in Group D, Kaplan-Meier analysis revealed a significant difference between groups in favour of Group D (p < 0.005). Using the endpoint death in Group A (excluding patients who underwent HTx) and Group D, Kaplan-Meier demonstrated a significant difference between groups in favour of Group D.

Conclusion Not in the short term (2 years) but in the long term (> 6 years) HTx seems to provide additional survival benefit in HTx candidates who tolerate uptitration of ACE-I and β-blockers.

Tabelle 9: J. Cup et al.

Kardiale Grunderkrankung		Medikamentöse Therapie	
DCM:	n = 45 (33 %)	ACEI:	99 (71 %)
ICM:	n = 58 (42 %)	ARB:	26 (19 %)
Hypertonie:	n = 20 (14 %)	BB:	113 (81 %)
HOCM:	n = 2 (1 %)	Furosemid:	106 (76 %)
TachyCMP:	n = 7 (5 %)	Spirono:	47 (34 %)
Andere:	n = 7 (5 %)	Digitalis:	31 (22 %)
		Statine:	48 (35 %)

4-V **118**

Einfluß einer optimierten klinischen Nachbetreuung auf die Rehospitalisierung von Herzinsuffizienzpatienten

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Die Mortalität von Herzinsuffizienzpatienten (CHF-Patienten) ist trotz spezieller Therapiemaßnahmen noch immer sehr hoch. Entsprechend liegt die Hospitalisierungsrate wegen ungeplanter Ereignisse nach Angaben in der Literatur abhängig vom NYHA-Stadium bei 0,6–8 Aufenthalten pro Jahr. Große Studien haben gezeigt, daß durch intensivierte ambulante Nachsorge entweder durch Heimbetreuung und/oder die Gründung von Herzinsuffizienzambulanzen (CHF-Amb) und eine spezielle Schulung der CHF-Patienten die Rehospitalisierung deutlich gesenkt werden kann. Ziel unserer retrospektiven Analyse war die Untersuchung des Einflusses einer neu organisierten CHF-Ambulanz in einem Wiener Gemeindespital auf die stationären Wiederaufnahmen wegen kardiovaskulärer Ereignisse. In einem Zeitraum von 09/02 (Ambulanzgründung) bis 03/04 wurden 139 konsekutive CHF-Patienten mit mindestens 1 Jahr Nachbeobachtung (FU) in der CHF-Ambulanz in die Untersuchung eingeschlossen. Es wurden die Anzahl der Hospitalisierungen 1 Jahr vor Gründung der Spezialambulanz mit den Spitalsaufnahmen im darauffolgenden Jahr verglichen.

Demographische Daten 108 Patienten männlich (78 %), 31 Patienten weiblich (22 %), mittleres Alter 65,7 ± 11,2 Jahre, mittlere LVEF 31 % **(Tabelle 9).**

Ergebnisse (1) Die Hospitalisierung im Jahr vor der CMP-Ambulanz-Gründung lag bei 67 Aufnahmen/Jahr und konnte im Jahr danach auf 49 gesenkt werden (p = 0,07). Dies entspricht einer Aufnahme von 0,48 vor und 0,35 nach CMP-Ambulanz-Gründung pro Patient. (2) Die Dauer der Aufenthalte wegen kardiovaskulärer Ereignisse lag mit 744 Tagen nach CMP-Ambulanz-Gründung gegenüber 1129 Tagen davor deutlich niedriger (–34 %).

Schlußfolgerung Die intensivierte Betreuung von CHF-Patienten durch Spezialambulanzen mit Umsetzung der in Richtlinien verankerten Therapieempfehlungen führt unmittelbar zu einer deutlichen Reduktion der Rehospitalisierungsrate mit entsprechender Verbesserung der Lebensqualität sowie einer Kostenreduktion.

4-VI **060**

Body Mass Index (BMI) and Bicycle Exercise Capacity after Heart Transplantation

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While patients undergoing heart transplantation (HTx) are affected by preoperative inactivity and postoperative deconditioning, 90 % report normal ability to perform daily activities on long term. Ergometer exercise tolerance, however, remains often limited.
A data base study was performed to investigate the potential impact of obesity on physical fitness of 177 stable, ambulatory HTx recipients (147 ♂/30 ♀, 57 ± 11 yrs) referred throughout 2002–2004 for graded symptom-limited upright bicycle exercise tests. Patients were subgrouped in exercise capacity (EC) levels I–IV using percent of predicted EC values according to standardized height, weight, age and gender scales **(Table 10).**

Table 10: B. Stanek et al.

	All 0–115 %	Level I 0–49 %	Level II 50–69 %	Level III 70–84 %	Level IV 85–115 %
n	177	14	55	65	43
% EC	74 ± 17	41 ± 7	61 ± 5	77 ± 4	96 ± 9 *
% peak HR	87 ± 12	76 ± 8	82 ± 13	89 ± 10	95 ± 10 **
BMI	28.3 ± 1.5	27.4 ± 3.6	28.1 ± 4.3	30.4 ± 2.4	25.8 ± 2.9
syst BP (mmHg)	133 ± 20	124 ± 22	135 ± 21	135 ± 19	131 ± 20
diast BP (mmHg)	89 ± 13	84 ± 14	90 ± 14	91 ± 13	88 ± 13
HR (bpm)	91 ± 13	94 ± 14	91 ± 14	91 ± 13	90 ± 11

*p < 0.001; **p = 0.006 between groups, Mean ± SD

The study demonstrates gratifyingly high physical fitness levels in 61 % of the HTx recipients. BMI, as well as age, gender, resting blood pressure (BP), and heart rate (HR) were similar in all groups. Thus, postHTx weight gain does not as a rule predict low fitness in this patient population.

4-VII **094**

Congestive Heart Failure in Austria: Is There a Ray of Hope at The End of the Tunnel?

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Background and Aim Chronic Heart Failure (CHF) as a clinical syndrome represents a major public health problem due to increasing costs and limited resources. Increasing life expectancy due to the improvement in management of coronary artery disease, acute myocardial infarction and arterial hypertension thereby have contributed to an increased number of patients (pts). Nearly 160,000 people in Austria have CHF and the incidence is increasing.

Methods Data acquired from the Austrian Department of Statistics between 2000 and 2002 from pts admitted to a hospital in Austria because of acutely decompensated Heart Failure (with the appropriate ICD-10 Code) in-hospital mortality were investigated. During this time span specific outpatient services for Heart Failure (HF) pts were implemented.

Results In the first year (2000) 31,243 consecutive pts with CHF were registered and 5,026 pts (19 %) died in the hospital. In 2001, there was a significant decrease in hospitalisations to 26,787 pts and as well as in mortality to 3,809 pts (17 %). Finally in 2002, 25,766 pts were admitted of whom 3,474 pts died (16 %) resulting in a decrease of 18 % of hospital admissions and a 31 % reduction of the in-hospital mortality during this 3 years period **(Figure 7).**

Conclusion The decline of hospital admissions and in-hospital mortality in HF pts reflects not only the evolving interest and improved medical treatment in CHF pts but also the increasing implementation becaused CHF outpatient units resulting in a better management of these high risk pts. This development in specific patient care reduced not only the total number of hospitalisations but also the in-hospital mortality due to CHF nearly in all regions of Austria. Further efforts will be mandatory not only to increase the number of specific outpatient services for CHF but also to improve the organisations of these services (rooms, equipment, special trained CHF

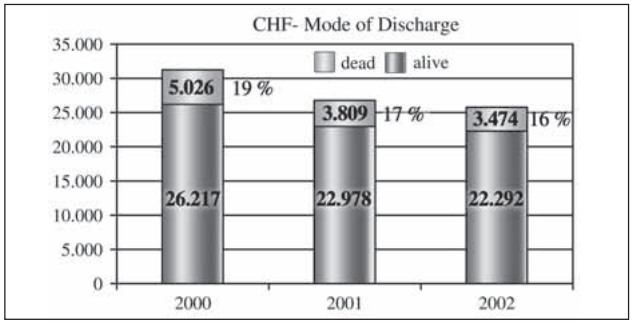

Figure 7: I. Kozanli et al

nurses) and to offer new opportunities of patient care e.g. mobile CHF nurses and home care, respectively.

4-VIII **112**

Survival in Patients with Chronic Thromboembolic Pulmonary Hypertension

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Background A series of medical conditions have recently been identified as risk factors for the development of chronic thromboembolic pulmonary hypertension (CTEPH). The impact of these medical conditions on prognosis is unknown.

Methods 129 consecutive CTEPH patients diagnosed between 1994 and 2003 (67 ♀/62 ♂) were studied. Prior splenectomy, ventriculo-atrial shunt (VA-shunt), chronic inflammation, elevated plasma factor VIII and anti-cardiolipin-antibodies/lupus anticoagulant were considered risk factors. Kaplan-Meier estimates of the survival distribution were performed. The influence of pulmonary thromboendarterectomy (PEA) on survival was tested by the Cox proportional hazards model.

Results Mean patient age at diagnosis was 55 ± 16 years. Median observation time was 56 months. In 85 patients (66 %) an underlying medical condition was identified (splenectomy: n = 12, VA-shunt: n = 7, inflammatory bowel disease (IBD): n = 8, elevated plasma factor VIII: n = 42, and APL: n = 16). Right heart hemodynamics were not significantly different in the patients with and without associated risk factors (pulmonary vascular resistance: 906 ± 426 dynes × s^{-1} × cm^{-5} versus 888 ± 427 dynes × s^{-1} × cm^{-5}, p = 0.2). Because of distal thrombus localisation only 4 patients with splenectomy or IBD underwent PEA. PEA reduced the risk to die by 62 % (HR = 0.38; 95 %-CI: [0.16–0.87], p = 0.025). Patients died from right heart failure (n = 21), malignancy (n = 1) or after PEA (n = 12). While the overall median survival time was 113 months, survival time in patients with splenectomy or IBD (n = 20) was significantly shorter (55 months; p = 0.015).

Discussion The data show that there exist several CTEPH entities. CTEPH associated with splenectomy or IBD carries the worst prognosis. The predominantly distal thrombus localisation and associated pulmonary vascular disease in these patients may account for this observation.

4-IX **111**

Bosentan Therapy for Inoperable Chronic Thromboembolic Pulmonary Hypertension

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Background Bosentan, a dual endothelin-1-receptor antagonist that can be administered orally, has been shown to be effective in the treatment of idiopathic pulmonary arterial hypertension. The aim of the present study was to evaluate its safety and efficacy in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH).

Methods This was a prospective uncontrolled cohort study. The effect of bosentan therapy was tested in 16 patients (9 ♀/7 ♂, mean age 70 ± 13 years) with inoperable CTEPH. After six months, changes from baseline in (1) liver enzymes, (2) NYHA functional class, (3) six-minute-walking distance and (4) NT-brain-natriuretic peptide (pro-BNP) were evaluated.

Results NYHA functional class improved by one class in 11 patients. Six-minute walking distances increased from 299 ± 131m to 391 ± 110 m (p = 0.01). In parallel, proBNP decreased from 3365 ± 2923 pg/mL to 1755 ± 1812 pg/mL (p = 0.01). Neither AST (25 ± 2 versus 25 ± 2U/L, p = 0.25) nor ALT (23 ± 12 versus 24 ± 9 U/L, p = 0.57) showed significant changes.

Conclusions Our initial experience with bosentan therapy in patients with inoperable CTEPH is promising and urges the need for a randomized, placebo-controlled trial.

Sitzung 5 – Interventionelle Kardiologie II

5-I **121**

Time to Treatment and In-hospital Mortality in Patients with acute STEMI: Preliminary Results of the Vienna Registry of Reperfusion Strategies in acute STEMI

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Background and Aim Recently published guidelines of ACC/AHA recommend urgent thrombolytic therapy (TT) in patients (pts) with STEMI if primary PCI (PPCI) cannot be performed within 90 min after first medical contact or to door-to-balloon-time. The aim of this study was to compare the relation of time to treatment and in-hospital mortality of patients treated with TT or PPCI.

Methods All pts with STEMI of < 12 hours (h) duration presenting at the participating departments were included. Impact of time to treatment (1st balloon inflation or injection of the thrombolytic agent) on in-hospital mortality was investigated according to time of presentation: early (< 2 h from start of pain), moderately delayed (2 to 6 h), and late (> 6 h).

Results Of the 1053 consecutive pts (61.8 ± 13.5 yrs; ♀/♂ = 71.6/28.4 %) with STEMI, 59.9 % (n = 631) underwent PPCI. If PPCI could not be offered within 90 min of 1st medical contact (time of diagnosis) TT was performed (n = 281, 26.7 %; 12.1 % prehospital) with subsequent angiography ± PCI between day 1 and 7 for responders to TT. Data of TT include also pts with immediate adjunctive PCI (either "rescue" or "facilitated") which was performed in 52 % of pts with TT. The mean time from onset of symptoms to treatment was 4.3 ± 2.5 h in the PPCI group and 2.0 ± 1.8 in the TT group. In 141 pts (13,4 %) no reperfusion therapy was offered, due to long presentation delays or contraindication against both reperfusion strategies. Mortality was 18,4 % in this group **(Table 11).**

Conclusion In-hospital mortality in both treatment groups, PPCI and TT, was time-dependent and lowest when treatment is offered within 2 hrs of onset of symptoms without significant differences between PPCI and TT at very early presentation. With increasing delay of treatment, mortality increased in both treatment groups but was smaller in PPCI treated pts compared to pts treated with TT. Therefore, pts with STEMI of < 2 hrs duration should be treated with the earliest available method while PPCI should be the preferred method in all other pts.

Table 11: K. Kalla et al. In-hospital Mortality of different treatment groups at various presentation delays (11.8 % of pts in the PPCI group and 12.7 % of pts in the TT group had clinical signs of shock at start of treatment)

Time to treatment	PPCI			TT		
	n	% of all PPCIs	% Mortality	n	% of all TTs	% Mortality
≤ 2 h	90	14.6	7.8	140	50.5	4.3
2 – 6 h	406	65.9	6.7	123	44.4	10.6
6 – 12 h	120	20.2	12.5	14	5.1	28.6
overall	616	97.6	8.1	277	98.6	8.2
overall without shock	552	87.5	2.9	240	85.4	2.1

5-II **057**

Association Between Response on Platelet Aggregation Therapy and Development of In-Stent Neointimal Hyperplasia in Porcine Coronary Arteries

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Aim The aim of the present study was to investigate the association between effectiveness of platelet aggregation therapy with Ticlopidine and Clopidogrel and development of neointimal hyperplasia after coronary stenting in pigs.

Methods Bare stents were implanted in the LAD and LCx coronary arteries of 22 pigs under general anaesthesia. During the 1-month follow-up (FUP), the pigs were treated daily with per os Aspirin (100 mg) and Ticlopidin (2 × 250 mg) (n = 15) or Clopidogrel (75 mg) (n = 7) after pre-treatment with loading doses. At FUP, neointimal volume obstruction by intravascular ultrasound and neointimal area and maximal neointimal thickness (MNT) by histomorphometry were measured. The aggregation profile of each animal was measured with the CARAT TX4 optical aggregometer at different time points (after loading dose of Aspirin and Ticlopidin, but before stenting and 1, 2, 3, and 4 weeks after stenting) as area under the curve (AUC) calculated from the ADP-induced (index of Ticlopidine and Clopidogrel treatment effectiveness) and collagen-induced (index of Aspirin treatment) aggregations. The mean aggregation level was calculated as the measured AUC in relation to the maximal AUC.

Results Significantly smaller neointimal volume obstruction (25 % vs. 38 %, $p < 0.05$), neointimal area (1.4 vs. 2.6 mm^2, $p < 0.05$), and MNT (0.33 vs. 0.62 mm, $p < 0.05$) was measured in pigs treated with Clopidogrel as compared with Ticlopidine. Similarly, Clopidogrel treatment resulted in significantly better aggregation profile in comparison with Ticlopidine (mean ADP-induced aggregation 28.4 ± 9.1 % vs. 51.2 ± 12.1 %, $p < 0.001$), while no difference was observed in collagen-induced aggregation (29.5 ± 5.9 % vs. 38.6 ± 16.4 %). The level of ADP-induced aggregation exhibited a significant correlation ($p < 0.01$) with the degree of neointimal hyperplasia (regression coefficient r = 0.82 for neointimal volume obstruction, r = 0.811 for neointimal area, and r = 0.859 for MNT). The collagen-induced aggregation exhibited significant ($p < 0.05$) but weak association with the amount of in-stent neointimal hyperplasia (r = 0.713 for volume obstruction, r = 0.721 for neointimal area, and r = 0.665 for MNT). The values of the aggregation profile at single time points showed no correlation with the neointimal amount, indicating the importance of repeated measurements of the aggregation levels during antiplatelet therapy.

Conclusions Repeated measurements of collagen- and ADP-induced platelet aggregation profile provides useful information on the effectiveness of antiplatelet therapy and might predict the outcome of stenting of coronary arteries.

5-III **051**

Gender-Specific Differences in Outcome after PCI in Acute Coronary Syndromes – Data from the Austrian Acute PCI Registry

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Background Subgroup analyses of randomised studies have shown gender specific differences regarding the benefits of percutaneous coronary intervention (PCI) in acute coronary syndromes (ACS). Few data exist about gender differences in outcome in "real-world" setting.

Methods The Austrian acute PCI registry includes data from 22 of 29 hospitals with PCI facilities. Between November 2003 and November 2004 1489 patients (mean age 62.3 ± 23.9 years) were registered. Acute PCI (intention-to-treat) was defined as invasive procedure within 24 hours after symptom onset of an ACS. Outcome data included primary success (TIMI-3 flow), reinfarction and in-hospital mortality rates.

Results 414 women (27.8 %) and 1074 men (72.2 %) were registered. PCI was performed in 82.4 %. Indications for PCI (STEMI, NSTEMI) were similar in men and women. Women were older than men (66.4 ± 13.0 years vs. 60.7 ± 12.5 years; $p < 0.001$) and more often had diabetes mellitus (18.6 % vs. 13.6 %; p = 0.001). Cardiogenic shock was more frequent in women (12.6 % vs. 7.6 %; p = 0.004). Conservative treatment was more often applied to women (11.4 % vs. 5.2 %; $p < 0.001$). PCI (83.4 % vs. 79.7 %; p = 0.09), and rescue PCI (11.9 % vs. 8.5 %; p = 0.06) tended to be performed more often in men. No difference was found between women and men in primary success rate (TIMI-3 flow) (82.9 % vs. 85.8 %) and reinfarction rate (1 % vs. 1 %). However, overall in-hospital mortality was higher in women than in men (11.4 % vs. 6.3 %; p = 0.001). After excluding patients in shock, no difference in mortality was found (5.2 % vs. 4.2 %; p = n. s.). After subdividing patients into STEMI and NSTEMI, mortality was higher in women versus men in STEMI (13.5 % vs. 6.3 %; $p < 0.001$), but equal in NSTEMI (4.5 % vs. 4.5 %). Using stepwise logistic regression analysis including age, gender, shock, diabetes mellitus and total treatment time, only age, diabetes and the presence of cardiogenic shock remained associated with mortality ($p < 0.001$).

Conclusion In this national registry of PCI in ACS, mortality of STEMI is higher in women than in men on univariate, but not on multivariate analysis. Worse in-hospital outcome for women following PCI for ACS is likely related to the higher co-morbid conditions seen in women (older age, shock, diabetes).

5-IV **120**

Sex-related Differences in Impact of Time to Treatment on In-hospital Mortality: Preliminary Results of the Vienna Registry of Reperfusion Strategies in acute STEMI

K. Kalla[1], G. Unger[1], R. Karnik[2], G. Christ[3], W. Schreiber[4], G. Norman[5], H. Pracher[6], R. Malzer[7], H. D. Glogar[3], A. Kaff[7], A. N. Laggner[4], H. Weber[5], J. Mlczoch[6], J. Slany[2], K. Huber[1], on behalf of the Viennese Reperfusion Strategies in STEMI Registry Group
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Background and Aim Several studies have shown that among patients with STEMI treated either with thrombolytic therapy (TT) or with primary PCI (PPCI), female sex is associated with worse outcome. The aim of this study was to investigate sex-related differences in impact of time to treatment on in-hospital mortality in patients treated with PPCI in comparison with TT.

Methods 1053 consecutive patients with STEMI of < 12 hours duration were included in the registry from March 2003 to December 2004. Impact of time to treatment (1st balloon inflation or injection of the thrombolytic agent) on in-hospital mortality was investigated in pts with early presentation (< 2 h from start of pain), moderately delayed presentation (2 to 6 h), and late presentation (> 6 h), respectively, and gender differences were calculated.

Results Among 1053 patients 299 (28.4 %) were women. Female sex was associated with more advanced age (67.4 ± 14.4 years vs. 59.6 ± 12.5 years), a higher incidence of shock at presentation (14.1 % vs. 11.2 %) and prolonged time of onset of pain to treatment (1st balloon inflation or injection of the thrombolytic agent) in both reperfusion groups (PPCI 4.4 ± 2.8 vs. 4.2 ± 2.8 and TT 3.0 ± 2.3 vs. 2.4 ± 1.7). No difference was observed in terms of infarct location. In 141 pts (13.4 %) no reperfusion therapy was offered, due to long presentation delays or contraindication against both reperfusion strategies. Mortality was 21.2 % (♀) vs. 16,9 % (♂) in this group **(Table 12).**

Table 12: K. Kalla et al. Time to treatment and mortality

		PPCI		Lysis	
		♂	♀	♂	♀
0–2 h	% Mortality	6.3	11.1	3.8	5.9
2–6 h	% Mortality	6.3	8.5	6.8	20.0
6–12 h	% Mortality	8.3	22.2	14.3	42.9

This data shows that in patients with STEMI women were associated with higher mortality rates in comparison with men, no matter with which reperfusion strategy they were treated, mainly because of their higher risk profile (age, incidence of shock, longer time to treatment). Increase in mortality with increased treatment delay was also higher in women for both treatment groups. But female sex did not emerge as an independent predictor of death.

5-V **052**

Perkutane intrakoronare Transplantation autologer Stammzellen nach akutem Myokardinfarkt – Klinischer und angiographischer Follow-up nach 6 Monaten

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Hintergrund Die Prognose nach akutem Myokardinfarkt wird wesentlich durch die Einschränkung der linksventrikulären Funktion und das Remodelling bestimmt. Rezente Publikationen konnten zeigen, daß die Transplantation autologer Stammzellen (SZ) in das nekrotische Areal die myokardiale Performance verbessern kann. In Zusammenarbeit mit der Blutzentrale entwickelten wir ein Verfahren, autologe SZ nach Stimulation mit G-CSF (Neupogen®) mittels Apherese aus dem peripheren Blut zu gewinnen und über einen Ballonkatheter via die infarktbezogene Koronararterie (IBK) zu transplantieren. Ziel dieser Untersuchung war es, den klinischen und angiographischen 6-Monats-Follow-up bei einer Serie von Patienten mit akutem Myokardinfarkt (AMI) und nachfolgender Transplantation von autologen SZ zu evaluieren.

Methodik Patienten (Pat.) mit AMI, erfolgreicher primärer Intervention der IBK und ventrikulographisch gesicherter Akinesie im Infarktareal wurden in die Studie eingeschlossen. Die Stimulation der Hämatopoese mittels G-CSF erfolgte ab dem 2. Postinfarkttag. Bei Erreichen eines Gipfels von CD34-positiven Zellen im peripheren Blut erfolgte die Apherese und Aufbereitung der SZ-Suspension. Spätestens am folgenden Tag wurden die SZ über einen Ballonkatheter, der innerhalb des Stents der vorhergehenden Akutintervention insuffliert wurde, in die IBK injiziert. Neben der Dokumentation des klinischen Verlaufs wurden eine Streßechokardiographie und eine Thalliumszintigraphie alle 3 Monate sowie eine invasiv durchgeführte Bestimmung der linksventrikulären Ejektionsfraktion (LVEF) und der Koronarmorphologie zum Zeitpunkt der SZ-Transplantation und nach 6 Monaten durchgeführt.

Ergebnisse Es wurden 22 Pat. mit einem mittleren Alter von 55 ± 9 Jahren (davon 19 männlich) in die Studie eingeschlossen. Die IBK waren der Ramus interventricularis anterior (n = 12), der Ramus circumflexus (n = 2), die rechte Koronararterie (n = 7) und ein Venen-Bypass zur rechten Koronararterie (n = 1); die mittlere LVEF vor SZ-Implantation betrug 46,4 ± 8,1 %. Pro Pat. wurden im Mittel 1,7 ± 1,1 Stents in die IBK implantiert, darunter 4 Drug-eluting Stents (DES). Die Apherese fand bei 21 Pat. 5,3 ± 1,3 Tage nach Beginn der Therapie mit G-CSF statt, bei einem Pat. konnte kein suffizienter Anstieg der ASZ im peripheren Blut nachgewiesen werden. Die Transplantation der SZ verlief bei 20 Pat. komplikationslos, bei einem Pat. unterblieb sie wegen eines asymptomatischen Reverschlusses der IBK. Nach 6 Monaten waren alle 20 Pat., die SZ erhalten hatten, am Leben. An klinischen Komplikationen fanden sich 1 Reinfarkt (5 %) zwei Monate sowie eine Hospitalisierung wegen Linksinsuffizienz (5 %) drei Wochen nach der SZ-Transplantation. Die LVEF verbesserte sich signifikant auf 54,3 ± 11 % (p = 0,0001), ebenso wie die Leistung der Pat. bei der Ergometrie (von 131 ± 27 auf 141 ± 38 Watt; p < 0,05). Bei der Koronarangiographie fanden sich signifikante Instent-Restenosen (ISR) bei 6 Pat. (30 %) und ein chronischer Verschluß der IBK bei 2 Pat. (10 %). Die 4 Pat. mit einem DES wiesen keine ISR auf.

Schlußfolgerung Nach AMI ist die Gewinnung von autologen SZ aus dem peripheren Blut nach Gabe von Wachstumsfaktoren und ihre transkoronare Transplantation mittels Ballonkatheter möglich. Im 6-Monats-Follow-up konnte eine signifikante Verbesserung der LVEF und der Leistungsbreite der Pat. nachgewiesen werden. Den Erfolgen der Methode steht das häufige Auftreten von ISR bei Verwendung nichtbeschichteter Stents entgegen.

5-VI **055**

Non-cardiac Surgical Patients with Severe Aortic Stenosis: Is There Still a Role for Palliative Balloon Valvuloplasty?

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Purpose This retrospective single-center study was performed to reevaluate the role of balloon aortic valvuloplasty in patients diagnosed with severe aortic stenosis before non-cardiac surgery.

Subjects and Methods 33 patients (26 female, 7 male, mean age 80.1 + 7.3 ranging from 63 to 94 years) with severe aortic stenosis (aortic valve area < 0.8 cm^2) who underwent balloon aortic valvuloplasty before non-cardiac surgery between July 1996 and March 2002 were identified. Procedure related morbidity and mortality, perioperative cardiovascular complications and one-year follow-up were assessed.

Results All patients had at least one cardiac symptom. Left ventricular ejection fraction was reduced in 24/33 patients (EF 48 ± 15 %, range 25–75). Main contraindications to preoperative aortic valve replacement were malignant disease in 12, advanced age in 9 and poor medical condition in 12 patients. After balloon aortic valvuloplasty aortic valve area increased from 0.56 ± 0.10 to 0.87 ± 0.16 cm^2 ($p < 0.01$) and mean transvalvular aortic gradient decreased from 55.1 ± 14.4 to 26.7 ± 8.8 mmHg ($p < 0.01$). Aortic balloon valvuloplasty could be performed successfully in 30/33 patients. Procedural related major complications were mainly vascular and occurred in 3 patients (9 %). Non-cardiac surgery could be performed with perioperative mortality of 6 % (2 patients) and minor cardiac complications in 24 %. Event-free survival rate after one year was 60 %.

Conclusion Balloon aortic valvuloplasty represents an effective preoperative tool for reducing perioperative morbidity and mortality in non-cardiac surgical patients with severe and symptomatic aortic stenosis who are unsuitable for aortic valve replacement.

5-VIII **48**

Interventionelle Behandlung von Nierenarterienstenosen im Herzkatheterlabor

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Die interventionelle Behandlung von Nierenarterienstenosen (NA-Stenosen) wird bei therapierefraktärem Blutdruck und/oder assoziierter progredienter Nierenfunktionseinschränkung empfohlen. Die Koinzidenz von koronarer Herzkrankheit und atherosklerotischen NA-Stenosen läßt es bei gegebener klinischer Indikation sinnvoll erscheinen, eine gleichzeitige angiographische Abklärung beider Gefäßregionen durchzuführen. Gegebenenfalls kann in einer Sitzung auch die interventionelle Behandlung von Koronar- und Nierenarterien angeschlossen werden. Wir berichten über unsere Erfahrungen mit einem derartigen Vorgehen im Katheterlabor unserer Abteilung.

Zwischen März 2003 und Februar 2005 wurden 3264 Patienten einer Herzkatheteruntersuchung unterzogen, bei 1149 Pat. (35 %) wurde zusätzlich eine Angiographie der NA durchgeführt. Bei 39 Patienten (Alter: 70,1 ± 8,6 Jahre; 18 Männer, 21 Frauen) wurde eine Intervention an den NA vorgenommen. Indikation zur NA-Intervention war das Vorliegen einer ≥ 70 % Stenose einer oder beider NA bei ungenügend eingestellter arterieller Hypertonie (≥ 3 verschiedene Antihypertensiva oder Unverträglichkeit der Medikation) mit oder ohne zusätzliche Nierenfunktionseinschränkung. Der mittlere Ausgangsblutdruck betrug 149 ± 17 mmHg systol. und 82,2 ± 8,3 mmHg diastol., durchschnittlich wurde mit einer Kombination von 2,7 ± 1,2 antihypertensiven Substanzen behandelt. Der Ausgangswert des Serumkreatinins (SKr) betrug 1,15 ± 0,42 mg/dl, 7 Pat. wiesen ein SKr > 1,5 mg/dl auf. Bei allen Patienten wurde in einer Sitzung zusätzlich die Koronarangiographie durchgeführt, bei 16 Patienten

erfolgte gleichzeitig eine Intervention an den Koronargefäßen. Insgesamt wurden 44 stenosierte NA behandelt, dabei wurde bei 34 Patienten an einer NA, bei 5 Patienten an beiden NA interveniert. Bei 13 von 44 Stenosen wurde primär eine Ballondilatation vorgenommen und anschließend ein Stent implantiert. Bei 30 Stenosen wurde primär ein Stent implantiert. Bei einem Patienten war eine Nachdilatation erforderlich. Der mittlere nominale Stentdiameter betrug 5,53 ± 0,73 mm, die mittlere Stentlänge 13,2 ± 2,27 mm und der maximale Ballondruck bei Implantation 12,4 ± 3,1 atm. Der angiographische Stenosegrad konnte von 78,8 ± 9,2 % vor auf 9,2 ± 7,8 % nach Intervention reduziert werden. Bei keinem Pat. kam es zum Auftreten einer periinterventionellen Komplikation. 2 Patienten verstarben 138 und 49 Tage nach der Intervention, ein Patient erlag einem plötzlichen Herztod, ein zweiter einem hämorrhagischen Insult. Bei den 37 überlebenden Patienten beträgt die mittlere Nachbeobachtungszeit 353 ± 207 Tage. 2 Patienten wurden aus kardialen Gründen nachangiographiert, bei keinem Patienten ergab sich angiographisch oder klinisch ein Anhaltspunkt auf das Vorliegen einer Restenose der NA. Das SKr blieb 6–12 Monate nach Intervention (1,19 ± 0,43 mg/dl; p = n.s.) gegenüber dem Ausgangswert (1,24 ± 0,34 mmHg) unverändert. Im Vergleich zum Ausgangswert vor Intervention (150,5 ± 17,9 mmHg) lagen die systolischen Blutdruckwerte 1 Monat (137,6 ± 14,8 mmHg; p = 0.007) und 6–12 Monate nach Intervention (137,1 ± 19,3 mmHg; p = 0,008) signifikant niedriger. In ähnlicher Weise kam es auch zu einem Absinken des diastol. Blutdrucks von 83,1 ± 8,5 mmHg vor der interventionellen Behandlung auf 75,2 ± 8,4 mmH 1 Monat (p = 0,01) und auf 75,2 ± 9,0 mmHg 6–12 Monate (p = 0,008) nach Intervention. Die Zahl der benötigten antihypertensiven Substanzen blieb dagegen mit 2,5 ± 0,8 Substanzen vor, 2,6 ± 0,8 Substanzen 1 Monat nach Intervention (p = n. s.) und 2,6 ± 1,0 Substanzen 6–12 Monate nach Intervention (p = n. s.) unverändert.

Schlußfolgerung Eine NA-Intervention kann im Rahmen der Herzkatheteruntersuchung mit und ohne zusätzlicher Koronarintervention in einer Sitzung mit einer sehr niedrigen Komplikationsrate durchgeführt werden. Bei entsprechender Indikationsstellung ist im Langzeitverlauf mit einer deutlich verbesserten Blutdruckeinstellung zu rechnen, eine Weiterführung der antihypertensiven Medikation ist jedoch meist erforderlich.

Sitzung 6 – Rhythmologie II

6-I **83**

Entwicklung der ICD-Implantationsraten in Österreich in den Jahren 2000–2003: Gibt es Unterschiede in den einzelnen Bundesländern?

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Hintergrund Bereits seit der Veröffentlichung von MADIT II, jedoch verstärkt durch die Ergebnisse der SCDHeFT-Studie herrscht eine rege Diskussion über die Umsetzung der ICD-Therapie in die klinische Praxis. Die ICD-Implantationsrate (ICD-IR) ist in Österreich im Vergleich zu den USA sehr niedrig, aber auch beträchtlich geringer als beispielsweise in Deutschland. Marktabschätzungen über die vergangenen Jahre ließen einen Anstieg der ICD-Implantationen vermuten. Auch wenn eine Zuordnungsabschätzung durch die Implantationszahlen der Krankenhäuser möglich ist, sollte doch der eigentlich relevante Parameter für die tatsächliche Versorgung die ICD-IR der Patienten gemessen an ihren Wohnorten sein. Eine frühere Untersuchung hatte diesbezügliche bundesländerspezifische Unterschiede aufgezeigt. Ziel dieser Auswertung war es, die Entwicklung der ICD-IR allgemein festzustellen sowie über den Beobachtungszeitraum zu eruieren, ob die Bundesländerunterschiede (gemessen am Wohnort des Patienten) weiterhin bestanden.

Methoden Das Österreichische Bundesinstitut für Gesundheitswesen (ÖBIG) stellt auf Anfrage Daten in anonymisierter Form zur Verfügung. Der dieser Auswertung zugrundeliegende Datensatz enthält sämtliche Fälle von österreichischen Fondskrankenanstalten zwischen 01.01.2000 und 31.12.2003. Für jeden Aufnahmefall werden unter anderem folgende Daten gespeichert: Wohnbundesland und Wohnbezirk, Alter und Geschlecht des Patienten, Bundesland der Krankenanstalt, Hauptdiagnose sowie die durchgeführten medizinischen Einzelleistungen (MELs). Für diese Auswertung wurden die MELs 2356 (Implantation eines automatischen ICDs) sowie 2361 (Aggregatwechsel eines automatischen ICDs) herangezogen. Zur Berechnung der ICD-IR (Implantationszahl pro Million Einwohner) wurden die Daten der Statistik Austria (Stand 2000) herangezogen.

Tabelle 13: Perthold W. Implantationsraten (Neuimplantationen pro Million Einwohner) bezogen auf den Wohnort des Patienten

	Wien	NÖ	B	Stmk.	OÖ	Sbg.	K	T	V	Ö gesamt
2000	42.9	50.6	46.6	36.6	40.6	42.6	28.4	28.4	40.2	40.8
2001	29.8	54.5	39.4	34.1	42.8	67.8	28.4	35.9	43.0	41.1
2002	61.6	83.1	39.4	34.1	61.6	46.5	40.8	28.4	51.6	55.3
2003	81.5	99.9	68.1	44.1	66.7	44.5	35.5	49.4	85.1	68.5
2000–2003	53.9	72.0	48.4	37.2	52.9	50.3	33.2	35.5	55.2	51.4

Ergebnisse In den Jahren 2000 bis 2003 wurden insgesamt 2194 ICD-Implantationen durchgeführt, davon waren 1667 (76 %) ICD-Neuimplantation. Die Zahl der Gesamtimplantationen stieg von 417 in 2000 auf 735 in 2003. Die Zahl der Neu-Implantationen stieg von 331 in 2000 auf 555 in 2003 **(Tab. 13)**. Sowohl der Anteil der Neuimplantationen (74–79 %) als auch der Anteil der Frauen (18–23 %) war über die beobachteten 4 Jahre relativ konstant.

Zusammenfassung Die Zahl der ICD-Neu-Implantation stieg im Zeitraum 2000 bis 2003 um insgesamt 68 % auf 555. Dieser Trend war mit kleinen Schwankungen in den meisten Bundesländern zu beobachten. Es gab jedoch weiterhin große regionale Unterschiede in der ICD-IR, wobei vor allem die Steiermark, Salzburg, Kärnten und Tirol weit unter dem österreichischen Durchschnitt lagen.

6-II **087**

Implantable Loop Recorder use for Detection of Arrhythmias Causing Syncope: Differences between Patients with and without Structural Heart Disease

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Aim To evaluate the diagnostic value of the implantable loop recorder (ILR) in patients with unexplained syncope with structural heart disease (SHD) compared to patients without SHD.

Methods and Results 52 patients (26 male/26 female, age 53 ± 16 years) with unexplained syncope were enrolled in a prospective study involving automatic arrhythmia detection with an ILR. SHD was present in 23 patients (44 %) (coronary artery disease in 12 patients, hypertrophic cardiomyopathy in 6 patients and dilated cardiomyopathy in 5 patients). The remaining 29 patients (56 %) had no structural heart disease. Non-invasive testing included neurologic work-up, Holter-ECG and provocative testing (tilt table test and Carotis Sinus massage) in all patients. An electrophysiologic study was performed in 12/23 patients (52 %) with SHD and in 11/29 patients (38 %) without structural heart disease. During a mean implantation time of 18 ± 9 month syncope was recorded 3.2 ± 2.9 months after implantation in 19/23 patients with SHD (83 %) and in 20/29 patients without SHD (69 %) while no further symptoms occurred in the remaining patients. Sinus-rhythm during syncope was recorded in 14/23 patients with SHD (61 %) and in 13/29 patients without SHD (45 %). Significant arrhythmias while syncope were detected in 22 % of patients with SHD: AV-nodal block III in three patients and sinus arrest in two patients. Significant arrhythmias during syncope were detected in 24 % of patients without SHD: AV-nodal block III in three patients, sinus arrest in one patient and Sick-Sinus-Syndrom in three patients. Thus, in these 12 patients a permanent pacemaker was implanted.

Conclusions In 83 % of patients with SHD the ILR allows to establish a symptom-rhythm correlation. However, normal sinus

rhythm during symptoms is more frequent in patients with SHD as compared to patients without SHD. The diagnostic yield of the ILR in detecting significant arrhythmias leading to pacemaker therapy ranges between 22 % and 24 %, irrespective of an underlying SHD.

6-III **85**

The Value of the Implantable Loop Recorder in Patients with Syncope

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Background Syncope is a complex clinical syndrome that can be very challenging with respect to a definite diagnosis. The implantable loop recorder (ILR) is a useful tool to define an arrhythmic etiology, but also to exclude arrhythmias as reason for fainting and syncopal episodes.

Methods Between April 1998 and February 2005 an ILR (Reveal®, Medtronic) was implanted at our institution in 38 pts (16 female, 22 male; mean age 63 ± 3 years) with unexplained syncope (n = 36) or palpitation (n = 2). Prior to implantation all pts underwent detailed neurological and cardiac work-up without significant findings.

Results 24 pts (63.2 %) had a recurrence of syncope, near-syncope or dizziness. In 9 of these pts (37.5 %) an arrhythmia has been excluded as explanation for the recurrent clinical event. However, in 15 pts (62.5 %) the ILR revealed an underlying arrhythmia, such as sick sinus syndrome with bradycardia (n = 2) or significant pauses (n = 4), paroxysmal AV block (n = 3), paroxysmal supraventricular tachycardia (n = 2), ventricular tachycardia or Torsades de Pointes (n = 4). Nine of these pts were treated with a dual chamber pacemaker and 4 pts with an implantable cardioverter defibrillator. One of the ICD pts underwent RF-ablation of Purkinje extrasystole as trigger for repetitive Torsades de Pointes. The mean follow-up period from implantation to occurrence of the arrhythmia was 11,5 ± 2,4 months.

Conclusion Significant brady- or tachyarrhythmias were diagnosed within the life-expectancy of the device in nearly two thirds of patients who received an ILR for unexplained and recurrent syncope. Consequently, the ILR helped efficaciously to determine the appropriate therapy for syncopal patients.

6-IV **116**

Mortalität nach Schrittmacherimplantation bei AV-Block – Vergleich verschiedener Stimulationsarten im Langzeitverlauf

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Einleitung Einsonden-VDD-Systeme haben sich gegenüber DDD-Systemen in der Behandlung des AV-Blocks als sichere und effiziente Therapieform erwiesen. In einer prospektiv randomisierten Studie gibt es sogar Daten für eine geringere Mortalität von Patienten mit VDD-Systemen. Seit 1994 werden an unserem Zentrum VDD-Schrittmacher implantiert, die den Vorteil einer kürzeren Operationsdauer sowie niedrigerer Kosten haben. Wir analysierten retrospektiv die Mortalität bei den unterschiedlichen Stimulationsformen.

Methodik Zwischen Jänner 1994 und März 2005 wurde an unserer Abteilung bei insgesamt 571 Patienten (Durchschnittsalter 77,8 ± 10,9; 50,4 % weiblich) mit AV-Block ein Schrittmachersystem implantiert. Kriterien für die Auswahl eines VDD-Systems waren eine normale Sinusknotenfunktion (≥ 70/min) sowie eine fehlende

Tabelle 14: B. Fellner et al.

	DDD	VDD	VVI
Anzahl der Patienten	162 (28,4 %)	343 (60,1 %)	66 (11,6 %)
Mortalität in %	33,3	39,1	57,6
Alter bei Implantation	73,6 ± 11,2 **	78,5 ± 10,4	84,1 ± 8,8
Alter zum Zeitpunkt d. Todes	80,3 ± 8,8 *	83,7 ± 9,0	86,9 ± 7,1
Tragedauer in Monaten	44 ± 34 *	37,2 ± 34,4	25,7 ± 25,4

* $p < 0.05$; ** $p < 0.001$ (Vergleich DDD vs VDD)

Anamnese/Dokumentation von atrialen Tachyarrhythmien. Die Entscheidung für ein VVI-System wurde bei älteren, comorbiden Patienten bzw. gleichzeitig vorliegendem permanentem VH-Flimmern getroffen. Die Patienten wurden regelmäßig in der Schrittmacherambulanz nachkontrolliert, die Daten der Mortalität beziehen sich auf telefonische Kontakte mit Angehörigen/Hausarzt/Klinik, Meldeamt sowie städtischer Bestattung.

Ergebnisse Fast 2/3 der Patienten erhielten ein VDD-System, der Anteil der VVI-Schrittmacher betrug 11,6 %. Details der Mortalität, die sich nicht signifikant zwischen VDD und DDD unterschied, sind in **Tabelle 14** zusammengefaßt.

Zusammenfassung Obwohl die Patienten der VDD-Gruppe im Vergleich zur DDD-Gruppe bei Erstimplantation deutlich älter waren (5 Jahre), zeigte sich kein signifikanter Unterschied in der Mortalität. Auch zum Zeitpunkt des Todes waren die VDD-Patienten signifikant älter, bei einer nur um 7 Monate verkürzten Schrittmacher-Tragedauer. VDD-Schrittmacher, für die bei sorgfältiger Selektion fast 2/3 der Patienten mit AV-Block in Frage kommen, sollten Patienten mit AV-Block und normaler Sinusfunktion nicht vorenthalten werden.

6-V **86**

Morbidity and Mortality in Implantable Cardioverter Defibrillator Patients: A Single Center Experience

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Background ICD recipients are in general a sick population with a high comorbidity in addition to the risk of sudden cardiac death (SCD). The purpose of this study was to determine the incidence and causes of mortality in ICD patients (pts) and to define their clinical characteristics.

Methods 70 consecutive pts (55 male, 15 female) underwent ICD implantation (39 single-chamber, 26 dual-chamber ICDs, 5 CRT-D) at our institution. Mean age was 67 ± 1.5 (range 25–83) years. Coronary artery disease was present in 41 pts, non-ischemic cardiomyopathy in 19 pts (3 of those had valvular heart disease), arrhythmogenic right ventricular dysplasia in 3 pts and no structural heart disease in 7 pts (one had Long QT Syndrome). Mean ejection fraction was 34 ± 1.5 % (range 15–60), mean QRS duration was 130 ± 4.2 ms. 44 pts (62.8 %) were in NYHA functional class I or II and 26 pts (37.2 %) in NYHA class III or IV. With respect to comorbidities 11 pts (15.7 %) had diabetes, 31 pts (44.2 %) paroxysmal or permanent atrial fibrillation. Two thirds of the pts (n = 48) were on beta blockers and 42 pts on amiodarone.

Results During a mean follow up of 23 ± 2,3 months 10 pts (14.2 %) died. Eight of these pts had an ejection fraction ≤ 35 %. All pts except one died related to non-arrhythmic causes, such as congestive heart failure (n = 2), cardiogenic shock (n = 2), sepsis (n = 3), cancer (n = 1) and cerebral bleeding (n = 1). One death occurred due to electrical storm despite delivery of all programmed ICD therapies. 39 pts (56 %) were treated with appropriate ICD therapies and 8 pts (11 %) experienced inadequate shocks. The Kaplan-Meier estimates of the 1, 2, 3, 4 year cumulative risk of survival were 89 %, 87 %, 82 %, 74 %, respectively. The mean duration from implant to death was 25 ± 1.9 months. Categorisation of the QRS duration above and below 120 ms and of the NYHA functional Class > II demonstrated a significant difference in total mortality. All other covariates (e. g., gender, underlying heart disease, diabetes, antiarrhythmic drug therapy) did not seem to have an influence on mortality.

Conclusion Despite clear reduction of the arrhythmogenic risk for sudden cardiac death concomitant comorbidities still play a major role for the survival of ICD recipients as shown in the investigated population. QRS duration > 120 ms and higher NYHA functional classes were associated with a higher overall mortality.

6-VI **107**

20 Jahre ICD-Therapie im Wilhelminenspital: ein Erfahrungsbericht

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Einführung Seit den 1980er Jahren ist die Implantierbare Cardioverter-Defibrillator (ICD-) Therapie die erste effektive Behandlung des plötzlichen Herztodes (SCD). Von unserer Arbeitsgruppe wurde 1985 der erste ICD in Österreich in Zusammenarbeit mit den Herzchirurgien AKH Wien und Lainz implantiert. Ziel dieser retrospektiven Analyse war, den Langzeitverlauf in diesem Patientengut zu untersuchen.

Patienten und Methodik Von 1985 bis 3/2005 wurden 336 Patienten (Pat.) – das mittlere Alter bei Implantation betrug 60,2 ± 13,5 Jahre, 77,1 % Männer, 22,9 % Frauen – mit einem ICD versorgt. Als kardiale Grunderkrankung bestand bei 53,8 % eine koronare Herzerkrankung, bei 28,6 % eine dilatative CMP und bei 17,6 % eine andere Erkrankung (Long-QT, ARVD, Brugada-Syndrom, primär elektrische Herzerkrankung). 126 Pat. (37,5 %) hatten eine linksventrikuläre Pumpfunktion von < 35 %. Bei 29,2 % der Patienten bestand Kammerflimmern (VF), bei 62,8 % eine Kammertachykardie (VT) und bei 5,3 % eine Synkope mit induzierbaren VT/VF als Indikation zur ICD-Implantation. Primär prophylaktisch erhielten 5 Pat. (1,5 %) einen ICD. 113 Pat. erhielten ein abdominell implantiertes Gerät (bis 1994), 223 Pt erhielten ein pektorales System. 282 Geräte waren Einkammer-ICDs, 44 DDD-ICDs, 1 VDD-ICD und 9 BIV-ICDs.

Ergebnisse In einem Follow-up (FU) von 25,6 ± 65,6 Mo (max. 175,2 Mo/Min 1 Tag) überleben 61 % der Pat., 34,8 % sind verstorben (4,3 % plötzlicher Herztod), 4,2 % „lost to FU". 2,4 % explantiert und 46,4 % sind auf unserer ICD-Ambulanz in regelmäßiger Kontrolle, 7,1 % werden in einem anderen KH kontrolliert. 74 Pa-

tiententen erhielten im FU eine antiarrhythmische Therapie, davon 59,5 % wegen supraventrikulärer Tachyarrhythmien (SVT) und 40,5 % wegen gehäufter VT/VF-Episoden. Eine adäquate Therapieabgabe durch das Gerät erfolgte bei 178 Pat. (47,1 %). Die erste Aktivierung erfolgte im Mittel 20,5 ± 26,5 Mo nach ICD-Implantation. 91 Pat. (28,2 %) erhielten keine antitachykarde Therapie.

Zusammenfassung Bei einem Drittel der ICD-Träger entsprach die Indikation der ICD-Implantation zwar den Guidelines, retrospektiv betrachtet aber bis dato nicht den klinischen Erfordernissen. Bei weniger als 25 % der Pat. wurde im Laufe der weiteren ICD-Nachsorge eine medikamentöse antiarrhythmische Therapie etabliert, in 2/3 der Fälle aufgrund von SVT. Trotz ICD-Therapie erlitten 4,3 % einen plötzlichen Herztod, wobei kein Hinweis auf eine Sonden- oder Generatordysfunktion vorlag. In einem vergleichbaren Kontrollzeitraum (ca. 2 Jahre) beträgt die SCD-Rate bei der allgemeinen Bevölkerung < 0,5 %, bei Herzinsuffizienz-Pat. mit EF < 35 % < 40 % und bei bekannter KHK < 12 %.

6-VII **093**

Hochdosierter intravenöser Amiodaronbolus bei Patienten mit Vorhofflimmern und tachykarder Ventrikelfrequenz

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Die Daten bezüglich Effektivität von intravenösem Amiodaron bei tachykard geleitetem Vorhofflimmern sind uneinheitlich. Vor allem der eindeutige Nachweis einer Wirksamkeit bezüglich Kardioversion steht aus. Der übliche klinische Einsatz mit einem Bolus, gefolgt von einer Dauerinfusion, ist durch die aufwendige Applikation über den empfohlenen zentralvenösen Zugang verkompliziert.

Methodik In einer offenen, randomisierten Studie wurden 100 Patienten (Pat.) mit Vorhofflimmern und einer Ventrikelfrequenz über 135/min mit Amiodaron (A) oder Digoxin (D) behandelt. 50 Pat. erhielten 450 mg A, 50 Pat. erhielten 0,6 mg D, jeweils als Bolus über einen peripheren Zugang. Lag die Ventrikelfrequenz nach 30 min über 100/min, folgte ein 2. Bolus mit 300 mg A oder 0,4 mg D. Alle Pat. wurden auf einer internistischen Intensivstation monitorisiert, die Herzfrequenz wurde kontinuierlich aufgezeichnet, der Blutdruck während der ersten Stunde in 5-Minuten-Intervallen gemessen. Der Zeitpunkt, zu dem ein Sinusrhythmus eintrat, wurde dokumentiert, der periphere Zugang bezüglich Inflammation klinisch observiert.

Ergebnisse Die mittlere Herzfrequenz vor der Therapie lag in beiden Gruppen bei 145/min. Bereits 5 Minuten nach Injektion unterschied sich die mittlere Herzfrequenz in den beiden Gruppen und blieb während des einstündigen Monitorings bei allen Vergleichspunkten (alle 10 min) statistisch signifikant unterschiedlich (p-Werte zwischen 0,0001 und 0,013). Nach 60 Minuten lag die mittlere Ventrikelfrequenz bei 94/min (A-Gruppe) und 105/min (D-Gruppe). Der Blutdruck unterschied sich zu keinem der Vergleichspunkte statistisch signifikant. Sinusrhythmus nach 30 Minuten war 14mal in der A-Gruppe vs. 3mal in der D-Gruppe nachweisbar, nach 60 Minuten hatten 21 Pat. in der A-Gruppe vs. 9 Pat. in der D-Gruppe Sinusrhythmus (p = 0,012). Bei keinem Pat. wurde eine Phlebitis festgestellt.

Schlußfolgerungen Die periphere intravenöse Bolusinjektion von 450 mg A bei Pat. mit tachykard geleitetem Vorhofflimmern scheint sicher zu sein und birgt kein klinisch relevantes Risiko einer Phlebitis. Die Wirkung hinsichtlich rascher Reduktion der Ventrikelfrequenz ist hochsignifikant ausgeprägter als bei D. Erstmals konnte ein statistisch signifikanter Effekt bezüglich Kardioversion zu Sinusrhythmus nachgewiesen werden.

Autorenindex

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