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Kardiologie im Zentrum

Fortbildung der Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

30. September – 1. Oktober 2016, Design Center, Linz

Abstracts

(in alphabethischer Reihenfolge nach Erstautor)

Die heurigen Gewinner des Posterpreises: T. Odeneg, J. Kellermair, B. Wernly (v. l. n. r.).
Foto: © RT Roman Kneidinger, Interne 1

1. Preis

Von Willebrand Factor Multimeric Structure Analysis in Patients with Severe Aortic Stenosis

J. Kellermair, H. Ott, J. Kammler, F. Obendorf, H. Blessberger, C. Reiter, S. Schwarz, A. Nahler, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Background Acquired von Willebrand Syndrome (AvWS) has been frequently found in patients with severe aortic stenosis (AS). In these patients, AvWS is characterized by proteolytic loss of high molecular weight (HMW) multimers of von Willebrand Factor (vWF) due to high shear force. In this study we aimed to determine the correct acquired von Willebrand AvWS subtype by vWF multimeric structure analysis, which has not been described in literature before.

Methods Consecutive patients with the diagnosis of severe AS (n = 20) were enrolled. Severe AS was defined as an echocardiographical peak aortic jet velocity ≥ 4 m/s, a mean transvalvular pressure gradient ≥ 40 mmHg and an aortic valve area (AVA; calculated by continuity equation) < 1 cm^2. vWF multimer analysis was performed using a Western blot: multimeric bands were electrophoretically separated using a low resolving (1%) and a high resolving (2%) agarose gel. For immunolocalization we used a polyclonal rabbit anti-vWF as the primary antibody and a Cy5-labeled ECL Plex goat anti-rabbit IgG as the secondary antibody. vWF multimeric bands were densitometrically quantified using a fluorescent laser scanner with 633 nm excitation.

Results In 18 out of 20 patients (90%) vWF multimeric pattern analysis revealed an isolated loss of high molecular weight bands. We did not find an additional decrease in middle and low molecular weight multimers. This finding is consistent with the diagnosis of AvWS 2B.

Conclusion AvWS in severe AS is a frequent finding and can be subcategorized into AvWS type 2B.

2. Preis

The Use of the Wearable Cardioverter Defibrillator in Austria. Results of the Austrian LifeVest Registry

T. Odeneg, M. Manninger, C. Ebner, D. Moertl, H. Keller, A. Dirninger, G. Stix, B. Föger, G. Grimm, M. Stühlinger, C. Steinwender, C. Haider, H. Brussee, D. Scherr, on behalf of the Austrian WCD Study Group
Division of Cardiology, Medical University of Graz

Introduction The wearable cardioverter-defibrillator, WCD or LifeVest is a treatment option for patients at high risk for VT/VF, either in whom this risk may be temporarely or in whom an ICD implantation is currently not possible.

Methods Retrospective registry of patients in Austria who received a WCD 2009–2016.

Results The Austrian LifeVest Registry enrolled 451 patients (59 ± 14 years; 24% female), who received a WCD 2009–2016 in Austria. The main indications were: Newly diagnosed severe cardiomyopathy (21%), recent myocardial infarction (20%), ischemic cardiomyopathy with recent PCI/CABG (21%), delayed ICD implantation (12%), acute myocarditis (10%) and ICD-associated infection (10%). Left ventricular EF was 33 ± 15%, median CHA_2DS_2VASc-Score was 3 (2–5). 48% of all patients had VT/VF before the WCD period. The median WCD duration was 48 (1–436) days. There was no significant difference in WCD compliance between patients wearing the WCD < 60 days vs. > 60 days (23.5 [3–24] h/day vs 23.2 [1–24] h/day; p = n. s.). 11 patients (2.4%) received 21 adequate WCD shocks for VT/VF events. All of these VT/VF events were terminated to sinus rhythm with the first WCD shock. One (0.2%) inadequate shock occured. Only 55% of all 451 patients required ICD implantation after the WCD period. Of the 45 patients with myocarditis, only 8 patients (22%) required an ICD (p < 0.001).

Conclusion The WCD is an effective treatment option in patients at high risk for VT/VF and/or mandated wating period for ICD implantation. The ICD implantation rate was 55% with a significant lower implantation rate for patients with myocarditis with 22%.

3. Preis

Pre-Interventional sST2 Plasma Concentration Predicts One-Year-Mortality after Transcatheter Aortic Valve Implantation (TAVI)

B. Wernly[1], M. Lichtenauer[1], S. Eder[1], C. Edlinger[1], U. Landmesser[2], H. R. Figulla[3], Ch. Reiter[4], U. C. Hoppe[1], C. Jung[5], A. Lauten[2]
[1]Department of Cardiology, Paracelsus Private Medical University, Salzburg, Austria; [2]Department of Cardiology, Charité – Universitätsmedizin Berlin; [3]Department of Cardiology, University Hospital of Jena, Germany; [4]Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz, Austria; [5]Division of Cardiology, Pulmonology and Vascular Medicine University Duesseldorf, Germany

Introduction Degenerative aortic valve stenosis is the leading valvular heart disease worldwide. Transcatheter aortic valve implantation (TAVI) is a relativly new procedure for valve replacement in high risk patients who are not suitbable for conventional aortic valve replacement. sST2 has been introduced as a novel biomarker in patients suffering from heart failure for better risk stratification. We sought to investigate in our study whether sST2 can serve as a useful biomarker for the prediction of mortality of patients undergoing TAVI because of severe aortic stenosis.

Methods 274 patients (149 female; age 80.50 ± 0.51 SEM; EUROSCORE 23.83 ± 1.65 SEM) that underwent TAVI procedure and were followed-up over 12 months were retrospectively investigated in this study. Plasma samples were evaluated for sST2 using commercially available ELISA kits.

Results Plasma sST2 concentration correlated significantly with left ventricular ejection fraction (–0.21; p = 0.001) and EUROSCORE (r = 0.18; p = 0.006). Patients were divided in two groups: patients with sST2 plasma concentration below and above the cohort's median (6370 pg/ml): patients with sST2 plasma concentration above the median evidenced a significantly increased one-year-mortality rate after TAVI (22% vs. 40%, p < 0.05). ROC and "area under the curve" calculation to evaluate sST2 for its prognostic relevance (AUC 0.67;

95-%-CI: 0.59–0.75; p < 0.001) and to compare it with other tools for risk assessment like the EUROSCORE (AUC 0.60; 95-%-CI: 0.52–0.69; p = 0.02) were performed. In a multivariate COX regression analysis and after correction for EUROSCORE, diabetes, mean aortic valve pressure gradient, CRP, renal function, coronary heart disease, arterial hypertension, besides pre-interventional left ventricular ejection fraction (RR 0.98; 95-%-CI: 0.97–0.99) and major vascular complications (RR 3.70; 95-%-CI: 1,45–9,44) only a sST2 plasma-concentration above the median (RR 2.62; 95-%-CI: 1.30–5.31; p = 0.007) remained significantly associated with an elevated one-year-mortality after TAVI.

Conclusion Patients with a plasma sST2 concentration above the median (6370 pg/ml) evidenced a 2.6-fold increase of one-year-mortality after TAVI. sST2 plasma concentration remained predictive for mortality even after correction for relevant laboratory and echocardiographic parameters. We assume based on these results that sST2 could serve as very helpful indicator for assessing patients' risk before undergoing TAVI procedure. Measurements of pre-interventional biomarkers in patients undergoing TAVI could provide extra information. Comprehensive assessment of the patient's cardiovascular risk profile could be substantiated by measurement of plasma sST2 concentration.

♦ ♦ ♦

Einfluss von linksventrikulärer Auswurffraktion und Diabetesstatus auf das Langzeit-Outcome nach interventioneller ungeschützter Hauptstamminter-vention – ein retrospektives Langzeit-Follow-up

H. Blessberger, J. Kammler, D. Hrncic, S. Schwarz, J. Starnawski, A. Kypta, T. Lambert, A. Nahler, C. Reiter, J. Kellermair, D. Kiblböck, K. Kerschner, M. Grund, C. Steinwender

Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Einleitung Durch die demographische Entwicklung wird es in naher Zukunft zu einer deutlichen Zunahme der koronaren Herzkrankheit mit konsekutivem Anstieg von signifikanten Hauptstammstenosen kommen. Wenngleich ungeschützte Stenosen des linken Hauptstammes laut aktuellen Guidelines eine Domäne der chirurgischen Revaskularisation darstellen, ist es durch die technischen Entwicklungen der interventionellen Kardiologie dazu gekommen, dass immer häufiger Stenosen in dieser Lokalisation – gerade bei älteren oder multimorbiden Patienten – auch mittels Stentrevaskularisation saniert werden.

In unserer Untersuchung evaluierten wir, ob Patienten unabhängig von ihrer linksventrikulären Auswurffraktion (LVEF) und ihrem Diabetesstatus von einem interventionellen Eingriff in gleichem Maße profitieren.

Methoden Es wurden Patienten aus dem UNPROLEMA- (UNPROtected LEft MAin disease-) Register für ungeschützte Hauptstamminterventionen des Kepler Universitätsklinikums analysiert, die sich zwischen 11/2002 und 12/2013 einer ungeschützten Hauptstammintervention unterzogen hatten. Dabei wurden im Rahmen des Registers die Patientendaten durch Informationen aus Krankengeschichten sowie aus strukturierten Telefoninterviews und Meldeamtsanfragen bzgl. Follow-up komplettiert. Die Patienten wurde gemäß ihrer LVEF und ihres Diabetesstatus (DM) in 4 Gruppen unterteilt: 1 = normale LVEF > 55 % ohne DM, 2 = eingeschränkte LVEF < 55 % ohne DM, 3 = DM mit LVEF > 55 %, 4 = DM mit LVEF< 55 %. Die Gesamtmortalität und das Auftreten von „major adverse cardiac and cerebrovascular events" (MACCE: definiert als STEMI, NSTEMI, Zielgefäßrevaskularisation [interventionell oder mittels aortokoronarem Bypass], Insult/TIA oder Tod jedweder Genese) wurden mittels Kaplan-Meier-Kurven analysiert. Ein Log-rank-Test wurde zur Prüfung der statistischen Signifikanz ermittelt. Schließlich wurde ein Cox-Proportional-Hazards- (CPH-) Modell für das Auftreten von MACCE berechnet, in dem für potentielle Confounder wie Alter, Geschlecht, Nierenfunktion und kardiale Risikofaktoren adjustiert wurde.

Resultate Im genannten Zeitraum erhielten 256 Pat. eine ungeschützte Hauptstammintervention (Alter 71,0 ± 10,4 Jahre, 30,9 % weiblich, 47 [18,4 %] nicht-insulinpflichtige, 11 [4,3 %] insulinpflichtige Diabetiker), die sich auf die 4 Gruppen wie folgt aufteilten: 1 = 138 Pat., 2 = 60 Pat., 3 = 32 Pat., 4 = 26 Pat. Während einer medianen Follow-up-Zeit von 4,1 Jahren (IQR: 2,0–7,0, Spannweite: 0–12) unterschieden sich die Kaplan-Meier-Kurven für Tod jedweder Genese signifikant (p < 0,001), wobei Pat. aus Gruppe 1 ein besseres Überleben aufwiesen als die der Gruppe 3, und jene wiederum ein besseres Überleben als die der Gruppen 2 und 4. Von der Analyse der MACCE mussten 12 Pat. (4,7 %) ausgeschlossen werden, die am Leben, für die aber keine Follow-up-Daten erhebbar waren. Auch die Wahrscheinlichkeit für das Auftreten von MACCE unterschied sich signifikant zwischen den Gruppen (p = 0,006), wobei die Inzidenz in der Reihenfolge von Gruppe 1 zu 3 und nochmals zu 2 und 4 zunahm. In einem CPH-Modell zeigte sich entsprechend der zunehmenden Risikokonstellation (von Gruppe 1 zu 3, 3 zu 2 und 2 zu 4) ein zunehmendes Risiko der Entwicklung von MACCE (HR 1,29; 95-%-CI: 1,08–1,53, p = 0,004).

Diskussion Eingeschränkte Linksventrikelfunktion und das Vorliegen eines Diabetes mellitus waren in unserer Kohorte von Patienten mit ungeschützter Hauptstammrevaskularisation mit einer erhöhten Mortalität sowie dem vermehrten Auftreten von MACCE assoziiert.

Leadless Cardiac Pacing after Lead Extraction in Patients with Severe Device Infection

H. Blessberger[1], A. Kypta[1], J. Kammler[1], D. Hrncic[1], T. Lambert[1], A. Nahler[1], S. Schwarz[1], S. Hönig[1], K. Saleh[1], D. Kiblböck[1], J. Kellermair[1], M. Lichtenauer[2], C. Steinwender[1]

[1]Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz; [2]Abteilung für Kardiologie, Klinik Innere Medizin II, Paracelsus Universität Salzburg

Background Conventional pacemaker therapy is limited by short- and long-term complications, most notably device infection. Explantation of a pacemaker system and further management may be especially challenging in patients who are fully pacemaker dependent. Temporary pacemaker leads bear the risk of infection themselves, whereas epicardial lead placement requires chest surgery in these high risk patients. Leadless cardiac pacemakers (LCPs) may be beneficial in such cases as they eliminate the need for a device pocket and leads and thus may reduce the risk of re-infection.

Material and Methods We assessed a novel procedure in five patients with severe device infection who were pacemaker dependent. In a first step, leads were extracted using a mechanical rotation sheath as well as a lead locking device. Then, a single chamber LCP (Medtronic Micra®) was implanted into the right ventricle via a femoral vein access. We used a temporary pacemaker for bridging between step one and two in the first four patients. In the fifth patient the two steps were reversed eliminating the need for a temporary pacemaker. A follow-up PET scan of the heart and device pocket was performed 3 months after LCP implantation to detect ongoing or de-novo device infection in all patients.

Results Five patients underwent system removals with lead extraction due to severe device infection at our institution between September and December 2015. Patients were between 56 and 88 years old, only one of them being female. All removed systems were single chamber pacemakers (VVI-R). Three were diagnosed with a pocket infection only, whereas the other two showed signs of both pocket and lead infection. The infected pacemaker systems had been implanted 8.0 ± 4.3 years before removal on average. Successful lead extraction and LCP implantation could be accomplished in all patients. Mean procedure time for lead extraction and system removal was 41 ± 15 minutes, while the mean time for LCP implantation was 35 ± 12 minutes. The first four patients were bridged with a temporary pacemaker between two hours and three days after lead extraction. All patients stayed free of infection during the follow-up period of 151 ± 42 days. PET CT confirmed absence of ongoing or de-novo infection 3 months after the procedure in all patients.

Discussion Leadless cardiac pacemaker implantation was safe and feasible in our five patients. It may be an option for patients with se-

vere device infection, especially in those with blocked venous access paths and those who are pacemaker dependent. Direct implantation into the right heart chamber without any leads or a device pocket may reduce the risk of re-infection. Three months after lead extraction and LCP implantation our cohort of five patients stayed free from infection as confirmed by PET-CT.

Erfahrung und Langzeitergebnisse nach 100 Micra®-Implantationen

H. Blessberger, A. Kypta, J. Kammler, D. Hrncic, T. Lambert, A. Nahler, S. Schwarz, C. Reiter, S. Hönig, K. Saleh, D. Kiblböck, J. Kellermair, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Hintergrund Patienten mit einer Indikation zur VVI-Schrittmacherimplantation (v. a. aufgrund höhergradiger AV-Blockierungen bei Vorhofflimmern oder eines Sick-Sinus-Syndroms) können neuerdings auch mit einem sondenlosen Schrittmachersystem versorgt werden. Im Gegensatz zu einem konventionellen System bietet der sondenlose Schrittmacher den potenziellen Vorteil einer geringeren Inzidenz von Schrittmacher-assoziierten Komplikationen. Diese können bei konventionellen Systemen in einem Zeitraum von 5 Jahren nach Implantation bis zu 20 % betragen und umfassen unter anderem Sondenbrüche, Sondendysfunktionen, Taschеninfektionen oder Sondeninfektionen mit Endokarditis. Durch transfemorale Implantation fallen auch Implantations-assoziierte Komplikationen wie Pneumothorax, Hämatothorax oder Taschenhämatome weg. Allerdings birgt die femorale Implantation auch eigene Risken wie Wundinfektionen oder Leistenhämatome. Ziel unserer Erhebung war es, die Daten unseres Zentrums nach den ersten 100 Implantationen zu evaluieren.

Methoden Es wurden alle Patienten erfasst, die an unserem Zentrum einen sondenlosen Schrittmacher seit der ersten Implantation weltweit im Dezember 2013 erhalten haben. Alle Micra®-Schrittmacher wurden transfemoral in Sedoanalgesie von 2 erfahrenen interventionellen Kardiologen implantiert. Der Wundverschluss in der Leiste erfolgte mittels Tabaksbeutelnaht. Geräteparameter und Komplikationen wurden bei der Implantation sowie im Verlauf des ersten Jahres nach Implantation (3- und 12-Monats-Kontrolle) erhoben.

Resultate Zwischen Dezember 2013 und Juni 2016 wurden 100 sondenlose Schrittmacher an unserem Zentrum implantiert (Alter 80,1 ± 7,1 Jahre, 56 % männlich, 77 % wegen höhergradiger AV-Blockierungen, 6 % bei Linksschenkelblock und AV-Block I nach transfemoralem Aortenklappenersatz, 17 % bei Sick-Sinus-Syndrom). Bei 5 Patienten wurde der Micra® nach einer Infektion eines konventionellen Schrittmachersystems eingebaut. Lediglich eine Implantation musste aufgrund eines Perikardergusses abgebrochen werden. Sonst traten keine periinterventionellen Komplikationen auf. Die durchschnittliche OP-Zeit betrug 39 ± 17 min. mit einer Durchleuchtungszeit von 7 ± 5 min. Für 78 Patienten war ein 3-Monats-Follow-up bzw. für 51 ein 12-Monats-Follow-up verfügbar. Während des Beobachtungszeitraums verstarben 10 Patienten (Todesursachen: 7× dekompensierte Herzinsuffizienz, 1× Malignom, 1× akutes Nierenversagen, 1× akuter Myokardinfarkt). Es traten keine Schrittmacher-assoziierten Fehlfunktionen auf. Im Laufe des Follow-up kam es zu einem signifikanten Anstieg des R-Wellen-Sensings sowie zu einer signifikanten Abnahme von Impedanz und Reizschwelle (Sensing: 10,4 ± 4,5 mV auf 15,8 ± 4,5 mV nach 12 Monaten, p = 0,0001, Reizschwelle: 0,59 ± 0,83 V auf 0,54 ± 0,23 V nach 12 Monaten, p = 0,006, Impedanz: 678 ± 178 Ω auf 588 ± 98 Ω nach 12 Monaten, p < 0,00001).

Diskussion In der alltäglichen klinischen Anwendung erwies sich der sondenlose Schrittmacher als effektiv und sicher mit einer niedrigen Rate an Komplikationen. Bisher konnte kein infiziertes sondenloses Schrittmachersystem beobachtet werden.

Is there a Difference in Outcome in Patients Undergoing Ablation of Paroxysmal Atrial Fibrillation as 1st- vs 2nd-Line Treatment?

J. Ebner, M. Manninger, D. Zweiker, B. Mastnak, E. Bisping, P. Lercher, R. Riedlbauer, B. Rotman, H. Brussee, D. Scherr
Division of Cardiology, Medical University of Graz

Background Catheter ablation of atrial fibrillation (AF) is an established 2nd-line therapy (after failed antiarrhythmic drug treatment) for patients with symptomatic paroxysmal AF. According to the latest ESC guidelines, AF ablation may be considered in highly symptomatic, low-risk patients as a 1st-line therapy option.

The fact that AF is steadily progressing over time indicates, that patients who receive catheter ablation as a consequence of failed antiarrhythmic drug treatment (and therefore at a later time point) might be potentially sicker compared to the 1st-line therapy collective, which could result in a worse outcome of catheter ablation in the 2nd-line therapy group.

Our study investigated whether an earlier ablation approach may result in improved sinus rhythm maintenance after ablation.

Objectives To test whether there is a difference between the outcome of AF ablation as a 1st- and a 2nd-line therapy in patients with paroxysmal AF.

Methods A total of 113 patients with paroxysmal AF were included in the study (age 53 ± 12; 24% female) and were split up into a 1st- and a 2nd-line ablation group. Success was defined as the absence of documented episodes of AF lasting > 30 seconds during the follow-up time by means of serial ECG and Holter monitoring at 3, 6 and 12 months and at 6 months intervals thereafter. Statistical analysis was performed for single and multiple procedural successes.

Results Overall, 122 AF ablation procedures were performed in these 113 AF patients (1.1 ± 0.4/patient). 54 patients received 1st-line AF ablation and 59 patients underwent 2nd-line AF ablation after a failed trial of antiarrhythmic drugs. There was no difference in baseline characteristics such as age, gender, structural heart disease, AF duration, LA size, or LVEF between groups. The median follow up time was 321 (91; 1042) days in the 1st-line group vs. 318 (93; 842) days in the 2nd-line group (p = n. s).

There was no significant difference in arrhythmia-free survival between those patients who received AF ablation as a 1st- or those who received AF ablation as a 2nd-line therapy both in single procedure outcome and in multiple procedure outcome (success rate with antiarrhythmic drugs 82% in the 1st-line group vs. 81% in the 2nd-line ablation group; Log rank test p = 0,75; success rate off antiarrhythmic drugs 64% in the 1st-line group vs. 55% in the 2nd-line ablation group; Log rank test p = 0.97).

Summary/Conclusion Success of AF ablation does not seem to differ between patients who receive AF ablation as a 1st-line therapy and patients who receive AF ablation as a 2nd-line therapy. Based on these data, a trial of antiarrhythmic drug therapy before AF ablation may be justified in the majority of patients with symptomatic paroxysmal AF eligible for rhythm control.

Thrombektomie ohne Bridging-Lyse: Eine retrospektive Analyse aus dem Thrombektomie-Netzwerk Oberösterreich 2011–2014 bei Patienten mit Kontraindikation für i.v. tPA-Behandlung

H.-P. Haring[1], M. Baumgartinger[1], J. Trenkler[2], K. Nußbaumer[2], M. Sonnberger[2], D. Csillag[2], M. S. Stockinger[1], T. von Oertzen[1]
[1]Neurologische und [2]Radiologische Abteilung, Neuromed Campus, Kepler Universitätsklinikum Linz

Hintergrund Routinemäßig wird derzeit die Thrombektomie (TE) nach vorausgegangener i.v. Gewebe-Plasminogenaktivator- (tPA-) Behandlung durchgeführt. Unklar ist, ob eine alleinige TE gleich effizient und sicher ist.

Fragestellung Unterscheiden sich Sicherheit und Outcome bei Patienten mit alleiniger TE im Vergleich zu einer kombinierten tPA -und TE-Behandlung?

Methoden Retrospektive Analyse aus dem TE-Netzwerk OÖ. Zwischen 2011 und2014 wurden 289 Patienten thrombektomiert und in 2 Kohorten gegliedert:
Kohorte TE+ = TE mit tPA (n = 220; 76,1 %)
Kohorte TE– = TE ohne tPA (n = 69; 23,9 %)

Statistik Chi-Quadrat-Test und T-Test

Erhobene Parameter

– Klinisches Outcome
  • mRS (mod. Rankin-Skala) bei Aufnahme, Entlassung, 3 Monate
  • NIHSS („National Institute of Health Stroke Scale“) bei Aufnahme, Entlassung
– Radiologisches Outcome
  • TICI- („thrombolysis in cerebral infarction“-) Score
– Sicherheits-Outcome
  • Intrazerebrale Blutung (ICH) bei Entlassung, extrakranielle Blutung, Gefäßverletzungen der Leiste, Gefäßdissektion

Ergebnisse

Tabelle 1: H.-P. Haring et al. Studienpopulation

	Alter	NIHSS median bei Onset
alle	69,2	17
TE–	68,7	15
TE+	69,6	17

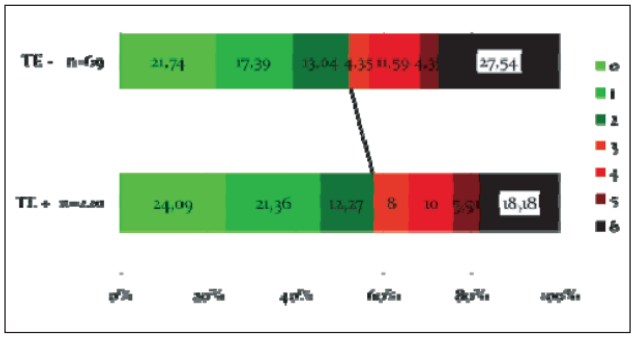

Abbildung 1: H.-P. Haring et al. Klinisches Outcome. (Shiftanalyse mRS nach 3 Monaten; statistisch nicht signifikant)

Tabelle 2: H.-P. Haring et al. Radiologisches Outcome

TICI 2b–3	%
alle	87,1
TE–	83,1
TE+	88,1

Tabelle 3: H.-P. Haring et al. Sicherheits-Outcome

Komplikation %	ICH	Bltg. extrakraniell	Gefäßverletzung Leiste	Dissektion
TE–	14,5	4,4	1,5	2,9
TE+	12,7	6,4	1,4	3,2

ICH: intrazerebrale Blutung

Schlussfolgerungen Zwischen den beiden Studienkohorten TE+ und TE– ergab sich kein signifikanter Unterschied in Bezug auf Sicherheit und Outcome. Eine tendenziell höhere Mortalität und geringere Rekanalisation in der TE-Gruppe erreichte kein statistisches Signifikanzniveau, wobei die Fallzahl berücksichtigt werden muss. In unserer Kohorte war für Patienten mit Kontraindikation zur Thrombolyse die alleinige Thrombektomie eine gleichwertige Therapieoption.

Todesursachenanalyse von Patienten nach interventioneller ungeschützter Hauptstamminterventionen – ein retrospektives Langzeit-Follow-up

D. Hrncic, H. Blessberger, J. Kammler, S. Schwarz, J. Starnawski, A. Kypta, T. Lambert, A. Nahler, C. Reiter, D. Kiblböck, K. Kerschner, M. Grund, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Hintergrund Gerade bei älteren Patienten mit einer Haupstammstenose ist eine interventionelle Sanierung aufgrund meist zahlreicher Komorbiditäten und folglich erhöhtem perioperativen Risiko attraktiv. Das wird auch von den aktuellen Guidelines befürwortet. Wir evaluierten, ob alle Patienten, unabhängig vom Lebensalter, in gleicher Weise von diesem Eingriff profitieren und an welchen Erkrankungen die Patienten letztendlich versterben.

Methoden Daten aus dem UNPROtected LEft MAin- (UNPROLEMA-) Register des Kepler Universitätsklinikums von Patienten, die sich zwischen 11/2002 und 12/2013 einer ungeschützten Hauptstamintervention unterzogen haben, wurden analysiert.

Die Follow-up-Daten wurden mittels Durchsicht der verfügbaren Krankengeschichten, eines strukturierten Telefoninterviews sowie mittels Anfragen beim Meldeamt erhoben. Die Gesamtsterblichkeit und das Auftreten von Major Adverse Cardiac and Cerebrovascular Events (MACCE) wurde mittels Kaplan-Meier-Analysen – stratifiziert für die Altersquartilen – evaluiert. Als MACCE wurden folgende Ereignisse klassifiziert: STEMI, NSTEMI, aortokoronare Bypassoperation, Re-Intervention im Zielgefäß, TIA/Insult und Tod jedweder Ursache. Der Log-rank-Test wurde zur Evaluierung eines statistisch signifikanten Unterschiedes herangezogen. Die Todesfälle wurden nach Ursachen aufgeschlüsselt.

Resultate Von den 256 untersuchten Patienten mit ungeschützten Hauptstamminterventionen verstarben insgesamt 89 (34,8 %) im Beobachtungszeitraum von bis zu 10 Jahren.

Das mittlere Alter war bei 71,0 ± 10,4 Jahre (Altersquartilen: Q1 bis 63,1, Q2 bis 73,3 Jahre, Q3 bis 79,0 und Q4 > 79,0 Jahre). Die Kaplan-Meier-Überlebensanalyse zeigte einen signifikanten Anstieg der Mortalität mit steigender Altersquartile ($p < 0{,}001$).

Von den 256 Patienten konnten 12 Patienten nicht nachverfolgt werden, wobei anhand der Meldeamtsanfragen erhebbar war, dass diese nicht verstorben waren. Diese wurden von der Analyse der MACCE-Daten ausgeschlossen.

Von den verbliebenen 244 Patienten betrug die mediane Follow-up-Zeit 4,1 Jahre (IQR: 2,0–7,0; Spannweite 0–2). Die Kaplan-Meier-Analyse konnte einen statistisch signifikanten Anstieg der MACCE-Rate mit steigender Altersquartile zeigen ($p = 0{,}005$). In einem multivariaten Cox-Regressionsmodell zeigte sich nach Adjustierung für potentielle Confounder wie linksventrikuläre Auswurffraktion, Diabetes mellitus und glomeruläre Filtrationsrate eine Hazard-Ratio von 1,3 für das Auftreten von MACCE pro Anstieg einer Altersquartile (95-%-CI: 1,06–1,65; $p = 0{,}014$).

Die Auswertung der Todesursachen ergab, dass 56 Patienten (62,9 %) an kardialer Erkrankungen verstorben sind und 33 (37,1 %) der Patienten an nicht-kardialen Ursachen. Sechs Patienten verstarben an einer malignen Erkrankung (6,7 %), 4 an neurologischen Ursachen (4,5 %), 8 im Rahmen einer Infektion (9,0 %), 4 an einem Trauma (4,5 %) und 11 an anderen oder unbekannten Ursachen (12 %). Von den 7 Patienten (2,7 %), die im Rahmen des Indexaufenthaltes verstarben, erfolgte bei 3 die Hauptstammrevaskularisation aufgrund eines STEMIs (einmal in kardiogenen Schock), ein Patient verstarb an einer dekompensierten Herzinsuffizienz und 3 an einer Stentthrombose.

Diskussion MACCE-Raten und Mortalitätsrisiko nach ungeschützter Hauptstammintervention steigen in Abhängigkeit vom Alter des Patienten trotz niedriger intraprozeduraler Mortalität an. Etwa 2/3 aller Patienten verstarben nach Hauptstammintervention an kardialen Ursachen.

Diastolic Retrograde Flow in the Descending Aorta by Cardiovascular Magnetic Resonance Imaging for the Quantification of Aortic Regurgitation

A. A. Kammerlander, M. Wiesinger, F. Duca, S. Aschauer, C. Zotter-Tufaro, M. L. Schwaiger, R. Badre-Eslam, B. A. Marzluf, P. E. Bartko, D. Bonderman, J. Mascherbauer
Abteilung für Kardiologie, Universitätsklinik für Innere Medizin II, Medizinische Universität Wien

Background Echocardiography is the standard method for quantification of aortic regurgitation (AR). However, accurate estimation of the severity of AR by echo may be challenging due to inherent limitations of applied methods. Cardiovascular magnetic resonance imaging (CMR) has recently been advertised as an accurate method for AR quantification, irrespective of acoustic windows.

The present prospective study sought to evaluate the usefulness of CMR for the quantification of AR.

Methods and Results 206 consecutive patients (30% female, 55 ± 21 years old) with varying degrees of AR by echocardiography (83 mild, 52 moderate, and 35 severe, 36 with inconclusive echocardiographic results – "moderate to severe" AR) were invited to undergo CMR within 4 weeks. CMR consisted of standard protocols including phase-contrast velocity-encoded imaging for measurement of regurgitant volume (RegV), and regurgitant fraction (RegF) at the sinutubular junction, and assessment of holodiastolic retrograde flow (HRF) in the descending aorta.

Severe AR was defined as the presence of HRF in the descending aorta by CMR.

Left ventricular (LV) volumes by CMR significantly increased with increasing AR severity by echo (LV end-diastolic volume/body surface area: mild: 77 ± 24 ml/m^2, moderate: 96 ± 28 ml/m^2, "moderate to severe": 106 ± 43 ml/m^2, severe: 124 ± 34 ml/m^2; $p < 0.001$), as did RegV (mild: 6 ± 15 ml, moderate: 15 ± 17 ml, "moderate to severe": 23 ± 20 ml, severe: 48 ± 27 ml; $p < 0.001$) and RegF at the sinutubular junction (mild: 7 ± 15%, moderate: 14 ± 15%, "moderate to severe": 22 ± 17%, severe: 35 ± 15%; $p < 0.001$).

Among the 135 patients with non-severe AR by echo, 11 (8%) had HRF by CMR, indicating severe AR.

Among the 35 patients with severe AR by echo, 12 (34%) did not show HRF by CMR, suggesting overestimation of AR severity in these patients.

In patients with inconclusive echo results, 42% had HRF in the descending aorta, indicative for severe AR.

Presence of HRF by CMR was associated with significantly higher RegF at the sinutubular junction (10 ± 12% vs 37 ± 19%, $p < 0.001$) and more dilated LVs (86 ± 28ml/m^2 vs 124 ± 41ml/m^2; $p < 0.001$).

Conclusion Quantification of AR by CMR is feasible and highly reproducible. HRF in the descending aorta by CMR is an easy marker that helps to distinguish between severe and non-severe AR.

Echocardiographical Coronary Flow Reserve Measurement (CFR) in acute (Peri-) Myocarditis

J. Kellermair, D. Kiblboeck, J. Kammler, S. Schwarz, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Background In the present pilot study we aimed to evaluate echocardiographical CFR in a small group of patients with diagnosis of acute (peri-) myocarditis, which has not been described in literature before. We assumed that CFR is reduced in the setting of acute (peri-) myocarditis (due to inflammatory mediated endothelial cell dysfunction) and will return to normal values after complete recovery after 3 months. CFR is defined as the ratio between peak diastolic coronary blood flow corresponding to flow autoregulation plateau at rest (PDV1) and peak diastolic coronary blood flow after maximal vasodilatation with adenosine (PDV2) with normal values ranging from PDV2/PDV1 > 2.

Methods In patients with acute (peri-) myocarditis (n = 3) CFR was assessed at baseline and at 3 months follow-up. CFR was echocardiographically assessed by color-doppler-guided (color doppler velocity 10–30 cm/s; color frame rate: 20–40) pulsed-wave doppler (PW-doppler; sample volume 15 mm) of the mid to distal segment of the left anterior descending artery (LAD). At rest, peak diastolic velocity (PDV1) was measured. Hyperemic coronary flow was triggered by infusion of adenosine (140 µg/kg/min) and PDV2 was measured during hyperemia.

Results At baseline CFR was reduced (mean PDV2/PDV1 = 1,4) compared to follow-up CFR (mean PDV2/PDV1 = 2,6). The difference was driven by a lack of adenosine-induced vasodilatation at baseline (mean PDV2 baseline = 0,6m/s vs. mean PDV2 follow-up = 1,9 m/s). The finding indicates a reduced coronary vasodilatator capacity at baseline due to inflammatory affection of the coronary microvasculature.

Conclusion CFR is reduced in the acute setting of (peri-) myocarditis and recovers after 3 months. CFR should be evaluated in higher sample size studies.

Unrepaired Tetralogy of Fallot with Major Aorto-pulmonary Collateral Arteries Arising from a Left Brachiocephalic Trunk in a 52 year old Female

J. Kellermair, B. Wichert-Schmitt, K. Akbari, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Background Severe unrepaired congenital heart defects in adults are rare in countries with developed pediatric health systems. However, this medical topic has become of growing interest as the number of refugees is raising worldwide.

Case Report A 52 year-old-female refugee (who had given birth to 3 children) presented with mild dyspnoea, cyanotic lips and an arterial oxygen saturation of 82%. Her past medical history was only significant for a syncope without prodromal symptoms a few years ago. Laboratory results were normal except an elevated NT-proBNP level of 4151 pg/mL.

Transthoracic echocardiography showed a perimembranous ventricular septum defect (VSD), an overrinding aorta, right-sided aortic arch, right ventricular (RV) hypertrophy and pulmonary atresia (PA).

Cardiac magnetic resonance angiography (A/B) and computed tomography (C/D) confirmed the diagnosis of PA with VSD and showed an isolated vascular structure with a diameter of 21 mm arising from a left-sided brachiocephalic trunk (BCT) supplying blood to the complete left lung as well as the right lower and right upper pulmonary lobe through a complex vascular collateral network (G). Analysis of a 3D printed cardiac model (E/F; printer: ZPrinter 650,3D Systems, Rock Hill, USA; software: Mimics 19.0, Materialise, Leuven, Belgium) contributed to identify the correct anatomy of the pulmonary circulation: The middle lobe of the right lung showed retrograde blood supply by the left pulmonary artery (via confluent right pulmonary artery). The left pulmonary artery received the blood from a peripheral left-sided collateral artery that did not feature anatomical characteristics of a persistant ductus arteriosus (PDA). The arterial network showed dilatations and calcifications as signs of pulmonary vascular remodeling.

Conclusion In this palliative situation the patient was scheduled for frequent follow-up at our outpatient clinic without any drug treatment.

Endothelial and Platelet derived Microparticles in Patients undergoing Transcatheter Aortic Valve Implantation (TAVI)

M. Lichtenauer[1], C. Jung[2], H.-R. Figulla[3], B. Wernly[1], S. Eder[1], C. Edlinger[1], C. Reiter[4], B. Goebel[3], M. Förster[3], U. C. Hoppe[1], A. Lauten[5]
[1]Universitätsklinik für Innere Medizin II, Kardiologie und internistische Intensivmedizin, Paracelsus Medizinische Universität Salzburg, Österreich; [2]Abteilung für Kardiologie, Pneumologie & Angiologie, Universitätsklinikum Düsseldorf; [3]Abteilung für Kardiologie, Klinik für Innere Medizin I, Universitätsherzzentrum Thüringen, Friedrich-Schiller-Universität Jena, Deutschland; [4]Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz, Österreich; [5]Medizinische Klinik für Kardiologie, Charité Centrum Herz-, Kreislauf- und Gefäßmedizin, Berlin, Deutschland

Introduction Degenerative severe aortic stenosis (AS) is the most frequent form of acquired valvular heart disease worldwide. AS is known to entail endothelial dysfunction caused by increased mechanical shear stress leading to elevated circulatory levels of microparticles. Endothelial and platelet microparticles (EMP and PMP) are small vesicles that originate from activated cells and thrombocytes. The hypothesis of our study was to evaluate whether transcatheter aortic valve implantation (TAVI) procedure would elicit beneficial effects on endothelial function by reducing circulating EMP and PMP.

Materials and Methods 92 patients undergoing TAVI procedure for severe AS were included in this study. Samples were obtained at each visit before TAVI and after 1 week, 1, 3 and after 6 months. The collected samples were stained with antibodies against CD31, CD42b, CD62E and Annexin in order to analyze circulatory levels of CD31+/Annexin+, CD31+/Annexin-, microparticles using flow cytometry.

Results Clinical and functional results after TAVI procedure were good as shown by significantly reduced V_{max}, MPG and PPG ($p < 0.001$). Also a slight improvement in ejection fraction was documented during follow-up, from 55.9% (± 18.4 SD) before TAVI to 62.6% (± 14.3 SD) after 6 months ($p < 0.01$).

CD62E+ EMP concentration before TAVI was 21.11% (± 6.6% SD) and declined to 20.99% (± 6.8% SD) after 1 week, to 16.63 (± 5.4% SD, $p < 0.0001$) after 1 month, to 17.08% (± 4.6% SD, $p < 0.0001$) after 3 months and to 15.94% (± 5.4% SD, $p < 0.0001$) after 6 months (Fig. 2). CD31+/CD42b-, CD31+/Annexin+/-EMP remained unchanged.

Furthermore, pre TAVI levels of CD31+CD42b- and CD31+ Annexin-correlated with maximum velocity (0.258 and 0.245, $p < 0.05$), mean pressure gradient (0.301 and 0.288; $p < 0.01$) and peak pressure gradient (0.230 and 0.219; $p < 0.05$). CD62E+ EMP and CD31+CD42b+ PMP correlated with EF (0.228 and 0.248; $p < 0.05$).

Conclusions Apart from a procedure related improvement in echocardiographic parameters, TAVI procedure also led to amelioration in endothelial dysfunction as shown by a decline in CD62E+ EMP. The reduction in transvalvular pressure gradients with less hemodynamic shear stress seems also to have beneficially affected endothelial homeostasis.

As the shedding of microparticles is also associated with systemic inflammation and endothelial activation, a vicious circle of hemodynamic shear stress and endothelial dysfunction is present in the pathophysiological setting of AS. It was shown that inflammation might play a fundamental part in the progression of degenerative AS and microparticles also seem to play a role as signaling factors within the vascular compartment mediating inflammation, angiogenesis and coagulation. As levels of CD62E+ EMP were significantly reduced during follow-up, one could argue that one factor for the progression of vascular dysfunction was taken out of the equation, thusly leading to an improvement in endothelial function.

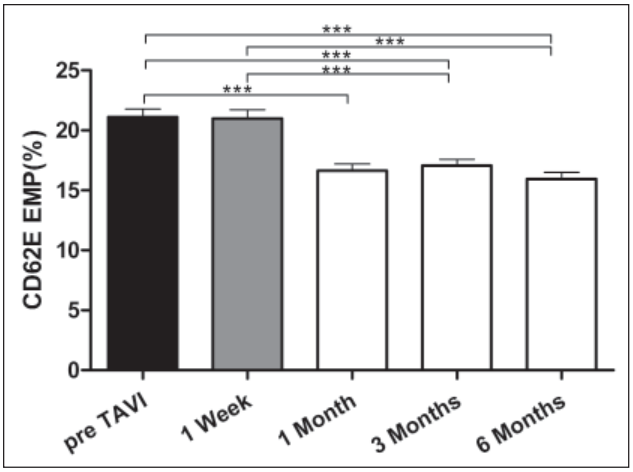

Figure 2. M. Lichtenauer et al.

Case Report of a Clopidogrel-Resistant Patient with Giant Thrombotic Saphenous Vein Graft Bypass Aneurysms

C. Reiter, B. Wichert-Schmitt, J. Kammler, T. Lambert, H. Blessberger, D. Kiblböck, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Case Report A 65-year-old multimorbid patient was referred to our department due to an incidental finding of two aneurysmatic saphenous vein coronary artery bypass grafts (SVG). At the age of 39, he had undergone surgery with a LIMA-to-LAD- as well as a SVG-to-RCA- and SVG-to-LCX-bypass due to acute myocardial infarction. At the age of 58, after percutaneous coronary intervention of a 90% stenosis of the SVG-to-LCX-bypass he was put on clopidogrel and aspirin. However, he autonomously stopped his aspirin intake.

Upon admission, the patient was widely symptom free. A cardiac CT scan revealed total obliteration of the SVG-to-LCX-bypass with a thrombosed aneurysm up to a diameter of 6.6 cm as well as a massively degenerated SVG-to-RCA-bypass with a thrombosed aneurysm up to a diameter of 2.8 cm. Both aneurysms did not compress any relevant structures.

Coronary angiography confirmed complete obstruction of the SVG-to-LCX-bypass and reduced blood flow (TIMI II) in the SVG-to-RCA-bypass, whist showing good collateralization. Due to the reasons stated in the discussion, we opted for a conservative approach. However, we recommended another cardiac CT scan in 6 months to rule out further progression.

Interestingly, after several days of controlled intake of clopidogrel, a VerifyNow-P2Y12-assay revealed a platelet inhibition rate of 0%. Since the patient strictly refused intake of aspirin, we decided switching to prasugrel. Subsequent reevaluation confirmed adequate response with a rate of 71%.

Discussion We opted for a conservative approach, due to the lack of symptoms and the high surgical risk based on the patient's multimorbidity. Considering the total obliteration of the SVG-to-LCX-bypass aneurysm and the subtotal obliteration of the SVG-to-RCA-bypass aneurysm with reduced blood flow, we estimated the risk of rupture to be low. In addition, due to good collateralization, we did not calculate a relevant extent of myocardial infarction in consequence of a potential total obliteration of the described bypass graft.

Considering that our patient was diagnosed with clopidogrel resistance, earlier evaluation of platelet inhibition might have prevented stent thrombosis. High prevalence of hyporesponsiveness to antiplatelet therapy has been demonstrated, especially when using clopidogrel, and adequate response can be achieved by an increased aspirin dose and/or changing to prasugrel of ticagrelor. Accordingly switch of antiplatelet agents did lead to adequate platelet inhibition in our patient. Therefore, a tailored approach might be a potential suitable option to improve the clinical outcome.

Proposal for a Novel Definition of "Ideal Response" to Renal Denervation and Analysis of the Optimal Length of Follow-Up

C. Reiter, T. Lambert, A. Nahler, C. Sautner, M. Grund, V. Gammer, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Introduction Renal denervation (RDN) has shown to be an effective treatment option for patients suffering from resistant arterial hypertension in numerous unblinded clinical trials. However, as the randomized sham-controlled Symplicity HTN-3 trial had failed to achieve its primary efficacy endpoint, studies like the Spyral HTN Global Clinical Trial were designed to address possible confounding factors like drug changes and adherence as well as patient population and procedural variability.

In this regard, the definition of response to treatment is crucial for the evaluation of the effect of RDN. In previous clinical trials, adequate response was defined as a reduction of the mean systolic ambulatory blood pressure of more than 5 mmHg at merely a single follow-up point after 6 months.

As it was observed that patients fulfilling these criteria showed increased blood pressure levels at other time points of follow-up, this approach may not reflect sustained blood pressure reduction. Therefore, we redefined the criteria for ideal respondership and tried to evaluate the optimal duration of follow-up after RDN.

Materials and Methods Patients with resistant hypertension, which was defined as a mean systolic office BP > 160 mmHg after 3 measurements, were treated with RDN.

All patients had to be on at least three antihypertensive drugs including one diuretic and secondary causes of hypertension were ruled out prior to the procedure.

For RDN, the Symplicity Flex™-RDN Catheter (Medtronic Inc.) was used. Depending on renal artery anatomy, a maximum of 10 ablations were performed in each renal artery. The individual blood pressure course after RDN was monitored by scheduled follow-up visits after 3, 6, 12 and 24 months. At all visits including baseline, ambulatory blood pressure measurement (ABPM) was performed.

According to the assumption that an ideal responder should have lowered blood pressure levels at every visit after RDN, ideal response was defined as a sustained reduction of the mean systolic blood pressure of at least 1 mmHg at each follow-up-visit compared to baseline levels. The number of patients fulfilling this definition was obtained by analyzation of their individual blood pressure course in order to evaluate the rate of sustained blood pressure reduction as well as to assess the optimal duration of follow-up necessary for the proposed novel definition of ideal respondership.

Results We investigated the effects of RDN on blood pressure levels in 42 patients suffering from resistant hypertension. 11 of these patients were excluded after baseline ABPM had revealed pseudo-resistance with a mean systolic blood pressure < 130 mmHg. By consideration of the proposed novel definition of "ideal response", 12 of 31 patients (38.7%) could be classified as ideal responders after 24 months. In this collective, there was a significant mean systolic blood pressure reduction at all follow-up points (3M: –21.4 mmHg, $p < 0.01$; 6M: –15.8 mmHg; $p < 0.01$; 12M: –19.9 mmHg; $p < 0{,}01$; 24M: –22.8 mmHg; $p < 0.01$). Of the 13 patients that could be classified as ideal responders after 12 months, 12 patients (92.3%) fulfilled the criteria with a sustained blood pressure reduction after 24 months.

Discussion As more than 90% of all patients undergoing RDN that met the definition of "ideal response" after 12 months were also ideal responders after 24 months, a follow-up period of 12 months seems to be adequate to confirm sustained blood pressure reduction.

Subcutaneous Absorbable Double Purse-String Suture for Femoral Vein Access Site Closure in Leadless Cardiac Pacemaker Implantation

S. Schwarz, A. Kypta, K. Saleh, H. Blessberger, J. Kammler, S. Hönig, T. Lambert, J. Kellermair, D. Kiblböck, C. Reiter, A. Nahler, C. Steinwender
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Background Leadless cardiac pacemakers (LCP) require large-caliber venous introducer sheaths for device placement. The sheath size of the Micra™ Transcatheter Pacing System (Medtronic Inc., Minneapolis, MN, USA) is 23 French (F) inner diameter and 27 F outer diameter. Common access site complications are hematomas, pseudoaneurysms and arterio-venous fistulas. Complete and secure closure of the venous access is an important step at the end of the procedure.

Methods After venous puncture and skin incision, two subcutaneous purse-string sutures were prepared for groin closure, using Novosyn® 3.0 (B. Braun Melsungen AG, Melsungen, Germany), a medium-term absorbable suture consisting of Polyglactin 910. Groin complications were evaluated during hospital stay, after 4 weeks and 3 months.

Results Between December 2013 and February 2016, 83 patients received a LCP. In 29 (34.9%) patients an unfractionated heparin bolus (UFH 4362 ± 1109 units) was given at the beginning of the procedure. 23 (27.7%) patients were on phenprocoumon in therapeutic range (INR 2.14 ± 0.41) and 10 (12%) patients on phenprocoumon not in therapeutic range (INR 1.84 ± 0.32). Access site complications occurred in 3 (3.6%) patients, 2 (2.4%) groin hematomas and one (1.2%) arterio-venous fistula. After 4 weeks, both hematomas resolved spontaneously and the fistula was not detectable by ultrasound anymore.

Conclusion Subcutaneous absorbable double purse-string suture closure is a simple, safe and cost-effective method to achieve appropriate hemostasis after removal of large-caliber venous sheaths as used in LCP implantation.

Procedure Time, Fluoroscopy Time and Deployment Rate in Leadless Cardiac Pacemaker Implantation: a 2-year Single-Centre Experience

S. Schwarz, C. Steinwender, K. Saleh, J. Kammler, H. Blessberger, T. Lambert, S. Hönig, D. Kiblböck, A. Nahler, J. Kellermair, C. Reiter, A. Kypta
Klinik für Kardiologie und Internistische Intensivmedizin, Kepler Universitätsklinikum Linz

Introduction Leadless cardiac pacemaker (LCP) implantation represents a novel technique in cardiac pacing therapy when it comes to vascular access via large-caliber venous introducer sheaths, handling with the delivery system and deployment of the pacemaker itself. Procedure and fluoroscopy time as well as the deployment rate were evaluated to specify the expected learning curve.

Methods Between December 2013 to February 2016, a Micra™ Transcatheter Pacing System (Medtronic Inc., Minneapolis, MN, USA) was implanted in 84 patients. All implantations were evenly distributed between 2 operators who were selected via assessment centre and trained on animal models prior to the start of the LCP program. Our cohort was divided chronologically into four equal groups of 21 patients to compare differences between groups over time.

Results Mean procedure time was 43.4 ± 16.1 (group 1), 35.2 ± 12.1 (group 2), 41.8 ± 22.9 (group 3) and 36.6 ± 14.8 (group 4) minutes with a mean fluoroscopy time of 8.2 ± 6.4, 6.0 ± 4.4, 7.5 ± 6.0 and 7.2 ± 4.4 minutes, respectively. Kruskal-Wallis test showed no statistical significance between groups, neither for procedure time ($p = 0.170$) nor for fluoroscopy time ($p = 0.243$). This finding also applied to the deployment rate ($p = 0.756$), though it has to be pointed out that the interprocedural fluctuation range of deployment rate was high, ranging from 1–20 attempts. Mean deployment rate in the 4 groups was 1.9 ± 1.9, 2.0 ± 1.7, 2.8 ± 4.1 and 1.9 ± 1.8.

Discussion High-level operator experience regarding handling with venous sheaths and suture techniques for groin closure as well as pre-

ceding training on animal models are considered influenceable factors. In contrast, considering our current experience, the deployment rate is an incalculable factor depending on individual anatomical conditions. A high interprocedural fluctuation range of deployment attempts can, in turn, influence procedure time and fluoroscopy time. The absence of the expected learning curve seems to have multifactorial causes. In our interpretation, a high-level operator experience plus the technical concept and practicability of the Micra™ TPS are the main contributing factors.

Effective Cerebrovascular Thrombectomy Requires Well Organized Structures – Real World Experiences of a Regional Stroke Network between 2012–2015

M. S. Stockinger[1], J. Trenkler[2], T. von Oertzen[1], K. Nussbaumer[2], M. Sonnberger[2], W. Schimetta[3], A. C. Pereira[4], G. Traxler[1], C. Dorninger[1], H.-P. Haring[1]
[1]Department of Neurology; [2]Department of Radiology, Neuromed Campus; [3]ASOKLIF, Department of Applied Systems Research and Statistics, Kepler University, Linz/Austria; [4]Department of Neurology, St. George's University Hospitals NHS Foundation Trust, London/UK

Background The objective of this study was to analyse the Neurothrombectomy Network registry of the Neuromed Campus (NMC) of the Kepler University Hospital in Linz (Austria). These data were compared to the results of recently published thrombectomy trials (MR CLEAN, ESCAPE, EXTEND-IA, SWIFT-PRIME and REVASCAT).

Patients and Methods We retrospectively studied 288 patients with acute large vessel ischemic stroke who underwent thrombectomy between January 2012 and December 2015 at the NMC in Upper Austria. The main outcome measures were modified Rankin Scale (mRS) 0–2, all-cause mortality and stroke- or thrombectomy-related mortality at discharge, as well as 90 days post discharge.

Results The median age was 70.4 years (IQR 59.9–76.7) and the median NIHSS at admission 17 (IQR 13–21). Thrombolysis in Cerebral Infarction (TICI) Scale 2b–3 Recanalization was achieved in 86.7%. 11.8% of the patients died in hospital and an additional 8.0% within 90 days after discharge. After 90 days, 55.6% had a mRS 0–2.

Conclusions These data suggest that the positive results of thrombectomy reported in several randomized controlled studies can be achieved in routine clinical practice. Therefore, the setting of an organized, regional stroke network proved an effective and appropriate method for delivering regional thrombectomy stroke treatment.

Blood Glucose Peaks are Associated with Increased both Intra-ICU and Long-Term Mortality in Non-Diabetic Patients with Myocardial Infarction

B. Wernly[1], M. Lichtenauer[1], M. Franz[2], M. Masyuk[3], J. Muessig[3], C. Reiter[4], B. Kabisch[2], U. C. Hoppe[1], H. R. Figulla[2], M. Kelm[3], C. Jung[3]
[1]Department of Cardiology, Paracelsus Private Medical University, Salzburg, Austria; [2]Department of Cardiology, University Hospital of Jena, Germany; [3]Division of Cardiology, Pulmonology, and Vascular Medicine, University Duesseldorf, Germany; [4]1st Medical Department – Cardiology, General Hospital Linz, Johannes Kepler University School of Medicine, Linz, Austria

Introduction Increased blood glucose levels at admission are associated with increased mortality in myocardial infarction patients. There is an ongoing debate whether increased glucose concentration constitutes an independent risk factor *per se* or if elevated blood glucose depicts only a severity parameter of illness. We therefore aimed to retrospectively analyze if blood glucose peaks are associated with both intra-ICU and long-term mortality.

Methods From 2006 to 2009 2034 patients (age 67.49 years +0.27 SEM; 1241 male; 271 patients suffering from type 2 diabetes [T2DM]) who were admitted because of myocardial infarction to our intensive care unit in a tertiary care hospital (University Clinic Jena) were retrospectively investigated in this study. Maximum blood glucose values were documented besides clinical and other laboratory parameters. We performed multivariate cox regression analysis to investigate long-term mortality and chi-square test to evaluate short-term mortality.

Results ROC and "area under the curve" calculation to evaluate maximum blood glucose concentration for its prognostic relevance (AUC 0.662; 95-%-CI: 0.64–0.69; $p < 0.001$) and to compare it with other tools for risk assessment like age (AUC 0.71; 95-%- CI: 0.69–0.73; $p < 0.001$) were performed. Patients with a maximum blood glucose concentration above the by means of Youden Index calculated cut-off (8.6 mmol/l) showed markedly increased intra-ICU mortality (3.4% vs 12.5%; $p < 0.01$) and long-term mortality (HR 2.82; 95-%-CI: 2.08–3.83; $p < 0.01$). Interestingly maximum blood glucose above the cut-off was associated with increased intra-ICU mortality only in patients without (3.1% vs 14.7%; $p < 0.01$) but not in patients with known T2DM (8.7% vs 5.6%; p = n. s.).

Regarding long-term mortality maximum blood glucose (alteration per unit in mmol/l) was associated with increased mortality (HR 1.1; 95-%-CI: 1.07–1.23; $p < 0.001$). After correction for age at admission, sex, occurrence of arrhythmias, cardial decompensation, sepsis, pneumonia, angina pectoris and presence of renal insuffiency and T2DM as well as maximum heart rate and maximum white blood count and highest lactate levels in a multivariate cox regression analysis (n = 1182) maximum blood glucose concentration remained predictive for mortality (HR 1.03; 95-%-CI: 1.00–1.06; p = 0.02).

Conclusion Hyperglycemic derailment is associated with increased intra-ICU and long-term mortality in patients without T2DM suffering from myocardial infarction and remained associated with increased long-term mortality after correction in a multivariate analysis. Elevated maximum blood glucose concentration was only associated with increased intra-ICU mortality in patients indicating a role of adaptation and resistance to high glucose levels in patients suffering from diabetes. We therefore conclude that hyperglycemia might constitute an independent risk factor per se in patients suffering from myocardial infarction.

Analysis of Ambient Influences Affecting Paracrine Mediators in Clinical Trials of Stem Cell Therapy for Myocardial Infarction

B. Wernly[1], C. Edlinger[1], V. Paar[1], M. Leisch[2], S. Eder[1], C. Reiter[3], U. C. Hoppe[1], M. Lichtenauer[1]
[1]Department of Cardiology, Clinic of Internal Medicine II; [2]Department of Oncology, Clinic of Internal Medicine III, Paracelsus Medical University of Salzburg; [3]1st Medical Department - Cardiology, General Hospital Linz, Johannes Kepler University School of Medicine, Linz

Background Contradictory results of large clinical trials of stem cell therapy in acute myocardial infarction (AMI) have impeded a wider clinical use. Whereas the REPAIR-AMI trial showed positive results, no relevant effects of stem cell administration were found in the ASTAMI-trial.

As signalling via paracrine factors in AMI has received more and more attention recently, we sought to compare processing protocols with special emphasis on paracrine factors such as Interleukin-8 (IL-8) and IL-6. It has also been shown that these mediators influenced angiogenesis after an ischaemic event. Many previous studies also focused on effects of IL-6 on intracellular signalling kinases being associated with ischemic conditioning and improving the cells tolerance against pro-apoptotic stimuli via STAT3, Erk1/2 and PI3K. However, only a transient peak in IL-6 or IL-8 concentrations seems to be cardioprotective in myocardial ischaemia. Chronically elevated levels lead to ongoing inflammation and fibrotic disorders and are associated with a worsened outcome.

Methods Bone marrow cells (BMC) and peripheral blood mononuclear cells were processed according to protocols used in the REPAIR-AMI and ASTAMI study. In short, mononuclear cells were obtained using density gradient centrifugation. Cells in the ASTAMI protocol were resuspended in sodium chloride solution supplemented with 20% of autologous plasma and were kept at 4, whereas in the REPAIR-AMI protocol cells were cultured in X-Vivo 10 medium supplemented with 20% serum at room temperature. IL-6 and IL-8

secretion was evaluated by ELISA. Effects of paracrine mediators on intracellular signaling factors in human cardiomyocytes were evaluated in Western Blots.

Results Supernatants of BMC processed in accordance with the REPAIR-AMI protocol evidenced higher levels of IL-6 and IL-8 (n = 9).

When incubating BMC at 37° Celsius and comparing the 2 study protocols, secretion of IL-6 and IL-8 further increased markedly (p = 0.007 and 0.03). Keeping cells at higher temperatures significantly boosted secretion of IL-6 and IL-8. Moreover, the use of autologous serum and X-Vivo medium was superior over reagents used in the protocol of the ASTAMI study (NaCl and autologous plasma). Additionally, supernatants obtained using the REPAIR-AMI protocol led to increased phosphorylation of cardioprotective signalling kinases (Akt and Erk1/2).

Conclusions External influencing factors (higher temperature, use of a modern cell culture medium supplemented with serum) led to higher concentrations of paracrine mediators. These results could provide explanation for the superior results found in the REPAIR-AMI study. Based on these experimental results, protocols for stem cell handling could be further improved in order to increase the benefit for AMI patients by defining more refined protocols.

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