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

## Kardiologie im Zentrum Fortbildung der Klinik für Kardiologie und Internistische Intensivmedizin Kepler Universitätsklinikum Linz 11.–12. Oktober 2019, Design Center Linz Abstracts

*Journal für Kardiologie - Austrian Journal of Cardiology 2019; 26 (11-12), 317-327*

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# Kardiologie im Zentrum

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

## 11.–12. Oktober 2019, Design Center Linz

## Abstracts

(in alphabetischer Reihenfolge nach Erstautoren)

Die Preisverleihung.
Foto: © Roman Kneidinger

### 1. Preis

### Incidence of Left Atrial Appendage Thrombus in Patients with Severe Aortic Stenosis

*A. Fellner, T. Lambert, C. Reiter, A. Nahler, J. Kammler, J. Kellermair, D. Hrncic, H. Blessberger, M. Grund, S. Schwarz, J. Starnawski, C. Steinwender*
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**Background** Atrial fibrillation (AF) is the most common arrhythmia in elderly patients, especially in patients with severe aortic stenosis. In the last years, transcatheter aortic valve replacement (TAVR) has become an alternative treatment option for these patients. However, AF might lead to left atrial appendage (LAA) thrombus, which is a well known risk factor for periprocedural stroke, even in case of TAVR. We aimed to investigate the incidence of thrombotic formations in the LAA in a consecutive series of patients scheduled for TAVR and a history of AF.

**Methods** Transesophageal echocardiography (TEE) was performed in all patients with severe aortic stenosis and AF prior to TAVR since June 2018. The left atrial appendage (LAA) was visualized in a mid-esophageal two chamber view using a commercially available echocardiography system (Epiq7®, Philips Health Systems, Amsterdam, The Netherlands). Absence or presence of an LAA thrombus was assessed in two orthogonal planes (xPlane function). Live 3D imaging of the LAA and echo contrast (SonoVue®, Bracco International BV, Amsterdam, The Netherlands) was used if deemed necessary. The findings were classified into three categories: 1. well circumscribed LAA thrombus, 2. spontaneous echo contrast (SEC, not well circumscribed), and 3. LAA free of thrombus or SEC. Patients with LAA thrombi or SEC were not deemed eligible for TAVR before modification of the antithrombotic medication and TEE reassessment.

**Results** From June to December 2018, 38 patients (mean age: 81.55 ± 4.57 years; 42% female) were examined. According to the 2016 ESC Guidelines for the management of atrial fibrillation, AF was classified as permanent in 26 patients (68.4%), as persistent in 5 patients (5%), and as paroxysmal in 7 patients (18.4%), respectively. All patients were on sufficient oral anticoagulation for at least 4 weeks prior to the TEE (73.7% on novel oral anticoagulants and 23.7 % on phenprocoumon; no intake interruptions and all INRs in therapeutic range, respectively). TEE revealed LAA thrombi or SEC only in patients with permanent AF. Thrombi were found in 4 patients and SEC in 5 patients, respectively (23.7% of all studied patients and 34.6% of patients with permanent AF, respectively). In patients with paroxysmal or persistent fibrillation no thrombi or SEC were found.

**Conclusion** In patients scheduled for TAVR and a history of AF, TEE revealed a high incidence of LAA thrombotic formations despite sufficient oral anticoagulation in those with permanent AF (thrombi or SEC in 9/26 patients; 34.6%). No thrombotic formations were found in patients with paroxysmal or persistent AF. These findings underscore the importance of diligent pre-procedural cardiac imaging as well as post-procedural anticoagulation management in TAVR patients with permanent AF **(Tab. 1, Fig. 1)**.

**Table 1.** A. Fellner, et al.

| | Paroxysmal AF (n = /%) 7/18,4 | Persistent AF (n = /%) 5/13,2 | Permanent AF (n = /%) 26/68,4 |
|---|---|---|---|
| LAA Thrombus | 0 | 0 | 4 |
| Spontaneous echo contrast (SEC) | 0 | 0 | 5 |
| LAA free of thrombus and SEC | 7 | 5 | 17 |

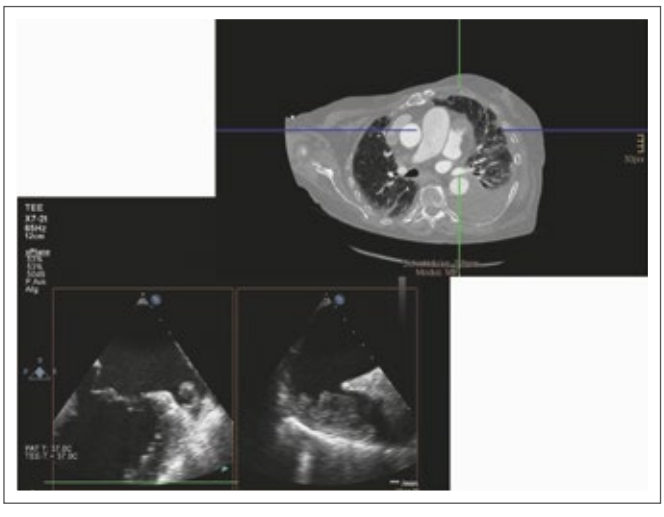

**Figure 1.** A. Fellner, et al.

### 2. Preis

### Laktat zur Mortalitätsprädiktion bei septischen Patienten: Baselinewerte versus Laktatclearance

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**Hintergrund** Die Höhe der Laktatkonzentration im Blut beim kritisch kranken Patienten ist proportional zur Schwere der Erkrankung und korreliert mit der Prognose. Ziel dieser Studie war es, die Baseline-Laktatkonzentration mit der Laktatclearance in Hinblick auf die Mortalitätsprädikation bei Patienten, die aufgrund einer Sepsis auf einer Intensivstation (ICU) behandelt wurden, zu vergleichen.

**Design** Retrospektive Analyse, Registerstudie mit den Daten der MIMIC-III-Datenbank.

**Setting** 6430 kritisch kranke Patienten mit dem Bild einer Sepsis, die auf einer ICU behandelt wurden.

**Methodik** 3583 (56 %) Patienten zeigten eine initiale Laktatkonzentration < 2,0 mmol/L, bei 2847 Patienten war diese > 2,0 mmol/L. Die Assoziation in Bezug auf die Mortalität wurde mit Hilfe der logistischen Regressionsanalyse und der „Area under the curve" (AUC) berechnet. Wir analysierten die Laktatkonzentration bei Aufnahme und die Laktatclearance bei 0, 2, 6, 12, 18 und 24 Stunden.

**Resultate** Die Mortalität im Gesamtkollektiv lag bei 19 % und war höher bei Patienten mit einem initialen Laktatspiegel von > 2,0 mmol/L (23 % vs. 11 %; p < 0,001). Im Kollektiv der Patienten mit einem initialen Laktat von > 2,0 mmol/L wiesen Non-Survivor höhere SAPS-Scores auf und waren klinisch kränker (p < 0,001). Zu allen Zeitpunkten waren die Laktatwerte höher in Non-Survivors (p < 0,001) und die Laktatclearance geringer (p < 0,001). Sowohl die Laktatkonzentration als auch die Laktatclearance waren assoziiert mit der Mortalität. Die Laktatclearance nach 2, 6 und 12 Stunden zeigte keine bessere Prädiktion als die Baseline-Laktatwerte.

**Konklusion** Die Laktatkonzentration war ein unabhängiger Prädiktor der Mortalität zu allen Zeitpunkten. Für die Prädiktion der Mortalität von Patienten mit Sepsis war die Baseline-Laktatkonzentration nicht-inferior zur Laktatclearance. Verglichen mit der Laktatclearance ist die Bestimmung der Baseline-Laktatkonzentration einfacher, leichter verfügbar und daher praktischer für den Einsatz in der klinischen Praxis.

## 3. Preis

### Metabolomic and MALDI Profiling of Thoracic Aortic Aneurysms and Dissections – Implications for Pathophysiology and Biomarker Discovery

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**Background** A deeper understanding of the pathogenesis of ascending thoracic aortic aneurysms (ATAA) and dissections is highly demanded for a better risk prediction, diagnosis and treatment. Modern clinical imaging cannot sufficiently predict the individual risk for dissection and ruptures; only disease progression can be observed. Metabolomic analyses offer an opportunity to increase our understanding of the ATAA and to find disease and progression markers.

**Methods** Using a targeted FIA-MS/MS metabolomics approach, we analysed the metabolic profiles of ascending thoracic aortic wall tissue of age-matched controls (n = 8), bicuspid aortic valve-associated aneurysms (BAV-A; n = 9), tricuspid aortic valve-associated aneurysms (TAV-A; n = 14), and tricuspid aortic valve-associated aortic dissections (TAV-Diss; n = 6). All together, the metabolite concentration of 182 single metabolites from various substance groups (sphingomyelins, glycerophospholipids, ceramides, amino acids, acylcarnitines) was determined.

Further, matrix-assisted laser desorption/ionisation (MALDI) imaging was used to investigate metabolite distribution in 60 µm diameter microdomains across unfixed cryostat sections of aortic wall tissue.

**Results** Out of 182 analysed metabolites only 5 could be used as markers to differentiate between controls, ATAA and dissections. Interestingly, MALDI screening revealed that many metabolites are not distributed equally across the aortic wall; some occurring only in the tunica media or the tunica adventitia, other metabolites show a characteristic distribution pattern within the tunica media.

**Conclusions** The analyses of aortic tissue revealed the usability of sphingolipids and glycerophospholipids for the identification and differentiation of ATAAs and dissections. MALDI imaging revealed that the aortas` tunica media is everything but a metabolically homogeneous structure, arguing for distinct functionally different sublayers within the aortic tunica media, which by means of classical histology seems to be a homogenous structure.

### Quantitative definition of severe functional mitral regurgitation – a matter of intercontinental debate

*G. Spinka, P. E. Bartko, G. Heitzinger, H. Arfsten, N. Pavo, J. Mascherbauer, C. Hengstenberg, M. Hülsmann, G. Goliasch*
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**Background** Recent divergence between AHA/ACC and ESC/EACTS guidelines of the quantitative definition for severe functional mitral regurgitation (sFMR) introduced uncertainty, inconsistency and continuing debate. The relation of each threshold with long-term outcome, in patients under guideline directed therapy (GDT) remains however uncertain.

**Methods** We enrolled 269 heart failure patients with reduced ejection fraction (HFrEF) and graded sFMR according to both guideline-recommendations [AHA/ACC: effective regurgitant orifice area (EROA) ≥ 40 mm² or regurgitant volume (RegVol) ≥ 60 ml/beat and ESC/EACTS: EROA ≥ 20 mm² or RegVol ≥ 30ml/beat]. All-cause mortality was defined as the primary endpoint.

**Results** According to AHA/ACC guidelines sFMR occurred in 17% by EROA with a median EROA of 0.5 mm² (IQR 0.4–0.6) and in 13% by RegVol with a median RegVol of 76 ml/beat (IQR 69–101). According to ESC/EACTS guidelines sFMR occurred in 53% by EROA with a median EROA of 0.4 mm² (IQR 0.2–0.4) and 40% according to RegVol with a median RegVol of 51 ml/beat (IQR 37–69). During 8-years follow-up, 165 patients died. We observed a significant association with outcome for sFMR according to AHA/ACC guidelines quantified by EROA (HR 1.66, 95-%-CI 1.13–2.43, P = 0.009) as well as RegVol (HR 2.02, 95-%-CI 1.34–3.05, P = 0.001). In contrast, the ESC/EACTS definition of sFMR was related with outcome exclusively if quantified by RegVol (HR 1.46, 95-%-CI 1.05–2.05, P = 0.026) but not for EROA (HR 1.30, 95-%-CI 0.91–1.86, P = 0.15).

**Conclusion** In this contemporary HFrEF cohort under GDT, there is significant association of the ACC/AHA proposed cut-off for severe FMR and long-term mortality. The ESC/EACTS definitions are associated with mortality exclusively for the RegVol. The lack of association between sFMR based on ESC/EACTS EROA cut-offs with mortality potentially results from incorporating patients where the regurgitant burden may still be compensated and has not yet become a driving force of disease progression. Contemporary definition of sFMR entails decision making for surgical/transcatheter repair. Cut-offs need to account for the competing risks of the procedure versus the potential benefit of reducing mortality. Lower thresholds may expose a significant proportion of patients to unnecessary risk of futile procedures and higher thresholds may withhold potentially life-extending therapies. The disagreement between the two guidelines does not only convey a source of uncertainty for treating physicians but also lead to inconsistent treatment allocation thereby hindering comprehensive and comparable research. Future studies need to approximate to the true nature of severe functional mitral valve disease in an attempt to facilitate a unifying definition of sFMR.

## Sonderpreis Medizindidaktik

### Needs Assessment of Residents in Cardiology at the Kepler University Hospital Linz

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**Background** In 2015 medical training regulations have been restructured for postgraduate medical training in Austria. Additionally, a restriction of working hours was implemented and both aspects affect the framework of postgraduate medical training in Austria so far. For adoption of the residency in cardiology at the Johannes-Kepler-University Hospital Linz a needs assessment of current residents was performed.

**Method** All residents of the Department of Cardiology were invited to participate at a needs assessment by a two-round Delphi method. In the first round, the residents were asked to draw up two lists each with positive and negative aspects of their cardiovascular training. Within four weeks the participants had to submit their results anonymously, and all issues were by categorized by two medical educators.

**Table 2.** T. Lambert, et al.

| Positive Aspects of Residency | Negative Aspects of Residency |
|---|---|
| High case load | Schedule of rotations |
| Possibility to take over responsibility | Missing of goals and objectives |
| Working atmosphere/climate | Missing mentorship |
| Support of attending physicians | Missing preparation for special tasks (cardiac consultations; device consultations) |
| Rotation in intensive care medicine | Missing discussion of complex cases |

In the second round, the list with all categories was transferred to residents again. The residents were able to review all issues and award a total of five points for prioritization. The second round was also conducted anonymously. This resulted in a ranking of the residents about the most important aspects of the cardiovascular training.

**Results:** All seven residents took part in both rounds of the needs assessment. The results of the second round were ranked and discussed together with the head of the department. The five most important positive and negative points are listed in **Table 2**.

**Discussion** Our assessment revealed important positive and negative aspects about the residency in cardiology. According to a high-volume center for cardiovascular diseases, the residents mentioned the high number of cases and the possibility of assuming responsibility in patient care as positive aspects. On the other hand, there are a lack of a mentoring program and deficits in the area of structured training.

In addition, the residents' feedback also underlines the need for a competency-based curriculum while at the same time moving away from a time-based concept in order to meet the challenges of demanding training and the needs of young physicians.

**Conclusion** Our needs assessment provides relevant information about the situation of our residents. Based on the results, a reform of the cardiovascular curriculum was initiated with the aim of better adapting the training to the needs of our young physicians.

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## Retrospective evaluation of pulmonary rehabilitation outcome parameters in 2595 consecutive patients – a single center experience

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*[2]Rehabilitation Clinic Enns, Enns*

**Introduction** Pulmonary rehabilitation (PR) has become an essential part in the management of COPD and other chronic respiratory diseases, supported by growing evidence about its efficacy.

In extension of a former study [1] evaluating first year results, we now report on the assessment of pulmonary rehabilitation outcome parameters collected within 44 months at the "Rehaklinik Enns", a PR center in close cooperation with a tertiary care university hospital.

**Methods** Patients attended an individually tailored three-week inpatient PR program according to the 2013 ATS/ERS guidelines [2] between June 2015 and January 2019. Spirometry, a 6-minute walk test (6MWT) and a COPD assessment test (CAT) were performed at the beginning and the end of the program. Changes were compared to the validated minimal clinically important difference (MCID) [3–5]. Additionally the smoking cessation rate and its association with outcome parameters were analyzed.

**Results** Among 2595 patients (mean age 61.9 y, 42.9% female) the most frequent diagnosis was COPD (64.1%), followed by asthma (13.5%), lung cancer (5.9%) and pulmonary embolism (2.7%). An increase in 6MWT above the MCID of 30 meters was observed in 51.8% of all patients. Greater benefits were seen in younger patients. A reduction in CAT score of at least the MCID of 2 points was evident in 74.4% of all patients. There were no differences for sex or baseline smoking status concerning 6MWT or CAT changes.

Of a total of 639 current smokers 166 (26.0%) stopped smoking at the end of PR, independent of age or sex. Successful cessation resulted in a greater increase in 6MWT (41.4 m vs. 30.1 m).

**Conclusions** PR showed beneficial effects irrespective of the entity and severity of pulmonary disease, sex and age. Patients who accomplished smoking cessation during PR had a greater 6MWT improvement than those who did not.

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## Large thrombus burden and persistently compromised flow in primary percutaneous coronary intervention

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**Case presentation** A 47-year-old man was referred for evaluation of recent-onset chest pain and shortness of breath during the previous three weeks. Medical history was unremarkable. Atherosclerotic cardiovascular risk factors included hypercholesterolemia and smoking.

**Clinical findings and results** At admission, the heart rate was 92 beats per minute and the patient had elevated jugular venous pressure. Blood pressure was 110/70 mmHg. ECG revealed AF with T-wave inversion in leads aVL, and V4 to V6 without ST-segment elevation or depression. Hs-troponin I was elevated.

A transthoracic echocardiogram showed severely reduced global left ventricular (LV) function with a calculated LV-ejection fraction of 24%. Wall motion abnormalities were present in all LV segements and not confined to a single coronary artery territory.

**Angiographic results** Urgent coronary angiography revealed occlusion of the circumflex artery (LCX) and a moderate stenosis in the proximal LAD. The occlusion of the proximal LCX could be crossed easily with a BMW wire. After inflation of a small semi-compliant balloon, TIMI I flow could be restored.

However, the entire vessel was filled with a huge thrombotic mass. ACT-guided heparin and abciximab were added to aspirin and ticagrelor. Several attempts of manual aspiration thrombectomy could only remove small thrombotic particles but were not sucessful to restore flow. Aspiration via the deeply engaged guiding catheter failed to remove the large thrombotic mass. However, the giant thrombotic mass migrated backward to the ostium of the LCX and jeopardized flow in the left main coronary artery **(Fig. 2)**.

**Procedural results** We proceeded with stenting using 2 metallic second generation drug eluding stents and suceeded to restore TIMI III flow without significant distal embolisation and a TIMI myocardial perfusion grade 2 to 3. Recovery was uneventful.

**Medical Therapy and Follow up** Beyond antiplatelet treatment, heart failure therapy including an angiotensin converting enzyme inhibitor, a beta blocking agent and eplerenone was started. Left ventricular ejection fraction markedly improved during 2 months follow up (LVEF 39%) and wall motion abnormalities remained in all LV segements.

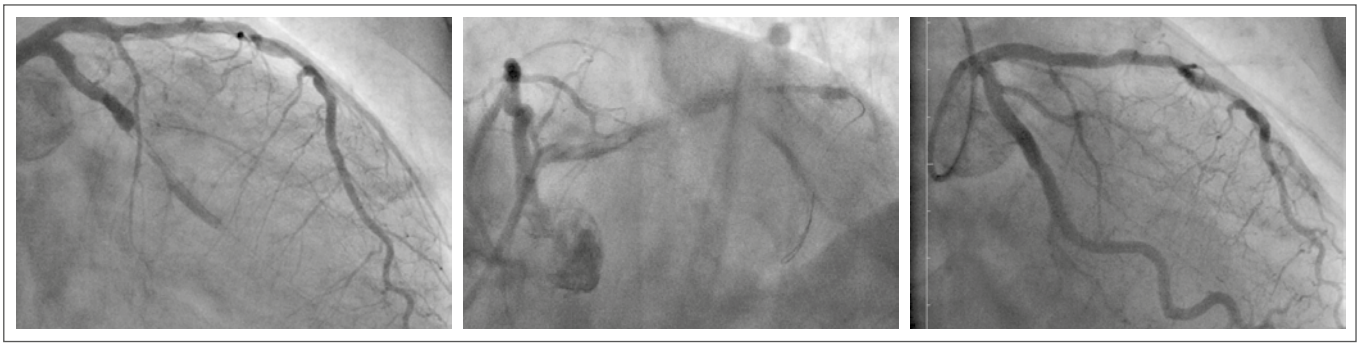

**Figure 2.** J. Auer

**Conclusion** Thrombus aspiration in the presence of antithrombotic and antiplatelet drugs is the default strategy to treat occluded coronary vessels with a large thrombus burden in the setting of an acute coronary syndrome. If thrombus aspiration fails, mechanical thrombectomy, stenting with drug eluting stents or novel mesh covered stents should be considered and can result in appropriate restoration of microvascular and tissue level perfusion.

## Disproportionate Functional Mitral Regurgitation: Advancing a Conceptual Framework to Clinical Practice

*P. Bartko, G. Heitzinger, H. Arfsten, N. Pavo, G. Spinka, M. Andreas, J. Mascherbauer, C. Hengstenberg, M. Hülsmann, G. Goliasch*
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**Introduction** A recently proposed conceptual framework [1] seeks to rearrange the effective regurgitant orifice area (EROA) and regurgitant volume (RegVol) cut-offs according to left ventricular end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF) in functional mitral regurgitation introducing "disproportionate FMR" to describe clinically meaningful FMR. The conceptual framework, however, remains hypothetical [1] **(Fig. 3)**.

**Purpose** To test the significance of disproportionate FMR.

**Methods** Data of 291 heart failure patients with reduced ejection fraction (HFrEF) under guideline directed therapy were embedded into this conceptual framework **(Fig. 4, Panel A and C)**. The black line represents a regurgitant fraction (RegFrac) of 50% at the median LVEF (25%) of the study population. For the EROA, the black line

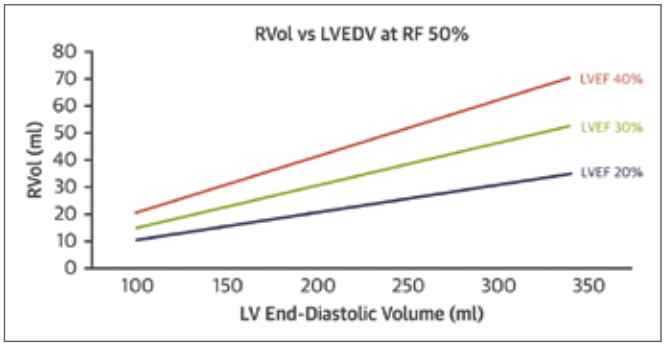


**Figure 3.** P. Bartko, et al. RegVol plottet versus LVEDV at a RegFrac of 50% by LVEF. Adapted from [1].

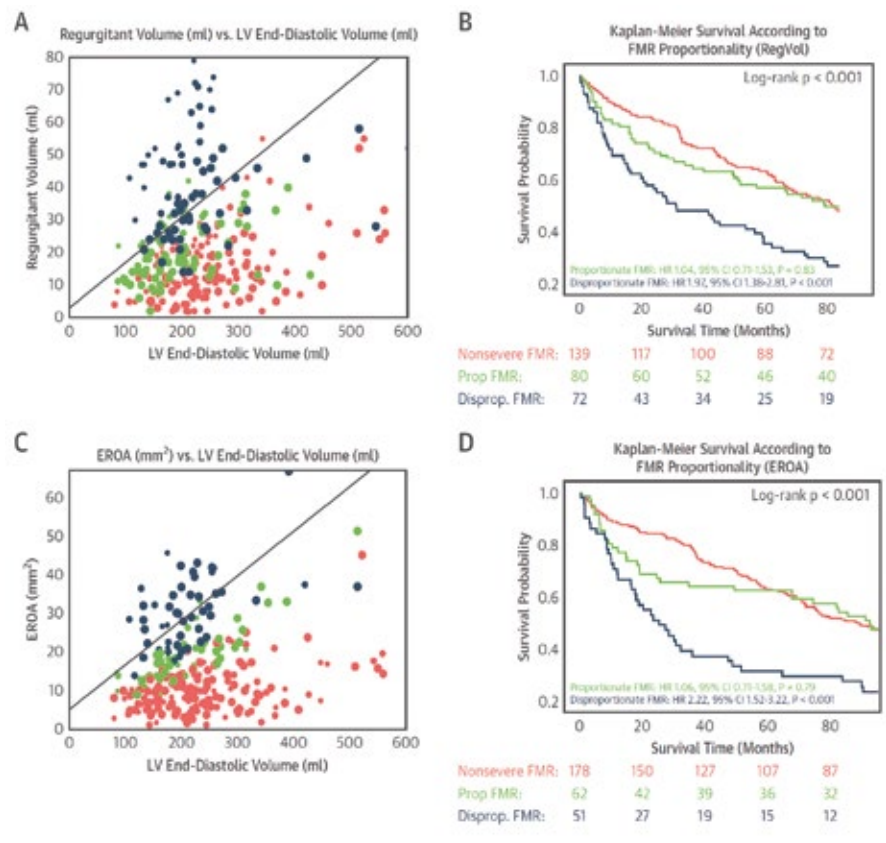


**Figure 4.** P. Bartko et al. **A:** Bubbleplot that plots disproportionate (blue) proportionate (green), and nonsevere (pink) functional mitral regurgitation according to left ventricular end-diastolic volume and FMR regurgitant volume. Bubble size is coded according to ejection fraction (large depicts an ejection fraction ≥ 35%; intermediate-sized, an ejection fraction of 25% to 35%; and small, an ejection fraction < 25%). The black line depicts a regurgitant fraction of 50% at the median ejection fraction (25%). **B:** Kaplan-Meier analysis according to nonsevere (pink), proportionate (green), and disproportionate functional mitral regurgitation (blue) as defined by regurgitant volume (RegVol) (log-rank p < 0.001). **C:** Bubble plot plotting disproportionate (Disprop) (blue), proportionate (Prop) (green), and nonsevere (pink) functional mitral regurgitation according to left ventricular end-diastolic volume and FMR effective regurgitant orifice area (EROA) assuming a median left ventricular ejection fraction of 30%. Bubble size is coded according to groups of maximum velocity (large depicts a maximum velocity ≤ 4 m/s; intermediate, a maximum velocity < 4–6 m/s; and small, a maximum velocity ≥ 6 m/s). The black line depicts a regurgitant fraction of 50% at the median maximum velocity (4.3 m/s). **D:** Kaplan-Meier analysis according to nonsevere (pink), proportionate (green), and disproportionate functional mitral regurgitation (blue), as defined by effective regurgitant orifice area (p < 0.001). A and C are adapted from [1].

represents a RegFrac of 50% at the median maximum velocity (4.3 m/sec) of the study population. Thus, above each individual center line, (illustrated by different bubble sizes), FMR severity is disproportionate. The gray area (not displayed because it is different for each individual patient) approximates the degree of uncertainty that is determined by the imprecision of the measurements defined as 2SD for inter- and intraobserver variability by Bland-Altmann analysis (equals ± 6.6%). The bubble size is coded according to groups of EF/$V_{max}$: largest EF ≥ 35%, $V_{max}$ ≤ 4 m/s; intermediate EF 25% to 35%, $V_{max}$ < 4 to 6m/s, and small EF < 25%, $V_{max}$ ≥ 6m/s.

**Results** Median age was 68 years (IQR 61–75), 77% were male. Median LVEF was 25% (IQR 18–33) and LVEDV was 214 ml (IQR 165–267). During a median follow-up of 84 months (IQR: 84 to 136 months), 166 patients died. Disproportionate FMR was associated with excess mortality (RegVol HR: 1.97; 95-%-CI: 1.38–2.81; P < 0.001; EROA HR: 2.22; 95-%-CI 1.52–3.22; P < 0.001) **(Fig. 4 B and D)** whereas proportionate FMR was not associated with increased long-term mortality: (RegVol HR: 1.04; 95-%-CI 0.71–1.53; P = 0.83; EROA HR: 1.06; 95-%-CI 1.71–1.58; P = 0.79) **(Fig. 4 B and D)**.

**Conclusions** In this contemporary cohort with heart failure and reduced ejection fraction, every fifth patient suffers from disproportionate FMR which conveys a two-fold increased risk of mortality that provides evidence for the validity of the conceptual framework. At the time of study enrollment, percutaneous mitral valve interventions were unavailable; therefore a selection bias can be excluded. Advancement of the conceptual framework to clinical practice has several implications: 1) EROA and RegVol are metrics that do not account for the contextual variability in LVEDV and LVEF; and 2) the RegFrac – not incorporated into the European Society of Cardiology guidelines – provides a metric proportionated to LV size and function, thus supporting its use to define clinically FMR. However, technical limits suggest its use on top of more robust metrics such as the EROA and RegVol. Future studies need to clarify whether disproportionate FMR reflects the subgroup of patients who would benefit from mitral valve repair and provide a robust algorithm [2] that integrates metrics of FMR severity in a complementary manner.

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## Influence of NT-PRO-BNP Serum levels on the long-term outcome after cryo pulmonary vein isolation

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**Introduction** Especially in the early course of atrial fibrillation (AF), pulmonary vein isolation (PVI) is an effective treatment modality to maintain sinus rhythm and is therefore endorsed by current guidelines. Both techniques, PVI using radiofrequency ablation or cryoablation, have recently been shown to be equivalent in terms of clinical outcomes. However, despite being more effective than conservative drug treatment, there is still a relapse rate of up to 35% in the first year after the procedure. Therefore, it is crucial to identify predictors of long-term outcome to provide a better individually-tailored treatment approach for patients. NT-pro-BNP is secreted into the bloodstream by atrial myocytes as a response to distension. NT-pro-BNP may thereby represent a surrogate parameter reflecting atrial stress or dilatation caused by increased atrial volume, pressure or a high atrial fibrillation burden. All these factors may, in turn, be associated with an inferior long-term outcome after PVI. The aim of this study was to assess baseline NT-pro-BNP serum levels as a predictor for long-term outcome after PVI using cryoablation.

**Methods** Data were retrieved from our institution's Atrial Fibrillation Cryo Ablation Registry (AFCAR). Patients were eligible if they had undergone a first-ever cryoablation for atrial fibrillation at least three months ago at our department and baseline NT-pro-BNP serum levels from the index stay prior to the ablation procedure were available. At first, demographic and peri-procedural data were collected retrospectively from the hospital's records. In a second step, follow-up data were collected by conducting telephone interviews (structured questionnaires) and by reviewing patients' charts. The primary outcome was defined as a combined endpoint of an ECG-documented relapse of an atrial arrhythmia or electrical cardioversion because of an atrial arrhythmia or a redo PVI procedure. Events within the first 90 days after the PVI were blanked out from the analysis. An exception to this rule was only made if a redo PVI was performed within three months after the index procedure. The impact of pre-procedural NT-pro-BNP serum levels on the primary endpoint was assessed with Kaplan-Meier survival analysis. Clinically significant effect modifiers, such as the type of atrial fibrillation, age, left ventricular ejection fraction, body mass index, kidney function or a history of coronary artery disease, were accounted for by applying a multivariate Cox proportional hazards model.

**Results** We identified 404 eligible patients. Of those, 4 (1%) patients refused the telephone follow-up, and 25 patients were alive, but no contact could be established (6.2% loss to follow-up). Three hundred seventy-five subjects were finally analyzed (median follow-up time: 2.1 years, IQR: 0.8-4.1 years, age 59.1 ± 10.8 years, 108 [28.8%] female, 327 diagnosed with [87.2%] paroxysmal and 48 [12.8%] with persistent or long persistent atrial fibrillation). One or more of the conditions pre-defined as combined endpoint were reached by 189 individuals (50.4%). An AF relapse was associated with persistent or long persistent AF, a history of coronary heart disease and intake of antiarrhythmic drugs at the time of follow-up. Baseline NT-pro-BNP levels ranged between 5 pg/ml and 3,309 pg/ml (tertile 1 ≦ 123.8 pg/ml, tertile 2 ≦ 342.2 pg/ml, tertile 3 > 342.2 pg/ml). The Kaplan-Meier survival analysis revealed a 1.45-fold risk to meet the primary endpoint per increase of one NT-pro-BNP tertile (Hazard ratio [HR] 1.45, 95-%-CI: 1.21–1.74, p = 0.0001). This statistically significant effect was preserved in the multivariate analysis that adjusted for major confounders (HR 1.40, 95-%-CI: 1.12–1.75, p = 0.003).

**Conclusion** NT-pro-BNP serum levels prior to a cryo pulmonary vein isolation may be used as a surrogate parameter of atrial stress. They proved to be a robust predictor of AF relapse in our cohort of patients.

## Association of adipocytokines with left atrial remodelling and thrombus formation in atrial fibrillation

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**Introduction** Atrial fibrillation is the most common sustained arrhythmia affecting 1.5–2.0% of the adult population on average. As low blood flow velocities in the left atrium during atrial fibrillation predispose to intra-cardiac thrombus formation, oral anticoagulation is an important and powerful therapeutic intervention in patients deemed to be at high thromboembolic risk. As every means of anticoagulation also bears the risk of bleeding, both the risk of thromboembolism and bleeding have to be balanced in every single patient. Risk scores like the $CHA_2DS_2VASc$ were shown to perform better in predicting thromboembolic risk in high-risk patients than in patients who are only at low risk. Thus, a further refinement would be desirable to better target oral anticoagulation therapy, especially in low risk patients. Novel serum markers reflecting the activation of platelets as a surrogate for intra-cardiac thrombus formation and subsequent thromboembolic events may be a possibility to accomplish this endeavor. Adipocytokines, like leptin, adiponectin, resistin or visfatin, are cell signaling proteins produced by human adipose tissue that are released into the blood stream. They were shown to influence platelet activation as well as arterial and venous thrombus

formation. By doing so, adipocytokine serum levels may predict the risk of intra-cardiac thrombus formation that may, in turn, lead to debilitating ischemic strokes.

**Methods** We conducted a prospective cross-sectional multi-center trial to assess the association between adipocytokine serum levels and the presence of spontaneous echo contrast (SEC) or left atrial thrombi as surrogate parameters for thromboembolic events. Participating centers were located in Germany (Heart Center Bad Neustadt a.d. Saale, University Hospitals in Duesseldorf, Bochum and Giessen) and Austria (University Hospital Linz). Patients were eligible for inclusion if they were diagnosed with paroxysmal or persistent atrial fibrillation and were referred to a transesophageal echocardiography (TEE) either before undergoing electrical cardioversion or pulmonary vein isolation. TEE was performed according to the respective standards at each institution. All patients had to be on some kind of oral anticoagulation. The primary outcome was defined as the presence of either spontaneous echo contrast (SEC) or left atrial appendage (LAA) or left atrial (LA) thrombus on TEE. Serum blood samples were drawn after an overnight fasting period and stored at –80°C until analysis. Members of the study team administered questionnaires to record baseline characteristics. Adipocytokine serum levels were measured by using commercially available ELISA kits. A logistic regression model was fitted to evaluate the association between adipocytokine serum levels and markers of intra-cardiac thrombosis.

**Results** 189 patients were enrolled in the study (33% females, mean age: 67.2 ± 11.1 years, BMI 28.6 ± 4.7). The majority of patients were diagnosed with persistent atrial fibrillation (102 [54.0%]). 48 individuals (25%) exhibited the primary outcome (one or more pre-defined endpoints on the transesophageal echocardiogram – 41 (21.7%) SEC, 3 (1.6%) LA thrombus, 13 (6.9%) LAA thrombus, group 1 (G1), whereas the others did not (group 2 = G2). The BMI was not statistically significantly different between both groups. Affected individuals were more likely to be in persistent atrial fibrillation ($p = 0.009$), diagnosed with chronic kidney disease ($p < 0.0001$), to have a lower left ventricular ejection fraction ($p < 0.00001$), to be on an oral anticoagulation with phenprocoumon (vs. NOAC, $p = 0.027$) or to have a history of stroke ($p = 0.018$). As opposed to adiponectin (G1: 31.3 µg/ml, G2: 26.9 µg/ml, $p = 0.126$) and visfatin (G1: 31.7 ng/ml, G2: 36.8 ng/ml, $p = 0.470$), leptin (G1: 22.6 ng/ml, G2: 12.0 ng/ml, $p = 0.025$) and resistin (G1: 6.52 ng/ml, G2: 5.31 ng/ml, $p = 0.016$) serum levels were significantly higher in patients with the primary outcome. In the logistic regression analysis, only resistin was statistically significantly associated with the primary outcome (OR 1.13, 95-%-CI: 1.02–1.25, $p = 0.021$), whereas leptin marginally missed statistical significance (OR 1.01, 95-%-CI: 0.99–1.02, $p = 0.061$).

**Conclusion** Leptin and resistin serum levels were associated with surrogate parameters of thromboembolic events in our cohort of patients with atrial fibrillation and may constitute a link between obesity and thromboembolism. These promising new serum parameters should be further investigated in larger prospective trials with hard endpoints.

## Leadless Pacemaker Implantation after Transcatheter Aortic Valve Replacement – Results of a Single Center Patient Cohort

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Leadless pacemakers (LP) have been recently introduced into clinical practice to overcome pocket- and lead-related complications of conventional pacing systems. The only commercially available LP today is the Micraä (Medtronic Inc.), an MR- conditional single-chamber LP with VVIR pacing capabilities. It is delivered to the right ventricle with a catheter through the femoral vein. Intermediate-term results of the Micra Investigational Device Exemption study and the Micra Post-Approval Registry demonstrated excellent safety and efficacy performance in more than 2,500 patients. Compared to a historical dataset of patients with conventional transvenous systems, major complications occurred 63% less often. Transcatheter aortic valve replacement (TAVR) has become a valid treatment option for selected patients (P) with severe symptomatic aortic valve stenosis. However, there still is a considerably high rate of postinterventional conduction disturbances caused by the valve prosthesis necessitating permanent pacemaker implantation. We investigated the safety and efficacy of LP implantation in P with a pacing indication after recent TAVR.

All P with recent (< 10 days) transfemoral TAVR and postinterventional conduction disturbances requiring pacemaker implantation were screened for LP implantation. As pacing indications were defined: (1) The new onset of a second-degree Mobitz II or third-degree AV-block, (2) development of left-bundle-brunch block (LBBB) plus prolongation of the PR-interval (> 200 ms) in P with sinus rhythm (SR) or (3) LBBB plus bradycardia or pauses in P with atrial fibrillation (AF). As suitable for LP implantation were defined: (1) P with preserved left ventricular ejection fraction (> 50%) and AF. (2) P with SR, if a low pacing rate was expected (back-up pacing for new LBBB plus PR-interval prolongation). Two experienced operators performed LP implantation during the same hospital stay like TAVR. Procedural, electrical and clinical follow-up data were prospectively collected for all P. As serious adverse events were defined: (1) Cardiac effusion requiring pericardiocentesis or surgery, (2) groin hematoma requiring transfusion, (3) LP dislocation after implantation, (4) loss of LP function after implantation due to a significant rise of the pacing threshold, (5) device infection. A Micra™ LP was implanted in 32 P with a pacing indication after TAVR. The sex was balanced (n = 16/50% males and females, respectively) and the mean age was 81 ± 4 years. All P had received a self-expanding TAVR (Evolut™, Medtronic or Portico™, Abbott) 7 ± 2 days before. All LP implantations were performed in a cathlab equipped for cardiac implantable electronic device implantations via the right femoral vein without serious adverse events. The mean implant procedure duration was 31 ± 6 min with a mean fluoroscopy time of 5.9 ± 2.3 min. After a mean of 1.5 ± 0.8 positions (100% septal), the LP showed a mean threshold of 0.49 ± 0.22 V, impedance of 805 ± 231 Ω and sensing of 10.9 ± 4.7 mV. No groin complications (hematoma, arterio-venous fistula, infection) occurred. All P could be discharged one to four days after LP implantation. At a mean follow-up of 1.1 ± 0.8 years, 31 P (97%) were alive. One P (3%) died 2 years and 10 months after LP implantation at home (cause of death unknown). Pacing thresholds and sensing remained stable in all P. No device-related serious adverse events occurred.In suitable patients with a pacing indication after TAVR, LP may be an attractive alternative to conventional transvenous systems due to the less invasive procedure and favorable intermediate-term results.

## Aluminium depleting anodisation of laser treated titanium as barrier against fibroblast overgrowth

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Miniaturized cardiac heart pacemakers are usually made from an aluminium and vanadium containing titanium alloy. Femtosecond pulse laser treatment followed by electrochemical anodisation yields a surface that is depleted in aluminium and effectively hinders an overgrowth by fibroblasts. In this way an explantation of the pacemaker is drastically simplified.

## Katheterablation von Herzrhythmusstörungen ohne Röntgenstrahlung – Wie wirkt sich der Einsatz von Zero-Fluoro-Technologien auf den klinischen Alltag aus?

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Tachykarde Herzrhythmusstörungen werden in der interventionellen Elektrophysiologie untersucht und therapiert. Ablationen können bei betroffenen Personen eine Heilung bewirken. Konventionell werden Katheterablationen unter Röntgenkontrolle durchgeführt. 3D-Mappingsysteme unterstützen bei der Orientierung im Herzen und ermöglichen Zero-Fluoro-Untersuchungen.

Diese Arbeit vergleicht anonymisierte Untersuchungsdaten von konventionellen elektrophysiologischen Untersuchungen und Zero-Fluoro-Prozeduren hinsichtlich der Untersuchungsdauer, -sicherheit und Dosis.

## CLARA – COPD in Österreich/Austria – Lebens-quAlität und EinschRänkungen im Alltag – Quality of Life and Limitations in Daily Life

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**Background** COPD patients suffer from respiratory symptoms and limitations in daily life. We aimed to characterize COPD outpatients regarding the impact of their disease on overall health, daily life, and perceived well-being.

**Methods** A national, multicentre, cross-sectional study was conducted in offices of pulmonologists and general practitioners. The St. George's Respiratory Questionnaire for COPD patients (SGRQ-C) was used. Inclusion criteria were spirometrically defined COPD and age ≥ 40 years. Subjects with a history of lung surgery, lung cancer or a last four weeks COPD exacerbation were excluded.

**Results** 67 pulmonologists and 6 general practitioners participated and collected data from 1,175 COPD patients.; of those 77 were excluded due to missing data, and 248 patients were found unobstructed (FEV1/FVC ≥ 0.7). Finally, 850 patients (62.8% men; mean age 66.2 ± 0.3 [SE] years; mean FEV1%pred. 51.5 ± 0.6 [SE]) were analysed. 55.4% had at least one exacerbation in the last year, and 12.5% were therefore hospitalised. 50.3% reported not being able to do any sports and only 21.3% stated that their chest symptoms allow them doing anything they would like to do.

**Conclusion** In Austria, COPD patients are strongly symptomatic and experience grave limitations in daily life due to their disease **(Fig. 5)**.

**Acknowledgements** The authors wish to express their gratitude to all investigators who contributed to the conduct of the CLARA study. Funding was provided by A. Menarini Pharma GmbH.

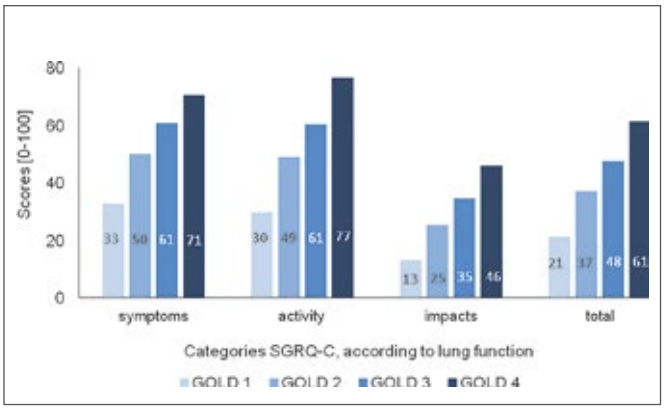


**Figure 5.** A. Horner et al. Components and total score of SGRQ-C (scores range from 0 to 100, with higher scores indicating more limitations).

## Einfluss des Vorhofflimmerstatus auf das Langzeit-Outcome nach interventioneller ungeschützter Hauptstammintervention – ein retrospektives Langzeit Follow-up

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**Einleitung** Die koronare Herzkrankheit ist ein Haupt-Risikofaktor für das Auftreten von Vorhofflimmern. Es ist wenig bekannt, wie das Langzeit-Outcome von Patienten nach perkutaner Intervention einer Stenose des Hauptstamms der linken Koronararterie durch das Vorliegen einer Vorhofflimmerdiagnose zum Interventionszeitpunkt beeinflusst wird.

**Methoden** Es wurden Patienten aus dem UNPROLEMA-(UNPROtected LEft MAin disease) Register unserer Klinik untersucht, bei denen zwischen 11/2002 und 08/2014 eine ungeschützte Hauptstammintervention durchgeführt wurde. Dabei wurden die Patientendaten durch Informationen aus Krankengeschichten sowie aus strukturierten Telefon-Interviews und Meldeamtsanfragen bzgl. Follow-up komplettiert. Die Patienten wurden anhand des Vorhofflimmerstatus zum Zeitpunkt der Intervention in eine Vorhofflimmer- (AF) und eine Sinusrhythmus-Gruppe (SR) unterteilt. Die Gesamtmortalität und das Auftreten von „major adverse cardiac and cerebrovascular events" (MACCE: definiert als Myokardinfarkt, 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 durchgeführt. Zudem wurde mittels Cox-Proportional-Hazards-Modell für potentielle Confounder (Alter, Diabetes-Status, linksventrikuläre Auswurffraktion, Raucherstatus, periphere arterielle Verschlusskrankheit, Hypercholesterinämie) adjustiert.

**Resultate** Insgesamt wurde bei 293 Patienten eine ungeschützte Hauptstammintervention durchgeführt. Davon war bei 237 zum Zeitpunkt der Intervention sowie aus der Anamnese kein Vorhofflimmern bekannt (SR-Gruppe, 80,9 %), während bei 56 (19,1 %) Vorhofflimmern bekannt war (AF-Gruppe: 30 paroxysmal, 5 persistierend und 21 permanent). Der $CHA_2DS_2$-VASc-Score, als Indikator einer größeren Komorbiditätslast, war in der AF-Gruppe mit 4,3 ± 1,6 signifikant höher, als in der SR-Gruppe mit einem virtuellen mittleren Score von 3,4 ± 1,7 (p = 0,0002). Während einer medianen Follow-up-Dauer von 3,4 Jahren (IQR 1,4–6,3, Spannweite 0–12,1 Jahre) zeigte die Kaplan-Meier-Analyse bei insgesamt 90 Todesfällen jedweder Ursache (30,7 %) einen signifikanten Unterschied (p = 0,002), wobei AF-Patienten ein 2,1-fach erhöhtes Mortalitätsrisiko aufwiesen (Hazard Ratio [HR] 2,1, 95-%-CI: 1,29–3,26). In der multivariaten Analyse mit Adjustierung für potentielle Confounder zeigte sich ein Verlust der statistischen Signifikanz (HR 0,46, 95-%-CI: 0,09–2,37, p = 0,350). Von der MACCE-Analyse mussten 5 Patienten ausgeschlossen werden, da die Follow-up-Daten nicht vollständig erhoben werden konnten. Auch hier konnte ein signifikanter Unterschied (p = 0,046) mit einem 1,51-fach erhöhten Risiko für das Auftreten von MACCE in der AF-Gruppe beobachtet werden (HR 1,51, 95-%-CI: 1,00–2,28). Nach Adjustierung für Confounder wurde wiederum ein Verlust der statistischen Signifikanz festgestellt (HR 0,75, 95-%-CI: 0,33–1,74, p = 0,506).

**Schlussfolgerungen** In der Analyse unserer Stichprobe beobachteten wir eine signifikante Erhöhung der Gesamtmortalität und der MACCE-Rate nach einer Hauptstammintervention bei Patienten mit Vorhofflimmern. Nach Adjustierung für potentielle Confounder konnte jedoch kein Einfluss des Vorhofflimmerns im Sinne eines unabhängigen Risikofaktors auf das Langzeit-Outcome festgestellt werden. Es ist daher davon auszugehen, dass die erhöhte Gesamtmortalitäts- und MACCE-Rate durch die mit Vorhofflimmern assoziierten Komorbiditäten bedingt ist. Der Vorhofflimmer-Status kann als wichtiger Prädiktor für das Langzeit-Outcome bei Patienten nach HauptstammInterventionen gesehen werden.

## Exercise Cancer and Cognition – The ECCO-Study; Excerpt of the Study Protocol: High-Intensity-Interval-Training in Oncology Patients

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For many decades cardiac-centric adverse consequences as arrhythmias, dose-dependent overt heart failure (HF), and/or sudden cardiac-related death in breast cancer patients undergoing systemic chemotherapy have been described in the literature. Especially cardiorespiratory fitness (CRF), seen as an assessment of global cardiovascular function, declines up to 26% during exposure to various systemic combination therapies, and may recover hardly after end of treatment. Such limitations may prone to non-cancer competing morbidities and its attendant symptoms persist for months or even years, after completion of medical treatment, impairing daily functioning, limiting ability to return to work and decreasing overall quality of life.

Exercise training, as a non-pharmacological therapy, has been introduced to improve CRF, quality of life and to reduce rehospitalization and death in oncology patients. Few interventional studies have included patients undergoing chemotherapy as the majority of conducted studies have involved women with breast cancer after completed cytostatic treatment. Further, studies typically investigated effects of moderate intensities, such as walking or low-intense cardiovascular training.

High intensive interval training (HIIT) accompanying systemic chemotherapy might be an effective and time efficient way to enhance patients' physical capacity and and shows promising effects in preclinical and small sampled phase I-II studies.

Against this backdrop the ECCO study investigates the influence of an intensive, individualized, structured and supervised exercise program during chemotherapy on patients' cardiac performance and potential structural and mechanistic underpinnings.

## Evaluation of Workload and Working Environment of Young Physicians at the Kepler University Hospital Linz

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**Background** Since 2015 the framework of postgraduate medical training in Austria has changed considerably. Through implementation of both, the new medical training regulations and the restriction of working hours according to the Europeans Unions working hour limitation requirements the overall training duration was shortened. On the other hand, the clinical routine has also changed. The increase in complex and multimorbid patients represents a major challenge for the healthcare system in general and for young physicians in particular. That is why we have carried out a self-assessment of young physicians with regard to their professional burdens.

**Method** An in-hospital questionnaire was conducted anonymously between February and May 2019 at the Kepler University Hospital Linz, Austria. Most items were ranked on a 7-point Likert-scale. Participants were recruited from medical students in their sixth academic year who were attending their internship, physicians in their basic training (common trunk), physicians in training in general medicine and residents in their first 18-months of training.

**Results** While students rated their workload as moderate, the workload significantly increased during medical training, with the highest ratings in physicians in training in general medicine and residents ($p = 0.001$). This was also reflected by the questions of whether it is possible to take regular breaks and to have lunch in daily work-life. While almost all students take regular breaks and can eat lunch, this is only possible for about a third of physicians in training in general medicine and residents ($p = 0.001/p = 0.001$). These data were further supported by the results of the question about sleeping disturbances, in which physicians in general medicine training scored very high ($p = 0.023$).

**Discussion** It seems important to adapt the training programs for general medicine and residents in order to cope with the high workload and to improve the working environment. Especially in the transition zone after completion of basic medical training, the stress level of young physicians rises due to the challenges of their new roles. Mentoring and feedback as well as adapted clinical tasks depending on the level of competence could offer young physicians prospects for further significant improvement.

## Standardized Semi-Quantitative Computed Tomography Findings and Associated Changes in FVC and DLCO in a Real-Life Cohort of Interstitial Lung Disease Patients

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**Background** Forced Vital Capacity (FVC) and Diffusion Capacity for Carbon Monoxide (DLCO) are standard parameters used to measure functional impairment in interstitial lung diseases (ILD). Both correlate with disease severity and mortality and can be used to assess disease progression. Still, it is largely unknown which exact features routinely described in high-resolution computed tomography (HRCT) chest scans determine those functional alterations.

**Methods** HRCT scans of 128 subsequent patients (mean age 65 years, 65% male) discussed by the local ILD board were reviewed and scored by an expert ILD radiologist, creating a semi-quantitative mapping of HRCT findings: Each lung was divided into three equally large portions defined by the maximum cranio-caudal diameter, each part was subdivided into a subpleural (< 10mm within the pleura), central and peripheral area (separated by half distance hilus-supleural space). Standardized patterns included noduli, reticulation, honeycombing, ground glass, consolidations, emphysema, bronchiectasis, visual signs of volume reduction and pulmonary hypertension (pulmonary artery/aorta ≥ 1). Using the Akaike information criterion, cut-off values for each semi-quantified HRCT finding were created regarding FVC and DLCO. Multivariate stepwise regression-analyses were used to evaluate the predictive value of HRCT findings on FVC and DLCO.

**Results** FVC was significantly determined by the extent of bronchiectasis ($F = 8.25$;$p < 0.001$) and consolidations ($F = 6.53$; $p = 0.012$). Including age and sex into the model, bronchiectasis remained the only significant HRCT variable ($F = 11.49$; $p < 0.001$), next to age ($F = 10.43$; $p = 0.001$). DLCO was significantly influenced by the extent of emphysema ($F = 16.27$; $p < 0.001$), reticulation ($F = 4.99$; $p = 0.008$), bronchiectasis ($F = 3.61$;$p = 0.016$) and signs of pulmonary hypertension ($F = 5.34$; $p = 0.023$). Age and sex did not have significant implications on the DLCO model.

**Conclusions** FVC was found to be mainly determined by the extent of bronchiectasis and age, while emphysema, reticulation, bronchiectasis and signs of pulmonary hypertension predicted DLCO.

## Zero-Fluoroscopy bei elektrophysiologischen Untersuchungen und Katheterablationen von rechtsseitigen Arrhythmien

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**Einleitung** Die Katheterablation ist bei supraventrikulären Tachykardien meist die Therapie der Wahl. Zur adäquaten endokardialen Positionierung und Darstellung der Katheter wird dabei eine fluoroskopische Bildgebung durchgeführt. Trotz zunehmend niedrigerer Strahlendosen in der Elektrophysiologie (EP) führt Röntgenstrahlung nachgewiesenermaßen bei langjähriger Anwendung mit hohen kumulativen Dosen bei dem im EP-Labor beschäftigten Team zu erhöhten Inzidenzen von zerebralen Tumoren oder einer Kataraktbildung. Weiters können die notwendigen Schutzmaßnahmen

(Bleischürzen) zu beträchtlichen muskuloskelettalen Beschwerden führen. Durch die rasante Entwicklung der virtuellen 3D-Mappingsysteme ist inzwischen eine sehr akkurate Steuerung aller Katheter auch ohne Verwendung von Fluoroskopie möglich (Zero-Fluoroscopy-Technologie, ZF) und bereits in einigen wenigen EP-Laboren weltweit in Verwendung. An unserer Institution wurde im Verlauf des letzten Jahres damit begonnen, den Großteil der rechtsatrialen und -ventrikulären Katheterablationen mittels ZF durchzuführen. Ziel dieser Analyse war es, die Sicherheit und Effektivität der ZF bei einer konsekutiven Serie von Patienten zu evaluieren.

**Methoden** Seit September 2018 wurden in unserem EP-Labor alle geplanten Untersuchungen mit dokumentierter Tachykardie, welche ihren Ursprung im rechten Vorhof oder Ventrikel vermuten ließ, ohne Verwendung von Röntgenstrahlung (ZF) durchgeführt. Zur Steuerung der Katheter fand das NAVX Ensite Precision System (Abbott) Verwendung. Bei Notwendigkeit einer Kontrolle der Katheterführung mittels Fluoroskopie war dies zu jeder Zeit der Prozedur mittels einer monoplanen bodenmontierten Röntgenanlage (Artis Q Zen, Siemens) möglich.

**Resultate** Es wurden insgesamt 43 konsekutive Untersuchungen mittels ZF durchgeführt. Das mittlere Alter der Patienten war 61 ± 14 Jahre mit einem Frauenanteil von 42 %. An wesentlichen Komorbiditäten fand sich eine arterielle Hypertonie bei 22 (51 %), eine koronare Herzkrankheit bei 14 (32 %) und eine eingeschränkte Linksventrikelfunktion bei 7 (16 %) der Patienten. Folgende Arrhythmien wurden abladiert: AV-Knoten-Reentrytachykardie (n = 17/40 %) und typisches Vorhofflattern (n = 17/40 %), Ektope rechts-atriale Tachykardie (n = 2/4 %), rechtsseitige akzessorische Leitungsbahn (n = 2/4 %) rechts-ventrikuläre Extrasystolie (n = 1/2 %). In vier Fällen wurde lediglich eine diagnostische Untersuchung durchgeführt (10 %). Alle Ablationen waren erfolgreich, keine Prozedur musste wegen Komplikationen abgebrochen werden, auch die peri- und postinterventionelle Komplikationsrate lag bei 0 %. Die mittlere Prozedurdauer betrug 98 ± 32 Minuten (Median 90 [75; 120] Minuten). In keinem Fall war von der ersten Lokalanästhesie bis zum Ziehen der Schleusen eine fluoroskopische Durchleuchtung erforderlich.

**Konklusion** Die Katheterablation von rechts-atrialen und ventrikulären Substraten mittels ZF ist sicher und effektiv. Durch die Vermeidung von Röntgenstrahlung stellt sie für das gesamte Team eines EP-Labors die Vorgangsweise der Zukunft dar. Ihre Anwendung auch bei linksseitigen Substraten wird derzeit untersucht.

## The role of volume status in patients undergoing transcatheter aortic valve replacement: acute kidney injury and outcome

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**Background** Acute kidney injury (AKI) represents a major complication following transcatheter aortic valve replacement (TAVR). Low body fluid levels have been described to predispose for AKI after percutaneous coronary interventions. Conversely, volume overload and cardiac decompensation are cardinal signs indicating the necessity of intervention in patients with valvular heart disease. Systemic fluid status can be easily assessed by bioelectrical impedance spectroscopy (BIS). The impact of fluid status on AKI and outcomes in TAVR is unknown.

**Methods** Consecutive patients with aortic stenosis scheduled for TAVR underwent systemic fluid status assessment using BIS, serum and urine analysis on the day preceding intervention, and were prospectively followed. Fluid overload (FO) was defined as relative FO of ≥7% (Rel. FO = FO/extracellular water × 100). AKI was defined as a > 1.5-fold and/or > 0.3 mg/dL increase in serum creatinine within 7 days post TAVR compared to baseline. AKI and a composite of death and heart failure hospitalizations were selected as study endpoints. Pearson correlation, binary logistic, Cox regression and Kaplan-Meier analyses were used as statistical methods.

**Results** 220 consecutive patients (81.1 ± 7.4 years; 46.7% female) with valid BIS data were included. Increased body fluid levels were associated with higher levels of serum creatinine and urine albumine/creatinine ratios by Pearson correlation analysis (r = 0.156 and 0.203, $p < 0.05$, respectively). AKI was diagnosed in 14.1% (n = 31/220), and during follow-up (26.7 ± 22.8 weeks) 18.2% (n = 40/220) experienced an event. By multivariate binary logistic regression, the use of low-osmolar contrast medium ($p = 0.000$), increased body mass index ($p = 0.007$), levels of C reactive protein ($p = 0.007$), and post-TAVR pacemaker implantation ($p = 0.016$), but not body fluid levels ($p > 0.05$) were significantly associated with AKI development. Patients with FO or AKI were more likely to experience an event, and subjects suffering from FO+AKI displayed the worst outcomes (log-rank, $p = 0.000$). Also, among all relevant cardiovascular and periprocedural characteristics, FO and AKI ($p = 0.003$ and 0.022, respectively) had a significant impact on event-free survival by multivariate Cox regression.

**Conclusions** In TAVR, OH is associated with renal dysfunction. Post-TAVR AKI develops irrespective of volume status and significantly worsens the clinical course, as does the presence of fluid overload. Therefore, BIS-guided pre- and postprocedural decongestion therapy might help to improve outcomes following TAVR.

## Klappenerhaltender Aortenwurzelersatz nach Ross-Operation bei Autograft-Aneurysmen

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**Hintergrund** Häufigste Langzeitkomplikation nach der Ross-Operation ist die aneurysmatische Dilatation des pulmonalen Autografts. In vorliegender Studie erfolgte eine retrospektive Analyse aller Ross-Operationen am Johannes-Kepler-Universitätsklinikum mit Fokus auf Reoperationen am Autograft.

**Methodik** Zwischen 1991 und 2016 erhielten 153 Patienten (29,6 ± 16,6 Jahre; 29,4 % Kinder) eine Ross-Operation mit Implantation des pulmonalen Autografts als freier Wurzelersatz. Das Follow-up ist 98,7 % komplett mit einer mittleren Dauer von 12,2 ± 5,5 Jahren.

**Ergebnisse** Die 30-Tage-Mortalität war 2,0 %. Die echokardiographische Kontrolle bei Entlassung zeigte bei 99,3 % der Patienten keine oder eine nur minimale Aortenklappeninsuffizienz. Die Überlebenswahrscheinlichkeit lag bei 85,4 % nach 20 Jahren. Es trat keine Endokarditis am Autograft auf. Die Freiheit von Reintervention am Autograft lag bei 75,3 % nach 15 Jahren. Die linearisierte Degenerationsrate des Autografts lag bei 2,01 % pro Patientenjahr. Eine Reoperation aufgrund einer aneurysmatischen Dilatation des Autografts war bei 35 Patienten (22,9 %) im Intervall von 11,1 ± 4,6 Jahren nach der Ross-Operation erforderlich. Ein klappenerhaltender Aortenwurzelersatz konnte bei 77 % dieser Patienten durchgeführt werden (17 Yacoub und 10 David-Operationen). Die perioperative Mortalität lag bei 0 %. Im Verlauf war bei 3 Patienten nach Yacoub-Operation aufgrund einer hochgradigen Aortenklappeninsuffizienz ein prothetischer Klappenersatz erforderlich. Zum Zeitpunkt des letzten Follow-up hatten 92 % aller Patienten noch ihre Autograftklappe. Die Freiheit von prothetischem Klappenersatz lag bei 92,1 % nach 15 Jahren.

**Schlussfolgerung** Durch eine David- oder Yacoub-Operation kann die Autograftklappe bei der Mehrzahl der Patienten mit einem Aneurysma der Neoaortenwurzel nach einer Ross-Operation erhalten werden. Diese Reoperationen können mit einer niedrigen Morbidität und Mortalität, einem guten funktionellen Ergebnis und einer geringen Reinterventionsrate durchgeführt werden.

## Periinterventionelle Dynamik der kardialen Reizleitung bei transfemoralem Aortenklappenersatz

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**Hintergrund** Der transfemorale Aortenklappersatz (TAVI) gilt seit Jahren als etablierte Behandlungsoption bei Patienten mit hochgradiger Aortenklappenstenose. Trotz der seit Jahren vorangetriebenen technischen Evolution der am Markt befindlichen Klappenprothesen

ist die Rate an periinterventionellen Reizleitungsstörungen, die eine Herzschrittmacherimplantation erfordern, weiterhin beträchtlich.

**Methodik** Diesbezüglich wird im Zuge einer noch laufenden prospektiven klinischen Studie an unserer Abteilung bei PatientInnen, die sich einem transfemoralen Aortenklappenersatz unterziehen, mittels mobilem EP-System (SJM WorkMate Claris 56 System) die Dynamik der AH-, HV- und QRS-Intervalle während unterschiedlicher Prozedurzeitpunkte ermittelt. Dazu ist eine zusätzliche Punktion einer Femoralvene erforderlich, über die ein His-Katheter eingeführt wird. Des Weiteren erfolgt bis zum dritten postinterventionellen Tag ein kontinuierliches Rhythmusmonitoring. Nach Abschluss der Studie sollen die EKG-Veränderungen mit diversen anatomischen und funktionellen Parametern, die vor Prozedurbeginn erhoben wurden, korreliert werden, um mögliche Prädiktoren für das Auftreten signifikanter Reizleitungsstörungen zu erheben.

**Resultate** Bis dato wurden 108 Patienten (66 Frauen, 42 Männer) mit einem mittleren Alter von 80,2 Jahren in die Studie eingeschlossen. Die statische Aufarbeitung der erhobenen Parameter zeigt einen signifikanten Anstieg der infrahisären HV- und QRS-Intervalle sowohl unmittelbar nach Ballondilatation, als auch nach Implantation der Klappenprothese, während die AH-Zeit weitgehend konstant bleibt. Des Weiteren zeigt sich auch an den drei Folgetagen eine signifikante Zunahme der PQ- und QRS-Dauer **(Abb. 6, Tab. 3)**.

**Diskussion** Soweit anhand der publizierten Studienlage bekannt, sind wir das erste Forschungsteam, welches mittels mobilem EP-System die intraprozeduralen Veränderungen am kardialen Reizleitungssystem während transfemoralem Aortenklappenersatz ermittelt. Bis dato wurde dies lediglich mittels eigenständiger EP-Prozeduren vor bzw. nach dem Eingriff durchgeführt. Die vorzeitige Analyse unserer erhobenen Daten nach Rekrutierung von nunmehr 108 Patienten zeigt eine hochsignifikante Beeinträchtigung der infrahisären Reizleitung durch die mechanische Einwirkung am His-Bündel bzw. dem linken Tawara-Schenkel infolge der Ballondilatation und Klappenimplantation. Da es sich bei den angewandten Prothesen um selbst-expandierende Systeme handelt, könnte die radiale Ausdehnungskraft neben einer möglichen Ödembildung am Myokard die Ursache für die Veränderungen der PQ- und QRS-Dauer an den Folgetagen sein. Deren klinische Relevanz spiegelt sich in verzögert auftretenden höhergradigen AV-Blockierungen wider. Ob sich ein Prädiktor für das Auftreten signifikanter periinterventioneller Reizleitungsstörungen herauskristallisiert, wird sich im Zuge der statischen Aufarbeitung nach Abschluss der Studie zeigen.

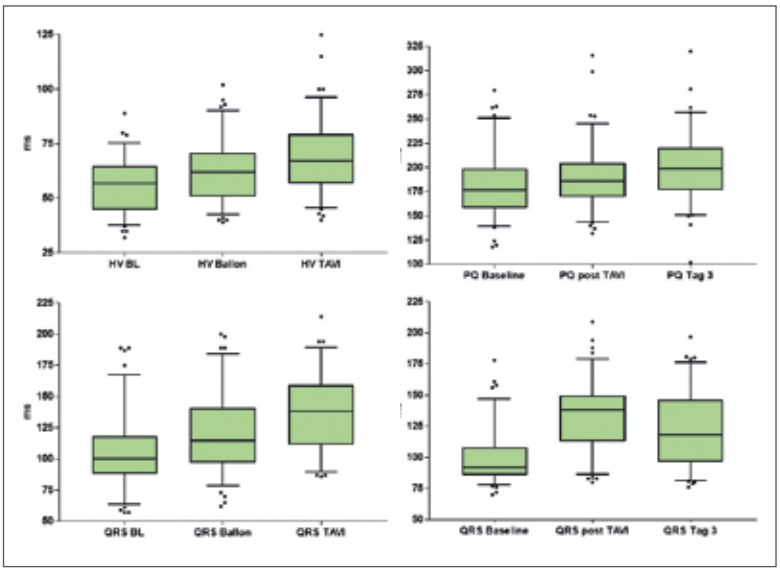


**Abbildung 6:** C. Reiter, et al.

**Tabelle 3:** C. Reiter, et al. Intra- bzw. periinterventionelle Dynamik der kardialen Reizleitung.

| | | | |
|---|---|---|---|
| **AH-Intervall (Intraprozedurale EP-Messung)** | | | |
| #1 | Baseline | 105,4 ± 33,3 ms | |
| #2 | Post Ballondilatation | 102,6 ± 29,8 ms | P = 0,178 (#1 vs. #2) |
| #3 | Post Klappenimplantation | 104,4 ± 29,4 ms | P = 0,164 (#2 vs. #3) |
| #4 | Prozedurende | 105,0 ± 29,6 ms | P = 0,983 (#3 vs. #4)<br>P = 0,723 (#1 vs. #4) |
| **HV-Intervall (Intraprozedurale EP-Messung)** | | | |
| #1 | Baseline | 56,7 ± 14,8 ms | |
| #2 | Post Ballondilatation | 63,2 ± 14,3 ms | P < 0,001 (#1 vs. #2) |
| #3 | Post Klappenimplantation | 69,1 ± 16,6 ms | P < 0,001 (#2 vs. #3) |
| #4 | Prozedurende | 69,8 ± 16,2 ms | P = 0,230 (#3 vs. #4)<br>P < 0,001 (#1 vs. #4) |
| **QRS-Intervall (Intraprozedurale EP-Messung)** | | | |
| #1 | Baseline | 105,8 ± 28,4 ms | |
| #2 | Post Ballondilatation | 120,8 ±32,0 ms | P < 0,001 (#1 vs. #2) |
| #3 | Post Klappenimplantation | 137,6 ± 32,1 ms | P < 0,001 (#2 vs. #3) |
| #4 | Prozedurende | 138,2 ± 32,1 ms | P = 0,681 (#3 vs. #4)<br>P < 0,001 (#1 vs. #4) |
| **PQ-Intervall (12-Kanal-EKG)** | | | |
| #1 | Baseline | 180,9 ± 32,3 ms | |
| #2 | Post TAVI-Prozedur | 190,5 ± 31,5 ms | P < 0,001 (#1 vs. #2) |
| #3 | Postinterventioneller Tag 3 | 200,6 ± 34,3 ms | P < 0,001 (#2 vs. #3)<br>P < 0,001 (#1 vs. #3) |
| **QRS-Intervall (12-Kanal-EKG)** | | | |
| #1 | Baseline | 100,1 ± 21,5 ms | |
| #2 | Post TAVI-Prozedur | 133,5 ±27,5 ms | P < 0,001 (#1 vs. #2) |
| #3 | Postinterventioneller Tag 3 | 122,7 ± 29,5 ms | P < 0,001 (#2 vs. #3)<br>P < 0,001 (#1 vs. #3) |

## Erste Erfahrungen beim Aufbau eines HIS-Bündel-Pacing-Programms

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**Einführung** Die rechtsventrikuläre Stimulation verursacht je nach Stimulationsanteil und Patientencharakteristika bei bis zu 15 % der Herzschrittmacher-Patienten eine Schrittmacher-induzierte Kardiomyopathie. Als Mechanismus wird die durch die Stimulation bedingte linksventrikuläre Dyssynchronie angegeben. Um diese zu verhindern, wird seit Jahren am Konzept des HIS-Bündel-Pacings (HBP) gearbeitet, bei dem die rechtsventrikuläre Stimulationselektrode nicht ins Myokard, sondern direkt in das HIS-Bündel geschraubt wird. Damit sollen eine konzentrische Aktivierung der Ventrikel bewirkt und die deletären Folgen der linksventrikulären Dyssynchronie verhindert werden. Die Technik des HBP wurde und wird durch eine eingeschränkte Steuerbarkeit der Sonden bei der Implantation sowie hohe Reizschwellen des HIS-Bündels im Vergleich zum Myokard erschwert. Mit neuen verfügbaren Tools wie der 4F Schraubelektrode SelectSecure™ Model 3830 mit den entsprechenden Schleusen C315HIS™ oder C304Deflectable™ (Medtronic) kann das HIS-Bündel bei der Implantation leichter erreicht und mit Reizschwellen unter 2,5 V stimuliert werden. Mit dieser Technologie wurde an unserer Institution ein HBP-Programm initiiert.

Ziel dieser Analyse ist es, die Ergebnisse der ersten eigenen Serie von Patienten (P) mit HBP in Hinblick auf Machbarkeit und Sicherheit zu beleuchten.

**Methoden** Eingeschlossen wurden nur P mit Sick-Sinus-Syndrom und niedrigem Wenckebach-Punkt bei der atrialen Stimulation,

um Erfahrungen mit der neuen ventrikulären Sondenposition bei nicht Schrittmacher-abhängigen P zu sammeln. Mit der Helix der SelectSecure™-Elektrode in einer Schleuse wurde dabei mittels kleiner Bewegungen die HIS-Region gemappt, bis am Analysiergerät und einer Elektrophysiologie-Messeinheit ein eindeutiges HIS-Signal nachweisbar war. Dann wurde die Elektrode durch Einschrauben fixiert, die Schleuse in den Vorhof zurückgezogen und die Sensing- und Reizschwellenwerte ermittelt. Waren diese akzeptabel (Impedanz 400–2000 Ohm, Sensing >2 mV, Reizschwelle < 2,5 V@1,0 ms), wurde eine Reizschwelle mit entsprechender Sicherheits-Marge programmiert. Anhand der Breite der stimulierten QRS-Komplexe wurde das Ergebnis als (1) selektives HBP: QRS-Komplexe ident zu denen bei AV-Eigenüberleitung bzw. als (2) para-HBP: QRS-Komplexe breiter als bei AV-Eigenüberleitung definiert.

Sämtliche Prozeduren wurden von einem sehr erfahrenen Implanteur über einen linksseitigen Zugang durchgeführt. Es wurden die Prozedurdauer, Durchleuchtungszeit und periprozeduralen Komplikationen sowie die elektrischen Parameter und klinischen Ereignisse im Follow-up erfasst.

**Ergebnisse** Von Mai bis inklusive Dezember 2018 wurden 8 P (5 weiblich, mittleres Alter 72 ± 8 Jahre) in die prospektive Beobachtung eingeschlossen. Bei allen P gelang es, ein HIS-Potenzial abzuleiten und die Elektrode an dieser Stelle einzuschrauben. Eine stabile Reizschwelle < 2,5 V@1,0ms wurde bei 4 P (50 %) gesehen, während bei den anderen 4 P nach erfolglosen HBP-Versuchen eine septale rechtsventrikuläre Position mit jeweils guten Parametern gewählt wurde. Die mittlere Prozedurdauer betrug 115 ± 32 min, die Durchleuchtungszeit 19 ± 10 min. Bei den 4 P mit HBP waren die mittleren elektrischen Messwerte bei der Implantation: Reizschwelle 1,65 V@1,0ms, Impedanz 728 ± 164Ω, Sensing 7,4 ± 2,7 mV. Der programmierte ventrikuläre Output war bei allen 4 P mit HBP jeweils 3,5 V@0,4ms und führte bei 3 P (75 %) zu selektivem HBP und bei 1 P (25 %) zu para-HBP. Es traten keine peri- oder postinterventionellen Komplikationen – insbesondere keine Sondendislokationen – auf. Bei allen P wurde ein 3-Monats-Follow-up durchgeführt, das stabile elektrische Messwerte (im Trend sinkende Reizschwellen) und keine Komplikationen ergab.

**Schlussfolgerungen** Der Aufbau eines HBP-Programms erfordert neben einer großen Implantations-Expertise sorgfältige Vorbereitung, Material-Know-how und Geduld während der Prozeduren. Die HIS-Region ist über einen linksseitigen Zugang mit den beschriebenen Devices und Techniken gut erreichbar. Limitierend für das Erzielen eines anhaltenden selektiven HBP scheint weniger die Stabilität der Elektroden-Fixation als das Erreichen einer ausreichend niedrigen Reizschwelle zu sein. Die Ergebnisse der ersten Implantationen und vor allem das Potential des HBP rechtfertigen fortgesetzte Bemühungen in Richtung dieser Implantationstechnik.

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