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Kardiologie im Zentrum

Fortbildung der Klinik für Kardiologie und
Internistische Intensivmedizin,
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5.–6. Oktober 2018, Design Center Linz

Abstracts

(in alphabetischer Reihenfolge nach Erstautoren)



Die Preisverleihung.
Foto: © Roman Kneidinger

1. Preis

Determinants of Bioprosthetic Heart Valve Degeneration

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Background Bioprosthetic heart valves are increasingly used for valve replacement therapy. Structural valve degeneration (SVD) remains the major determinant of bioprosthetic valve durability. The present long-term prospective study investigated incidence and mode of SVD, as well as associated factors, using thorough echocardiographic and clinical follow-up.

Methods 502 consecutive patients (73.4 ± 7.9 years; 56.9% female) underwent surgical bioprosthetic aortic (n = 466) or mitral (n = 36) valve replacement between 1994 and 2014. Clinical assessment, transthoracic echocardiography, and laboratory testing were performed at baseline and follow-up. SVD was defined as mean transprosthetic gradient ≥30 mmHg for aortic, ≥ 10mmHg for mitral valves and/or at least moderate valvular regurgitation on echo. Patient prosthesis mismatch (PPM) was defined as an effective orifice area indexed to body surface area ≤ 0.8 cm²/m² for aortic and ≤ 1.2cm²/m² for mitral valves.

Results Patients were followed for a median of 112.3 (Interquartile range [IQR] 57.7–147.7) months. 78 patients (19.0%; 4.7% per valve year) developed SVD after a median of 31.0 months (IQR 10.0–91.9; stenosis: n = 51; regurgitation: n = 17; or both: n = 10). Factors associated with SVD by multivariable regression analysis: serum creatinine > 1.27 mg/dl (OR = 2.038; 95% confidence interval [CI] 1.064–3.904; p = 0.032), PPM (OR = 2.262; 95% CI 1.241–4.123; p = 0.008), and porcine tissue valves (OR = 2.474; 95% CI 1.394–4.390; p = 0.002). Median delay to SVD was shorter in the elderly (< 70 y: 47.4 months, 70–80 y:40.5 months, > 80 y:22.0 months; p = 0.005). By multivariable Cox regression, age, diabetes, concomitant CABG, and creatinine (p < 0.05) were significantly associated with mortality.

Conclusions Based on echocardiography, every fifth patient developed SVD within 9 years of surgical bioprosthetic heart valve replacement. SVD was associated with PPM, renal impairment, and use of porcine tissue valves. Patients younger than 70 were not affected by faster SVD (Figure 1).

2. Preis

Significant Intraprocedural Alterations of HV- and QRS-Intervals during Transcatheter Aortic Valve Replacement

C. Reiter¹, T. Lambert¹, M. Grund¹, A. Nahler¹, S. Schwarz¹, H. Blessberger¹, J. Kellermaier¹, D. Hrnčić¹, D. Kiblböck¹, K. Kammler¹, C. Sautner¹, M. Patrasso¹, C. Steinwender^{1,2}

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3. Preis

Pharmacologically Active Storage Solution for the Preservation of Myocardial Function in Transplantation

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Introduction Heart transplantation is often the last life-saving therapeutic resort to an otherwise deadly condition for many patients with severe heart failure. An important factor for a successful transplantation is the quality of the donor heart. A major problem, however, is the limited extracorporeal durability of the donor heart during ischemia due to hypoxia and lack of nutrients. Further harmful influences to which the graft is exposed to include ischemia-reperfusion injury (IRI), as well as other factors such as acute and chronic allograft vasculopathy.

Therefore, the aim of this study was to investigate a pharmacologically active storage solution to protect heart grafts from ischemic injury caused by prolonged cold ischemia and IRI in a model of murine heterotopic cervical heart transplantation.

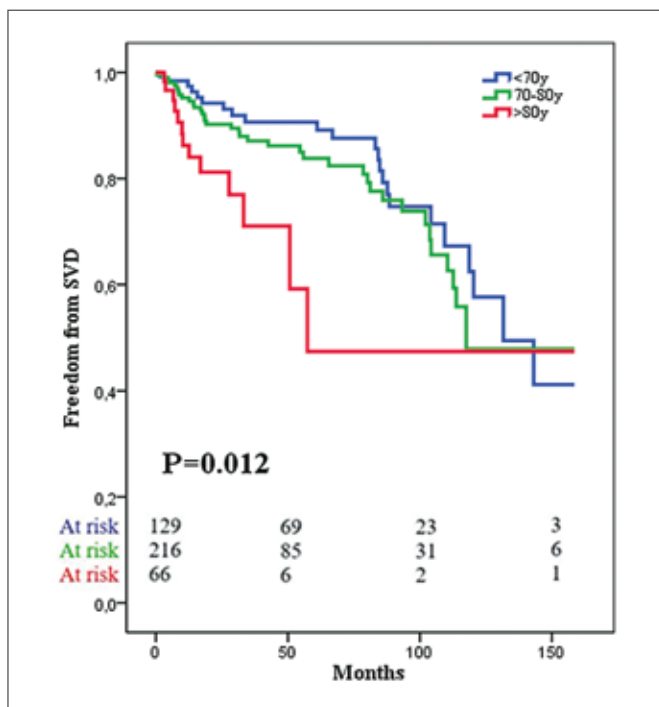


Figure 1. C. Nitsche et al. Kaplan-Meier plot. Freedom from structural valve degeneration according to age. SVD indicates structural valve degeneration; y, years;

For this purpose 5'-methoxyoleigin (5'-ML), a secondary plant metabolite from Edelweiss was chosen. 5'-ML has been shown to be a promising candidate for therapeutic application in cardiovascular diseases [1, 2].

Methods Heart transplantations were carried out on non-genetically altered male inbred C57BL/6J mice using a cuffed heterotopic cervical technique as described by Oberhuber et al. [3]. Transplant recipients encompassed four groups with grafts which were kept in HTK-storage solutions with 30 μ M 5'-ML or DMSO (solvent control) under cold ischemia for 6 or 9 hours before implantation to induce significant levels of IRI. On day 10 after transplantation, graft recipients were sacrificed and hearts were harvested for histological analysis.

Results and Discussion Histological analysis showed that the addition of 5'-ML to the preservation solution significantly reduced fibrosis after 9h of cold ischemia. This suggests less ischemia-induced necrosis and diminished cardiac remodeling, indicating protection of the myocardial tissue from major reperfusion injury caused by prolonged ischemia. Additionally, the 5'-ML treated group displayed an accelerated weight gain after 9 hours of cold ischemia compared to the control group. This might be a systemic effect due to decreased IRI and reduced cardiac remodeling.

Conclusion The obtained data point to significant protection against IRI by 5'-ML, which leads to an extension of the tolerance time against ischemia. Thus this compound may be a useful additive in graft preservation solutions preventing ischemic damages to the heart and possible other organs. Further applications could be in the context of other ischemic events like myocardial infarction, or warm ischaemia during surgery.

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Speckle Tracking Derived Longitudinal Strain – Validation and Influence of Scanner Settings

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Introduction Speckle tracking based strain analysis is on the verge of clinical routine for the assessment of left ventricular function. However, it is unclear if the methodology is affected by factors other than myocardial mechanics. We evaluated the impact of ultrasound machine settings on the quality and reliability of strain measurement in routine clinical practice.

Materials and Methods We recruited 35 consecutive patients with various degrees of left ventricular function and cardiac diagnoses. In each patient the four chamber view was recorded several times with different ultrasound settings (modification of gain, frame rate, depth, and transducer frequency) with a commercially available ultrasound imaging system (Vivid 7; GE Healthcare). In addition, inter- and intra-observer variability was assessed. Global longitudinal peak systolic strain (GLPSS) values were calculated offline (EchoPac[®] software, GE Healthcare). For each modified variable, we estimated a linear regression model with a random intercept and a random slope. The two observers were compared via Bland-Altman analysis.

Results Ejection fraction ranged between 10% and 76% and correlated well with GLPSS ($r = -0.70$). Modification of gain (mean effect: -0.019% , 95% CI: -0.112% to 0.073% , p -value = 0.680) and frame rate (mean effect: 0.002% , 95% CI: -0.011% to 0.015% , p -value = 0.747) exhibited no effect on measurements of GLPSS. Conversely, a higher depth setting led to slightly higher GLPSS values (mean effect:

-0.156% , 95% CI: -0.239% to -0.072% , p -value < 0.001). Higher harmonic and fundamental imaging transducer frequencies were associated with lower GLPSS values (mean effect: 1.102% , 95% CI: 0.605% to 1.600% , p -value < 0.001 , and mean effect: 0.522% , 95% CI: 0.172% to 0.872% , p -value = 0.003 , respectively). Bland-Altman analysis did not indicate statistically significant differences in variances between two measurements of a single observer (observer A: mean difference: -0.200% , 95% CI: -0.609 to 0.209 , and observer B: mean difference: -0.103% , 95% CI: -0.871 to 0.664 , respectively) or between measurements of two skilled observers in the same patient (observer A vs. B: mean difference: -0.527% , 95% CI: -1.116% to 0.062%).

Conclusion Speckle tracking based GLPSS analysis provides reproducible and robust parameters of left ventricular function if extreme depth and transducer settings are avoided.

MIMICRY – Monocenter Investigation Micra[®] MRI Study – Feasibility Study of the MRI Compatibility of a Leadless Pacemaker System

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 *Deceased.

Background As in vivo real-life data are still scarce, we conducted a study to assess the safety and feasibility of cardiac MRI in patients with a leadless pacemaker system.

Methods In this prospective non-randomized interventional trial, we enrolled 15 patients with an MRI conditional Micra[®] leadless pacemaker system to undergo either a 1.5T or 3.0T cardiac MRI scan. Clinical adverse events as well as device parameters such as pacing threshold, sensing, impedance and battery life were assessed at baseline as well as 1 and 3 months after the scan. Device parameter changes between different time points were tested for statistical significance and compared with pre-set cut-off values.

Results Fourteen patients underwent the cardiac MRI scan according to the protocol as well as the scheduled follow-up visits. One participant was excluded from analysis, as the MRI scan was not possible because of severe claustrophobia. Other clinical events did not occur during the scan and the follow-up period. Device parameters stayed stable and changes during the observational period were statistically not significant (changes vs. baseline: pacing threshold: 0.01 ± 0.05 V, $p = 0.308$, 0.01 ± 0.07 V, $p = 0.419$, sensing: -0.15 ± 1.11 mV, $p = 0.658$, -0.19 ± 1.17 mV, $p = 0.800$, impedance: -7.86 ± 30.7 Ohm, $p = 0.447$, -7.86 ± 25.77 Ohm, $p = 0.183$, at 1- and 3-month follow-up, respectively). Parameter changes were not statistically different between patients who underwent imaging at 1.5T ($n = 7$) or 3.0T ($n = 7$).

Conclusion In our set of patients with a Micra[®] leadless pacemaker, cardiac magnetic resonance imaging at either 1.5T or 3.0T proved feasible and safe with no relevant changes in device parameters within 3 months of follow-up.

Laser-Structured and Anodized Ring around Ti Cylinders as barrier against Overgrowth by Fibroblasts

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The invention of new miniaturized and smart medical devices continues in all medical fields, including miniaturized pacemakers which

are directly implanted into the heart. These pacemakers with a Ti casing may have to be removed after several years and shall therefore not be completely overgrown by the cells or scar tissue after implantation [1]. Scar tissue is mainly formed by fibroblast cells and extracellular matrix proteins like collagen produced by them. Suppression of fibroblast growth at Ti surfaces could be achieved by 790 nm fs laser-ablation creating self-organized sharp spikes with dimensions in the 10 µm-range which are superposed by fine sub-µm parallel ripples. Compared to flat surfaces, the cell density on the microstructures was significantly lower, the coverage was incomplete and the cells had a clearly different morphology. The best results regarding suppression of cell growth were obtained on spike-structures which were additionally electrochemically anodized under acidic conditions. Cell cultivation with additional shear stress could reduce further the number of adherent cells [2]. When flat Ti cylinders with a similar diameter (8 mm) as the miniaturized pacemakers (7 mm) were placed upright in a culture of murine fibroblasts, a multi-layer cell growth up to a height of at least 1.5 mm occurred within 19 to 22 days. We could demonstrate that a laser-structured and anodized ring around the Ti cylinder surface, beginning at a height of 0.5 mm, is an effective way to create a barrier that mural fibroblasts were not able to overgrow within this time. These results are very promising for future miniaturized pacemakers with controlled ingrowth into the heart wall.

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Adherence to Inhaled Therapy and Mortality in COPD

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Rationale COPD (chronic obstructive pulmonary disease) is characterized by non-reversible airflow limitation. Currently, no cure is available, and treatment aims to delay disease progression, to treat exacerbations, and to improve quality of life. Adherence to inhaled therapy is supposed to have a significant impact on treatment outcomes. Therefore, we aimed to investigate the adherence to COPD therapy and its association with mortality.

Methods A retrospective analysis of all patients hospitalized for COPD in a tertiary care hospital in Linz, Austria, in 2012 was performed to examine the association between adherence to inhaled therapy and mortality 36 months after discharge. Adherence to inhaled therapy was defined according to the percentage of prescribed inhalers dispensed to the patient. A patient was classified as non-adherent if less than 50% of the prescribed inhalers were dispensed in a pharmacy, i.e. the patient did not collect them. Drug dispense, and mortality data was recorded by the Upper Austrian Health Insurance. Patients with incomplete data, patients, who died within 6 months of the start of follow-up, and patients using only a short-acting bronchodilator on demand were excluded. Patients were classified into mild (post-bronchodilator FEV1 ≥ 50% predicted, GOLD 1–2) and severe COPD (FEV1 < 50%, GOLD 3–4).

Results Data of all 592 patients discharged was analyzed. 263 patients were excluded due to missing data (n = 116), death within 6 months (n = 82) or short-acting bronchodilators only (n = 65).

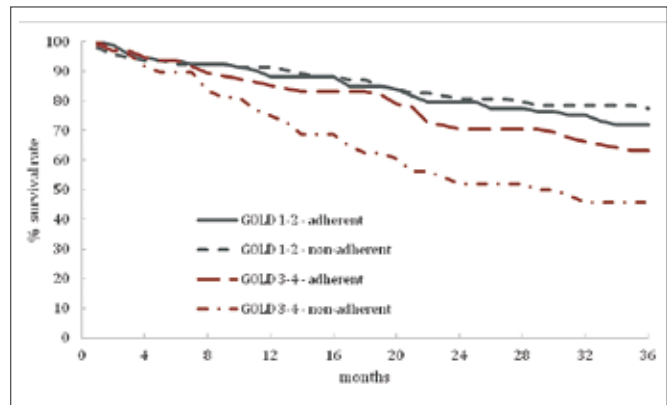


Figure 2. A. Horner, et al.

Among the remaining 329 patients aged 67.0 ± 0.6 years, 66.0% were men, 35.9% current and 56.8% former smokers. 43.5% were diagnosed with severe COPD (GOLD 3–4). There was no significant difference in age between severe and mild COPD ($p = 0.523$).

A total of 57.1% of all patients were regarded as adherent, significantly more in the group of severe COPD (66.4% vs. 50.0%, respectively; $p = 0.003$; OR = 2.02 [1.26; 3.23]).

After 36 months, 66.9% of all patients were still alive, significantly less in the group of patients with severe COPD (56.6% vs. 74.7%, respectively; $p < 0.001$).

For mild COPD, there was only a small difference in survival according to adherence (72.0% vs. 77.4%; $p = 0.496$). However, in severe COPD, adherent patients had significant higher survival rates (62.1% vs. 45.8%; $p = 0.030$).

Conclusion Adherence to inhaled therapy in severe COPD is significantly associated with higher survival rates after 36 months of hospital discharge (Figure 2).

Ressourcenplanung und medizindidaktische Konsequenzen – Unterschiedliche Lektoren-Anzahl und Auswirkungen auf den Studienerfolg am Beispiel der studentischen Lehre an der Klinik für Kardiologie des Kepler Universitätsklinikums Linz

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Hintergrund Im Herbst 2014 wurde an der Johannes-Kepler-Universität Linz eine Medizinische Fakultät gegründet. Die Aufgabe, neben dem klinischen Alltag einen studentischen Lehrbetrieb zu implementieren, stellt eine große organisatorische Herausforderung dar, da Lektoren zeitgerecht von ihrer klinischen Tätigkeit freigestellt werden müssen, um die Agenden des Lehrbetriebs wahrnehmen zu können.

Methodik Im März 2018 wurden die Studierenden der Humanmedizin im 3. Studienjahr für das Seminar „Falldemonstrationen kardiovaskulärer Erkrankungen“ in 2 Gruppen aufgeteilt. Eine Gruppe (G1) wurde während des Seminars von verschiedenen Lektoren unterrichtet, während die zweite Gruppe (G2) nur von einem einzigen Lektor betreut wurde. Im Anschluss an das Seminar wurden ein Fragebogen und die Prüfungsergebnisse der Studierenden ausgewertet. Als Endpunkte unserer Studie wurden dabei die Evaluation der Lehrveranstaltung durch die Studierenden, die Notenverteilung, die Zeitdauer bis zur Beantwortung der Prüfungsfragen und ein Leistungs-Score der Abschlussprüfung (Punkte pro Minute) definiert.

Ergebnisse Die Auswertung des Fragebogens ergab, dass die Studierenden die Lehrveranstaltung insgesamt sehr gut bewertet haben und es in den Kategorien „Aktives Anwenden von Wissen anhand von Fallbeispielen“ (Note 1,3; $p = 0,347$) und „Planung und Aufbau

der Lehrveranstaltung“ (Note 1,1; $p = 0,208$) keine statistischen Unterschiede gab.

In der Kategorie „Rahmenbedingung und Atmosphäre während der Lehrveranstaltung“ wurde die G2 statistisch signifikant besser bewertet ($p = 0,015$). Die Zeitdauer bis zur Abgabe der Abschlussprüfung und der Leistungs-Score waren in der G2 ebenfalls signifikant besser (G1: $49,1M \pm 14,8$ min vs. G2: $41,8 \pm 10,6$ min; $p = 0,045$ und G1: $0,7 \pm 0,35$ vs. G2: $0,793 \pm 0,25$; $p = 0,052$). Bei der Notenverteilung selbst fanden sich statistisch keine Unterschiede ($p = 0,469$).

Schlussfolgerung Die Ergebnisse unserer Studie belegen einen tendenziell besseren Studienerfolg jener Studierenden, die im Seminar nur von einem Lektor unterrichtet wurden. Die insgesamt hohe Bewertung beider Gruppen spiegelt das hohe Engagement des gesamten Lektorenteam wider. Insgesamt erscheint es zudem organisatorisch einfacher, einen Lektor für die Dauer der Lehrveranstaltung von seinen klinischen Aufgaben zu entlasten, als verschiedene Lektoren abwechselnd.

Implementierung eines universitären Lehrbetriebs im Rahmen der Neugründung einer Medizinischen Fakultät am Beispiel einer kardiologischen Klinik

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Problemstellung Im Herbst 2014 wurde an der Johannes-Kepler-Universität Linz eine Medizinische Fakultät gegründet. Die Herausforderung, einen Lehrbetrieb mit stufenweise steigenden Studierendenzahlen an den klinischen Abteilungen des Kepler Universitätsklinikums zu implementieren, soll anhand der Klinik für Kardiologie dargestellt werden.

Projektbeschreibung Im dritten Studienjahr des Bachelorstudiums Humanmedizin ist die Abhaltung eines 4-Wochen-Moduls „Erkrankungen des kardiovaskulären Systems“ vorgesehen. Für die Planung und Implementierung dieses Moduls wurde eine Analyse mittels „conceptual framework of Force Field Analysis by Kurt Lewine“ durchgeführt und anschließend ein Aktionsplan erstellt.

Ergebnisse Folgende „Driving Forces“ konnten identifiziert werden: intrinsische Motivation einiger Mitarbeiter, Reputation der Abteilung für Kardiologie, akademische Karriereoptionen. Dem gegenüber standen folgende „Restraining Forces“: limitierte zeitliche Ressourcen, fehlende Expertise, fehlender finanzieller Anreiz.

Der anschließend erstellte Aktionsplan umfasst 3 Phasen. In der ersten Phase wurde eine Arbeitsgruppe bestehend aus 4 Kardiologen gegründet und ein erster Lehrplan für das Modul erstellt. Im Anschluss wurde dieser von der Arbeitsgruppe mit konkreten Inhalten gefüllt und erstmals abgehalten.

Der Fokus der zweiten Phase besteht in einer personellen Erweiterung des Lehrteams innerhalb der kardiologischen Abteilung sowie der Professionalisierung eines Mitarbeiters durch Absolvierung eines MME-Lehrgangs. In der dritten Phase wird der Pool der Lektoren weiter vergrößert und deren didaktische Ausbildung abgeschlossen, um im Vollbetrieb 300 Studierende pro Jahr auszubilden.

Schlussfolgerung Die Implementierung eines Lehrbetriebs stellt eine hohe organisatorische und personelle Herausforderung im klinischen Alltag dar. Mitarbeitermotivation und -einbindung ist ein zentraler Erfolgsfaktor.

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Quantification of Fluid Status using Bioelectrical Impedance Spectroscopy: A Step Towards Personalized Medicine in Valvular Heart Disease

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Background Volume overload is a main cause for chronic disease burden in patients with valvular heart disease (VHD). Fluid overload requiring hospitalization is not only associated with high mortality rates but also a major economic challenge for the healthcare system. So far, clinical assessment of fluid status is limited to presence of leg edema, distension of jugular veins, progression of dyspnoea, or weight gain, lacking both specificity and reliability.

Bioelectrical impedance spectroscopy (BIS) is a validated non-invasive way to assess fluid status in patients undergoing haemodialysis. However, the usefulness of BIS in VHD patients has not been studied so far.

Methods Patients with moderate or severe VHD by transthoracic echocardiography were invited to undergo fluid status assessment using BIS at baseline and were prospectively followed. Patients with clinically overt cardiac decompensation were excluded. The primary end-point was a composite of heart failure requiring hospitalization and cardiovascular death. Kaplan-Meier estimates and multivariable Cox-regression analysis were used to identify factors associated with outcome. This study was registered at clinicaltrials.gov (NCT03372512).

Results 164 (53% female, 72 ± 13 years) were included. 39.0% suffered from mitral regurgitation, 29.3% from aortic stenosis, and 27.4% from tricuspid regurgitation. The remaining 4.3% were patients with aortic regurgitation, mitral stenosis, or combined lesions.

The median of overhydration (OH) was +0.7 liters and patients were stratified by this cut-off into two groups. There was no association between fluid status and comorbidities like diabetes, arterial hypertension, coronary artery disease, the type of valve lesion, renal function, left ventricular, or left and right ventricular. Interestingly, NYHA class did not correlate with fluid status ($p = 0,333$). However, NT-proBNP levels were significantly elevated in patients with OH $\geq 0,7$ liters (7228 ± 7798 vs 3680 ± 4897 ng/l, $p < 0,001$). A total of 38 events (23.3%) occurred during a follow-up of 16 ± 11 weeks.

Patients with a fluid overload were more likely to experience an event (32.9% in OH $\geq 0,7$ liters vs 14.3% in OH $\leq +0,7$ liters; log-rank, $p = 0,009$). By simple Cox-regression analysis, previous myocardial infarction, NT-proBNP levels, renal function, and fluid status were associated with outcome. In a multivariable model, only fluid status remained significantly associated with outcome within these parameters.

Conclusion Quantitative assessment of fluid status using BIS is significantly associated with cardiovascular events in patients with VHD and outperformed NT-proBNP as a predictor of outcome in our cohort. Routine use of this non-invasive technique could help to adjust diuretic treatment and reduce disease burden.

Von Willebrand Factor Multimer Ratio for the Differentiation between True-Severe and Pseudo-Severe Low-Flow, Low-gradient Aortic Stenosis

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Background Subclassification of low-flow, low-gradient (LF/LG) aortic stenosis (AS) into a true-severe (TS) and a pseudo-severe (PS) subform bases on dobutamine stress echocardiography (DSE) and multi-detector computed tomography (MDCT). However, uncertainty about stenosis severity frequently persists even after DSE and MDCT, therefore, there is a need for a biomarker-based discrimination to expand the diagnostic portfolio. Unfortunately, valueable parameters have not been identified so far.

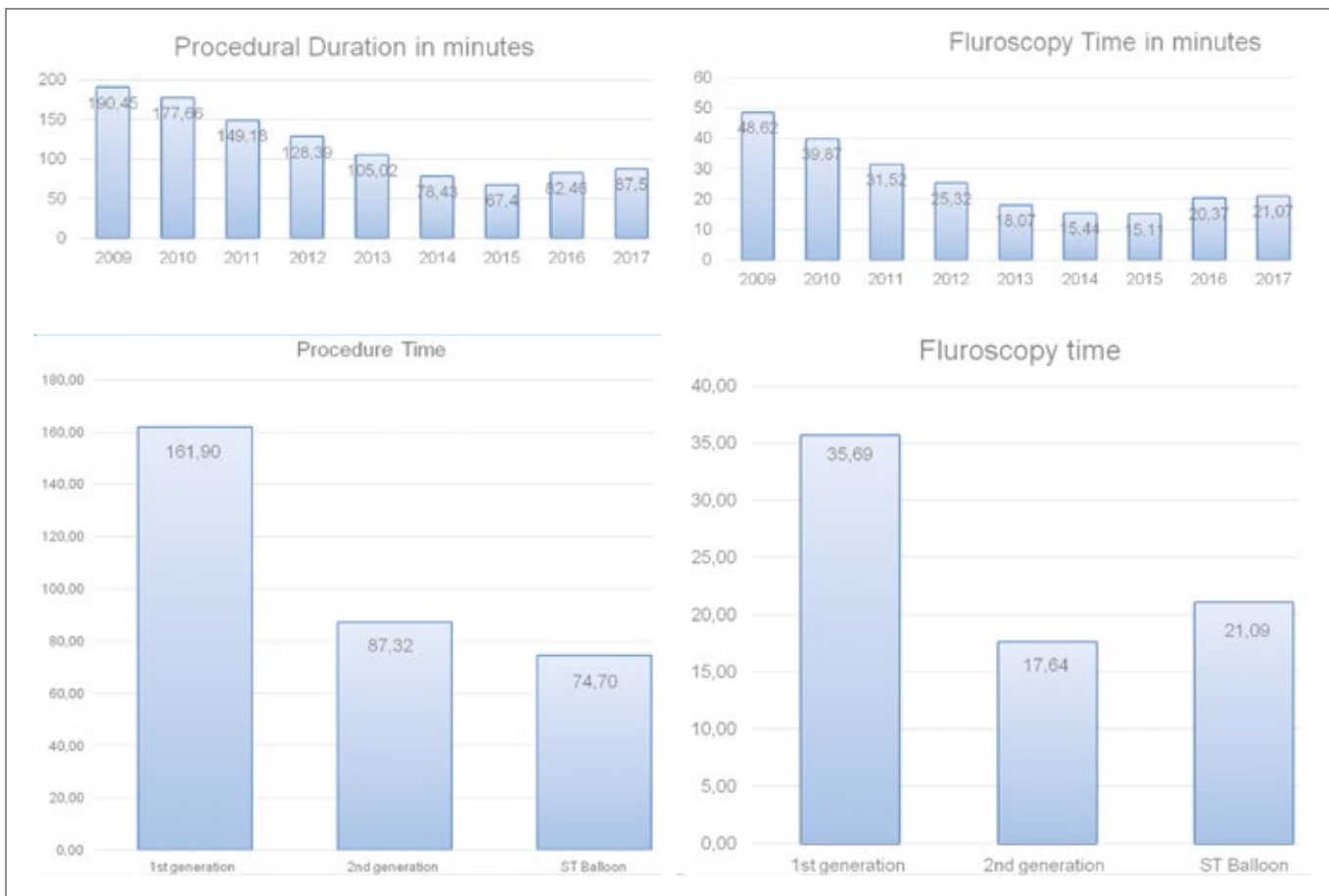


Figure 3. A. Nahler, et al.

Shear-stress induced degradation of high-molecular-weight (HMW) von Willebrand factor (VWF) multimers is a frequent phenomenon at the site of AS, thus, it might represent a valuable biomarker. The present study analysed the value of HMW VWF multimer ratio for LF/LG AS subcategorization.

Methods Sixty consecutive patients with diagnosis of LF/LG AS (defined by a peak aortic jet velocity < 4m/s + a mean transvalvular pressure gradient < 40 mmHg + an AVA < 1 cm² + a stroke volume index of < 35 ml/m² + left ventricular ejection fraction < 50%) were prospectively recruited and subclassified using DSE and/or MDCT. HMW VWF multimers of all patients were analysed using a densitometric quantification of Western Blot bands and HMW VWF multimer ratio was calculated.

Results Patients were subclassified into TS LF/LG AS (n = 36) and PS LF/LG AS (n = 24) using DSE in 44 patients and MDCT in 16 patients. Patients with PS LF/LG AS showed a mean HMW VWF multimer ratio of 1.07 ± 0.09 while in patients with TS LF/LG AS the mean ratio was 0.82 ± 0.28 ($p < 0.001$). HMW VWF ratio presented a ROC-AUC of 0.780 (95%CI: 0.667–0.894; $p < 0.001$) with a calculated sensitivity of 0.47 (95%CI: 0.30–0.65) and a specificity of 1.00 (95% CI: 0.86–1.00) at the optimal cut-off < 0.91 for diagnosis of the TS subform.

Conclusion The present study introduces HMW VWF multimer ratio as a novel biomarker for LF/LG AS subclassification. HMW VWF multimer ratio identifies patients with a TS pattern without the use of other imaging modalities, and, therefore, may be integrated in an early stage of the diagnostic work-up of patients with LF/LG AS.

Pulmonary Vein Isolation by Cryotechnology in Patients with Atrial Fibrillation – Evaluation of Total Procedure Duration and Fluoroscopy Time in a Long-Term Follow-Up

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Background Atrial Fibrillation (AF) has become the most important supraventricular arrhythmia in the last years. An incidence of 2–3% in adults and the aging population underlines the high clinical relevance of AF concerning a significant higher risk for stroke and death. The relevance of pulmonary vein isolation (PVI) increased in the last years next to pharmacological treatment. Therefore, the ESC Guidelines on the “Management of Atrial Fibrillation” indicated PVI as a treatment option after failure of medical treatment and as first line therapy, mainly in patients with paroxysmal AF on their choice. The data of the Fire and Ice trial published in 2016 by Krum et al. showed, that PVI by cryotechnology (CRYO) was non-inferior to point-by-point ablation performed by radiofrequency technology. The need for only one transeptal puncture and the short duration of the procedure are important advantages of CRYO. However, we have to keep in mind the need for longer fluoroscopy time for navigation of the cryoballoon. Therefore, we performed an analysis of procedure and fluoroscopy time of all patients treated with PVI by CRYO at our department.

Methods All patients with AF treated with PVI by CRYO (Medtronic Cryoballoon®) were analysed due retrograde evaluation of the procedure and fluoroscopy times in dependence of different Cryoballoon catheters and in dependence of different operators.

Cardiac CT for evaluation of pulmonary vein anatomy and transesophageal echocardiography for exclusion of left atrial appendage thrombus were done before PVI. Procedures were performed

under sedanalgesia and all pulmonary veins were treated with at least one freeze, until electrical isolation was achieved. For statistical analysis Graph Pad Prism 7 was used.

Results Since 2009 519 patients were treated for AF with PVI using CRYO. Mean age was 59 ± 10.68 years and 29,09% of patients were female. Main comorbidities were hypercholesterolemia ($n = 345/66.47\%$), hypertension ($n=270/52.02\%$) and coronary artery disease ($n=228/43.93\%$). First generation cryoballoon was used in 145 patients while PVI with second generation cryoballoon was done in 340 patients. The cryoballoon ST catheter was used in 34 patients. In total, the mean procedure and fluoroscopy time for all procedures was 107.42 ± 49.16 and 22.9 ± 13.22 minutes. A first analysis of procedure and fluoroscopy times by the different generations revealed a constant decrease of both over years due to technical improvements of newer generation devices. (First generation cryoballoon: mean procedure time: 161.9 ± 46.73 minutes and mean fluoroscopy time 35.54 ± 14.9 minutes; second generation cryoballoon (mean procedure time: 87.13 ± 30.33 minutes and mean fluoroscopy time 17.62 ± 7.95 minutes, $p < 0.0001$); cryoballoon ST catheter (mean procedure time: 73.16 ± 24.44 minutes and mean fluoroscopy time 20.78 ± 10.07 minutes ($p < 0.0001$)). In a second analysis total procedure and fluoroscopy times were evaluated in dependence of the operators over the last years. Thereby we also found a decrease of both times, as a result of the learning curve of the devices. The procedure duration decreased from 190.4 ± 33.54 minutes in 2009 to 87.5 ± 35.95 minutes in 2017 ($p < 0.0001$) and fluoroscopy time decreased from 48.62 ± 15.4 minutes to 21.07 ± 9.73 minutes in 2017 ($p < 0.0001$).

Conclusion We were able to show a significant decrease of procedure duration and of fluoroscopy time in PVI with CRYO due to improvements of devices and a high operator experience (Figure 3).

Native T1 mapping of the Anterior Right Ventricular Insertion Point is a Strong Predictor of Outcome in Heart Failure Patients with Preserved Ejection Fraction: Insights from a Cardiovascular Magnetic Resonance Study

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Background In pulmonary hypertension (PH), increased afterload for the right ventricle (RV) is reported to induce fibrosis at the RV insertion points (RVIPs), detectable by cardiac magnetic resonance (CMR) using late gadolinium enhancement (LGE). In contrast to LGE imaging, T1-mapping, as a relatively new CMR technique, allows quantitative assessment of myocardial native T1 times and extracellular volume (ECV). However, the prognostic value of T1-mapping and ECV of the RVIPs in heart failure patients is unknown.

Methods We prospectively investigated 167 consecutive patients with heart failure and preserved ejection fraction (HFpEF), a patient population frequently suffering from PH, who underwent CMR including T1-mapping. Of these, 155 (92,8%) underwent right heart catheterization (RHC) for hemodynamic assessment. Native T1-times were measured at the anterior and inferior RVIP and ECV was calculated. The prognostic value of T1-mapping of the RVIPs was investigated by multivariable Cox regression analysis.

Results Native T1-times were 995 ± 73 ms at the anterior and 1040 ± 90 ms at the inferior RVIP and ECV was $30.3 \pm 5.8\%$ and $34.3 \pm 7.7\%$, respectively. RVIP T1 times were correlated with pulmonary artery pressures (PAP), pulmonary artery wedge pressure (PAWP) and right atrial pressure (RAP), by linear regression analysis (p for all < 0.05).

Patients were followed for 43.2 ± 22.6 months. In total, 30 (18.0%) subjects died during follow up. By Kaplan-Meier analyses, T1 times at both RVIPs (log-rank, p -values: 0.002 and 0.039 for anterior and inferior RVIP, respectively) were associated with mortality while for ECV this was only the case for the anterior (log-rank, $p=0.020$), but not the inferior RVIP (log-rank, $p = 0.063$).

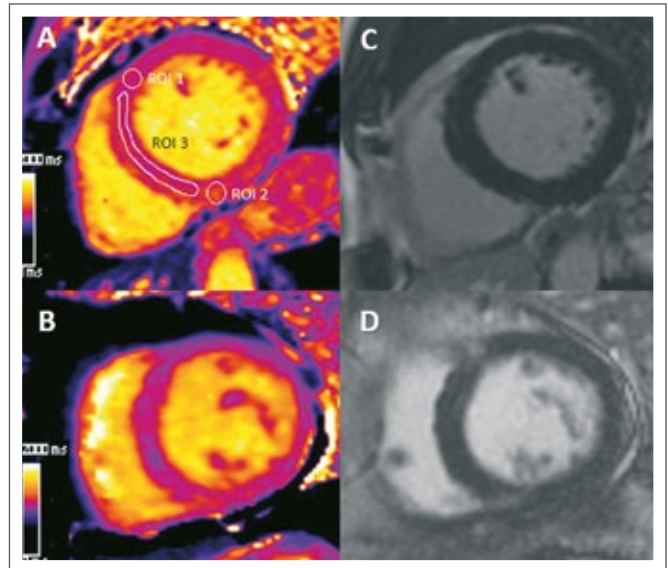


Figure 4. C. Nitsche et al. Panels A and B show precontrast T1 mapping images of 2 HFpEF patients. ROI indicates “region of interest” and demonstrates assessment of RVIPs (ROI 1 and 2 for anterior and inferior RVIP, respectively) and the IVS (ROI 3). Panels C and D show corresponding LGE images. No LGE can be detected in panel C, whereas panel D shows clear LGE in both RVIPs.

By multivariable Cox regression analysis, including imaging, invasive hemodynamic, and clinical parameters, NTproBNP serum levels ($p = 0.021$), sPAP ($p = 0.016$), native T1 time of the anterior RVIP ($p = 0.029$), and RVEF ($p=0.021$) remained significantly associated with outcome.

Conclusions Fibrosis of the anterior RVIP as detected by T1-mapping is associated with pulmonary hypertension, and appears to be independently related with prognosis in HFpEF (Figure 4).

Prevalence of Transthyretin and Immunoglobulin Light Chain Cardiac Amyloidosis in Patients undergoing Transcatheter Aortic Valve Replacement

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Background A significant number of aortic stenosis (AS) patients suffer from coexisting cardiac amyloidosis (CA). Only transthyretin (TTR) CA has so far been described in AS although immunoglobulin light chain (AL) is the most common CA form. The present study evaluated the prevalence of TTR- and AL-CA in AS patients scheduled for transcatheter aortic valve replacement (TAVR).

Methods 106 consecutive patients (81.0 ± 9.0 years; 55.6% female) were screened for CA between October 2017 and June 2018 and were prospectively enrolled. Patients underwent cardiac magnetic resonance imaging (CMR), ^{99m}Tc-DPD bone scintigraphy, serum and urine free light chain assessment and echocardiography with strain analysis. Myocardial biopsy was performed in AL-CA.

Results CA was found in 9.1% ($n = 9$) of patients, including TTR-CA ($n = 7$) and two cases of AL-CA. By CMR, extracellular volume (ECV) and native T1 relaxation time did not differ significantly between AS and CA-AS patients (p for both > 0.05), and typical pattern of late gadolinium enhancement was only present in 26.8% of CA. Furthermore, there were no significant differences with respect to

relative apical longitudinal strain by echocardiography between patients with and without CA (median, 0.87 [IQR 0.84–1.10] vs. 0.80 [IQR 0.74–0.90]; $p = 0.099$). Among patients with AL-CA, 99mTc-DPD bone scintigraphy showed Perugini grade 1 cardiac uptake in one patient and was negative in the other patient.

Conclusions A significant proportion of AS patients scheduled for TAVR suffered not only from TTR-CA but also AL-CA. As our patients were elderly, AL-CA may even be more prevalent in younger patients undergoing surgery for AS.

Neue diagnostische und therapeutische Ansätze bei Kindern mit plastischer Bronchitis nach Fontan-Operation – Darstellung des Lymphgefäßsystems mittels „Lymphatic Imaging“

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Hintergrund Die plastische Bronchitis (PB) stellt eine seltene, aber schwerwiegende Komplikation bei Kindern mit angeborenen Herzfehlern in Form einer „Single Ventricle Physiologie“ und Fontanzirkulation dar, die nach wie vor mit einer sehr hohen Morbidität und Mortalität behaftet ist. Ursächlich werden Veränderungen im Lymphgefäßsystem, ausgelöst durch einen erhöhten zentral-venösen Druck in der Fontanzirkulation, angesehen.

Die kontrastmittelgestützte Magnetresonanztomographie (MR-) Lymphangiographie mit dynamischer Bildakquisition, kurz „Lymphatic Imaging“, stellt seit einigen Jahren eine minimal-invasive Methode zur Darstellung der Lymphgefäße mit viel Potential dar, die nicht nur diagnostische, sondern auch therapeutische Relevanz besitzt. Mittels „Lymphatic Intervention“ können erkannte Lymphfisteln selektiv verschlossen werden.

Fallbericht Wir berichten über einen 4 Jahre alten Knaben mit hypoplastischem Linksherzsyndrom nach extrakardial fenestrierter Fontan-Operation. Dieser entwickelte 3 Monate postoperativ erstmalig rezidivierende Hustenepisodes ohne Fieber und ohne erhöhte Entzündungswerte. Zwei Monate später musste er aufgrund zunehmender Dyspnoe und Hypoxämie stationär aufgenommen werden und es erfolgte bei radiologischem Verdacht auf Pneumonie eine antibiotische Therapie. Erst als der Patient Kasts aushustete, konnte die Diagnose einer plastischen Bronchitis gestellt werden.

Zur weiteren Abklärung erfolgte ein „Lymphatic Imaging“, bei dem zunächst in Narkose ultraschallgezielt inguinale Lymphknoten punktiert und mit Zugängen versehen wurden. Nach nativen MR-Sequenzen erfolgte eine Applikation von Kontrastmittel (KM) in diese Lymphknoten, der Abfluss des KM in das angrenzende lymphatische System wurde in dynamischen MR-Kontrollbildern dokumentiert. So konnten die zugrundeliegenden Lymphfisteln aus dem Ductus thoracicus in Mediastinum und Pleuraraum dargestellt werden. In weiterer Folge können diese mittels „Lymphatic Intervention“ gezielt behandelt werden. Dabei erfolgt ultraschall- und durchleuchtungsgezielt die intrafistuläre Applikation eines Gewebeklebers. Dadurch wird ein selektiver, minimal-invasiver Fistelverschluss möglich.

Diskussion Die plastische Bronchitis stellt eine lebensbedrohliche Komplikation bei Patienten mit Fontanzirkulation dar, die durch einen unkontrollierten Proteinverlust in die Lunge mit konsekutiver Kastbildung und Obstruktion der Atemwege gekennzeichnet ist. Therapeutisch stand bis vor Kurzem eine polypragmatische Therapie (u. a. Sildenafil, inhalative Steroide, inhalative Fibrinolytika) mit nur mäßigem Erfolg im Vordergrund.

Mittels „Lymphatic Imaging“ können nun die zugrundeliegenden Veränderungen des lymphatischen Gefäßsystems dargestellt werden. Dies ist somit ein wesentlicher Baustein in der Therapieplanung.

Erste Ergebnisse der „Lymphatic Interventions“ aus dem führenden Zentrum in Philadelphia (Children’s Hospital of Philadelphia, USA), bei denen Lymphfisteln in die Lunge gezielt mit einem Gewebekleber-Lipiodol-Gemisch verschlossen werden, zeigen vielversprechende Ergebnisse.

Neben einer deutlichen Verbesserung der Beschwerden kommt es zumindest vorübergehend zum Verschwinden der Kasts und somit zu einer deutlichen Besserung der Lebensqualität. Die Beurteilung eines längerfristigen Erfolges bleibt aufgrund der Natur des Eingriffes, der die Ursache nicht zu beheben vermag, abzuwarten.

Zusammenfassung Mittels „Lymphatic Imaging“ können bei Patienten mit PB die zugrundeliegenden anatomischen und funktionellen Veränderungen des Lymphsystems dargestellt werden, um anschließend gegebenenfalls mittels „Lymphatic Intervention“ Lymphgefäße gezielt zu verschließen.

Neue diagnostische und therapeutische Ansätze bei Kindern mit proteinverlierender Enteropathie nach Fontan-Operation – Darstellung des Lymphgefäßsystems mittels „Lymphatic Imaging“

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Hintergrund Die Protein verlierende Enteropathie (PLE) stellt eine seltene, aber schwerwiegende Komplikation mit hoher Morbidität und Mortalität bei Kindern mit angeborenen Herzfehlern in Form einer „Single Ventricle Physiologie“ und Fontanzirkulation dar, bei der es aufgrund eines unkontrollierten Lymphverlustes in den Darm zu Hypoalbuminämie, Hypogammaglobulinämie sowie ausgeprägter Lymphopenie kommt. Ursächlich werden Veränderungen im Lymphgefäßsystem, ausgelöst durch einen erhöhten zentral-venösen Druck in der Fontanzirkulation, angesehen.

Die kontrastmittelgestützte Magnetresonanztomographie (MR-) Lymphangiographie mit dynamischer Bildakquisition, kurz „Lymphatic Imaging“, stellt seit einigen Jahren eine minimal-invasive Methode zur Darstellung der Lymphgefäße mit viel Potential dar.

Fallbericht Wir berichten über einen 19-jährigen Patienten mit „Single Ventricle“ nach Fontan-Operation, der im Alter von 15 Jahren erstmalig aufgrund einer Hypoproteinämie mit Ödemen vorstellig wurde. Im Labor zeigten sich zu diesem Zeitpunkt neben dem Eiweißmangel zusätzlich eine Hypogammaglobulinämie sowie eine Lymphopenie. In der weiteren Abklärung konnte bei unauffälliger Herzfunktion sowohl eine Nierenerkrankung als auch eine Leberfunktionsstörung als Ursache des Proteinmangels ausgeschlossen werden und somit wurde die Diagnose einer PLE gestellt.

Beim „Lymphatic Imaging“ mit Zugang über inguinale Lymphknoten konnte initial, abgesehen von einer kleinen Lymphleckage in die Darmwand, keine nennenswerte Pathologie gefunden werden. Zwei Jahre später gelang es in Zusammenarbeit mit Dr. Y. Dori, durch direkten perkutanen Zugang von Lymphbahnen im Bereich des Leberhilus, Lymphfisteln in den Darm darzustellen. Im Rahmen einer „Lymphatic Intervention“ konnten diese im Anschluss durchleuchtungsgezielt durch Instillation eines Gewebekleber-Lipiodol-Gemischs verschlossen werden.

Bereits innerhalb der ersten Woche nach Intervention kam es zu einem deutlichen Anstieg sowohl des Gesamteiweißes von initial 37,6 g/l auf 50,6 g/l (Referenz: 66–87g/l), als auch des Immunglobulin G von initial 189 mg/dl auf 414 mg/dl (Referenz: 450–1700 mg/dl). Der Patient ist acht Monate nach Intervention aktuell beschwerdefrei, seine Gesamteiweißwerte und auch seine Immunglobulin-G-Werte haben sich mit 61 g/l bzw. 500 mg/dl annähernd normalisiert. Die vorbestehende Lymphopenie wurde von der Intervention hingegen nur wenig beeinflusst (Anstieg von initial 0,26 G/L auf maximal 0,6 G/L [Referenz: 1,00–4,00 G/L] nach der Intervention).

Diskussion Die proteinverlierende Enteropathie stellt eine schwerwiegende Komplikation bei Patienten mit Fontanzirkulation dar, die derzeit nur unzureichend therapiert werden kann.

Das „Lymphatic Imaging“ mit Zugang über die Leistenlymphknoten stellt seit einigen Jahren ein bildgebendes Verfahren zur Darstellung lymphatischer Veränderungen zentraler Lymphbahnen dar, anhand dessen lymphatische Eingriffe geplant werden können. Die bei der

PLE maßgeblichen Veränderungen der hepatischen Lymphwege können durch diesen Zugang nur ungenügend dargestellt werden. Erst durch die gezielte perkutane Punktion von Lymphwegen im Bereich des Leberhilus gelingt es, auch diese Veränderungen zu finden und zu verschließen.

Erste Erfahrungen der „Lymphatic Intervention“ bei PLE zeigen neben einer deutlichen Verbesserung der Hypoproteinämie und Hypogammaglobulinämie auch eine Besserung der Beschwerden und

somit eine deutliche Besserung der Lebensqualität. Die Beurteilung eines längerfristigen Erfolges bleibt aufgrund der Natur des Eingriffes, der die Ursache nicht zu beheben vermag, abzuwarten.

Zusammenfassung Das „Lymphatic Imaging“ stellt eine vielversprechende, minimal-invasive Methode zur Darstellung anatomischer und funktioneller Veränderungen des Lymphsystems dar. Mittels „Lymphatic Intervention“ können abgebildete Lymphfisteln gegebenenfalls selektiv verschlossen werden.

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Mitteilungen aus der Redaktion

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