Introduction: Since the introduction of catheter ablation (CA) of atrial fibrillation (AF), knowledge has increased and techniques and technologies have developed. The aim of our analysis was to investigate, whether these advances resulted in reduced recurrence rates of atrial tachyarrhythmias over time.

Methods: From 2001 to 2014, all patients undergoing a first radiofrequency (RF) CA of AF at our institution were analyzed using our prospective AF registry. Patients were included if an objective follow-up (FU) using serial 7-days-ECGs or a 12-lead-ECG in case of recurrence were available. The follow-up period was 12 months in all patients to allow for comparison over time, and because the recommended long-term ECG FU was most dense within the first year (3, 6 and 12 months). A blanking period of 3 months was applied. Recurrence was defined as any atrial tachyarrhythmia lasting > 30 seconds, irrespective of symptoms.

Results: Out of 883 patients undergoing a first RF CA of AF, 766 (87%) fulfilled inclusion criteria. Paroxysmal AF was present in 529 (69%) and persistent AF in 237 (31%). Mean age of the study population was 58±10 years and 577 (75%) were males. The recurrence rates in patients with paroxysmal and persistent AF are given in the figure. A decrease of recurrence was observed in both groups, but it was more pronounced in patients suffering from paroxysmal AF.

Conclusion: These single center real world data show that all combined advances and developments of RF CA of AF resulted in a decrease of recurrence rates over time within the first year after ablation. This decrease was more pronounced in patients with paroxysmal AF. However, there is still room for improvement.

Disclosure of Interest: H. Servatius Grant/ research support from: Biosense Webster, SJM, Sorin, L. Roten Grant/ research support from: Biosense Webster, BostonScientific, J. Seiler Grant/ research support from: Biosense Webster, BostonScientific, F. Noti: None Declared, V. N. Tran: None Declared, A. Medeiros Domingo Grant/ research support from: Sorin, A. Haeberlin: None Declared, A. Lam: None Declared, J. Fuhrer Grant/ research support from: AstraZeneca, Bayer, Bristol-Myers Squipp, Medtronic, SanofiAventis, Sorin, Biosense Webster, SJM, BostonScientific, Biotronik, H. Tanner Grant/ research support from: Biosense Webster, SJM, BostonScientific, Biotronik
Revised manuscript:

Introduction: Contrast injections to demonstrate pulmonary vein (PV) occlusion are routinely performed during cryoballoon (CB) ablation of atrial fibrillation (AF). The aim of this study was to assess the feasibility and impact of a procedural protocol without routine cine acquisitions and without contrast injections during CB ablation of AF.

Methods: Consecutive patients with paroxysmal AF undergoing pulmonary vein isolation (PVI) using a 2nd generation CB and a single 3-minute freeze approach were studied. Patients undergoing PVI using a novel procedural protocol without routine contrast injections and without cine acquisition (group 1) were compared to a set of consecutive patients undergoing PVI with routine contrast injections and cine acquisitions to demonstrate PV occlusion (group 2). The main outcome measures were the feasibility of the low radiation procedural protocol and the impact of the protocol on radiation dose (dose area product, air kerma), fluoroscopy time, procedure time, mid-term efficacy and safety.

Results: Twenty-four patients (age 61±10 years, ejection fraction 0.61±0.07, left atrial size 40±7 mm) with paroxysmal AF were included. Baseline data were not significantly different between the groups. In group 1, the novel low-radiation protocol was feasible in 11 of 12 patients (92%), and median contrast use was 0 ml (IQR 0-0) compared to 35 ml (IQR 23-48) in group 2 (p<0.0001). Dose area product was 2.0 (1.7-3.8) Gy*cm² in group 1 compared to 7.8 (3.2-16.5) Gy*cm² in group 2 (p<0.05). Total procedure time and fluoroscopy time were 54±9 minutes and 9.3±3.0 minutes in group 1 and 72±10 minutes and 13.8±4.0 minutes in group 2, respectively (all p<0.05). There were no complications in both groups.

Conclusion: Performing CB ablation without using contrast injections and without cine acquisitions to demonstrate PV occlusion is feasible in the majority of patients and is associated with nearly 4-fold decrease in radiation exposure.

Disclosure of Interest: M. Kühne Grant/ research support from: Biosense Webster, Consultant for: Bayer, Daiichi-Sankyo, Paid Instructor for: Medtronic, S. Knecht: None Declared, T. Reichlin: None Declared, A. Mühl: None Declared, B. Schaeer: None Declared, S. Osswald: None Declared, C. Sticherling: None Declared

OR02
2. Pacemaker, defibrillator and electrophysiology
Reduction of radiation exposure during cryoballoon ablation of atrial fibrillation
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1University of Basel, Basel, Switzerland

Introduction: Contrast injections to demonstrate pulmonary vein (PV) occlusion are routinely performed during cryoballoon (CB) ablation of atrial fibrillation (AF). The aim of this study was to assess the feasibility and impact of a procedural protocol without routine cine acquisitions and without contrast injections during CB ablation of AF.

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2. Pacemaker, defibrillator and electrophysiology
Catheter ablation of ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy – experience of a tertiary care center

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Introduction: Sustained Ventricular Tachycardia (VT) is common in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC/D), and associated with frequent ICD interventions, hospitalizations, and reduced quality of life. Antiarrhythmic drugs are not always effective in suppressing ventricular arrhythmias in ARVC/D.

Aim: We assessed outcomes of radiofrequency catheter ablation (RFA) for VT in a single-center cohort of patients with ARVC/D.

Methods: All RFA procedures addressing VT performed in our tertiary-care center between 1998 and 2015 in 40 patients (49±16 years of age; 83% male) with definite (n=32) or borderline (n=8) ARVC/D were analyzed.

Results: 71 RFA procedures using a 3D mapping system were performed (mean 1.8 per patient), of these 55% (n=39) using an endocardial, 34% (n=24) using a combined endo-epicardial, and 11% (n=8) using an epicardial approach (table). VT was inducible in 86% of patients. In 44% of ablations, >1 sustained VT was inducible, and multiple VT morphologies (mean 1.5±1) were common (38%). The mean cycle length of induced VT was 351±78ms. Most VT had a LBBB morphology and superior axis, correlating with the subtricuspid area as the most frequent VT exit site. Although fibro-fatty infiltration typically begins subepicardially, an endocardial substrate with low voltage (bipolar <1.5 mV) and fragmented/late potentials was found in the majority (55%).

RFA was successful (defined as abolishment of all inducible sustained VTs) in 86%, and partially successful (defined as abolishment of all clinical VTs) in 10%. 3 procedures on two different patients were not successful. VT ablation was generally safe with 1 (1.4%) pericardial tamponade occurring after epicardial puncture, and 9 minor complications (pericardial effusion n=2, mild pericarditis n=4, mild femoral hematoma n=3). The number of sustained VT significantly decreased after RFA compared to before RFA (27±38 vs. 4±12, p<0.05). The percentage of patients on antiarrhythmic drugs did not change before and after RFA (93% vs. 90%, p=ns).

Picture/Graph:
**Conclusion:** RFA is an effective strategy to reduce VT burden in patients with ARVC/D. Although the pathologic process begins in the subepicardium, the majority of patients referred for VT ablation has rather advanced disease, and thus presents with an endocardial substrate amenable to endocardial RFA. Endocardial RFA has a high acute success rate, potentially obviating the need for an epicardial approach in some of these patients.

**Disclosure of Interest:** None Declared

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**Abstract - Table. Electrophysiologic data**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablation procedures</td>
<td>71</td>
</tr>
<tr>
<td>&gt; endocardial</td>
<td>39 (55%)</td>
</tr>
<tr>
<td>&gt; epicardial</td>
<td>8 (11%)</td>
</tr>
<tr>
<td>&gt; endo- &amp; epicardial</td>
<td>24 (34%)</td>
</tr>
<tr>
<td>Number of VTs induced</td>
<td></td>
</tr>
<tr>
<td>&gt; 0</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>&gt; 1</td>
<td>30 (42%)</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>13 (18%)</td>
</tr>
<tr>
<td>&gt; ≥3</td>
<td>18 (26%)</td>
</tr>
<tr>
<td>Only PVCs</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Mean cycle length of induced VT (ms)</td>
<td>351±78</td>
</tr>
<tr>
<td>Induction method including</td>
<td></td>
</tr>
<tr>
<td>&gt; Extrastimuli</td>
<td>35 (75%)</td>
</tr>
<tr>
<td>&gt; High-dose isoprotensol ± burst pacing</td>
<td>6 (8.3%)</td>
</tr>
<tr>
<td>&gt; Spontaneous</td>
<td>6 (8.3%)</td>
</tr>
<tr>
<td>&gt; Multiple induction methods</td>
<td>0 (0.3%)</td>
</tr>
<tr>
<td>VT morphology including</td>
<td></td>
</tr>
<tr>
<td>&gt; LBBB inferior axis</td>
<td>12 (18%)</td>
</tr>
<tr>
<td>&gt; LBBB superior axis</td>
<td>18 (28%)</td>
</tr>
<tr>
<td>&gt; RBBB inferior axis</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>&gt; RBBB superior axis</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>&gt; Multiple separate morphologies</td>
<td>25 (38%)</td>
</tr>
<tr>
<td>&gt; PVCs only</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Treatment duration (minutes)</td>
<td>271,0±100,7</td>
</tr>
<tr>
<td>Radiation time (minutes)</td>
<td>17,1±12,5</td>
</tr>
<tr>
<td>Dose of radiation (cGy x cm²)</td>
<td>3009,8±3173,2</td>
</tr>
<tr>
<td>Amount of contrast agent (ml)</td>
<td>76,6±79,1</td>
</tr>
<tr>
<td>Amount of RFA applications</td>
<td>19,2±15,0</td>
</tr>
</tbody>
</table>

Values are means ± standard deviation and numbers (percentages).
Abbreviations: VT, Ventricular tachycardia; PVC, Premature ventricular contraction; LBBB, Left bundle branch block; RBBB, Right bundle branch block; RFA, Radiofrequency ablation
Introduction: Numerous irrigated ablation catheters are currently available for the ablation of atrial flutter (AFL). The aim of this study was to compare 3 different irrigated-tip catheters used for ablation of AFL.

Methods: An observational dataset of consecutive patients referred for radiofrequency (RF) ablation of AFL from two centers was analysed using a propensity score weighting method to reduce potential confounding. Two analyses were performed: 1) A comparison of the established irrigated platinum-iridium tip catheter (Thermocool, group 1) to the pooled group of the more recent designs of a porous irrigated (56 irrigation holes) platinum-iridium tip catheter (Thermocool SF, group 2) and a dedicated irrigated Gold-tip catheter (AlCath Flutter Gold, group 3) (group 1 vs. pooled group 2 & 3), and 2) a second comparison between the newer catheters (group 2 vs. group 3). The primary endpoint was acute efficacy (net RF time) to achieve complete block across the cavo-tricuspid isthmus. Secondary endpoints were total procedure time, complications, and recurrence of AFL.

Results: 219 consecutive patients (age 69±10 years, 27% female) with typical AFL were included in the analysis. Net RF time to achieve complete block was neither significantly different between group 1 (793±503 s) and pooled group 2 & 3 (798±534) (p=0.733) nor between group 2 and group 3 (807±563 vs 726±458 s; p=0.425). Total procedure time was not significantly different between group 1 (70±27 min) and pooled group 2 & 3 (73±31) (p=0.195) nor between group 2 and group 3 (76±35 vs 70±26 s; p=0.183). There were no major complications in the 3 groups. During a follow-up of 6 months, recurrence of AFL occurred in 1 of 66 (2%) in the Thermocool group, in 0 of 65 (0%) in the SF group, and in 2 of 88 (2%) in the Gold group (p=ns).

Conclusion: In a triple propensity weighted comparison of irrigated-tip catheters for ablation of AFL, acute and chronic efficacy of Gold-tip vs. standard platinum-iridium vs. porous-tip platinum-iridium catheters were comparable.

Disclosure of Interest: S. Knecht: None Declared, F. Burch: None Declared, A. Mühl: None Declared, T. Reichlin: None Declared, U. Celikyurt: None Declared, B. Schaer: None Declared, D. Altmann: None Declared, P. Ammann: None Declared, S. Osswald Grant/ research support from: Medtronic, Boston Scientific, Biotronik, and St Jude Medical, Speakers bureau: Medtronic, Boston Scientific, Biotronik and St Jude Medical, C. Sticherling Grant/ research support from: Medtronic, Biotronik, Medtronic, Biosense Webster, Sorin, Speakers bureau: Medtronic, Biotronik, M. Kühne Grant/ research support from: Biosense Webster, Speakers bureau: Boston Scientific, St Jude Medical, and Biotronik, Paid Instructor for: Medtronic
Introduction: The Rhythmia mapping system was recently launched and allows for rapid ultra high-resolution electroanatomical mapping of cardiac chambers. We evaluated the feasibility, acute efficacy and safety of this novel mapping system for ablation of atrial fibrillation (AF) and left atrial tachycardia (AT).

Methods: A total of 35 consecutive patients (17 female, mean age 64.3±8.6 years, mean LA-diameter 44.4±5.8 mm) underwent catheter ablation for AF and/or AT. All procedures were performed using the Rhythmia mapping system in conjunction with the Orion mini-basket catheter, which incorporates 64 electrodes. An electroanatomical shell of the LA including the LA-PV junction and the proximal PVs was created. Pulmonary vein isolation (PVI) and linear lesions were performed applying radio-frequency (RF) energy. PVI was confirmed by presence of entrance and exit block using the mini-basket catheter. In addition, pacing maneuvers assessed bidirectional conduction block across linear lesions.

Results: Acute PVI was achieved in all patients (Figure, left panel: LA voltage map before PVI; right panel: LA voltage map after PVI, white arrow showing basket catheter in left superior PV; lower panel: tracings showing entrance block on basket catheter, red arrow: PV spike, black arrow: atrial far field). Procedure duration was 110.3±33 min., fast acquisition mapping (FAM) time was 19±9 min. A mean number of 10165±5904 mapping points were acquired during the initial map and 6379±3191 for a remap. A total number of 31±15 radiofrequency applications were delivered within 45±22 min. Total fluoroscopy time was 21±5 min, 5±2 min. were used for FAM. We observed a significant learning curve for mapping duration (p=0.01). Correction of automatic annotation was not necessary to reach procedural endpoints. Complications included pericardial tamponade (n=1), transient air embolism in the right coronary artery (n=1), and mild groin hematoma (n=2).

Picture/Graph 2:
Conclusion: To the best of our knowledge, this is the largest study evaluating the feasibility, acute efficacy and safety of the Rhythmia mapping system for PVI and ablation of left AT. PVI was achieved in all patients. Applying this ultra high-resolution electroanatomical and activation mapping system under routine conditions leads to a high level of confidence. More data will be mandatory before final conclusions can be drawn.

Disclosure of Interest: None Declared
Introduction: Atrial fibrillation (AF) has been shown to be associated with changes in left atrial (LA) anatomy. The aim of the current study was to investigate the relationship between symptomatic AF burden and LA dimensions obtained from pre-procedural cardiac imaging.

Methods: LA assessment was performed in consecutive patients using pre-procedural imaging (Computed tomography and Magnetic Resonance Imaging) in 3D (sphericity, volume, indexed volume), 2D (anterior-posterior (AP) diameter) and from echocardiography in 1D (parasternal long axis (PLAX)). AF burden was classified based on a novel AF burden score (1 = minimal, 2 = mild, 3 = moderate, 4 = severe) introduced by Koci and Ruskin [1] including the frequency and duration of AF episodes and the number of cardioversions.

Results: We analysed 204 consecutive patients referred for catheter ablation of AF (147 male (72%), age 61±9 years, BMI 27±4). Time since first AF detection was 57±61 months. Forty-nine patients (24%) suffered from dyspnea, 114 (56%) from effort intolerance, 150 (74%) from palpitations, 15 (7%) from tachymyopathy and 14 (7%) had chest pain. AF was classified as persistent in 71 patients (35%). AF burden score in 197 patients was 1 in 8 (4%), 2 in 107 (53%), 3 in 56 (27%), and 4 in 26 (13%) subjects. Patients with persistent AF had a significantly higher AF burden score (p<0.001) than paroxysmal ones. A significant correlation was found between the burden score and LA volume, indexed volume, AP diameter, sphericity, and LA in PLAX (ρ=0.368 (p<0.001), ρ=0.351 (p<0.001), ρ=0.378 (p<0.001), and ρ=0.294 (p<0.001), respectively). Using multivariate analysis, the AF burden score could be predicted by the indexed volume and sphericity (R=0.447, p<0.05) by a multiple linear regression model.

Conclusion: For the novel classification scheme of AF burden, a significant association with LA anatomy was found and can be predicted based on the indexed volume of the LA and sphericity.


Disclosure of Interest: S. Knecht: None Declared, M. Pradella: None Declared, A. Mühl: None Declared, T. Reichlin: None Declared, U. Celikyurt: None Declared, B. Stieltjes: None Declared, J. Bremerich: None Declared, S. Osswald: Grant/ research support from: Medtronic, Boston Scientific, Biotronik, St Jude Medical, Speakers bureau: Medtronic, Boston Scientific, Biotronik, St Jude Medical, C. Sticherling: Grant/ research support from: Biosense Webster, Biotronik, Boston Scientific and Sorin, Speakers bureau: Medtronic, M. Kühne: Grant/ research support from: Biosense Webster, Speakers bureau: Boston Scientific, St Jude Medical, and Biotronik, Paid Instructor for: Medtronic
Introduction: Patient with heterozygous familial hypercholesterolemia (FH) may be at particular risk of recurrence after acute coronary syndrome (ACS), but the strategy to identify those remains unclear. The identification of patients with the highest cardiovascular risk is required to personalize the intensity of lipid-lowering therapies.

Methods: We studied 4,534 men and women from a prospective cohort of patients hospitalized with ACS in Switzerland between 2009 and 2014, in whom we applied three algorithms for FH diagnosis based on clinical criteria only: (1) the latest American Heart Association (AHA) algorithm, (2) the Simon Broome Register algorithm, and (3) the Dutch Lipid Clinic Network algorithm to assess probable/definite FH (>5 points). For each algorithm, we used multivariable adjusted Cox proportional models to assess risk of first major adverse cardiovascular events defined as cardiovascular death, myocardial infarction, or ischemic stroke. Restricted analyses were conducted in 1,369 patients with premature coronary heart disease, defined as below 55 years for men, and below 60 years for women.

Results: Over the year after ACS, 275 (6.1%) patients had a cardiovascular event, 217 (4.8%) had a fatal or non-fatal myocardial infarction, and a total of 153 (3.4%) died. Prevalence of clinical FH was 2.5% (95% confidence interval (CI) 2.1-3.0) using the AHA algorithm, 5.5% (95% CI 4.9-6.2) using the Simon Broome algorithm, and 1.6 (95% CI 1.3-2.0 ) using the Dutch Lipid Clinic algorithm. The risk of cardiovascular event after ACS was higher in patients with FH, as compared patients without FH, with multivariable adjusted hazard ratio (HR) of 2.19 (95% CI 1.02-4.73, p=0.046) for the AHA algorithm, 2.61 (95% CI 1.49-4.95, p=0.001) for the Simon Broome algorithm, and 2.64 (95% CI 0.9-7.35, p=0.06) for the Dutch Lipid Clinic algorithm. Similar associations but with larger CI were found after further adjustment for the GRACE risk score, or when restricting the analyses to patients with premature ACS.

Picture/Graph:
Conclusion: Patients with FH identified at the time of hospitalization for ACS using convenient clinical criteria not relying on genetics tests have more than two-fold risk of recurrence of cardiovascular events within the first year after discharge than patients without FH. Patients with both ACS and FH may benefit most from new intensive lipid-lowering therapies.

Disclosure of Interest: None Declared
OR08

5. Epidemiology, risk factors, rehabilitation, thromboembolic disease

Prognostic value of pcsk9 levels in patients with acute coronary syndromes

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Introduction: Proprotein convertase subtilisin kexin9 (PCSK9) is an emerging target for the treatment of hypercholesterolaemia, but the clinical utility of PCSK9 levels to guide treatment is unknown. We aimed to prospectively assess the prognostic value of plasma PCSK9 levels in patients with acute coronary syndromes (ACS).

Methods: Plasma PCSK9 levels were measured in 2030 ACS patients undergoing coronary angiography in a Swiss prospective cohort. At 1 year, the association between PCSK9 tertiles and all-cause death was assessed adjusting for the Global Registry of Acute coronary Events (GRACE) variables, as well as the achievement of LDL cholesterol targets of 1.8 mmol/L.

Results: Patients with higher PCSK9 levels at angiography were more likely to have clinical familial hypercholesterolaemia (rate ratio, RR, 1.21, 95% confidence interval, CI, 1.09–1.53), be treated with lipid-lowering therapy (RR 1.46, 95% CI 1.30–1.63), present with longer time interval of chest pain (RR 1.29, 95% CI 1.09–1.53) and higher C-reactive protein levels (RR 1.22, 95% CI 1.16–1.30). PCSK9 increased 12–24 h after ACS (374±149 vs. 323±134 ng/mL, P < 0.001). At 1 year follow-up, HRs for upper vs. lower PCSK9-level tertiles were 1.13 (95% CI 0.69–1.85) for all cause death and remained similar after adjustment for the GRACE score. Patients with higher PCSK9 levels were less likely to reach the recommended LDL cholesterol targets (RR 0.81, 95% CI 0.66–0.99).

Conclusion: In ACS patients, high initial PCSK9 plasma levels were associated with inflammation in the acute phase and hypercholesterolaemia, but did not predict mortality at 1 year.

Disclosure of Interest: None Declared
OR09
5. Epidemiology, risk factors, rehabilitation, thromboembolic disease
Serum uromodulin predicts cardiovascular events both in patients with and in subjects without type 2 diabetes
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1VIVIT-institute, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, 2Medicine, Private University of the Principality of Liechtenstein, Triesen, Liechtenstein, 3Medicine & Cardiology, 4Medical Central Laboratory Feldkirch, Academic Teaching Hospital Feldkirch, Feldkirch, Austria, 5College of Medicine, Drexel University, Philadelphia, United States

Introduction: Uromodulin is a protein produced exclusively by the kidneys, and the serum uromodulin/creatinine ratio recently has attracted interest as a marker of kidney disease. Whether this ratio also is associated with cardiovascular event risk is unknown.

Methods: We therefore measured uromodulin in a series of 529 patients who were undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD) and prospectively recorded cardiovascular events in these patients over 6.6±1.8 years.

Results: At baseline, the uromodulin/creatinine ratio both among patients with type 2 diabetes (T2DM; n=146) as well as among non-diabetic subjects (n=383) correlated significantly with proBNP (r=0.388; p<0.001 and r=0.141; p=0.022, respectively) and, in diabetic patients, with the extent of CAD (r=0.201; p=0.015 and r=0.096; p=0.061, respectively). Prospectively, cardiovascular events occurred in 145 patients; event rates were 37.7% in patients with T2DM and 23.5% in non-diabetic subjects (p=0.001). The uromodulin/creatinine ratio predicted the incidence of cardiovascular events after multivariate adjustment including proBNP, the baseline extent of CAD and baseline creatinine in patients with T2DM (standardized adjusted HR 1.41 [95%CI 1.03-1.91]; p=0.031) as well as among non-diabetic subjects (standardized adjusted HR 2.00 [95%CI 1.06-3.78]; p=0.033).

Conclusion: We conclude that the uromodulin/creatinine ratio is a novel predictor of cardiovascular event risk both in patients with T2DM and in non-diabetic subjects.

Disclosure of Interest: None Declared
Introduction: Early recognition of diseases or syndromes related to aortic aneurysms is crucial for a timely surgical indication and to prevent spontaneous aortic dissection. Genetic disorders characterized by prevalent root enlargement imply early indication for surgical treatment based on aortic root dimensions. At the time being, in asymptomatic and not genetically related aneurysms, elective surgery is recommended with diameters ≥ 5.5 cm. In addition, the ASI (aortic size index, i.e. aortic diameter divided by body surface area) may be useful to predict the risk of rupture.

Methods: We retrospectively analysed ascending aorta morphology and diameters on preoperative CT scan of patients who underwent emergency surgery for type A aortic dissection (AADA) at our center. Morphology has been used to distinguish pure ascending aorta aneurysms from aorta with prevalent root dilation. Available intraoperative transesophageal echocardiographies were also employed to size aortic root dimensions. ASI (aortic size index, i.e. aortic size/body surface area) was calculated for patients with post-junctional dilation of the ascending aorta.

Results: From January 2001 to December 2015, 108 patients (73 males; mean age of 63.6±13 yrs) were operated in emergency for spontaneous type A aortic dissection. We were able to access and analyse the preoperative CT scans of 95 of these patients. Patients with bicuspid valves were excluded from further analysis (5/95 - 5.2%). Among the 17/95 patients (17.9%) with predominant aortic root dilation, 7/17 (41.2%) had AADA at diameters <5.0 cm (mean 4.4±0.3 cm, median 4.4). In the remaining 73/95 patients with ascending aorta dilation, 20/73 (27.4%) presented with a post-junctional ascending aorta of ≥ 5.5 cm, 50/73 (68.5%) had a diameter of <5.5 cm (mean 4.7±0.3 cm, median 4.8) and 3/73 (4.1%) presented with normal aortic dimensions (mean 3.3±0.1 cm). The ASI was < 2.75 cm/m² (mean 2.3± 2.3 cm/m², median 2.3) in 49/70 (70%), between 2.75 and 4.25 cm/m² (mean 3.0 ± 3.4 cm/m², median 3.0) in 20/70 (28.5%) and >4.25 cm/m² in 1/70 (1.5%).

Conclusion: In our clinical experience, 68.5% of patients with post-junctional aortic dilation acutely dissected despite a diameter below 5.5 cm and 70% had an ASI of less than 2.75 cm/m² (low risk for rupture, 4%/year). Our findings challenge the recently released clinical guidelines, as well as the ASI-based prediction of risk.

Disclosure of Interest: None Declared
Introduction: Time, cost and geographical restrictions currently limit on-site teaching and training. Telementoring, which delivers the requested medical service at the desired time, cheaply and despite geographical distances, may represent a feasible strategy to support skill introduction, especially in remote health care sites.

Methods: A telementoring protocol using a stepwise introduction of EVAR had been implemented between a university care center and a remote vascular health care site. From March 1999 to April 2003, 49 EVAR procedures were telementored at the remote center. Telementoring was performed using three online audio-video-facilities and 4 ISDN lines allowed image transmission. After the telementoring period, the remote team independently performed 86 EVAR interventions from May 2003 to July 2011. Patients’ follow-up lasted till May 2013.

Results: No significant difference was appreciated between telementored and not-telementored procedures neither in peri-interventional mortality rate (4.1% vs 2.3%, χ2 test p=0.621) nor in the initial technical success rate (93.9% vs 97.7%, p=0.353). The telementored group showed no significant difference compared to not telementored procedures in the overall aneurysm-related mortality (6.1% vs 2.3%, p=0.353), neither in the overall complication rate (p=0.985) nor in the number of patients developing endoleaks (p=0.722). The reintervention rate was significantly lower among not-telementored procedures (11.6% vs 32.7%, p=0.004).

Conclusion: The telementoring program, providing distant teaching by a university care center team, allowed excellent EVAR skill acquisition into the routine practice of a remote health care site. The learning curve achievement further improved technical results, significantly reducing the reintervention rate during follow-up. Telementoring, with its broad applications, may represent a cheap and time-saving teaching tool in remote health care sites.

Disclosure of Interest: None Declared
5. Epidemiology, risk factors, rehabilitation, thromboembolic disease

iPhone-app compared to standard blood pressure measurement – trial design and pilot data of the iparr trial

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Introduction: Smartphones and smartwatches allow to measure and track vital signs traditionally assessed with dedicated equipment. As these devices and health-related apps become increasingly used by the general population, it is essential to assess the accuracy of new measuring methods. A recently developed algorithm calculates systolic blood pressure (SBP) from the pulse wave recorded with a smartphone camera. This app is the only smartphone based tool worldwide that needs no calibration measurement or additional peripheral devices to calculate SBP. This study aimed to compare the accuracy of this method with a traditional professional blood pressure monitor.

Methods: In this prospective, blind, single-center trial, 1000 adult subjects are recruited until February 2016. Seven sequential blood pressure measurements are performed after five minutes of rest in a quiet room and in sitting position. The series starts with a standard device (Omron HBP-1300 professional blood pressure monitor, appropriate cuff size) alternating with the tested smartphone app (Preventicus, iPhone 4s). The photoplethysmographic signal is recorded by placing the finger on the iPhone camera for 2 minutes. During this recording the finger is illuminated by the integrated LED-light. Based on the pulse wave morphology and five additional parameters (age, size, weight, sex, tobacco use) the algorithm calculates the SBP. Additionally information about cardiovascular risk factors, concomitant disease and medication, are collected.

Results: In a retrospective analysis pilot data of 500 patients shows a correlation of r=0.81 and mean error of <10mmHg between the SBP measured with a standard device and a smartphone. A first pilot validation cohort of 85 subjects confirms the proof of concept with a correlation of r=0.76 and a mean error of 13.6mmHg (Figure 1). Repeated measurements of the same patients with a smartphone are reproducible (Figure 2).

Conclusion: Pilot data of an ongoing prospective blinded validation trial (iPARR) shows that SBP measurement with a smartphone app is a promising innovative tool that will be tested and developed further to be implemented in a smartwatch. Analysis of additional data should reveal whether the accuracy is maintained within subpopulations (e.g. age, sex and hypertensive). A validation cohort following ESH criteria will follow.
**OR13**

7. **Clinical cases (All clinical cases have to be submitted in this topic)**

Cardiac contractility modulation therapy for patients with reduced ejection fraction heart failure and normal qrs duration: report of two cases

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**Introduction:** Cardiac resynchronisation therapy improves symptoms in patients suffering from ventricular dysynchrony with widened QRS. It failed however to improve symptoms in patients with normal QRS duration. In these latter patients, cardiac contractility modulation (CCM) is now considered as new add-on therapy. CCM signals are non-excitatory impulses of high voltage applied during the absolute refractory period, which is thought to improve strength of muscle contractility.

**Methods:** We report hereby two cases of CCM device implantation at our institution.

**Results:**

**Case #1.** A 49-year-old patient without any past medical history presented with acute heart failure. Baseline transthoracic echocardiography revealed a severe dilated left ventricle with reduced left ventricular ejection fraction (EF) to 25%. No secondary cause could be found despite thorough evaluation including infectious, autoimmune, endocrine and ischemic assessment. At 3-month follow-up and despite optimal medical therapy (OMT), severe dyspnea persisted even though EF improved to 35%. Serial follow-up electrocardiograms showed normal QRS duration (86 ms). After careful consideration, this patient was implanted with CCM (Impulse Dynamics N.V.) and implantable cardioverter defibrillator (ICD). One-hour intermittent periods of 7.5Volts CCM signals were applied for a total duration of 7 hours per day. At 6 months, the patient reported NYHA functional class improvement (decreasing from class III to II), though no change of EF was observed.

**Case #2.** A 72-year-old patient with long-standing ischemic heart disease and a history of multiple coronary revascularizations was complaining of increasing dyspnea. Transthoracic echocardiography revealed severe left ventricular dilation with reduced EF to 20%. In the context of persistent symptoms despite OMT with normal QRS duration (96 ms) and an increased risk of sudden death, a CCM device (Impulse Dynamics N.V.) was implanted together with ICD. CCM signals were applied along the same modules as the first case. At 4 months, the patient revealed significant improvement of dyspnea and quality of life, and EF increased to 35%

**Picture/Graph:**
Conclusion: When CCM therapy might be effective for quality of life improvement in patients with reduced EF heart failure and normal QRS duration, patient selection still remains challenging and perhaps the primary determinant of success.

Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Transient para-aortic hematoma during transseptal puncture for atrial fibrillation ablation: a characteristic echocardiographic image

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Introduction: Ablation of atrial fibrillation (AF) requires puncture of the inter-atrial septum (IAS) to gain access to the left atrium (LA). Rare complications include laceration of the aortic root or perforation of the LA, which are associated with a high morbidity as they usually require urgent surgery.

Methods: A 75-year old male patient was referred for radiofrequency isolation of the pulmonary veins (PV) under general anesthesia because of symptomatic paroxysmal AF. A trans-oesophageal echocardiography (TEE) was performed to exclude thrombus of the LA appendage; both ventricles had normal function and the aortic root was normal (fig A). After femoral venous punctures and 100 U/kg of unfractionated heparin, an SL0 guiding sheath and a needle were dragged against the septum secundum (SS) creating a typical tenting (Fig B). The transseptal puncture (TSP) was uneventful and a guidewire was introduced into the left upper PV. The ablation catheter and its guiding sheath were then advanced along the guidewire to cross the IAS without the need for a second TSP. An unusual resistance was felt while advancing the ablation catheter. On TEE, the orientation of the sheath was somewhat different, more parallel to the IAS and pointing anteriorly toward the ascending aorta (Fig C). Simultaneously, a new echo-lucent space appeared between the aortic wall and the LA wall, raising the suspicion of an aortic laceration (Fig D). The sheath was retrieved but no pericardial effusion occurred at TEE. The catheter was repositioned posteriorly, which allowed to easily cross the IAS (Fig E). Five minutes later, TEE control of the aortic root showed complete resolution of the para-aortic echo-lucent space (Fig F), allowing to proceed with AF ablation.

Results: The thin SS is the only fully intracardiac part of the IAS that is safe for puncture and LA access. Conversely, the thick part of the IAS merely represents an infolding of the atrial wall. Puncture of the thick IAS may create a communication with the extracardiac fatty space that separates the atrial wall and the aortic root. A hematoma occurring into this virtual space may be confused with an aortic root dissection, but may spontaneously resolve without the need for heparin reversal if immediately recognized.

Picture/Graph:
Conclusion: Dissection of the thick part of the IAS is a less well-known complication that can easily be detected on TEE. Our case suggests that such a complication may be benign and self-limited if immediately recognized.

Disclosure of Interest: None Declared
OR15
7. Clinical cases (All clinical cases have to be submitted in this topic)
Emergency epicardial-only vt ablation using image integration in a patient with vt storm.
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Introduction: Few data are known about the efficacy and safety of epicardial-only ablation, which is mostly performed in the presence of an endocardial LV thrombus. We present a case in which image integration guided us towards an epicardial-only approach.

Methods: We present a case of a 60-yrs old male patient with non-ischaemic cardiomyopathy (LVEF 25%) after myocarditis in 2010 with basal inferolateral epicardial scar). The patient entered the hospital with an electrical storm (monomorphic VT) and 6 ICD shocks before urgent admission to our center. Urgent MDCT imaging was performed at the referral center and the MUSIC (MUltimodality platform for Specific Imaging in Cardiology) platform was used to create a high-resolution personalized 3D model with the coronary artery system and the left phrenic nerve. The decision was made to perform a subepicardial only procedure, due to a huge subepicardial-only scar (142cm²) on his personalized model. The patient was intubated after 3 new ICD-shocks at our centers. Image integration into the CARTO 3 system (Biosense Webster) was performed and fusion with the voltage map performed using the following anatomical landmarks: the aortic root and cusps, the coronary sinus and the left phrenic nerve.

Results: High-density (2017points) low bipolar voltage mapping (<1.5mV) and LAVA (local abnormal ventricular activity,389points) was performed using a multipolar catheter (PentaRay) trough a steerable sheath (epicardial Agilis) during sinus rhythm and VT. The phrenic nerve was tagged using local phrenic capture at 10mA and 2ms. Anatomical imaging channels (differences in wall thinning) in the border zone were analyzed in detail. In the main channel, the clinical VT was mechanically induced, mid-diastolic potentials were observed and VT was ablated and terminated during RF. After 82 min RF time and 300min procedure time, non-inducibility was reached and all epicardial LAVA were ablated, except around the phrenic nerve. Amiodarone was stopped. After 1month follow-up, no recurrence of VT was observed. No complications occurred.

Picture/Graph:
Conclusion: Image integration is critical to achieve anatomical substrate modification by guidance of the approach, by improvement of efficacy with the demonstration of heterogeneity and anatomical channels and by improvement safety of epicardial ablation due to phrenic nerve and coronary artery segmentation. An epicardial only approach can be used in a highly selective subset of patients with good outcome.

Disclosure of Interest: None Declared
Introduction: A 62 yo hypertensive woman (47kg, 150cm) underwent an elective isolation of the pulmonary veins (PVI) because of paroxysmal atrial fibrillation (AF). The procedure was successfully performed in general anesthesia using a cooled-tip (8ml/min) ablation catheter (SmartTouch SF, BW). An accessory PV was found postero-medially to the right superior (RS) PV (arrow, panel A of the figure). Ablation was performed at 20W at the posterior and 25W at the anterior left atrium (LA) for 40sec, with Visitag set at 5mm spatial averaging and FTI targeting ≥400gs. Note that the ablation included the accessory RSPV (panel A, pink-red dots).

Methods: Ten days after the procedure, the patient complained of AF recurrence, followed by a transfixing chest pain 48h later. A transthoracic echocardiogram showed a minor pericardial effusion. A CAT scan revealed a pneumo-mediastinum and a pneumo-pericardium suggestive of an esophageal perforation (arrows, panel B).

Results: Because of the absence of neurological symptoms, she underwent a gastroscopy that showed an esophageal perforation 34 cm below the dental arch. A right exploratory thoracotomy revealed an eso-pericardial fistula complicated by a pyopericardium (green arrows, panel C), but no perforation of the posterior LA wall. The esophageal perforation (blue arrow, panel C) was sutured and the esophagus (black arrows, panel C) wrapped with a diaphragmatic patch. Postoperative evolution was favorable under antibiotics over 4 weeks.

Conclusion: Eso-atrial fistula is one of the most lifethreatening complications following PVI. Herein, we report a rather unique case of eso-pericardial fistula without perforation of the posterior LA. As recently shown, the catheter cooling limits local tissue damages but can shift RF energy delivery to adjacent unprotected tissue. Interestingly, an accessory PV forced us to medially extend the ablation, which might have moved the RF energy closer to the esophagus.

Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Induction of life-threatening arrhythmias by automatic threshold monitoring by an implantable cardioverter-defibrillator

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Introduction: It is well-known that antitachycardia therapies of implantable cardioverter-defibrillators (ICDs) can be proarrhythmic. We describe a case where an automatic threshold monitoring (ATM) feature of an ICD caused life-threatening arrhythmias.

Methods:

Results: Case presentation:

A 57-year old male patient with status post myocardial infarction 17 years earlier with formation of a posterior aneurysm and depressed left ventricular function sustained recurrent myocardial infarction. A coronary angiogram showed three-vessel disease. He underwent coronary bypass surgery with additional reduction of the aneurysm, mitral valve repair, and closure of a persistent foramen ovale 5 days later. Sustained monomorphic ventricular tachycardia (VT) occurred 4 days after surgery. A repeat coronary angiogram revealed one occluded venous graft.

A VDD-ICD was successfully implanted 8 days after cardiac surgery. Sustained monomorphic VT occurred during implantation necessitating cardioversion via the ICD. After initial VVI stimulation at 100 bpm, antibradycardia programming was set to VVI 45 bpm, output was set to 3.5V @ 0.4ms, ATM was programmed "ON", and antitachycardia therapy was programmed starting at 125 bpm. Early after ICD implantation, the patient had several episodes of VT, treated with antitachycardia pacing and ICD shocks.

On the fourth day after ICD implantation, sustained monomorphic VT at a rate of 141 bpm occurred. On the telemetric monitoring, pacing artifacts precede VT, (Figure 1, telemetric rhythm monitoring strip). Antitachycardia pacing by the ICD was unsuccessful, accelerated the VT, and induced ventricular fibrillation (VF), which was successfully defibrillated by the ICD. VT resumed during post-shock pacing, which was eventually successfully treated via ICD.

ICD interrogation showed that ventricular stimulation during ATM induced the VT (Figure 2, printout of ICD interrogation, the same episode as in Figure 1 is displayed, ventricular stimulation is indicated by *, FF denotes far field, RA, right atrium, RV, right ventricular, respectively). An unrelated finding was undersensing of atrial fibrillation. There was no evidence of device malfunction. Subsequently, ATM was programmed "OFF".

Picture/Graph:  

Picture/Graph 2:
Conclusion: ATM by an ICD may induce sustained VT, that may be accelerated or degenerate into VF by attempts of the ICD to terminate the arrhythmia. It may be prudent to disable this feature in patients at high risk of frequent recurrent ventricular arrhythmias.

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Silencing of the activated protein-1 transcription factor JunD exacerbates ischemia/reperfusion-induced cerebral injury


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Introduction: The activated protein-1 transcription factor JunD mediates inflammation, apoptosis and oxidative stress, which are crucial components to ischemia/reperfusion brain damage. In this study we investigate the role of vascular JunD in ischemia/reperfusion-induced brain injury using a mouse model of ischemic stroke, primary human brain microvascular endothelial cells (HBMVECs) as well as peripheral blood monocytes (PBMs) from ischemic stroke patients.

Methods: Twelve-week-old male C57BL/6 mice underwent JunD silencing (siJunD, n=10) using small interfering RNA (siRNA) before transient (45min) middle cerebral artery occlusion (MCAO) followed by 24hours of reperfusion was performed to induce ischemia/reperfusion brain damage; stroke size was assessed by TTC staining and neuromotor function by neurological score and Rotarod tests and compared to scramble siRNA-injected control animals (siScr, n=8).

To investigate the role of JunD in the human cerebral endothelium, JunD was silenced in HBMVECs and cell death was evaluated by lactate dehydrogenase (LDH) release after exposure to 4hours hypoxia (0.2% oxygen) and 4hours reoxygenation (21% oxygen). Lastly, we examined vascular JunD responsiveness to ischemia/reperfusion in C57BL/6 wild-type (WT) mice, to hypoxia/reoxygenation in HBMVECs, and to ischemic stroke in PBMs isolated from patients.

Results: JunD silencing provided a 40±8% reduction of JunD protein expression in murine aortae. After transient MCAO, JunD-silenced mice showed increased stroke volumes (siScr, 42±7mm3; siJunD, 69±9mm3) and decreased neuromotor function, compared with control animals. Likewise, JunD-silenced HBMVECs exposed to hypoxia/reoxygenation revealed increased cell death, compared with control cells. After transient MCAO, JunD expression was decreased in middle cerebral arteries of WT mice. Similarly, JunD was reduced in HBMVECs exposed to hypoxia/reoxygenation and in PBMs of ischemic stroke patients after 24hours of symptom onset, as compared to age- and sex-matched control subjects.

Conclusion: Brain ischemia/reperfusion reduces vascular JunD expression in WT mice as well as in primary human cerebrovascular endothelial cells and monocytes from patients with ischemic stroke. Vascular JunD silencing in mice augments stroke volumes and neuromotor deficits suggesting its involvement in the pathogenesis of ischemia/reperfusion-induced brain injury.

Disclosure of Interest: None Declared
Phosphodiesterase 5 inhibitor attenuates pulmonary and right ventricular remodeling due to pulmonary hypertension through an antiproliferative mechanism

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Introduction: Hypoxic pulmonary hypertension is one of the devastating diseases characterized by pulmonary vascular remodeling that leads to right ventricular hypertrophy (RVH) and failure. We performed to assess the role of sildenafil on pulmonary and right ventricular remodeling in a preclinical model of chronic hypoxic pulmonary hypertension.

Methods: Adult male Sprague-Dawley rats were exposed 2 weeks to chronic hypoxia (CH, 10% O2) or normoxia (N, 21%O2, n=10). CH rats received sildenafil (1.4 mg/kg/day ip, n=10) or saline (n=10). The effects of CH on cardiopulmonary hemodynamics were assessed by Doppler echocardiography and RV catheterization. Lungs and RV were removed and frozen for biochemical analysis or formalin-fixed and paraffin-embedded for immunofluorescence staining (IF).

Results: Compared to N, Doppler echocardiography revealed reduced pulmonary artery (PA) acceleration time and velocity time integral (-41±4% and -0.74±0.03%, respectively) and increased PA systolic pressure (+2.0±0.08%) in CH rats, which rescued by sildenafil. Although CH resulted in a 1.7-fold increase in RV systolic pressure and in RVH accompanied by a 1.5-fold increase in medial wall thickness of pulmonary arterioles, these were significantly attenuated by sildenafil. This was associated with blunted proliferation of cells in response to stress, as judged by BrdU incorporation that was higher in CH rats. Additionally, a double IF showed an increase in the BrdU+alpha-SMA+cells (a vascular smooth muscle cell-specific marker) in CH compared to N tissues, which inhibited by sildenafil. Compared to N, RT-PCR showed an mRNA up-regulation of Type I and Type III collagen in the RV (+2.0 fold) tissues after CH, confirmed by RV interstitial fibrosis, which was substantially reduced by sildenafil. In contrast, no change was observed for lung tissue. Moreover, both in the lung and RV tissues obtained from CH rats, the expression of LC3II (an established autophagy index) and p62 (an adaptor protein targeting ubiquitinated proteins to autophagosomes) were significantly increased compared to N rats. More interestingly, the treatment of CH rats with sildenafil substantially increased the activation of LC3II only but not p62 protein in RV and not in lung tissues.

Conclusion: Our data provide evidence that sildenafil rescues the proliferation of new fibroblasts both in the lung and RV tissues, and promotes the activation of autophagy to induce the intracellular degradation of RV collagen.

Disclosure of Interest: None Declared
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Need for support for patients with chronic heart failure, the development and implementation of self management strategies at home- a qualitative research study in Switzerland

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Introduction: Introduction
Chronic heart failure (CHF) is characterized by a wide range of symptoms, high prevalence in the elderly, poor (quality of life Qol) and frequent hospitalisations. Managing one’s condition at home is important to successful treatment. Multiprofessional patient education programs have shown positive effects on self management strategies (SMS), Qol, mortality and costs although a lack of congruency exists in methods, quantity and duration of programs. It is unclear what support these patients need to integrate and maintain SMS at home. This survey explored the support needed to maintain SMS at home for CHF patients who have completed a self-management (SM) course during hospitalisation. Additionally, it evaluated which available social networks support SMS at home.

Methods: Methods
A qualitative study was utilized to explore the subjective perspective of patients. Grounded theory was chosen to examine patients’ perspectives in SM at home.

Twenty two interviews were conducted at the participants’ homes after hospital discharge. Various methods of coding, open, axial and selective were used. The process was completed after the main phenomenon has been identified.

Results: Results
The results show intrinsic motivation as the main phenomenon. This motivation gives patients strength and energy to develop SMS for achieving a good Qol. SM is influenced by the patient’s relationship with the health care providers, and their personal experiences shape their behaviour. Confidence is the key factor for cooperation between patients and health care providers. It results from behaviours such as reliability, feeling encouraged to ask questions, listening, attentiveness and friendliness, being able to talk to each other and taken seriously, knowing each other and more. In the critical event of transitions from inpatient to outpatient, the social network and the collaboration between the patient and the health care provider may be the key element for successful SMS at home.

Conclusion: Conclusion
Results show a wide range of factors influence intrinsic motivation for effective SMS at home with the aim of a high Qol and preventing hospitalisation. Professionals need to be aware of influencing factors and should build networks to provide patient support. Each patient situation requires a comprehensive assessment to provide individualised help with SMS at home and to establish a supportive social network.

Disclosure of Interest: None Declared
Introduction: Percutaneous mitral valve repair (PMVR) using the MitraClip-system has become a valid alternative for patients with severe mitral regurgitation (MR) and high surgical risk. For a lack of evidence deriving from randomized trials, data from high volume registries is therefore of interest. Herein, we report the updated results of the ongoing national MitraClip registry (MitraSwiss).

Methods: Consecutive patients with moderate to severe MR and high surgical risk (as discussed within a Heart-team) or declined for surgical repair were included in the registry. PMVR was performed under general anesthesia in the cath-lab or hybrid operating room with fluoroscopic and transesophageal echocardiography guidance. Transthoracic echocardiography, 6 min walking distance (6MWD), and a Minnesota Living With Heart Failure (MLWHF) score were recorded at baseline and after 6 months (mo). Clinical endpoints were analyzed after 6 mo and included death, hospitalization for heart failure, surgical mitral valve repair/replacement and “redo” PMVR.

Results: So far more than 500 patients (mean age 77±10 years; 37% female) underwent PMVR and were included in the registry by 10 institutions. Left ventricular ejection fraction (LVEF) was 46.4±16.6%. The origin of the MR was functional in 53%, degenerative in 40% and mixed 7%. In 38% of the procedures, 1 clip was implanted, whereas in 50% of the interventions ≥2 clips were necessary to achieve an acute procedural success (APS) rate of 91% (placement of ≥1 clip; discharge MR grade of ≤2+). 30 days survival was 98% (95%CI: 96.2- 98.9%) and 6 mo survival was 93% (95%CI: 90.3-94.9%). At 6 mo 79.4% of the patients were in NYHA class 2 and 72.6% had MR grade ≤2+ and significant reduction in pulmonary pressure. 6MWD improved from 332±145m at baseline to 375±137m at 6 mo (p< 0.001) and the MLWHF score improved from 35±20 points to 24±19 points (p< 0.001). The origin of the MR and pulmonary pressure at bl did not predict event-free survival. In a multivariate analysis only a good procedural result (MR grade ≤ 2+) figures as a potential predictor of event-free survival (p = 0.081).

Conclusion: The results of the nationwide, prospective MitraSwiss registry indicate that PMVR using the MitraClip-system, is safe, has a high procedural success rate and provides durable reduction of MR severity and improvement in symptoms, functional capacity and quality of life. A good procedural results seems to predict event-free survival.

Disclosure of Interest: None Declared
OR22
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation
Characterization of the natural history and outcomes of lamin a/c cardiomyopathy over
long term follow up: insights from a multi-centre study
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Introduction: Although the cardiac phenotype of Lamin A/C (LMNA) mutations is recognized as highly malignant, detailed natural history studies of associated arrhythmic and non-arrhythmic outcomes are limited.

Methods: 122 consecutive LMNA mutation carriers evaluated at 5 international referral centres were assessed for the development of atrioventricular block (AVB), atrial arrhythmias (AA), sustained ventricular arrhythmia (VA), heart failure (HF)/left ventricular (LV) dysfunction, thromboembolic (TE) events, end stage heart failure and overall mortality.

Results: From first clinical contact to median follow up of 7 years, the incidence of AVB increased from 44% to 55%, AA from 42% to 63%, VA from 16% to 34%, HF/LV dysfunction from 43% to 57% and TE events from 3% to 10%. During follow up, 22% reached end stage HF and 18% died, predominantly from complications related to end stage HF or its therapies. New defibrillator device implant or upgrade was required in 59% of patients paralleling the increasing incidence of LV dysfunction and complete AVB. Male gender (HR 3.2, 95% CI 1.3-8, P=0.01), LVEF ≤50% at first clinical contact (HR 3.5, 95% CI 1.5-8.1, P=0.004) and non-missense mutations (HR 2.5, 95% CI 1.1-1.6, P=0.03) were independently associated with sustained VA in follow up. LVEF≤50% at first clinical contact was the only factor associated with death or MCS/transplant (HR 5.2, 95% CI 2.1-13, P<0.001).

Conclusion: Death or life-threatening arrhythmias occur in more than half of patients with LMNA related heart disease 7 years after the index presentation. Male gender, non-missense mutations and LV dysfunction are important predictors of clinical events. Careful follow-up with early planning for advanced heart failure therapies seem warranted.

Disclosure of Interest: None Declared
OR23

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Intermittent scheduled low-dose levosimendan infusions enhance survival with advanced chronic heart failure: a propensity score matching analysis.

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Introduction: Advanced chronic heart failure (ACHF) is characterized by poor quality of life (QOL) and high mortality. Improved QOL can be obtained with usual inotropes like Dobutamine, but at the price of lower survival. As opposed to classic inotropes, Levosimendan (Levo) doesn’t increase myocardial O2 demand. Nevertheless, neither single 24h nor short intervals (2 weeks) repeated 6h infusions of high dose Levo (0.1-0.2 µ/kg/min) showed any survival benefit in phase III randomized-controlled trials (RCT), possibly because of dose-related side effects. In this study, we sought to assess the efficacy of long intervals repeated 24h low dose Levo infusions on 1 year survival.

Methods: we conducted a retrospective case control study based on our database of acute HF. Cases (n=38) were eligible if they had their 1st Levo infusion at the time of decompensated HF in addition to standard of care (SOC) with at least 1 further infusion scheduled, and if they had ACHF defined as HF with reduced left ventricular ejection fraction (LVEF<40%) not responding to > 3 months optimal therapy. They received 4.37 (range 2 - 12) 24h 0.05 µg/kg/min Levo infusion at 3-4 weeks intervals after initial hospitalization. These cases were compared 1 to 1 with SOC controls with ACHF that were matched for age, sex, ischemic heart disease, LVEF, sinus rhythm and creatinine on the basis of a propensity score matching analysis. Outcome was defined as 1-year survival.

Results: demographic and biological variables were not different between the 38 SOC+levo cases and the matched 38 SOC controls (Table 1). Repeated low dose Levo therapy conferred significantly better 1-year survival as compared to SOC (94.7% vs. 76.3%; HR=0.21; 95% CI 0.045-0.97) (Figure 1).

<table>
<thead>
<tr>
<th>Age (years, SD)</th>
<th>SOC + Levo</th>
<th>SOC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>89,5%</td>
<td>84,2%</td>
<td>1,0</td>
</tr>
<tr>
<td>Ischemic Heart Dis</td>
<td>53%</td>
<td>55%</td>
<td>0,10</td>
</tr>
<tr>
<td>Sinus rythm</td>
<td>66%</td>
<td>73%</td>
<td>1,0</td>
</tr>
<tr>
<td>LVEF (% SD)</td>
<td>21,8 (4,2)</td>
<td>21,4 (5,9)</td>
<td>0,72</td>
</tr>
<tr>
<td>Creatin (µmol/L SD)</td>
<td>137,1 (89)</td>
<td>134,7 (74)</td>
<td>0,31</td>
</tr>
</tbody>
</table>

Picture/Graph: 

Picture/Graph 2:
Conclusion: low dose 24h Levo (0.05 µg/kg/min) during hospitalisation for decompensated HF and regularly repeated on a scheduled basis thereafter may confer survival benefit as compared to SOC in ACHF patients. These data must be confirmed by larger RCTs.

Disclosure of Interest: None Declared
**OR24**

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation  
Prognostic power of proBNP in left ventricular non-compaction cardiomyopathy

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**Introduction:** Left ventricular non-compaction cardiomyopathy (LVNC) is a potentially life threatening disease of the left ventricular myocardium characterized by a thin, compacted, epicardial layer and a thick endocardial layer with deep recesses between prominent trabeculations. While left ventricular ejection fraction, heart failure symptoms, and exercise capacity are known to correlate with clinical outcome in LVNC patients, the role of proBNP has never been assessed.

**Methods:** A total of 153 patients with isolated LVNC were identified from the clinical databases at the University Hospitals Zurich and Basel (1988 and 2015). After a median follow-up of 6.6 years 23 (15%) patients reached the composite endpoint of all-cause mortality and heart transplantation. All available values for proBNP, left ventricular ejection fraction (LVEF, biplane Simpson’s method), NYHA functional class, and exercise capacity by bicycle ergometer (percent of target performance) were analyzed using unadjusted and adjusted (for age and gender) Cox regression models as well as a combined covariate analysis.

**Results:** Time to event analysis (death or transplantation) revealed a highly significant positive correlation for proBNP levels (adjusted HR 2.44 for every doubling, 95%CI 1.45-4.09, p=0.0007) and a negative correlation for LVEF (adjusted HR 2.57 for 10% decrease, 95%CI 1.67-3.59, p<0.0001). Using proBNP and LVEF as combined covariates, a very strong influence of proBNP on the hazard ratio was revealed (adjusted log2 HR 2.89, 95%CI 1.33-6.26, p=0.007), whereas LVEF was no longer significant (adjusted HR 1.02, 95%CI 0.95-1.09, p=0.66) indicating a favorable prognostic power of proBNP over LVEF. The prognostic power of proBNP was underscored by the finding that no event was recorded in patients with normal proBNP levels whereas proBNP levels >2000 ng/l were associated with a 40 times higher risk of death or transplantation as compared to proBNP <2000 ng/l. A higher NYHA functional class was associated with a worse outcome (adjusted HR 3.58, 95%CI 1.57-8.15, p = 0.002). Exercise capacity revealed a trend in the same direction.

**Conclusion:** This study provides evidence that an increase in proBNP is a strong predictor of outcome in patients with LVNC. The prognostic power of proBNP was stronger than that of LVEF, indicating a particularly high prognostic relevance in this patient population. Hence, proBNP measurement improves risk assessment in patients with LVNC.

**Disclosure of Interest:** None Declared
Introduction: Endothelial dysfunction appears to play an important pathophysiological role in heart failure. Previous studies focused on the relevance of brachial endothelial dysfunction in disease pathogenesis. Less is known about the extent of endothelial dysfunction in other vascular beds, the retinal microcirculation in particular. Retinal vessel analysis (RVA) is a new method allowing study of the retinal microcirculation in a standardized way using high-resolution caliber measurements of retinal vessels. The primary goal of this study was to evaluate the extent of retinal microvascular endothelial dysfunction as assessed by flicker-induced dilatation of retinal vessels in heart failure patients compared to age- and sex matched healthy controls.

Methods: In this prospective, observational, single-center study, patients with a diagnosis of heart failure on stable pharmacological therapy and currently compensated status, healthy controls were recruited for the assessment of vascular function. RVA was conducted using an Imedos retinal vessel analyzer (Jena, Germany) with the assessment of retinal flicker-induced vasodilatation (FID) using an established stimulation protocol and the measurement of retinal arteriovenous ratio (AVR) calculated using fundus photographs.

Results: 45 heart failure patients (mean age 60.3 ± 10.4 years, 24 % female, mean left ventricular ejection fraction 36.9 ± 14.2 %) and 31 healthy controls (mean age 57.4 ± 15.3 years, 26% female) were included in this analysis. Heart failure patients showed significantly reduced FID of retinal arterioles and venules compared to healthy controls (mean arteriolar FID 1.2±1.9% vs. 3.2±2.0%; mean venular FID 2.8±1.8% vs. 4.8±2.1, both p<0.0001 respectively). No significant difference in retinal AVR was found between both groups (mean AVR 0.84±0.07 in heart failure patients and 0.85±0.06 in healthy controls, p=0.32).

Conclusion: Heart failure patients are characterized by a profound alteration in retinal microvascular endothelial function as assessed by FID of retinal arterioles and veins. RVA may be a useful tool for the non-invasive assessment of microvascular function in heart failure.

Disclosure of Interest: None Declared
Late and very late presenting transposition of the great arteries: transition from atrial to two-stage arterial switch

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Introduction: Ventricular retraining and arterial switch has been described in late presenting transposition of the great arteries (TGA) has been described in older infants who couldn’t undergo neonatal arterial switch (ASO), or late survivors of atrial switch with systemic RV dysfunction. There is relatively little data available on patients presenting between these two groups, and our program recently transitioned from performing atrial switches to two-stage ASO in this patient group. This study aims to review the early and mid-term outcomes of the management late-presenting TGA.

Methods: From 2000 to 2014, 36 patients were referred for management of late-presenting TGA. 20 patients underwent a Senning procedure, while 16 patients underwent a two-stage ASO by pulmonary artery banding and modified Blalock-Taussig shunt, followed by ASO. Baseline demographic, echocardiographic, surgical and follow-up data were reviewed. The primary outcome measure was early mortality and ECMO requirement.

Results: Patients in the Senning group were slightly older, with a mean age of 36.2 months, compared to 15.2±11.9 months in the ASO group. The mean time of LV retraining was 126.9±183.7 days. There were 2 early deaths (10%) in the Senning group, and 2 in the ASO group (12.5%, P = >0.99), one after LV retraining and one after the ASO. Two patients in the ASO group required ECMO after ASO. During follow-up, there were 2 late deaths, 1 in the Senning group (5%) and 1 in the ASO (6.3%, P = >0.99), and 2 re-interventions for baffle obstruction (1 systemic, 1 pulmonary venous pathway) in the Senning group. All surviving patients in both groups had normal biventricular function at late follow-up.

Conclusion: Although a challenging group of patients, both Senning and two-stage ASO can be performed with acceptable outcomes and a low rate of reinterventions. LV retraining and ASO is a reasonable option for late presenting TGA, although longer-term follow-up is required to assess late LV function.

Disclosure of Interest: None Declared
Introduction: The atrial switch operation (Senning) has been the main surgical repair technique for d-transposition of the great arteries for many years. The Senning procedure results in a subsystemic morphologic right ventricle (RV) and a subpulmonary morphologic left ventricle (LV). This can be regarded as a model for the effects of long-term pressure overload on the RV, and of ultimately decreased afterload on the LV. We sought to determine the impact of these chronically altered loading conditions on the myocardial deformation of the RV and LV.

Methods: 26 patients after Senning (age 28.4± 7.5y) and 18 normal controls (age 22.2± 11.4y; p=0.034) underwent cardiac magnetic resonance (CMR) imaging. 2D SSFP cine images were acquired in an horizontal long axis and in a short axis covering both ventricles and post-processed with a feature tracking software (TomTec 2D CPA). Global circumferential strain was measured on a short axis mid-ventricular slice. Global longitudinal strain was measured in a long axis, separately for each ventricle.

Results: When comparing RV in either position, subsystemic circumferential strain was higher than subpulmonary circumferential strain (-16.1± 2.9% vs. -13.1± 4.3%; p<0.01), and subsystemic longitudinal strain was lower than subpulmonary longitudinal strain (-12.8± 3.3% vs. -18.3± 3.8%; p<0.001). In contrast, LV global strain in subsystemic vs. subpulmonary position was similar: LV circumferential strain (-23± 13.1% vs. -20.2± 3.9%; n.s.); LV longitudinal strain (-17.5± 4.6% vs. -16.1± 5.3%; n.s.).

The subsystemic RV showed lower circumferential (-16.1± 2.9% vs. -23± 13.1%; p<0.05) and lower longitudinal strains (-12.8± 3.3% vs. -17.5± 4.6%; p<0.001) than the subsystemic LV. The subpulmonary LV exerted greater circumferential strains (-20.2± 3.9% vs. -13.1± 4.3%; p<0.001) but similar longitudinal strains compared to the subpulmonary RV (-16.1± 5.3% vs. -18.3± 3.8%; n.s.).

Conclusion: In discordant ventriculo-arterial connection, the subsystemic RV adapts to the increased afterload with an increase in circumferential strain and an impaired longitudinal deformation. This may represent the effect of a positive interventricular interaction due to the shared circumferential fibers, since the LV shows higher circumferential strain than the RV even in subpulmonary position.

Disclosure of Interest: None Declared
Introduction: The arterial switch operation (ASO) for repair of transposition of the great arteries (TGA) requires transsection of the great arterial trunks and reimplantation of the coronary arteries (CA) into the neo-aortic root. This results in sympathetic denervation of the CA and thus may affect myocardial blood flow (MBF) regulation. We sought to evaluate sympathetic (re-)innervation in young adults after ASO and its impact on MBF.

Methods: Ten patients (age 22.8±1.8 years) after ASO for TGA in the neonatal period and ten healthy controls (age 22.0±1.7 years) were included. Cardiac sympathetic innervation was measured using $^{11}$C-meta-hydroxyephedrine (HED) positron-emission tomography (PET) and MBF was measured with $^{15}$O$_2$O PET at rest, during adenosine stimulation and during sympathetic nerve stimulation with cold pressor test.

Results: Global uptake of HED was significantly lower in patients compared to controls (median and interquartile range 4.2 [3.3-4.9] vs 8.7 [7.3-9.1], p<0.001) without differences between vessel territories. As illustrated in figure 1, global MBF was lower in patients compared to controls at rest and during adenosine-induced hyperemia (p=0.006 and 0.012, respectively). However, there was no difference in MBF during cold pressor test between patients and controls (p=0.829).

Figure 1 Global myocardial blood flow at rest, during adenosine-induced hyperemia and during cold pressor test in young adult patients after arterial switch operation and healthy controls.
**Conclusion:** Although sympathetic innervation of the coronary arteries in young adults after the ASO is markedly reduced compared to healthy controls, MBF during sympathetic stimulation is comparable to healthy controls, suggesting an adequate blood flow response to sympathetic stimulation despite reduced innervation.

**Disclosure of Interest:** None Declared
Introduction: The arterial switch operation (ASO) is currently the surgical technique of choice for repair of d-transposition of the great arteries. The main pulmonary artery is moved forward (Lecompte maneuver) and its branches are stretched on either side of the ascending aorta. The coronary arteries are removed from and reinserted into the aorta. We sought to assess myocardial deformation changes in the right (RV) and left ventricles (LV) as signs of subclinical myocardial functional impairment after ASO and re-positioning of the coronary arteries.

Methods: Patients after ASO and normal controls underwent cardiac magnetic resonance (CMR) imaging including 2D SSFP for ventricular function. 2D SSFP cine images were post-processed with a feature tracking software (TomTec 2D CPA). Global circumferential strain was measured on short axis mid-ventricular slices and global longitudinal strain on horizontal long-axis images, separately for each ventricle. Patients with pulmonary arteries stenoses or history, symptoms, or CMR findings suspicious for coronary compromise were excluded.

Results: Eighteen patients after ASO (age 16.8± 6.7y) were compared to 18 normal controls (age 22.2± 11.4y; p=0.098). RVs of ASO patients showed lower longitudinal strains (-14.1± 6.4% vs. -18.3± 3.8%; p<0.05) but higher circumferential strains (-16.6± 3.2% vs. -13.1± 4.3%; p<0.01) compared to normal RVs. LV longitudinal strain (-15.4± 5.1% vs. -17.5± 4.6%; n.s.) and LV circumferential strain (26± 5.6% vs. -23± 13.1%; n.s.) were not significantly different in patients vs. controls. There were no differences between ASO patients and controls regarding ejection fractions of the RV (54± 6% vs. 52%± 5%; n.s.) and LV (58± 8% vs. 60%± 5%; n.s.) or regarding end-diastolic volumes of the RV (91± 21ml/m2 vs. 94± 12ml/m2; n.s.) and LV (87± 26ml/m2 vs. 80± 11ml/m2; n.s.) indexed to body surface area, respectively.

Conclusion: LV deformation is preserved after the ASO operation, despite coronary artery surgery. In contrast, even in the absence of significant pulmonary artery stenosis, RV deformation is altered with decreased global longitudinal strain and increased circumferential strain, while preserving RV volume and ejection fraction. This may be the result of abnormal ventriculo-arterial coupling after the Lecompte maneuver and its changes in the outflow tract geometry.

Disclosure of Interest: None Declared
**OR30**

**6. Cardiac imaging, congenital and pediatric cardiology**

Prenatal diagnosis of single ventricle physiology impacts morbidity and mortality

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**Introduction:** Single ventricle (SV) lesions are most often detected in fetal echocardiography. We sought to evaluate the impact of prenatal diagnosis on morbidity and mortality.

**Methods:** All consecutive patients born between 2001 and 2013 with pre- or postnatal diagnosed SV and birth weight >1800g from 1/2001 until 6/2013 were reviewed. Primary endpoint was 30days survival rate after Hemifontan palliation. Secondary endpoints were condition at admission, neonatal mortality (30d) and hospital morbidity after the first operation.

**Results:** 259 cases with SV physiology 160(62%) were prenatally diagnosed. After termination of pregnancy, intrauterine demise and comfort care a total of 181 alive newborns were admitted to our center for treatment. One patient died for non-cardiac cause. Thus 87 fetal cases and 93 postnatal cases were analysed. Prenatal and postnatal anatomical diagnoses showed similar distribution, including hypoplastic left heart syndrome 40/35%, atrioventricular septal defect 10/11%, tricuspid atresia 15/10%, double inlet left ventricle 14/13%, double outlet right ventricle 9/13%, others 12/18% and right ventricular predominance 56/55%. High-risk patients were equally present in both groups, and consisted of restrictive foramen or obstructive pulmonary veins 8/8%, right atrial isomerism 3/2%, left atrial isomerism 4/2%. Patients with a prenatal diagnosis were born earlier (38.2±1.4 versus 39.3 ±1.5, p<0.0001), but birth weight was not significantly different (3033±453g versus 3167±613,g p=0.09). Lactate at admission was more often >10mmol/l in postnatal cases (9/93 versus 1/87; p=0.02). PH at admission was more often <7.20 in postnatal cases than in prenatal diagnosed cases (10/93 versus 1/87; p=0.001). Postnatal diagnosed children presented ad admission with higher dose of prostaglandin ≥0.05mcg/kg/min (14/93 versus 2/87, p=0.003) and required more often mechanical ventilation (25/93 versus 2/87; p<0.0001). Neonatal mortality was significantly higher in postnatal diagnosed children (14% versus 4.6%, p=0.03). Overall mortality until 30d after Hemifontan palliation, including transplantation in one prenatal case, was also higher in postnatal diagnosed patients (24.7% versus 12.6%; p=0.04).

**Conclusion:** Prenatal diagnosis helps reducing neonatal morbidity and mortality in children with single ventricle physiology. Overall mortality remains significantly lower until 30 days after Hemifontan palliation in prenatal diagnosed compared to postnatal diagnosed cases.

**Disclosure of Interest:** None Declared
Introduction: In Switzerland there are an estimated 300-500 adults living with a systemic (subaortic) right ventricle (RV). This includes adults with prior atrial switch operations for complete transposition of the great arteries (D-TGA) and adults with congenitally corrected TGA (ccTGA). Although midterm survival is favorable, late outcome is compromised by RV dysfunction. The loading conditions of the subpulmonary left ventricle (LV) altered by interatrial shunting through baffle leaks or by obstruction of the LV outflow tract impact on the position of interventricular septum and hence, the geometry of the RV. We retrospectively investigated exercise capacity and RV function in patients with a systemic RV in relation to LV loading conditions.

Methods: We identified 161 adults with cc-TGA or d-TGA with prior atrial switch operations from a nation-wide registry. In 79 stable patients (pts), a cardiopulmonary exercise study and cardiac MRI or transthoracic echocardiography (in patients with a pacemaker) was performed within 12 months. Volume load (VOL) of the subpulmonic LV was defined as baffle leak with Qp:Qs > 1.5, and pressure load (PRESS) as LV outflow tract peak gradient > 20 mmHg. Exercise capacity (peak-VO2) and RV function (RV-EF) were compared between pts with LV pressure or volume load and those without (CONTR). For RV-EF measurement we used only MRI data (available in 66 pts).

Results: Mean age was 33±10 y, 70% were male. N=9 (11%) had cc-TGA, n=70 (89%) D-TGA and an atrial switch procedure. N=60 (76%) were in the CONTR group, n=12 (15%) in the PRESS group and n=7 (9%) in the VOL group. Cardiac MRI was done in 58 pts (73%), 21 pts (27%) had a pacemaker. Mean VO2max in all 79 pts was 25±7 ml/min/kg (70% of predicted) and did not differ between CONTR and PRESS (Fig). However, pts with a baffle leak (VOL) had a lower exercise capacity (VO2max 21±3 ml/min/kg [p=0.038] or 63% of predicted). Mean RV-EF was 48±9% and mean LV-EF was 62±9%. RV-EF did not differ between CONTR and VOL, but was higher in pts with a LV outflow tract obstruction (46±9% in CONTR and VOL [n=44] vs. 52±8% in PRESS [n=12], p=0.048). The VOL group had larger LV volumes, and the PRESS group smaller RV volumes compared to the others.

Picture/Graph:
Conclusion: In adults with a systemic RV, a pressure loaded subpulmonary LV seems to have a beneficial effect on systemic RV-EF. In contrast, a volume loaded LV has no effects on RV-EF, but is associated with decreased exercise capacity.

Disclosure of Interest: None Declared
Lung function in patients with primary ciliary dyskinesia (pcd): a multinational study

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Introduction: Data on lung function in patients with PCD are few and contradictory. Within the EU project BESTCILIA, we compared lung function (FEV1) of patients with PCD to the Global lung function initiative (GLI) 2012 reference values and to published data from UK patients with Cystic Fibrosis (CF; Goss et al. Thorax 2015).

Methods: We calculated z-scores and %predicted values for FEV1 using the GLI reference, and used a multilevel linear regression model, adjusted for age, sex and study centre, to account for repeated measurements.

Results: We obtained 4683 FEV1 measurements of 648 PCD patients from 15 centres. The median age was 16 years (range 6-70), 295 (46%) were females. In the multilevel model FEV1 z-scores (95% CI) were significantly lower than GLI values (FEV1 -1.5 (-1.6 to -1.4); p<0.005). Both sexes and all age groups were affected, with a smaller difference for children aged <10 years (FEV1 z score -1.18 (-1.3 to -1.05). Compared to published data for CF, FEV1 %predicted (95% CI) was similar in children (e.g. age 6-9: PCD: 87% (86 - 89%); CF: 90% (88 - 91%)); but better in adult PCD patients (age 18-21: PCD: 76% (73 - 80%); CF: 66% (65 - 68%)).

Conclusion: This is the largest study ever conducted on spirometry in patients with PCD. FEV1 was significantly reduced compared to normal reference values for all age groups and both sexes. Young children with PCD and CF both had a low FEV1, which later in life remained relatively stable in PCD unlike in CF. In the ongoing study, we will analyse determinants of lung function, particularly age at diagnosis, time since diagnosis, and diagnostic certainty.

Funding: FP7 grant 305404, SNF32003B-144068

Disclosure of Interest: None Declared
8. Pneumology and Thoracic Surgery

Altitude related adverse health effects in lowlanders with copd travelling to 3200 m. Randomized trial of preventive dexamethasone treatment

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Introduction: We investigated the incidence of altitude related adverse health effects (AAHE) in lowlanders with COPD during a stay at 3200m, and evaluated effects of preventive treatment with dexamethasone, a drug known to alleviate acute mountain sickness (AMS) in healthy subjects.

Methods: 112 COPD patients (mean±SD age 54.7±9.3y, FEV1 85±21 %pred, SpO2 95±2%) were studied in Bishkek (760m), Kyrgyz Republic, and after travelling within 6h to Tuja Ashu clinic (3200m) and staying there for 3 days. Patients received dexamethasone (2x4mg/d, p.o.) or placebo before ascent and during stay at 3200m according to a double-blind randomized, placebo-controlled trial. Main outcome assessed during 3 days at 3200m was the cumulative incidence of one of the following AAHEs: AMS (AMSc environmental symptom cerebral score ≥0.7), severe hypoxemia (SpO2 <75% for >30min) or discomfort requiring descent to low altitude. ClinicalTrials.com NCT02450968

Results: During 3 days at 3200m, 21 patients (19%), 11 (20%) using placebo, 10 (18%) using dexamethasone (p=ns), had AAHEs (table). In the 1st 12h at 3200m, the cumulative incidence of severe hypoxemia or discomfort was lower with dexamethasone than with placebo (2 vs. 8 patients, p=0.04).

Table1. Altitude related adverse health effects in COPD patients

<table>
<thead>
<tr>
<th>Altitude</th>
<th>AAHE</th>
<th>AMSc score ≥0.7</th>
<th>H or D</th>
<th>AMSc score</th>
<th>SpO2,%</th>
<th>AAHE</th>
<th>AMSc score</th>
<th>H or D</th>
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<td>90.7±3.5*</td>
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<td>11</td>
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<td>3200m</td>
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<td>15</td>
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<td>89.2±3.4*</td>
<td>14</td>
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<td>0.09±0.15†</td>
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<td>91.4±2.6*</td>
<td>16</td>
<td>11</td>
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<td>0.09±0.16¶</td>
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<td>90.0±3.4*</td>
<td>18</td>
<td>12</td>
<td>9</td>
<td>0.09±0.24¶</td>
</tr>
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AAHE: altitude related adverse health effect including acute mountain sickness, severe hypoxemia or discomfort requiring descent to low altitude; H or D: severe hypoxemia or discomfort; *p<0.05 vs. 760m; †p<0.05 vs. day 1 at 3200m; ‡p<0.05 vs placebo at the same time of altitude exposure

Conclusion: In lowlanders with COPD, GOLD grade 1-2, staying 3 days at 3200m the cumulative incidence of clinically relevant AMS, severe hypoxemia or discomfort requiring descent to lower altitude was low (19%). Preventive dexamethasone treatment did not alter the cumulative incidence or severity of AAHEs although it improved severe hypoxemia and discomfort in the 1st 12h at 3200m.

Disclosure of Interest: None Declared
OR34

8. Pneumology and Thoracic Surgery

Hyaluronic acid and its degrading enzyme hyaluronidase as systemic biomarkers to predict COPD progression and severity

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Introduction: Hyaluronic acid (HA) is an abundant molecule in the human lung, which plays a key role in airway remodelling in COPD. The biological functions of HA depend on its molecular weight (MW). High-MW HA exhibits anti-inflammatory and immune-suppressive effects, while low-MW HA is pro-inflammatory. The aim of our study was to investigate if serum levels of HA and serum enzymatic activity of hyaluronidase (HYAL), the enzyme that degrades HA, can be used as systemic biomarkers to predict COPD progression and severity.

Methods: We prospectively evaluated 638 patients with stable COPD for ≥ 6 weeks, GOLD II-IV, > 10 PY seeking care in pulmonary tertiary hospitals in 8 European countries and included in the PROMISE cohort. The primary outcome of the study was exacerbation and/or death. Median observation time was 24 months. Serum levels of HA were measured at baseline by ELISA and hyaluronidase activity in serum by reverse HA zymography.

Results: Serum levels of HA were positively correlated with FEV1% pred (p=0.002) and FEV/FVC (p=0.025) while HYAL activity was negatively correlated with FEV1% pred (p=0.034). Furthermore, HA was associated significantly (p<0.001) with the time to death (Exp(B) 1.019 95% CI 1.009-1.029). Cox-regression multivariate analysis revealed that this association was independent of adjusted Charlson score, annual exacerbation rate and BODE index components.

Conclusion: Our results indicate that HA and its degrading enzyme HYAL may be used as systemic biomarkers to predict COPD progression and severity.

Disclosure of Interest: None Declared
OR35

8. Pneumology and Thoracic Surgery

A multicentre validation of the 1-minute sit-to-stand test in patients with chronic obstructive pulmonary disease

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Introduction: The 1-minute sit-to-stand (1-min STS) test is a simple exercise capacity test, which can be performed in almost any clinical setting. However, the 1-min STS test has not yet been comprehensively validated in patients with chronic obstructive pulmonary disease (COPD). We aimed to assess the measurement properties of the 1-min STS test in two populations of COPD patients.

Methods: Patients with COPD were included from two studies (Switzerland (CH): n=52 and Germany (D): n=205) in pulmonary rehabilitation (PR) clinics where all patients took part in an inpatient PR programme ranging from 10 days to 4 weeks. Patients were assessed with the 1-min STS test and additional exercise capacity tests (6MWT, five-repetition sit-to-stand test [5STS]), a muscle function test (QMVC) and patient reported outcomes (CRQ, SGRQ, CAT CCQ, FT, HADS, BDI/TDI) at the beginning and end of PR. We calculated intraclass correlation coefficients (ICCs) between two 1-min STS tests (learning effect and test-retest reliability; CH), Pearson correlation coefficients of the 1-min STS test scores and change scores with previously validated measures (cross-sectional and longitudinal validity), standardised response means (SRM) (responsiveness to change), and calculated the minimal important difference (MID) with anchor and distributional methods. In the Swiss study, we compared the 1-min STS test with the 5STS using Pearson correlation coefficients.

Results: The mean of the 1-min STS test scores at baseline were 16.5 ± 6.6 (CH) and 24.2 ± 7.5 (D). The change scores were 3.6 ± 4.1 (CH) and 4.0 ± 4.3 (D). The ICC for learning effect between two 1-min STS tests conducted at baseline was 0.93 (95% CI: 0.83 to 0.97) and for test-retest reliability at follow-up was 0.99 (95% CI: 0.97 to 1.00). The Pearson correlation coefficients between the 1-min STS test and 6MWT at baseline were 0.59 (CH) and 0.64 (D), and at follow-up were 0.67 (CH) and 0.68 (D). The SRMs were 1.16, 95% CI 0.86 to 1.45 (CH) and 0.92, 95% CI 0.78 to 1.07 (D). Based on estimates from both studies, the MID of the 1-min STS test was estimated as 3 repetitions. The 1-min STS test was highly correlated with the 5STS at both baseline and follow-up (Pearson correlation coefficients -0.59 and -0.70, respectively).

Conclusion: The 1-min STS test is a reliable and valid test for measuring exercise capacity in COPD patients. The test is responsive to PR and we suggest an MID of 3 repetitions for this patient population.

Disclosure of Interest: None Declared
**OR36**

**8. Pneumology and Thoracic Surgery**

**Longitudinal assessment of physical activity in patients with COPD**

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**Introduction:** Physical activity is an important clinical parameter related to morbidity and mortality in COPD. Although the benefits of participation in physical activity are widely recognized, most COPD patients do not engage in regular activity. Cross-sectional analysis has demonstrated that physical activity is severely reduced, however, little is known about longitudinal changes in physical activity in the context of disease progression.

**Methods:** This prospective, multicenter cohort study annually measured lung function, exacerbations and physical activity (steps per day with a multisensory armband over one week). Univariable regression was performed to investigate associations between annual change in steps per day and possible confounders. Multivariable analysis included regression of variables that showed a p-value of p<0.1 in univariable analysis.

**Results:** The mean observation time in 198 patients (137 males) with COPD was 2.5 (1/5) years. Mean (SD) age 63.5 (7.2) years, BMI 26.2 (6.0) kg/m2 and FEV1%pred. 49 (20). The mean (CI) daily step count decreased significantly during the 2.5 years of follow up by -556 (-740/-373) steps per day. Univariable regression revealed that age, pack years of smoking, FEV1%pred. at baseline and frequent exacerbations were significantly associated with the decrease in steps per day. However, changes of FEV1%pred. (adjusted for baseline FEV1%pred.) were not associated with changes in physical activity. Multivariable analysis demonstrated that age, pack years of smoking and baseline FEV1 were independently associated with changes in steps per day. Frequent exacerbations did not independently confound this relationship.

**Conclusion:** Physical activity substantially decreases over time in COPD patients independent of changes in lung function. Innovative strategies and efforts to increase the number of physically active COPD patients who successfully maintain their level of activity for a substantial length of time are needed.

**Disclosure of Interest:** None Declared
Therapy with proton-pump inhibitors for gastroesophageal reflux disease does not reduce the risk of severe exacerbations in copd

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Introduction: Gastroesophageal reflux disease (GERD) symptoms are associated with a higher risk of exacerbation of COPD. We hypothesize that treatment with proton pump inhibitors (PPIs) reduces the risk of exacerbation in patients with stable COPD.

Methods: We prospectively evaluated 638 patients with stable COPD for ≥6 weeks, ≥10 pack year of smoking and GOLD II-IV seeking care in tertiary hospitals in 8 European countries in the PROMISE-COPD cohort. Comorbidities including associated medical treatment were assessed at baseline, at exacerbation and at biannual visits. Median observation time was 24 months. The primary outcome of the study were exacerbation and/or death.

Results: A total of 85 (13.3%) of COPD patients were on anti-GERD therapy. These patients had higher annual and higher severe exacerbation rates (p=0.009 and p=0.002), decreased quality of life (SF-36: activity score p=0.004, SGRQ: physical functioning p=0.013, social functioning p=0.007), higher BODE-index (p=0.033) and MMRC scores (p=0.002), shorter 6 MWD (p=0.0004) and a higher adjusted Charlson score (p<0.0001). Anti-GERD therapy was associated with a shorter time to severe exacerbation (HR 2.05 95%CI 1.37-3.08). Using 3 multivariable cox-regression models, this association was independent of: (a) adjusted Charlson score and FEV₁% pred (HR 1.91 95% CI 1.26-2.90); (b) adjusted Charlson score, BODE index and MMRC (HR 1.62 95% CI 1.04-2.54) and (c) adjusted Charlson score, FEV₁% pred and 9 classes of medication for comorbidities (HR 1.63 95% CI 1.04-2.53).

Conclusion: These findings suggest that patients with stable COPD receiving acid-suppressive therapy with PPIs remain at high risk of frequent and severe exacerbations.

Disclosure of Interest: None Declared
Introduction: ProAdrenomedullin (ProADM) serum levels were associated with reduced survival and frequent exacerbations in COPD patients. This clinical observation is in some contradiction to the assumed beneficial anti-inflammatory effect of active adrenomedullin (ADM) in the lung. Intracellular signaling of ADM is mediated via the receptor activity modifying protein (RAMP)-1, 2, 3 and calcitonin receptor like receptor (CRLR). The study aimed to investigate the discrepancy of high ProADM levels in COPD patients and the missing beneficial effects of ADM. We characterized the response to ADM of primary human epithelial cells isolated from lung tissue biopsies obtained from patients with asthma (n=16), COPD (n=14) and controls (n=9), in regard to inflammation and remodeling.

Methods: The expression of ADM and its receptors was analyzed by immunohistochemistry and western blotting. Primary bronchial epithelial cells (BEC) were isolated from endo-bronchial biopsies and stimulated with ADM (10^-6 M). Secreted levels of CXCL1, CXCL5, IL-6, IL-8, IL-10 and TNFα were determined by ELISAs at 0, 24, and 48 hours and the activity of matrix metalloproteinase (MMP-2, MMP-9) by zymography. The activation of extracellular signal-regulated kinases 1/2 (ERK), p-38 mitogen-activated protein kinases (MAPK) and cyclic adenosine monophosphate response element-binding protein (CREB) was determined by western blotting.

Results: Immunohistochemistry showed equal ADM expression in all lung tissue sections. CRLR was expressed in epithelial cells and sub-epithelial cells. RAMP-1, 2 and 3 were expressed only by sub-epithelial cells. Recombinant ADM significantly induced pro-angiogenic cytokine (CXCL1 and CXCL5) secretion only by asthmatic cells. ADM did not significantly induce the secretion of pro-inflammatory cytokines (IL-6, IL-8, IL-10, TNFα). In the same BEC, ADM stimulated MMP-9 expression in a disease specific pattern with an increase of active MMP-9 in the asthmatic BEC as compared to healthy control and COPD cells. ADM did not activate any of the tested intra cellular signaling proteins, but instead it inhibited Erk1/2 phosphorylation in asthma cells, and had no effect on either CREB, or p-38.

Conclusion: Our results suggest a novel regulatory system of a cell-type and disease-specific response to ADM regulating inflammation, angiogenesis and remodeling in the human lung. Therefore, understanding the ADM system biology may lead to novel therapeutic and diagnostic targets.

Disclosure of Interest: None Declared
Cell-specific interactions between the novel myokine irisin and hyaluronic acid in chronic obstructive pulmonary disease

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Introduction: Physical activity is a principal target in the treatment for chronic obstructive pulmonary disease (COPD). Irisin, a recently identified myokine, has been controversially associated chronic exercise training (CET): meta-analysis of randomized controlled trials showed that CET leads to significantly decreased circulating serum levels of irisin, while CET in COPD patients was linked to a significant increase in serum levels of irisin. In order to clarify the role of irisin in COPD we investigated its interaction with hyaluronic acid (HA), a glycosaminoglycan that plays a key role in airway remodeling in COPD.

Methods: We used primary cultures of airway smooth muscle cells (ASMC) and fibroblasts from patients with COPD, and skeletal muscle cells (SkMC) that are known to produce irisin, as controls. Cells were stimulated with various concentrations of irisin for 24 and 48 h and secreted HA was measured by ELISA. Furthermore, we assessed irisin and HA serum levels in 638 patients with stable COPD, GOLD II-IV, >10 PY, included in the PROMISE cohort. The primary outcome of the study was exacerbation and/or death. Median observation time was 24 months.

Results: We observed that irisin stimulates significantly (p<0.001) in a time- and dose-dependent manner the secretion of HA by ASMC and SkMC, but not by fibroblasts. Circulating irisin was significantly higher in patients with severe exacerbations as compared with patients without severe exacerbations (1480 ± 121 μg/ml vs 1265 ± 88 μg/ml p=0.009). Furthermore, there was a significant (p=0.002) correlation (rho=0.142) between HA and irisin serum levels. HA was associated significantly (p<0.001) with the time to death (Exp(B) 1.019 95% CI 1.009-1.029), while irisin was associated significantly (p=0.004) with the number of severe exacerbations per year (OR 0.134 95% CI 0.051-0.269).

Conclusion: Our results indicate that irisin stimulates HA secretion, in a cell-specific way, and this is associated with COPD progression and severity. It may be postulated that the beneficial effects of CET in COPD patients may be attributed to reduced levels of HA associated with decreased levels of irisin.

Disclosure of Interest: None Declared
**OR40**

**8. Pneumology and Thoracic Surgery**

Bacterial endotoxin fine-tunes macrophage-fibroblast tissue remodeling activity

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**Introduction:** Long-term management of lung transplantation remains limited by Chronic Lung Allograft Dysfunction (CLAD), a poorly understood entity associated with inflammation and pathological remodeling. We hypothesized that the cross-talk between the pulmonary microbiota and host macrophages-fibroblasts is a key determinant in the control of lower airway remodeling.

**Methods:** Using in vitro mono- and co-culture experimental models of monocyte-derived macrophage (differentiated THP1) and fibroblast (MRC5) stimulation, we quantified by RT-PCR the expression of a panel of remodeling genes. Expression profiling was assessed in the presence of low- or high-dose *Escherichia coli* endotoxin, to mimic different levels of microbial stimulation, under baseline conditions or upon exposure to pro-remodeling factors (TGFβ and immunosuppressive drugs).

**Results:** In monocultures, macrophages and fibroblasts presented a range of pro-remodeling activation states that culminated under immunosuppressive conditions combined with TGFβ stimulation. Bacterial endotoxin played a protective role in macrophages, in marked contrast to fibroblasts, by reducing the rate of remodeling gene expression. Importantly, in coculture experiments enabling macrophage-fibroblast cross-talk, the dose-dependent protective effect of endotoxin was transmitted to fibroblasts, as detected by a lower gene expression of markers of fibroblast to myofibroblast differentiation (e.g. alpha smooth muscle actin, collagen I, fibronectin 1), a hallmark of tissue remodeling.

**Conclusion:** Our data suggest that a fine-tuned interplay between microbes and host cells in the transplanted lung is required to prevent the acquisition of an exaggerated pro-remodeling activation profile in macrophages and fibroblasts, key effector cells in fibrogenesis. Prevention of lung microbiota dysbiosis might be considered as an important therapeutic objective during long-term post-transplant follow-up.

**Disclosure of Interest:** None Declared
Mesenchymal stem cells isolated from human lung tissue inhibit proliferation and collagen expression by lung fibroblasts

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Introduction: The pathomechanisms leading to idiopathic pulmonary fibrosis (IPF) are not fully understood, but they ultimately result in enhanced numbers of fibroblasts and the accumulation of extracellular matrix (ECM) components in the lung interstitium. Therapeutic approaches therefore target fibroblast proliferation and ECM deposition. In animal models of lung fibrosis, beneficial effects of exogenously administrated stem cells have been demonstrated. Mesenchymal stem cells have been identified in the human lung; however, their role in lung disease is not clear. In this study we isolated and characterized for the first time mesenchymal stem cells from lung tissue obtained from patients with fibrotic lung diseases and from emphysema patients and studied their in vitro properties.

Methods: Mesenchymal stem cells were cultured from fibrotic (n=17), emphysema (n=12), and from normal control lungs (n=3). The characterization of cells was performed by immunofluorescence stainings. The effect of conditioned media obtained from mesenchymal stem cells (n=7) on proliferation of primary human lung fibroblasts and on collagen mRNA expression by real time RT-PCR was studied.

Results: Expression of CD44, CD90, CD105, Oct3/4, and NANOG characterized the cells as mesenchymal stem cells. In addition to their mesenchymal differentiation potential (adipocytes, osteoblasts, myoblasts, chondroblasts), stem cells were able to differentiate into epithelial cells. Significantly more mesenchymal stem cells were obtained from fibrotic lungs than from emphysema or control lungs (p<0.001). Conditioned medium obtained from these mesenchymal stem cells significantly inhibited the proliferation of lung fibroblasts by 29% (p=0.0001). Expression of collagen type I mRNA was markedly decreased in the presence of stem cell-derived conditioned medium by 40% (p<0.0001).

Conclusion: Our data demonstrate that conditioned medium obtained from lung mesenchymal stem cells exhibits significant anti-fibrotic properties via the inhibition of proliferation and collagen expression by fibroblasts. Furthermore, we found enhanced numbers of mesenchymal stem cells in fibrotic lung tissue as compared to emphysema and normal lung, suggesting a pivotal role of these cells in local repair mechanisms. Our data indicate that lung resident mesenchymal stem cells have fibro-protective properties and might therefore be a novel therapeutic approach for patients with idiopathic pulmonary fibrosis.

Disclosure of Interest: None Declared
Pneumology and Thoracic Surgery
Virosomes coupled to antigen induce enhanced specific CD4+ T cell activation compared to liposomes in an in vitro model of pulmonary dendritic cells
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Introduction: Nanocarriers provide a promising approach for vaccinations, therapies and prognostic tools. Virosomes and liposomes represent degradable bio-mimetic antigen carriers with great potential for antigen delivery and virosomes additionally with immunostimulatory properties derived from the incorporated hemagglutinin (HA) from influenza virus. In this study, we set out to study the interaction of these particles with antigen presenting cells.

Methods: Virosomes and liposomes were fluorescently labelled for detection and/or coupled with ovalbumin (OVA) as a model antigen. Murine bone marrow-derived and in vitro differentiated dendritic cells (BMDCs) were treated with virosomes or liposomes prior to determining particle uptake, cell viability and BMDC phenotype. Co-Cultures of pre-incubated BMDCs and OVA-specific CFSE-labeled CD4+ T cells were analyzed for T cell activation, proliferation and polarization.

Results: Rapid particle uptake occurred with virosomes, whereas uptake of liposomes was slower. Neither virosomes nor liposomes affected BMDC viability, nor did the moderate degree of activation differ for CD40, CD80, CD86. BMDCs pre-incubated with OVA-coupled virosomes induced strong CD4+ T cell proliferation compared to DCs pre-incubated with empty virosomes and soluble OVA protein or liposomes with coupled OVA. Specific CD4+ T cell proliferation by OVA-coupled virosomes was achieved with 100-fold lower antigen concentration than with corresponding soluble OVA. Intracellular staining revealed increased IFN-g production and upregulation of FoxP3 when treated with OVA-coupled virosomes compared to OVA-coupled liposomes.

Conclusion: Taken together, both virosomes and liposomes were successfully taken up by DCs and induced similar upregulation of co-stimulatory markers. Specific CD4+ T cell proliferation was achieved by OVA-coupled virosomes, only. Antigen-coupled virosomes therefore represent a promising approach to modulate mucosal immune responses by interacting with DCs.

Disclosure of Interest: None Declared
Introduction: Idiopathic pulmonary fibrosis (IPF) is a devastating lung disease with poor survival. There is an urgent need to better diagnose and monitor IPF patients as new treatments are available. Exhaled breath condensate (EBC) is easily and non-invasively collected, but analysis of potential biomarkers is difficult due to low concentrations and methodological limitations. Nevertheless, initial studies have shown differences in levels of lysophosphatidic acid in EBC in IPF compared to controls. We now used a non-targeted metabolomics approach to identify discriminatory metabolic profiles between IPF and controls.

Methods: We collected EBC from 10 stable IPF and 10 lung healthy controls. Samples were analyzed by ultra-performance liquid chromatography coupled to high-resolution mass spectrometry (UPLC-MS) in positive and negative ion mode. An in-house established bioinformatics pipeline was applied for data processing and analysis. Briefly, raw data were processed with Progenesis QI (v2.0, Nonlinear Dynamics). Multivariate analysis was applied to visualize trends and outliers within observations and to identify discriminative metabolites between IPF and controls using principal component analysis (PCA) and orthogonal projection to latent structures-discriminant analysis (OPLS-DA) with SIMCA (v14, Umetrics). The discriminative metabolites were reviewed and excluded if they failed standardized acceptance criteria.

Results: In total 31 metabolites were found to be discriminative between IPF and controls (FDR corrected Mann-Whitney q-value ≤0.05). Of them, 20 were detected in positive, and 11 in negative mode, respectively. Changes up to 5-fold were observed and the majority of candidates (84%) were down-regulated in IPF compared to controls. Even though a discriminative metabolite signature was found between IPF and controls, the identities of the individual metabolites still remain elusive.

Conclusion: Our preliminary results identified a distinguished EBC profile of IPF patients compared to controls. Although these results need to be confirmed in additional individuals, EBC sampling as a method to diagnose and/or monitor IPF patients would be an exciting new technic which deserves further exploration.


Disclosure of Interest: None Declared
OR44

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Three-dimensional self-navigated T2 mapping for the detection of acute cellular rejection after orthotopic heart transplantation


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Introduction: Magnetic resonance imaging with measurement of the T2 signal detects myocardial edema, which accompanies acute cellular rejection (ACR). The present study tests three-dimensional (3D) self-navigated T2 mapping at an unprecedented resolution of 1.7mm3 for the detection of focal ACR.

Methods: High-resolution 2D T2 maps were acquired in 3 short-axis slices; self-navigated 3D radial whole-heart isotropic T2 maps (flip angle 70°/35°, voxel size 1.7mm3) were obtained during free breathing. Both 2D and 3D T2 maps were segmented in accordance with the AHA guidelines. The highest segmental 2D and 3D T2 values of each patient were compared statistically. Patients were divided into groups with no (OR), mild (1R), and moderate (2R) ACR; groups were then tested for differences in T2 value. 3D T2 maps were rendered as 3D images (Figure), after which they were inspected for foci of T2 elevation.

Results: Results:
A total of 26 HTx recipients in the stable phase after HTx were included (mean age: 52±9 years; 3 females; mean donor age: 42±12 y; mean time post-transplant: 699±674 days). Four 3D T2 maps were discarded due to insufficient image quality. OR was present in 18 EMBs, 1R in n=3, 2R in n=1; no EMB presented acute humoral rejection. The reformatted 3D T2 values agreed well with the 2D T2 values for all patients (p>0.51 for all paired t-test comparisons with Bonferroni correction). The highest 2D segmental T2 values of the 3 ACR groups were 49.9±4.0ms (0R), 48.9±0.8ms (1R), and 65.0ms (2R). Rendered 3D T2 maps of the 3 cases with 1R ACR showed foci with significantly elevated T2=58.2±3.6ms that were not visible on the 2D T2 maps (Figure 1B, black arrow). Of note, 3D self-navigated T2 mapping showed patches of increased T2 value in 5/18 patients (44%) without histological signs of ACR in the EMB.

Figure 1. 3D & 2D T2 maps of cardiac allograft rejection. A-C) rendered 3D T2 maps segmented along the center of the endocardium of the left ventricle. D-F) Corresponding basal 2D T2 maps. Segmental T2values in 2D T2 maps of the patients with 1R (by EMB) were not elevated whereas the corresponding 3D T2 maps showed myocardial areas with significantly elevated T2 values (black arrow). The color bar indicates T2 values in ms for all maps.

Conclusion: This pilot study indicates the potential of 3D self-navigated T2 for ACR detection with higher sensitivity when compared with EMB.

Disclosure of Interest: None Declared
OR45
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation
Predictors of procedural outcomes of left atrial appendage closure in patients with atrial fibrillation
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Introduction: Percutaneous left atrial appendage closure (LAAC) is a valuable treatment option for stroke prevention in patients with atrial fibrillation (AF). Determinants of procedural safety events with AMPLATZER occluders are not well established, and the possibly interrelating effect of LAA anatomy is unknown. This study sought to assess predictors of adverse peri-procedural outcomes and determine the effect of LAA morphology following LAAC with AMPLATZER devices.

Methods: Between 2009 and 2014, 500 consecutive AF patients ineligible or at high risk for oral anticoagulation underwent LAAC using AMPLATZER devices at two Swiss centers. In-hospital outcomes were recorded. Major adverse events (MAE) were defined as death, stroke, major or life-threatening bleeding, cardiac tamponade, major access-site vascular complication, need for cardiovascular surgery, or grade-3 kidney injury within 7 days following the intervention.

Results: Patients (age 73.9±10.1 years) were treated with AMPLATZER Cardiac Plug (n=408, 82%) or Amulet devices (n=92, 18%). Procedural success was 97.8% and MAE occurred in 24 patients (4.8%). Independent predictors of MAE included device repositioning (OR 4.01; 95% CI 1.16-13.9; p=0.028) and baseline warfarin treatment (OR 2.12, 95% CI 0.87-6.07; p=0.07) with no effect of device type or size. Angiographic LAA morphology, characterized as cauliflower (33%), cactus (32%), windsock (20%) or chicken-wing (15%), was not associated with procedural success (p=0.51) or the occurrence of in-hospital MAE (p=0.89).

Conclusion: Peri-procedural major adverse events following LAAC with AMPLATZER devices occurred at relatively low rates and were predicted by patient- and procedure-related factors. While LAA morphology displayed substantial heterogeneity, procedural outcomes were comparable across the spectrum of LAA anatomies.

Disclosure of Interest: None Declared
**OR46**

**3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation**

Iron deficiency based on high soluble transferrin receptor index identifies patients at the highest risk of death in chronic heart failure patients

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**Introduction:** Iron deficiency (ID), irrespective of anaemia, is an important predictor of mortality in heart failure (HF) patients. Previous studies defined ID in HF as ferritin ≤ 100 µg/L or ferritin 100–299 µg/L with transferrin saturation (Tsat) < 20%. However, ferritin and Tsat are both affected by chronic disease and inflammation and represent only surrogates of ID. In contrast, soluble transferrin receptor (sTfR) reflects the cellular iron demand and therefore is a sensitive indicator of ID. The aim of this study was to define the role of sTfR in the prediction of ID associated mortality in HF patients.

**Methods:** Patients with chronic HF and reduced left ventricular ejection fraction (LVEF <40%) were prospectively analysed for ferritin, Tsat and sTfR and followed for one year in the Registry Analysis of Iron Deficiency (RAID) at the University Hospital Basel. The ID diagnosed based on sTfR (ID-sTfR) was defined as the combination of sTfR >3.5 mg/L and sTfR/log ferritin (sTfR index) > 1.55. The ID-sTfR prevalence and impact on mortality were compared with the traditional definition of ID based on ferritin and Tsat (ID-ferritin/Tsat).

**Results:** A total of 187 patients (75% men, age 72 ± 12, LVEF 28± 8%) completed the 1-year follow up. The prevalence of ID-sTfR was similar as ID-ferritin/Tsat (45% and 46% patients, respectively). The ID-sTfR patients did not differ in terms of NYHA-classification, B-type natriuretic peptide (BNP), haemoglobin and creatinine clearance from ID-ferritin/Tsat patients. During the 12-month follow-up, 25 patients (13 %) died. Patients with ID-sTfR exhibited a significantly higher mortality [HR=2.68, CI: 1.15- 6.30, p=0.02], when compared with patients with ID-ferritin/Tsat [HR=1.68, CI: 0.75- 3.79, p=0.21]. Patients with preserved iron status had the lowest mortality [HR=0.41, CI: 0.16- 1.03, p=0.06]. The prognostic value of ID-sTfR persists even after adjustment for haemoglobin and BNP. When both definitions of ID in patients with ferritin > 100 µg/L, were included in one Cox proportional hazard model, only ID-sTfR was a significant predictor of 12-month mortality (HR=3.43, CI: 1.23- 9.21, p=0.01).

**Conclusion:** ID-sTfR is common in chronic HF and identifies patients at higher risk of death compared to those diagnosed by the traditional definition based on ferritin and Tsat. Therefore, sTfR and sTfR-index should be included into the diagnostic work-up and may help to guide iron supplementation therapy in HF patients with ID.

**Disclosure of Interest:** None Declared
Introduction: Frailty and associated comorbidities are often prohibitive surgical risk factors in symptomatic severe aortic stenosis. Transcatheter aortic valve replacement (TAVR) is a viable treatment option for such patients. Neopterin, a pteridine synthesized by activated macrophages reflecting Th1-dependent interferon-γ production, has been associated with prevalent frailty in elderly patients. Moreover, immune activation-mediated tryptophan degradation is associated with frailty in diverse chronic disease states.

Methods: We thus prospectively investigated a total of 392 patients undergoing TAVR and measured neopterin, kynurenine, tryptophan, tyrosine and phenylalanine levels at baseline and at day 1-3 post intervention. In the derivation cohort of 185 patients, neopterin, plasma kynurenine/tryptophan ratio (KTR) and plasma phenylalanine/tyrosine ratio (Phe/Tyr) were dichotomized at the upper quartile, and Royston-Parmar proportional hazards models were employed relating biomarkers to all-cause mortality.

Results: In bivariate analysis adjusted for EuroSCORE II, belonging to the upper quartile of neopterin (HR 5.7, 95% CI: 2.0-16.5, P < 0.01), KTR (HR 3.1, 95% CI: 1.1-8.5, P = 0.02) and Phe/Tyr ratio (HR 2.8, 95% CI: 1.0-7.7, P = 0.03) emerged as independent predictors of mortality. A similar finding on neopterin and KTR was obtained in the 207 patients of an external validation cohort.

Conclusion: Increased Th1-type immune activation and associated tryptophan degradation serve as biochemical signatures of frailty underscoring the prognostic role of baseline inflammation for outcome in patients with severe aortic stenosis undergoing TAVR, and thus may provide a future therapeutic target in this elderly patient population.

Disclosure of Interest: None Declared
Introduction: Early mortality is high after hospitalization for heart failure (HHF). Clinical improvement with HHF suggests that prediction of postdischarge mortality based on admission variables is not appropriate. This study compares prediction of early postdischarge mortality based on pairs of admission and discharge variables.

Methods: This study enrolled consecutively a total of 407 HHF patients hospitalized with HHF at a tertiary center (mean age 78±7 years, 57.4% males). At admission, patients presented with cardiogenic shock (4.1%), pulmonary edema (25.5%), right heart failure (10.8%), hypertensive crisis (10.3%), and global decompensation (49.3%). Mean length of stay was 10±5 days. In-hospital mortality was 6.4%, the outcome parameter was mortality at 30 and 180 days postdischarge (2.2% / 17.3% / 25.2%, respectively). Association between discharge variables and early postdischarge mortality at 30 and 180 days was assessed using a logistic regression model.

Results: Heart rate (95% CI :1-1.09 ; p=0.0404), potassium (95% CI :0.02-0.89; p=0.0347), use of loop diuretic (95% CI :0.02-0.6; p=0.011), and eGFR <60 ml (95% CI :0.14-0.72; p=0.0058) were merged in a risk score for prediction. Receiver operating characteristic (ROC) curve compared model performance in pairs of admission and discharged values. The area under curve was always increased when based on discharge parameters most clearly for postdischarge mortality at 30 days (0.53 to 0.89) and morderately at 180 and 365 days (0.54 to 0.69; 0.51 to 0.63, respectively).

Conclusion: Prediction of postdischarge mortality after HHF is improved when based on discharge parameters.

Disclosure of Interest: None Declared
OR49

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation
Renal function post tavi, a significant predictor of mortality: introducing the acef-7 score
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Introduction: Impact of Worsening in renal function post TAVI as a predictor of long term all-cause mortality, by means of a modified ACEF score, using the highest creatinine level obtained within one week post the procedure, here referred to as the ACEF-7 score.

Methods: 456 consecutive TAVI patients were included. Patients who died within one week after TAVI were excluded (n=17 (3.7%)), leaving a study population of 439 patients. All-cause mortality at 1-year and 6 months were 17.5% (80) and 12.5% (57) respectively. The surviving 439 (96%) patients one week post valve implantations were stratified according to ACEF-7 score.

Results: Baseline Euroscore II, STS, ACEF, ACEF-Modified had AUC for 1 year all-cause mortality of 0.562, 0.588, 0.598, 0.621 respectively. Hence we formulated the ACEF-7 score to improve prediction of mortality, which resulted in an AUC 0.675 and 0.7 for 1-year and 6 month all-cause mortality. Patients were then stratified into ACEF-7 low (score<2.1, n=108), ACEF-7 mid (score 2.2-3.48, n=116), and ACEF-7 High groups (score>3.48, n=48.7). 1-year and 6 month all-cause mortality was significantly higher in the ACEF-7 High compared to the other groups (21.5% vs 10.3% vs 6.5%, p<0.001) and (9.6% vs 5.2% vs 3.7% p=0.001) respectively. Euroscore II and STS score were both not predictors of mortality post TAVI. ACEF-7 in a multivariable Cox regression model corrected for gender, baseline mean aortic valve gradient, Post-TAVI aortic regurgitation grade ≥2, and baseline ACEF modified, was the only independent predictor of 1-year all-cause mortality as a per point increment HR 1.6 [95% CI 1.604 – 1.176, p=0.003] and as ACEF-7 High group HR 3.10 [95% CI 1.36 – 7.04, p=0.007].

Conclusion: The ACEF-7-score was the best predictor of long-term outcome in survivors one week post TAVI which outperformed standard pre-TAVI scores by simply adjusting for worsening in renal function post the procedure.

Disclosure of Interest: None Declared
Introduction: Acute decompensated heart failure is a significant cause of recurrent hospital admissions and mortality, and rapid diagnosis and risk stratification in these patients is important. The angle between the vectors of the QRS complex and the T wave in the 12-lead surface ECG is a measure for an abnormal depolarization–repolarization relationship. Its value for diagnosis and prognosis in patients with symptoms suggestive of acute decompensated heart failure (ADHF) are unknown.

Methods: We prospectively enrolled 1188 consecutive patients with symptoms suggestive of ADHF. The QRS-T angle was automatically calculated from a digital 12-lead ECG recorded at presentation to the ED. Patients were followed up for all-cause mortality for 2 years.

Results: ADHF was the final diagnosis in 62% of patients. The median QRS-T angle was significantly greater in patients with ADHF compared to those without (35° (IQR 16-66) vs. 102° (IQR 43-157), p<0.001). The area under the ROC curve for the diagnosis of ADHF was 0.74. Overall, 2-year survival rate was 69.8%. A greater QRS-T angle was significantly associated with a worse prognosis after 2 years (Survival rates 78%, 73%, 60% for patients with a QRS-T angle <50°, 50-100° and >100°, p<0.001). In multivariable analysis, the prognostic value of the QRS-T angle was independent of other important predictors such as age, sex or the QRS-duration.

Picture/Graph:
**Conclusion:** In patients with symptoms suggestive of ADHF, the QRS-T angle automatically derived from the 12-lead ECG was elevated in patients with ADHF. It significantly predicted all-cause mortality during 2 years of follow-up independently of age, sex or QRS-duration and therefore has the potential to improve immediate risk stratification in these patients.

**Disclosure of Interest:** None Declared
OR51
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation
First experience with the ozaki technique in europe: creating a stentless aortic valve by reconstructing leaflets using autologous pericardium
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Introduction: To demonstrate smooth and straight-forward clinical implementation and preliminary results of a novel technique for stentless aortic valve replacement by reconstructing leaflets using autologous pericardium, the Ozaki Technique.

Methods: Between 10/2015 and 12/2015 a total of 11 patients (6male, 70.5±9years) suffering from aortic stenosis (AS, n=8) or regurgitation (AR, n=3) were operated using glutaraldehyde treated autologous pericardium that was intraoperatively customized and tailored according to individual sinus measurements and appropriate OZAKI templates (CE marked). Peak / mean preoperative gradient in AS was 75.75±29.7 and 48.63±21.16mmHg respectively, effective orifice area 0.89±0.35cm² and ejection fraction (EF) was preserved with 56.3±16.9%. 9/11 valves were tricuspid, 2/11 bicuspid and 3/11 patients had concomitant cardiac surgery (mitral valve repair, replacement of ascending aorta). Data are in-hospital data.

Results: Success rate for valve reconstruction was 100%. Mean cross-clamp time for mere replacement was 78.12±12.22min; mean perfusion time 107.5±17.36min. Size of left coronary cusp (CC) was 27.0±2.36mm, right CC 27.0±2.68mm and non CC 28.8±2.75mm. Peak / mean postoperative gradients decreased to 12.9±4.7mmHg and 6.5±2.71mmHg respectively, mean effective orifice area increased to 3.02±0.66cm². Regurgitation of reconstructed valves was graded nil/trace in 7/11 and mild in 4/11. EF remained unaltered with 54±14.39%.

picture/graph:

Conclusion: The implementation of this since recently available aortic valve reconstruction technique in aortic valve surgery shows a quick increment of skills without tedious training and already has become part of our routine clinical armamentarium. The preliminary results are favorable in terms of decreasing pressure gradients and increasing effective orifice area. The use of autologous pericardium in combination with excellent hemodynamics might have the potential to overcome structural failing of biological aortic valves.

Disclosure of Interest: None Declared
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Predicting right ventricular failure in the era of continuous flow assist devices: why we are always wrong.

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Introduction: In the era of continuous flow left ventricular assist devices (LVAD), the decision of whether a patient will tolerate isolated LVAD support or will need biventricular support (BIVAD) can be challenging. Several risk stratification tools have been recently developed to predict the need of right assist device (RVAD) implant concomitant to continuous flow LVAD implantation, but none seems to outperform the others. We reviewed our experience to validate the most recent strategies identifying patients at risk of post LVAD right ventricular failure (RVF).

Methods: We collected hemodynamic and echocardiographic variables for 34 consecutive patients who underwent VAD implant from 2010 through June 2015 (LVAD=32, BIVAD=2). We defined pre-op RVF based on echocardiographic parameters, taking into account RV contractility, tricuspid regurgitation, and tricuspid annular motion (TAPSE). Post-operative RV failure was defined according to INTERMACS Protocol 3 definition (CVP>18 mmHg, CI<2 l/min/m², need for NOx or inotrope therapy>7 days after LVAD). For each patient, we calculated the CRITT score (CVP>15 mmHg, RV dysfunction, Intubation preoperatively, Tricuspid regurgitation, Tachycardia>100) and applied the Pittsburgh Decision Tree (PDT). We assessed score performance by entering it in a logistic regression model with RV failure as the outcome. The PDT was entered as a single binary predictor.

Results: The mean age was 52±12; 70.5% were men. The indication was bridge to transplant in 100%. Etiology was ischemic in 42%; 14.7% required additional mechanical circulatory support after LVAD implant (BVAD=2, ECMO=3). All patients received continuous flow LVADs (HeartMate II=13, HeartWare=21). By 30 days, 22 patients (64.7%) developed RVF defined as the need for RVAD (n=2); pulmonary vasodilator use >48h (n=18); inotropes for >14 days post LVAD (n=22). According to CRITT score the RVF expected rate was 29% (10 patients had 4 or 5 corresponding to 80% risk of RVF). According to PDT, 8 patients needed BVAD. CRITT score achieved best performances: C stat=0.60; CI 95%; sensitivity=90%; specificity=8.3%.

Conclusion: These data indicate that even clinical RVF risk prediction models developed in the era of continuous flow pumps have rather limited clinical applicability. We need new clinical test based on quantitative pre-operative imaging data, able to quantify the functional reserve of RV to drive our clinical decision about using an isolated LVAD versus BIVAD, especially in the destination therapy perspective.

Disclosure of Interest: None Declared
OR53

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Prognostic impact of aortic regurgitation after tavi: effect of kidney function

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Introduction: To evaluate the impact of aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) on short- and long-term outcome in patients with reduced kidney function.

Methods: Short- and long-term outcome was obtained in 546 patients (mean age 81.9±7.7 years) undergoing TAVI for severe aortic valve stenosis. Short-term outcome was defined as a combined early safety endpoint at 30 days according to the valve academic research consortium-2 (VARC-2) criteria, long-term outcome as mortality at 1 year. Post-implant AR was classified as none/mild or moderate/severe using transthoracic echocardiography. Aortic valve calcification was determined using computed tomography. Uni- and multivariate logistic regression analyses were performed in patients with none/mild (estimated glomerular filtration rate [eGFR] ≥30ml/min/1.73m2, 487 patients [89%]) and moderate/severe (eGFR <30ml/min/1.73m2, 59 patients [11%]) chronic reduction in kidney function.

Results: The 30 day endpoint occurred in 88 patients (16%). Moderate/severe post-implant AR was documented in 66 patients (12%). In patients with eGFR <30ml/min/1.73m2, moderate/severe AR was the only independent predictor of the 30 day endpoint (odds ratio [OR] 7.091, 95% confidence interval [CI] 1.144-43.962, p=0.035). In contrast, in patients with normal/mildly reduced kidney function, the degree of AR was not predictive of short-term outcome, while the levels of hemoglobin (OR 0.994 per 1g/L increase, 95% CI 0.989-0.999; p=0.017) and NT-proBNP (OR 1.023 per 500ng/L increase, 95% CI 1.003-1.043; p=0.026) before intervention were independent predictors of the 30 day endpoint. Similarly, moderate/severe post-implant AR contributed to impaired long-term outcome only in patients with moderately/severely reduced kidney function (p<0.001), but not in patients with normal/mildly reduced kidney function. Aortic valve calcification was comparable in patients with none/mild and moderate/severe reduction in eGFR. Logistic regression analysis revealed aortic valve calcification as the only independent predictor of moderate/severe post-implant AR, both in the overall population and in the subgroups with various kidney function.

Conclusion: Moderate/severe AR after TAVI independently predicts short-term outcome in patients with moderate/severe chronic reduction in kidney function, but not in patients with normal or mildly reduced kidney function.

Disclosure of Interest: None Declared
OR54

6. Cardiac imaging, congenital and pediatric cardiology

Prognostic value and the optimal ischemic threshold of adenosine stress-perfusion CMR in patients with suspected myocardial ischemia. The experience of the CMR center at university hospital of lausanne, switzerland. 

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Introduction: Perfusion-CMR is increasingly used in daily practice while the ischemic burden indicating a need for revascularization is not well defined. We aimed to correlate the ischemic burden in perfusion-CMR with the outcome in patients with suspected myocardial ischemia.

Methods: Between January and December 2012, 310 consecutive patients referred to adenosine stress-perfusion CMR were prospectively enrolled in our data registry. A 16-segment left ventricular model was used for assigning myocardial ischemia and scar. Myocardial ischemia was defined as perfusion defect in at least one segment. Late gadolinium enhancement (LGE) technique was used to detect myocardial scar. The primary end-point was a composite of all-cause of death, non-fatal myocardial infarction (MI) and late coronary revascularization (>30 days post stress-CMR).

Results: One-hundred-seventy-three patients (56%) had a previous history of MI or coronary revascularization and a myocardial scar was detected in 192 (62%) patients. During a mean follow-up of 371±97 days, the primary end-point occurred in 35 (11%) patients (5 cardiac and 2 non-cardiac deaths, 4 non-fatal MI and 28 late revascularizations). Myocardial ischemia was diagnosed in 134 patients (43%) and the median number of ischemic segment was 2.0 (25th-75th 1-4 segments). Receiver operating characteristic curve showed that the cut-off of 1.5 ischemic segments had a sensitivity of 77% and a specificity of 75% for predicting the primary end-point. The occurrence of primary end-point was similar between patients without ischemia and those with only 1 ischemic segment (4.0% vs 2.5%, HR: 0.621, 95% CI 0.076-5.050, P=0.656). Conversely, the presence of ischemia in more than 1 segment was associated with high rate of primary end-point (28%, HR: 8.593, 95% CI 3.902-18.923, P<0.001) (Kaplan Meyer curve shown in Figure 1). At multivariate analysis, ischemia in more than 1 segment remained a strong and independent predictor of adverse clinical outcome (HR 8.632, 95% CI 3.810-19.555, P<0.001) even after correction for age, LV ejection-fraction and myocardial scar.

Picture/Graph:
**Conclusion:** In patients referred to adenosine stress CMR, the detection of ischemia in more than 1 segment strongly influences the outcome. This ischemic threshold should be recommended for patients' management in the clinical practice.

**Disclosure of Interest:** None Declared
**Introduction:** The Edwards Sapien 3 heart valve prosthesis (S3) is commonly used for transcatheter aortic valve implantation (TAVI) and is available in 3 sizes. To date, however, no data has been published on the effective orifice area (EOA) of the different sizes of this prosthesis. The aim of this study was to measure the size-specific EOA and hemodynamic performance of this prosthesis in short and midterm follow up.

**Methods:** 113 consecutive patients treated by TAVI with a S3 prosthesis at the Heart Clinic Zurich between May 2014 and July 2015 were included. Clinical data were extracted from the Swiss TAVI register. The EOA was calculated using Doppler echocardiography (baseline, discharge) and by 3D-biplane transesophageal echocardiography (peri-interventional). Mean transvalvular gradients (dPmean) were additionally measured at 30 days and 1 year. Results were analysed separately for the 23mm, 26mm and 29mm prostheses.

**Results:** The study populations’ mean age was 83 ± 4.9 years, and 50% were male. The mean body surface area (BSA) was 1.8 ± 0.2 m², and the baseline mean left ventricular ejection fraction was 56 ± 14%. Of the 113 patients, 42 (37%) received a 23mm S3, 46 (41%) a 26mm S3, and 25 (22%) a 29mm S3. The results of the EOA and dPmean per prosthesis size are given in figure 1. At the time of implantation, the EOA were 1.7 ± 0.2 cm² (23mm S3), 2.2 ± 0.2 cm² (26mm S3), and 3.0 ± 0.2 cm² (29mm S3), p < 0.001. The mean EOA indexed to BSA was 1.2 ± 0.3 cm²/m². Despite the differences of EOA, the dPmean did not differ between prosthetic sizes at discharge (p = 0.21), 30 days (p= 0.26) and 1 year (p = 0.11).

**Conclusion:** This is the first study to describe the in vivo EOA and transvalvular gradients of the Edwards Sapien 3 TAVI prosthesis in short-term and 1 year follow-up differentiated by prosthesis size. While the EOAs significantly differ between the three prosthesis sizes, the transvalvular gradients are comparable. Mean transvalvular gradients remain stable over
time and document good prosthesis function after 1 year. The results of this study are relevant for clinical follow up and to avoid patient prosthesis mismatch.

**Disclosure of Interest:** None Declared
Multimodality imaging causes reclassification of aortic stenosis severity in patients undergoing TAVI: effect on aortic valve area and energy loss index

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Introduction: This retrospective study assessed whether the combined evaluation of data from transthoracic echocardiography (TTE) and multidetector computed tomography (MDCT) affected the grading of aortic stenosis (AS) severity under consideration of the energy loss index (ELI) in patients undergoing TAVI.

Methods: 194 consecutive patients with symptomatic severe AS undergoing TAVI were included in this study.

Results: LVOT diameters measured by TTE were comparable to the minimal diameter and consistently smaller than the maximal diameter measured in MDCT. The sphericity index (diameter min/max in MDCT) confirmed the ovoid configuration of the LVOT (sphericity index = 0.75±0.1). LVOT area derived from TTE was smaller than the LVOT area assessed by planimetry in MDCT. Measurement of the sinotubular junction (ST-junction) in TTE by inner edge to inner edge (ITI) versus leading edge to leading edge (LTL) method demonstrated that LTL measurements were larger than ITI values. LTL ST-junction diameter was similar to maximum, minimum, and mean ST-junction diameters determined by MDCT. Sphericity index was 0.94±0.4 indicating a circular anatomy of the ST-junction. ST-junction area derived from LTL measurement was similar to the planimetric ST-junction area in MDCT. Fusion aortic valve area index (AVAi) assessed by inserting MDCT derived LVOT area in the continuity equation was significantly higher in all patients as compared to conventional AVAi. 62 patients were reclassified from severe to moderate AS because AVAi was >0.6 cm2/m2. Energy loss index (ELI) was calculated for conventional AVAi and fusion AVAi each with ST-junction area determined by TTE and MDCT. Calculation of ELI using conventional AVAi resulted in larger AVA irrespective of whether the ST-junction area was determined by TTE or MDCT. AVAi was >0.6 cm2/m2 in 31 patients (ST-area from echo) and 44 patients (ST-area from MDCT). Calculating ELI using fusion AVAi resulted in even larger AVA, with values >0.6 cm2/m2 in 83 patients (ST-area from echo) and 85 patients (ST-area from MDCT). Reclassified patients had lower mean transvalvular gradients, less myocardial mass, less symptoms according to NYHA classification, and lower proBNP levels.

Conclusion: TTE underestimates LVOT area as compared to MDCT, while both modalities are comparable with regard to ST-junction area. Integration of TTE and MDCT derived values for calculation of ELI reclassifies the severity of AS in 44% of patients initially diagnosed with severe AS.

Disclosure of Interest: None Declared
Introduction: The prevalence of severe low flow low gradient aortic stenosis with reduced ejection fraction (LFLG AS) and with preserved ejection fraction (paradoxical LFLG AS) may be overestimated due to underestimation of the indexed stroke volume (SVI) assessed by echocardiography (echo). Calculation of SV from echo measurements is affected by errors occurring due to the ovoid shape of the left ventricular outflow tract (LVOT) and due to foreshortened views of the left ventricle. This study evaluated whether there is a reclassification of severe (paradoxical) LFLG AS when comparing SVI assessed by echo with that by fusion of data from echo and multidetector computed tomography (MDCT).

Methods: SVI was calculated in 186 preinterventional TAVI patients using a) biplane Simpson’s method (BSM), b) LVOT area calculated from echo LVOT diameter, and c) LVOT area measured by planimetry in MDCT either with calcification included or excluded. LVOT area determined by either method was multiplied with LVOT velocity time integral for calculating SV. Patients were classified according to SVI (cut-off 35ml/m²) and mean transaortic systolic pressure gradient (cut-off 40mmHg).

Results: SVI obtained by the biplane Simpson’s method (29.52±0.61ml/m²) was smaller than that determined by the echo LVOT area (34.89±0.75ml/m², p<0.01). In contrast, SVI was considerably larger when the planimetric LVOT area from MDCT was used. When calcification was included, SVI equalled 47.5±1.36ml/m² (p<0.01), when it was excluded, SVI was 43.6±1.27ml/m² (p<0.01). Patients were classified for severe LFLG AS according to SVI. 71 patients exhibited a severe LFLG AS according to the BSM, 53 patients according to the echo LVOT calculation, 30 patients according to the MDCT LVOT planimetry with calcification included, and 32 patients according to those with calcification excluded. When patients with ejection fraction>50% were analyzed, there were 43 patients classified as paradoxical LFLG AS with the BSM, 29 patients with the echo LVOT calculation, 14 patients with the MDCT LVOT planimetry with calcification included and 15 patients with calcification excluded.

Conclusion: Due to systematic errors in the echocardiographic calculation of SVI, the prevalence of LFLG AS is overestimated by up to 60% and that of paradoxical LFLG AS by up to 67%. Fusion of data from echocardiography and MDCT is a more accurate method for determining stroke volume and should be applied for classification of patients in the different forms of AS.

Disclosure of Interest: None Declared
Introduction: 8 of 1000 children are born with a heart disease. That makes heart defects to the most common birth defect. In the wake of progresses in open heart surgery almost 90 percent of children with complex congenital heart disease nowadays survive into adulthood. Most important is the patient's adherence to the therapeutic regimen. Previous research shows that particularly adolescents have troubles with being adherent to their drugs. Although there is a consensus about the importance of medication adherence there is little known about how adolescents feel towards medication intake and how this influences their adherence. The research question focuses on this subject: How do adolescents with a heart disease experience medication taking?

Methods: In order to grasp the perspectives of adolescents towards their medication intake the design of this study was qualitative. The data collection was performed by semi-structured interviews with a narrative character. Ten adolescents with heart disease from the children’s university hospital Zurich participated. Including criteria were: The necessity to take medicine every day because of the heart disease and age between 11 to 18 years. The interviews were tape recorded and transcribed. Analysis was conducted following the principles of theoretical coding of the grounded theory methodology.

Results: Adolescents who are experiencing a strong exposure to their heart disease seem to consider their medication more important than adolescents who are in a more stable state of health. What significance the drugs have, largely depends on existing experiences of how adolescents feel without medication. Having experienced positive consequences like gaining more strength fosters growing acceptance of medication intake, which consequently positively influences adherence to the therapeutic regimen. Therefore these adolescents have a significantly higher adherence than adolescents who always took medication.

Another important factor which influences the adherence is the acceptance of the heart disease. The more adolescents accept their disease, the better is their adherence.

Conclusion: If the medication adherence of adolescents with a heart disease should be improved, interventions in the educative sector are useful only to a certain degree. More important seems to be the support of the adolescents considering different aspects influencing the acceptance of the disease so that they can optimize their medication management.

Disclosure of Interest: None Declared
Introduction: In 2013, an initiative was started to develop a nation-wide registry of adults with congenital heart disease (CHD) in Switzerland (SACHER). The aim of this registry is to prospectively collect data on long-term outcomes of patients with CHD, use this registry as the basis for future national clinical studies and finally to improve the long-term outcomes of these patients. For the purpose of this study we analyzed the growth of the cohort and baseline data of patients enrolled until the end of 2015.

Methods: All adults with CHD, including inherited connective tissue disease with associated aortic disease, attending specialized adult CHD clinics (University Hospitals of Basel, Bern, Lausanne and Zurich; Kantonsspital St. Gallen) were asked to participate. After written informed consent, each patient was anonymized and the data entered in an online registry (secuTrial®). The secuTrial® software is internet-based with options for support for query management, monitoring, reporting and coding. SecuTrial® server and technical support are maintained by a university based clinical trial center. Baseline data of interest included age at inclusion, gender, main and secondary diagnosis, type of prior cardiac repair and late complications amongst other.

Results: From May 2014 to December 2015 2073 patients were included into the registry. For 1743 patients (54% male) complete baseline data were available and were analyzed for this study. Mean age was 32±12 years; more than 83% were younger than 40 years. Fifty-seven percent (n=987 patients) had lesions of moderate or great complexity. Isolated aortic valve disease (congenital aortic stenosis or bicuspid aortic valve) was the most prevalent main diagnosis (n=277, 16%), followed by tetralogy of Fallot (n=208, 12%), aortic coarctation (n=188, 11%), D-transposition of the great arteries (n=169, 10%) and isolated ventricular septal defects (n=159, 9%). A total of 1257 patients (72%) had prior cardiac surgery, of those 51% (n=638) needed subsequent cardiac surgery or interventions after their main repair. In 8% of patients, devices had been implanted (109 pacemaker and 35 ICD/CRT). The most common late complications were previous atrial arrhythmias (11% intraatrial re-entrant tachycardias and 8% atrial fibrillation), pulmonary hypertension (6%), previous stroke (6%) and previous endocarditis (5%).

![Patients over time](image)
Conclusion: The SACHER registry facilitates research on the prevalence and long-term outcome of congenital heart disease in Swiss adults.

Disclosure of Interest: None Declared
**OR100**

**6. Cardiac imaging, congenital and pediatric cardiology**

**Quality of life, general self-efficacy and health status in adults with congenital heart disease**

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**Introduction:**

During recent years, the focus of research in congenital heart disease (CHD) has shifted from reducing CHD related mortality to additionally improving quality of life (QoL). In many chronic health conditions, perceived self-efficacy has been shown to be an important modifiable predictor of QoL. Self-efficacy describes a person’s belief in his or her ability to respond to difficult life situations and deal with adverse situations. The aim of this study was to investigate interrelationships between self-efficacy, QoL and health status among adults with CHD.

**Methods:**

As a cross-sectional sub-study of an international multi-centre study of patient-reported outcomes in CHD (APPRAOCH-International Study), data from 454 patients were collected from two tertiary centers in Switzerland and Canada. Here, we report patient responses to 3 measures: (i) a 10-item measure of general self-efficacy (GSE), (ii) the EQ-5D-3L measure of health status, which assesses overall health status with a 0-100 Visual Analog Scale and also includes items pertaining to 5 dimensions (mobility, self-care, usual activity, pain/discomfort and anxiety/depression), and (iii) a 0-100 Linear Analog Scale assessment of QoL. Higher scores on the analog scales reflect better health status/QoL.

**Results:**

The mean age of the sample was 35±13.5 years (range = 18 to 81 years) and 55% were male. Eighty percent had defects of moderate or great complexity. Overall, patients reported good QoL (median 80, 1=66, 3=90) and overall health status (median 80, 1=65, 3=90). In a univariate analysis, there was a significant interrelation between QoL, health status and GSE: QoL and health status, \( r^2 = 0.530, p<.001 \); QoL and GSE, \( r^2 = 0.211, p<.001 \); GSE and health status, \( r^2 = 0.140, p<.001 \). In a multivariate regression model with QoL as main outcome, QoL correlated not only positively with self-efficacy but also with 4 of the 5 assessed health dimensions: mobility (p<.001), usual activity (p<.001), pain/discomfort (p<.001) and anxiety/depression (p<.001). Self-efficacy was an independent predictor of QoL (p<.001) after controlling for the dimensions of health status.

**Conclusion:**

There is a positive correlation between self-efficacy and QoL in adults with CHD, independent of perceived health status. Therefore, interventions aiming at strengthening patients’ self-efficacy should be developed and investigated to determine their potential to improve QoL.

**Disclosure of Interest:** None Declared
**OR60**

**8. Pneumology and Thoracic Surgery**

Telemetrically triggered interventions in the first month of cpap treatment - a prospective, randomized controlled intervention trial in patients with a new diagnosis of obstructive sleep apnea syndrome.

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¹Kantonsspital St.Gallen, Center for Sleep Medicine, ²Kantonsspital St.Gallen, Pneumologie, St.Gallen, Switzerland

**Introduction:** CPAP is the standard treatment for OSAS. Long term adherence with CPAP is relatively low, many patients abscond in the first months of treatment (1). In a pilot study, we observed an improvement in 1-month adherence for patients supported with telemetrically triggered interventions (2). A subsequent prospective randomized controlled intervention study is presented here.

**Methods:** Symptomatic OSAS patients with an apnea-hypopnea index of >5/h were started CPAP with a structured instruction session of 1 hour, including a trial period in bed. After 1-3 nights at home, patients who agreed for long-term CPAP were included in the study. According to the sample size calculation for the primary endpoint of 1-month adherence, 240 patients were randomized 1:1 to a telemedicine (TM) or control group (non-TM). For the TM group, CPAP usage, mask leakage and residual AHI were checked on an online data depository 3 times per week. Phone calls were undertaken if there were 2 nights of usage <4h or if excessive leakage was present for 2 consecutive nights.

**Results:** 240 patients were randomized. According to the predefined protocol, 17 early absconders (11 TM, 6 non-TM) were excluded from analysis. Baseline characteristics of the study population were comparable in both groups (Table 1).

Among TM patients, 28 (26%) had no indication for calls, 40 (37%) received 1 or 2 calls and 41 (37%) 3 or more calls. Usage data at 1 month for TM and non-TM patients are given in Table 2. Usage differences between groups were not statistically significant. In a subgroup analysis, we found that for the quartile of patients with low baseline scores in the Epworth sleepiness scale (ESS), a significant increase in usage was observed.

**Conclusion:** Targeted patient support to patients with usage problems did not result in a statistically significant increase in CPAP usage during the first month of treatment, but a significant improvement was observed in the subgroup of patients with low ESS scores. Usage data at 6 months are currently analyzed.

**References:**

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</thead>
<tbody>
<tr>
<td>N</td>
<td>109</td>
<td>114</td>
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<tr>
<td>Sex ratio (M/F)</td>
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<td>83.3%</td>
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<tr>
<td>Age</td>
<td>55.1 [44.1-63.9]</td>
<td>57.3 [47-65.3]</td>
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<td>BMI</td>
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<td>31 [28-34.9]</td>
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<tr>
<td>ODI</td>
<td>31 [18-58]</td>
<td>36 [21.5-59.5]</td>
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<tr>
<td>AH1</td>
<td>37 [23-68]</td>
<td>49.9 [27-67.5]</td>
</tr>
<tr>
<td>ESS</td>
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</table>

**Picture/Graph:**

**Picture/Graph 2:**

<table>
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<tr>
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<td>N</td>
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<td>114</td>
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<td>Daily Usage (h)</td>
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<td>4.93 [3.69-6.56]</td>
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<td>Prop. night with CPAP used</td>
<td>0.967 [0.8-1]</td>
<td>0.967 [0.8-1]</td>
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<tr>
<td>Prop. night with efficient CPAP use</td>
<td>0.767</td>
<td>0.733 [0.5-0.933]</td>
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</table>

| [0.467-0.933] |


Disclosure of Interest: O. Schoch Grant/ research support from: PANGAS Switzerland, G. Benz Grant/ research support from: PANGAS Switzerland, F. Baty Grant/ research support from: PANGAS Switzerland, J. Niedermann Grant/ research support from: PANGAS Switzerland, M. Brutsche Grant/ research support from: PANGAS Switzerland
OR61

8. Pneumology and Thoracic Surgery

Dexamethasone reduces pulmonary artery pressure in lowlanders with copd travelling to 3200m. Randomized, placebo-controlled trial.

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Introduction: COPD is associated with increased pulmonary artery pressure (PAP) at lowlands and affected patients may be at risk of symptomatic pulmonary hypertension when travelling to altitude. Since dexamethasone prevents pulmonary edema due to PAP rise in susceptible subjects at high altitude1 we performed a randomized, placebo-controlled trial evaluating the hypothesis that preventive treatment with dexamethasone mitigates the altitude-induced PAP rise in COPD patients.

Methods: Patients with COPD Gold grade 1-2 living below 800m, SpO2 >93%, in stable condition were included. Participants were randomized to receive dexamethasone (4mg, bid) or placebo one day before ascent from 760m and during a sojourn to 3200m in Tuja Ashu, Kyrgyz Republic. Echocardiography was performed at 760m and after the first night at 3200m. The main outcome was the tricuspid pressure gradient (TPG).

Results: 109 patients were randomized (mean±SD age 56±9, BMI 26±4 kg/m2, FEV1 89±21%pred, SpO2 95±2%). The TPG and systolic PAP increased from 760 to 3200m, dexamethasone mitigated the altitude-induced increase in TPG vs. placebo while the increase in cardiac output was similar with dexamethasone and placebo. The smaller increase in TPG with dexamethasone was associated with a higher SpO2 at peak walk test. Regression analysis confirmed that dexamethasone was associated with a reduced altitude-induced increase in TPG even when controlled for age and FEV1%pred (R2=0.58, P=0.02).

<table>
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<tr>
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<th>Dexamethasone (n=58)</th>
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<tr>
<td></td>
<td>760m</td>
<td>3200m</td>
<td>760m</td>
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<tr>
<td>TPG, mmHg</td>
<td>18 ± 5</td>
<td>26 ± 6*</td>
<td>20 ± 5</td>
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<td>Systolic PAP, mmHg</td>
<td>31 ± 6</td>
<td>39 ± 8*</td>
<td>32 ± 6</td>
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<td>4.9 ± 0.7</td>
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<td>4.6 ± 1.1**</td>
<td>4.1 ± 1.1</td>
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<td>6 MWT, m</td>
<td>500 ± 76</td>
<td>486 ± 93</td>
<td>502 ± 77</td>
</tr>
<tr>
<td>SpO2 peak walk, %</td>
<td>95.0 ± 2.5</td>
<td>85.1 ± 4.2*</td>
<td>95.0 ± 1.5</td>
</tr>
</tbody>
</table>

Discussion: Mild pulmonary hypertension due to PAP rise is common in patients with COPD travelling to high altitude. Dexamethasone mitigates this altitude-induced increase in PAP while maintaining cardiac output with a favorable effect on oxygenation during exercise.

Conclusion: In lowlanders with COPD, GOLD 1-2, travelling to 3200m induces mild pulmonary hypertension. Dexamethasone mitigates this altitude-induced increase in PAP while maintaining cardiac output with a favorable effect on oxygenation during exercise.

Disclosure of Interest: None Declared
Introduction: Systemic sclerosis (SSc) is associated with pulmonary hypertension (PH). The significance of exercise induced PH in SSc is unknown.

Methods: Exercise RHC from SSc-patients from 2005-15 were reviewed and clinical characteristics, NYHA class and 6 minute walk distance (6MWD) assessed at 0, 3 and 12 month and transplant-free survival until 11/2015 noted.

Results: Exercise RHC of 84 patients (72 females) median (quartiles) age 62 (51;75), NYHA 2 (2;3), FVC 90 (81;105), DLCO 58 (43;64)%pred. were analyzed. 17 had resting precapillary, 2 resting postcapillary PH (mean pulmonary artery pressure ≥25mmHg). From the 65 without resting PH, 28 had exercise precapillary PH (ΔmPAP/ΔCO>3mmHg/l/min & mPAP> 30mmHg) and 10 exercise postcapillary PH (Wedge>20mmHg). Patients with resting precapillary PH achieved a lower workload than patients with exercise precapillary PH or no PH (20 (15;30) vs. 30 (30;40) resp. 30 (20;40) Watt, p=0.043. The pressure-flow ratio was lowest without PH (3.7 (1.9;7;9) intermediate in exercise PH ( 8.3 (6.1;30)) and highest in resting PH 24 (12.6;82.2) mmHg/l/min (P=0.000 resting& exercise vs. no PH, P=0.027 resting vs. exercise PH).

All patients with resting and 16/28 patients with exercise precapillary PH received PH-targeted therapy for at least 3 months. Patients with resting PH had an improved NYHA class at 3 but not 12 months but unchanged 6MWD. In exercise PH, changes in 6MWD and NYHA from baseline to follow-up were not significant. During 1167±878 observational days, 12 patients died and 2 were transplanted. Transplant-free survival was better in patients without PH compared to patients with resting or exercise precapillary PH (p=0.019 or 0.48) but was similar for treated vs. untreated exercise PH.

Conclusion: SSc patients with resting, but also exercise precapillary PH have worse transplant free survival compared with SSc without PH. The increased pressure/flow-ratio during exercise in SSc with exercise-PH may suggest early pulmonary vascular disease for which treatment might be considered if confirmed by randomized trials.

Disclosure of Interest: None Declared
OR63

8. Pneumology and Thoracic Surgery

Asa score and preoperative icu admission are the only predictors of mortality after surgical biopsy for interstitial lung disease

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Introduction: Recently, an aggregate risk score for predicting mortality after surgical biopsy for interstitial lung disease was developed (Fibla, et al. 2012, Interactive Cardiovascular and Thoracic Surgery). This score includes four independent parameters; age ≥67, pre-operative intensive care unit (ICU) admission, immunosuppressive treatment and open surgery.

Methods: All patients with interstitial lung disease who underwent diagnostic surgical lung biopsy between 2000 and 2014 were included in the study. ROC-curve and multivariate analyses were applied to determine the predictors of mortality. Variables included were age, type of surgery (VATS vs open), immunosuppressive treatment, number of biopsies, American Society of Anaesthesiologist (ASA) physical status score, smoking history, pre-operative ICU admission, preoperative lung function test (FEV1%, DLCO%) and coronary artery disease. A risk score was calculated and classified as low risk or high risk. Statistical significance was set at p<0.05.

Results: 294 patients (121 females and 173 males) with an average age of 55.7±14.9 years (range 19 – 85) were included in the study. 161 (54.7%) of the patients were immunocompromised. 39 (13.2%) patients were admitted to the ICU preoperatively. 30- and 90-day mortality were 6.8% (n=20) and 10.2% (n=30), respectively. ROC-Curve analysis for 30-day mortality revealed ASA score (area under the curve 0.792, p=0.009) and preoperative ICU admission (area under the curve 0.847, p=0.02) as the only predictors for mortality. For the 30-day and 90-day mortality, 255 patients were low risk with 3 and 12 deaths, respectively and 39 patients were high risk with 17 and 18 deaths, respectively. Open lung biopsy was not an independent predictor of mortality. Age, smoking history, immunocompromised status, number of biopsies, pre-operative lung function and coronary artery disease were not independent predictors as well.

Conclusion: In contrast to previously described scores, only preoperative ICU admission and ASA score were the most important predictors of mortality. The high risk group constituted only a small percentage of our patient population.

Disclosure of Interest: None Declared
Introduction: Bronchoscopy is a basic procedure that every pulmonologist must acquire during training. Familiarization with endoscopic aspects requires visual educational support. Bronchoscopy atlases in the form of textbooks are not easily updated. Some online resources do exist but they are either incomplete or not very user friendly. To date no online atlas covers subjects relevant to bronchoscopy combining extensive photographic material and links to educational resources.

Methods: The online platform was developed using the program ‘Gallery’. An extensive literature research was conducted to identify educational resources on bronchoscopy. Thematic files were created in an exhaustive organizational tree format. After approval of the ethics committee, anonymized photos were collected directly by the bronchoscopists and by the images archive of the endoscopy department (Endobase). Educational resources were selected by two bronchoscopists from literature and internet research. Quality control of the images, links and their relevance to the created files was done by the project coordinator and three dedicated site reviewers.

Results: Out of more than 2000 bronchoscopies conducted each year in our department and from the Endobase archive used systematically since 2012, more than 400 photos were selected for the atlas. Two bronchoscopists screened approximately 700 articles and websites related to bronchoscopy to choose the educational links. Photographs and links were grouped in the following thematic items: materials/techniques, normal anatomy, anatomical variations, descriptive terminology, specific disease states, post-operative bronchoscopy, trauma-foreign bodies-inhalation injuries, pediatric bronchoscopy cases and quiz. Specific subjects can be easily retrieved using the ‘search box’ and ‘common tags’. Users can write their comments under a file or an image.

Conclusion: The created online bronchoscopy atlas (http://bronchoscopyatlas.ch/atlas/index.php/), is constantly updated and completed to cover a wide spectrum of techniques and pathologies relevant to bronchoscopy. It is expected to become an invaluable educational tool for pulmonologists both nationally and internationally.

Disclosure of Interest: None Declared
Recurrence hypercapnia and hypoxemia in congenital central hypoventilation syndrome (undine syndrome) likely acts as endothelial preconditioning


1Cardiology, Inselspital, Bern, Switzerland, 2Cardiology, Inselspital, Bern, South Sudan, 3Medicine interne, CHUV Lausanne, Lausanne, Switzerland

Introduction: Undine syndrome (US) is a rare disease with severely impaired central autonomic control of breathing and dysfunction of the autonomous nervous system. The incidence is estimated to be at 1 of 200,000 livebirths. Due to recurrence hypercapnia and hypoxia we hypothesized that these patients have higher risk for pulmonary arterial hypertension (PHT) and longterm systemic vascular dysfunction. We examined 14 patients with US at baseline and high altitude in regards to pulmonary artery pressure and systemic vascular disease and compared them with 15 age and sex matched healthy subjects.

Methods: 14 patients with US (18.6±4.1 y) and 15 age and sex matched healthy controls (17.9±1.5 y) were examined at 550m and at 3883m above sea level with echocardiography (to measure pulmonary artery pressure). Vascular function was assessed by pulse wave velocity (PWV) and carotid intima-media thickness (IMT).

Results: US patients had mildly elevated RV/PA gradients at 550m above sea level while no relevant RV/PA gradient was found in the controls (25.8±8.0 vs. 20±4.3 mmHg, P=0.03). In 3883m above sea level all US subjects showed only mild increase in RV/PA gradients similar to the controls (33.5±17.8mmHg vs.29±21mmHg). Systemic vascular function was impaired in US subjects as shown by an increased PWV (8.0±1.2 vs. 7.0±0.9 m/s, P=0.02, US vs. control) and IMT (418.4±34.2 vs. 367.7±50.6 µm, P<0.01, US vs. control).

Conclusion: US patients show impaired systemic vascular function. Despite this findings Undine patients do not show evidence for marked pulmonary hypertension during rapid ascent to high altitude. We speculate that endothelial preconditioning due to intermittent hypoxemia might have a protective effect.

Disclosure of Interest: None Declared
Introduction: Reports on PCSK9 levels in HIV-infected patients are scarce, and HIV-infected individuals have typically been excluded from trials investigating anti-PCSK9 monoclonal antibodies. High prevalence rates of tobacco or recreational drugs consumption, such as marijuana or alcohol, have been reported in observational studies in HIV-infected individuals. Marijuana has demonstrated anti-inflammatory properties, yet no study has assessed the association between marijuana consumption and PCSK9 levels, in particular with regard to HIV-patients.

Methods: All HIV-infected individuals included in the SHSC (www.shcs.ch) were screened for PCSK9 levels based on a routine blood sample collected in 2014 during a clinical visit at Geneva University Hospitals. Marijuana consumption was investigated based on a physician-administered questionnaire and information was gathered regarding frequency (daily, less frequently and never). Continuous PCSK9 levels were transformed into a logarithm scale as the dependent outcome for linear regression and three models were built, based on the following independent variables: (1) unadjusted marijuana consumption, (2) adjusted for the calculated Framingham risk score and (3) additional adjustment for available clinical variables relevant to HIV-individuals.

Results: Among 239 HIV-infected individuals who met the inclusion criteria with available PCSK9 levels, 35 (14.6%) reported marijuana consumption, of whom 20 (57.1%) reported daily consumption and 15 (6.3%) occasional use. Median value of PCSK9 was 263.4 ng/ml in HIV-patients, which was significantly higher than reference values in non-HIV controls (P<0.001). Patients with marijuana consumption had significantly higher levels of PCSK9 levels (P < 0.001). A dose-response effect was observed between marijuana consumption and PCSK9 levels (P < 0.001); the association persisted after adjustment for the calculated Framingham risk score (P=0.003) and additional adjustment for clinical variables (P=0.027).

Conclusion: In HIV-infected individuals naïve of statin treatment, marijuana consumption is associated with higher PCSK9 levels independently of CV risk factors and clinically relevant confounding factors. Our findings are the first to suggest an association between marijuana consumption and PCSK9 levels.

Disclosure of Interest: None Declared
OR67
5. Epidemiology, risk factors, rehabilitation, thromboembolic disease
Endothelial protective properties of hdl improve early after roux-en-y gastric bypass but not after diet-induced weight loss: the superior cardiometabolic benefits of rygb
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¹Centre for Molecular Cardiology, University of Zurich, Schlieren- Zurich, Switzerland, ²Institute of Cardiovascular Sciences, London, United Kingdom, ³Department of Endocrinology, Diabetology and Metabolism, Antwerp University Hospital, Antwerp, Belgium

Introduction: Background. Roux-en-Y gastric bypass (RYGB) reduces cardiometabolic risk through different mechanisms. The current understanding suggests that the beneficial metabolic effects of RYGB likely result from changes in intestinal physiology rather than from surgery induced body weight (BW) loss alone; however, the exact mechanisms for these benefits are not clear. Changes of high density lipoprotein (HDL) properties might explain part of this benefit. Aim. We assessed the effect of RYGB on HDL vaso-protective properties in comparison with a hypocaloric diet-induced weight loss.

Methods: Methods. HDL was isolated from serum of obese patients (BMI > 35 kg/m²) before and 6 months after RYGB (n=32) or diet (n=32). In endothelial cells, we quantified HDL-stimulated nitric oxide (NO) production by DAF-2 fluorescence and paraoxonase-1 antioxidant activity (PON-1). Total cholesterol (T-CHOL), low density lipoprotein (LDL-C), HDL-C, and triglycerides (TG) as well as glucose plasma fasting levels were measured.

Results: Results. There was no significant difference in mean BW and BMI between RYGB and diet patients either at baseline (119.9 Kg; 42kg/m² vs. 110.9 kg; 37.4 kg/m², respectively, p=0.06) nor after 6 months (RYGB: 94kg; 33 kg/m²; diet: 99kg; 33.4 kg/m², p=ns). In both groups, mean T-CHOL and TG were reduced; LDL-C decreased only after RYGB. Total HDL-C increased after both interventions. Only RYGB improved the vasoprotective HDL-stimulated NO production (RYGB: 234.2±178.0 vs diet 98.8±76.4 arbitrary units, p=0.0001) and PON-1 activity (RYGB: 40% vs diet: 9% increase vs. baseline; p<0.0001). Fasting glycemia improved in both groups and were not different at 6 months.

Conclusion: Conclusion. Although HDL concentration increased after both interventions, only RYGB restored endothelial protective HDL properties. This suggests that BW loss is not sufficient to improve the protective properties of HDL, unless accompanied by yet unknown surgery-specific effects.

Disclosure of Interest: None Declared
Introduction: Improvement of transplantation techniques and supportive care lead to an increasing number of long-term survivors after allogeneic hematopoietic stem cell transplantation (HSCT). Recipients of allogeneic HSCT have a higher prevalence of cardiovascular risk factors including arterial hypertension (HT). The prevalence of ambulatory hypertension in patients after HSCT is unknown.

Methods: All patients with hematologic malignancies at least one year after allogeneic HSCT at the University Hospital Basel were included during their annual check. Blood pressure (BP) was measured in the office after 5 minutes rest on both arms. Arterial hypertension was defined as ≥140/90 mmHg. 24h ambulatory BP measurement (ABPM) by SomnoTouch® device was performed on the same day. 24h-, day- and nighttime hypertension was defined as ≥130/80, ≥135/85 and ≥120/70 mmHg, respectively.

Results: Sixty-six patients were enrolled between April 2015 and December 2015. 47% were female. Median age at study entry was 56 (range 22-73) with median 9 (range 1-29) years after transplantation. Nine patients had a body-mass-index ≥30 kg/m2. Fifteen patients took calcineurin inhibitors and 4 patients took cortison. Thirty patients (45.5%) had office hypertension: 17 patients with isolated systolic HT, 2 patients with isolated diastolic HT and 11 patients with systolic and diastolic HT. An ambulatory hypertension was documented in 41 patients (62%) with 6 systolic, 8 diastolic and 27 systolic and diastolic HAT patterns. Day- and nighttime HT was diagnosed in 32 (48%) and 54 (82%) patients, respectively. Two patients (3%) had white coat HT and twelve patients (18%) had masked HT. All patients with eGFR<60 ml/min (n=17) and microalbuminuria (n=22) were hypertensive during ABPM. Thirty-two patients (48%) were on antihypertensive drugs whereas 17 of these patients still had office HT.

Conclusion: Arterial hypertension is common in patients after allogeneic HSCT and is often missed by office BP measurements only. ABPM detects patients with relevant night-time hypertension. ABPM may lead to better treatment of hypertension.

Disclosure of Interest: None Declared
Selective heart rate reduction with ivabradine increases central blood pressure in stable coronary artery disease

D. Cerny¹, F. Messerli¹, S. Laurent², C. Seiler¹, S. Rimoldi¹

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Introduction: Heart rate (HR) lowering by betablockade was shown to be beneficial after myocardial infarction. In contrast heart rate lowering with ivabradine was found to confer no benefits in two prospective randomized trials in patients with coronary artery disease (CAD). We hypothesised that this inefficacy could be in part related to ivabradine’s effect on central (aortic) pressure. Aim of this study was to assess the HR lowering effect of ivabradine on invasively measured central blood pressure.

Methods: A total of 46 patients with chronic stable CAD who were randomly allocated to placebo (n=23) or ivabradine (n=23) in a single-blinded fashion for 6 months. Concomitant baseline medication was continued unchanged throughout the study except for β-blockers, that was stopped over the study period. Central blood pressure and stroke volume were measured directly by left heart catheterization at baseline and after 6 months. For the determination of resting HR at baseline and at follow-up, a 24 h ECG monitoring was performed.

Results: Patients on ivabradine showed an increase of 11 mmHg in central systolic pressure, from 129 ± 22 mmHg to 140 ± 26 mmHg (p=0.02) and in stroke volume by 86 ± 21.8 to 107.2 ± 30.0 ml (p=0.002). In the placebo group central systolic pressure and stroke volume remained unchanged. Despite a HR decrease of 8 ± 12 beats/min no significant change in the double product (central systolic pressure x HR) was observed in the ivabradine group. The decrease in HR from baseline to follow up correlated with the concomitant increase in central systolic pressure (r=-0.41, p=0.009) and in stroke volume (r=-0.61, p<0.001) in the whole patient population.

Conclusion: The decrease in HR with ivabradine was associated with an increase in central systolic pressure, which may have antagonized possible benefits of heart rate lowering in CAD patients.

Disclosure of Interest: None Declared
Introduction: Heart failure (HF) affects an increasing number of individuals, with strong links to complex health care needs, morbidity and premature mortality. As self-care is recognized as an important modifiable factor influencing morbidity and mortality, baseline data, i.e., on patients’ healthcare support needs and self-care are essential to patient-specific education interventions. While international research has shown sub-optimal self-care in HF populations, data are rare in Switzerland. This study aims to describe the prevalence of HF symptoms, complex needs, self-care, vulnerable profiles and past unplanned healthcare utilization, and to explore the relationships between these variables.

Methods: This ongoing cross-sectional study will include a convenience sample of 150 adult HF patients recruited from 4 sites of one Swiss acute care hospital. Complex needs relate to both symptoms (M.D. Anderson Symptom Inventory–HF instrument) and needs (Heart Failure Needs Assessment Questionnaire). Self-care is measured via the Self-Care of Heart Failure Index and the European Heart Failure Self-care Behavior Scale. Vulnerable individuals’ profiles are investigated regarding socio-demographic and clinical variables. Unplanned healthcare utilization reflects the number of emergency department admissions, non-selective all-cause hospitalizations and re-hospitalizations over the past year. Descriptions of patients’ overall needs will reflect the mean scores and comparative rankings of support needs; and the mean scores of HF symptoms’ severity and distress. Description of self-care will reflect mean scores for self-care. Frequencies will summarize unplanned healthcare utilization. Latent class analysis will identify vulnerable patients’ profiles. Multiple regression analysis will explore relationships between complex needs, self-care and unplanned healthcare utilization.

Results: So far, the study has included 50 patients. We will present preliminary results of this study using data of patients included until March 1st 2016.

Conclusion: Significance of this study: This study is among the first in Switzerland to examine the levels of complex needs and self-care in HF patients. Its results will increase our understanding of the interrelations between HF patients’ profiles, their levels of self-care and their healthcare needs. As part of our research programme, this study’s results will guide us in the development of an intervention targeted at needs and self-care capabilities.

Disclosure of Interest: None Declared
**OR71**

5. Epidemiology, risk factors, rehabilitation, thromboembolic disease

Effect of permanent internal mammary artery occlusion on extracardiac coronary collateral supply

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**Introduction:** The structural existence of anastomoses between the internal mammary artery (IMA) and the coronary circulation has been confirmed by pathological examinations and, rarely, by angiographic cases in patients with severe coronary artery disease (CAD). Most often these pre-existing connections have been documented to occur ipsilaterally, that is, right IMA to right coronary artery (RCA) and left IMA to a branch of the left coronary artery (LCA). Before the advent of coronary artery bypass grafting, augmenting the function of these pre-existing extracardiac collaterals has been attempted by bilateral distal IMA ligation. This study aimed to examine the effect of permanent distal right IMA occlusion on right and left coronary collateral function in patients with coronary artery disease (CAD).

**Methods:** 50 patients with CAD underwent catheter-based right IMA occlusion by placement of an Amplatzer vascular plug 4 distal to the offtake of the pericardiophrenic branch. Coronary collateral function was determined in the right coronary artery (RCA) and a branch of the LCA at baseline (before IMA occlusion) and at follow-up after 6 weeks by coronary collateral flow index (CFI) during a 1-minute coronary balloon occlusion.

**Results:** Right coronary CFI (n=50) increased from 0.071±0.089 at baseline to 0.129±0.115 at follow up (p<0.0001). Left coronary CFI (n=42) remained unchanged, 0.095±0.085 at baseline vs 0.096±0.038 at follow-up (p=0.95).

**Conclusion:** This first-in-man study provides the proof of concept of the augmenting effect of permanent distal right IMA occlusion on right coronary collateral function. The role of catheter-based distal IMA occlusion as an alternative to established revascularization procedures has to be defined in further, randomized studies.

**References:** Stoller, Michael; de Marchi, Stefano F.; Seiler, Christian (2014). *Function of Natural Internal Mammary-to-Coronary Artery Bypasses and Its Effect on Myocardial Ischemia.* Circulation, 129(25), pp. 2645-2652.

**Disclosure of Interest:** None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Genetic testing in sudden cardiac death: never give up

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Introduction: Genetic tests remain often negative in patients (pt) having suffered an aborted Sudden Cardiac Death (SCD). We here report the case of a young male where genetic testing gave the clue of the problem after an initially negative result.

Methods: The pt suffered an aborted SCD in 2004 when he was 26y old. The extensive cardiac work-up was negative for an underlying cardiopathy; in particular, no arrhythmia was documented during stress test or electrophysiological study (EPS). However, the familial history was positive as his father died suddenly aged 33y when the pt was 4 y old; the necropsy did not find any underlying cardiac disease. The initial genetic testing performed in 2004 for LQT1, LQT2 and LQT3 was negative.

Results: The pt was implanted with a single chamber Implantable Cardiovertor Defibrillator (ICD). The clinical evolution was uneventful and the pt had a totally normal life until September 2015 when he suffered a first episode of ventricular fibrillation correctly detected and treated by the ICD. Full cardiac investigations excluded again any underlying cardiopathy. Genetic testing was repeated and extended using next generation sequencing (NGS). A pathogenic mutation was found in RYR2 allowing the diagnosis of Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT). The pt is now treated by beta-blocker.

Conclusion: In pts having suffered a SCD, genetic testing has to be regularly updated according to the ongoing progress in the field. In these pts, CPVT has to be suspected even in absence of any arrhythmia during stress test or EPS. The identification of a mutation allows genetic counseling of blood relatives and is particularly important in cases where no other test is available to identify at-risk carriers.

Disclosure of Interest: None Declared
OR73

7. Clinical cases (All clinical cases have to be submitted in this topic)

A rare manifestation of right heart endocarditis of the Chiari network in a patient with iv drug abuse diagnosed and followed up by transthoracic echocardiography (TTE) and treated in an unconventional way

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Introduction: Bacterial endocarditis is a serious condition with high morbidity, requiring intravenous antibiotic treatment. Only 10% affect the right heart. We report a case of patient with an unusual right heart endocarditis, diagnosed and followed up by transthoracic echocardiography (TTE), successfully treated with a long-term oral antibiotic therapy.

Methods: A 38-years old female with known intravenous drug abuse was admitted to our emergency department with fever up to 40°C for 4 days, myalgia and headache. TTE quality was good and a pedunculated vegetation of 2.1x1.2cm in size adherent to the Chiari net could be seen. The valves, were free of vegetations. Blood cultures yielded continuous growth of a penicillin-sensitive Staphylococcus aureus (SA). Chest x-ray showed septic pulmonary emboli.

Results: Long-term intravenous antibiotic therapy with penicillin could not be completed due to the patient’s refusal of prolonged hospitalisation. Instead, an unconventional oral treatment with amoxicillin 1g every 6hours, combined with probenecid 250mg twice daily was started. After 6 weeks of oral therapy TTE showed a pronounced reduction of the vegetations size. The patient’s condition and the inflammatory parameters have returned to normal. Oral antibiotic treatment was continued until complete resolution of the vegetation, which was documented by TTE after 13 weeks of therapy. Follow up blood cultures remained sterile.

Conclusion: Only three cases of right sided endocarditis limited to the Chiari network were published according to our literature research. In most cases the Chiari network and anomalies in the right atrium is documented by transesophageal echocardiography (TEE). In our patient, diagnosis as well as follow-up was performed by TTE. In this patient oral treatment with amoxicillin and probenecid was a successful alternative treatment. Historically, it was common to use probenecid to enhance plasma concentrations of beta-lactams by reducing renal excretion.


Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Transapical aortic and mitral valve implantation with severe left ventricular outflow tract obstruction and complete retraction of the repositionable lotus® valve system in mitral position

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Introduction: Transapical aortic and mitral valve implantations (TAVI, TAMVI) have become an alternative approach in patients with high operative risk. In selected groups with severe aortic and mitral valve stenosis, a simultaneous treatment of both is considered an alternative. We present a case of a 59-year-old woman who underwent a double transapical TAVI/TAMVI implantation in native aortic and mitral valve positions, followed by imminent severe LVOT-obstruction upon deployment of the TAMVI.

Methods: A 59-year-old female with severe aortic stenosis, severe mitral stenosis with mild mitral insufficiency, persistent atrial fibrillation, severe chronic obstructive pulmonary disease and NYHA class of IV was evaluated by our interdisciplinary heart team. Due to the calculated Euroscore II, logistic Euroscore with 10% and 17% a decision was made towards a transapical TAVI approach.

Results: The procedure was performed under general anaesthesia utilizing both fluoroscopic and TEE guidance. The implantation of an Edwards Sapien 3 valve in the aortic position was performed and the perioperative TEE showed a good result. Afterwards a predilatation of the stenotic mitral valve was done. The echocardiography revealed a slight improvement of the mitral valve gradient, combined with a moderate mitral valve regurgitation. Due to the insufficient dilatation of the mitral valve a repositionable Lotus Valve (BostonScientific) was chosen. However, immediately postimplantation, the patient developed severe refractory hypotension. In TEE a severe obstruction of the LVOT by the anterior native mitral valve leaflet was observed. Therefore, the Lotus valve was completely retracted, leaving the native stenotic mitral valve. The patient was extubated on table and made an uneventful postoperative recovery.

Conclusion: The case shows that thorough preoperative diagnostics are essential, especially for planning of correct type and size of the chosen valve, and for an efficient preparation for potential complications. In this patient the LVOT was evaluated as a high-risk for LVOT-obstruction. Accordingly, it was decided against the use of balloon-expanding valves in the interdisciplinary team, as it is not repositionable. Instead, it was decided for the use of a Lotus Valve, as it is repositionable and therefore possible to retract in case of LVOT obstruction. In patients at high-risk of developing a LVOT-obstruction after the deployment of a transcatheter mitral valve, we recommend the use of retractable transcatheter valves.

Disclosure of Interest: None Declared
OR75
7. Clinical cases (All clinical cases have to be submitted in this topic)
Vasopastic angina : a forgotten acute coronary syndrome
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Introduction: A 30 years old male, smoking one pack per day, went to the emergency with an acute chest pain radiating into left arm with accompanying dyspnoea. Electrocardiogram showed anterior ST elevation.

Methods: Then, the coronary artery angiography showed proximal left anterior descending artery thrombus with subocclusion. (Images 1) Left circumflex artery and right coronary artery were without lesions. The periprocedural complications were a third degree atrioventricular block requiring a provisional pacemaker implantation, then a cardiopulmonary arrest with ventricular fibrillation requiring resuscitation using an automated chest compression device (LUKAS), intubation and successful defibrillation. Finally, successful intracoronary application of 2 mg adrenalin was done to stabilise the blood pressure and implantation of two DES in the proximal left anterior descending artery with restoration of TIMI III flow. Patient had a good neurologic and cardiac outcome after 2 days in the intensive care unit.

Results: However, 48 hours later patient had a recurrence of typical chest pain with signs of inferior STEMI. Patient finally confessed consuming occasionnaly methylamphetamines. The coronary artery angiography showed RCA vasospasm, which was resistant Nitroglycerin or Verapamil (systemic and intracoronary). (Images 2) An Angioplasty with balloon only was done.

Left ventricular ejection fraction was 50% and patient was discharged with calcium channel blocker and antiplatelet therapy.

Picture/Graph:
Conclusion: Vasospasm leading to blood stasis could explain formation of thrombus in the proximal LAD explaining the first STEMI. To conclude vasospasm – likely having been induced by Methylamphetamine consumption - causing 2 subsequent acute coronary syndromes and even a cardiac arrest in a young patient

Disclosure of Interest: None Declared
Complete regression of liver cirrhosis after heart transplantation in a patient with prior Fontan surgery for complex congenital heart disease.

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Introduction: Palliative Fontan surgery offers enhanced survival and quality of life for patients not candidates for biventricular repair. It restores a noncyanotic state by directing the systemic venous return passively to the lungs at the expense of elevated central venous pressure and decreased cardiac output. Progressive failure of the Fontan circulation is characterized by ventricular dysfunction, systemic complications and chronic Fontan failure. Heart transplantation (HTx) is the only potential treatment for many of these patients. Fontan-associated liver disease (FALD) is increasingly reported in this population and raises concerns when considering HTx. We report the case of histological and functional reversal of liver cirrhosis after HTx in a patient with previous Fontan palliation.

Methods: A 20 years old male patient with complex congenital heart disease and Fontan palliation for single ventricle physiology presented with chronic Fontan failure and liver cirrhosis diagnosed by liver biopsy. Liver histology (fig.1) revealed extensive bridging fibrosis with centro-lobular and portal fibrosis, sinusoidal dilatation and patchy area of architectural changes.

Results: Patient underwent HTx at the age of 24 and presented an unremarkable post-operative course. After 18 months of follow-up free of any post transplantation complication, liver biopsy (fig.2) revealed nearly complete regression of liver fibrosis and remnant of disturbed hepatic architecture compatible with reversion of previous established cirrhosis.

Picture/Graph:

Picture/Graph 2:
**Conclusion:** Our case of a young patient with single ventricle physiology, Fontan palliation and liver cirrhosis on hepatic biopsy nicely demonstrates that liver cirrhosis might be entirely reversible post HTx. In selected Fontan patients, liver cirrhosis might not be absolute contraindication for HTx only, which might be the procedure of choice instead of heart-liver transplant. This emphasizes the need for detailed assessment of FALD in Fontan patients candidate for HTx.

**Disclosure of Interest:** None Declared
OR77
7. Clinical cases (All clinical cases have to be submitted in this topic)
Unrestrictive aortopulmonary window: extreme presentation as non-eisenmenger in a 30 year-old patient
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Introduction: An aortopulmonary window, a failure of septation between the aorta and the pulmonary artery, is a rare congenital cardiac anomaly. Patients usually present in the first week of life. Late or extremely late presentation is unusual, but has rarely been reported in adults at the stage of Eisenmenger syndrome. We report the rare presentation of symptomatic aortopulmonary window with an unrestrictive left-right shunt at 30 years of age successfully repaired surgically.

Methods: A 30 year-old lady was referred for management of an aorto-pulmonary window. Her history was notable for chronic atrial fibrillation treated by amiodarone and coumadin anticoagulation. Peripheral oxygen saturation was 95%. The echocardiogram showed a large, 15 mm aorto-pulmonary (AP) window, approximately 25 mm above the aortic valve between the ascending aorta and main pulmonary artery (type I) with an unrestrictive, exclusively left-right shunt and a peak gradient of 30 mmHg. Cardiac catheterization showed a pulmonary systolic pressure 40% of systemic pressure (44/20 mmHg, mean 32), pulmonary capillary wedge pressure (PCWP) of 20 mmHg, cardiac index of 3.04 ml/min/m2, pulmonary vascular resistance (PVR) of 1.79 Woods units (WU)/m2, PVR:SVR ratio of 0.21. After acute vasodilator testing with inhaled nitric oxide, the PVR decreased to 1.54 WU/m2 and PVR:SVR ratio of 0.11. The hemodynamics met criteria suggestive of operability.

Results: The AP window was closed with a 14 mm circular GoreTex patch under cardiopulmonary bypass and cardioplegic arrest. The patient was weaned uneventfully from cardiopulmonary bypass. Her postoperative course was uneventful. Cardiac catheterization 20 days after surgical repair showed a pulmonary artery pressure of 68/27 mmHg (mean 41), PCWP of 11 mmHg, cardiac index of 2.5 l/min/m2, PVR of 5.5 WU/m2 with a PVR:SVR ratio of 0.34, and normal end-diastolic left ventricular pressure (6 mmHg). PA pressure and PVR normalized with inhaled nitric oxide, and she was placed on sildenafil. At follow-up 13 months after repair and after discontinuing sildenafil, she denies any symptoms. Cardiac catheterization showed normalized pulmonary artery pressure (31/8 mmHg, mean 18 mmHg), a mean PCWP of 8 mmHg, pulmonary vascular resistance of 1.6 WU/m2, with a PVR:SVR ratio of 0.03.

Conclusion: We report the rare presentation of an aortopulmonary window with an unrestrictive left-right shunt at 30 years of age, still at the stage of reactive pulmonary hypertension and who underwent successful surgical repair.

Disclosure of Interest: None Declared
**Introduction:** Subclavian artery aneurysms (SAA) are uncommon and usually caused by thoracic outlet syndrome and atherosclerosis. Despite the common occurrence of aortic aneurysms in patients with Marfan’s syndrome (MFS), SAA are not a typical finding unless aortic dissection with involvement of the supraaortic vessels has occurred.

**Methods:** A 23-year-old Marfan patient with a history of several prior aortic procedures due to aortic valve insufficiency and various dilatations of the aorta but not dissection presented with bilateral SAA during follow-up. CT-angiography (CTA) revealed de novo aneurysm of the total aortic arch, the proximal descending aorta and the maximal diameters of both subclavian arteries were 5 cm (Figure A). Echocardiography showed severe aortic regurgitation. The decision for elective surgical correction as a re-re-do operation was taken. After replacing the aortic valve with a mechanical prosthesis and cooling down to 26 °C, the aortic arch was opened during hypothermic circulatory arrest. To replace the aortic arch and proximal descending aorta, a hybrid graft (Thoraflex Hybrid, Vascutek Deutschland GmbH) was used. Both SAA were excised and the vertebral arteries were prepared for later re-implantation. The subclavian arteries were reconstructed with end-to-end anastomoses to the branches of the hybrid prosthesis. Both vertebral arteries were re-implanted into the subclavian branches using autologous saphenous vein grafts. After a prolonged recovery due to postoperative bleeding and subsequent rethoracotomy, the patient was discharged on the 27th postoperative day. Twelve months follow-up, the patient had well recovered with a satisfying physical state and quality of life. Follow-up CTA displayed no recurrence of SAA (Figure B).

**Results:**

**Picture/Graph:**
Conclusion: Multiple reoperations for aneurysms in Marfan-patients and surgical correction of SAA are feasible. Our case demonstrates that reestablishment of the regular anatomy of aortic arch and supraaortic vessels is difficult but can be successfully performed in patients with MFS.

Disclosure of Interest: None Declared
Left ventricular non-compaction cardiomyopathy mimicking a myocardial infarction

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Introduction: Left ventricular non-compaction (LVNC) cardiomyopathy is an infrequently encountered cardiomyopathy, characterized by numerous prominent trabeculations and deep intertrabecular recesses in the ventricular myocardium with a variable clinical presentation ranging from asymptomatic to heart failure, arrhythmias, thromboembolic events, and death.

Methods: We present a case of a 76-year-old man who was referred for cardiac evaluation because of progressive signs of heart failure associated with frequent ventricular ectopic beats.

Results: A cardiac ultrasound showed a slight dilatation of the left cardiac cavities and a moderate left ventricular (LV) systolic dysfunction (40-45%) associated with an hypertrabeculated aspect of the infero-lateral (IL) LV wall, raising the question of a possible LV non-compaction (LVNC) cardiomyopathy. A CMR 1.5 tesla exam was performed confirming a LVNC cardiomyopathy with involvement of the IL wall which was severely hypokinetic showing marked trabeculation and intertrabecular recesses within the non-compacted layer, with moderate systolic LV dysfunction (Figure 1). Furthermore, late gadolinium enhancement (LGE) was found involving almost transmurally the IL LV wall (Figure 2). Because of the age of the patient and the clinical presentation, an associated myocardial infarction (MI) was suspected. A subsequent coronaryography was therefore performed which revealed normal coronary arteries, ruling definitively out an associated coronary artery disease.

Picture/Graph:
Picture/Graph 2:
**Conclusion:** This case shows that a LVNC cardiomyopathy can be associated with a transmural LGE involvement thereby mimicking a transmural MI. Thus, we should be aware of this possibility in the global cardiac evaluation of these patients.

**Disclosure of Interest:** None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Livedo reticularis and iris flocculi would have predicted the risk of aortic dissection during pregnancy

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Introduction: We report about a 26-year old female who developed acute type A aortic dissection (AAAD) during pregnancy. The patient showed two specific clinical features, livedo reticularis and iris flocculi (Figure 1a, b).

Methods:

Background:
The patient complained of acute back pain during pregnancy, which was misdiagnosed and treated with analgetics. 4 weeks later she underwent cesarean due to intrauterine growth retardation. 2 weeks after delivery she again suffered from acute severe back pain. Computed tomography scan showed AAAD. We performed emergent aortic surgery with ascending and hemiarch replacement in moderate hypothermic circulatory arrest combined with an antegrade stent delivery into the proximal descending aorta. Physical examination revealed two specific clinical features, livedo reticularis of all extremities and iris flocculi. Her father, who has livedo reticularis as well, had undergone aortic surgery for ascending aortic aneurysm. Paternal family members had suffered from sudden unexplained deaths. The combination of the clinical features and AAAD let us suspect a familial thoracic aortic aneurysm predisposition. Genetic analysis confirmed this suspicion in demonstrating an ACTA2 mutation.

Results:

Discussion:

Most young patients who develop AAAD have a genetic predisposition, with variable clinical expression and without syndromic features. Various genes have been identified leading to the description of familial thoracic aortic aneurysm and dissection (TAAD) with ACTA2 mutation in 14%. ACTA2 gene encodes for a vascular smooth muscle cell (SMC) specific protein, α-actin. α-actin mutation can impair the aortic structure by causing dysfunction in contractility, thus leading to aneurysms and AAAD. Women with an ACTA2 mutation have a higher risk of AAAD during pregnancy. Interestingly this mutation can also cause dermal capillary occlusion by an increased proliferation of SMCs leading to livedo reticularis. The other feature was iris flocculi, which are hyperpigmented cystic outgrowths of the iris aggregated at the pupillary margin. Iris flocculi has been described to be an ocular marker of TAAD.

Picture/Graph 2:

Conclusion: Livedo reticularis and iris flocculi can be associated with TAAD and therefore would have predicted the risk of aortic dissection during pregnancy.

Disclosure of Interest: None Declared
OR81

7. Clinical cases (All clinical cases have to be submitted in this topic)

First neonatal cardiac transplantation in Switzerland

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Introduction: Neonatal cardiac transplantation is rarely offered in Europe due to the paucity of donors compared to North America.

Methods: We report about a female term newborn baby (3.3 kg, body surface area 0.21 m²) who rapidly deteriorated 90 min after birth following an uncomplicated pregnancy and caesarian delivery. Respiratory failure with subsequent intubation was necessary.

Results: Echocardiographic examination revealed a huge tumor within the free wall of the left ventricle (LV) (24x52 mm) and obstructing 90% of the main left bronchus. Surgical tumor resection was performed on the sixth day of life. During surgery partial enucleation of tumor including mitral valve, was done. After resection the free wall of the LV was thin and collapsed. Therefore, a Berlin Heart Excor (BH) left ventricular assist device (VAD) had to be implanted (left apex, aorta ascendens). Histology of the tumor revealed a Fibroma. The neonate was listed for cardiac transplantation 12 days after surgery (3.3kg) since myocardial recovery was unlikely. Six days after listing a donor organ was accepted. The 11 months old donor weighed 11.3 kg and died from severe brain injury. Uncomplicated bicaval cardiac transplantation with an ischaemic time of 3.45 hours was performed. For right ventricular support iNO and intropics were given and slowly weaned. Control bronchoscopy showed a 70% stenosis of the main left bronchus, however the patient was successfully extubated 12 days after transplantation. Immunosuppressive therapy included rATG for 3 days and steroids for 7 days followed by Tacrolimus (day 3) and Mycophenolate. The patient was transferred to a normal ward 20 days after transplantation. The first routine biopsy on postoperative day 30 showed no rejection (ISHLT 0R).

Conclusion: In this case a newborn with a single ventricle physiology due to a massive tumor and severe left main bronchus stenosis had to be managed. After partial tumor resection the child was bridged with a BH for 16 days to transplantation. Transplantation with an organ-donor/recipient size mismatch of >200% was successful and extubation was possible. This is the youngest child transplanted within Switzerland so far (Swisstransplant data).

References: * First two authors share first authorship

Disclosure of Interest: None Declared
OR82

4. ACS, PCI, CABG

Fast-track management: dexmedetomidine provides effective pain modulation and rapid extubation in patients after off-pump coronary artery bypass grafting

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Introduction: Dexmedetomidine (DEX) is a highly selective, shorter-acting alpha-2 agonist with 10-fold greater alpha-2 to alpha-1 receptor selectivity than clonidine. Many desirable effects of DEX, including analgesia, anxiolysis, improvement of hemodynamic stability, and potential myocardial and renal protection have been proven. The aim of this study was to retrospectively investigate the effect of dexmedetomidine on patients undergoing off-pump coronary artery bypass grafting (OPCAB).

Methods: From January 2012 till March 2015, 464 patients after OPCAB were included for retrospective analysis of early postoperative outcome. After propensity matching (1:1) to mitigate selection bias in DEX infusion, including cardiovascular risk factors, baseline laboratory values and operative strategy, two groups (DEX vs DISO, n=129) could be compared. DEX patients received immediately after chest closure an infusion of dexmedetomidine (1µg/kg/h) while disoprivan was reduced and stopped in the OR. DISO patients were transferred with disoprivan to the ICU, routinely. Continuous and categorical variables were reported as mean ± SD or percentages, and compared with the chi-square test and the Mann-Whitney test, respectively.

Results: In the DEX group less use of pain medication in the initial phase at ICU could be observed. During the first 2 hours, DEX patients received significantly more intravenous nicomorphine (DEX 8 mg ± 3.2 vs DISO 6 mg ± 4, p<0.001), while in the following two hours the pain medication was significantly reduced (DEX 3.2 mg ± 2.8 vs DISO 4.7 mg ± 3.3, p<0.001). After 12 hours there was no difference in both groups, although remifentanil was stopped considerably earlier in the DEX group (DEX 238 min ± 209 vs DISO 353 min ± 266, p<0.001). Additionally, DEX led to earlier extubation (DEX 208 min ± 106 vs DISO 307 min ± 230, p<0.001). Furthermore, there was a significant difference in the occurrence of postoperative atrial fibrillation, which was rarer after DEX application (p=0.01). Delirium occurred only once in the DEX group and five times in the DISO group, which was statistically not significant (p=0.098). There were no differences between both groups in postoperative CK, CKMB or TropT and in Creatinine.

Picture/Graph:
Conclusion: Early postoperative application of DEX supports the fast-track strategy in OPCAB patients by rapid extubation, less need of pain medication, rarer occurrence of atrial fibrillation and a tendency to less delirium.

Disclosure of Interest: None Declared
Skeletonized bima grafts in cabg surgery: a single centre fifteen-year experience.
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Introduction: During the last decades, several clinical studies have shown a long-term survival benefit from multiple arterial grafts use during coronary artery bypass grafting (CABG), especially in diabetic patients. Despite this evidence, at the time being only 10% of patients eligible for CABG receive a second arterial graft in the USA, 12% in Europe and 32% in Australia. We retrospectively reviewed and analysed the surgical outcome of CABG operations performed with bilateral internal mammary artery (BIMA) grafts in our centre during the last fifteen years.

Methods: Between January 2001 and December 2015, 540 selected patients (out of 3560 CABG performed) received BIMA grafts. In all patients the mammary arteries were harvested in a skeletonized fashion and were preferentially employed to revascularize the left coronary system. The right mammary artery was used as a free graft in case of inadequate length, with the proximal anastomosis stemming from the top of a vein graft. Univariate analysis was performed by Student’s T-test.

Results: Mean age was 60.5±10.1 years, 43.1% of patients were in CCS class ≥3 and the mean number of diseased vessels was 2.8±0.4. Mean ejection fraction was 57.7±9.2%. Hundred eight patients (18.7%) were diabetics (12 treated with insulin) and 27 (5%) cases required a combined procedure. Mean grafts per patient was 3.4. Mean pulmonary bypass time and aortic cross-clamp time were 69.7±45.5 and 44.2±30.3 min, respectively. Hospital mortality was 0.4% (2 pts). With regards to postoperative complications, one patient suffered from a stroke and 2 patients needed permanent dialysis. In 49 cases (9.1%) a re-exploration for bleeding was performed postoperatively. Sternal wound dehiscence rate was 8% (43 pts.). Among them, there were 37 superficial dehiscences and 6 (1.1%) deep sternal wound infections. Would cultures were positive in 21% of them. Univariate analysis did not revealed significant correlations between sternal wound dehiscence/infection and preoperative clinical conditions except for the presence of previous percutaneous coronary intervention (p 0.05), associate surgical procedures (p 0.07) and peripheral vascular disease (p 0.09).

Conclusion: In our restrospective analysis of clinical outcomes after BIMA use in selected patients, we did not observe an increased risk of sternal wound infection compared to standard CABG patients treated with single IMA. These results are encouraging for extending the indication for BIMA use.

Disclosure of Interest: None Declared
Heart string reduces stroke rate and enables complete revascularization in off pump coronary artery bypass graft surgery

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Introduction: Stroke is very devastating complication of coronary artery bypass grafting. According to literature it appears in up to 4% of the patients after isolated bypass surgery. The most common cause is the microemboly mobilized by aortic manipulation during cannulation and in particular by performing proximal anastomosis. Off pump surgery as well as aortic no touch technique have been proposed to avoid aortic manipulation and aortic side clamping. Using both mammary arteries as T or Y graft is very demanding and not suitable for every patient to perform fully revascularization. The heart string proximal anastomotic device allows creation of the proximal anastomosis without side clamping of aorta.

Methods: We analyzed retrospectively the prospective collected data of 2420 consecutive patients who underwent isolated off pump coronary artery bypass graft surgery, from January 2003 till December 2014. Primary end point was incidence of stroke during hospitalization.

Results: The overall mortality was 1.4% varying from 0.9% to 1.8% per year. The perioperative myocardial infarction occurred in 67 patients (2.8%). The mean number of distal anastomosis was 3.8 and of proximal 1.6. Bima was used in 40% of the patients with an upward trend in the last four years.

The stroke incidence was 0.83% (20 patients). 13 suffered hemiplegia with or without dysarthria, showing their symptoms directly after operation. Five patients suffered visual disturbances such as diplopia, hemianopsia or even complete blindness (1), which appear rather later postoperatively on the ward. All patients with stroke had a structural brain damage in computed tomography. Overall mortality caused by stroke was 0.16% (4 patients), two of them never waking up after operation and the other two developing coma in the following course. There was one aortic dissection and one massive bleeding, both device related. Conversion rate to on pump was 4%.

Conclusion: Use of heart string is safe and reduces dramatically the incidence of stroke compared to literature data. It enables complete revascularization regardless on number of necessary distal anastomosis.

Disclosure of Interest: None Declared
Introduction: Sternal instability, dehiscence, wound infection and mediastinitis are feared complications in cardiac surgery. Inadequate sternal healing can influence these complications. It has been shown that a certain number of asymptomatic patients show sternal abnormalities (SAs). We assessed by multi-planar CT-scans (CTs) the sterna of asymptomatic patients with no postoperative complications. Potential related causes were analyzed to identify possibilities for more optimized sternal healing.

Methods: We analysed CTs from 131 asymptomatic consecutive patients performed between 2007 and 2009 who underwent cardiac surgery via median sternotomy. CTs were performed after 11.9±4.5 years post sternotomy. Age of the cohort was 59.5±11.2 years. Patients' selection was limited to CABG (n=83) and aortic valve (AV) procedures (n=48). To identify SAs, CTs were analysed in axial view. To perform a detail analysis of SAs, CTs were 3D reconstructed. A chart review analysis for well-established risk factors for sternal complications was also performed.

Results: 32.1% of sterna showed abnormalities (n=42). 49 SAs were identified: 24 offsets, 18 gaps and 7 impactions. 532 wires were implanted for sternal closure (4.2±0.5 wires/patient). 96.1% of implanted wires (n=511) were figure-of-8 wires (4.1±0.5 wires/sternum); only 3.9% (n=21) of implanted wires were single wires (0.2±0.6 wires/sternum). Wire count in normal sterna (M=4.2±0.5) and abnormal sterna (M=4.3±0.6) were not statistically different (t(123)=1.3, p>0.05, 95% CI[-0.3,0.1]). 65% SAs were found in the manubrium (n=32). Distance from the first wire to proximal edge of the manubrium in normal sterna (n=61, M=11.2±4.2mm) and abnormal sterna (n=24, M=10.9±4.8mm) showed no statistical difference (t(83)=0.3, p>0.05, 95% CI[-1.8,2.4]). CABG-patients presented a higher risk for SAs (OR=2.4, p≤0.05,95% CI[1.2,4.9]). BIMA (OR=4.4, p≤0.05,95% CI[1.1,17.9]) and BMI>31kg/m² (OR=3.4, p≤0.01,95% CI[1.4,8.3]) significantly increased the risk of SAs.

Conclusion: Sternal healing after median sternotomy is a mayor problem. In our study, >30% of asymptomatic patients showed SAs with potential higher risk of complications. CABG, BIMA and BMI>30kg/m² were identified as independent risk factors for SAs. The area around the manubrium seems of higher risk for SAs. Our analysis of sternal wiring in this area did not show influence on the outcome of SAs. Different closure techniques in these risk groups, as well as on the manubrium—such as osteosynthesis plate—should be considered.

Disclosure of Interest: None Declared
Introduction: Hybrid coronary artery revascularization (HCAR) consists of minimally invasive direct coronary artery bypass grafting (MIDCAB) of the left anterior descending artery (LAD) and percutaneous coronary intervention (PCI) of non-LAD vessels in a single or staged procedure. It combines the excellent long-term patency of the left internal mammary artery (LIMA) to the LAD and the similar long-term results of stented non-LAD to the patency of aorto-coronary venous grafts. Here we present our specialized single centre experience with HCAR.

Methods: Between January 1st 2009 and December 31st 2015 a total of 47 patients were scheduled for HCAR after discussion in the heart-team due to stentable multi-vessel disease or patient request for a minimally invasive approach. All operations were performed in our hybrid theatre. MIDCAB was performed first followed by PCI using DES. Preoperative, intraoperative, postoperative and follow-up information about major adverse cardiac and cerebrovascular events (MACCE) and need for re-intervention were collected.

Results: Mean age was 66.7±10.4 years, median Euroscore 4(0-10), 85.1% were male patients. HCAR was performed in all patients without procedural complications. There were nine coronary interventions of two non-LAD vessels (19.1%). Angiography confirmed patency of all LIMA grafts intraoperatively. Twenty-three patients (48.9%) were extubated in the theatre and 22 (46.8%) on the day of surgery. Twelve patients (25.5%) were transferred directly to intermediate care. Median intensive care unit stay was 0.8(0-7) day and hospital stay 7(1-20) days. Thirty-day mortality was 0% and there was no stroke. Four patients required one unit of red blood cells each (8.5%). No early stent thrombosis occurred. Median follow up was 25 (1-75) months and was completed in 47 patients (100%) with 93%±3.6 survival (three non-cardiac deaths). One patient (2.1%) had a re-intervention of the LAD and four (8.5%) a re-intervention of non-LAD vessels due to late stent-thrombosis.

Conclusion: HCAR is a safe procedure in specialized centres with low postoperative morbidity, mortality and favourable mid-term MACCE-free survival and freedom from re-intervention in selected patients. However, our results demonstrate that the incidence of re-intervention due to late stent-thrombosis is still higher than the need for re-intervention due to LIMA-LAD failure and that complete surgical revascularisation might had resulted in a higher patency rate.

Disclosure of Interest: None Declared
Introduction: Coronary artery bypass grafting (CABG) remains the gold standard for complex revascularization in multivessel disease. The concept of Miniaturized extracorporeal circulation circuit (MiECT) was introduced to minimize pathophysiological side effects like complement activation or inflammatory reaction. This study presents early and long term outcome after CABG using the MiECT in a single center sequential patients cohort.

Methods: From January 1st 2005 to 31st December 2010, 2130 patients underwent CABG with a MiECT at our center. We collected morbidity and mortality follow-up data with a median follow-up of 3.6 years, maximum 9.7 years. Kaplan-Meier estimates were calculated for the primary endpoint of death and compared the general Swiss population: we used published data about life expectancy in Switzerland, stratified for gender and year of birth. For each patient in the study cohort, we matched a corresponding record from the general cohort.

Results: Mortality in the CABG patients was comparable to the general Swiss population beginning one year after surgery for the whole seven year observation period. All-cause mortality was 0.8% 30 days after CABG. With 445 patients (20.9%) being female, mean age was 65.8±9.8 years. Comorbidities were prevalent in this population: arterial hypertension (79.2%), dyslipidemia (77%), diabetes (30.5%), peripheral arterial disease (16.7%), prior cerebro-vascular event (5.9%) and chronic renal failure (5.8%). 463 patients (23%) suffered from myocardial infarction within seven days prior to the operation. The mean operative risks estimated by the standard, logistic and EUROSCORE II were 4.6±3.3, 5.8±9.6, 3.0±5.1 respectively. Mean perfusion time was 71.1±23.8 min. with a cross-clamp time of 44.9±16.3 min. Mortality was predicted by the presence of diabetes mellitus 1.85 [1.40 to 2.46] (p<0.001), peripheral arterial disease 2.36 [1.64 to 3.38] (p<0.001), severe obstructive pulmonary disease 3.21 [1.42 to 7.24] (p=0.005), chronic renal failure 3.68 [2.49 to 5.43] (p<0.001) and transfusion of more than one erythrocyte concentrate in the perioperative period 1.46 [1.09 to 1.95] (p=0.015). Cerebrovascular events occurred in 29 patients (1%).

Conclusion: CABG using MiECT is associated with low postoperative mortality rate comparable with the overall mortality rate of the general Swiss population. A stroke rate of 1% in the study population is compatible to the international baseline.

Disclosure of Interest: None Declared
Introduction: Recently, novel quadripolar coronary sinus leads (Acuity X4 family) have been introduced for cardiac resynchronization therapy (CRT). These leads potentially allow to overcome issues related to high thresholds and phrenic nerve stimulation. Three models (with different shapes and inter-electrode spacing) are currently available: the spiral long (Spiral L), spiral short (Spiral S) and Straight. The performance of these leads after implantation has not yet been reported. Our aim was to evaluate the electrical parameters and requirements for repositioning after at least 3 months follow-up.

Methods: First consecutive 201 patients with a standard indication for CRT enrolled in the RALLY-X4 multicenter study following successful implantation of an Acuity X4 lead for standard CRT indications were followed-up prospectively. The protocol of this post-market follow up registry with > 800 enrolments specified an initial mandated analysis for a 200 patient dataset collected after at least 3 months post implantation.

Results: A total of 201 patients (169 males, mean age 67.1±9.6 years) were followed-up for a mean of 6.9± 4.5 months). No dislodgements were observed which required repositioning. Only 1/201 (0.5%) patient required reintervention due to phrenic nerve stimulation which could not be resolved by reprogramming.

The electrical parameters (at the programmed configuration) are shown in the table. At 3 months, 95% of patients with available threshold data had an LV threshold of <2.5V/0.4ms at the programmed configuration. A non-distal electrode was used for pacing in 71% of cases.

Conclusion: These first follow-up data show that the Acuity X4 lead family has good electrical performance, which is comparable between the different models. Stability of the leads was excellent with no clinically relevant dislodgments. Freedom from re-reposition for lead-related issues was >99%.

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2. Pacemaker, defibrillator and electrophysiology
The torpedo-pacemaker – towards blood flow driven lead- and batteryless right ventricular outflow tract pacing
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Introduction: Leadless pacemakers (PM) have been introduced recently. They overcome the need for the failure-prone pacing leads and therefore confer an advantage over conventional PMs. However, contemporary leadless PMs are powered by batteries offering only a limited energy storage capacity. When the battery approaches its end of life, the device has to be replaced (or another device has to be implanted if the leadless PM cannot be explanted). This Achilles’ heel is accentuated by the limited volume in the right ventricle restricting the battery size. To overcome this limitation, a lead- and batteryless PM is desirable.

We investigated the feasibility of energy harvesting by a blood flow driven generator in the right ventricular outflow tract (RVOT). This approach would allow building lead- and batteryless PM’s for catheter-based implantation.

Methods: We developed a torpedo-like pacemaker generator for implantation in the RVOT. The device (diameter 6.2mm, weight 3.9g) features four self-expanding nitinol-struts for a centered alignment in the RVOT (figure 1). The blood flow drives a propeller which actuates a microgenerator (MG 4.0, Kinetron, Netherlands). The microgenerator converts the propeller rotation into electrical energy. The 3D printed propeller (outer diameter 18mm) was designed for physiological flow conditions in the RVOT. To transfer the mechanical power while ensuring impermeability of the device, we built a magnetic coupling mechanism. This allows a permanent through-flow of blood which is aimed to reduce blood trauma (and the associated risk of thrombosis).

The prototype was tested on a flow bench mimicking hemodynamic conditions in the RVOT. Energy output of the generator was measured.

Results: Even at a low cardiac output of 2.0l/min (heart rate 60 beats/min, stroke volume 33±1.6ml; figure 2), the generator delivered a mean power of 16.5±2.1µW (the typical power consumption of modern leadless PMs is in the range of 5µW). No significant RVOT stenosis was induced (mean pressure drop over the generator was <1mmHg). The mean propeller speed was 4'084±656 rotations per minute.

Picture/Graph:
Conclusion: Blood flow in the RVOT provides sufficient energy to power a pacemaker, enabling lead- and batteryless RVOT pacing. However, long-term tests are required to minimize the thrombogenicity of the device. Furthermore, the nitinol-struts need to be improved to serve as electrical interface for myocardial stimulation. *In vivo* implantation is targeted in summer 2016.

Disclosure of Interest: None Declared
Introduction: Transcatheter Leadless Pacemakers (TCLP, Micra®, Medtronic) have been recently introduced for patients (pts) requiring right ventricular (RV) pacing as an alternative to conventional lead-based pacing. TCLP has been shown to reduce local and periprocedural complications compared to traditional pacemakers. We aimed to assess the clinical safety and efficacy of TCLP in a real-world clinical practice.

Methods: All consecutive pts treated with TCLP at both institutions were enrolled in the present registry between June and December 2015. The choice for TCLP or regular lead pacemaker implantation was left to operators’ discretion. TCLP implantation was performed according to manufacturer guidelines. Baseline pts and procedural characteristics and clinical presentation were collected at the index procedure. Follow-ups were performed as outpatient visits. The primary safety endpoint included the occurrence of major complications defined as death or resuscitated cardiac arrest, major bleeding (BARC>2), prolonged hospitalization or loss of device function. Efficacy endpoints were defined as a capture threshold <1.75 V at a pulse width of 0.24 msec at discharge and at 4-8-week follow-up.

Results: A total of 25 pts (75±22-91 years old, 72% male gender) were implanted with a TCLP during the study period. Most pts presented with syncope (48%) or symptomatic bradycardia (33%) due to atrial arrhythmias, sick sinus syndrome, AV node disease or AV node ablation. The procedure was successful conducted in 92% (23/25) of the cases. Procedure time was 51±20-129 minutes with a fluoroscopic time of 7.78±2-21 minutes. Safety endpoints occurred in two (8%) pts who developed an hemodynamic collapse due to cardiac tamponade that was fatal in one (4%) and resulted in a prolonged hospitalization in the other case. No other complication was noticed. Among the 23 implanted pts, 96% (22/23) reached the efficacy endpoint (pacing threshold <1.75 V/0.24msec) on the first post-operative day and 91% (20/22) at 4-8 weeks.

Conclusion: TCLP is an attractive alternative for pts requiring RV pacing with efficient short-term pacing thresholds. Device-related serious adverse events occurred in 8% of the cases during the initial experience. As TCLP is a new technique, one is expecting a reduction in procedural complications rate with increasing experience. Randomized studies comparing both systems are needed including the need for case replacement and new TCLP implantation at end of life (EOL).

Disclosure of Interest: None Declared
Introduction: Pericardial effusion (PE) may be a life-threatening complication of lead extraction procedure (TLE). Little is known on possible causal mechanisms of PE formation during TLE.

Methods: From January 2009 to June 2015, TLE of 267 leads in 187 patients (mean age 69±14 years, 131 male, mean BMI 27±11 m²/kg, LVEF 43±27%) was performed. Indications for TLE included lead dysfunction (60.4%), upgrade (18.9%), infection (13.2%), or other (6.3%). TLE was first attempted using mechanical approach, and eventually combined with laser technique. Extraction procedures were performed under general anesthesia with continuous invasive arterial blood pressure and transesophageal echocardiography (TEE) monitoring. Severity of PE was defined as mild (<10 mm), moderate (11–20 mm), or severe (≥20 mm).

Results: TLE was complete for 259 of 267 leads (97.0%). PE developed in 12 pts (6.4%): mild in 6 pts (3.2%) and severe in 6 pts (3.2%). All patients with severe PE experienced hemodynamic instability; 2 pts required urgent cardiac surgery, 2 pts were treated with pericardiocentesis, and 2 patients were treated medically. Key differences between these patients was the site of lesion, namely RV in all patients treated in a conservative manner (fluid infusion and repeated echocardiographic examinations). Laceration of the superior vena cava (2 pts) resulted in rescue surgery; lesions of the right atrial free wall (1 pt) and coronary sinus ostium (1 pt) were treated with pericardiocentesis. Pre-discharge transthoracic echocardiography excluded PE evolution in all cases and no recurrences occurred during follow-up.

Conclusion: Sudden onset of severe PE during TLE is a life-threatening condition. Evolution and subsequent pt management depends on the site of lesion, with RV site lesions being self-limiting.

Introduction: High failure rates have been reported for the Medtronic Sprint Fidelis lead (Fi), the St. Jude Medical Riata/Riata ST leads (Ri) and recently for the Biotronik Linox lead (Li).

Methods: We compared lead failure rates and lead failure manifestations of all patients implanted with one of the abovementioned leads at our centre.

Results: A total of 93 Li leads (median patient age at implant 60 years; 77% males), 86 Ri leads (62 years; 91% males) and 81 Fi leads (61 years; 79% males) were implanted. Median follow up was 46 months, 84 months and 61 months for Li, Ri and Fi leads, respectively. Lead survival at 3 years was 96% (Li), 95% (Ri) and 90% (Fi), and at 5 years was 88% (Li), 92% (Ri) and 71% (Fi) (Log Rank Test: p=0.95 for Li vs. Ri; p=0.061 for Li vs. Fi; p=0.077 for Ri vs. Fi; see Figure). Lead failures showed non-physiological high-rate signals in 73% (Li), 27% (Ri) and 80% (Fi) of cases (p=0.001). Inappropriate shocks were delivered in 64% (Li), 5% (Ri) and 32% (Fi) of failed leads (p=0.001) and a device alarm was noted in none (Li), 5% (Ri) and 52% (Fi) of cases (p=<0.001).

Conclusion: At our centre, lead survival of the Linox lead is not different to that of the Riata/Riata ST leads. Non-physiological high-rate signals are often present in Linox and Sprint Fidelis lead failures and inappropriate shocks are delivered as a consequence. Inappropriate shocks are rare during Riata lead failures.
Introduction: High failure rates of the Biotronik Linox defibrillator lead have been reported by others and by our group. This study gives an update on the Linox lead (Li) performance at our centre and also includes the newer Linox Smart lead (LiSm).

Methods: We assessed lead performance of all Li and LiSm leads implanted at our centre. Linox and Linox Smart leads are also marketed by the Sorin Group as Vigila and Volta leads, respectively, these leads were also included in our analysis.

Results: A total of 93 Li leads (median patient age at implant 60 years; 77% males; 24% dual coil) and 115 LiSm leads (62 years; 79% males; 26% dual coil; 24% DX leads) were implanted. Median follow up was 46 months and 20 months for Li and LiSm leads, respectively. Lead survival at 3 years was 96% (Li) and 93% (LiSm) (Log Rank Test: p=0.88). Of a total of 11 Li lead failures, 7 presented with non-physiological signal sensing. We observed three LiSm lead failures, two of those affected Linox Smart DX leads. All LiSm lead failures showed non-physiological signal sensing (on the atrial and far-field channel in one DX lead and on the ventricular channel in the remaining two leads). All failed LiSm leads were explanted and an insulation failure within the pocket was observed in two leads. Analysis of the remaining LiSm DX lead did not reveal any abnormality.

Picture/Graph:
Conclusion: The Biotronik Linox Smart lead may also be prone to insulation failure and consecutive non-physiological signal sensing. At our centre, lead performance of the Linox Smart lead after 3 years is not different to that of the Linox lead.

Tanner Conflict with: Biosense Webster, SJM, BostonScientific, Biotronik, L. Roten Conflict with: Biosense Webster, BostonScientific
Electrophysiology study tailored pacemaker or loop recorder implantation and follow up of patients with left bundle branch block after transcatheter aortic valve implantation

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Introduction: Left bundle branch block (LBBB) after transcatheter aortic valve implantation (TAVI) is common and has been associated with a higher incidence of syncope, complete AV-block and death. The aim of this study was to determine the site of conduction delay and to evaluate a tailored management strategy in patients with LBBB after TAVI based on the measurement of the His-ventricular interval (HV).

Methods: 143 patients undergoing TAVI (Core valve: n=7 (0.5%); Edwards-Sapien: n=102 (71%); Jenavalve: n=7 (0.5%); Lotus: n=35 (25%); Portico: n=19 (13%)) were screened for LBBB after TAVI. In case of persistent LBBB, patients underwent measurement of the HV-interval within 24 hours after TAVI. If HV was >55ms, pacemaker implantation (lower rate limit programmed to 40bpm) was performed. If HV was ≤55ms, an implantable loop recorder (ILR) with remote monitoring capabilities (Medtronic Reveal LINQ) was inserted at the end of the 72-hour telemetry period. The primary outcome measures were the development of high-grade AV-block (Mobitz II or complete AV-block) in the ILR-group and the need for pacing (>1%) in the pacemaker-group. Secondary outcome measures were syncope and death.

Results: Of 143 patients, 55 had LBBB after TAVI (age 81±6, 56% female). Of these 55 patients, the HV-interval was >55ms in 17 patients (31%) whereas the HV-interval was ≤55ms in 35 patients (64%). HV interval measurements were not available in 3 patients (5%). None of the 35 patients with LBBB and HV-interval ≤55ms developed high-grade AV-block during a median follow-up of 7 months. Syncope occurred in one of the 35 patients with HV ≤55ms, but no AV-block or significant bradycardia (<40bpm) was detected on the ILR. In the 17 patients with HV>55ms, 6 patients (35%) required ventricular pacing (median 9% ventricular pacing). 3 patients died in the ILR-group (cause of death was other than sudden cardiac death in all of these patients). None of the patients died in the pacemaker group.

Conclusion: A patient-tailored strategy based on the measurement of the HV-interval in patients with LBBB after TAVI successfully identified patients with no need for pacemaker implantation during a follow-up 7 months after TAVI. These preliminary findings suggest that patients with LBBB and HV-interval ≤55ms may be followed clinically without further rhythm monitoring.

Introduction: Therapy with an implantable cardioverter defibrillator (ICD) is an established therapy for the prevention of sudden cardiac death (SCD) in high risk patients. The therapy is costly, shows vast regional differences and 2/3 of contemporary patients will never receive appropriate shocks. Women have been consistently underrepresented in all major trials. We therefore analysed the outcome of women with primary preventive ICD therapy by analysing registry data from 14 centres in 11 European countries compiled between 2002 and 2013.

Methods: A total of 4'689 pts (female 885 pts (19%); mean age 64±11 yrs; LVEF < 0.25 60%; ischaemic cardiomyopathy 64%, CRT-D 44%) with a primary preventive ICD indication were included in the retrospective EU-CERT ICD registry and followed for a mean of 27 months (IQR 13-48 months). Demographic and follow-up data from 14 local registries were compiled and analysed from a central database. Survival curves and hazard ratios with multivariable correction for baseline parameters and testing for heterogeneity between centers were calculated.

Results: During follow-up 885 pts (19%) died. The risk of death for women (n=120) was significantly lower than that for men (n=765; adjusted HR 0.69:054-0.87; fig.1). Women also received significantly fewer first appropriate ICD shocks than men (60, 7% vs. 484, 13%, shocks; adjusted HR 0.64:0.46-0.88; fig2).

Picture/Graph:
Conclusion: Women with a primary preventive ICD have a significantly lower total mortality and receive significantly fewer first appropriate ICD shocks than men. Our data indicate that the cost effectiveness of primary preventive ICD therapy is lower in women and that better risk stratification is urgently needed.

Disclosure of Interest: None Declared
Introduction: In Switzerland, ECG screening has been recommended for national squad athletes in 1998, since 2001 it has become mandatory in selected professional sports (e.g. ice hockey). The impact on sudden cardiac death (SCD) rates in athletes is unknown. We aimed to study the incidence, causes and trends of sports-related SCD in comparison to cases of SCD unrelated to exercise.

Methods: We reviewed all forensic reports of the German-speaking part of Switzerland (overall population of 5,617,963 inhabitants) in the age-group 10 to 39 years between 1999 and 2010. Cases compatible with SCD were included and classified in three groups based on the relation to sports: none (NONE), recreational sports (REC), and competitive sports (COMP). COMP was defined as SCD during competitions in organized team or individual sports. REC was defined as SCD during physical activities, excluding competitions. Yearly incidences were calculated per 100,000 person for the average population of the observed period. Nominators were adjusted for the average autopsy rate (47.5%); denominators were derived from surveys of the Federal Offices of Statistics and Sports. The analysis was done using the statistical software R (R Core Team, 2015); trends were calculated using Poisson regression analysis.

Results: Over the 12-year study period, 349 SCD cases were recorded (mean age 30±7 years, 76.5% male, 97.6% white). 297 occurred in NONE, 31 in REC, and 21 in COMP. Incidences of SCD were the lowest in REC (mean±SD 0.43±0.14), followed by COMP (1.16±0.62) and NONE (2.47±0.68). In all three groups, coronary artery disease (CAD) with or without acute myocardial infarction (MI) was the most common cause of SCD (incidences were 0.91±0.38, 0.11±0.15, and 0.45±0.44 for NONE, REC and COMP, respectively), followed by hypertrophic cardiomyopathy (HCM). HCM was the most common cardiomyopathy observed; incidences in NONE, REC and COMP were 0.24±0.16, 0.09±0.15 and 0.11±0.27, respectively. In young competitive athletes (YCA, age≤35 years) acute MI was the most common cause of SCD. No time trend, for incidences of SCD caused by CAD with or without acute MI and cardiomyopathies, could be demonstrated in neither group (p≥ 0.268 for all groups).

Conclusion: In our cohort, incidence of sports-related SCD was low. CAD with or without acute MI was the most common cause of SCD in all groups, also in YCA. No time trend could be demonstrated in neither group for incidence of SCDs, caused by CAD or cardiomyopathies.

Disclosure of Interest: None Declared
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4. ACS, PCI, CABG
High-intensity statin therapy stabilizes vulnerable plaques in patients after st-elevation myocardial infarction patients (ibs-4): a serial multivessel optical coherence tomography study (oct)
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Introduction: The clinical benefit of statins is associated with only modest reductions of plaque burden, suggesting additional vascular effects not detected by IVUS. Fibrous cap thickness and macrophages represent important indices of plaque vulnerability and can be reliably assessed by optical coherence tomography (OCT). The aim of this study was to investigate the effect of high-intensity statin therapy on measures of plaque stability including cap thickness and macrophage accumulation using serial OCT imaging in patients after STEMI.

Methods: A total of 103 STEMI patients underwent OCT and IVUS of the proximal segments of two non-infarct-related coronary arteries (non-IRA) after successful primary PCI at 5 European centers. All patients were treated with high-intensity rosuvastatin (40 mg/day) throughout 13 months and serial imaging was available for 83 patients with 153 non-IRA. The primary endpoints were changes in minimal fibrous cap thickness and macrophage accumulation. Analysts were concealed for the time-point of data acquisition. Cap thickness was assessed using a semi-automated method. Statistical analysis was performed using linear mixed models.

Results: At 13 months, low-density lipoprotein cholesterol (LDL-C) had decreased from a median of 128 mg/dl to 73.6 mg/dl (P<0.001). The matched region of interest in 153 non-IRA amounted to 28.4±10.2mm. The minimal cap thickness increased from 64.4 ±18.0mm to 83.6 ±30.3mm (p<0.001) and the mean cap thickness increased from 254.4±62.3mm to 309.7±79.4mm (p<0.001) over 13 months. The change in cap thickness was associated with a decrease in the proportion of frames with thin cap fibroatheroma (BL 2.8%±5.39, FUP 0.69%±1.49, p=0.019). A decrease in lipid pool angle (BL 54.5°±34.9, FUP 42.4°±31.5, p=0.02) was noted. Macrophage accumulation was observed in 16.4% of frames at BL and 12.0% of frames at FUP, corresponding to a reduction of 26.8% (p<0.001). Similarly, the mean macrophage angle decreased from 10.3° to 6.6° (p<0.001). Macrophage frequency and angle reduction correlated with reductions in LDL over 13 months (p-value linear trend p<0.05 for both).

Conclusion: High intensity statin therapy is associated with a relevant increase in fibrous cap thickness and decrease in macrophage accumulations among STEMI patients. These findings provide direct evidence of non-culprit plaque stabilization in STEMI patients under high-intensity statin therapy, which may have important clinical implications.

Disclosure of Interest: None Declared
Multi-analysis with OCT and vasomotion in everolimus-eluting synergy coronary stents - the moves trial
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Introduction: We sought to compare endothelium-dependent and -independent vasomotor function and vascular healing 15 months after implantation of 2 new-generation everolimus-eluting stents and 1 everolimus-eluting bioresorbable vascular scaffold.

Methods: A total of 28 patients previously treated with a SYNERGY stent, a PROMUS stent or a bioresorbable ABSORB scaffold for coronary artery disease underwent control coronary angiography and optical coherence tomography, coupled with supine bicycle exercise during 2 minutes at 50 and 100 Watts, 15 months after device implantation. Intracoronary nitroglycerin was administered after exercise testing. Coronary vasomotor response was assessed using quantitative coronary angiography at rest, during supine bicycle exercise and after nitroglycerin. The primary endpoint was the percent change in mean lumen diameter of the stented segment and the persistent regions at maximum exercise compared to baseline. Secondary endpoints were strut coverage and apposition as assessed by OCT imaging.

Results: Of 28 included patients, 10 had previously been treated with SYNERGY, 10 with PROMUS and 8 with ABSORB. There were no significant differences with regard to baseline characteristics, lesion or procedural characteristics at the index procedure between the treatment groups.

There was no significant difference in vasomotor response between the 3 treatment groups. However, patients with PROMUS showed significant vasoconstriction of the proximal (-10±5%, p=0.02) but not at the distal (-3±9%, p=0.37) persistent segment at maximum exercise. ABSORB- and SYNERGY- treated patients did not show significant vasoconstriction around proximal (ABSORB: -3±6%, p=0.40; SYNERGY -4±13%, p=0.36) or distal (ABSORB: -1±12%, p=0.67; SYNERGY -2±9%, p=0.41) persistent regions at maximum exercise.

Mean neointimal thickness over struts was 82±22μm, 135±50μm and 82±33μm for ABSORB, SYNERGY and PROMUS, respectively. SYNERGY (4%) and ABSORB (3%) showed less uncovered struts than PROMUS (14%, p=0.03 and 0.08 respectively). Malapposed struts were more frequent with ABSORB (2±1%) than with SYNERGY (1±1%, p=0.02). Malapposition in patients with PROMUS (2±3%) was not significantly different from any of the other treatment arms.

Conclusion: ABSORB and thin-strut SYNERGY have a reassuring vasomotion profile suggesting minimal endothelial dysfunction 15 months after implantation.

Disclosure of Interest: None Declared
Diagnostic and prognostic value of the v-index, a novel ecg marker quantifying spatial heterogeneity of ventricular repolarization, in patients with symptoms suggestive of acute myocardial infarction


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Introduction: The V-index is an ECG marker quantifying the spatial heterogeneity of ventricular repolarization. We aimed to prospectively assess the diagnostic and prognostic value of the V-index in patients with symptoms suggestive of acute myocardial infarction (AMI).

Methods: In a prospective observational study, we enrolled 582 patients presenting with suspected AMI to the emergency department (ED). Twelve lead ECG’s of five minutes were recorded at presentation to the ED. The V-index was calculated in a blinded fashion. Final diagnosis was adjudicated by two independent cardiologists. Patients were followed for the endpoint of all-cause mortality.

Results: AMI was the final diagnosis in 16% of patients. Values for the V-index at presentation were higher in patients with AMI compared to other causes of chest pain (23ms (IQR 18-28) vs. 18ms (IQR 15-24), p<0.001). The diagnostic accuracy of the V-index at presentation for the diagnosis of AMI as quantified by the area under the receiver operating characteristic curve (AUC) was 0.64 (95% CI 0.58-0.70). Median V-index levels in deceased patients were significantly higher as compared to survivors (28ms (IQR 22-37) vs. 19ms (IQR 15-24), p<0.001). Cumulative 24-month mortality rates were 99.5%, 97.2% and 90.4% according to tertiles of the V-index (p<0.001). In multivariable Cox proportional hazard analysis, the V-index significantly predicted mortality independently of age and high-sensitive cardiac Troponin T (hs cTnT).

Picture/Graph:
Conclusion: The V-index, an ECG marker quantifying the spatial heterogeneity of ventricular repolarization, predicts mortality in patients with suspected AMI independently of age and hs-cTnT, but does not seem to help in the early diagnosis of AMI.

Disclosure of Interest: None Declared
Exosomes from human cardiac-resident progenitor cells are more cardioprotective than exosomes from bone marrow mesenchymal stem cells via a pregnancy-associated plasma protein-a-dependent mechanism

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Introduction: Cardiac-derived progenitor cells (CPC) and bone marrow mesenchymal stem cells (BMC) have been evaluated in clinical trials in patients after myocardial infarction (MI). The most beneficial cell type, however, has not been determined yet. Available evidence suggests that both cell types may exert beneficial effects in injured hearts primarily by releasing secreted factors, particularly exosomes (Exo; nanosized vesicles). Thus, a comparison of cardioprotective activities of Exo from these cellular sources is important for cell heart therapy.

Methods: Right atrial appendage and sternal BM samples were collected from patients who underwent heart valve surgery to derive CPC and BMC, respectively. Exo were isolated from culture media conditioned by these cells. They were tested in cardiomyocyte (CMC) apoptosis and angiogenesis models in-vitro, and in-vivo after MI in rats. miRNA and proteomics analyses were performed.

Results: Exo-CPC were more cardioprotective and proangiogenic than Exo-BMC both in-vitro and in-vivo, moreover Exo-CPC improved cardiac function after MI to a greater extent than Exo-BMC. Both Exo types were highly enriched in a set of cardioprotective miRNA (miR146a, miR210, miR132, miR181a) compared to Exo derived from human dermal fibroblast, which were not cardioprotective. Pregnancy-Associated Plasma Protein-A (PAPP-A) was identified as one of the most highly enriched proteins in Exo-CPC vs. Exo-BMC. PAPP-A on Exo-CPC induce the release of bioactive insulin-like growth factor-1 (IGF-1) that activate IGFR, leading to the phosphorylation of Akt and ERK in recipient CMC, resulting in reduced apoptosis under stress conditions. Knocking-down of PAPP-A using siRNA abrogated benefits of Exo-CPC.

Conclusion: Exo-CPC are more cardioprotective and proangiogenic than Exo-BMC, which also show some degree of activity. The mechanism of benefit of Exo-CPC involves PAPP-A-mediated activation of IGF-1 and Akt/ERK signalling pathways.

Disclosure of Interest: None Declared
PP-002

1. Cardiovascular biology (Including all abstracts with in vitro or in vivo investigations)

The ryanodine receptor type 2 can also cause recessive catecholaminergic polymorphic ventricular tachycardia (cpvt)


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Introduction: Mutations in the Ryanodine Receptor type 2 (RYR2) gene are known to produce Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) type 1, an inherited arrhythmia syndrome characterized by dysfunctional ryanodine receptor and impaired calcium regulation, leading to catecholamine induced ventricular arrhythmias and/or sudden cardiac death in young people with otherwise normal hearts. The RYR2 gene is known to provide an autosomal dominant pattern of inheritance. Here we present a novel recessive RYR2 mutation.

Methods: After obtained informed consent, DNA was extracted from peripheral blood. Clinical exome was performed in the index case using the TrueSight One Sequencing Panel from Illumina® which includes 4,813 genes associated with known clinical phenotypes. 42 genes associated previously with cardiac channelopathies were analyzed. Read alignment and local realignment of indels was performed using CLC Workbench v7.5.1. Variant prediction was done using Polyphen2, SIFT and Mutation Taster and following databases were used for data interpretation: human gene mutation database (HGMD, Biobase), 1000 genomes and ExAC browser. After the identification of a putative mutation, extensive family screening was performed.

Results: In the index case, a novel RYR2 homozygous mutation c.365G>A (p.Arg122His) was identified. This mutation was predicted to be pathogenic by SIFT, Polyphen2, Mutation Taster and absent in HGMD, 1000 genomes and ExAC Browser encompassing >60,000 sequenced whole exomes. The patient had several syncopes under emotional stress and physical activity in childhood beginning at age of 12 and was successfully resuscitated from cardiac arrest at age of 17. Both parents were asymptomatic heterozygous carriers, not known to be related, but originating from the same region. At least 6 additional heterozygous asymptomatic carriers have been identified in the family.

Conclusion: The Ryanodine Receptor type 2 encoded by RYR2 gene, known to provide primarily autosomal dominant CPVT, is able to cause recessive CPVT. In isolated families in whom heterozygous carriers did not exhibit the phenotype, the homozygous carriers had a severe form of the disease.

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1. Cardiovascular biology (Including all abstracts with in vitro or in vivo investigations)

Ticagrelor, but not clopidogrel active metabolite, exerts antithrombotic properties on left atrial endocardial cells of patients with atrial fibrillation


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Introduction: Atrial Fibrillation (AF) is the most common cardiac arrhythmia in Europe and is associated with an increased risk for thromboembolic complications. Thrombi are mainly formed in left as compared to right atrial appendages and increased expression of prothrombotic factors including tissue factor (TF) and plasminogen activator inhibitor-1 (PAI-1) in left atrial appendage endocardial cells (LAAECs) have recently been proposed as a potential mechanism for this observation. We have previously reported on pleotropic antithrombotic properties of P2Y12 receptor antagonists on endothelial cells. In this study we show that specific P2Y12 receptor antagonists blunt the prothrombotic profile displayed by LAAECs from patients with atrial fibrillation.

Methods: Fourteen left atrial appendages were removed from patients with known AF undergoing elective cardiac surgery at the University Hospital Zurich after informed consent, before LAAECs were isolated and cultured. Endocardial cells were treated with clinically relevant concentrations of ticagrelor (10⁻⁷, 10⁻⁶, 10⁻⁵M) or clopidogrel active metabolite (CAM, 1.5x10⁻⁸, x10⁻⁷, x10⁻⁶M), and stimulated with tumor necrosis factor-alpha (TNF-α, 10 ng/mL) to mimic the prothrombotic and proinflammatory environment in AF patients. Effects on procoagulant TF expression and activity, its counter-player TF pathway inhibitor (TFPI) and antifibrinolytic PAI-1 protein expression and activity were investigated.

Results: Ticagrelor, but not CAM, dose-dependently reduced TF protein expression in TNF-α-stimulated LAAECs without affecting TFPI expression. Correspondingly, TF enzyme activity was reduced by ticagrelor, but not CAM. Similarly, ticagrelor decreased PAI-1 protein expression in LAAECs, whereas no effects were observed in CAM-treated cells. In line with the reduced protein expression, also PAI-1 activity was decreased by ticagrelor.

Conclusion: Ticagrelor, unlike clopidogrel active metabolite, reverses the prothrombotic profile in endocardial cells of left atrial appendages from patients with atrial fibrillation. Such properties may be of potential interest in patients with atrial fibrillation and needing antiplatelet therapy.

Disclosure of Interest: None Declared
Introduction: Environmental influences acting early in life predispose to premature cardiovascular disease. Assisted reproductive technologies (ART) involve the manipulation of early embryos at a time when they are particularly vulnerable to external disturbances. In line with this concept, we recently showed that ART induces endothelial dysfunction, premature vascular ageing and arterial hypertension in humans and mice. These problems are related to epigenetic modifications of the eNOS gene resulting in decreased vascular nitric oxide (NO) bioavailability. However, it is unknown if others mechanisms also contribute to ART-induced alteration of the cardiovascular phenotype. In rodents, restrictive diet during pregnancy or prenatal nicotine exposition induce arterial hypertension in the offspring by increasing the vascular angiotensin II (ANG II) sensitivity. We speculated that a similar mechanism could be involved in ART-induced arterial hypertension.

Methods: To test this hypothesis, we assessed ANG II sensitivity in ring preparations of the distal aorta of ART and control mice by measuring the vasoconstrictor responsiveness to stepwise increasing doses of ANG II in the presence of an endothelial nitric oxide synthase inhibitor (L-NMA). Moreover, we also assessed endothelial function (mesenteric-artery responsiveness to increasing doses of acetylcholine) and arterial blood pressure (using a carotid catheter) in the 2 groups.

Results: As expected, ART mice displayed marked mesenteric-artery endothelial dysfunction (P=.03, vs. control) in vitro and arterial hypertension in vivo (121.8±7.3 vs. 114.6±4.5 mmHg, P=.02, vs. control). Most importantly, the vasoconstrictor response to ANG II, independently of endothelial function, was almost 2-fold greater in ART than in control mice (P<.01, vs. control).

Conclusion: We show for the first time that ART increases the angiotensin II sensitivity in the aorta. Hence, we identified a new mechanism, independent of the NO pathway, that appears to be involved in the pathogenesis of ART-induced premature vascular ageing and arterial hypertension in mice. We speculate that exaggerated vascular sensitivity to ANG II could also be involved in ART-induced premature vascular ageing and arterial hypertension in humans.

Disclosure of Interest: None Declared
Exosomes from human cardiac progenitor cells, but not those from patient-matched bone marrow-derived mesenchymal stem cells, improve cardiac function after myocardial infarction in vivo

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**Introduction:** Both human cardiac progenitor cells (CPC) and bone marrow-derived mesenchymal stem cells (BM-MSC) have been tested in clinical trials of cell transplantation in patients with myocardial infarction (MI). We have recently shown that exosomes (Exo) from (CPC) account for cardioprotective and proangiogenic activities of these cells, both in vitro and in vivo. The aim of this study is to compare Exo-CPC and Exo-MSC in terms of cardioprotective activity and functional improvement after MI.

**Methods:** CPC and BM-MSC were derived from right atrial appendage and bone aspirate from patients undergoing heart valve surgery. From each patient, samples of both tissues were obtained for a patient-matched comparison of Exo from the two tissue sources. Exo were isolated by differential ultracentrifugation of conditioned media from CPC or BM-MSC. Anti-apoptotic and proangiogenic activities of Exo-CPC, Exo-MSC were assessed in-vitro and compared with exosomes from human dermal fibroblast cell line (Exo-F). Exo-CPC and Exo-MSC from 8 patients were injected intramyocardially in 8 rats each after permanent ligation of the left anterior descending (LAD) coronary artery. Left ventricular ejection fraction (LVEF) was measured by echocardiography 1 and 4 weeks after MI. Statistical analysis was performed by Student’s T-test.

**Results:** Although both Exo-CPC and Exo-MSC inhibited cardiomyocyte (CM) apoptosis, following serum starvation in vitro the former showed superior efficacy (Exo-CPC 21±4%; Exo-MSC 28±4%; Exo-F 40±5%). Exo-CPC, but not Exo-F, were proangiogenic in HUVECs. In vivo, hearts injected with Exo-CPC showed an improved LVEF compared to those injected with patient-matched Exo-MSC at 1 week (87.0±9.9% vs 61.1±11.9; p<0.05) and 4 weeks after MI (75.4±8.9% vs 58.7±18.4%; p<0.05).

**Conclusion:** These results from patient-matched analyses show, for the first time, that Exo-CPC is superior to Exo-MSC at inhibiting CM apoptosis in vitro, and at improving cardiac function after MI in vivo. More advanced clinical research is needed to demonstrate the cardiac regenerative capacity of this cell-free approach.

**Disclosure of Interest:** None Declared
1. Cardiovascular biology (Including all abstracts with in vitro or in vivo investigations)

Safety and efficacy improvement of xeno-allogenic cardio-vascular prosthesis by decellularization and pathogen agents inactivation.

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Introduction: Although the glutaraldehyde is currently the gold standard treatment for prosthesis preservation, calcifications appearance and the absence of tissue growth remain the major limitations. Our study assessed the biocompatibility of human/porcine tissues treated with a chemical/physical procedure for decellularization and non-conventional pathogens inactivation.

Methods: Human (fascia lata, pericardium) and porcine (pericardium, peritoneum, arteries) tissues were treated with chemical agents and gamma-irradiation. First, biopsies (n=4/tissue) were performed before and after treatment to assess decellularization (HE/Dapi/DNA/MHC-I) and mechanical integrity (elongation test). Secondly, 50 rats received an abdominal aortic patch of native tissues, treated tissues or bovine glutaraldehyde fixed pericardium (control). Finally, a patch or a tubularized prosthesis (on carotid and abdominal arteries) was performed in porcine recipient with: decellularized human fascia lata (n=4)/pericardium (n=9) and decellularized porcine peritoneum (n=7)/arteries (n=3) and control(n=3). AngioCT were performed at weeks 2 and 4 post-implantation and implants were explanted and processed for HE/von Kossa staining and immunohistochemistry for von Willebrand factor/CD3 (lymphocytes)/CD68 (macrophages).

Results: 95% of decellularization was obtained for all tissues excepted for fascia lata (75%). Mechanical properties were slightly altered by the treatment in all groups excepted for fascia lata (p<0.05). In the rodent, a significant increase of CD3 and CD68 was found in the patch for native and control tissues in comparison to decellularized tissues (p<0.05). Von Kossa staining demonstrated calcifications in 3 controls. After porcine intravascular implantations, no deaths, aneurysms or pseudoaneurysm formations were observed. A significant higher CD3 and CD68 infiltration for human fascia lata and the control group was found in the reconstructed wall.

Conclusion: This treatment reduces significantly the immunogenicity of tissues and improves the biocompatibility and the tissue remodelling of allogenic (pig to pig) as well as xenogenic (human to pig) decellularized tissues in comparison to glutaraldehyde-treated xenogenic graft. Interestingly, the human fascia lata elicited a significant higher immune response following a lower rate of decellularization. Therefore, biological cardiovascular tissues must be controlled in term of decellularization before implantation.

Disclosure of Interest: None Declared
1. Cardiovascular biology (Including all abstracts with in vitro or in vivo investigations)

Cardioprotective reperfusion strategies improve recovery after normothermic global ischemia in an isolated working rat heart model of donation after circulatory death

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Introduction: The use of hearts obtained with donation after circulatory death (DCD) could potentially improve the currently insufficient cardiac graft availability. But DCD hearts undergo an inevitable warm ischemic period and for ethical reasons, most cardioprotective strategies can only be applied at reperfusion (procurement). Therefore, we investigated whether cardioprotective reperfusion strategies could improve heart recovery after warm global ischemia in our isolated working rat heart model of DCD.

Methods: Isolated hearts of adult male Wistar rats were perfused in working-mode with modified Krebs-Henseleit buffer for 20 min (baseline), then subjected to 27 min global warm ischemia (37°C) and 60 min reperfusion (n=43). Mild hypothermia (MH; 30°C, 10 min), mechanical postconditioning (MPC; 2x30 sec reperfusion/ischemia), low pH (pH 6.8-7.4, 3 min) and hypoxia (HY; no O2, 2 min) were applied at the onset of reperfusion and compared with controls (i.e. no strategy applied). Hemodynamic and biochemical parameters were monitored. Data (mean±SD) were compared using t-tests; p-values were corrected for multiple comparisons.

Results: Compared to controls, post-ischemic recovery was higher in MPC, MH and HY treated hearts, but similar for low pH (see Table below).

<table>
<thead>
<tr>
<th></th>
<th>LV Work [%]</th>
<th>Cardiac Output [%]</th>
<th>dPdt max [%]</th>
<th>O2 cons. [%]</th>
<th>Coronary Flow [mL/min]</th>
<th>LDH release [U/min•10^3•g wet•1]</th>
<th>Cyt c release [ng/min•10^3•g wet•1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>44±7</td>
<td>5±8</td>
<td>57±10</td>
<td>41±15</td>
<td>13±3</td>
<td>396±276</td>
<td>45±20</td>
</tr>
<tr>
<td>MH</td>
<td>62±7*</td>
<td>20±18</td>
<td>74±12*</td>
<td>55±13</td>
<td>14±2</td>
<td>112±128*</td>
<td>31±23</td>
</tr>
<tr>
<td>MPC</td>
<td>65±8*</td>
<td>27±19*</td>
<td>74±7*</td>
<td>61±14*</td>
<td>17±3*</td>
<td>303±357</td>
<td>44±17</td>
</tr>
<tr>
<td>HY</td>
<td>61±11*</td>
<td>8±16</td>
<td>85±20*</td>
<td>50±12</td>
<td>16±3</td>
<td>265±318</td>
<td>28±10</td>
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<tr>
<td>Low pH</td>
<td>45±13</td>
<td>12±11</td>
<td>60±14</td>
<td>44±10</td>
<td>15±3</td>
<td>449±628</td>
<td>38±18</td>
</tr>
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</table>

All parameters are reported as 60 min reperfusion. Values are expressed as percentage recovery of baseline, except for coronary flow, cytochrome c (Cyt c) and lactate dehydrogenase (LDH) release, expressed as the absolute value at 10 min reperfusion.

*p<0.05 vs control; left ventricular (LV) work (developed pressure•heart rate) / dPdt max (maximum contraction rate) / O2 cons (O2 consumption)

Conclusion: Mechanical postconditioning, mild hypothermia and hypoxia, but not low pH, appear to improve hemodynamic recovery when applied immediately at reperfusion. Reduced necrosis (MH), increased oxidative metabolism (MPC) and decreased mitochondrial damage (HY) may contribute to improved functional recovery. In DCD heart transplantation, strategies applied at graft procurement could improve overall recovery of ischemic grafts by limiting/preventing additional reperfusion injury; optimal reperfusion strategies remain however to be further identified.

Disclosure of Interest: None Declared
1. Cardiovascular biology (Including all abstracts with in vitro or in vivo investigations)

Enalapril, eplerenone or their combination: finding the best paradigm to protect against doxorubicin-induced cardiotoxicity

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Introduction: Anticancer therapy with Doxorubicin (Dox) is complicated by the generation of reactive oxygen species (ROS) in cardiomyocytes, causing early and late cardiac dysfunction. Dox treatment is associated with activation of the renin-angiotensin-aldosterone system which may further increase ROS load and fibrosis upon activation of the mineralocorticoid receptor (MR) by aldosterone. Using mice, we assessed the ability of MR blockade, ACE inhibition or their combination to protect against Dox-induced cardiotoxicity (DIC).

Methods: Acute and chronic DIC were induced in wild type (WT) mice by a single injection of Dox (15 mg/kg) or five weekly injections of Dox (4 mg/kg), respectively. MR blockade was achieved in WT mice with an Eplerenone-enriched diet and in transgenic mice with cardiac-specific deletion of the MR gene. ACE inhibition was provided by adding Enalapril in drinking water. Left ventricular (LV) systolic function was assessed using 2D echocardiography and magnetic resonance imaging and diastolic function by Doppler imaging. Changes in levels of proteins production were assessed by western blot. Plasma aldosterone levels were measured by LC-MS and radio-immunoassay.

Results: Acute and chronic models of DIC triggered cardiac atrophy associated with reduced cardiomyocyte cell size and decreased activation of mTOR. DIC was further characterized in both models by cardiac diastolic and systolic dysfunction, as shown by decreased mitral inflow velocities and decreased cardiac output, respectively. MR blockade with Eplerenone was not sufficient to prevent cardiac dysfunction. It drastically increased plasma aldosterone levels and was associated with an increased production of CTGF and of angiotensin II (AgII) receptor type I, suggesting that interplay between aldosterone and AgII signaling diverts the effect of MR blockade. Enalapril treatment, however, decreased the severity of both diastolic and systolic dysfunction in the chronic model of DIC. Combination of Enalapril and Eplerenone similarly protected Dox-treated animals which, however, featured intermediate levels of plasma aldosterone and of cardiac CTGF, between those of mice treated with Eplerenone or Enalapril alone.

Conclusion: Our data show that blocking MR with Eplerenone does not prevent DIC in mice. However, blocking AgII production with Enalapril limits the severity of cardiac dysfunction in a clinically relevant model of chronic DIC. Our results suggest that treatment with Enalapril in human may protect against DIC.

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Neuregulin1β promotes glucose uptake via PI3K/Akt in neonatal rat cardiomyocytes
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Introduction: Nrg1β is critically involved in cardiac development and also maintains function of the adult heart. Studies conducted in animal models showed that it improves cardiac performance under a range of pathological conditions, which led to its introduction in clinical trials to treat heart failure. Recent work also implicated Nrg1β in the regenerative potential of neonatal and adult hearts. The molecular mechanisms whereby Nrg1β acts in cardiac cells are still poorly understood. In the present study we analyzed if and how Nrg1β activates mTOR and Akt and tested whether these pathways regulate glucose uptake.

Methods: Neonatal rat ventricular myocytes were pretreated with inhibitors for 30 min, stimulated with Nrg1β, IGF-I or insulin for 30 min, followed by 3H-deoxyglucose for 30 min. Glucose uptake was measured after extraction of the cells and the counts per minute were normalized for cellular protein. Additional samples were extracted after hormone treatment for analysis of signaling pathways by Western blotting.

Results: We show that Nrg1β activates mTORC1, mTORC2 and Akt. Nrg1β enhances glucose uptake as efficiently as IGF-I and insulin and all three factors act via PI3K-Akt. Although Nrg1β activates mTORC2 and thereby causes Akt-S473 phosphorylation, this effect seems not important for the glucose uptake. For Nrg1β, activation of PI3K-Akt is associated with phosphorylation of focal adhesion kinase (FAK) at Y861. Knockdown experiments with siRNA indicate that ErbB2/ErbB4 heterodimers mediate Akt activation and glucose uptake in response to Nrg1β. Src inhibition with PP2 or Dasatinib decreases Nrg1β-induced phosphorylation of FAK, Akt and AS160 as well as the glucose uptake, which suggests that Src-family kinases are implicated.

Conclusion: These novel insights into pathways by which Nrg1β regulates cardiomyocyte glucose uptake contributes to the understanding of its protective function in heart failure.

Disclosure of Interest: None Declared
A model of platelets in the aging: increased platelet counts and activation are associated with reduced clearance

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Introduction: Aging is associated with multiple vascular risk factors. The global percentage of >60 y olds will rise to >20% in 2050. Platelets hold a central role in the development of (adverse) cardiovascular events, the prothrombotic phenotype of aging, primary hemostasis and inflammation. A model that distinguishes between age and associated diseases is desirable. We therefore evaluated the role of platelets in a mouse model of aging.

Methods: We investigated
a) The age-dependent changes of platelet function
b) The degree and mechanisms of platelet-clearance involved

We analyzed old (aged >20 months) C57BL/6 mice compared to their young (12 w) littermates. Blood was collected terminally and total blood cell count was performed (EDTA). Reticulated platelets were determined using thiazole orange staining and analyzed by FACS. For platelet activation studies, washed platelets were obtained from citrate-anticoagulated blood, activated with thrombin or collagen and incubated with specific antibodies against P-selectin, activated integrin αIIbβ3 and GPIb. Samples were analyzed by FACS. Soluble glycocalcin and circulating GPVI were determined by ELISA.

Results: Our preliminary data indicate significantly increased platelet counts in old vs. young mice (1719 vs. 791 x 10³/μl, fig 1), while reticulated platelets were decreased in old mice (4 vs. 11%, fig 2), indicating a lower clearance. The flowcytometric data show a greater reactivity to stimulation with thrombin in old mice with higher expression of GPIIb/IIIa (mean fold-increase 139 vs. 52) and P-selectin (mean fold-increase 18 vs. 7), and a greater number of GPIb on the surface, whereas GPVI appeared lower, indicating increased cleavage, as reflected by corresponding concentrations of glycocalcin and soluble GPVI. Basal expressions of GPIIb/IIIa and P-selectin tended to be insignificantly lower in old mice.

Picture/Graph:
Conclusion: Our model of aging indicates increased platelet counts via a mechanism of reduced clearance despite of an increased reactivity to stimulation and a similar baseline expression of typical receptors. This constellation calls for further analysis of platelet clearance in aging, especially the activity of the Ashwell-Morell receptor which mediates the hepatic elimination after loss of sialic acid from the platelet surface (mainly GPIb); the Fc-receptor mediated clearance by the spleen; platelet senescence due to an imbalance of pro- and anti-apoptotic proteins (Bak/Bax & Bcl) and the newly described endothelial engulfment of platelets.

Disclosure of Interest: None Declared
Introduction: The existence of an increased platelet aggregability in the first part of the morning is well demonstrated but whether this has an impact on antiplatelet therapy is unknown. Therefore, the aim of the study was to observe if platelets aggregability with ticagrelor follows a circadian rhythm.

Methods: 25 healthy volunteers (11 female; 14 male) were included in the study. Physical activity, food intake and sleep were standardized. Blood samples were collected every 4 hours from an antebrachial venous catheter and were mixed in vitro with ticagrelor using half maximal inhibitory concentration of in vitro ticagrelor previously determined. Platelets aggregability test was then performed using VerifyNow System Platelet Reactivity Test®. Diurnal changes in platelets total count, percentage of platelets inhibition, von Willebrand antigen concentrations as well as volunteers’ physiological parameters were analyzed by fitting individual data to a sine curve with a 24-h period. A circadian rhythm was deemed to be present if the amplitude of the fitted curve was significantly different from 0 (Wald test).

Results: Volunteers physiological parameters (heart frequency [bpm], blood pressure [mmHg] and body temperature [Celsius] followed a significant circadian pattern [amplitude (p-value)] of 6 bpm (<0.001), 5 mmHg/7 mmHg (<0.002) and 0.3° (<0.001) respectively (Figure 1). Platelets inhibition with ticagrelor was significantly lower at 8AM (38.4%) as compared to any other time (45.2%) (p=0.018). Percentage of inhibition plotted against time followed a circadian pattern (p<0.001) with minimal values observed between 8AM and 12AM (Figure 2a). Similarly, von Willebrand antigen concentrations followed a circadian pattern (p<0.001) with an amplitude of 12.24 U/dL (Figure 2b). Its concentration was maximal between 8AM and 12AM. These differences were not explained by total platelets count (minimal value in the morning (Figure 2c)).

Conclusion: Platelets inhibition with ticagrelor follows a circadian rhythm with lower values observed between 8AM and 12AM.

Disclosure of Interest: None Declared
Cardiac-specific overexpression of junD leads to an enlarged infarcts in ischemia/reperfusion model in mouse
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Introduction: Myocardial injury during short-term ischemia and reperfusion has become clinically important with the use of primary percutaneous coronary angioplasty (PCI) as a first-line strategy in patients with acute coronary syndrome (ACS). The Jun family of activator protein 1 (AP-1) transcription factors (c-Jun, JunB, JunD) is involved in fundamental biological processes such as proliferation, apoptosis, tumor angiogenesis, and hypertrophy. The AP-1 member junD is specifically expressed in the developing heart and cardiovascular system. Current evidence suggests a complex role for junD in different processes in the adult heart. However, there is little direct and in vivo evidence about how exactly junD acts in the myocardium. In the present study we analyzed the specific role of junD in the mouse heart using transgenic mouse line with cardiac-specific overexpression of junD subjected to ischemia/reperfusion.

Methods: 8-12-week-old male mice selectively overexpressing junD in the myocardium (cJunDTG) and corresponding C57Bl/6 wild-type (WT) control mice were subjected in vivo to 30 min of ischemia (I) followed by 24h of reperfusion (R).

Results: After 30 min of ischemia, cJunDTG mice developed markedly larger infarcts as compared to WT (Fig. 1A and 1B). This was further associated with increased post-ischemic levels of serum cardiac troponin I (Fig. 1C). However, the observed effect on infarct size was not due to initial impaired contractility of transgenic heart since there was no difference in both left ventricular end systolic (LVESD) and end diastolic (LVEDD) diameters and thus ejection fraction was similar in both groups as assessed by MRI at basal level in both cJunDTG and WT mice. In addition, capillary density observed in transgenic hearts after I/R was significantly decreased compared to WT hearts as has been assessed by CD31 and smooth muscle actin staining on heart cross sections.
Conclusion: Thus, *junD* seems to promote the increased sensitivity to myocardial infarction when expressed at unphysiological levels. Such *junD*-associated cardiac phenotype seems likely to be driven by the impaired angiogenesis. It is also well possible that such phenotype could be due to the impaired function of apoptosis-related (p53) or prosurival (RISK and SAFE) pathways. Therefore, *junD* might represent a potential therapeutic target to protect human heart from myocardial infarct in future.

Disclosure of Interest: None Declared
Introduction: The advantage of a septal right ventricular (RV) lead position compared to an apical position is still controversial. Cardiac magnetic resonance imaging (CMR) has several advantages over echo to assess markers of left ventricular (LV) performance, especially better endocardial border detection and tracking. We studied the acute effect of a septal compared to an apical lead position on LV strain and torsion.

Methods: All patients had a dual chamber Accent MRI™ (St Jude Medical) pacemaker (PM) implanted. Patients were scanned with the PM switched on, immediately after they had a second scan with the PM switched off. Dedicated imaging analysis software was used to analyze LV strain and torsion from the CMR images (2D CPA analysis, TomTec).

Results: 10 patients were included in the study (mean age 71.9 ± 9 yrs; 50% female). 5 patients had a septal lead position (verified by chest x-ray in 2 planes) and 5 patients an apical RV lead position. When the PM was switched on, LV longitudinal strain decreased significantly with apical pacing (-8.2%; P=0.04) but not with septal pacing (-0.7%; p=NS). Radial and circumferential strain was not affected significantly by either lead position. LV torsion decreased from 6.6 degree to 4.1 degree in the apical group and from 8.4 degree to 8.2 degree in the septal group when the PM was on, which was not significant in both groups. Interestingly, apical pacing abolished predominantly the basal clockwise rotation compared to a septal lead position (-5.7 degree in the septal group compared to + 2.4 degree in the apical group; p=0.04). Additionally, LVEF and RVEF both decreased significantly with RV apical pacing (LVEF -8.7%; p=0.04, RVEF -8.7%; p=0.04) but not with septal pacing (LVEF -2.9%; p=NS, RVEF +0.9% p=NS).

Conclusion: Using CMR imaging with the PM on versus off, we demonstrated a decrease of LV longitudinal strain with apical pacing. LV torsion is also affected by apical pacing, especially the basal clockwise rotation. Additionally, there is a significant decrease in LVEF and RVEF with apical pacing when the PM was switched on. Most of these negative effects of RV apical pacing can be avoided with a septal lead position.

Disclosure of Interest: None Declared
Introduction: Sex hormones have been reported to play a role in the pathophysiology of ventricular arrhythmias. Male patients with ARVC/D develop more severe symptoms than females at similar ages. We hypothesized that serum levels of sex hormones might contribute to major adverse cardiovascular events in patients with ARVC/D.

Methods: Serum levels of testosterone, dehydroepiandrosterone, sex hormone binding globulin (SHBG), androstenedione, estradiol (E2), and progesterone as well as a routine panel of biochemical markers were measured in 50 patients from the Swiss ARVC/D registry. Sex hormone levels were correlated with major adverse cardiovascular events (MACE), defined as the occurrence of cardiac death, heart transplantation, survived sudden cardiac death, ventricular fibrillation, sustained ventricular tachycardia or arrhythmogenic syncope. We further used an established human ARVC/D induced pluripotent stem cell-derived cardiomyocyte (iPSC-CM)-based model to demonstrate the effects of testosterone and E2 on cardiomyocytes.

Results: Twenty-six patients (52%) experienced MACE prior to determination of sex hormone levels. In male patients with MACE, testosterone levels and SHBG levels were significantly increased, whereas dehydroepiandrosterone levels were decreased. In females, E2 levels were lower in patients with MACE. In males, increased testosterone levels remained significantly associated with MACE after adjusting for age, BMI, dehydroepiandrosterone and SHBG. In males, a cut-off value for total serum testosterone of >13.5 nmol/l was associated with MACE with a sensitivity of 84% and a specificity of 76%. In our ARVC/D iPSC-CM based model, normal premenopausal E2 levels decreased ARVC/D pathologies, yet high testosterone levels worsened ARVD cardiomyocyte apoptosis and lipogenesis in culture.

Conclusion: Our study shows for the first time that elevated testosterone and/or decreased E2 serum levels are associated with clinical MACE and might permit disease progression in patients with ARVC/D. Thus, determining the levels of these two sex hormones might be useful for risk stratification of patients with this disease.

Disclosure of Interest: None Declared
Introduction: The subcutaneous implantable cardioverter defibrillator (S-ICD) does not require a vascular access for the defibrillation electrode. Some intra, peri, and post-procedural risks are therefore significantly reduced. Mid-term safety and efficacy was evaluated.

Methods: All patients (pts) treated with S-ICD at our Center were included. Safety was evaluated considering the incidence of peri-procedural implantation complications and the rate of inappropriate shocks during follow-up. Efficacy was evaluated considering defibrillation test (DT) success and successful therapies during follow-up.

Results: From September 2014 to December 2015, 12 patients (pts) were implanted with S-ICD (54±12 years, 7 pts with ischemic heart disease, LVEF 38±17%); secondary prevention for sudden cardiac death was the main ICD indication (7 pts). DT was effective in each case with a single shock and a mean energy delivered of 60 Joules. During an observation period of 7 months (IQR 4.0-8.8) no complications linked to the implantation procedure occurred. One patient presented an appropriate shock that effectively terminated a sustained fast ventricular tachycardia, while another patient, with unknown intermittent RBBB, experienced repeated inappropriate shocks due to dynamic changes of the QRS/T wave complex ratio, hence resulting in double-counting during sinus rhythm.

Conclusion: S-ICD showed a good safety and efficacy profile in correctly selected patients. It is imperative to exclude, through provocative testing (stress test, ajmalin or isoproterenol infusion), dynamic changes of the QRS/T wave complex ratio that may trigger inappropriate interventions.

Introduction: We hypothesized that organization indices based on the analysis of atrial ECG harmonic components may help identify patients (pts) with persistent AF (pAF) unresponsive to pulmonary vein isolation (PVI) and left atrial (LA) ablation. Using adaptive harmonic frequency tracking schemes, we computed on the atrial ECG: 1) the variance of the phase difference (aPD) between the dominant frequency (DF) and the 1st harmonic (H1), and 2) the organization index (AOI) defined as the ratio of the power of the DF and H1 over the total power of the unprocessed atrial signal as measures of AF regularity.

Methods: In 34 consecutive pts (61±7 y, pAF duration: 19±11 m), PVI and LA ablation were performed until AF termination. 40-sec ECG time series devoid of QRST were recorded at baseline (BL), after PVI (end_PVI) and at the end of LA ablation (end_ABL). APD and AOI were estimated on leads V1 and V6b (placed on the pts back).

Results: pAF was terminated within the LA in 68% (23/34 LT - left terminated) of the pts, while 32% (11/34 NLT - not left terminated) did not. The figure shows that: 1) LT pts displayed higher AOI values at BL indicative of greater atrial ECG organization that increased significantly (p<0.05 for V1 and V6b) during LA ablation as opposed to NLT pts, and 2) NLT pts displayed higher APD values at BL indicative of greater atrial ECG disorganization that decreased during LA ablation, but did not reach LT pts values.

Conclusion: Estimation of the level of organization of atrial ECG based on adaptive harmonic schemes appears as promising tools for the measure of pAF complexity and prediction of procedural outcome.

Disclosure of Interest: None Declared
Introduction: Permanent pacemaker (PPM) implantation after isolated aortic valve replacement (AVR) is reported to be 3–8.5%. Incidence may be lower in standard AVR, excluding complex surgery. The implantation, i.e. suture technique may have an impact on postoperative PPM implantation.

Methods: AVR with a standard surgical suture approach have been reviewed. Thirty days PPM implantation for rhythmic disorders was analyzed, with focus on indications for AVR, pre-existing conduction disorders and surgical technique.

Results: 995 AVR, operated from 2007 to 2015, have been reviewed. Overall PPM incidence was 2.9% (29 patients). Indications for AVR were degenerative in 18, infectious endocarditis of the native valve in three, endocarditis of a previous implanted prosthesis in three and re-operation for prosthetic degeneration (other than infectious) in five patients. 35% of the PPM implantation occurred after complex surgical procedures: active endocarditis with para-valvular abscess, endocarditis of previous implanted prosthesis and complex (more than first) re-operation for prosthesis degeneration. The remaining 65% had PPM implantation after simple AVR (18 patients) or at first redo surgery (one patient), corresponding to an incidence 1.9% after standard AVR. Pre-existing rhythmic disorders have been observed in 17% of the group requiring PPM versus 6% in the control group (p<0.02). Septal myectomy was not associated to PPM implantation (17% versus 12.8%; p=0.5). Suture techniques had, with 1.4% PPM implantation in continuous sutured valves (12/852) versus 5% in interrupted mattress sutured valves (7/143; p<0.005) an impact on outcome.

Conclusion: PPM implantation rate of 2.9% is in the lower range compared to reported incidences. In this large patients’ cohort, complex surgical AVR have been included and the incidence for PPM after simple AVR was almost lower (2%). The majority of the prostheses were implanted using continuous suturing techniques (85%) avoiding mattress sutures and the incidence in this group was, with 1.4% considerably lower than in literature. PPM after standard AVR is rare and results should be confronted with rhythmic disorders after TAVI procedures, with observed PPM implantation rates from 8 (Sapien®, Edwards Life-sciences) to up to 30% (Core Valve®, Medtronic). This should be kept in mind balancing cost effectiveness of treatment strategies.

Disclosure of Interest: None Declared
Introduction: Catheter ablation is an established therapy for the treatment of symptomatic atrial fibrillation (AF). Current guidelines recommend catheter ablation for drug-refractory paroxysmal AF (PAF) in adults, and as first-line therapy in selected patients. However, long-term data on the efficacy and safety of catheter ablation for PAF in young adults is very limited.

Methods: From 2005 to 2014, 52 consecutive young adults (32 men, 20 women) with symptomatic PAF underwent pulmonary vein isolation (PVI). The procedure end point was complete PVI (entrance block) verified by circular catheters placed within the PVs. Follow-up was based on regular outpatient clinic visits including 24h Holter-ECGs and telephone interviews at last follow-up. Recurrence was defined as any symptomatic and/or documented atrial tachyarrhythmia episode [30 s following a 3-month blanking period].

Results: Mean patient age at the time of the index procedure was 30±4 years (range 19-35). Complete PVI by either radiofrequency current guided by 3-dimensional mapping (n=50) or cryoballoon (n=2) was achieved in 51/52 patients (98%). Six patients were lost to follow-up. During a mean follow-up period of 4.9 years (range 1.0-9.7 years) stable sinus rhythm was achieved in 65% after a single procedure, and in 83% after multiple procedures (mean 1.5; range 1-3). Success rate at last follow-up off anti-arrhythmic drugs was 74%. Eight patients (17%; 3 with stable sinus rhythm) were taking antiarrhythmic drugs (AAD; only class I) at last follow-up compared to 26 patients (57%, p<0.01) before the index procedure. A second procedure was performed in 19, and a third procedure in 2 patients. PV reconduction was observed in 16 patients (84%) during the second, and in 1 patient (50%) during the third procedure. EHRA score significantly improved at last follow-up (mean 3.2 to 1.2, p<0.001). Major periprocedural complications occurred in 3 patients (tamponade in 1, PV stenosis in 2). No patient progressed towards persistent AF.

Conclusion: In the majority of very young adults ≤35 years of age, catheter ablation for PAF is effective during long-term follow-up and associated with a low complication rate. These findings support the concept of PVI in very young adults with symptomatic PAF.

Disclosure of Interest: None Declared
Epicardial fibrosis enhances endo-epicardial dissociation and breakthrough in an atrial computer model

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Introduction: Recent work has shown that the transition from persistent to permanent AF in goats coincides with an increase in fibrosis in the outer millimeter of the atrial wall. Macroscopically this leads to reduced electrical conductivity orthogonal to the dominant fiber orientation. A causal relation has not been established yet. Our purpose was to test if subepicardial fibrosis can explain the increased incidence of epicardial breakthroughs, which is also observed in permanent AF.

Methods: We constructed a detailed geometry of the human atria including all major bundle structures and two layers of fiber orientation. Computer simulations were run with a mesh of 0.2 mm resolution and an ionic current formulation specific for the human atrial myocyte. Subepicardial fibrosis was modeled by assigning zero transverse conductivity to a random selection of model elements. Simulations were performed with 0, 50, and 70\% affected elements. Fibrillation was induced with incremental rapid pacing. Simulations were repeated with 10 different pacing locations, for a total of 30 simulations of 5 seconds each. We tested in the first place whether AF was induced by this protocol. In those simulations where fibrillation occurred, we computed the number of waves, number of phase singularities, percentage dyssynchrony, and number of breakthroughs in the 3 seconds after pacing.

Results: An increased percentage of fibrotic tissue markedly increased AF susceptibility, conduction pattern complexity, and increase in epicardial breakthrough occurrence. Detailed results are given in the figure.

Conclusion: Subepicardial fibrosis can account for an increased susceptibility for AF as well as for the remarkable increase in epicardial breakthrough observed in experimental studies.

Disclosure of Interest: None Declared
Introduction: To better appreciate the role of the novel oral anticoagulants (NOACs) for real-life patients with non-valvular atrial fibrillation (AF) knowledge of the quality of the traditional coumarin-based oral anticoagulation (cOAC) in daily practice is important. We aimed to assess the percentage of INR values within the therapeutic range of 2.0-3.0 and to assess predictors of high (≥80%) and low (≤50%) percentage of INR values within this range in unselected patients with AF treated with cOAC.

Methods: In a cross-sectional study, clinically stable patients either seen as outpatients or electively admitted as inpatients with cOAC treatment for non-valvular AF for at least six months, documentation of INR values over a period of at least three months with at least two INR values were included.

Results: We studied 332 patients (62% male, mean age 74±9 years). The median (interquartile range) CHA2DS2-Vasc and HAS-BLED scores were 4 (3-5) and 3 (2-4) points. The median number of INR values per patient was 8 (5-14) during an observation period of 158 (103-246) days with a median average interval between INR measurements of 20 (13-27) days. The median percentage of INR values between 2.0 and 3.0 was 67 (50-83)%; 105 (32%) patients had ≥80% INR values in this range, and 82 (25%) patients had <50% of values in this range. Independent predictors of ≥80% INR values between 2.0 and 3.0 included a longer interval between INR measurements [odds ratio (OR) 5.94 (95% confidence interval [CI] 3.34-10.56) per ln-transformed unit for day; p<0.001] and the non-use of Spironolactone [OR 0.43 (95%CI 0.20-0.92); p=0.03]. The only independent predictor of <50% of values in the therapeutic range was a shorter interval between INR measurements [OR (95%CI 0.28 (0.18-0.44); p<0.001]. The use of Amiodarone was a predictor of <50% of values in the therapeutic range in the univariable but not in the multivariable analysis (p=0.08). Other patient characteristics were not independently related to a high or low percentage of INR values in the therapeutic range.

Conclusion: The quality of cOAC in Switzerland is highly variable. There are little clinical predictors of this quality. The better quality of cOAC in patients with less frequent INR measurements is most likely explained that the fact that patients with better cOAC quality have less INR measurements rather than the opposite. The association between Spironolactone use and worse cOAC quality needs further investigation.

Disclosure of Interest: None Declared
Introduction: Pulmonary vein isolation (PVI) is an important treatment option for symptomatic atrial fibrillation (AF). A new remote catheter system (RCS), which allows remote robotic manipulation of standard electrophysiology catheters, has recently become available to perform this intervention. Robotic ablation can significantly reduce operator fluoroscopy exposure. Furthermore, enhanced tissue contact and catheter stability may improve outcomes of PVI with RCS. The aim of this study was to assess safety and success rates of electroanatomic mapping and PVI using a RCS compared with manual catheter ablation.

Methods: 143 patients (mean age 62 +/- 10 years, 67% male) with paroxysmal (n=98) or persistent (n=45) AF were included in a prospective cohort study. Wide-area circumferential PVI was performed by RCS in 53 pts. and in 90 pts. using a standard manual approach (MA). Procedural end-point was demonstration of entry- and exit block using a circular mapping catheter. Procedural success, adverse events, and follow-up after 3 months, including 48 hour Holter ECG recordings, were compared between the two groups.

Results: Complete PVI was achieved in all patients in both groups. Success rates at three months tended to be higher with RCS among patients with paroxysmal AF (RCS 76% vs. MA 56%, P=0.05) whereas among patients with persistent AF, success rates were similar in both groups (RCS 50% vs. SA 55%, p=0.7). Procedure time (minutes; median (IQR)) was not significantly longer with RCS among patients with paroxysmal AF (RCS 200 (85) vs. SA 180 (65); P=0.113), and similar in both groups among patients with persistent AF (RCS 193 (80) vs. SA 210 (79); P=1.0). Periprocedural complications were similar in both groups (groin hematoma, RCS 5.7% vs. SA 4.4%; AV fistula, RCS 1.9% vs. SA 1.1%. P=0.7). No other adverse events occurred during the procedure and follow-up period. Fluoroscopy time (minutes; median (IQR)) was similar in both groups (RCS 16 (6) vs. SA 12 (4); P=1.0), whereas operator fluoroscopy exposure tended to be lower in the RCS group (8 (16) vs. 12 (24) minutes P=0.7).

Conclusion: Three-dimensional electro-anatomic mapping and PVI using remote catheter navigation with standard electrophysiology catheters was safe in patients with paroxysmal and persistent AF. Procedural success defined as complete pulmonary vein isolation was similarly high using RCS and a standard manual approach. In patients with paroxysmal AF, PVI with the RCS was associated with higher success rates at 3 months follow-up.

Disclosure of Interest: None Declared
Introduction: Subcutaneous implantable cardioverter-defibrillator (S-ICD) can avoid important complications associated with transvenous leads. This is particularly interesting for patients with Brugada syndrome (BrS) who do not need pacing therapy. Due to the dynamicity of the diagnostic Brugada type 1 ECG, S-ICD sensing evaluation is crucial to avoid inappropriate shocks. Aim of this study was to analyze whether patients with drug-induced BrS are suitable for an S-ICD.

Methods: Consecutive patients with suspected BrS and non-diagnostic baseline ECG were screened as potential candidate to S-ICD. Analysis of QRS complex and T wave morphology was performed in both standing and supine position at baseline and during ajmaline challenge. Ajmaline was administrated at a dosage of 1 mg/kg over 5 minutes. Morphology analysis was defined appropriate when ≥1 sense vector was acceptable in both supine and standing position. Results: A total of 21 patients (mean age: 48±6 years; 15 males) underwent ajmaline challenge. Four patients (19%) were tested because of previous syncope or ventricular fibrillation. At baseline 18 (86%) patients had a normal ECG, 2 (9%) had a type 3 Brugada ECG and 1 (5%) had a type 2 Brugada ECG. All patients had appropriate morphology analysis at baseline. Ajmaline challenge unmasked type 1 ECG in 6 patients (28%). In 2 patients (33%), morphology analysis was inappropriate after appearance of Brugada type 1 ECG. In both patients, the reason for inappropriateness was the more pronounced T-wave during Brugada type 1 ECG.

Conclusion: S-ICD sensing can change in 33% of patients with BrS and non-diagnostic baseline ECG. Morphology analysis during ajmaline challenge is an important tool in this setting to evaluate sensing appropriateness and avoid inappropriate shocks.

Disclosure of Interest: None Declared
Introduction: In patients undergoing epicardial catheter ablation (CA) for ventricular tachycardia (VT), the current consensus guidelines advocate that pericardial access is avoided in anticoagulated patients and should be performed prior to systemic heparinisation. Recent studies have shown that pericardial access may be safe in heparinised patients. However, no data exists for patients on oral anticoagulants.

Methods: This was a retrospective study of consecutive patients undergoing catheter ablation for VT in whom epicardial access was attempted. All patients were heparinized with a target activated clotting time (ACT) of 300-350 seconds. Patients who had procedures performed on continuous warfarin (in addition to heparin) were compared to those not taking an oral anticoagulant. Clinical data, procedural data and complications occurring up to 3 months were analyzed from a prospective registry with additional review of notes and electronic health records.

Results: 46 patients were included of which 13 were on warfarin during the procedure. There was no significant difference in clinical and procedural characteristics (except INR) between the two groups. No patients had a history of prior cardiac surgery. Pericardial access was achieved in all patients. Acute ablation success was similar in the two groups with an identifiable epicardial target (although non-inducibility was not sought in all patients). A small proportion of patients required a repeat procedure after 3 months follow-up (8.3% warfarin vs 22.6% no-warfarin group). There were no deaths and no patients required surgery. There was a trend towards a higher proportion of patients in the warfarin group who had a drop in haemoglobin of >2g/dL compared to the no-warfarin group (38.5% versus 27.3%; p = 0.74), and a trend towards more delayed pericardial drain removal (defined as > 24 hours post procedure end) due to ongoing drainage [3% vs 7.8%, p = 0.53]. However, there was no difference in the overall procedure complications including bleeding, RV puncture, coronary damage and delayed drain removal.

Conclusion: Pericardial access can be achieved safely and effectively in patients anticoagulated with warfarin and heparinized with a therapeutic ACT. This may be an attractive option for a cohort with a high stroke risk. Further larger studies will be required to confirm these findings and to investigate the safety of the newer oral anticoagulants in this setting.

Disclosure of Interest: None Declared
Introduction: The SGK congress is the most important national platform for young and established Swiss researchers where they present their work to a broad scientific public. An increasing number of abstracts are submitted every year and eminent reviewers rate them to the best of their knowledge. Accepted abstracts and talks or posters presented at the congress are praiseworthy, but more important is their publication in important international journals. Aim of this study was to determine publication rates and impact factors (IF) and analyse the temporal trend in the field of electrophysiology.

Methods: In November 2015 we downloaded the abstract books (available as PDF under http://www.cardiovascular-medicine.ch) and extracted all talks and posters presented during the SGK congresses 2011 to 2014. We assessed in PubMed whether a paper has been published and, when yes, in which journal with which IF (always determined in the respective publication year). We excluded case reports, papers published more than at least 6 months before the congress and all abstracts presenting national data from a multicentre study (unless the first author of the published paper was from Switzerland). The percentage of published papers and their mean and median IF was calculated overall and per year.

Results: Rates ranged from 29% to 50% and mean IF from 2.8 to 5.4. Table 1 shows the rate of published papers and IFs across the four years in more detail.

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Conclusion: Abstracts in the field of electrophysiology presented during the SGK congresses have a high likelihood of being published, usually in papers with a good IF. This indicates the good quality of cardiology research in Switzerland.

Disclosure of Interest: None Declared
PP-025
2. Pacemaker, defibrillator and electrophysiology
First-degree av block is mainly due to intraatrial conduction delay in patients with atrial fibrillation, right atrial flutter and supraventricular tachycardia
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Introduction: AV block I (PR interval >200ms) may be due to AV nodal/His-Purkinje system conduction delay or intra-atrial conduction delay. The purpose of this study was to identify the site of conduction delay by standard electrophysiologic measurements.

Methods: 465 consecutive patients (age 58±15 years, 35% female) referred for ablation were included in the study (225pts (49%) with atrial fibrillation (AF), 81 pts (17%) with right atrial flutter (AFlu), and 159 pts (34%) with paroxysmal supraventricular tachycardia (PSVT)). P wave duration, PR interval, atrium-His (AH) intervals and His-ventricular (HV) intervals were measured in sinus rhythm. Right intra-atrial conduction (RIAC) was defined as the interval from the beginning of the P wave on the 12 lead ECG to the onset of the atrial electrogram on the His catheter.

Results: AV block I of any cause was present in 64 patients with AF (28%), in 34 patients (42%) with AFlu and in 12 patients (8%) with PSVT. RIAC, P-waves and PR intervals were significantly longer in AF and AFlu pts compared to SVT pts with the greatest values measured in the AFlu group (table 1). Analyzing the number of patients with AV block I but normal (not prolonged) AH and HV showed an RIAC delay (“Pseudo 1st degree AV block”) only in 36 of 64 patients (53%) in the AF group and in 10 of 34 patients (30%) in the AFlu group. If present in SVT, AV Block I is mainly due to RIAC delay (5 of 12 pts).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SVT (n=159)</th>
<th>AFlu (n=81)</th>
<th>AF (n=225)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR prolongation [n (%)]</td>
<td>12 (8)</td>
<td>34 (42)</td>
<td>64 (28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PR interval [ms]</td>
<td>156 (138-174)#, §</td>
<td>196 (168-232)#, *</td>
<td>178 (163-206)#, *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P-wave duration [ms]</td>
<td>104 (96-117)#, §</td>
<td>142 (123-155)#, *</td>
<td>124 (114-132)#, *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AH interval [ms]</td>
<td>80 (70-94)#</td>
<td>92 (77-114)#, *</td>
<td>82 (68-102)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HV interval [ms]</td>
<td>40 (38-46)#, §</td>
<td>48 (42-54)#</td>
<td>48 (42-52)#</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RIAC interval [ms]</td>
<td>33 (24-44)#, §</td>
<td>54 (43-66)#</td>
<td>50 (40-62)#</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SVT – supraventricual tachycardia, AFlu– right atrial flutter, AF – Atrial fibrillation, AH – atrium-His; HV - His-Ventricle; RIAC – right intra-atrial conduction. Median (interquartile range); § - p<0.01 between SVT and AF, # - p<0.01 between SVT and AFlu; *- p<0.01 between AF and AFlu.

Conclusion: In patients with AF and AFlu, PR prolongation is frequent and caused by RIAC delay (“Pseudo-1st degree AV-block”) and not conduction delay in the AV node/His-Purkinje system in half of the AF and in one third of the AFlu patients.

Disclosure of Interest: S. Knecht: None Declared, A. Mühl: None Declared, T. Reichlin: None Declared, N. Pavlovic: None Declared, U. Celikyurt: None Declared, B. Schaer: None Declared, S. Osswald Grant/ research support from: Medtronic, Boston Scientific, Biotronik, and St Jude Medical, Speakers bureau: Medtronic, Boston Scientific, Biotronik and St Jude Medical, C. Sticherling Grant/ research support from: Biosense Webster, Biotronik, Boston Scientific and Sorin, Speakers bureau: Medtronic, M. Kühne Grant/ research support from: Biosense Webster, Speakers bureau: Boston Scientific, St Jude Medical, and Biotronik, Paid Instructor for: Medtronic
Mobile application versus sms alert in out-of-hospital cardiac arrest: efficiency and impact on survival

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Introduction: Out-of-hospital cardiac arrest (OHCA) is an acute urgent medical condition that requires immediate care. First responders (FR) and bystander involvement in the resuscitation care is crucial to improve survival. Purpose of the study was to assess the efficiency and the prognostic impact of a new automatic alarm system for FR recruitment based on mobile application (APP), compared to short message service (SMS) system, in which the emergency medical system (EMS) dispatch center was directly involved in the management of FR.

Methods: EMS dispatched CPR, times of intervention (time to first BLS, time to EMS arrival, time to ROSC) and survival were measured in all OHCAs occurred in the year 2012, in which SMS system was used to alert FR and compared to the year 2014, in which mobile APP system became available.

Results: 145 and 137 cardiac OHCA occurred in 2012 and in 2014, respectively. No differences were observed in mean age, gender and location of OHCA. 61% of victims received a BLS before EMS arrival in 2012, versus 70% in 2014. 44 patients (26%) received a chest compression-only approach in 2012 and 50 (37%) in 2014. No differences were observed in times of intervention and in AED use between the 2 years. Overall survival increased from 15% in 2012 to 30% in 2014. Utstein survival increased from 36% to 55%.

Conclusion: Mobile APP alert system is highly efficient in the FR management, leading to a significant impact on survival.

Introduction: The Medtronic MICRA transcatheter pacing system (TPS) is a new leadless single-chamber pacing system. Recently, results have been published proving the efficacy and safety of this device. We hereby present a patient with multiple complications during/after implantation of a MICRA TPS pacemaker system.

Methods: The 86-year old woman suffered from sick sinus syndrome and severe aortic stenosis. She received a transfemoral aortic valve implantation (23mm CoreValve Evolut R) and developed left bundle branch block after the procedure. Due to insufficient rate control of her atrial fibrillation with episodes of sinus bradycardia, a MICRA TPS was implanted. During the implantation she developed persistent complete heart block without ventricular escape rhythm due to the manipulation with the large bore delivery catheter. A temporary pacemaker wire was placed via the opposite groin immediately. After several repositioning maneuvers of the MICRA TPS, a satisfactory pacing threshold was obtained in an inferoapical position. Sensing was 6.5 mV (with right ventricular pacing over the temporary wire), threshold 0.88 V / 0.24 msec, and impedance 630 ohm. Two out of four tines were attached to the myocardium. At hospital discharge, pacing threshold was 1.25 V / 0.24 ms, impedance 560 ohm, and sensing not measurable due to lack of intrinsic rhythm >30/min. Correct device location was confirmed by chest x-ray.

Results: Two weeks later, the patient came back in cardiogenic shock due to bradycardia/asystole. The ambulance crew installed an external/transdermal pacemaker. The pacemaker interrogation revealed an increase of the pacing threshold to 2.13V/1.0ms, impedance increased to 830 ohm. Pacing threshold was not rate dependent nor was it dependent on the patient’s position. Device dislocation and myocardial perforation were ruled out by chest x-ray and transthoracic echocardiography. The output was set to 5V/1.0ms, autocapture was switched off. During telemetric monitoring recurrent capture failure was seen. We implanted a conventional dual chamber pacemaker system via the left subclavian approach. The patient recovered well and could be discharged several days later to a nursing home.

Conclusion: In patients with preexisting left bundle branch block the implantation of a MICRA TPS can lead to a persistent complete heart block. A late massive increase in pacing threshold without obvious pacemaker dislocation is a new complication occurring with this leadless pacemaker system.

Disclosure of Interest: None Declared
Introduction: Image integration defines the substrate for VT and can help to guide the safety and efficacy of VT ablation. Ablation of local abnormal potentials (LAVA) is a technique that can be performed during sinus rhythm and VT. High-density mapping is more sensitive to near field and demonstrates more LAVA activity and channels. We report our first clinical results using image-integrated LAVA-based VT ablation.

Methods: This is a single center prospective study at Klinik Im Park, Switzerland, using the MUSIC (MUltimodality platform for Specific Imaging in Cardiology) platform and the CARTO 3 system (Biosense Webster). High-density mapping with a multipolar catheter (PentaRay) and a LAVA-based ablation approach was used. Acute results and short-term follow-up were analyzed.

Results: In total, 7 patients (69±11yrs, 86% male; ICD, n=86%; post-myocarditis, n=1; ischaemic cardiomyopathy, n=6; endocardial, n=6 and epicardial n=1; use of extracorporeal membrane oxygenation, n=1) were included. Of them, 4 patients (57%) presented in emergency with VT storm. Mean procedure time was 199±54min. Mean RF time was 35±27min. Mean fluoroscopy time was 35±15min. A PentaRay catheter was used in 71%. LAVA were found and ablated in 89%. Good correlation between LAVA and scar on imaging was found (90% within scar and 100% within 1cm border around the scar). Clinical VT was ablated during VT inside an anatomical channel shown with imaging in 2pts. A septal VT was ablated from both sides of the septum in 1pt. The right bundle was ablated in 1pt with bundle branch reentry VT. Complete LAVA elimination was obtained in 57% and non-inducibility was obtained in 86% (inducible non-clinical VT). After a mean follow-up of 2±1months one patient (13%) had 1 non-clinical VT episode. No complications or mortality were observed.

Picture/Graph:
Conclusion: Routinely used image integrated VT ablation is feasible and demonstrates good short-term outcome without any complications in this small cohort. The efficacy and safety needs to be confirmed in multicenter trials.

Disclosure of Interest: None Declared
Introduction: In selected patients CRT is a mainstay of heart failure therapy and often a CRT-D is chosen. However, some patients have important comorbidities and carry the risk of dying early without ever being in need of the ICD. They would be candidates for a CRT-P and still experience benefit of CRT. Competing risk methodology (cumulative incidence function approach) is an established estimation for this. Aims of the study were to determine competing risks and to construct a mortality risk score in a large CRT-D cohort.

Methods: We used merged data from ICD registries conducted by 2 large tertiary care hospitals. CRT-Ds were implanted for primary or secondary prevention. No patient was excluded. Baseline parameters consisted of demographic data, heart disease, drug therapy and comorbidities. Primary endpoint was time from implantation to the 1st appropriate ICD therapy or death. We used Fine and Gray regression models of subdistribution hazard and R version 3.2.1 and its competing risk library cmprsk.

Results: 904 pts were studied. Median age was 65 yrs, median follow up 5.8 yrs. 30% died, 28 % had ICD therapies (ICD-T). 5/10 yr cumulative incidences of ICD-T and death were 29/40% and 16/25% respectively. Pts with comorbidities were at higher risk of prior death (e.g. impaired renal function: HR, 2.06; peripheral artery disease: HR, 2.57). Risk scores are shown in table 1. They allowed categorizing patients in 3 classes of predicted benefit. Patients e.g. in risk class 1 for prior death b in class 2 or 3 for ICD-T have a high predicted benefit from CRT-D. So, 25% of pts have a high, 50% an intermediate, and 25% a low predicted benefit from ICD therapy (figure 1). Low risk for appropriate ICD-T is a score of ≤0, for prior death ≤7, high risk for appropriate ICD-T ≥6, for prior death ≥10

<table>
<thead>
<tr>
<th>Any appropriate ICD therapy</th>
<th>Diuretic</th>
<th>5</th>
</tr>
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<tbody>
<tr>
<td>NYHA class 3 or 4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Age at implantation</td>
<td>-0.1 x Age</td>
<td></td>
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<tr>
<td>Secondary prevention</td>
<td>10</td>
<td></td>
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<tr>
<td>Prior VF</td>
<td>-3</td>
<td></td>
</tr>
<tr>
<td>Presence of diabetes</td>
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<td></td>
</tr>
<tr>
<td>Ischemic cardiopathy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Prior death</td>
<td>Age at implantation</td>
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</tr>
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<td>Systolic blood pressure &lt;=100</td>
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<tr>
<td>Renal failure</td>
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<tr>
<td>History of cancer</td>
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<td></td>
</tr>
<tr>
<td>History of peripheral artery disease</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>-2</td>
<td></td>
</tr>
<tr>
<td>BMI &gt;= 30</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion: This easy competing risk model predicts chances of appropriate ICD therapy and prior death in patients with CRT-D.

Disclosure of Interest: None Declared
Introduction: Leadless transcatheter pacing has emerged as a novel alternative to standard transvenous pacing in order to avoid a permanent transvenous lead and a pacemaker pocket. The aim of the current study was to compare the initial experience with leadless pacing to standard transvenous pacing at a tertiary care center.

Methods: Ten patients with an indication for implantation of a VVI-pacemaker based on current guidelines underwent implantation of a Micra™ transcatheter pacing system (Micra-group) and compared to a previous series of ten consecutive patients undergoing implantation of a standard transvenous VVI-pacemaker (standard group). Thresholds, total procedure time (skin-to-skin or stick-to-sheath removal), fluoroscopy time, radiation dose (dose area product (DAP)) and complications were compared.

Results: Twenty patients (25% female, age 81±5 years, ejection fraction 0.57±0.09) were included. All procedures were completed successfully without complications, specifically no lead dislodgement or Micra™ embolization or dislodgement requiring retrieval occurred. Sensing thresholds were 9 mV (interquartile range (IQR) 6-17 mV) and 9 mV (IQR 8-11 mV) whereas pacing thresholds were 0.6±0.3 V (@0.24ms) and 0.6±0.3 V (@0.5ms) in the Micra-group compared to the standard group, respectively (all p=ns). In the Micra-group, procedure time was 35 min. (IQR 32-47 min.) compared to 33 min. (IQR 24-44 min.) in the standard group (p=0.38). The fluoroscopy time of 5.5 min. (IQR 3.5-8.6 min.) was higher in the Micra-group compared to 1.7 min. (0.6-2.8 min.) in the standard group (p<0.0001), and DAP was markedly higher in the Micra-group (2625 (IQR 1256-4159) Gy*cm²) compared to the standard group (33 (IQR 16-51) Gy*cm²; p<0.0001).

Conclusion: During an initial experience with leadless transcatheter pacing, implantation of the Micra™ VVI pacemaker compared to a standard transvenous VVI pacemaker was associated with equal implantation success and similar procedure duration, but markedly longer fluoroscopy time and higher radiation dose.

Disclosure of Interest: None Declared
Introduction: In patients with cavotricuspid isthmus (CTI) ablation and atrial flutter (AFl) as the only documented arrhythmia, the decision to hold oral anticoagulation (OAC) often becomes an issue. There is mounting evidence, however, that atrial fibrillation (AF) very often goes along with AFl. The purpose of this study was to a) assess the incidence of subsequent development of AF in an unselected population without previous AF referred for typical AFl ablation and b) to compare CTI ablation in patients with AFl only and those with AFl and previous AF.

Methods: A total of 302 patients (223 male; mean age 66±11 yrs) with documented AFl only (group A) and 74 patients (53 male; mean age 63±11 yrs) with AFl and previously documented AF (group B) underwent successful CTI ablation at a tertiary referral center were included in the study.

Results: Over a mean follow-up of 23±20 months, 193 (64%) patients in group A and 40 (54%) patients in group B had no documentation of a recurrent atrial arrhythmia (p=0.14). AF developed in 85 patients (28%) in group A and in 29 (39%) patients in group B (p=0.005). AFl recurred in 24 patients (8%) and in 5 patients (7%) in group A and B, respectively (p=ns). 22 (7%) patients in group A and 17 (23%) in group B had undergone pulmonary vein isolation (PVI) at the end of the follow-up period (p=0.004).

Conclusion: Our results indicate, that new-onset AF develops in a significant proportion of patients undergoing CTI for AFl. One should therefore be careful to withhold OAC. Furthermore, since patients with previous AF have significantly more AF recurrences after CTI, PVI should be considered in conjunction with CTI.

Disclosure of Interest: U. Celikyurt: None Declared, S. Knecht: None Declared, M. Kuehne Grant/ research support from: Biosense Webster, T. Reichlin: None Declared, A. Muehl: None Declared, S. Osswald Grant/ research support from: Medtronic, Boston Scientific, Biotronik and St Jude Medical, Speakers bureau: Medtronic, Boston Scientific, Biotronik and St Jude Medical, C. Sticherling Grant/ research support from: Biosense Webster, Biotronik, Boston Scientific and Sorin, Consultant for: Medtronic
Introduction: Red cell distribution width (RDW) and B-type natriuretic peptide (BNP) are strong predictors of mortality in a broad spectrum of patients with heart failure (HF). However, little is known about their respective value in predicting mortality in most advanced HF patients. Thus, the aim of this study was to determine the prognostic value of RDW in comparison to BNP in different stages of HF.

Methods: Patients with chronic HF and LVEF <40% were prospectively followed for one year in the Evidence based treatment in HF (EVITA-HF) registry in Basel. According to BNP quartiles at baseline, patients were divided into two groups: “advanced HF” (highest quartile of BNP) and “stable HF” (BNP quartiles 1-3). The association of baseline RDW and BNP with co-morbidities (iron deficiency (ID), renal failure) and 1-year mortality were determined in the two groups using multiple regression and cox proportional hazard models.

Results: A total of 199 patients (77% men, age 71 ± 12, LVEF 28± 8%) completed the 1-year follow up. Forty-six patients (23%) were classified as “advanced HF” with a median BNP of 3621±3377 ng/L and NYHA ≥ III (81%), the reminder of patients were classified as “stable HF” with a median BNP of 587±477 ng/L and NYHA ≤ II (48%). In the total cohort, RDW and BNP were both independently associated with all-cause mortality (p< 0.001). However, in the subgroup of “advanced HF” patients only RDW significantly predicted mortality (HR=1.24, CI: 1.01- 1.46, p=0.04). The area under the receiver operating characteristic curve for RDW for predicting mortality was 0.70 (95%CI 0.53-0.87) and the best cut-off point for RDW was 14.5% (sensitivity 93% and specificity 73%). Importantly, patients with RDW >14.5% and BNP> 2000 ng/l had significantly higher mortality compared to others (HR=5.85, CI: 2.62- 13.05, p< 0.001). In “stable HF” the strongest relationship for RDW was obtained with markers of ID [Beta=0.29, p< 0.001 for soluble transferrin receptor (sTfR)], however in patients with “advanced HF”, beside ID, renal failure became a strong driver of RDW increase (Beta=0.49, p< 0.001 for creatinine clearance; Beta=0.51, p< 0.001 for sTfR).

Conclusion: RDW is a convenient and powerful marker predicting outcome better than BNP in advanced stages of HF. While ID is the principal driver of RDW in stable HF, cardiorenal syndrome potentiates RDW increase in advanced HF.

Disclosure of Interest: None Declared
Introduction: The distensibility of the aortic root has been shown to contribute to valve cusp stress reduction and a gradual and smooth opening and closure of the aortic valve (AV). The objective of this study was to investigate the effects of aortic root distensibility on the hemodynamic parameters and valve kinematics of an Edwards Intuity sutureless valve (Edwards Lifesciences, Irvine, CA) in a controlled \textit{in vitro} experiment.

Methods: Three transparent aortic root phantoms with different wall thicknesses (0.55, 0.85, 1.50 mm) were created using silicone. Their resulting distensibility was 0.50, 0.30 and 0.15 \%/mmHg, respectively. An Edwards Intuity sutureless 21 mm valve was inserted in these phantoms and hemodynamic measurements were performed in an \textit{in vitro} left heart flow loop. The AV kinematics were assessed using a high speed camera which captured the movement of the cusps in a retrograde axial view of the AV. The geometric orifice area (GOA) was measured by counting the pixels frame by frame in the lumen of the open AV. The opening and closing speed of the AV were calculated from the GOA. The effective orifice area (EOA) was calculated as \( EOA = \frac{Q_{rms}}{51.6 \sqrt{dP_{mean}}} \) \( \text{cm}^2 \) where \( dP_{mean} \) \( \text{mmHg} \) is the mean systolic trans-valvular pressure gradient and \( Q_{rms} \) \( \text{ml/s} \) is the root-mean-square value of the systolic AV flow. Hemodynamic measurements were performed at a heart rate of 60 bpm, a cardiac output of 3.5 l/min, and an aortic pressure of 100/60 mmHg.

Results: The GOA increases with decreasing distensibility (1.560±0.004, 1.790±0.005, 1.800±0.010 cm\(^2\)) while the EOA is constant (1.64±0.01, 1.64±0.01, 1.64±0.01 cm\(^2\)). Additionally, the AV opening (158±7, 165±8, 173±18 cm\(^2\)/s) and closing speed (38.1±5.9, 45.6±9.7, 48.8±12.7 cm\(^2\)/s) increase with decreasing distensibility. The hemodynamic parameters \( dP_{mean} \) (9.9±0.2, 9.6±0.1, 10.0±0.1 mmHg), \( Q_{rms} \) (267±2, 262±2, 268±2 ml/s), and the heart rate (59.9±0.2, 58.4±0.2, 58.5±0.3 bpm) were nearly the same for all phantoms.

Conclusion: The GOA is bigger for the less distensible aortic root phantoms (even though the hemodynamic parameters \( Q_{rms} \), \( dP_{mean} \) and EOA are the same). The resulting mean systolic flow velocity \( Q_{rms}/\text{GOA} \) in the AV orifice is lower for the
stiffer aortic root such that the systolic wall-shear-stress acting on the cusps is expected to be lower. However, the higher opening and closing speeds of the cusps in these aortic roots lead to higher mechanical load on the cusps.

**Disclosure of Interest:** None Declared
Assessment of flow patterns and hydrodynamic stresses in a novel right heart model

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Introduction: The pathophysiologic processes leading to structural alterations of the right ventricle (RV) in the athlete's heart and in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) are incompletely understood. The main aim of this study is to assess flow patterns and hydrodynamic stresses in a novel in-vitro silicone right heart model.

Methods: Among the in-vitro methods available to quantify mean and fluctuating velocities, 3D Particle Tracking Velocimetry (3D-PTV) has gained much attention as it permits studying complex flow fields in chambers and vessels. In this study, 3D-PTV has been applied to a silicone replica reconstructed from a 3D volume rendering of a high-resolution magnetic resonance (MR) scan (Fig.1). The pulsatile ventricular blood flow was investigated in this model. The obtained in-vitro results were then compared with those obtained from a healthy proband by in-vivo MR flow measurements.

Results: Our results show that the in-vitro pathlines of flow during peak systole are similar to physiological flow patterns. A substantial portion of the flow is directed towards the RV outflow tract. The velocity magnitudes are higher along the RV outflow tract and the subtricuspid area – typical predilection sites in ARVC/D - and the spatial distribution of the flow field is qualitatively uniform. Local rotational regions develop in the vicinity of the subtricuspid area.

Conclusion: The study of flow dynamics and hydrodynamical stresses in our novel in-vitro right heart model may improve the understanding of processes that initiate structural alterations in RV diseases and the athlete's heart.

Disclosure of Interest: None Declared
PP-035

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

3F enable and perceval s: a single centre comparison of two bioprosthetic valves for sutureless aortic valve replacement

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¹Inselspital Bern, Bern, Switzerland

Introduction: The 3F Enable and the Perceval S aortic valves are both nitinol-stented bio prosthesis designed for sutureless aortic valve replacement (AVR). Direct comparison of such bio prosthesis is lacking. Primary objective of this observational clinical trial was to assess intra-operative performance and to compare hemodynamic follow-up parameters.

Methods: In our institution 111 patients (pat) with severe aortic stenosis underwent sutureless AVR either with the an 3F Enable (n=57) or a Perceval S bio prosthesis (n=54). Intraoperative surgical and echocardiographic assessment as well as follow-up including echocardiography were performed at discharge, after 3-6 months, and annually thereafter.

Results: Demographic data (age, NYHA, EuroSCORE, cardiovascular risk factors) were comparable. Concomitant procedures (CABG, PFO closure, carotid endarterectomy) were performed in 14 pat of the 3F Enable group (25%) and in 18 pat of the Perceval S group (33%), respectively (p=.402). Mean aortic cross-clamp time was longer in the 3F Enable group, regardless whether pat underwent isolated AVR [3F Enable, 41±14 min vs Perceval S, 31±10 min; p=.002] or AVR with a concomitant procedure (3F Enable, 42±16 min vs Perceval S, 35±11 min; p=.01]. Mild transprosthetic leaks were very frequent in the Perceval S group (p<.001). No difference was found for mild paraprosthetic leaks (p=.613). During follow-up of 3.4±2.3 years, 7 deaths occurred in the 3F Enable group (12%) and 3 (6%) in the Perceval S group. All deaths were not device related. Prosthesis replacement due to endocarditis, early degeneration and symptomatic leaking was required in 5 pat (9%) of the 3F Enable group and in 4 pat (7%) of the Perceval S group. Higher transvalvular gradients and smaller effective orifice area (EOA) was documented for the Perceval S prosthesis (mean systolic gradient after 5y: Perceval S, 16.4 ±9.7 mmHg vs 3F Enable, 7.9±2.2 mmHg [p=.001]; EOA: Perceval 1.5±0.5 cm² vs 3F Enable, 2.0±0.5 cm² [p=.006]).

Conclusion: The 3F Enable and Perceval S valves are both suitable bio prosthesis for sutureless AVR. The Perceval S device offered advantageous intra-operative procedural characteristics, whereas hemodynamic performance of the 3F Enable prostheses during follow-up appeared more favourable.

Disclosure of Interest: None Declared
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Treatment of severe aortic stenosis with a new generation recapturable and repositionable self-expanding transcatheter aortic valve system: a single centre experience of consecutive patients

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¹Cardiology, ²Anesthesiology, ³Cardiovascular surgery, ⁴Radiology, Hôpitaux Universitaires de Genève, Geneva, Switzerland

Introduction: The purpose of the present study is to report prospectively collected safety data and clinical outcomes of the new generation recapturable and repositionable CoreValve Evolut R System (Medtronic, Inc.)

Methods: Between February and December 2015, 51 consecutive patients underwent TAVI at a tertiary centre. All were treated using the CoreValve Evolut R System for symptomatic severe aortic stenosis. Clinical endpoints were independently adjudicated according to the Valve Academic Research Consortium (VARC)-2 criteria. Primary outcomes consisted of the VARC-2 early safety composite endpoints at 30 days and device success. Device success was defined as the absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical location and intended performance (absence of prosthesis patient mismatch, mean aortic valve gradient <20 mmHg, peak velocity <3 m/s, and absence of moderate or severe prosthetic valve regurgitation). The incidence of new pacemaker implantation was also reported.

Results: The median population age was 82 [IQR: 78.5-86] years and 42.2% were females with a median EuroSCORE II and STS score of 3.6% [IQR: 2.1-4.8] and 3.4% [IQR: 2.4-5.0], respectively. A previous pacemaker was present in 11.8% of patients. A fully percutaneous vascular approach was preferred in 90.2% of patients and the EnVeo R delivery catheter was advanced sheathless in 88.2% of patients. All attempts (11/51) of valve repositioning were successful. At 30 days, 2 patients (4.7%) had died and 4 patients (8.7%) presented a stroke including one disabling stroke (Rankin score of 4). Two patients (3.9%) experienced major vascular complications and 3 (5.9%) had life-threatening bleeding. Overall device success was reported in 88.2% of patients. Paravalvular leakage at 30 days was less than moderate and moderate in 97.7% and 2.3% of patients respectively. No severe paravalvular leakage was reported. The CoreValve Evolut R System was effective in reducing mean transvalvular aortic gradient from 43.7 ± 14.3 at baseline to 7.8 ± 3.7 at discharge (p<0.0001 vs. baseline) and 7.5 ± 4.0 at 30 days. New permanent pacemaker implantation was required in 21.6%.

Conclusion: The first experience with the new generation CoreValve Evolut R System shows high device success and acceptable morbidity and mortality. The reduced sheath size and recapture properties have the potential to improve clinical outcomes, though this will have to be demonstrated in larger multicentre studies.

Disclosure of Interest: None Declared
Introduction: Transcatheter aortic valve prostheses may impact coronary perfusion owing to the proximity of the coronary ostia to the valve stent frame. In this in vitro study, we aim at quantifying the hemodynamic effects of transcatheter aortic valve implantation (TAVI) stent frames on the coronary perfusion.

Methods: A pulsatile left heart flow loop was used to reproduce physiological flow in a silicone phantom of the aortic root containing a 27 mm Carpentier-Edwards 2625 aortic valve (Edwards Lifesciences, Irvine CA, USA). The aortic root phantom featured left and right coronary ostia which were connected to an in vitro network mimicking the coronary circulation. Physiological coronary flow was achieved in both branches by adjustable hydraulic resistors and a model of intramyocardial collapsing vessels whose resistance was regulated by the left ventricular pressure. The potential hydraulic obstruction through TAVI stent frames was modelled by mesh frames of different heights (15 mm, 25 mm) which were mounted on the aortic valve. The struts of these mesh frames were thicker than commercially available TAVI stent struts and therefore expected to be more obstructive. The trans-valvular pressure gradient, the aortic flow as well as pressure and flow in the two coronary branches were measured for both mesh frames and were compared to a baseline measurement without a mesh frame. The measurements were performed under physiological conditions with 5 l/min cardiac output at 60 bpm and an aortic pressure of 125/85 mmHg.

Results: The in vitro flow loop reproduced physiological flow in the left and the right coronary branch. The two mesh frames had no significant effect on the coronary flow rates and pressures compared to the baseline measurement without a mesh frame. However, the presence of a mesh frame reduced the fluttering of the valve cusps in the open position.

Picture/Graph:
Conclusion: We developed an *in vitro* model which reproduced physiological flow in the aortic root and in the coronary circulation. Our experiments with mesh frames suggest that TAVI prostheses have no obstructive effect on the coronary perfusion.

Disclosure of Interest: None Declared
Surgical antegrade transcatheter mitral valve implantation for symptomatic mitral valve disease and heavily calcified annulus: a case series

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Introduction: Surgical techniques for the treatment of mitral valve regurgitation (MR) has continuously evolved and includes several approaches to safely repair or replace the mitral valve. However, anatomical specifications like severe annular calcification remain challenging and require sophisticated surgical strategies. Herein we report the first series of successful antegrade transcatheter mitral valve implantation among four patients with extensive calcification of the mitral annulus.

Methods: Among patients with symptomatic mitral valve disease referred for surgical valve repair or replacement, four of them (73 ± 9.2 years) presented with severe calcification of the mitral annulus precluding conventional surgical techniques. After interdisciplinary discussion, all of them were successfully treated by implanting a conventional balloon expandable transcatheter aortic bioprosthesis using a surgical antegrade access. Concomitant procedures included atrial fibrillation ablation, coronary artery bypass grafting and septal myectomy with a cardio-pulmonary bypass time of 147 ± 38 minutes and an aortic cross clamp time of 105 ± 25 minutes. The perioperative course was uneventful in all patients.

Results: No serious adverse events were reported during a mean follow-up duration of 12.8 ± 9.4 months (max. 24/min. 4). Echocardiographic follow-up assessment confirmed a well seated valve in appropriate position with a normal function and a mean transvalvular gradient of 4.5 ± 0.6 mmHg. All patients presented in NYHA functional class I and II at the respective follow-up.

Conclusion: Surgical mitral valve replacement using a balloon-expandable transcatheter aortic bioprosthesis can be a valuable and attractive bailout strategy in patients with a heavily calcified mitral annulus and provides excellent hemodynamic results and favorable short- to midterm clinical outcomes.

Disclosure of Interest: None Declared
PP-039
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation
Long-term progression of cardiac allograft vasculopathy
a serial quantitative coronary analysis

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Introduction: Cardiac allograft vasculopathy (CAV) adversely affects the long-term prognosis after heart transplantation. Only limited data is available regarding the serial long-term progression of CAV by means of angiography. The primary objective of our study was to investigate the progression of CAV assessed by 3-vessel quantitative coronary analysis (QCA) in a heart transplantation cohort of a tertiary care center.

Methods: A total of 70 heart transplant recipients were enrolled between January 1994 and August 2014 at Bern University Hospital. We retrospectively performed 3-vessel QCA analysis for every segment according to the modified AHA/ACC classification at three timepoints: at baseline (donor angiography or within 6 months after heart transplantation), at 1 year and at the latest follow up (FUP) available. CAV was visually classified according to the definition of the International Society for Heart and Lung Transplantation.

Results: Mean age at heart transplantation for donor was 43.2±13.2 years and for recipients was 46.6±15.9 years. Either everolimus (52.9%) or tacrolimus (47.1%) was prescribed as immunosuppressive drug in combination with mycophenolate mofetil and steroids. The primary cause of heart transplantation was dilated cardiomyopathy (48.6%), followed by coronary artery disease (34.3%). Mean follow-up time was 8.62 ± 3.59 years. Serial angiography at all three timepoints was available in 40 patients (57%). In the QCA analyses, the change in minimal lumen diameter (MLD) was analyzed in 510 matched segments. The mean segment level MLD significantly decreased from baseline to 1-year follow up (Δ-0.22mm/year [95%CI -0.28 to -0.16], p<0.001) and from 1-year to the latest follow-up (Δ-0.08mm/year [95%CI -0.11 to -0.05], p<0.001). (Figure 1) The ISHLT-visual Score at the latest follow-up was CAV-0 in 16 (40%), CAV-1 in 17 (42.5%), CAV-2 in 7 (17.5%) and CAV-3 in no patient. Mean MLD and mean percent diameter stenosis was 1.89±0.32mm and 15.9±3.2% in patients with CAV-0, 1.82±0.28mm and 20.1±3.9% for CAV-1, and 1.63±0.24mm and 23.8±5.0% for CAV-2.

Picture/Graph 2:
Conclusion: A prevailing lumen loss was observed in the first year after heart transplantation followed by a low but steady decrease in MLD up to 17 years. How early and late angiographic changes associate with prognosis require further investigation.

Disclosure of Interest: None Declared
Introduction: To analyze our experience with the repair of leaking bicuspid aortic valves (AV) since 2013.

Methods: Among a total of 40 patients who underwent a Tirone David operation in this time period, 18 patients (median age: 42 +/- 12 years) had this procedure - along with a valve reconstruction - for a leaking bicuspid AV. Among them, 12 patients had a severe aortic insufficiency due to a leaflet prolapsus (18 pts) and/or a root dilatation (12 pts). Prolapsus of leaflets was corrected by central plications. The leaflets were thinned out and the raphe resected in 12 patients. A neo-commissure was built with autologous pericardium in 3 patients. A commissure was moved to release the left coronary ostium in a patient. The aortic root was replaced by Valsalva prosthesis (diameter between 28 and 32 mm) in every patient. Replacement or reinforcement of the entire ascending aorta was performed in 5 patients. The median duration of aortic clamping was 142 +/- 37 min and the cardiopulmonary bypass time was 167 +/- 42 min.

Results: The aortic valve was competent in all patients. The transvalvular gradient was measured between 7 and 15 mmHg. A pacemaker was implanted in two patients, for intermittent and for a constant atrioventricular block. Two patients had to be re-operated for a suture dehiscence in the first two months. A new repair and valvular replacement were performed in each. One patient, known for a non-compaction of the left ventricle required a transient mechanical support to get a complete recovery of the ventricle. The echocardiography findings remained stable in the other patients.

Conclusion: The repair of bicuspid aortic valve is possible with good short and medium results. It should be considered as the procedure of choice in young patients. Indications for surgery might be extended.

Disclosure of Interest: None Declared
Introduction: During the last 15 years, minimally invasive surgery using the right anterolateral mini-thoracotomy access has emerged as an accepted approach for the management of mitral valve disease alone or in combination with tricuspid valve disease, defects of the atrial septum or atrial rhythm disorders. We report our single institution experience with minimally invasive mitral valve surgery.

Methods: Between 2010 and 2015 a total of 152 patients underwent minimally invasive mitral valve surgery using right anterolateral approach in our institution. Additionally 3 patients received TKR, PFO closure in 8 patients, resection of left atrial myxoma in 1 patient and maze operation in 7 patients. 124 patients received mitral valve repair, 19 patients mitral valve replacement. The Operation was performed in 101 male patients (mean age 59.98±11.48 years) and 51 female patients (mean age of 60.75±11.49 years). In 106 (85.5%) cases, the pathology of valve prolapse was addressed to the posterior leaflet; in 5(4%) cases to the anterior leaflet, in 2(1.6%) cases a prolapse of both leaflets was seen and in 10(8.06%) cases the cause was annular dilatation and 1(0.8%) patient with other pathology.

Results: In 33(21.7%) patients repair was performed via tri- or quadrangular resection of the prolapsing valve leaflet in combination with a ring, in 71(46.7%) patients annuloplasty was combined with insertion of neo-chordae, 19(12.5%) patients just received an annuloplasty, 19(12.5%) - mechanical valve. Mean perfusion time was 156.7±40.6 min, mean ischemic time is 98.5±20.9 min. In 11% of cases the patients needed blood products. Mortality rate was 1.9% and reoperation rate was 1.9%.

In 3 patients with primarily planned mitral-valve repair the valve had to be replaced (repair/intention to repair rate of 98%). Other postoperative complications: seroma in the groin after femoral cannulation in 1.3%, hemotorax in 1.3%, SIRS in 0.65%, successful resuscitation due to cardiac arrest in 1.3% and laparotomy for abdominal bleeding (venous injury after cannulation) in 0.65%.

Conclusion: Mitral valve surgery can be safely performed through a right minithoracotomy with good early and intermediate results. The avoidance of extensive surgical dissection, optimal valve exposure, low infection rates, low number of blood transfusion and patient comfort are the main advantages of this technique. Therefore we strongly recommend the anterolateral approach whenever possible.

Disclosure of Interest: None Declared
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Arrhythmogenic right ventricular cardiomyopathy versus dilated cardiomyopathy: implications of next generation sequencing in appropriate diagnosis

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Introduction: Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC) is a rare, familial heart-muscle disease that causes sudden death and is characterized by progressive replacement of myocardium by fibrofatty tissue. In advanced stages of the disease, it is difficult to differentiate ARVC from idiopathic dilated cardiomyopathy (DCM). In this study we aim to evaluate potential differences in the genetic profile of cases with definite, borderline and possible ARVC phenotype by 2010 Task Force criteria using a custom genetic panel after whole exome analysis.

Methods: We performed whole exome sequence analysis in 14 unrelated, consecutive patients enrolled in the Zurich ARVC Program (www.arvc.ch) with ARVC diagnosis based on the Task Force criteria of 2010 and categorized them as “definite”, “borderline” or “possible”. Exome sequencing was performed at Atlas Biolabs, Berlin, Germany, using an “Illumina HighSeq 2000” system. The analysis included alignment to the human reference sequence, delivering Binary Alignment/Map files (BAM) and variant call format files (VCF). We presented our initial results focused on 96 known cardiomyopathy and channelopathy genes. For detailed sequence analysis and interpretation of sequence variations we used Alamut-Batch (including HGMD Professional) and visualized by the Alamut Viewer 2.2 (Interactive Biosoftware, Rouen, France). Additional analyses were performed with Sequence Pilot (JSI, Medical Systems, Kippenheim, Germany), SeqScape (Applied Biosystems, Rotkreuz, Switzerland), the Human Genome Browser at UCSC, and the ENSEMBL database.

Results: According to the 2010 Task Force criteria, 7/14 cases (50%) were classified as “definite” phenotype, 4/14 (29%) were “borderline”, and 3/14 (21%) were diagnosed with the “possible” phenotype. 9/14 patients (64%) were males, and all were Caucasians, with an average age at genetic diagnosis of 50 ± 15 years. Among the 7 cases with the “definite” phenotype, 6 (86%) had a putative desmosomal mutation while none of the 7 patients with a “possible” or “borderline” task force classification phenotype hosted putative mutations in desmosomal genes. Four (57%) of them had rare variants in other dilated cardiomyopathy (DCM) genes.

Conclusion: Most of the patients with definite ARVC phenotype by task force 2010 host mutations in desmosomal genes. Weaker ARVC phenotypes host variants/mutations in other DCM genes and result in a disease spectrum, including DCM or phenocopies of ARVC.

Disclosure of Interest: None Declared
Introduction: The Symetis ACURATE neo transcatheter heart valve (Symetis SA, Ecublens, Switzerland) has received CE mark in 2014. Since then, more than 1300 implants have been performed worldwide. The valve is available in three different sizes (S, M, L), and is delivered through an 18F sheath. Here, we report 30 day outcomes of procedures performed at three centers in Switzerland.

Methods: All patients undergoing transfemoral transcatheter aortic valve implantation (TAVI) with the ACURATE neo at three Swiss centers (Luzerner Kantonnspital, Herzklinik Hirslanden, Inselspital Bern) were analyzed based on data entered in the prospective SwissTAVI registry.

Results: A total of 31 patients (52% females, mean age 83 ± 5 years) underwent transfemoral TAVI with the ACURATE neo for the treatment of severe aortic stenosis (n = 29), severe aortic regurgitation (n = 1), and mixed disease (n = 1). Among 29 patients with aortic stenosis, aortic valve area increased from 0.8 ± 0.2 cm² to 2.1 ± 0.5 cm² (p < 0.01), and the mean gradient dropped from 40 ± 12 mmHg to 6 ± 4 mmHg (p < 0.01). Paravalvular regurgitation was none/trace in 9 (31%), mild in 18 (62%), and moderate in 2 (7%). In two patients with predominant aortic regurgitation, the degree of regurgitation was reduced from severe to mild and from moderate-severe to none. A total of 3 patients (10%) required implantation of a new permanent pacemaker. Median length of hospital stay was 8 days. After 30 days of follow-up, rates of serious adverse events were low. All-cause mortality was 0%, one patient (3.2%) had a disabling stroke, one (3.2%) had a major vascular complication, and there were two patients with major bleeding (6.4%). The rates of VARC-2 device success, early safety (30 days) and clinical efficacy (30 days) were high with 94%, 90%, and 94%, respectively.

Conclusion: Implantation of the Symetis ACURATE neo transcatheter heart valve resulted in very promising clinical and hemodynamic outcomes with very low residual gradients and a low pacemaker rate.

Disclosure of Interest: S. Toggweiler Conflict with: Proctor for Symetis SA, T. Pilgrim: None Declared, P. Biaggi: None Declared, F. Cuculi: None Declared, P. Wenger Müller: None Declared, J. Grünenfelder: None Declared, R. Kobza: None Declared, S. Windecker: None Declared, P. Jamshidi: None Declared, R. Corti: None Declared, S. Stortecky: None Declared
Percutaneous treatment options for high risk patients with recurrent mitral valve disease after failed mitral valve surgery

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Introduction: The management of recurrent mitral valve (MV) pathology after failed MV surgery can be challenging. Percutaneous treatment options have been described as an alternative to redo-surgery in surgical high-risk patients. We aim to analyze the outcome of percutaneous MV interventions of such a cohort.

Methods: 17 consecutive patients with recurrent symptomatic MV disease treated at the Heart Clinic Zurich or the University Heart Center Zurich between 2011 and 2015 were analyzed retrospectively. Clinical and echocardiographic data were gathered by reviewing patients' charts. All patients were judged high-risk surgical candidates by a HeartTeam or refused redo open-heart surgery. Consequently, percutaneous MV repair using a MitraClip device was performed in 11 patients, and 6 patients needed percutaneous MV replacement as either valve-in-ring (n=3) or valve-in-valve (n=3) treatment (fig 1).

Results: The median age at the time of intervention was 75.8 years (range 53.6 to 89.4 years) and 65% of patients were male. The median EuroSCORE II and STS mortality score were 4.5% (range 0.5% to 14.4%) and 4.9% (range 1.5% to 20.9%), respectively. Mitral regurgitation (MR) grade at baseline was moderate-severe (n=4, 24%) or severe (n=13, 76%). Interventional success was obtained in all but one case (94%), where a MitraClip insertion was converted to a valve-in-ring implantation. 30 day survival rate was 100%. Median time to last clinical follow up was 130 days (range 31 to 807 days). At last follow up, MR grade was none-mild in 81% and moderate in 19% of patients. Reduction of dyspnea according to New York Heart Association classes was achieved in all but 2 patients (88%). Of those, a dyspnea reduction by 1, 2 or 3 classes was described in 38%, 54% and 8% of patients, respectively. The median gradient across the tricuspid valve was reduced from 49.2 mmHg (range 20.1 to 70.0 mmHg) to 39.3 mmHg (range 19.8 to 60.1 mmHg). The overall survival rate was 76%, with 3 patients dying from non-cardiac death at days 31, 427 and 1093, respectively, and one patient from unknown cause at day 394. The median age at death was 88.1 years (range 86.5 – 90.5 years).

Picture/Graph:
Conclusion: Percutaneous MV treatments instead of redo MV surgery are feasible and associated with a lower than expected peri-interventional mortality in selected high-risk surgical patients. The interventions proved effective regarding reduction in mitral regurgitation and symptoms as well as lowering of pulmonary pressure.

Disclosure of Interest: None Declared
PP-045

3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation

Local versus general anesthesia for transfemoral transcatheter aortic valve implantation

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Introduction: To investigate patient characteristics and clinical outcomes of patients undergoing transfemoral transcatheter aortic valve implantation (TAVI) with local or general anesthesia.

Methods: The SWISS TAVI Registry (NCT01368250) is a national, prospective, multicenter, centrally monitored registry assessing procedural and clinical outcomes of CE approved devices. Data are entered into a web-based database (www.swisstaviregistry), which is maintained and monitored by an independent Clinical Trials Unit.

Results: Between February 2011 and September 2015, a total of 2,553 patients undergoing transfemoral TAVI were included into the Swiss TAVI registry and prospectively followed. Local anesthesia with conscious sedation (LA) was used for the majority of procedures (64.2%, n=1640), whereas 35.8% (n=913) of procedures were performed in general anesthesia with orotracheal intubation (GA). Conversion from local to general anesthesia was observed in 3.7% of patients. Patients with GA were at higher surgical risk according to the STS risk score compared with LA patients (6.3%±4 vs. 5.7%±3, p=0.003). Although there were no differences with respect to age (GA 82.5±7 vs. LA 82.2±6, p=0.37) and body mass index (26.7±6 vs. 26.6±5, p=0.55), patients undergoing LA were less frequently female (48.4% vs. 53.0%, p=0.031) and had higher rates of coronary artery disease (57.3% vs. 51.1%, p=0.014) when compared with GA patients. Patients with LA had a shorter procedure time (67.5±31 vs. 78.4±38 minutes, p<0.001), shorter length of stay at intensive care unit (0.8±1.8 vs. 1.3±2.1 days, p<0.001) and a reduced overall length of hospital stay (9.6±6 vs. 10.3±6 days, p=0.003) when compared with GA.

At hospital discharge, patients with LA had favorable clinical outcomes with low rates of all-cause mortality (GA vs. LA 3.4% vs. 1.3%, HR adj 2.65, 95%CI 1.55-4.53), disabling stroke (1.4% vs. 1.7%, HR adj 0.83, 95%CI 0.43-1.61), life-threatening bleeding (5.1% vs. 4.2%, HR adj 1.24, 95%CI 0.86-1.79) and major vascular complications (9.0% vs. 8.9%, HR adj 1.00, 95%CI 0.77-1.29). At 30 days, patients with LA sustained lower rates of all-cause and cardiovascular mortality (4.1% vs. 2.4%, HR adj 1.78, 95%CI 1.12-2.80 and 3.9% vs. 2.0%, HR adj 2.01, 95%CI 1.23-3.26).

Conclusion: Local anesthesia with conscious sedation is safe and effective among patients undergoing transfemoral transcatheter aortic valve implantation and is associated with favorable clinical outcomes.

Disclosure of Interest: None Declared
**Introduction:** Discrepancies between echocardiographic and invasive assessment of aortic stenosis have been recently reported in the elderly. We sought to investigate the amplitude of these discrepancies in a real-world setting.

**Methods:** We examined data from 71 consecutive patients (mean age 84 ± 6 years; 54% women) with moderate or severe aortic stenosis (mean aortic valve area at echocardiography 0.75 cm², range 0.41 to 1.29 cm²) who underwent both transthoracic echocardiogram and right-and-left heart catheterization within an interval of 8 ±12 days. All patients were evaluated by our institution’s Heart Team and clinical decision-making was based upon these data along with symptomatic status.

**Results:** There were no significant differences in mean arterial pressures (94 ± 16 vs. 96 ± 17 mmHg, p=0.37) and heart rates (74 ± 14 vs. 76 ± 13 bpm, p=0.15) between the two examinations. Mean transaortic gradients were not statistically different using the two methods, albeit with broad limits of agreement (ICC=0.69, bias -1.8 mmHg, LOA -21.7 to 18.1 mmHg, p=0.14), only 31 patients (44%) having a mean gradient difference <5 mmHg. We found a modest correlation between aortic valve area at echocardiography and at catheterization using directly measured oxygen consumption with a small overall bias but wide, clinically relevant limits of agreement (ICC=0.47, bias 0.06 cm², LOA -0.32 to 0.44 cm², p=0.01). In addition, stroke volume index, valvuloarterial impedance, systemic arterial compliance and systemic vascular resistance showed poor correlation between the two methods (ICC between 0.20 and 0.31).

**Conclusion:** In a real-world setting and among multimorbid elderly patients, discordances between echocardiographic and hemodynamic measurements are of clinical importance. Thus, the two methods cannot be used interchangeably in this population.


**Disclosure of Interest:** None Declared
3. Cardiac failure, valvulopathies, cardiomyopathies, pericardiopathies, heart transplantation
The impact of the multidisciplinary team approach on early mortality and acute cellular rejection after heart transplantation

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Introduction: Background:
In 2008, the University Hospital of Lausanne established the multi-disciplinary Heart Transplantation (HTx) team to improve quality of respective pre- and postoperative care. This study investigates its impact on mortality and morbidity early post-transplant.

Methods: Methods:
A total of 140 patients underwent HTx between 2000-8/2014 with 66 patients operated between 2000-2007 and 74 thereafter. Mean age was 53.5 years (IQR 47.3-59.8 years), 80% were males, donor/recipient gender mismatch was 38.3%, length of in-hospital stay was 34 days (IQR 26-61 days), donor age was 41 years (IQR 26-51 years); characteristics were not different between groups. In HTx recipients of 2008-2014, dilated cardiomyopathy of non-ischemic origin was less prevalent (43.2 vs 63.6%; p=0.024), assist device treatment was more frequent (24.3 vs. 9.1%; p=0.030). Cardiovascular risk factors, burden of comorbidity, and baseline hemodynamic, clinical, and echocardiographic parameters were not different between groups.

Results: In-hospital and 1-year all-cause mortality (ACM) was lower in HTx recipients of 2008-2014 (22.2 vs. 16.2%; p=0.4711/0.4708). Diabetes mellitus was a predictor of in-hospital and 1-year ACM in patients operated 2000-2007, acute cellular rejection (ACR) of moderate grade was associated with in-hospital mortality in 2000-2007 but not in 2008-2014; mean individual grade of ACR was lower in 2008-2014 (0.2 vs. 0.65; p<0.0001).

Conclusion: The multidisciplinary HTx team approach increased the number of HTx recipients and increased quality of care in HTx with a lower mean ACR grade within the first year post-transplant, improved treatment of risk factors, and non-significant decrease of in-hospital and 1-year ACM.

Disclosure of Interest: None Declared
Introduction: Ventricular arrhythmias (VA), atypical flutter and/or conduction disorders may be life-threatening manifestations of Cardiac Sarcoidosis (CS), whose etiologic assessment represents a challenge encompassing biological and histological findings as well as imaging biomarkers. Considering the frequent virus-negativity, autoreactive immunopathogenesis besides CS may cause a progressive arrhythmogenic cardiac fibrosis whose clinical presentation remains poorly defined.

Methods: We report a series of 21 consecutive pts (57±13.4 y, n = 4 females) addressed at our tertiary university center because of VA, atypical flutter and/or conduction disorders, who underwent a diagnostic work-up including coronary angiography (CA) and Cardiac Magnetic Resonance (CMR) in those without an ICD. 18F-FDG PET scan (PET) was performed in pts with normal CA and evidence for delayed enhancement (DE) within the left ventricle (LV) at CMR. Pts displaying focal hypermetabolic activity at PET underwent directed cardiac biopsies.

Results: DE within the LV was observed in 18 pts with normal CA and no contraindication for CMR. A DE within the interventricular septum suggestive of CS was reported in 11 (52%) pts only. A PET, performed in 21 pts, revealed a hypermetabolic LV activity in 20 pts (95%) of whom 4 (19%) displayed a focal hypermetabolic right ventricle activity as well. The figure below illustrates an example of septal and lateral DE at CMR (A) and focal hypermetabolic LV activity at PET (B). Directed myocardial biopsies, performed in 19 pts, were abnormal in 14 (74%) cases consisting in 2 (14%) CS and 3 (21%) lymphocyte myocarditis. The 9 remaining pts showed fibrosis. Cases of biopsy-proven CS showed a more aggressive clinical presentation leading to a faster diagnosis compared to cases in whom cardiac biopsies were CS negative (14±11 vs 35±41 months). Despite the lack of criteria fulfilling the diagnosis of CS, immunosuppressive treatment has been introduced in 14 (67%) pts up to now, resulting in complete suppression of focal hypermetabolic activity in 9 (64%) pts and a partial reduction in the remaining 5 (36%) ones (Figure C).

Picture/Graph:

Conclusion: A multi-modality assessment based on CMR and FDG-PET allowed the detection of a new focal hypermetabolic syndrome sharing several features with CS including a favorable response to immunosuppressive treatment. In contrast to CS, clinical presentation seems to be more insidious, representing a challenge for diagnostic assessment.

Disclosure of Interest: None Declared
Introduction: Hemodynamically irrelevant pericardial effusion (PE) is a known predictor of negative outcome in heart failure patients. In contrast, the clinical relevance of non-surgery related PE in heart transplanted patients remains unknown. This study was designed to assess the prognostic value of PE occurring later than one year after heart transplantation.

Methods: All 313 patients who underwent heart transplantation in Zurich between August 1989 and July 2012 were retrospectively assessed for PE in our echocardiography database. Exclusion criteria were death within the first year after transplantation (64 patients), age <16 years at heart transplantation (8 patients), and lack of echocardiography follow-up (89 patients, mostly due to transfer to a different clinic after transplantation). Cox proportional hazard models were performed to analyze both mortality and unscheduled hospitalization for patients with and without PE. For analysis of mortality, the data was adjusted for gender and age at transplantation.

Results: A total of 152 patients was included, of which 25 developed PE. The median follow-up was 11.9 years with a PE incidence of 14.4 per 1000 patient-years. Absolute number of deaths was 6 in the PE group and 46 in the non-PE group. The occurrence of PE was associated with an increased risk of death (HR 2.49, 95%CI 1.02 - 6.13, p<0.05). Cause of death was cancer (28.8%), infections (15.4%), heart failure (13.4%), cardiovascular events (11.5%), and transplant rejection (3.8%). Absolute number of unscheduled hospitalizations was 306. In patients with PE, the risk of hospital admission was increased (HR 2.53, 95%CI 1.57 - 4.1, p=0.0002). The main reason for hospitalization was infection in 47.6% followed by cardiovascular events (10.4%) and cancer (6.9%).

Conclusion: This study reveals that the echocardiographic finding of PE in heart transplanted patients is associated with a 2.5 times higher risk of either death or hospitalization as compared to patients without PE. Thus, small PE which may be observed during routine echocardiography – even though hemodynamically irrelevant – are associated with a negative outcome.

Disclosure of Interest: None Declared
Introduction: Sarcoidosis is a systemic noncaseating granulomatous disease (etiology unknown). Cardiac sarcoidosis (CS) is occurring in < 20% of these patients (pts) however, CS is prognostically important due to possible AV block, atrial and ventricular arrhythmias or rarely heart failure. Treatment involves immunosuppressants, thus, early and reliable diagnosis of CS is essential. There are few data on the impact of changes of the diagnostic approach in the current era.

Methods: Findings of ECG, echocardiography (echo) and cardiac CMR of all 48 pts referred with possible or suspected CS were reviewed. Pts with only pulmonary sarcoidosis and no definite (biopsy proven, scar by CMR) or possible CS (pulmonary sarcoidosis combined with arrhythmias, pericardial effusion, AV block etc.) were excluded leaving 31 pt in the study.

Results: Mean age was 58 years, 17 females (55%). ECG and transthoracic echo was performed in all; 23 pt had≥1 cardiac magnetic resonance imaging (CMR), 8 had myocardial biopsy. Myocardial scars were found in 12 pt, involving the septum in 6 pt. Right bundle branch block (RBBB) was present in 5 pts, left bundle branch block in 1. Total AV block was seen in 5 pts, 3 pts had 1st degree AVB, ventricular tachycardia (VT) 8 pts (2 pt needed ICD), atrial tachyarrhythmias in 5 pt. Pericardial effusion/thickening was seen in 7 pts (one pt with severe constriction). In the 8 pt with VT, scars were seen in 5 pt (3 pt had no scar by CMR) and pericardial effusion in 1 pt (without a scar). Four pt had ≥moderate mitral regurgitation (in 3 functional, in 1 pt prolapse).

Results of myocardial biopsy showed in 2 pt nondiagnostic findings after prior steroid treatment. Immunosuppressant treatment was given in 15 pts including steroids in all, additionally azathioprine in 2 and infliximab in 1 pt.

Panel A shows a typical example of CS with total AV block, RBBB and ventricular tachycardias (VT) explained by huge scars (arrow) in the septum. Panel B is an example of a man with impressive constrictive pericarditis (yellow arrow) and RBBB in whom there is only a tiny scar inferolaterally (orange arrow).
Conclusion: CS is still often associated with significant arrhythmias, variable myocardial scars, and/or pericardial effusion. With the help of CMR and myocardial biopsy diagnostic accuracy can be improved, however, quite often uncertainty remains. CS is a very diverse, still amazing cardiac disease.

Disclosure of Interest: None Declared
Introduction: Concomitant mitral regurgitation (MR) is common among patients with aortic stenosis (AS). While MR often improves after correction of AS, some patients require percutaneous double valve treatment.

Methods: Patients undergoing transfemoral transcatheter aortic valve implantation (TAVI) and percutaneous treatment of the mitral valve (MitraClip) at five centers in Switzerland (Inselspital Bern, HerzKlinik Hirslanden, Luzerner Kantonsspital, Cardiocentro Ticino, and University Hospital Basel) were analyzed.

Results: A total of 20 patients (age 84 ± 6 years) underwent percutaneous double valve interventions. All patients had grade 3 or 4 MR and concomitant severe AS (n = 14), moderate AS (n = 5), or severe aortic regurgitation (n = 1). Five patients underwent treatment of both valves during the same hospitalization, two even during the same procedure. The remaining patients were treated during different hospitalizations, with TAVI performed 48-581 days prior to MitraClip in 10 patients and MitraClip performed 27-825 days prior to TAVI in 5. TAVI was performed using the Sapien / Sapien 3 (n = 10), CoreValve (n=6), ACURATE neo (n=2), Lotus (n=1), and Allegra NVT (n=1). Aortic valve area increased from 0.8 ± 0.3 cm² to 2.0 ± 0.5 cm², and there was mild or less paravalvular regurgitation in 18 (90%). The mitral valve was effectively treated with one clip (n=14), two clips (n=5), or three clips (n=1) with a reduction of MR to grade 1 in 13 (65%), grade 2 in 5 (25%), and grade 3 in 2 (10%). Major in-hospital complications included acute delirium after TAVI in 2 (10%), and two deaths caused by ischemic stroke and kidney failure (10%). Mid-term clinical outcomes were favorable. After a median follow-up of 268 days, 16 (80%) of patients were alive.

Conclusion: In patients with concomitant aortic stenosis and mitral regurgitation, the preferred strategy was to treat the aortic stenosis, and wait if mitral regurgitation improves. Therefore, only a minority of patients underwent percutaneous double valve treatment. In those undergoing treatment for both valves, both the aortic stenosis and mitral regurgitation were effectively treated, in most during different hospitalizations.

Disclosure of Interest: None Declared
**Introduction:** In functional mitral regurgitation (MR), valve leaflets are normal and deficient coaptation results from mitral annular dilatation (left atrial (LA) remodelling) and tethering of the leaflets (ventricular remodelling). As the relative importance of these mechanisms in ischemic (I-DCM) and non-ischemic (NI-DCM) dilated cardiomyopathy is not well known, we aimed to identify the specific morphological changes that correlate with MR in these two groups.

**Methods:** By retrospective review of our echocardiography database, patients with DCM (LV end-diastolic volume index >75ml/m² and LV ejection fraction <45%) were identified. Patients with primary MR, previous valve surgery, or aortic valve disease were excluded, as were datasets obtained during hemodynamic instability or poor quality datasets. One hundred consecutive patients with I-DCM (=with history of myocardial infarction) and 100 with NI-DCM were selected for analysis. All measurements including LV and LA dimensions and volumes, annular diameter, tenting area and MR quantification (PISA method), were re-acquired by one experienced examiner. An effective regurgitant orifice (ERO) >20 mm² defined severe functional MR. Factors independently correlated with ERO were identified in both groups by stepwise multiple linear regression.

**Results:** I-DCM were older (68±12 vs 61±16 y; p<0.001) and more frequently male (90% vs 67%; p<0.001) than NI-DCM patients. Atrial fibrillation was found in 37% and 34%, and MR was severe in 29% and 28% of NI-DCM and I-DCM patients, respectively. Other echocardiographic measurements are summarized in the table. In NI-DCM, the LA volume (coeff 0.001, 95%CI 0.0004 to 0.002; p<0.01) and the LV posterior wall thickness (PWT, coeff -0.29, 95%CI -0.49 to 0.10; p<0.01) were independently correlated with ERO. In I-DCM, only the tenting area showed a significant correlation (coeff 0.03, 95%CI 0.002 to 0.06 ; p<0.05).

**Picture/Graph:**
Conclusion: Severe MR was equally frequent in I-DCM and NI-DCM. Our data suggest that MR merely results from atrial (annular) dilatation than from ventricular remodelling in NI-DCM. We hypothesized that the correlation with reduced basal PWT might indicate that NI-DCM patients with a more extensive LV remodelling involving the basal LV segments also have impaired mitral annular contraction. On the other, hand leaflet tethering appears as the most relevant mechanism in I-DCM. Although significant, these weak correlations only allow to generate hypothesis.

Disclosure of Interest: None Declared
Publication rates and impact factors of accepted abstracts presented during the SGK congresses 2011 to 2014 in the field of interventional cardiology

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Introduction: The SGK congress is the most important national platform for young and established Swiss researchers where they present their work to a broad scientific public. An increasing number of abstracts are submitted every year and eminent reviewers rate them to the best of their knowledge. Accepted abstracts and talks or posters presented at the congress are praiseworthy, but more important is their publication in important international journals. Aim of this study was to determine publication rates and impact factors (IF) and analyse the temporal trend in the field of interventional cardiology.

Methods: In November 2015 we downloaded the abstract books (available as PDF under http://www.cardiovascular-medicine.ch) and extracted all talks and posters presented during the SGK congresses 2011 to 2014. We assessed in PubMed whether a paper has been published and, when yes, in which journal with which IF (always determined in the respective publication year). We excluded case reports, papers published more than at least 6 months before the congress and all abstracts presenting national data from a multicentre study (unless the first author of the published paper was from Switzerland). The percentage of published papers and their mean and median IF was calculated overall and per year.

Results: Rates ranged from 35% to 74% and mean IF from 4.3 to 6.5. Table 1 shows the rate of published papers and IFs across the four years in more detail.

<table>
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<tr>
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<td>2.6 - 11.3</td>
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Conclusion: Abstracts in the field of interventional cardiology presented during the SGK congresses have a high likelihood of being published, usually in papers with a good IF. This indicates the good quality of cardiology research in Switzerland.

Disclosure of Interest: None Declared
PP-054

4. ACS, PCI, CABG

Type 2 myocardial infarction: incidence, presentation, treatment and outcome in routine clinical practice.

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Introduction: The universal definitions of myocardial infarction (MI) introduced in 2007, classifies MI into 5 types and defines type 2 (MI2) as caused by an imbalance between oxygen demand and supply. However, this type of MI has been the subject of considerable clinical discussion without clear consensus, and no specific guidelines are available for treating these patients. The aim of this study was to assess differences in presentation and outcome of patients with type 1 MI (MI1) and MI2 in routine clinical practice.

Methods: Using data from the AMIS Plus Registry (2009-2015) where MI types were defined prospectively by clinicians in a “real world situation”, we compared baseline characteristics, therapies and outcomes in patients with MI1 to those with MI2 using propensity score matching.

Results: Of 14,919 patients from 53 Swiss hospitals, 13,829 were classified as having MI1 and 1091 (7.3%) as having MI2. Patients with MI2 were older, more frequently female, with more risk factors and comorbidities, and presented less frequently with ST-segment elevation MI. After matching using these variables (1091 patients per group), patients with MI2 less often presented with typical chest pain, and had higher systolic blood pressure and faster heart rate at admission. Atrial fibrillation was more frequent (MI2 15.6% vs. 4.9% in MI1) and so was anemia (33.5% vs. 23.3%); (both P<0.001). Patients with MI2 less frequently received percutaneous coronary interventions (PCI) (51.1% vs. 76.4%; P<0.001) and antplatelet treatment. No differences were found for in-hospital mortality (5.8% vs 5.6%; OR 1.04; 95%CI 0.72-1.49), cardiac death (3.1% vs 3.5%; P=0.72) and 1-year mortality (11.2% vs. 7.2%; P=0.38) between patients with MI1 or MI2, respectively.

Conclusion: Patients with MI2 presented less frequently with typical symptoms, but often with atrial fibrillation and anemia. They were less aggressively treated with anticoagulants, platelet inhibitors or PCI. However, there were no differences in complications and mortality in hospital and 1 year after discharge. Patients with MI2 are a heterogeneous group that requires further investigation to better define appropriate therapeutic approaches.

Disclosure of Interest: None Declared
Introduction: The European Society of Cardiology strongly recommends transradial approach in patients presenting with acute myocardial infarction (AMI) with- and without ST-elevation. This report summarizes feasibility of the transradial approach in an all-comers population presenting with AMI including those with previous coronary artery bypass surgery (CABG).

Methods: Transradial coronary catheterization was established in 2012 in our centre. Transradial coronary angiography is performed using 4F diagnostic catheters, while percutaneous coronary intervention (PCI) is routinely performed using 6.5 F sheathless catheters. The right radial approach was used as default in patients without previous CABG, while patients with previous CABG were examined using the left radial artery. The main criterion to use the transradial approach was a palpable radial pulse. Allen-Test was not routinely performed.

Results: In the time-period July 2014 to December 2015 a total of 893 AMI patients underwent cardiac catheterization in our institution. The mean age was 66±13 years, 26 % were female and 292 patients (33 %) had ST-elevation myocardial infarction (STEMI). In 716 patients (80.2 %) primary approach was transradial, while in 177 patients (19.8 %) primary approach was transfemoral. In 76 % of patients with STEMI primary approach was transradial. 61 patients (6.8 %) had previous CABG and in 27 (44.3 %) the primary approach was transradial. Overall crossover rate from radial to femoral was 3 % in the total population, 3.4 % patients with STEMI and 3.3 % in patients with previous CABG.

Conclusion: Transradial coronary angiography and PCI is feasible in the vast majority of patients including patients with previous CABG. Crossover rates are low in selected patients with good radial pulse. Efforts should be made to further increase the rate of ACS patients undergoing transradial coronary catheterization and treatment.

Disclosure of Interest: None Declared
Introduction: Robotic-assisted minimally invasive left internal thoracic artery (LITA) to left anterior descending (LAD) bypass takes advantage of the survival benefit of the LITA-to-LAD bypass while decreasing the morbidity of the procedure associated with the spreading of the sternum. The objective was to assess the clinical outcomes and graft patency at 3 years.

Methods: From March 2011 to July 2014, 17 consecutive patients were operated with robotic LITA harvesting and then manually anastomosed to the LAD on the beating heart through a small anterior thoracotomy. Patients underwent a coronarography (n=6) or CT angiography (n=11) at 1 year after the operation.

Results: All patients were successfully revascularized as planned. There were no early or late deaths. All the patients were fast tracked, with extubation during the first 2 hours in the ICU and for 6 of them in the operating room. The mean hospital stay was 4 ± 1.1 days. No patient required reoperation or re-exploration for bleeding. Follow-up ranged from 24-36 months. At 1 year, all patients had a patent LITA-LAD anastomosis.

Conclusion: Robotic LITA takedown and minimally invasive off-pump revascularization results in excellent perioperative outcomes, high graft patency and freedom from angina during follow-up.

Disclosure of Interest: None Declared
4. ACS, PCI, CABG

Omitting aspirin in patients requiring oral anticoagulation and undergoing percutaneous coronary intervention is safe in an all-comers population

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Introduction: Triple therapy with phenprocoumon (OAC) or direct oral anticoagulants (DOAC) with aspirin and clopidogrel is associated with a high rate of major bleedings reaching almost 25 % in the first 30 days after initiation. It is not clear whether a combination of OAC/DOAC plus clopidogrel (double therapy) is a safe option regarding thrombotic events, especially stent/scaffold thrombosis (ST) in an all-comers population undergoing PCI.

Methods: In 2014 the acute coronary syndrome (ACS) working group of central Switzerland decided not to apply triple therapy in every PCI patient requiring OAC/DOAC. The decision whether a double- or triple therapy is used is made on an individual basis after a careful bleeding- and ischemic risk assessment. A regional registry with 3- and 12-months follow-up was established. Ischemic events were defined as probable or definite ST. Bleeding events were categorized using the GUSTO definition: severe (life-threatening, intracranial or hemodynamic compromise) or moderate (requiring blood transfusion but not resulting in hemodynamic compromise). In this abstract 3-months follow-up for ST and bleeding rates are reported.

Results: In the period September 2014 to November 2015 a total of 122 patients were included in this registry. The mean age of the patients was 73±9 years and 31 (22 %) were women. 57 patients (47 %) had stable angina, 65 patients (53 %) had ACS including 19 patients with ST-elevation myocardial infarction. 97 patients (80.2 %) had double therapy with OAC/DOAC and clopidogrel, whereas 24 patients (19.8 %) had triple therapy with OAC/DOAC, clopidogrel and aspirin. Two of 97 patients (2.1 %) receiving double therapy had definitive ST: one 10 days post PCI on rivaroxaban plus clopidogrel and one 7 days post PCI on phenprocoumon plus clopidogrel. Both ST had a mechanical reason. No ST was seen in patients on triple therapy. In the double therapy group a total of three severe (3.1 %) and three moderate bleedings (3.1 %) were seen. In the triple therapy group there was one moderate (4.2 %) and no severe bleeding.

Conclusion: Omitting aspirin in patients requiring OAC/DOAC seems to be a safe option in all-comers. Two ST were observed within 10 days in the double therapy group but both had mechanical reasons. Bleeding rates within three months were low in the double and triple therapy group - however patients at high risk for bleeding were not treated with triple therapy.

Disclosure of Interest: None Declared
Introduction: Little is known about mechanisms underlying very late bioresorbable vascular scaffold (BVS) thrombosis (VLScT). We performed a systematic literature review to identify all reported cases of VLScT BVS with available intracoronary imaging at the time point of thrombosis.

Methods: By systematically reviewing the literature a total of 13 reports were identified reporting of 18 patients with VLScT.

Results: The median time between index implantation and thrombosis was 18 months (range 12 to 44 months). Seventeen patients underwent optical coherence tomography at the time point of VLScT, and one was assessed by intravascular ultrasound. Malapposition was reported in 10 patients (56%). Of those, strut discontinuity was observed in 6 patients (33%). Discontinued struts were completely apart from the luminal surface into the coronary artery (isolated struts) in 4 patients, and layered struts suggesting discontinuity were observed in 2 patients. Lumen loss characterized by small scaffold lumen area relative to reference vessel area at the time point of thrombosis was observed in 8 patients (44%). Uncovered struts were reported in 5 patients (29%). Neoatherosclerosis was observed in 2 patients (11%), of which neointimal rupture with mural thrombus with proximal neoatherosclerotic lesions were reported in one patients, and OCT-derived macrophages as an innocent bystander in the other patient. At the time point of VLScT, 3 patients (25%) were reported to be on dual antiplatelet therapy (DAPT) and 6 patients (50%) on acetylsalicylic acid (ASA) alone with the remaining 4 patients (33%) without any antiplatelet therapy, while no medication status have been reported in 5 patients.

Conclusion: Malapposition was the leading mechanism underlying VLScT identified by intracoronary imaging with scaffold strut disintegration as the most frequent cause. Late lumen loss was an additional resorption-related cause of VLScT. The majority of patients suffering from VLScT were on ASA or DAPT, emphasizing the central role of local (scaffold-related) factors for development of the complication.

Disclosure of Interest: None Declared
Double wall-less cannulas for veno-venous ecmo
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Introduction: Contribution of veno-venous ECMO to gas transfer is flow dependent. Cannula design is a key factor for optimal pressure/flow rate relationship.

Methods: Two cannulas with modern design (dual-lumen 27F Avalon catheter versus wall-less Smartcanula 36F constricted to 27F plus wall-less Smartcanula 20F) were compared. Flow, pump inlet-pressure and outlet-pressure were determined at 1000, 2000, and 3000 RPM.

Results: At 1000, 2000, and 3000 rpm, double lumen catheter showed inlet flow values of 1.46±0.01, 3.14±0.02, 4.75±0.01 l/min versus 3.89±0.01*, 7.65±0.01*, and 11.52±0.01*l/min: p<0.05* for wall-less 36F constricted to 27F. The pump inlet negative-pressure values were -2.38±0.26, -28.89±0.66, -70.29±1.58 mmHg for double lumen versus -21.62±0.1*, -34.55±0.13*, and -83±0.13* mmHg, for wall-less- 36F restricted to 27F respectively. The outlet-pressure values for double lumen catheter were 33.22±0.11, 114.14±0.54, and 245.60±0.80 mmHg versus 4.16±0.08*, 23.75±0.06* and 68.68±0.09* mmHg for wall-less 24F. Double lumen catheter demonstrated outlet-flow values of 1.45±0.01, 3.04±0.01, and 4.63±0.01 l/min versus 3.92±0.01*, 7.83±0.01*, and 11.59±0.02* l/min for virtually wall-less 24F.

Conclusion: For this hydrodynamic study, double wall-less cannula provide up to 2.5 times more flow than the double lumen design despite similar access orifices (27F). Likewise, lower inlet and outlet pressure are generated with the wall-less design at corresponding flow rates.

Disclosure of Interest: None Declared
**Introduction:** Cardioplexol™ (formerly Cardioplex) was originally conceived to fit the emerging concept of minimally invasive extra-corporeal circulation (MECC). With its simple formulation essentially combining Potassium, Magnesium, Procain and Xylitol in a final volume of only 100 mL, it rapidly demonstrated numerous advantages including the quasi-immediate cardioplegic arrest that allows surgeons to perform their cardiac geste without any delay. Cardioplexol™ is currently used in a few centres in Switzerland. Until the end of 2015, more than 8'000 procedures have been performed in Bern with this solution. We report here on our experience between September 2008 (corresponding to the introduction of the final and current formulation of Cardioplexol™) to December 2014 (minimum follow-up of one year).

**Methods:** All consecutive cardiac surgical procedures (including ascending aorta and aortic arch) performed on-pump under cardioplegic arrest were considered. Transplantation, GUCH, trauma, pulmonary embolectomy and other non-typical procedures were excluded. Demographics, pre-, per- and post-operative data were retrieved from our prospectively maintained cardiovascular registry. After cleaning and checking for possible implausibility, data were analysed using Stata software and traditional statistics methods were applied. Data are presented as mean±SD.

**Results:** Isolated CABG with MECC and Cardioplexol was performed in 2'393 patients. From the 3'550 other (non-isolated CABG) procedures Cardioplexol was used to induce cardiac arrest in 3'261 patients and complemented with further regular (every 20 minutes) administration of Buckberg reperfusion solution. Cardioplexol was used alone in 171 cases that could be seen as straightforward (lower EUROScore, shorter X-clamp time). Buckberg was still used alone in 119 special situations (higher EUROScore, longer X-clamp time. Details of these groups are presented in Table 1. All surgical procedures could be performed without complication related to the Cardioplexol™ solution. Outcomes are similar to the best results to be found in the literature. Specific analysis of subcategories of risk groups will be presented in detail.

**Conclusion:** The currently cumulated 10 years experience of cardiac surgery with Cardioplexol™ at Inselspital show very satisfactory results and seem to confirm the reliability of this simple cardioplegic approach.

Immediate treatment and outcome of cancer patients with acute myocardial infarction

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Introduction: Cancer disease and its corresponding treatment have an important impact on the cardiovascular health of these patients. However, little is known on whether cancer patients receive adequate treatment and care after suffering an acute myocardial infarction (AMI). The aims of this study were to investigate whether AMI patients with a history of cancer receive the same kind of therapy as those without, and to determine how this affects outcome.

Methods: All patients with ST-elevation MI (STEMI) and non-STEMI (NSTEMI), enrolled since 2002 in the AMIS Plus registry with available data on co-morbidities based on the Charlson Comorbidity Index (CCI) were included in the analysis. Patients were classified as having cancer if one of the cancer diseases of the CCI was indicated. Immediate treatment and in-hospital outcome were compared between groups using propensity score matching.

Results: Of 35,249 patients, 1981 (5.6%) had a history of cancer. After propensity score matching for age, gender, Killip class>2, STEMI, and moderate to severe renal disease (1981 patients in both groups), there were no longer significant differences in hypertension, diabetes, cardiac insufficiency, cerebrovascular disease and past history of MI between cancer and non-cancer patients. No significant differences were found for a left ventricular dysfunction (angiographic ejection fraction below 35%: 10.9% vs. 9.5%; p=0.33 or echocardiographic below 30%: 11.9% vs. 11.4%; p=0.79). However, cancer patients underwent less frequently percutaneous coronary intervention (67.8 vs. 73.4%, OR 0.76; 95% CI 0.67-0.88) and received less frequently P2Y12 blockers (70.3% vs. 74.3%, OR 0.82; 95% CI 0.71-0.94) and statins (67.5% vs. 70.4%, OR 0.87; 95% CI 0.76-0.99). The use of aspirin (92.7% vs. 94.1%, OR 0.80; 95% CI 0.62-1.03) and beta blockers (60.4% vs. 60.9%, OR 0.98; 95% CI 0.86-1.11) was similar in both groups. In-hospital complications (cardiogenic shock, re-infarction, stroke and bleeding) did not differ between the groups. However, in-hospital mortality was significantly higher in cancer patients (10.7% vs. 7.6%, OR 1.45; 95% CI 1.17-1.81). The main cause of death was cardiac with no difference between the groups (p=0.06).

Conclusion: These results showed that cancer patients with AMI were less likely to receive evidence-based treatment and had worse in-hospital outcomes than non-cancer patients. This shows that there could be room for improvement in the treatment of cancer patients with AMI.

Disclosure of Interest: None Declared
Impact of new onset atrial fibrillation in ACS patients. Insights from the Swiss AMIS Plus Registry

L. Biasco, D. Radovanovic, H. Rickli, M. Roffi, F. Eberli, R. Jaeger, T. Moccetti, M. Moccetti, P. Erne, G. Pedrazzini

Introduction: Atrial fibrillation (AF) may be present either at admission or appear during hospitalization in patients with Acute Coronary Syndromes (ACS). In the present analysis, we aim to evaluate the impact of new onset AF in patients enrolled in the AMIS Plus registry.

Methods: Among 35,958 patients enrolled in the nationwide Acute Myocardial Infarction in Switzerland (AMIS) Plus registry between 2004 and 2015, 1,953 showed AF. Out of them, 1,644 showed AF at admission while 309 new onset of AF during hospital stay. Groups were compared with regard to clinical characteristics and outcome (in-hospital and 12 months mortality).

Results: Patients with new onset AF were younger (74.6±10.9 vs 76.8±10.7, p<0.001), less frequently hypertensive (RR 0.86; 95%CI 0.79-0.93, p=0.003) or with history of coronary disease (RR 0.77; 95%CI 0.65-0.91, p=0.002), heart failure (RR 0.51; 95%CI 0.31-0.85, p=0.009) or renal impairment (RR 0.72 95%CI 0.58-0.99, p=0.04), presented more frequently with STEMI (RR 1.29 95%CI 1.16-1.43, p<0.001) and needed more frequently hemodynamic support with vasopressors (RR 1.56 95%CI 1.18-2.07, p=0.002) and balloon counterpulsation (2.42 95%CI 1.67-3.51, p<0.0001). In hospital bleedings (6.5% vs 3.2%, RR 2.04 95%CI 1.23-3.38, p=0.005) and cerebrovascular events (4.2% vs 1.3%, RR 3.13 95%CI 1.59-6.15, p=0.001) were more common in new onset AF pts. In hospital (13.1% vs 10.7%, RR 0.9 95%CI 0.57-1.14, p=0.22) and one year (landmark) mortality (13.7 vs 12.1, RR 1.1 95%CI 0.53-2.38, p=0.73) were comparable among groups.

Conclusion: ACS Patients with new onset AF showed a lower baseline risk profile but a greater need of hemodynamic support and higher incidence of serious in-hospital complications with mortality rates comparable to pts with pre-existing AF.

Disclosure of Interest: None Declared
Abstract:

**Introduction:** Neutrophils are being recognized to contribute to the pathogenesis of atherosclerosis and ischemia-reperfusion injury after myocardial infarction. However, for risk stratification of patients with acute coronary syndromes (ACS), it remains unclear whether measuring the absolute neutrophil blood count provides incremental information when added to total leukocyte count, high-sensitive C-reactive protein (hsCRP) or high-sensitive Troponin T (hsTnT).

**Methods:** Between December 2009 and October 2012 a total of 2168 patients with the diagnosis of ACS referred for coronary angiography to 4 University Hospitals were enrolled into the Biomarker Cohort 1 of the Swiss SPUM-ACS study. Based on blood drawn at coronary angiography, total leukocyte, neutrophil (absolute and relative) and lymphocyte counts as well as neutrophil to lymphocyte ratio (NLR), hsCRP and hsTnT data were available in 1429 patients. The primary endpoint was defined as the adjudicated composite of cardiac death, myocardial infarction, or stroke within 30 days and 1 year after the index ACS. Correlations were assessed using uni- and multivariate logistic regressions. Prognostic accuracy of these biomarkers was determined using Receiver Operating Characteristic (ROC) curves at distinct cut-offs and Areas Under the Curve (AUC) were calculated. Comparison of two correlated AUCs was performed using DeLong's test.

**Results:** Absolute neutrophil count is an independent predictor for adverse events during 30 days post-ACS compared with total leukocyte count (OR 1.318, CI 1.043 – 1.713; p = 0.03), hsCRP (OR 1.093, CI 1.026 – 1.159; p = 0.004) and hsTnT (OR 1.094, CI 1.028 – 1.16; p = 0.004). Prognostic accuracy is moderate for all examined biomarkers to predict adverse events during 30 days (AUC 0.565 - 0.616) and 1 year (AUC 0.529 - 0.601). Combining absolute neutrophil count with hsCRP, hsTnT or total leukocyte count yields no improvement to predict adverse events during short- and long-term follow-up after an ACS.

**Conclusion:** In patients with an ACS referred for coronary angiography, absolute neutrophil count is an independent risk predictor, but does not improve risk stratification when added to total leukocyte count, hsCRP or hsTnT.

**Disclosure of Interest:** None Declared
A novel, low-volume cardioplegia is safe in protecting the myocardium during coronary artery bypass surgery

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Introduction: A novel, low-volume (100ml) crystalloid cardioplegia (CARDIOPLEXOL) is used to protect the myocardium during ischemia in coronary artery bypass surgery (CABG). We hypothesised that this novel cardioplegic strategy is safe and associated with low postoperative myocardial ischemia parameters independent of the severity of the coronary artery disease.

Methods: All consecutive patients undergoing CABG using the novel, low-volume cardioplegia and the minimised extracorporeal circulation (MECC) at the University Hospital Basel from 2013 to 2015 were included in the study. All clinical and laboratory data was prospectively collected. Myocardial ischemia parameters including creatine kinase MB (CK-MB) and troponin T (TnT) were compared among patient groups (isolated left main trunk stenosis (MT), severe three vessel disease (3VD) and those with combined MT and 3VD) using statistical tests as appropriate.

Results: A total of 387 patients underwent CABG, of those 11% were emergent procedures. The mean (±SD) age was 67 (±10) years, 86% of patients were male, the preoperative logistic EuroSCORE was 6 (±10). Aortic clamping time (=myocardial ischemic time) was 56 (±20) minutes, and the MECC perfusion time 91 (±31) minutes. ICU time was 4 (±7) days. 30-day mortality was 3%. Postoperative maximum values of CK-MB in those with MT (n=37) were 86 ug/l (±162), with 3VD (n=179) were 32 ug/l (±45) and those with combined MT and 3VD (n=128) 41 ug/l (±95); CK-MB in those with MT was increased compared to both other groups (p<0.04). Postoperative maximum values of TnT in those with MT (n=37) were 2.2 ug/l (±5.3), with 3VD (n=179) were 0.8 ug/l (±1.8) and those with MT and 3VD (n=128) were 1 ug/l (±3); TnT in those with MT was increased compared to those with 3VD (p<0.003), but not to those with combined MT and 3VD (p=0.06).

Conclusion: Use of the novel, low-volume cardioplegia (CARDIOPLEXOL) for elective and emergent CABG with the MECC is safe. However, patients with underlying isolated left main trunk disease might be less well protected compared to those with 3VD and combined MT and 3VD[ST1].

Disclosure of Interest: None Declared
Implantation of a modern drug eluting stent over a covered stent to treat coronary aneurysms: angiographic and optical coherence tomography follow-up of 3 patients

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Introduction: Covered Stents (CS) are being used to treat coronary aneurysms but they have relatively high event rates of in-stent-restenosis (ISR, up to 25-30 %) and stent thrombosis (ST, up to 6 % mostly occurring in the subacute phase). Delayed endothelialisation and susceptibility to thrombus formation are thought to be the reason for this phenomenon. Using a modern drug-eluting stent (DES) over a covered stent could facilitate endothelialisation and achieve a less thrombogenic surface in the long term. We describe our experience of 3 patients with coronary aneurysms treated with a combination of CS and DES.

Methods: After pre-dilatation with a non-compliant (NC) balloon a Polytetrafluorethylene (PTFE)-CS was implanted to seal the aneurysm. The CS was post-dilated using an NC balloon and a modern DES was implanted overlapping the edges of the CS. The procedure was finished with a final post-dilatation using a NC balloon. Clinical and angiographic follow-up was scheduled 6 months post PCI. Additionally optical coherence tomography (OCT) was performed.

Results: A total of three patients were treated, two with a post-stenotic aneurysm (one in a protected left main stenosis with a patent LIMA graft and one in right coronary artery), while one aneurysm was due to an ectatic form of coronary disease located in the right coronary artery but without stenosis. We used Papyrus CS (Biotronik) in two patients and BeGraft (Bentley) in one patient. Orsro sirolimus eluting stent (Biotronik) was used in two and Xience everolimus eluting stent (Abbott Vascular) in one patient to "overstent" the CS. Angiographic follow-up at 6 months demonstrated no in-stent-restenosis or thrombosis. OCT imaging showed a thin neointima without stenosis.

Conclusion: We describe a new method to treat coronary aneurysm using a combination of CS and DES. The DES surface might offer a more controlled endothelialization compared to CS. The encouraging results of this series need to be confirmed in a larger case series or randomized study.

Disclosure of Interest: None Declared
Introduction: Many millions of high altitude dwellers are exposed to chronic hypoxia. Recent data show that the presence of patent foramen ovale (PFO) in high altitude dwellers is associated with more severe hypoxemia and pulmonary hypertension. Chronic hypoxemia per se induces systemic and pulmonary vascular dysfunction. Aim of our study was to investigate if the presence of PFO in high altitude dwellers was associated with more severe hypoxemia and consequent systemic vascular dysfunction.

Methods: We included 46 Bolivian high altitude dwellers (mean age 42± 16 y.) without classical cardiovascular risk factors. The presence or absence of PFO was assessed by trans-esophageal echocardiography. To assess systemic vascular function we measured flow-mediated vasodilation (FMD) of the brachial artery, carotid-femoral pulse-wave velocity (PWV) and carotid intima-media thickness (IMT).

Results: PFO was present in 17/46 subjects (37%). The presence of PFO was associated with more severe hypoxemia (SaO₂ 86±6 vs. 89.5±3 %, P=0.04) and systemic vascular dysfunction (FMD: 6.6±2.9 vs. 5.0±1.6%, P=0.03; PWV: 10.0±2.2 vs. 8.5±1.1 m/s, P=0.03; IMT: 578±158 vs. 595±140 um, P=0.71). There was a significant positive correlation between SaO₂ and FMD (r=0.52, P<0.001) and an inverse relationship between SaO₂ and PWV (r=-0.66, P<0.001) and IMT (r=-0.47, P=0.001).

Conclusion: In high altitude dwellers without classical cardiovascular risk factors, the presence of PFO is associated with more severe hypoxemia and consequent systemic vascular dysfunction. We speculate that the presence of PFO in conditions associated with chronic hypoxemia accelerate the development of arteriosclerosis.

Disclosure of Interest: None Declared
PP-067

5. Epidemiology, risk factors, rehabilitation, thromboembolic disease

Non-alcoholic fatty liver disease strongly predicts incident diabetes in patients with coronary artery disease

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Introduction: Both coronary artery disease (CAD) and non-alcoholic fatty liver disease (NAFLD) are associated with type 2 diabetes. Whether NAFLD predicts future diabetes in CAD patients who do not have diabetes yet is unknown.

Methods: We therefore prospectively recorded diabetes incidence in a large cohort of 1018 consecutive non-diabetic patients with angiographically proven CAD; for the diagnosis of NAFLD we used the validated fatty liver index (FLI); diabetes was diagnosed according to ADA criteria.

Results: At baseline, 44.3% of our patients had impaired fasting glucose (IFG) and 55.2% had an HbA1c of 5.7-6.4% and thus were at risk of diabetes according to ADA categories. The prevalence of NAFLD was significantly higher in patients with IFG than in those with normal fasting glucose (46.8 vs. 34.0%; p<0.001) but not between patients with an HbA1c of 5.7-6.4% and those with an HbA1c <5.7% (40.8 % vs. 38.5 %; p=0.478). Prospectively, 11.2% of our patients newly developed diabetes during a follow-up period of 6.3±3.7 years; both IFG (OR 3.24 [2.03-3.32]; p=0.001) and an HbA1c of 5.7-6.4% (OR 5.90 [1.50-5.61]; p=0.002) significantly predicted incident diabetes. Importantly, diabetes incidence was significantly higher in patients with NAFLD than in those who did not have NAFLD (18.4 vs. 8.5 %; p<0.001), and NAFLD strongly predicted incident diabetes both univariately (OR 2.41 [1.56-3.73]; p<0.001) and after multivariate adjustment including both baseline fasting glucose and HbA1c (OR 1.76 [1.11-2.79]; p=0.017).

Conclusion: We conclude that NAFLD in patients with CAD strongly predicts incident diabetes independently from the baseline glycemic state.

Disclosure of Interest: None Declared
Introduction: Data on non-alcoholic fatty liver disease (NAFLD) in patients with the combination of both impaired glucose metabolism and established cardiovascular disease are scarce.

Methods: We therefore aimed at investigating its association with the glycemic state as well as its impact on cardiovascular event risk in a large series of 1791 patients with established cardiovascular disease (1472 patients with angiographically proven coronary artery disease and 319 patients with sonographically proven peripheral arterial disease) using the validated fatty liver index to diagnose NAFLD.

Results: At baseline, 42.5%, 36.5%, and 19.8% of our patients had normal fasting glucose (NFG), impaired fasting glucose (IFG), and type 2 diabetes (T2DM), respectively. The prevalence of NAFLD significantly increased from 34.2% over 52.2% to 62.7% through these categories of the glycemic state (p<0.001). Prospectively, we recorded 701 cardiovascular events over a mean follow-up period of 5.6±3.3 years. Cardiovascular event risk significantly (p<0.001) increased from 30.7% in patients with NFG over 33.3% in patients with IFG to 46.5% in patients with T2DM. NAFLD significantly predicted cardiovascular event risk both univariately and in age- and gender adjusted analyses (HRs 1.23 [1.05–1.45]; p=0.012 and 1.27 [1.08–1.50]; p=0.005, respectively), but not after additional adjustment for the glycemic state (HR 1.15 [0.97–1.37]; p=0.098).

Conclusion: We conclude that the prevalence of NAFLD in CAD patients is high and gradually increases with a worsening glycemic state; however, it does not predict cardiovascular events independently from impaired glucose metabolism in this patient population.

Disclosure of Interest: None Declared
Does prenatal detection screening influence the incidence of congenital heart disease (CHD)?

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Introduction: Detection rate for CHD in utero remains despite all efforts outside the perimeter of tertiary centers around 20-30% (FETCH data Switzerland 2005). To evaluate the screening success in the catchment area of the University Hospital in Bern we reviewed all in utero screenings from July 2009 to December 2014. In addition we looked at the incidence of CHD which should be around 0.8%. In Switzerland the current incidence of CHD is 0.5%.

Methods: Retrospective data analysis from July 2009 to December 2014 including all in utero and postnatal diagnosed new CHD at the Center of Perinatal Medicine at the University Hospital in Bern.

Results: 1522 in utero screenings have been performed. Of n=339 patients with new CHD, n=130 were born with an in utero diagnosis of CHD. n=43 died in utero (detection rate of 51.03%). Median RACHS for prenatal diagnosed children was higher than in the postnatal detected CHD patients (2.4 vs. 3.1). The current incidence of CHD in the catchment area of Bern lays with 0.25% significantly below the expected incidence of 0.5% in Switzerland.

Conclusion: This data clearly show that prenatal screening in the last years significantly improved from around 25% to currently 51% detection rate. In utero detected CHD has an overall higher RACHS in comparison with prenatally missed CHD, indicating that complex CHD is as of today better diagnosed in utero. Interestingly with a higher in utero detection rate we observe a decrease in the incidence of CHD postnatailly.

Disclosure of Interest: None Declared
5. Epidemiology, risk factors, rehabilitation, thromboembolic disease

Oxidative stress mediated systemic vascular dysfunction in offspring of preeclampsia evolve into arterial hypertension and may be prevented by anti-oxidants

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Introduction: Epidemiological studies have shown an association between pathologic events in early life and cardiovascular disease in adulthood. Previously, we showed that offspring of mothers with preeclampsia display vascular dysfunction related to increased oxidative stress and decreased plasma nitric oxide (NO) bioavailability. We hypothesized that systemic vascular dysfunction evolve into arterial hypertension and may be prevented by anti-oxidants.

Methods: Therefore, we measured 24h ambulatory blood pressure (ABPM) and assessed the effects of an acute intravenous infusion of antioxidant vitamins C (1 g) on systemic endothelial function (flow-mediated vasodilation (FMD)) in 10 offspring of preeclampsia and 12 age- and gender-matched controls.

Results: As expected FMD was impaired in offspring of preeclampsia (6.5±2.9 vs. 10.2±2.3 %, P<0.01). This vascular dysfunction translated into increased 24h systolic blood pressure (BP, 113±11 vs. 105±5 mmHg, P=0.02, offspring of preeclampsia vs. controls) and diastolic BP (72±9 vs. 65±5 mmHg, P=0.04, offspring of preeclampsia vs. controls). Importantly, vitamin C improved systemic vascular function (6.5±2.9 vs. 7.5±2.4 %, P=0.02) in offspring of preeclampsia, whereas it had no effects in controls.

Conclusion: Systemic vascular dysfunction in offspring of preeclampsia evolve into arterial hypertension and is, at least in part, related to increased oxidative stress. Accordingly, anti-oxidant administration improve endothelial dysfunction indicating that this problem is partially reversible. We speculate that early intervention aiming to decrease oxidative-stress prevent the development of arterial hypertension in offspring of preeclampsia.

Disclosure of Interest: None Declared
Combining high-sensitive C-reactive protein, high-sensitive troponin T and NT-pro B-type natriuretic peptide with the pulmonary embolism severity index risk score marginally improves risk stratification of elderly patients with pulmonary embolism


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Introduction: Inflammation, myocardial damage and heart failure are associated with prognosis after pulmonary embolism (PE). Yet, it remains unclear whether the combination of high-sensitive C-reactive protein (hsCRP), high-sensitive cardiac Troponin T (hsTnT) and NT-pro B-type natriuretic peptide (NT-proBNP) improves risk stratification of patients with acute PE beyond the Pulmonary Embolism Severity Index (PESI) risk score.

Methods: We analysed 232 patients aged ≥ 65 years with newly diagnosed PE enrolled into the prospective SWISS venous Thromboembolism COhort (SWITCO 65+) study with available blood samples drawn within 1 day after diagnosis. Associations between hsCRP, hsTnT and NT-proBNP and the primary outcome defined as 6-month mortality were assessed. The discriminative power of the PESI risk score and its combination with hsCRP, hsTnT, and NT-proBNP for all-cause mortality at 6 months was compared using the integrated discrimination improvement (IDI) index and the net reclassification improvement (NRI).

Results: Compared with the lowest quartile, patients in the highest quartile had a higher risk to die during the first 6 months (significant adjusted Hazard Ratio (HR) for both, hsTnT (12.03; 95% CI 2.09-69.24; p=0.005) and NT-proBNP (5.6; 95% CI 1.21-25.91; p=0.028), with a trend for hsCRP (3.04; 95% CI 0.83-11.07; p=0.092). Compared with the three biomarkers (c-statistic of 0.57 for hsCRP (not significant), 0.71 for NT-proBNP and 0.72 for hsTnT), the PESI risk score (c-statistic 0.78 (95% CI 0.71-0.85) had the highest prognostic accuracy for 6-month mortality. The combination of all three biomarkers individually or combined did not improve risk stratification when added to the PESI risk score as assessed by NRI. A marginal improvement was found when combining hsTnT with the PESI risk score as assessed by IDI (IDI 0.049, 95% CI 0.003-0.095; p=0.036) and the combination of all three biomarkers (IDI 0.067, 95% CI 0.015-0.119; p=0.011).

Conclusion: 6-month mortality can be predicted by the PESI risk score alone and is only marginally improved when combining it with hsCRP, hsTnT and NT-proBNP.

Disclosure of Interest: None Declared
Introduction: Recently, eHealth programs have become popular alternatives for phase II preventive cardiac rehabilitation (CR) programs. Additionally or even more importantly, eHealth training may provide optimal support for phase III maintenance training. Efficacy studies provide limited evidence in the absence of knowledge on patient acceptance.

Methods: A questionnaire including 7 questions was designed and distributed to patients who attended a 12-week ambulatory structured CR program at the conclusion visit between June 2013 and October 2015.

Results: Questionnaires of 478 patients were included in the analyses. Patients’ etiologies included coronary artery disease, chronic heart failure, grown-up with congenital heart disease (GUCH), diabetes, cancer, stroke, and peripheral artery disease. Mean age of the included population was 57.9±8.8 years, with 77% being male and 58% using a mobile phone. Travel distance to the center was 13±12 km linear distance corresponding to 42±24 min by public transport. Only 8% of the patients considered eHealth alone as a valid alternative to the ambulatory centre-based phase II CR and another 15% would welcome a combination of eHealth and structured ambulatory program in phase II. A greater percentage, namely 39% welcomed eHealth training for phase III. There was a greater acceptance of phase III eHealth training among patients younger than 65 years (46%) compared to only 25% in those 65 years and older. Patients willing to use an eHealth phase III training program were more likely to be male (p=0.017), mobile phone users (p<0.001), younger (p<0.001) and fitter (p=0.005). On a scale of € 10-100 per month, patients considering phase III eHealth training as an option would pay an average of € 27 per month for this service. Travel distance to the center had no influence on acceptance of eHealth training, neither for phase II nor phase III.

Conclusion: EHealth CR programs have poor patient acceptance for phase II training and moderate acceptability for phase III training. In a typical Swiss CR setting, travel distance has no influence on eHealth acceptance. Patients interested in eHealth CR training in phase III are younger than 65 years, and more likely to be male and fit.

Disclosure of Interest: None Declared
Introduction: Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are non-obese. We prospectively investigated the single and joint effects of obesity and of the MetS on diabetes incidence in patients with angiographically proven coronary artery disease (CAD).

Methods: Diabetes incidence was recorded over 6.1±3.7 years in a large cohort of 1063 patients with angiographically proven CAD. Obesity was defined as a BMI ≥30kg/m²; presence of the MetS was defined according to the harmonized consensus definition.

Results: From our patients, 698 were non-obese and did not have the MetS, 62 were obese but did not have the MetS, 184 were non-obese but had the MetS, and 119 were obese and had MetS. During follow-up, the overall incidence of diabetes was 12.1%, corresponding to 1.9% per year. Diabetes incidence was 6.7% in non-obese patients without the MetS. It was significantly higher in obese patients without the MetS (16.0%; p<0.001), in non-obese patients with the MetS (22.3%; p=0.009), and in obese patients with the MetS (24.4%; p<0.001). Diabetes incidence however did not differ significantly between obese or non-obese MetS patients (p=0.303) or between obese patients with and obese patients without the MetS (p=0.674).

Conclusion: We conclude that the incidence of diabetes in patients with CAD is high except among subjects who neither are obese nor have the MetS. Both, obesity and the MetS, increase diabetes risk; a metabolically healthy obese phenotype does not protect against the development of diabetes in this population.

Disclosure of Interest: None Declared
Diastolic rather than systolic or systolic/diastolic combined hypertensive response to exercise is more frequently observed in 2,476 consecutive exercise tests in a large tertiary referral center in Switzerland.

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Introduction: Irrespective of apparent ‘normal’ resting blood pressure (BP) in patients without diagnosed arterial hypertension or with optimally treated arterial hypertension, some individuals show an excessive elevation in BP with exercise, a condition termed exercise hypertension or ‘hypertensive response to exercise’ (HRE). So far, systolic HRE was reported more often than diastolic or systolic/diastolic (combined) HRE.

Methods: Between January 2009 and May 2012, 2,476 consecutive exercise tests were performed in our institution, a tertiary general cardiology all-comers outpatient clinic. We systematically analyzed all exercise tests with respect to elevated blood pressure at rest (>140/90 mmHg) and at maximal exertion or during the recovery period after exercise (i.e. systolic BP ≥ 210 mmHg in men or ≥ 190 mmHg in women or diastolic BP ≥ 110 mmHg in men or women). Clinical characteristics of all subjects that showed HRE were collected.

Results: Of 2,476 exercised patients, 484 (19.5%) patients had elevated BP during exercise (64.0±14.7 years, 70.5% males, coronary artery disease: 48.4%, valvular heart disease: 26.9%, diabetes: 21.9%, BMI 28.1±5.7 kg/m²), of whom 334 (69.0%) had a previously known arterial hypertension. An elevated office blood pressure was found in 172 (35.5% of all patient with elevated BP during exercise) subjects and therefore did not fulfill the criteria for HRE. The remaining 312 subjects with HRE, that represented 12.6% of all exercise tests, subdivided in 189 (60.6%) optimally treated hypertensive patients and 123 (39.4%) subjects without known arterial hypertension. Of all subjects with HRE, 128 had elevated diastolic (5.2% of all exercise tests, 41.0% of all that fulfilled criteria for HRE), 108 (4.3%/34.6%) elevated systolic and 76 (3.1%/24.3%) elevated combined (diastolic and systolic) response to exercise. Subjects with diastolic, systolic or combined HRE did not differ with respect to age, gender, body mass index, creatinine clearance, left ventricular ejection fraction; presence of coronary artery disease, valvular heart disease, diabetes, sinus rhythm; or positive family history of arterial hypertension.

Conclusion: In our institution, hypertensive response to exercise was found in 12.6% of all exercise tests. Contrary to previous observations, diastolic HRE was found more often than systolic or combined HRE, and subjects with diastolic, systolic or combined HRE did not differ significantly.

Disclosure of Interest: None Declared
Introduction: Remnant cholesterol recently has attracted interest as a marker of cardiovascular event risk and is associated with the metabolic syndrome as well as with type 2 diabetes (T2DM). However, it is unknown whether remnant cholesterol also predicts the development of diabetes in patients who do not have diabetes yet.

Methods: We prospectively recorded incident diabetes over 6.1±3.7 years in 861 consecutive non-diabetic Caucasian patients with angiographically proven coronary artery disease (CAD). Diabetes was diagnosed according to ADA criteria.

Results: At baseline, 41.3% of our non-diabetic CAD patients had impaired fasting glucose (IFG); remnant cholesterol was significantly higher in IFG than in NFG patients (23±21 vs. 19±22 mg/dl; p<0.001). During follow-up, diabetes was newly diagnosed in 111 patients, i.e. in 12.9% of the study population. Remnant cholesterol strongly predicted diabetes both univariately (OR 1.88 [1.56-2.27]; p<0.001) and after multivariate adjustment including both fasting glucose and HbA1c values (OR 1.40 [1.40-2.11]; p<0.001).

Conclusion: We conclude that the incidence of diabetes is high in patients with established CAD and that remnant cholesterol strongly and independently predicts the development of diabetes in this population.

Disclosure of Interest: None Declared
Introduction: Acute type A aortic dissection (ATAAD) is the most frequently diagnosed lethal condition of the aorta. Malperfusion of aortic side branches is among others the cause of a significant burden of morbidity and mortality. Bronchial arteries are small aortic branches following the bronchial tree to irrigate the lung parenchyma. They can be visualized by computed tomography (CT) and play a role notably in lung infection defense, mucociliary clearance and post-ischemic re-perfusion oedema clearance.

Our hypothesis was therefore to evaluate whether bronchial artery malperfusion was associated with postoperative pulmonary complications in patients operated on for ATAAD.

Methods: We reviewed the pre-operative CT of the last 40 consecutive patients with ATAAD operated at the CHUV between March 2014 and December 2015. Bronchial arteries permeability on CT, postoperative intubation time, intensive care unit (ICU) stay as well as respiratory complications were collected. 15 patients were excluded due to lack of imagery or data.

Results: 25 operative survivors were included in the study. Bronchial malperfusion was observed on preoperative CT scan in 9 (36%) patients. Mean postoperative ventilation time and duration of ICU averaged 3.24 (±3.31) and 6.6 (±5.02) days respectively. We found no difference in the postoperative duration of ICU stay in patient with (6.22±2.74 days) and without (6.81±5.92 days; p=0.39) bronchial malperfusion. In contrast, postoperative mechanical ventilation time was significantly shorter for patient with bronchial artery malperfusion on the preoperative CT than in those without (1.56±1.26 vs 4.18±3.71 days respectively; p=0.03). Respiratory complications (pneumonia, atelectasis or respiratory failure) were noted in 11 (44%) patients. Their incidence was not statistically different between patients with (5 patients, 55.5%) or without bronchial artery malperfusion (6 patients, 37.5%; p=0.38).

Conclusion: We couldn’t demonstrate any significant relationship between bronchial artery malperfusion and the outcomes measured. Limitations of our analysis came from the limited number of patients and the difficulties to visualize the whole bronchial circulation on CT due to the size of those arteries and their numerous existing anatomic variations. Moreover, anastomoses between bronchial arteries and pulmonary alveolar microvessels originating from the pulmonary arteries, called bronchopulmonary arteries, could explain the lack of impact of their malperfusion.

Disclosure of Interest: None Declared
5. Epidemiology, risk factors, rehabilitation, thromboembolic disease

Publication rates and impact factors of accepted abstracts presented during the sgk congresses 2011 to 2014 in the field of risk factors and epidemiology

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Introduction: The SGK congress is the most important national platform for young and established Swiss researchers where they present their work to a broad scientific public. An increasing number of abstracts are submitted every year and eminent reviewers rate them to the best of their knowledge. Accepted abstracts and talks or posters presented at the congress are praiseworthy, but more important is their publication in important international journals. Aim of this study was to determine publication rates and impact factors (IF) and analyse the temporal trend in the field of risk factors and epidemiology.

Methods: In November 2015 we downloaded the abstract books (available as PDF under http://www.cardiovascular-medicine.ch) and extracted all talks and posters presented during the SGK congresses 2011 to 2014. We assessed in PubMed whether a paper has been published and, when yes, in which journal with which IF (always determined in the respective publication year). We excluded case reports, papers published more than at least 6 months before the congress and all abstracts presenting national data from a multicentre study (unless the first author of the published paper was from Switzerland). The percentage of published papers and their mean and median IF was calculated overall and per year.

Results: Rates ranged from 39% to 57% and mean IF from 3 to 5. 1. Table 1 shows the rate of published papers and IFs across the four years in more detail.

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>Overall</th>
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<tr>
<td>Submitted</td>
<td>24</td>
<td>17</td>
<td>16</td>
<td>19</td>
<td>76</td>
</tr>
<tr>
<td>Excluded</td>
<td>3</td>
<td>3</td>
<td>8</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>Published (%)</td>
<td>9 (42.9)</td>
<td>8 (57.1)</td>
<td>4 (50)</td>
<td>7 (38.9)</td>
<td>28 (45.9)</td>
</tr>
<tr>
<td>IF mean</td>
<td>4.7</td>
<td>5.1</td>
<td>3</td>
<td>3.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>±3.5</td>
<td>±4.7</td>
<td>±0.7</td>
<td>±1.2</td>
<td>±3.2</td>
</tr>
<tr>
<td>IF median</td>
<td>3.8</td>
<td>4.2</td>
<td>2.9</td>
<td>3.5</td>
<td>3.4</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>1.9-7.3</td>
<td>2.1-6.4</td>
<td>2.3-3.7</td>
<td>2.3-4.7</td>
<td>2.2-5.9</td>
</tr>
</tbody>
</table>

Conclusion: Abstracts in the field of risk factors and epidemiology presented during the SGK congresses have a high likelihood of being published, usually in papers with a good IF. This indicates the good quality of cardiology research in Switzerland.

Disclosure of Interest: None Declared
PP-078
5. Epidemiology, risk factors, rehabilitation, thromboembolic disease
The visceral adiposity index predicts cardiovascular events both in coronary artery disease patients with and in coronary artery disease patients without diabetes
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Introduction: The visceral adiposity index (VAI) is a validated tool for the evaluation of visceral adiposity, using waist circumference, serum triglycerides, age and gender to diagnose this metabolic abnormality. It has recently been associated with cardiovascular risk in primary care patients. No data are available on the association of the VAI with mortality in patients with established CAD.

Methods: We therefore calculated the VAI in 1472 consecutive patients with angiographically proven stable CAD according to the Amato formula. T2DM was defined according to the ADA definition. The incidence of vascular events was recorded over 10 years.

Results: At baseline, the VAI was significantly higher in CAD patients with T2DM than in those without diabetes (362±330 vs. 247±224; p <0.001). Prospectively, 539 vascular events occurred; the event rate were significantly higher in patients with T2DM than in those who did not have diabetes (44.8% vs. 33.7%; p<0.001). The VAI significantly predicted cardiovascular events in CAD patients with T2DM (standardized adjusted hazard ratio (HR) 1.16 [1.01-1.33]; p=0.037) as well as in those without T2DM (HR 1.14 [1.02- 1.27]; p=0.018).

Conclusion: We conclude that the VAI predicts cardiovascular events both in CAD patients with and in CAD patients without diabetes.

Disclosure of Interest: None Declared
Introduction: Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker in various patient populations. Its power to predict cardiovascular events in metabolic syndrome (MetS) patients undergoing coronary angiography is unclear.

Methods: We therefore measured serum proBNP in 752 patients who underwent coronary angiography for the evaluation of suspected or established coronary artery disease (CAD). Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing ≥50%. Presence of the MetS was defined according to the current harmonized consensus definition. Prospectively, we recorded vascular events over 5.1±2.4 years.

Results: ProBNP was significantly higher in patients with (n=591) than in subjects without significant CAD at baseline (715±1361 vs. 652±1842 pg/ml; p=0.003). Prospectively, we recorded 185 cardiovascular events. The incidence of vascular events significantly increased over tertiles of proBNP in patients with the MetS (15.8%, 24.2%, and 60.0% respectively; p=0.033) as well as in subjects without the MetS (13.3%, 22.2%, and 64.4%, respectively; p=0.004). Concordantly, serum proBNP significantly predicted the incidence of cardiovascular events after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol, HDL cholesterol and the eGFR both in patients with the MetS (standardized adjusted HR 1.34 [1.14-1.58]; p<0.001) and in subjects without the MetS (HR 1.24 [1.11-1.39]; p<0.001). These results were not attenuated after further adjustment for the angiographically determined baseline CAD state in patients with the MetS nor in subjects without the MetS (HRs 1.34 [1.14-1.57]; p<0.001 and 1.42 [1.24-1.63]; p<0.001, respectively).

Conclusion: We conclude that serum proBNP predicts cardiovascular events independently of established cardiovascular risk factors and of the baseline CAD state both in patients with and in subjects without the MetS.

Disclosure of Interest: None Declared
Introduction: Elevated thyroid stimulating hormone (TSH) is associated with cardiovascular risk factors, in particular with hypercholesterolemia, diabetes and obesity. We investigated the association between TSH and cardiovascular mortality in non-obese patients with or without type 2 diabetes (T2DM).

Methods: We measured TSH in a high-risk cohort of 1741 non-obese patients undergoing coronary angiography for the evaluation of suspected coronary artery disease. Prospectively, the incidence of vascular events was recorded over 10 years.

Results: At baseline, TSH was not significantly different between patients with T2DM (n=502) and those who did not have T2DM (2.31±4.59 vs. 2.06±2.66 µU/ml; p=0.446). During follow-up, 553 patients suffered vascular events; the event rate was significantly higher in patients with T2DM than in non-diabetic subjects (40% vs. 29%; p<0.001). TSH proved to be a strong and independent predictor of vascular events in non-obese patients without T2DM (standardized adjusted HR 1.34 [1.03-1.66]; p=0.013), but not in those with T2DM (HR 0.963 [0.894-1.037]; p=0.315). An interaction term TSH x T2DM was significant (p=0.026), indicating that TSH was a significantly stronger predictor of vascular events in non-obese subjects without T2DM than in those with T2DM.

Conclusion: We conclude that the power of thyroid stimulating hormone to predict cardiovascular mortality in non-obese patients is significantly modulated by the presence of T2DM.

Disclosure of Interest: None Declared
Introduction: The purpose of this study was to compare the safety and efficacy of intracardiac echocardiography (ICE) as an alternative imaging modality to transesophageal echocardiography (TEE) for left atrial appendage occlusion (LAAO).

Methods: All consecutive single center, single operator LAAO candidates were analyzed. Baseline clinical and procedural characteristics and in-hospital outcomes were compared between patients in whom a Watchman was implanted with ICE versus TEE guidance.

Results: Of 65 patients scheduled for LAAO three were excluded because of unsuitable anatomy in two and thrombus in the appendage in one patient. In 62 consecutive patients the Watchman device was deployed under ICE in 20 patients (32%) and under TEE guidance in 42 patients (68%). Baseline characteristics and clinical indications were comparable between groups, except that patients in the TEE group were older than those in the ICE group (79 ± 9 years vs. 74 ± 9 years, p = 0.02). Of the TEE guided LAAO 16 (38%) were combined with transcatheter aortic valve implantation. The CHA2DS2-VASc score (3.95 vs. 4.24; p = 0.3) and the HAS-BLED score (3.55 vs. 3.67; p = 0.59) did not differ between ICE and TEE patients, respectively. Total injected contrast media as well as fluoroscopy time were comparable between groups (94.2 ml vs. 89.5 ml, p = 0.612 and 10 min 11 sec vs. 9 min 29 sec, p = 0.574, for TEE versus ICE, respectively). However, time from femoral venous puncture to transseptal puncture and to closure was longer in the ICE group than the TEE group (8.03 min vs. 14.93 min, p = 0.003 and 37.9 min vs. 47.18 min, p = 0.014, respectively). In the TEE group one patient suffered esophageal erosion with bleeding, which was managed conservatively and one non-LAAO related in-hospital mortality occurred in an 88-year-old patient after multiple other interventions. Device implantation success rate was 100% in both groups. No device embolization, no significant peri-device leak, no new pericardial effusion, no tamponade, no stroke and no access site bleeding occurred in any patient. Total hospital stay for stand-alone LAAO was comparable between groups (2.3 ± 1.3 days vs. 2.8 ± 1.5 days, p = 0.168, in ICE versus TEE, respectively).

Conclusion: ICE guidance for LAAO with the Watchman device was safe and effective compared to TEE. Furthermore, ICE guidance for LAAO precludes the need for general anesthesia and may become the preferred imaging modality for LAAO.

Introduction: Diseases characterized by chronic intermittent hypoxemia are associated with increased cardiovascular morbidity and mortality, but the exact contribution of hypoxemia per se to these problems is unknown and difficult to investigate due to the presence of confounding factors. Congenital central alveolar hypoventilation syndrome (CCHS) is characterized by chronic intermittent hypoxemia in the absence of any other known potential confounding cardiovascular risk factor. CCHS, therefore, offers a unique opportunity for testing the hypothesis that intermittent hypoxemia per se causes vascular dysfunction in young apparently healthy humans.

Methods: To test this hypothesis, in the systemic circulation, we assessed pulse wave velocity (PWV, a proxy of vascular stiffness) and carotid intima-media thickness (IMT) in 14 patients with CCHS (age: 18.6±4.1 y) and 15 healthy age and sex matched controls (17.9±1.5 y). To assess pulmonary vascular function, we measured the right-ventricular-to-right-atrial (RV/RA) pressure gradient using transthoracic echocardiography.

Results: The main new finding was that in patients with CCHS, both the systemic and pulmonary vascular function were altered, as evidenced by 1) an increased PWV (8.0±1.2 vs. 7.0±0.9 m/s, P=.02, CCHS vs. control) and IMT (418.4±34.2 vs. 367.7±50.6 µm, P<.01, CCHS vs. control) in the systemic circulation and 2) an increased RV/RA pressure gradient (25.8±8.0 vs. 20.0±4.3 mmHg, P=.03, CCHS vs. control).

Conclusion: These findings provide the very first evidence that young apparently healthy patients suffering from congenital central alveolar hypoventilation syndrome, in the absence of any additional known cardiovascular risk factor, display systemic and pulmonary vascular dysfunction. These findings indicate that chronic intermittent hypoxemia per se causes generalized vascular dysfunction in humans. Moreover, our findings suggest that patients with CCHS may be at increased cardiovascular risk.

Disclosure of Interest: None Declared
Introduction: Presumed paradoxical embolism (PPE) includes stroke, brain abscess or myocardial infarction; and can occur in patients (pts) with interatrial shunting. It is more common in those with right-sided heart disease and previous pacemaker implantation. Previous small cohort studies have shown a substantial risk in patients (pts) with Ebstein Anomaly (EA).

Methods: We performed a retrospective analysis of 982 pts with EA from a single institution treated between 1963 and 2013. Perioperative strokes were not included as PPE.

Results: The average age at most recent follow-up was 30±20 years. PPE was recognized in 108 pts (11%); including stroke/transient ischemic attack in 100 pts (10.2%); brain abscess in 8 pts (0.8%); and embolic myocardial infarction in 3 pts (0.3%). Median age at occurrence was 31.5 years (0.1-73 years); with 52 (48%) events occurring in pts below the age of 30 in this group. The strongest predictor of PPE using univariate analysis was interatrial shunting (p <0.0001) and migraine/headaches (p = 0.0048) (Table). Reduced left ventricular function, left atrial enlargement and/or atrial arrhythmia trended to be more common in the patient with PPE. Pacemaker implantation was not predictive (p 0.23). 86% of these pt needed cardiac operation.

Legend: EA = Ebstein anomaly; PPE = presumed paradoxical embolic event; PFO = patent foramen ovale; ASD = atrial septal defect; LV = left ventricle

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>All pt</th>
<th>No PPE</th>
<th>PPE</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Age last control, years</td>
<td>30±20</td>
<td>28±20</td>
<td>42±19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female sex</td>
<td>58%</td>
<td>51%</td>
<td>61%</td>
<td>ns</td>
</tr>
<tr>
<td>Severity EA</td>
<td>80%</td>
<td>79%</td>
<td>86%</td>
<td>ns</td>
</tr>
<tr>
<td>PFO/ASD</td>
<td>78%</td>
<td>76%</td>
<td>94%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left atrial enlargement</td>
<td>14%</td>
<td>13%</td>
<td>21%</td>
<td>0.06</td>
</tr>
<tr>
<td>Decreased LV function</td>
<td>19%</td>
<td>18%</td>
<td>28%</td>
<td>0.05</td>
</tr>
<tr>
<td>Atrial/flutter</td>
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<td>25%</td>
<td>35%</td>
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</tr>
<tr>
<td>Arterial hypertension</td>
<td>9%</td>
<td>9%</td>
<td>15%</td>
<td>ns</td>
</tr>
<tr>
<td>Smoking</td>
<td>13%</td>
<td>13%</td>
<td>17%</td>
<td>ns</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>10%</td>
<td>9%</td>
<td>16%</td>
<td>ns</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>21%</td>
<td>25%</td>
<td>23%</td>
<td>ns</td>
</tr>
<tr>
<td>Migraine/headache</td>
<td>21%</td>
<td>20%</td>
<td>33%</td>
<td>0.0048</td>
</tr>
</tbody>
</table>

Conclusion: The incidence of PPE in pts with Ebstein Anomaly is substantial, and especially in the younger pt. This has important implications for the management of this group, and should likely influence the timing of the cardiac operation.

Disclosure of Interest: None Declared
Prosthetic pulmonary valve endocarditis: increasingly recognized but often with delayed diagnosis

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¹UniversitätsSpital Zürich, Zürich, Switzerland

Introduction: Among adults with congenital heart disease, a growing number of patients have pulmonary valve replacement (PVR) with bioprosthetic valved conduits. Recent studies have shown a high risk of infective endocarditis in this cohort. As pulmonary valve endocarditis is uncommon in patients with acquired heart disease, diagnosis of infective endocarditis in patients after PVR may be delayed. The aim of this study was to characterize patients with prosthetic pulmonary valve endocarditis with a focus on delay between onset of symptoms and diagnosis.

Methods: All patients with prosthetic pulmonary valve endocarditis between 2008 and 2015 were identified from our clinical database. Patient characteristics, clinical and echocardiographic presentation, causative organism, time from onset of symptoms to diagnosis of endocarditis and antibiotic treatment prior to diagnosis were assessed by chart review.

Results: A total of 11 patients with bioprosthetic pulmonary valve endocarditis were identified (mean age at diagnosis 28.5 ± 11.6 years, 73% male, at a mean of 80 ± 38 months after conduit implantation). Type of prosthetic conduits and type of causative organism are shown in figure 1 and 2. The majority of patients (72%) presented with valvar dysfunction (55% new or worsening obstruction, 18% with regurgitation). Median time from onset of symptoms to diagnosis was 28 days (range: 5-133 days). In 9/11 (82%) patients a delay of > 7 days was observed. Delay was caused mainly by the patient in 2 cases, mainly by physicians in 5 cases and by both in 2 cases. Before admission to the specialist center, 10 patients (91%) had undergone assessment at a local hospital or by a general practitioner. In these patients the diagnosis was not suspected or missed in 7/10 patients. Five patients (45%) received a course of antibiotics without prior blood cultures and 5 patients (45%) had an echocardiography before transfer to the specialist center. In 4 of these 5 echocardiographic studies the diagnosis of infective endocarditis was missed.

Picture/Graph:

Type of bio-prosthetic conduit

- Homograft 9%
- Stented bioprosthesis 18%
- Percutaneous pulmonary valve 18%
- Bovine jugular vein graft 55%

Picture/Graph 2:
Conclusion: The diagnosis of prosthetic pulmonary valve endocarditis is often delayed. Both, patients and physicians contribute to this delay. Better patient education and early referral to specialist centers may improve timely diagnosis and early initiation of appropriate therapy.

Disclosure of Interest: None Declared
Introduction: Population based studies show a steady increase in adult patients with congenital heart defects. The aim of this study was to assess the evolution of such a patient cohort and its burden on clinical care at a dedicated tertiary care center.

Methods: All patients with congenital heart disease followed by a dedicated multi-disciplinary team at our institution between 1996 and 2015 were identified (n = 1,725). Disease characteristics, the increase in patient numbers and interventions and the increase in selected complications were analyzed and compared between the first (1996-2005) and the second decade (2006-2015) of the study period.

Results: The majority of patients (1'125/1'750 patients, 65%) had lesions of moderate or great complexity. Between the first and the second decade of the study period, the number of patients under follow-up increased by 109%, and the number of outpatient visits increased by 195% (see figure 1). The number of patients who died more than doubled comparing the first decade of the study period (29 deaths) and the second decade of the study period (63 deaths). One fourth of all patients underwent at least one surgical procedure in adulthood and 14% had at least one percutaneous intervention. The increase in surgical procedures between the two decades was 27% and the increase in percutaneous interventions 159%. Between the two decades the number of patients requiring direct current cardioversion increased from 32 to 95 (+197%), the number of patients requiring admission for infective endocarditis increased from 7 to 29 (+314%) and the number of women followed during a pregnancy increased from 18 to 115 (+539%).

Conclusion: Due to the increasing number and complexity of adult survivors with congenital heart disease more resources will be needed to cope with the demands of this novel cohort of complex patients in adult cardiology.

Disclosure of Interest: None Declared
Patient characteristics and perceived self-efficacy in adult patients with congenital heart disease

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Introduction: Congenital heart disease (CHD) is a chronic disorder. During their lifetimes, most adults with repaired CHD will face long-term complications such as heart failure, arrhythmias, and re-operations. Perceived self-efficacy has been recognized as an important and positive element for people living with chronic diseases. It describes a person’s belief in one’s own competence to tackle difficult life situations and cope with hardships. Thus far, no study investigated the level of self-efficacy in adults with CHD. We aimed to assess perceived self-efficacy in adult CHD patients in relation to patients’ characteristics.

Methods: As a sub-study of the cross-sectional, multicentre study of patient-reported outcomes in CHD (APPROACH-International Study), data from 454 adults with CHD from Switzerland and Canada were included. The 10-item General Self-Efficacy (GSE) questionnaire was used to assess patients’ self-efficacy. We investigated whether GSE scores differed as a function of socio-demographic variables (sex, age, marital status, children, graduation, religion), mood disorders and/or CHD variables (severity of CHD, number of cardiac surgeries, cardiac devices, history of congestive heart failure or arrhythmias).

Results: Of the total sample, 45% of the patients were female and the mean age was 35 ± 13.5 years; 50% were highly educated. Twenty percent of the patients had mild, 49% moderate, and 31% severe CHD. The mean GSE score was 30.1 ± 3.3, which is close to GSE scores observed in the general population (mean = 29.4). There was a statistical difference in self-efficacy between males and females (GSE score 30.6 ± 4.9 vs. 29.5 ± 5.4, p<.02). No associations were found between GSE score and the other socio-demographic, mood disorders or CHD variables.

Conclusion: In CHD patients, the GSE score is not affected by disease severity and comparable to the GSE score in the general population. As explanation, we hypothesize that adults living with a pediatric-onset medical condition have grown up accustomed to the heart-related disease burden and have developed sufficient coping abilities. Although the mean score for males was higher than the mean score for females, the literature suggests that this is unlikely to be clinically meaningful.

Disclosure of Interest: None Declared
Flow pattern and vascular distensibility of the pulmonary arteries in patients after repair of tetralogy of fallot. Insights from 4d flow cmr
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Introduction: Pulmonary regurgitation is a frequent sequela after repair of tetralogy of Fallot (TOF). The regurgitant flow may lead to changes in the flow profile and in size and distensibility of the pulmonary arteries (Pas). We sought to assess Pa flow and distensibility in TOF patients (pts) by cardiac magnetic resonance (CMR) and to correlate them with the flow patterns provided by 4D flow CMR.

Methods: 18 TOF pts (mean age 28±11yrs, weight 63±12 kg) and 9 control subjects (age 17±7yrs, weight 63±24kg) underwent CMR. 2D Phase-contrast (PC) images were acquired through-plane in the main (MPA), right (RPA) and left pulmonary artery (LPA). A 4D PC dataset was acquired covering all the great arteries. Vessel areas and quantitative flow were measured on the 2D PC images. The flow patterns in MPA, RPA and LPA were qualitatively assessed for presence of helix or vortex on the reconstructed 4D images. Flow parameters, size and distensibility of the Pas were compared between TOF pts and controls and in the TOF group between RPA and LPA with regard to helix/vortex.

Results: In TOF pts, MPA mean regurgitant fraction (RF) was 25±17%. Compared to controls, both Pas were larger and distensibility was higher in LPA (p 0.048) but not in RPA. RF was greater in LPA than in RPA (29±19% vs 16±14%, p 0.001) and LPA area was larger than RPA area (316±134 vs 257±116 mm2/m2, p 0.0342). LPA net flow was lower than RPA net flow (p 0.0005). Distensibility was similar in LPA and RPA and significantly correlated with RF, regurgitant flow and minimum area in both Pas branches.

By 4D flow, vortex was observed in the LPA in 72% (13/18) of TOF pts, but not in normals. Helical flow was present in 44% (8/18) of pts and in 11% (1/9) of normals. Presence of vortex in the LPA was independent from any other parameter; LPA helix was more frequent in pts with higher distensibility (p 0.04).

RPA presented helical flow in 77% (14/18) of TOF pts and in 55% (5/9) of controls. Vortex was only detected in 11% (2/18) of TOF pts. RPA helical flow was not correlated to other parameters.

Conclusion: In pts after TOF repair, Pas size and distensibility are mainly determined by the amount of regurgitant flow and less by specific flow patterns, such as vortex or helix. Characteristic flow patterns are found in LPA and RPA, which seem to be more related to the geometry of the pulmonary bifurcation and its branches than to quantitative flow parameters.

Disclosure of Interest: None Declared
Introduction: The wall shear stress (WSS), defined as the force per unit area a flowing liquid exerts on a solid boundary, is being discussed as an essential feature of atherosclerosis plaque formation. In order to test this in the small animal model, the goal of this doctoral thesis is to develop and validate for the first time a method by which the WSS in the mouse aorta can be quantified via high field magnetic resonance tomography (17.6 T).

Methods: A 2D phase contrast magnetic resonance imaging (PC MRI), which enables the measurement of blood flow velocity in very narrow vessels, was optimized for the measurement of the WSS via several flow phantoms. The method was validated via comparison with the calculated WSS of well known flow profiles. Subsequently, C57BL/6N mice (n = 5, age 11-18 weeks, weight 22.8-24.9 g) were examined using this technique (sequence parameters: TR = 5 ms, slice thickness = 1 mm, flip angle = 35°, matrix size = 250 x 200, FOV = 25 x 20 mm, 2 averaging, spatial resolution 0.1 mm/pixel x 0.1 mm/pixel). The MR section planes were located in the ascending aorta, before the descension of the brachiocephalic artery, in the descending aorta, after the descension of the left subclavian artery, and in the abdominal aorta (figure 1). The heartbeat and breath were triggered via a pressure balloon on the mouse’s chest. The WSS and the flow were measured throughout the whole cardiac cycle. The flow and WSS were then used to calculate the oscillatory shear index (OSI), which quantifies the change of direction of the WSS within a cardiac cycle as a further potentially important predictor of plaque formation.

Results: The validation experiment in flow phantoms showed that the determination of the WSS via MR can be reliably carried out. Both the wall shear stress and the oscillatory shear index were reliably quantifiable in vivo in the mouse aorta in the selected analysis levels. There was a correlation between the WSS or the oscillatory shear index (OSI) on the respective levels of analysis in the mouse aorta (figure 2).

Figure 1: Analysis level 1-4 (left) or 5 (right) in the mouse aorta, in which the WSS and OSI were determined

Figure 2:
Conclusion: Thus, it is now possible to sequentially study the influence of the blood vessel wall interaction on the atherosclerosis in the model.

Disclosure of Interest: K. Riedl Grant/ research support from: Otto-Hess-Scholarship from the German Cardiac Society, T. Kampf: None Declared, P. Winter: None Declared, V. Herold: None Declared, W. Bauer: None Declared
Association between hepatic stiffness by elastography and liver fibrosis in adult fontan patients
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Introduction: Liver disease has been identified as an important long-term complication in patients after Fontan palliation. Hepatic ultrasound with measurement of hepatic stiffness has been proposed as a screening method.

Methods: Since 2014 all Fontan patients followed at our center undergo screening for liver disease by hepatic ultrasound with measurement of hepatic stiffness by elastography. Patients with elevated liver stiffness are offered transjugular liver biopsy with concomitant measurement of Fontan pressures and transhepatic pressures. For the purpose of this study, all adults with Fontan palliation, who had undergone hepatic ultrasound with elastography were identified from our registry. Findings on hepatic ultrasound and correlation with liver fibrosis in those who had undergone biopsy were analyzed.

Results: A total of 16 patients underwent hepatic ultrasound with elastography (mean age 31.9 +/- 8.0 years, 43% males, mean duration after Fontan operation 25.2 +/- 3.9 years). Median hepatic stiffness was 24.4 kPa (IQR: 16.5-26.3) and all patients had hepatic stiffness > 7kPa. A total of 11 patients underwent transjugular liver biopsy. In 5/11 patients (45%) advanced changes with bridging fibrosis were identified on histology. There was a trend towards higher hepatic stiffness in patients with bridging fibrosis compared to those without (see figure, p 0.082). No difference was found for Fontan pressures, transhepatic gradients or time since Fontan operation between patients with and those without bridging fibrosis (p > 0.1 for all analyses).

Conclusion: Elevated liver stiffness is found almost universally in adults late after Fontan operation. On histology, a large proportion of these patients are found to have bridging fibrosis. Liver stiffness may be a tool to identify high risk patients but larger patient numbers are required to draw conclusions.

Disclosure of Interest: None Declared
6. Cardiac imaging, congenital and pediatric cardiology

Clinical variability of cmr-measurements of right ventricular volumes and function in patients with repaired tetralogy of fallot and severe pulmonary regurgitation

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Introduction: Cardiac magnetic resonance imaging (CMR) is the reference method for assessment of right ventricular (RV) volumes and ejection fraction (RVEF) in patients with repaired tetralogy of Fallot (rTOF). Clinical decision making regarding pulmonary valve replacement is often based on changes of RV volumes indexed to body surface area (RVEDVi) and changes in RVEF. The aim of this study was to assess the clinical variability of CMR measurements of RV volumes and RVEF in adults with rTOF and severe pulmonary valve regurgitation.

Methods: We identified 10 clinically stable adults with severe pulmonary regurgitation who had undergone >2 CMR studies (5 patients with 3 CMRs, 4 with 4 CMRs, 1 with 5 CMRs, accounting for a total of 26 pairs of CMR studies). Time interval between first and last CMR study was 8.8 +/- 2.9 years. We compared changes in RV volumes (expressed as cc/m²) and changes in RVEF (expressed as %) between all pairs of CMR studies, changes from first to the last CMR study of each patient and maximal changes between two studies. Significant changes were defined as change >10% of RVEDVi or >10% in RVEF. All CMR studies were performed by a dedicated specialist team with extensive experience in the field (EV and CK).

Results: Consecutive measurements for RVEDVi and RVEF for the 10 individual patients and the average of all 10 patients are shown in figure 1. The average increase in RVEDVi from first to last CMR study was 0.8 ± 11.2 cc/m². An increase of >10% in RVEDVi was observed in 3 study pairs and a decrease of >10% in 4 study pairs. Maximum increase and maximum decrease of RVEDVi between two studies in individual patients is depicted in figure 2. Similar observations were made for RVEF: While on average, RVEF remained stable (change of RVEF between all study pairs: -0.6 +/- 5.8%) there was substantial variation between studies in individual patients. No patient had a decrease of RVEF >10% but in 2 patients an increase >10% between 2 study pairs was observed.

Picture/Graph:
Conclusion: In clinically stable Fallot patients with severe pulmonary regurgitation, changes in RV volumes and RVEF, as measured by CMR show substantial variations. In individual patients measurements swing around an individual baseline that does not significantly change over time. These data importantly highlight that changes in RVEDVi or RVEF between two CMR-studies in an individual patient must not be used alone for clinical decision making.

Disclosure of Interest: None Declared
Introduction: Our objective was to assess the impact of bileaflet mitral valve prolapse on left ventricular (LV) volume measurement and mitral regurgitation (MR) quantification with cardiac magnetic resonance (CMR).

Methods: MR severity was quantified in 23 patients with bileaflet mitral valve prolapse by calculating the regurgitant volume (RVol= LV stroke volume (LVSV) minus the reference SV) using CMR. LVSV was calculated as the difference between the diastolic and systolic LV volumes using the Simpson's method (from the mitral annulus to the apex: standard SV). A corrected LV systolic volume was also calculated as the sum of the standard systolic LV volume plus the prolapse volume, i.e. the volume included between the mitral annulus and the prolapsing mitral valve (corrected SV). The prolapse volume was calculated as the area of the basal LV slice times the prolapse height measured on a 2-chamber cine slice (Fig 1). We compared the differences in MR grading with these two methods, using the right ventricular (RV) SV as a reference.

Results: 23 patients (mean age 40±23 years, 8 males) were included, and 13 had no detectable MR jet. The mean prolapse height was 10±4 mm. RVSV was measured in all patients and showed an excellent agreement with the aortic SV measured by phase contrast (bias 0.2 ml, 95%CI -7 to +8 ml; n=14). In the 13 patients with no detectable MR jet, the corrected SV showed an excellent agreement with the reference SV (bias 0.6 ml; 95%CI -4.0 to +5.2 ml) and was therefore consistent with the diagnosis of absent MR. Conversely, the standard SV showed a significant overestimation (Fig 2A; bias 16.3 ml; 95%CI -5.1 to 37.9 ml). Likewise, over the whole group, the standard and corrected methods provided significantly different results for LV ejection fraction (67±7% vs 53±9%, p<0.0001), RVol (27±17 vs 7±12 ml, p<0.0001) and regurgitant fraction (RF, 27±16 vs 9±15%, p<0.0001). The distribution of the MR grades - absent or trace (RF<5%), mild (RF 5-29%), moderate (RF 30-50%) and severe MR (RF>50%) - among the 23 patients was 0/13/8/2 with the standard and 12/8/3/0 with the corrected method (Fig 2B). Overall, the 2 methods were concordant in only 3 (13%) patients, as the standard method overestimated MR severity by 1 grade in 19 (83%) and by 2 grades in 1 (4%) patient.

Picture/Graph:

Figure 1

Picture/Graph 2:
Conclusion: In patients with bileaflet mitral prolapse, SV corrected for the prolapse volume better reflects the true LVSV. This may improve MR severity grading by preventing a systematic overestimation of RVol and RF.

References:

Disclosure of Interest: None Declared
Introduction: Mitral annular plane systolic excursion (MAPSE) is an established echocardiographic parameter representing a marker of left ventricular (LV) longitudinal systolic function. However, studies indexing MAPSE in a healthy population are scarce. Hence, the purpose of this study was to determine the best parameter for indexing MAPSE exhibiting the strongest correlation to LV ejection fraction (LVEF) in a normal population.

Methods: Normal transthoracic two-dimensional echocardiography studies of 561 patients (49.7% males) performed between January 2012 and May 2015 were analysed. The influence of age on LVEF, body surface area (BSA) and LV length was evaluated. Moreover, the impact of age, BSA and LV length on MAPSE was determined to identify the best correlation between MAPSE and LVEF.

Results: Mean LVEF was 61.9% (range: 55% - 78%) and mean MAPSE was 15.3 mm (range: 12 mm - 24 mm). There was a positive correlation between LVEF and patient's age ($r=0.21$, $p<0.001$), while a negative correlation was observed between LV length and patient's age ($r=-0.15$, $p<0.001$). No correlation existed between BSA and patient's age ($r=0.065$, $p=n.s.$). The MAPSE values per se exhibited a negative correlation with age ($r=-0.14$, $p<0.01$) and did not correlate with LVEF ($r=0.84$, $p=n.s.$) When MAPSE was indexed to BSA, no correlation with LVEF was found ($r=0.07$, $p=n.s.$), while there was a negative correlation of MAPSE/BSA with age ($r=-0.18$, $p<0.001$). If MAPSE was indexed to LV length, there was a significant positive correlation with LVEF ($r=0.10$, $p<0.05$), while there was no correlation of MAPSE/LV length with age ($r=-0.06$, $p=n.s.$).

Conclusion: Normal values for MAPSE should be indexed to LV length, but not to BSA, because LV dimensions change with increasing age in the normal population.

Disclosure of Interest: None Declared
Impact of stroke volume assessment by three-dimensional echocardiography and multi-detector computed tomography on the classification of aortic stenosis severity

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Introduction: Echocardiographic assessment of indexed stroke volume (SVI) is important in aortic stenosis (AS) patients to identify those with low flow severe stenosis. Three-dimensional (3D)-imaging may improve diagnostic accuracy.

Methods: In 37 patients with severe AS evaluated for transcatheter aortic valve replacement, SVI was calculated using a) the biplane Simpson’s method, b) left ventricular outflow tract (LVOT) velocity time integral and area derived from i) two-dimensional transthoracic echocardiography (2D-TTE) LVOT diameter, ii) 2D transesophageal echocardiography (2D-TEE) LVOT diameter, iii) 3D-TEE LVOT area, or iii) multi-detector computed tomography (MDCT) LVOT area.

Results: SVI as assessed by the biplane Simpson’s method was larger than that obtained from 2D-TTE LVOT diameter (30.5±1.3 vs 25.5±1.5 ml/m²; p=0.01), similar to that calculated from 2D-TEE LVOT diameter (30.2±1.5 ml/m², p=0.87), and smaller than that determined by LVOT area planimetry in 3D-TEE (44.0±1.8 ml/m², p<0.001) or MDCT (47.9±2.1 ml/m², p<0.001 versus Simpson and p=0.008 versus 3D-TEE), respectively. SVI calculations based on MDCT correlated best with 3D-TEE (r=0.73, p<0.001 vs 3D-TEE; r=0.67, p<0.001 vs 2D-TEE; r=0.46, p=0.009 vs 2D-TTE; and r=0.25, p=0.18 vs Simpson). Low flow severe AS was diagnosed in 78% of patients using the biplane Simpson’s method, in 83% using 2D-TTE, and in 68% using 2D-TEE, as opposed to 23% and 9% with 3D-TEE and MDCT, respectively.

Conclusion: 3D-TEE and MDCT echo data fusion are more accurate for the determination of stroke volume than 2D-TTE or 2D-TEE and affect the classification of AS patients due to larger stroke volumes.

Disclosure of Interest: None Declared
Introduction: Our aim was to assess the overall burden of congenital syndromes and non-cardiac comorbidities among adults with congenital heart disease and to assess their impact on living conditions and outcomes.

Methods: Within a cohort of 1725 adults with congenital heart defects (65% defects of moderate or great complexity, median age at first visit 26.4 years, IQR: 19.9-38.8 years) followed at a single tertiary care center, congenital syndromes and comorbidities were identified by chart review. The association of disease complexity, congenital syndromes and comorbidities with arrhythmias, living conditions and survival was analyzed.

Results: Within the study cohort, 232 patients (13%) had a genetic syndrome, 51% a comorbidity and 23% >1 comorbidity. Type and frequency of syndromes are depicted in figure 1. Most prevalent comorbidities were systemic arterial hypertension (11%), thyroid dysfunction (9%), psychiatric disorders (9%), neurologic disorders (7%) chronic lung disease (7%) and a previous stroke (6%). In contrast to higher disease complexity, the presence of comorbidities had no impact on living conditions but patients with comorbidities were less likely to work full-time. Atrial arrhythmias were more common among patients with moderate/great disease complexity and those with comorbidities but were less common among patients with congenital syndromes (p < 0.01 for all comparisons). Figure 2 shows survival estimates stratified for disease complexity, associated syndromes and comorbidities. Patients with complex lesions and patients with >1 comorbidity had lower survival estimates compared to those with none or only one comorbidity (p < 0.001 and p = 0.013, respectively).

Picture/Graph:
Conclusion: Congenital syndromes and comorbidities are highly prevalent in adults with congenital heart disease followed at specialist centers and add to the overall complexity of care. The presence of these additional factors impacts on living conditions, is associated with arrhythmias and should be further explored as prognostic markers.

Disclosure of Interest: None Declared
Introduction: To compare the safety and performance of a novel hyperosmolar, small-volume single-shot cardioplegia (2 ml/kg) (SSC) compared to Buckberg blood cardioplegia (BC) in pediatric patients undergoing congenital heart surgery.

Methods: Retrospective analysis and propensity score matching of pediatric patients undergoing corrective surgery of ASD, VSD, CAVC, TOF, TGA with mild hypothermic ECC) by using either BC or SSC. Intra-, peri-, and postoperative data were collected.

Results: Propensity score matching identified 71 children - 32 patients with SSC and 39 with BC (age p=1.0; weight: p=0.97; procedure time: p=0.1, ECC time: p=0.4, cross-clamp-time: p=0.11). In-hospital mortality was 0%; follow-up is complete with all patients alive. SSC group was found to show higher Hematocrit values (p=0.06), while potassium values were significantly lower (p<0.001). SSC patients required significant less catecholamine support one (Adrenalin: p=0.02, Dobutamin: p=0.02) and six hours postoperatively (Dobutamin: p=0.01); after 24 hours there was no difference between the two groups. Furthermore no difference was observed for Troponin-T (p=0.2) and lactate values (p=0.8) postoperatively. Intubation time was slightly lower in the SSC group (p=0.09), whereas hospitalization time was comparable in both groups (p=0.7).

Conclusion: The novel small-volume single-shot cardioplegia provides safe and effective cardio-protection compared to established blood cardioplegia during corrective cardiac surgery in pediatric patients.

Disclosure of Interest: None Declared
Introduction: Therapy of choice of patients with complete atrioventricular septal defect (CAVSD) is surgical repair during early infancy. Survival without repair falls to 20% after two years of age, mainly because of pulmonary hypertension and cardiac failure. Experience with corrective surgery beyond the first year of life and particularly for adult patients, is extremely limited. We present our experience with correction of CAVSD in older children and adults.

Methods: Retrospective analysis of all patients with CAVSD, who underwent corrective surgery beyond one year of age at our center.

Results: 8 patients (2 male, mean age 19.6 years, range: 2-43 years) were identified between 2009 and 2014. 5 of the patients had trisomy 21. Follow up is complete (mean: 37.6 months). Prior to the operation, 6 patients had left atrioventricular valve (AV) regurgitation (5 moderate, 1 severe) and 4 right AV valve regurgitation (2 mild, 2 moderate). Moderate pulmonary hypertension (PHT) was found in 4 of the patients, severe PHT in 2. One patient presented in profound cardiac shock due to chordae ruptures.

A 2-patch technique was used for repair in 3 patients, and a 1-patch technique in 5. Replacement of the left AV valve was necessary in 2 patients. Postoperative ECMO support was needed in one case for 4 days. Average time on the intensive care unit was 8 days, hospitalization time 22 days. Pacemaker implantation due to postoperative complete AV-block was necessary in 1 patient. 30 days mortality is 0%. In the long-term, one patient died due to severe thromboembolic complication of his mechanical mitral valve 51 months after repair. At last follow-up, all patients were in functional status NYHA I-II with normal left ventricular function. Residual left AV valve insufficiency is mild in 3, and moderate in 1 patient. Moderate PHT persists in 1 patient.

Conclusion: Late correction of CAVSD is challenging but feasible, and can provide good results. Careful preoperative evaluation and a dedicated interdisciplinary approach in a specialized center are mandatory for success.

Disclosure of Interest: None Declared
Introduction: A latest generation 256-slice CT scanner (Revolution CT, GE Healthcare, Waukesha, WI, USA) combines single-beat coverage, a more powerful x-ray generator, faster gantry rotation times and ASiR-V allowing a protocol with minimized radiation and contrast agent exposure. The purpose of the present study was to assess the impact of such a protocol on interpretability and image quality in unselected patients referred for exclusion of suspected coronary artery disease (CAD).

Methods: Coronary computed tomography angiography (CCTA) was performed in 89 consecutive patients (61% male; mean age 55±11 years) using prospective ECG triggering. Tube voltage (80-120 kVp), tube current (180-310 mA) as well contrast agent volume (25-45 mL) and flow rate (3.5-5 mL/s) were adapted to BMI. Mean attenuation was quantified by placing a region of interest in the aortic root. Two independent blinded readers semi-quantitatively evaluated the study interpretability and image quality regarding motion, noise and contrast on a four-point scale.

Results: Median contrast agent volume and median effective radiation dose were 35 mL (IQR, 30-40 mL) and 0.5 mSv (IQR, 0.4-0.6 mSv). Mean attenuation in the aortic root was 412 ± 89 HU. Diagnostic image quality was acquired in 1050 of 1067 (98.4%) coronary segments and, on an intention-to-diagnosis basis, in 85 of 89 (95.5%) patients. Below a cut-off heart rate of 67 beats/min, only 1 of 974 (0.1%) coronary segments was non-diagnostic.

Conclusion: CCTA on a latest generation 256-slice CT scanner with minimized radiation and contrast agent exposure yields diagnostic image quality in patients referred for CAD exclusion in daily clinical routine.

Disclosure of Interest: None Declared
Introduction: There are scarce data on pregnancy in patients with complete atrioventricular (block (CHB) without a pacemaker (PM). This conduction abnormality is frequently complicated by associated congenital heart disease(CHD), and perinatal care can be highly complex.

Methods: A retrospective, multi-center study design was utilized to identify all pregnant women with CHB and no permanent PM. Data on cardiac function, pregnancy outcome and peri-natal complications was retrospectively collected and analyzed.

Results: Congenital CHB was present in 4 of the patients, while 1 patient acquired CHB following an atrial switch operation (pt #1). No patient had a pacemaker. The average age at pregnancy was 34 years (range: 20-46 years). All patients carried a single pregnancy, yet one patient was included for both her pregnancies., pt #5). Left ventricular size and function were normal in all prior to pregnancy. The ECG, Holter, and other baseline characteristics are shown in in Table 1. Serum BNP was elevated in 2 of the 5 women (both with concomitant hypertension). The single patient with CHD presented with clinical symptoms prior to pregnancy, yet the remainder was asymptomatic at baseline. No QRS prolongation was seen. During pregnancy, all women were controlled at least every 2 months; no change in ventricular function and no new onset of arrhythmias was observed. At birth, there were no complications. Caesarean section was performed in 4 of the 5 women. Transient class II NYHA heart failure was noted after C-section in a single patient (prior atrial switch procedure) with mild anemia.

Legend Table: HR = heart rate; LVEDD = left ventricular enddiastolic diameter; HTN = hypertension; VT ever = ventricular tachycardia; NYHA = New York Heart Association class

<table>
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<th>LVEDD cm/EF %</th>
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<th>VT ever</th>
<th>NYHA</th>
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Conclusion: Pregnancy in women with CHB appears to be feasible despite a mean age of 34 years. In isolated CHB without associated congenital heart disease pregnancy is tolerated well. In the presence of associated congenital heart disease, management remains a challenge. Based on this cohort alone, prophylactic implantation of a permanent pacemaker is likely unnecessary in the clinical stable patient in anticipation of pregnancy.

Disclosure of Interest: None Declared
Introduction: In ARVC/D, unlike other cardiomyopathies, aborted sudden cardiac death due to ventricular tachyarrhythmia (VT) can be the first clinical manifestation of the disease and often precedes development of myocardial dysfunction. These patients may often benefit from catheter ablation by classical endocardial approach. Nonetheless, many patients still experience recurrence of VTs many years after ablation therapy. Recent autopsy studies in patients with ARVC have shown that the arrhythmogenic substrate is located within the epicardial layers of the right ventricle and may be responsible for reentrant VT circuits. In those patients, where an isolated endocardial catheter approach may not eliminate VTs, an approach combining endo- and epicardial access for catheter ablation may be considered.

Methods: This case shows that the combination of endo- and epicardial ablation can successfully address the ventricular tachyarrhythmic burden in an ARVC patient after failure of multiple drug therapy.

Results: Case: A 65-year old male patient with previously diagnosed definite ARVC, according to the 2010 Task Force Criteria, presented with multiple implantable cardioverter defibrillator shocks due to electrical storm with recurrent monomorphic VTs (Figure 1). Subsequently, the patient was taken to the electrophysiology laboratory for VT ablation, during which four different monomorphic VTs with left bundle-branch block pattern could be induced. Initial endocardial mapping did not reveal potential ablation targets. Therefore, epicardial mapping was performed (Figure 2). This demonstrated scar tissue and late potentials dominantly in the subtricuspid and inferior regions of the RV and in the right outflow tract. Epicardial catheter ablation rendered all four VTs non-inducible by programmed stimulation with up to four extrastimuli. The patient was discharged off any antiarrhythmic medication. No further VTs occurred during a follow-up of 10 months.

Picture/Graph:
Conclusion: For a selected group of patients with ventricular tachycardia the combination of endo- and epicardial catheter mapping and ablation has become an established successful therapy.

Disclosure of Interest: None Declared
Missing coronary arteries -
an extreme variant of an anomalous left coronary artery from the pulmonary artery (alcapa)


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Introduction: Coronary artery anomalies (CAAs) are a diverse group of congenital cardiac malformations. Depending on the origin and course some are considered to be clinically irrelevant and are only diagnosed accidentally by echocardiography or angiography. Others are more clinically important and can lead to sudden cardiac death.

Methods: We report the case of an 8 days old female newborn with a functional single left ventricle (hypoplastic right ventricle) with malposition of the aorta overriding a ventricle septum defect (VSD) and a persistent ductus arteriosus (PDA). Further chromosomal rearrangement with partial trisomy 8q and partial monosomy 8p was diagnosed. Decision was made to palliate with univentricular correction. After installing cardiopulmonary bypass signs of cardiac ischemia appear. Application of cardioplegic solution via aortic root could not been established. Neither, aortotomy and search for coronary ostia for the application of selective cardioplegia, nor in a postoperatively performed cardiac catheter (CC) examination the origin of the coronary arteries could be identified. When all attempts to resuscitate the ventricle had failed, the patient expired. Autopsy examination of the heart showed an abnormal origin of the left coronary artery arising from the pulmonary trunk. The right coronary artery could not be detected.

Results: CAAs represent a very heterogeneous group of lesion with varying clinical significance. To the best of our knowledge this is the first report of an abnormal left coronary artery arising from the pulmonary trunk in combination with an agenesia of the right coronary artery. Surprisingly the child had no signs of myocardial ischemia during the first eight days of life.

Conclusion: Congenital cardiac surgeons should be aware of known fatal events due to CAAs. In the presented case even with MRI done the missing coronary ostia of the aorta were not diagnosed until CC. While it is not feasible to perform CC in every child undergoing CHD surgery in case of diagnosed severe chromosomal anomalies CAAs should be kept in mind and CC might be necessary.

Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Emergency assessment of proximal left anterior descending coronary stent permeability using transthoracic echocardiography

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Introduction: Techological advances in echocardiography allow direct visualization of all coronary arteries by transthoracic echocardiography. In particular, left anterior descending artery (LAD) can be assessed using color and pulsed wave Doppler in >90% of echograms performed by skilled operators¹.

Methods: A 44-year-old man with acute anterior ST elevation myocardial infarction underwent emergency PCI and stenting of an occluded ostial LAD, restoring a TIMI 3 flow. Initial echocardiographic assessment showed anterior septal and apical akinesis. Thirty-six hours later, he developed a crushing chest pain that radiated to the back and the abdomen. Serial 12-lead ECGs showed persistence of ST segment elevation that hadn’t resolved since the admission in the coronary unit. An emergency echocardiogram was performed in order to exclude an early mechanical complication and assess coronary flow in the LAD.

Results: Using the left parasternal acoustic window, a short axis view at the level of the aortic valve was obtained and slightly modified by superiorly tilting the probe. Color Doppler flow mapping with the Nyquist limit lowered at 14 cm/s allowed identification of the mid-LAD and its bifurcation with a large septal branch. Antegrade LAD flow was demonstrated using pulsed wave Doppler with the sampling volume placed inside the LAD. As ECG was in this situation non contributing, these echocardiographic findings allowed to demonstrate at least partial permeability of the ostial LAD, excluding a complete occlusion of the stent, and provided time to obtain serial troponin samples. A decreasing troponin trend and further clinical evaluation oriented investigations to the upper abdominal region and an acute cholecystitis was finally diagnosed by means of a thoraco-abdominal CT scan. An acute aortic process was excluded at the same time.

Conclusion: Direct visualization of antegrade blood flow in the coronary arteries is feasible and can directly influence clinical decision making.


Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Two successful pregnancies in a female with d-TGA, prior atrial switch (Senning), severe muscular subpulmonary outflow tract obstruction and non-sustained ventricular tachycardias

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Introduction: Whereas pregnancy after atrial switch procedures (ASP) is possible, outcome is limited by increased complications including fetal loss, deterioration of right ventricular (RV) function, increase in tricuspid regurgitation (TR), arrhythmias or thromboembolism. Data on pregnancy outcome of patients (pt) with subpulmonary (left ventricular outflow tract; LVOT) obstruction after ASP are lacking.

Methods: Findings of ECG, exercise tests, transthoracic echocardiography (echo), cardiac magnetic resonance imaging (CMR) and laboratory before and after pregnancy were analyzed in a pt with prior ASP and severe LVOT.

Results: A female with d-TGA had ASP (Senning) at 13 months. She always had significant muscular LVOT (60% systemic pressure) with normal left ventricular (LV) function. For years, she had a stable course with dyspnea NYHA II, a trivial baffle leak and a history of nonsustained ventricular tachycardias treated (beta blocker). A double switch procedure was declined by the surgeon. ICD implantation was refused by the pt. She insisted on pregnancy. Exercise testing showed good working capacity and Holter monitoring did not reveal VTs. CMR showed a RV size of 107ml/m², EF of 55%, max. velocity LVOT 3.6m/sec and LV EF of 72% compatible with echofindings (see Table). There was no baffle obstruction. Eventually she had 2 healthy full-term babies in 2011 and 2013. The results of her echos before, during and after pregnancy are shown in the Table. During the 2 pregnancies, she was in functional class II-III. Now, she is in functional class II. Holter ECG and CMR show no changes.

Conclusion: This is the first case of pregnancy after ASP with significant LVOT. It remains open to discussion if the gradient in the left ventricle helps to improve the situation for the systemic right ventricle by its impact on geometry. Still, careful monitoring and delivery in a tertiary care center is essential in such patients.

Disclosure of Interest: None Declared
PP-103
7. Clinical cases (All clinical cases have to be submitted in this topic)
Multimodal imaging of anomalous pulmonary venous return in a patient with ventricular tachycardia
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Introduction: We present a clinical case with multimodal imaging of an anomalous pulmonary venous return in a patient with ventricular tachycardia.

Methods: A 53-year-old asymptomatic male was referred for investigation of a monomorphic ventricular tachycardia. The referring cardiologist revealed dilated right-sided cardiac chambers and ruled out an atrial septal defect by transthoracic echocardiography. He nicely showed an anomalous pulmonary venous return from the left upper pulmonary vein into the left brachiocephalic vein by suprasternal views. Computed tomography confirmed the diagnosis. Chamber saturations from catheterization demonstrated an elevated saturation in the vena cava superior. Given a relevant left-to-right shunt with a pulmonary (Qp) to systemic blood (Qs) flow ratio of 1.3:1 the patient underwent surgical correction with redirection of the pulmonary venous return. Eight months after surgery, dimensions of the right-sided cardiac chamber had normalized. Holter monitoring excluded further tachycardia. This case clearly underlines the importance of completing transthoracic echocardiography by suprasternal views in order to obtain a correct diagnosis.

Results: This case clearly underlines the importance of completing transthoracic echocardiography by suprasternal views in order to obtain a correct diagnosis.

Conclusion: This case clearly underlines the importance of completing transthoracic echocardiography by suprasternal views in order to obtain a correct diagnosis.

Disclosure of Interest: None Declared
Clinical cases (All clinical cases have to be submitted in this topic)

Cladribine treatment for progressive pulmonary langerhans cell histiocytosis

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Introduction: Pulmonary Langerhans cell histiocytosis (PLCH) is a rare diffuse cystic lung disease mainly affecting young active smokers, and characterized by the accumulation of differentiated cells of the monocyte-macrophage lineage (Langerhans cells, LC) in bronchiolocentric granulomatous nodules. 30% of cases express the BRAF V600E mutation in LC. Smoking cessation is essential but may not prevent disease progression to respiratory insufficiency, lung transplantation or death. Corticosteroids and immunosuppressive agents are of unproven efficacy, and no standard therapy exists. A few case reports have shown a beneficial effect of cladribine, a purine nucleotide analogue that down-regulates histiocyte proliferation, in PLCH.

Methods: Case presentation

Results: A 32 year-old man was diagnosed with PLCH by surgical lung biopsy after a spontaneous pneumothorax in 2012. Chest CT showed typical multiple lung cysts and excavated nodules sparing the lung bases. At histopathology, LC did not bear the BRAF V600E mutation. Initial lung function showed: FEV1 72 %pred, FVC 77 %pred, FEV1/FVC 79%, DLCO 46 %pred. After smoking cessation, lung function and chest imaging remained stable for 2 years. In 2015, the patient complained of progressive dyspnea to NYHA class III and weight loss of 7 kg over 3 months. Lung functions tests showed a 1000 ml decline of FEV1 and 1200 ml decline of FVC. Chest CT showed marked disease progression. After patient’s consent, cladribine 0.1 mg/kg/d was administrated subcutaneously on 5 consecutive days every 4 weeks for 4 cycles under prophylaxis of co-trimoxazole and valacyclovir (maintained for 6 months after the last cycle). Treatment was well tolerated without any infectious or hematological side effects.

After 4 months, we observed improvement of dyspnea to class II, a weight gain of 6 kg, a 800 ml increase of FEV1, and a 1300 ml increase of FVC. DLCO did not improve. Chest CT showed a marked regression of excavated nodules.

Conclusion: Cladribine as a single agent may be an effective therapy for PLCH progressing despite smoking cessation, and may delay the occurrence of respiratory insufficiency and the need for lung transplantation. Administration requires experience in chemotherapy, anti-infectious prophylaxis, and close monitoring. The beneficial effect of cladribine appears independent of the BRAF V600E mutation, which could theoretically constitute another, yet unstudied, therapeutic target, but which is found in only 30% of cases of PLCH.

Disclosure of Interest: None Declared
Introduction: Acute pulmonary embolism (PE) is a common pathology with high morbidity and mortality rates. Diagnosis must be done without delay so that treatment can be started immediately. Transthoracic echocardiography (TTE) is one of the most often used diagnostic tools in emergency departments. McConnell’s sign, described in 1996 as an echocardiographic indicator for acute PE, is defined by preserved contractility of the right ventricular (RV) apex with severe hypokinesia or akinesia of the free wall. Despite the high sensitivity found by McConnell, this sign can be found in others conditions than PE, as it was the case in our patient.

Methods: NA

Results: An 83-year-old man was admitted to the emergency department after sudden cardiac arrest. He was hemodynamically stable with an ECG showing sinus rhythm and ST depression < 1 mm in DIII and aVF, 1 mm in V1-V2, 2 mm in V3, and 1 mm in DI - aVL - V6. TTE showed a small hyperdynamic left ventricle (LV), partially compressed by the RV, with normal ejection fraction and regional wall-motion, except for a paradoxical septal motion. The RV was moderately to severely enlarged, with severe hypokinesia of the free wall and presence of McConnell’s sign. Right ventricular systolic pressure could not be estimated. At this point, we performed a thoracic CT-scan and ruled out a PE. With a differential diagnosis of right ventricular infarction, we performed a coronary angiogram, showing occlusion of the proximal right coronary artery which is a small vessel that gives branches exclusively to the RV. Angioplasty was performed with a drug eluting balloon because of the small diameter of the vessel.

Conclusion: McConnell’s sign can lead one toward a diagnosis of PE, but it is not pathognomonic. The mechanism remains unclear, but it may be due to free wall ischemia secondary to any cause of RV afterload elevation. And as in the case of our patient, we must not forget that the differential diagnosis is inferior myocardial infarction with RV involvement even if LV regional wall motion is not, or only slightly altered.

Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)
Spontaneous regression of a large iatrogenic ascending aorta intramural hematoma.
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Introduction: Acute aortic syndrome (AAS) is wide-spectrum identity that includes classic aortic dissection (AD) with true and false lumen, intramural haematoma which is an hematoma of the aortic wall without circulating blood flow, discrete AD which is a very local bulging of the aortic wall, ulceration of aortic wall following plaque rupture and traumatic or iatrogenic AD illustrated by catheter-induced lesion of the intima. AAS involving ascending aorta is a life-threatening condition that currently requires surgery to avoid pericardial effusion, coronary arteries dissection or acute aortic regurgitation, but spontaneous regression could happen in some rare situation.

Methods: Iatrogenic AD can be induced when the catheter is pushed into the vessel wall during the introduction of a diagnostic or guiding catheter, and is usually located in the abdominal aorta. In some cases it involves the ascending aorta, starting usually close to the coronary ostia. If its extension is not too large in association with a very small intimal tear and no circulating blood flow in the false lumen, a spontaneous regression could happen under medical therapy.

Results: We present herein the case of a 74 year old woman who was admitted for elective right coronary angioplasty. During the procedure, she complained about chest pain on the attempt of the right coronary injection. A control by contrast injection of the ascending aorta showed an iatrogenic AD (Figure 1) caused by a very small intimal tear above the right coronary sinus. An enhanced-contrast CT-Scan confirmed the AD with a intramural hematoma involving nearly the entire ascending aorta (figure 2A). Considering that the patient remained hemodynamically stable and totally asymptomatic we opted for a medical therapy. A control CT-Scan, realized three days later, showed a complete regression of the hematoma (Figure 2B) without related-complication.

Picture/Graph:
Conclusion: This case suggests that uncomplicated ascending iatrogenic AD with a minimal intimal tear may be managed conservatively under careful medical supervision, even in large extension. A long term follow-up is needed to detect further aortic dilatation.

Disclosure of Interest: None Declared
Multimodality imaging evaluation of a mitro-aortic fibrosa pseudo-aneurysm fistulizing into both atria
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Introduction: A 44-year-old asymptomatic man was referred from abroad to our hospital for a surgical correction of a pseudo-aneurysm of the mitro-aortic intervalvular fibrosa (P-MAIVF). The mitro-aortic intervalvular fibrosa (MAIVF) is the region of fibrous tissue between the left coronary or noncoronary aortic cusp and the anterior leaflet of the mitral valve, and its pseudo-aneurysm communicates with the left ventricular outflow tract (LVOT). P-MAIVF was first described in 1962 by Abrahams et al after post-mortem examinations (1).

Methods: The patient developed this P-MAIVF a year earlier, after a paravalvular abscess complicating an aortic bacterial endocarditis. Despite the replacement of his native bicuspid aortic valve and a first surgical repair of this P-MAIVF, it progressed and further fistulized into both atria.

Results: P-MAIVF is a rare complication favoured by the presence of a bicuspid aortic valve, endocarditis and iatrogenic trauma, mainly during aortic valve surgery, being the most common causes. Although fistulization has been described into the left atrium and the aorta, it has never been reported into the right atrium (2,3).

Conclusion: Preoperative assessment of the precise anatomy of this acquired malformation was performed by different imaging modalities including a transthoracic echocardiogram (TTE), a transesophageal echocardiogram (TEE) and a cardiac CT scan. In order to avoid further potential complications (rupture, compression of a coronary artery or other cardiac structure, further fistulization...), the patient underwent a successful surgical repair with reconstruction of his mitro-aortic fibrosa by a bovine patch. A permanent pacemaker had to be implanted post-operatively due to a third-degree atrio-ventricular block, and immediate follow-up was otherwise unremarkable.

Images: 4 to 6 images of the multimodality imaging (TTE, TEE and CT scan) will illustrate this case


Disclosure of Interest: None Declared
Introduction: Cardiac transplantation is the gold standard treatment of end-stage cardiac insufficiency, but the shortage of donor organs has led to the development of left ventricular assist devices (LVAD) as destination therapy or bridge to transplantation.

Methods: In Switzerland about 150'000 patients, mostly over 65 years of age, suffer from heart failure. The younger ones are referred for heart transplantation. Some may require a LVAD as a bridge to transplantation in view of the potentially long waiting time for an organ. The challenge is to define the optimal time for LVAD implantation. We present the first two cases in whom the new Thoratec HeartMate III LVAD was implanted in Switzerland, in very different clinical settings: a stable and an unstable patient.

Results: The first patient had dilated cardiomyopathy post myocardial infarction in 2001 with diminished LVEF despite two revascularization procedures with drug-eluting stents. He was put on the heart transplantation waiting list in September 2015. In November 2015, his clinical situation deteriorated rapidly due to ventricular tachycardia. On 19th November 2015, he underwent implantation of a HeartMate III LVAD. He was discharged from the ICU on day 8, and home on day 22. The second patient had idiopathic dilated cardiomyopathy diagnosed in 2009. He was admitted to hospital in November 2015 for global cardiac decompensation with generalized oedema and acute renal failure. Despite aggressive inotropic therapy, including administration of levosimendan, the patient remained unstable and was operated on an emergent basis on 4th December 2015 in order to implant a HeartMate III LVAD. The patient also had severe right ventricular dysfunction, such that a temporary right assist device was necessary during nine days. The patient is still hospitalized in the ICU due to several post-operative complications potentially induced by delay in LVAD implantation. No device related complication as thromboembolism, infection or LVAD failure was noted in both of these cases.

Conclusion: These two cases show the utility of VAD in the armamentarium of a transplantation program. They highlight the importance of timing of implantation, in particular in case of acute cardiac decompensation. Moreover the second case
illustrates that right ventricular dysfunction may be present after left VAD implantation and should be treated by transient circulatory support since this may be reversible.

**Disclosure of Interest:** None Declared
Coronary anomaly: successful challenge for off-pump coronary artery bypass grafting with complete revascularisation

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Introduction: Anomalies of coronary arteries demonstrate a surgical challenge in revascularisation of coronary heart disease and may require adjustment of the standard technique, especially in patients in need of total revascularisation.

Methods: A 78-year-old man was admitted for diagnostic angiography suffering from angina pectoris CCS 3 and increasing dyspnea NYHA III. The angiography was complicated to perform. Finally, beside severe stenoses of all branches, the angiography revealed a coronary anomaly. The CX derived from the dominant RCA ostium, while the LAD was spreading fanwise into numerous fragile twings (Fig. 1). Because of the fragile anatomy of the LAD, that appeared as small vessel disease, and the abnormal course of the CX deriving from the ostium of the RCA, we discussed the strategy for revascularisation and decided, finally, to perform an off-pump coronary artery bypass grafting as the standard procedure in our clinic.

Results: As standard approach the patient was operated off-pump using the right internal thoracic artery and two vein grafts (Fig. 2a+b). Exposition of the affected vessels for anastomoses, as shown precisely in the images, was comfortably to achieve without hemodynamic compromising. First, three dominant branches of the RCA spreading to the posterior wall were sequentially anastomosed by a vein (Fig. 2a: Graft A: vein graft to the marginal branch, RIVP and RPLD). The “fan” of the LAD consisted of one branch with larger calibre, that could be anastomosed without difficulties to the right internal thoracic artery (Fig. 2b: Graft B). On the anterolateral wall a venous graft to the CX and intermediate branch was anastomosed (Fig. 2b: Graft C). The patient was extubated immediately after operation and could be discharged at 7th postoperative day to cardiac rehabilitation. The CT scan confirmed a good patency of the grafts.

Picture/Graph:
Conclusion: The coronary anomaly led to further discussion about on- or off-pump strategy, especially concerning the need of total revascularisation in this severe coronary artery disease. If adequate intraoperative exposition and stable hemodynamics can be achieved as required criteria, a coronary disease complicated by anatomic anomaly may be treated without cardiopulmonary bypass for the advantages of off-pump surgery.

Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)
Large aneurysm of the right sinus of valsalva
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Introduction: Sinus of Valsalva aneurysms (SVA) are infrequent cardiac anomalies which are usually diagnosed following rupture and then constitute a cardiac emergency. Non-ruptured SVA's are found incidentally because of the silent clinical course. Surgical correction of this rarity constitutes either the closure of the defect by direct sutures, patch-plasty or a complete root replacement with a valved conduit.

Methods: A 57-year-old man presented to our institution for a routine medical examination following sudden deaths of his two brothers. On admission, the patient was free of complaints and asymptomatic. A genetic disorder was negated. Echocardiography revealed an isolated 62-mm dilatation of the aortic root in the presence of a normally functioning aortic valve and a normal ascending aorta. Computed tomography (CT) demonstrated an enormous right SVA. The patient was referred for an operative correction. A careful dissection was made between aorta and pulmonary trunk along the aorta towards aortic annulus. Here the distally migrated right coronary artery was found (Fig. A). After aorta was opened transversely at the level of the sinotubular junction, the aneurysm was inspected (Fig. B). Inner surface of the aneurysm consisted of only a pseudointima, that rested directly on the right ventricular myocardium. During the further preparation of the right coronary button it became apparent that there was no true edge between the aortic annulus and the coronary sinus (Fig. C-D). A bovine pericardial patch was thus fixed directly to the aortic annulus thereby establishing the continuity of the aortic wall (Fig. E). Re-anastomosis of the supracommissural aorta to the sinotubular junction (Fig. F) was followed by the reimplantation of the right coronary ostium into the bovine patch (Fig. G-H). After an uneventful recovery and a control CT-angiography with normal findings, the patient was discharged on the 8. postoperative day. Six months later, the patient was free of complaints. CT-angiography displayed a normal looking aortic root as well as unobstructed right coronary artery.

Results:

Picture/Graph:
Conclusion: A non-ruptured SVA may progress to rupture and thus lead to acute cardiac tamponade and sudden death and they should therefore be repaired. Our case demonstrates that reestablishment of the aortic wall continuity using a bovine pericardial patch and the re-implantation of the right coronary artery button can safely be performed in patients with isolated SVA.

Disclosure of Interest: None Declared
**Clinical cases (All clinical cases have to be submitted in this topic)**

Norwood stage 1 with surgical ventricular reconstruction and mitral valve repair for neonatal idiopathic left ventricular dilated cardiomyopathy

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**Introduction:** Fetal cardiomyopathies are rare and carry a very poor prognosis. There are few reports on the management of isolated left ventricular fetal cardiomyopathy. We report the management of a patient with a prenatal diagnosis of isolated and idiopathic left ventricular (LV) dilated cardiomyopathy (DCM) presenting at birth.

**Methods:** A 3.1 kg neonate, with a prenatal diagnosis of isolated severe LV DCM diagnosed at 33 weeks of gestation, was born at 38 weeks of gestation from a cesarean section. Post-natal echocardiography confirmed the diagnosis, with a severely dilated left ventricle (end-diastolic diameter 3.2 cm, Z-score +3.3; end-systolic diameter 2.8 cm, Z-score +5.6) with severe systolic dysfunction (shortening fraction 12%) with global hypokinesis, a patent foramen ovale with left-right shunt, an unobstructed aortic arch, and a large ductus arteriosus with right-left shunt and retrograde flow in the aortic arch, and moderate mitral regurgitation from tethering of the leaflets by the dilated left ventricle (see figure). The baby was placed on epinephrine and prostaglandins. Computed tomography showed normal proximal coronary arteries. The patient underwent stage 1 Norwood single ventricle palliation, which consisted of a Damus-Kaye-Stansel anastomosis, atrioseptectomy and a 3.5 mm right modified Blalock-Taussig shunt. A large portion of the left ventricular free wall was found to be severely thinned and scarred. This aneurysmal ventricular wall was resected. The mitral valve was repaired using an A2-P2 Alfieri stitch. The ventriculotomy was primarily repaired with double running 5-0 polypropylene suture, following a modified Batista technique.

**Results:** The patient had an uneventful post-operative recovery, followed by stage 2 - bidirectional Glenn and tricuspid valvuloplasty at 2.75 months of age. Histology of the resected left ventricular wall showed extensive endocardial fibroelastosis.

**Conclusion:** This reports the rare presentation of isolated LV DCM in a neonate, and it’s successful single ventricle palliation.

**Disclosure of Interest:** None Declared
Urgent laminectomy and off-pump cabg as salvage management of spontaneous spinal epidural hematoma complicating symptomatic left main coronary subocclusion

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Introduction: Spontaneous epidural hematoma is a rare complication of fibrinolysis or dual antiplatelet therapy which requires immediate decompression. We report the management of a patient with spontaneous epidural hematoma after receiving dual antiplatelet agents and anticoagulation while waiting for urgent coronary artery bypass grafting for symptomatic left main subocclusion.

Methods: A 79 year-old diabetic gentleman was admitted for a NSTEMI and was administered dual antiplatelets and anticoagulation. The coronary angiogram showed severe triple vessel disease, and the patient was referred for surgery. The following morning, the patient developed acute onset of incomplete tetraparesia due to a spontaneous epidural hematoma from C2 to Th2 compressing the spinal cord, detected at the spinal magnetic resonance. During the examination, the patient presented intermittent chest pain and ST-segment elevation. The patient was urgently brought to the operating room for left hemilaminectomies of C3 to Th2, evacuation of the epidural hematoma and placement of two drains, followed by off-pump triple coronary artery bypass grafting. A single bolus of 5000 UI of heparin was given prior to the coronary anastomoses, and reversed 1:1 with protamine.

Results: The patient had an uneventful post-operative course. His neurological examination showed improvement, with 3/5 strength of both lower limbs, 3/5 of the left arm and 4+/5 strength of the right arm, and improved sensitivity. The patient was placed on aspirin with no further bleeding episodes.

Conclusion: Rapid management of both the neurological and cardiac emergencies with a tailored approach allowed our patient to have a favorable outcome.

Disclosure of Interest: None Declared
7. Clinical cases (All clinical cases have to be submitted in this topic)

Pregnancy in pulmonary arterial hypertension: illustration of pluridisciplinary management at an expert center
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Introduction: Pregnancy during pulmonary arterial hypertension (PAH) is associated with high rate of mortality, thus guidelines for the management of pulmonary hypertension (PH) strongly recommend that PAH patients avoid pregnancy.

Methods: This 36 years old woman presented to the emergency room for a progressive dyspnea since the beginning of her pregnancy (24 wks). She also noted diffuse joint pain. Medical history was unremarkable except for a late miscarriage (26 wks) one year before. She gave birth to 2 others normal children without complication (7 and 9 years ago).

Results: Initial assessment by contrast-enhanced chest CT-scan ruled out pulmonary embolism and showed a normal lung parenchyma. Transthoracic echocardiography (TTE) revealed dilatation of right cavities with high probability for a pulmonary hypertension. V/Q scan excluded a chronic thromboembolic disease. Right heart catheterization (RHC) confirmed a severe precapillary PH (pulmonary artery mean pressure (mPAP) of 57 mmHg and elevated pulmonary vascular resistances (PVR) (6.6 WU)). Etiologic PAH investigation revealed presence of auto antibody (Anti Nuclear Antibodies 1/5000, positive anti-nucleosomes 127U) suggestive of a lupus associated PAH.

Upfront PAH specific bitherapy was initiated with sildenafil (20mg tid) and epoprostenol (14ng/kg/min), endotelin receptor antagonist being contraindicated due to potential fetal toxicity. Therapeutic anticoagulation was also started. Lupus was treated by oral corticotherapy. After multidisciplinary assessment, a caesarean section under spinal anaesthesia was planned between 30 and 31 weeks. The delivery occurred without complication at the scheduled date. Newborn adapted well and only necessitated continuous positive airway pressure (cPAP) in room air.

Post delivery was managed in intensive care unit (ICU) and was unremarkable. In particular, no hemodynamic degradation, even transitory, occurred. Central venous pressure was stable around 10 mmHg. RHC was repeated before transfer of the patient to standard unit. We observed hemodynamic improvement with a substantial PVR decrease (4.2 WU, -36%). Specific PAH triple combination therapy was then initiated by adjunction of macitentan (10 mg/d). Lupus treatment was intensified with cyclophosphamid. Since initiation of treatments, the patient remained in a stable clinical condition.

Conclusion: This case report illustrates that pregnancy management in PAH requires a complete multidisciplinary involvement and the cornerstone role of expert centers.

Disclosure of Interest: None Declared
**PP-114**

7. **Clinical cases (All clinical cases have to be submitted in this topic)**

Exclusion of thrombus from the left atrial appendage by cardiac magnetic resonance imaging and confirmation with intracardiac echocardiography in a patient after esophagectomy

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**Introduction:** Recently, intracardiac echocardiography (ICE) has been shown to be a safe and reliable imaging modality to rule out thrombi from the left atrial appendage (LAA). However, no data are currently available regarding the reliability of cardiac magnetic resonance imaging (CMR) in this manner.

**Methods:** The patient is a 70 year old man with esophageal cancer who underwent esophagectomy with pericardial reconstruction. After surgery, the patient was diagnosed with a new onset atrial flutter. Subsequently, oral anticoagulation (OAC) with rivaroxaban was started and an ablation was scheduled 4 weeks later. Due to questionable compliance with OAC and poorly tolerated symptoms related to the arrhythmia, we decided to exclude the presence of a thrombus in the LAA prior to the ablation.

Given the recent surgery, a transesophageal echocardiography (TEE) was contraindicated. As such, the patient underwent a CMR exam.

**Results:** The LAA was visualized by 2 Steady-state free precession (SSFP) cine stacks perpendicular to the LAA long axis in an oblique transaxial and an oblique sagittal orientation before and immediately after contrast medium injection. CMR did not show the presence of a thrombus in the LAA [Figure 1]. However, with a restricted resolution by a voxel size of 1.2x1.2x6mm, the presence of smaller sized thrombi could not be excluded by CMR. Subsequently, the patient was brought to the electrophysiology laboratory, where he underwent an ICE. After placing the ICE probe (AcuNav, Siemens AG Medical Solution, Munich, Germany; 5.5–10 MHz; 8F) in the pulmonary artery [Figure 2a], the LAA was visualized and the exclusion of a thrombus was confirmed [Figure 2b].

**Picture/Graph:**
Figure 1: Steady-state free precession (SSFP) cine still images of the LAA before (upper row) and after Gadolinium injection (lower row). Still frames from an oblique transaxial stack (A and C), from an oblique sagittal stack (B and D). LAA: left atrial appendage

Picture/Graph 2:
Conclusion: Currently, the gold standard modality to exclude a thrombus in the LAA remains TEE. Recently, several studies have demonstrated the non-inferiority of ICE over TEE in this regard. However, no data are currently available regarding the accuracy and reliability of CMR. This case demonstrated that CMR may be used to rule out a larger thrombus in the LAA in case of contraindication to TEE. Further data are required to validate the reliability of this imaging modality.

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PP-115

7. Clinical cases (All clinical cases have to be submitted in this topic)

A full cardiac evaluation in a patient with implanted cardioverter defibrillator: how adjustment of bandwidth improves image quality.


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Introduction: Cardiac magnetic resonance (CMR) is an important tool for follow-up of patients with coronary artery disease. It allows visualization of chronic myocardial infarction (MI), assessment of ischemia and of complications like intracavitary thrombus formation. The presence of implanted conventional internal cardioverter defibrillators (ICDs) precludes CMR. However, new MRI-conditional ICDs are now entering the market.

Methods: A 67 year-old patient known for an antero-septal MI in 2013, treated by stent implantation in the left anterior descending artery, was addressed to exclude myocardial ischemia before a planned lobectomy for a pulmonary tumor of unknown origin. One year ago an MRI-conditional ICD (Biotronic Ilesto™ 7) was implanted for primary prevention. After programming the ICD in ProMRI™ mode, a standard CMR protocol with function and viability assessment as well as with a stress first-pass perfusion study was performed on a 1.5T MRI scanner (MAGNETOM Aera, Siemens).

Results: CMR revealed the presence of an apical thrombus of 17x31mm on fast gradient echo cine sequence (figure 1a) and phase sensitive inversion recovery (PSIR, figure 1b) of a 4 chamber view. First-pass perfusion showed myocardial hypoperfusion in the chronic MI territory, no ischemia, as well as the large apical thrombus (figure 2).

Short axis PSIR images, however, were disturbed by a high signal in the anterior region of the left ventricle (figure 2a), mimicking late gadolinium enhancement (LGE). Increasing the bandwidth from 140 to 300Hz/pixel allowed elimination of this artifact (figure 2b).

Picture/Graph:
1a and 1b: 4 chamber view. 1a: Fast gradient echo cine sequence with mural thrombus (Th) and the artifact of the ICD electrode (black arrow). 1b: Standard phase sensitive inversion recovery with myocardial scar in septal and apical segments as well as the apical thrombus (Th) and the ICD electrode (white arrow).
1c and 1d: Myocardial perfusion map on motion compensated perfusion images. Visualization of hypoperfusion in the scar in the mid (1c) and apical septal segments and the thrombus (1d).

**Picture/Graph 2:**
Conclusion: New generation ICDs allow examination of patients by CMR as shown by recent trials. However, even if safety and efficacy has been proven, artifacts due to the ICD device and leads may disturb image quality, complicate image interpretation, and therefore may diminish the diagnostic power of the examination. Several technical adjustments allow reducing artifacts like the use of fast spin echo or fast gradient echo sequences instead of steady-state free precession sequences. Fast gradient echo based perfusion sequences can deliver excellent quality and increasing the bandwidth can reduce the typical high signal artifacts of LGE as demonstrated in this case, allowing in the presence of new generation ICDs a full cardiac evaluation by CMR including myocardial scar visualization.

Disclosure of Interest: None Declared

2a: Standard PSIR short axis view with the presence of the mural thrombus, artifact of the ICD lead (arrow head) and artifact in the anterior region (arrow).
2b: PSIR short axis view with increased bandwidth from 140 to 300Hz/pixel with elimination of the previously present artifact. Th: thrombus.
7. Clinical cases (All clinical cases have to be submitted in this topic)

Upright bitherapy with macitentan/tadalafil after monotherapy failure in idiopathic pulmonary arterial hypertension

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Introduction: Supported in particular by the results of the AMBITION study, Guidelines for pulmonary hypertension (PH) management outline the role of combination therapy in newly diagnosed patients with intermediate or high risk pulmonary arterial hypertension (PAH).

Methods: We present the case of a 77-year-old woman who presented with complaints of increasing shortness of breath since January 2013 (NYHA II). An ultrasound performed at this moment shows signs of pulmonary hypertension confirmed by right heart catheterization (Table 1). After a comprehensive assessment, the diagnosis of idiopathic pulmonary arterial hypertension (IPAH) is retained and bosentan, an endothelin receptor antagonist (ERA) was introduced. This treatment had to be discontinued after three months due to a significant elevation of liver enzymes. Ambrisentan, another ERA was then introduced. Hemodynamic assessment at 3 months (Table and Fig. 1) shows a discrete improvement but the patient decided to stop all treatment due to adverse events (abdominal pain, diarrhea, and edema). In November 2014 a breast cancer was diagnosed and a new hemodynamic assessment is carried out before scheduling a mastectomy. This new right catheterization confirmed severe hypertension (Table and Fig. 1) in a patient in functional class III. Given the risk of general anesthesia, dual therapy with another ERA (macitentan) and a PDE5 inhibitor (tadalafil) was started and well tolerated by the patient. We noted a dramatic clinical improvement, and in order not to further delay surgical intervention, a new right heart catheterization was performed after two months (Table and Fig. 1). This new assessment confirmed a near hemodynamic normalization. At the same time, the patient recover a functional class I and the distance of 6 min walking test was normalized.

Results: Faced with the imperative surgery, combination therapy was administered immediately to try to have a rapid clinical response in this functional class III patient. Clear clinical and functional improvements were observed and curative surgery performed without complication.

Conclusion: This case illustrates the possibility of an excellent clinical and hemodynamic response by combination therapy immediately combining macitentan and tadalafil and suggests that this strategy is beneficial.

Disclosure of Interest: None Declared
Post-operative right ventricular mechanical assistance with a heartmate ii device in Ebstein’s anomaly

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Introduction: Acute right ventricular failure is a life-threatening condition with poor prognosis. We report a case of Ebstein’s anomaly with severe right ventricular dysfunction after surgical correction of both tricuspid and pulmonary valve insufficiency.

Methods: A 45-year-old man with Ebstein’s anomaly and a previous history of surgical relief of associated pulmonary stenosis using a transannular patch was referred to us with marked decrease in exercise tolerance. He was found to have severe insufficiency of both tricuspid and pulmonary valves, severe right ventricular dilatation, but he was not cyanosed. He underwent surgery, which consisted in tricuspid and pulmonary valve replacement and direct closure of a patent foramen ovale. The operation was technically uneventful. His condition deteriorated rapidly with severe RV dysfunction leading to a significant leftward shift of the interventricular septum. He was stabilized with veno-arterial femoro-femoral extracorporeal life support (ECLS). In view of the mean gradient of 10 mmHg across the pulmonary bioprosthesis, we replaced it with a pulmonary homograft 4 days later. In the same act, his ECLS set-up was switched to a simplified short-term right ventricular support device.

After 14 days of isolated right ventricular support and several unsuccessful attempts to wean this, we decided to implant a long-term right ventricular assistance using the HeartMate II device as a bridge-to-transplant strategy.

Results: The patient’s condition slowly improved, including his RV function. On POD 47, despite adequate anticoagulation and antiplatelet therapy, the patient presented evidence of hemolysis and altered HMII pump parameters. This was strongly suggestive of HMII pump thrombosis. However, there appeared to be no hemodynamic compromise. Therefore, we decided to discontinue HMII RV support. The device was turned off and disconnected from its external battery, but it was left in place. He was discharged home on POD 88 and remains well.

Conclusion: The HM II device may be used to support the failing RV.

Disclosure of Interest: None Declared
**Introduction:** Flexible bronchoscopy (FB) is increasingly used for diagnostic and therapeutic purposes in patients with COPD. We aimed to compare the safety of FB in patients with and without COPD.

**Methods:** Prospective, longitudinal, case-control, single centre study including 1400 consecutive patients. Patients were categorized according to clinical variables and lung function in COPD or non-COPD. The primary end-point was the combined incidence of complications related to FB in COPD.

**Results:** The combined incidence of complications was similar in both groups (p=0.301) and independent of FEV1% predicted (p=0.789). Individually, the need for insertion of the insertion of a nasopharyngeal or oropharyngeal airway (7.4% vs. 11.7%, p=0.021) was more common in the group of patients with COPD. This difference was no longer significant after adjustment for age, gender, and duration of the procedure. Patients with and without COPD depicted distinctive hemodynamic responses to sedation. Hypotension (20.7% (n=135) vs. 29.8% (n=131), p<0.001) was significantly more common among patients with COPD. While the number of episodes of hypoxemia ≤ 90% was did not differ between COPD and non-COPD (p=0.125), patients with COPD had a lower median and lowest SO2 and persisted hypoxemic (SO2 <88%) longer than patients without COPD. Both peak pCO2 and time on pCO2>45mmHg were higher in COPD, but increase in paCO2 change over the time course of FB was similar in both groups (p=0.571). There were no differences in patient reported outcomes.

**Conclusion:** The safety of flexible bronchoscopy is similar in patients with and without COPD.

**Disclosure of Interest:** None Declared
**PP-119**

**8. Pneumology and Thoracic Surgery**

Effect of hyperoxia on exercise performance in patients with COPD: a randomized trial

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**Introduction:** The effect of supplemental oxygen on performance and mechanisms of exercise limitation in COPD are incompletely understood.

**Methods:** 20 COPD (11 women, age 65±6y, FEV1 64±19%pred.) performed 4 cardiopulmonary exercise tests (CPET) to exhaustion breathing oxygen enriched or ambient air (FiO$_2$ 0.5 or 0.21) and using progressively increased or constant load (75%Wmax, FiO$_2$ 0.21) bicycle protocols, according to a randomized, cross-over design. Pulmonary gas-exchange, oxygen saturation (SpO2), cerebral and muscle tissue oxygenation (CTO and MTO) and hyperinflation by respiratory inductance plethysmography were monitored.

**Results:** In progressive ramp tests with FiO$_2$ 0.50, mean maximal work rate was significantly increased to 108%, and oxygen uptake, SpO2, CTO and MTO exceed values during FiO$_2$ 0.21, while the ventilatory equivalent for CO2 and heart rate were reduced. In constant load tests with FiO$_2$ 0.5 endurance was increased to 159% vs. FiO$_2$ 0.21 (table). Dynamic hyperinflation was similar under FiO$_2$ 0.21 and 0.5 and it was negatively correlated with endurance in constant load exercise on FiO$_2$ 0.5 (r=-0.54, p=.002). At isotime corresponding to end of tests with FiO$_2$ 0.21, heart rate, breathing frequency and minute ventilation were lower and breathing reserve, SpO2, CTO and MTO higher when patients were breathing FiO$_2$ 0.5.

<table>
<thead>
<tr>
<th></th>
<th>End of progressive ramp</th>
<th>End of constant load</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FiO$_2$ 0.21</td>
<td>FiO$_2$ 0.50</td>
</tr>
<tr>
<td>Endurance, s</td>
<td>422±78</td>
<td>455±94*</td>
</tr>
<tr>
<td>Work rate, watts</td>
<td>96±21</td>
<td>104±28*</td>
</tr>
<tr>
<td>V’O$_2$, l/min</td>
<td>1.34±0.28</td>
<td>1.96±0.46*</td>
</tr>
<tr>
<td>Heart rate, 1/min</td>
<td>125±19</td>
<td>126±18</td>
</tr>
<tr>
<td>V’E, l/min</td>
<td>45±11</td>
<td>45±13</td>
</tr>
<tr>
<td>V’E/V’CO2</td>
<td>36±6</td>
<td>32±5*</td>
</tr>
<tr>
<td>Breathing reserve, %</td>
<td>24±22</td>
<td>23±21</td>
</tr>
<tr>
<td>SpO2, %</td>
<td>95±4</td>
<td>98±3*</td>
</tr>
<tr>
<td>CTO, %</td>
<td>64±7</td>
<td>74±6*</td>
</tr>
<tr>
<td>MTO, %</td>
<td>64±10</td>
<td>66±11*</td>
</tr>
<tr>
<td>Dynamic hyperinflation, ml</td>
<td>1±551</td>
<td>232±617</td>
</tr>
<tr>
<td>Borg CR10, dyspnea</td>
<td>6±2</td>
<td>6±2</td>
</tr>
</tbody>
</table>

Mean±SD values during final 30 sec of exercise; *P<0.05 vs. FiO$_2$ 0.21; V’O$_2$: oxygen uptake; V’E: minute ventilation; V’E/V’CO2: ventilatory equivalent for CO2; SpO2, CTO and MTO: arterial, cerebral and muscle tissue oxygenation. ERV = expiratory reserve volume; dynamic hyperinflation: exercise induced increase in end-expiratory lung volume

**Conclusion:** In COPD patients, breathing oxygen enriched air significantly improves exercise performance mainly by increasing the aerobic capacity. This is achieved by enhancing ventilatory efficiency, reducing mechanical ventilatory limitation and improving oxygen availability in the muscles and the brain.

**Disclosure of Interest:** None Declared
Mortality of patients with long term oxygen therapy due to chronic obstructive pulmonary disease - a population based cohort study

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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death worldwide. It is associated with substantial socioeconomic burden. Long term oxygen therapy (LTOT) has shown to reduce mortality in COPD patients with severe chronic hypoxemia and is recommended for this population by current treatment guidelines. The aim of this study was to assess the standardized mortality ratio of incident and prevalent LTOT users due to COPD and to identify predictors of mortality.

Methods: We conducted a 2-year follow-up population based cohort study of all COPD patients receiving LTOT in the canton of Bern (reference day March 12th, 2012). At that time LTOT was provided only by a single institution (Lungenliga Bern). Baseline data included demographics, pulmonary function tests, arterial blood gases, oxygen saturations, presence of cor pulmonale, type of oxygen delivery system and prescribed oxygen dose. Comparing age and sex adjusted standardized mortality ratios we analysed associations between all-cause mortality and patient characteristics at baseline. Data for the incident (receiving LTOT < 6 month prior to baseline) and prevalent LTOT users were analysed separately.

Results: At the reference day, COPD was the indication for LTOT in 475 out of 771 patients (62%) using LTOT in the canton of Bern (prevalence 48/100 000 inhabitants; 20% incident users, n=93). Two-year overall mortality was 29% (n=140). Mortality was significantly higher in the incident LTOT users (41% vs. 27%, p < 0.001). Standardized mortality ratios were 8.02, 95% CI 5.64 – 11.41 for incident and 5.90, 95% CI 4.79 – 7.25 for prevalent users, respectively. After adjusting for age and sex, the incident users were found to have a higher risk of death than the prevalent users (HR = 1.66, 95% CI 1.14 – 2.41, p = 0.008). Type 2 respiratory failure at LTOT initiation was associated with significantly higher rates of death among the incident LTOT user group (standardized mortality ratio 60.57, 95% confidence interval 11.82 to 310.45, p = 0.038).

Conclusion: Two-year mortality rate was notably lower in our study than in older cohorts but remained high compared to the general population, especially in patients receiving LTOT < 6 months. Patients recently started on LTOT should receive a closer follow-up in the first months.

Disclosure of Interest: None Declared
Postural control in copd patients travelling from 760 m to 3200 m; a randomized trial evaluating effect of dexamethasone.

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Introduction: The objective was to evaluate the effects of acute exposure to high altitude and of preventive dexamethasone treatment on the postural control in patients with chronic obstructive pulmonary disease (COPD).

Methods: In this randomized, double-blind trial, 104 lowlanders with COPD, GOLD 1-2, age 20-75 y, living near Bishkek (760 m), were assigned to receive either dexamethasone (2x4 mg/d p.o.) or placebo on the day before ascent and during a 3-day sojourn at Tuja-Ashu high altitude clinic (3200 m), Kyrgyzstan. Postural control was assessed with a Wii Balance Board™ at 760 m and one day after arrival at 3200 m. Patients were instructed to stand immobile on both legs with eyes open. Mean values from 5 tests of 30 sec per patient are reported.

Results: With ascent from 760 to 3200 m the center of pressure path length (PL) increased in the placebo group from median (quartiles) 29.2 (25.8;38.2) to 31.5 (27.3;39.3) cm (P<0.04); in the dexamethasone group the corresponding increase from 28.8 (22.8;34.5) to 29.9 (25.2;37.0) cm was not significant (P=0.10). The mean difference between dexamethasone and placebo group in altitude-induced changes (treatment effect) was -0.3 cm (95% CI -3.2 to 2.5 cm, P=0.41). Multivariate regression analysis confirmed a significant increase in PL with higher altitude (coefficient 1.6, 95% CI 0.16 to 3.0, P=0.03) but no decrease with dexamethasone (coefficient 0.01, 95% CI -3.8 to 3.8, P=1.00) when controlled for several potential confounders. PL changes were related more to antero-posterior than lateral sway. 22 of 104 patients had an altitude related increase in the antero-posterior sway velocity of >25% that was associated with a two-fold risk of falls in previous studies (Kwok, Clark et al. Clin Biomech 2015;30:481)

Conclusion: Lowlanders with COPD travelling from 760 to 3200 m revealed postural instability 24h after arriving at high altitude, and this was not attenuated by preventive dexamethasone treatment. In certain patients, the altitude related increase in antero-posterior sway velocity was in an order of magnitude raising concerns of an increased risk of falls.


Disclosure of Interest: None Declared
**PP-122**

8. Pneumology and Thoracic Surgery

Effectiveness of the “living well with copd” intervention on coping, smoking behavior and exacerbations in patients from swiss primary care: a non-randomized controlled study

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**Introduction:** Pivotal objectives of self-management programmes are behavior change, coping and better health related quality of life (HRQL). The aim of this study was therefore to compare the effects of the “Living well with COPD” (LWWCOPD) self-management program and usual care on coping, HRQL, smoking cessation rates and exacerbation frequency at 24 months in COPD patients from primary care.

**Methods:** Prospectively planned non-randomized controlled study with COPD patients who took part in the “Living well with COPD program” adapted to primary care in Switzerland. COPD patients from the primary care-based COPD Cohort ICE COLD ERIC (http://www.ClinicalTrials.gov with the identifier: NCT00706602) served as control group. The primary outcome was coping as measured by the mastery domain of the Chronic Respiratory Questionnaire (CRQ). We performed multivariate regression analyses where we accounted for the lack of randomization through propensity scores.

**Results:** 71 patients were in the self-management and 385 in the usual care cohort. Patients with the self-management program had significantly higher (i.e. better) mastery scores (0.71 (95% CI 0.28-1.13)) exceeding the minimal important difference of the CRQ of 0.5. Patients with the self-management program showed significantly less moderate to severe exacerbations over the course of two years (incidence rate ratio 0.68, 95% CI 0.48-0.97) and significantly more patients quite smoking at 24 months (odds ratio 0.26 (95% CI 0.07-0.95). There was a significant effect on fatigue (0.75, 95% CI 0.28-1.22) whereas the effect just did not reach statistical significance for dyspnea (0.50, 95% CI -0.03-1.03) and emotional function (0.40, 95% CI -0.03-0.82, all CRQ).

**Conclusion:** The LWWCOPD intervention in COPD patients in a primary care setting showed long-term benefits on coping, exacerbations and smoking cessation behavior.

**Disclosure of Interest:** C. Steurer-Stey Consultant for: GSK, Boehringer Ingelheim, Novartis, Speakers bureau: AstraZeneca, GSK, J. Braun: None Declared, V. Gaveikaite: None Declared, S. Markun: None Declared, K. DallaLana: None Declared, M. Puhan: None Declared
**Introduction:** Recruiting patients for research in general practice is particularly difficult in diseases that tend to remain underdiagnosed like chronic obstructive lung disease (COPD). Researchers may consider introducing case finding in patient recruitment but the impact on recruitment yield is largely unknown.

**Methods:** For a cluster RCT on COPD in general practice, an opportunistic case finding strategy was introduced in patient recruitment in addition to recruiting patients with previously diagnosed COPD. Recruitment process and performance of general practitioners (GPs) was analyzed. Numbers and characteristics of patients identified by case finding were compared with those of patients with previously diagnosed COPD.

**Results:** Thirty-five GPs approached 400 and successfully recruited 216 patients during one year. The mean number of patients recruited was 6.4 (range 0 to 16) patients per GP. Case finding contributed 71 (32.9%) patients that had significantly milder disease with FEV1 % +16.7 (95%CI: +11.3 to +22.0), 43.7 % GOLD I (vs 17.4%), CAT difference -4 points (95%CI: -2 to -6) and a significantly higher current smoking rate with 70.4% compared to 48.6 % (p=<0.002) than patients with previously diagnosed COPD.

**Conclusion:** Opportunistic case finding increased the number of recruited patients by almost 50%. The COPD patients identified by case finding differed importantly from those with previously diagnosed COPD. Researchers should be aware of the impact of case finding during recruitment, especially in healthcare settings with high rates of COPD underdiagnosis.

**Disclosure of Interest:** None Declared
**Introduction:** Chronic obstructive pulmonary disease (COPD) patients with acute hypercapnic respiratory failure (AHRF) treated in the intensive care unit (ICU) have a high risk of readmission and death. Exacerbations become more frequent as FEV1 decreases, but the prediction of subsequent risk is now better assessed by combining FEV1 values, history of previous exacerbations, and comorbidities. Dyspnea, a common symptom of COPD, is associated with poor outcome in the general population, because it is a proxy for important heart and lung diseases. Our objective was to investigate whether dyspnea per se is an independent predictor of life-threatening events in COPD after index ICU admission.

**Methods:** This study is part of a larger cohort looking at the impact of important co-morbidities in patients surviving AHRF in the ICU. Pulmonary function tests and transthoracic echocardiography were obtained 15 days after ICU discharge. Impact of dyspnea was measured using NYHA scale on the day of hospital discharge. Hospital readmission, ICU readmission, and death were recorded at regular intervals for 6 months. We constructed a Kaplan-Meier cumulative event curve for a combined event of readmission and death. The log-rank test was used to compare the curves in two groups and the Cox proportional hazard model was used to test the independent effects of factors related to dyspnea.

**Results:** 47 COPD patients were included (table 1). Among 17 patients with NYHA III-IV, 11 (65%; 95% CI: 38%-86%) were either readmitted or died during the observation period. Among 28 patients with NYHA I-II, 10 patients (36%; 95% CI: 19%-56%) were either readmitted or died during the same observation period (figure 1). NYHA III or IV was associated with adverse outcome compared to NYHA I or II (on log-rank test P=0.038). After multiple adjustments for age, body mass index, severity of COPD, and presence of heart failure, only NYHA III-IV remained associated with readmission and death (hazard ratio=2.70; 95% CI: 1.05-6.97; P=0.040).

**Conclusion:** Our data suggest that dyspnea is an important determinant of readmission and death in COPD patients surviving AHRF. This remains equally true after adjustment for the severity of obstruction and major co-morbidities associated with dyspnea.

**Disclosure of Interest:** None Declared
Introduction: The 6-Minute Walk Test (6MWT) is routinely used to quantify exercise capacity in patients with chronic cardio-pulmonary diseases. Cardiopulmonary exercise testing devices enable to measure breath-by-breath oxygen exchange (VO2) kinetics during exercise performance. From the original acquired oxygen exchange data, curves can be derived and parameters can be estimated by model fitting. Simultaneous modeling of multiple kinetics requires nonlinear mixed models methodology. To the best of our knowledge, no such curve-fitting approach has been used to analyze multiple VO2 kinetics in both research and clinical practice so far. The aim of this work was to describe functionality of a new statistical package that allows fitting nonlinear mixed models for automated curve fitting modeling.

Methods: Patients with COPD referred to the Department of Pulmonary Medicine of the University Hospital of Basel for a 6MWT gave informed consent to participate to the study. A six-parameter nonlinear regression model describing the 3 main phases of the oxygen kinetics (before, during and after 6MWT) was defined and fitted using the newly developed package medrc from the R statistical software. The new methodology was compared to a curve-by-curve approach.

Results: VO2 kinetics were measured in 61 patients with COPD who were classified into 3 disease severity stages (GOLD II, III and IV). The six-parameter model was jointly fitted to the set of 61 oxygen kinetics. Figure 1 displays the 61 raw oxygen kinetics data together with the fitted curves summarized within each COPD disease severity stage. Significant differences between disease stages were found regarding maximum oxygen uptake during exercise testing (II vs. IV: adj. p = 0.038), oxygen level after recovery (II vs. IV, adj. p = 0.0013) and inflection point in the recovery phase (II vs. IV, adj. p = 0.088). In comparison with the curve-by-curve approach, the estimates obtained by nonlinear mixed model regression shows that the standard errors are consistently smaller. Thus, the proposed mixed model methodology resulted in a gain in efficiency and power.

Picture/Graph:
Conclusion: The R package medrc provides a comprehensive and flexible framework for the parametrisation and inference of nonlinear mixed-effects regression models with various biological and medical applications, as exemplified by an application from pulmonary medicine. Physicians and clinicians may find it interesting to have access to and work with an all-integrated infrastructure for advanced modeling.

Disclosure of Interest: None Declared
Introduction: Functional deficiency of mannose-binding lectin (MBL) may contribute to the pathogenesis of chronic obstructive pulmonary disease. We hypothesized that specific MBL2 gene polymorphisms and circulating MBL protein levels are associated with clinically relevant outcomes in the Predicting Outcome using systemic Markers In Severe Exacerbations of COPD PROMISE-COPD cohort.

Methods: We followed 277 patients with stable COPD GOLD stage II-IV COPD over a median period of 733 days (IQR 641–767) taking survival as the primary outcome parameter. Patients were dichotomized as frequent (≥ 2 AECOPD/year) or infrequent exacerbators. Serum MBL levels and single nucleotide polymorphisms of the MBL2 gene were assessed at baseline.

Results: The MBL2-HYPD haplotype was significantly more prevalent in frequent exacerbators (OR: 3.33; 95% CI, 1.24 - 7.14, p=0.01). The median serum MBL concentration was similar in frequent (607 ng/ml, [IQR; 363.0 – 896.0 ng/ml]) and infrequent exacerbators (615 ng/ml, [IQR; 371.0 – 942.0 ng/ml]). Serum MBL was not associated with lung function characteristics or bacterial colonization in sputum. However, high serum MBL at stable state was associated with better survival compared to low MBL (p=0.046, log rank test).

Conclusion: In COPD, the HYPD haplotype of MBL2 gene is associated with frequent exacerbations and high serum MBL is linked to increased survival.

The PROMISE-COPD study was registered at www.controlled-trials.com under the identifier ISRCTN99586989.

Disclosure of Interest: None Declared
8. Pneumology and Thoracic Surgery
On-line breath analysis of copd patients reveals altered metabolic signatures between frequent and non-frequent exacerbators

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Introduction: Using real-time mass spectrometry, we investigated the profiles of volatile and semi-volatile organic compounds (VOC, sVOC) in exhaled breath of patients suffering from chronic obstructive pulmonary disease (COPD), with and without frequent exacerbations. The aim of the study was to discriminate between the two groups as well as getting an insight into underlying metabolic differences to better understand exacerbation events.

Methods: COPD patients with frequent exacerbations (defined as ≥ 2 exacerbations during the last 12 months) and non-frequent exacerbations were recruited and matched in terms of gender, age and smoking history. Their breath was analysed in real-time, using secondary electrospray ionization mass spectrometry (SESI-MS). Extensive data analysis was then applied to identify metabolic patterns which are significantly different between the two groups, which are then also used to train a classification algorithm.

Results: Using the preliminary data of 15 respectively 16 patients, we successfully identified metabolic patterns in exhaled breath, which are significantly different between COPD patients with and without frequent exacerbations. In total we observed approximately 65 significant (p<0.05) features. Amongst others, putative short-chained fatty acids, aldehydes and saturated polyols were detected. A correlation analysis revealed several highly correlating families, suggesting underlying metabolic influences.

Conclusion: The preliminary results suggest that breath analysis by real-time mass spectrometry allows the identification of mass-spectral features discriminating COPD patients with and without frequent exacerbations with good accuracy. Untargeted real-time mass spectrometry is a powerful and easily applicable method to get new insights into the pathophysiology of COPD exacerbations.

References: *These authors contributed equally to this work

Disclosure of Interest: None Declared
Introduction: There are concerns that altitude travel may induce cerebral hypoxia, in particular in patients with preexisting lung disease and during sleep. Therefore, we investigated cerebral oxygenation in lowlanders with COPD spending one night at 2590 m.

Methods: 37 COPD patients living below 800m (mean age±SD, 62.4±12.3y, FEV1 61±16 %pred.) underwent sleep studies with monitoring of arterial oxygen saturation (SpO2 by pulse oximetry) and cerebral tissue oxygenation in the prefrontal cortex (CTO by near-infrared spectroscopy) at 490m and in the first night after arrival at 2590m.

Results: At 2590m, both mean SpO2 and CTO were significantly decreased compared to 490m although the decrease in CTO was less pronounced. Moreover, oxygenation was unstable with frequent desaturation events (>4% dips) in SpO2 and, to a lesser extent, in CTO (table).

<table>
<thead>
<tr>
<th></th>
<th>490 m Means±SD</th>
<th>2590 m Means±SD</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean nocturnal SpO2, %</td>
<td>92.0 ± 2.2</td>
<td>83.6 ± 4.7</td>
<td>-8.4 (-9.7; -7.0)*</td>
</tr>
<tr>
<td>Mean nocturnal CTO, %</td>
<td>65.3 ± 5.6</td>
<td>61.7 ± 5.4</td>
<td>-3.6 (-5.6; -1.5)*†</td>
</tr>
<tr>
<td>SpO2-OD, 1/h</td>
<td>8.2 ± 9.3</td>
<td>41.6 ± 34.1</td>
<td>33.5 (23.3; 43.7)*†</td>
</tr>
<tr>
<td>CTO-OD, 1/h</td>
<td>0.9 ± 1.5</td>
<td>4.0 ± 5.8</td>
<td>3.1 (1.3; 4.9)*†</td>
</tr>
<tr>
<td>CTO-OD / SpO2-OD</td>
<td>0.14 ± 0.15</td>
<td>0.11 ± 0.16</td>
<td>-0.03 (-0.10; 0.05)</td>
</tr>
</tbody>
</table>

SpO2: arterial oxygen saturation; CTO: cerebral tissue oxygenation; OD: oxygen desaturation event; †p<0.05 versus altitude induced change in SpO2.

Conclusion: In lowlanders with COPD travelling to 2590m the arterial hypoxemia due to reduced barometric pressure and high altitude periodic breathing is associated with persistent and intermittent cerebral hypoxia. Although it is less pronounced than the drop in arterial oxygen saturation, the altitude induced cerebral deoxygenation may represent a risk of brain dysfunction.

Grant: Swiss National Science Foundation, Lung League Zurich

Disclosure of Interest: None Declared
A human in vitro airway epithelial model to study the effects of aerosolized multi-walled carbon nanotubes in chronic obstructive pulmonary diseased cells

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Introduction: The risks of occupational exposures at working places where engineered nanomaterials (one dimension below 100nm) are produced and processed, have received limited attention to date. There is, however, growing concern about health-effects in the lung of large-scale produced multi-walled carbon nanotubes (MWCNTs), when released into the environment. Special attention also should be paid on risks assessment for susceptible persons suffering from pulmonary disease such as chronic obstructive lung disease (COPD).

Methods: Primary human bronchial epithelial cells from healthy donors and COPD patients COPD were grown in vitro at the air-liquid interface (ALI). Cells were exposed to aerosolized MWCNTs resulting in two concentrations deposited onto the cell surface (0.12µg/ml; 0.4µg/ml). Differentiation, integrity, pro-inflammatory status and viability of cultures were monitored 24h after exposure using laser scanning microscopy, transmission electron microscopy (TEM), LDH analysis, ELISA and real-time qPCR. Ciliary beating frequency was measured before and after exposure to MWCNTs.

Results: Cultures of healthy and COPD patient showed a tight monolayer consisting of differentiated ciliated and mucus-producing cells, when cultured at the ALI. Differentiation and epithelial integrity was maintained even after exposure to MWCNTs as visualized by microscopy. TEM micrographs showed that MWCNTs were localized extra- but also intracellular inside vesicular structures in cultures from healthy and COPD subjects. Preliminary data revealed that neither release of LDH, RNA expression (IL-6, IL-8, IP-10) nor the secretion of pro-inflammatory cytokines was triggered by MWCNTs, both in healthy and COPD cells. Ciliary beating frequency of COPD and/or exposed cells did not deviate from healthy, untreated cells, showing an average value of 8.8±2.29Hz.

Conclusion: This in vitro model represents a appropriate tool to investigate effects of engineered nanomaterials on the human respiratory tract. Realistic occupational dosage of MWCNTs nebulised at the ALI representing an acute exposure did not cause any adverse effects in healthy or COPD cells.

Disclosure of Interest: None Declared
Exhaled breath analysis identifies altered metabolic signature in chronic obstructive pulmonary disease


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Introduction: Diagnosis of chronic obstructive pulmonary disease (COPD) is currently based on fixed airflow limitation in spirometry, respiratory symptoms and an appropriate history of exposure to risk factors. New mass spectrometry techniques analysing exhaled breath might have the potential to better define airway diseases in terms of pathophysiological and clinical phenotyping. We aimed at defining profiles of volatile organic compounds (VOCs) in exhaled breath from patients suffering from COPD using real-time mass spectrometry.

Methods: In this prospective cohort study, patients with COPD GOLD stage 1-4 were recruited from our outpatient clinic. Exhaled breath analysis by untargeted mass spectrometry was performed using secondary electrospray ionization-mass spectrometry (SESI-MS). Breath prints were matched to healthy controls according to age, gender and smoking state. The primary outcome was the ‘COPD specific’ exhaled breath pattern.

Results: Exhaled breath from 22 patients with COPD (mean age 58.6±6.9 years, FEV₁ 58.5±19.9% predicted, 32.4±19.2 pack years) and 14 controls (mean age 58.1±8.1 years, FEV₁ 102.5±11.3% predicted, 23.6±12.5 pack years) was analysed using secondary electrospray ionization-mass spectrometry. 14 features were found to be highly specific to differentiate COPD patients from healthy controls, the most discriminating features showed a prediction accuracy of 88.9% (95% CI 73.9% - 96.9%) with a sensitivity of 92.9% and a specificity of 86.4%. Metabolites from oxidative stress processes like fatty acids and amino acid-related compounds were found to differ significantly between COPD patients and healthy controls.

Fig. 1. Real-time breath analysis (left boxes): time traces of a selected feature (m/z 105.1) for a healthy control and a COPD Patient. The breath signals from the patient are enhanced in comparison to the ones from the healthy control. Between group comparison (right box) for the same feature for all study participants showing a distinct difference between both groups (pFDR = 0.02).
Conclusion: Breath analysis by real-time mass spectrometry allows the identification of mass-spectral features discriminating COPD patients from matched, healthy controls with a high sensitivity and specificity within a few minutes. Real-time mass spectrometry is a powerful and easily applicable method to get new insights into the pathophysiology of the disease.
* These authors contributed equally to this work

Disclosure of Interest: None Declared
Introduction: Hospitalizations because of acute exacerbated COPD (AECOPD) are a major burden to patients and the healthcare system. Adherence to recommended interventions of acute and post-acute care targeting at preventive and chronic care measures is crucial for improving short-, medium- and long-term outcomes.

Methods: Twenty-four months (1.1.2012-31.12.2013) retrospective medical chart review of patients hospitalized to 3 public hospitals in the Canton of Zurich with a principle diagnosis of AECOPD. We assessed the documentation of guideline-recommended acute and post-acute interventions before discharge.

Results: Data from 263 patients (61% male, mean age 68.5 years, 47% active smokers) were analyzed. Severity of COPD was GOLD I 2%, GOLD II 23%, GOLD III 37%, GOLD IV 38%. The mean length of stay was 10 days (SD 6.05). Documentation of acute care interventions: radiologic imaging 96 %, arterial blood gas analysis 75 %, treatment with systemic corticosteroids 79%, prescription of antibiotic therapy 76% with appropriate prescribing according to GOLD guidelines in 56% consisting in 38% overuse and 6% underuse. Documentation of post-acute care interventions: patient education and self-management support 2%, influenza vaccination/recommendation 11% , physical activity counseling 13% , assessment of inhalation technique 20%, referral for pulmonary rehabilitation 24% and smoking cessation intervention or counselling 47%.

Conclusion: This study shows low adherence to post-acute care interventions for AECOPD. Fostering these interventions is investing in medium and long-term prognosis, opportunities that should not be missed in hospital care.

Disclosure of Interest: None Declared
Introduction: Patients with chronic obstructive pulmonary disease (COPD) may be severely limited in daily life but exercise tests may not adequately reflect this limitation. We therefore assessed whether daily activity monitored with an acceleration sensor at the arm correlates with exercise capacity and nocturnal oxygen saturation in patients with COPD.

Methods: COPD patients underwent activity monitoring (Sensewear™), a maximal bicycle exercise test (CPET), a 6 minute walk distance (6MWD) and an ambulatory respiratory sleep study. Senswear™ derived activity was quantified by the mean count of steps/day, daily estimated energy expenditure (EE) over 24h and average of metabolic equivalents (METs) per day. Pearson correlations of activity with exercise parameters or sleep were calculated.

Results: 20 COPD patients (11 female, age 65±6y, FEV1 64±19%pred) were recruited. Patients were moderately active (7120±3492 steps/day), estimated EE was 9166±1085kJ and METs 1.4±0.2. Mean nocturnal oxygen saturation was 92±2%, oxygen desaturation index was 4.4±4.6. The steps/day correlated with FEV1%pred (r=0.51, p<.05) but not with the 6MWD. The EE was positively correlated with the maximal workload during CPET and the apnea/hypopnea index but not with mean nocturnal SpO2 or the 6MWD. Conversely, the METs were negatively correlated with the nocturnal oxygen desaturation index and mean nocturnal oxygen saturation.

<table>
<thead>
<tr>
<th></th>
<th>Maximal workload</th>
<th>6 minute walk distance</th>
<th>Apnea/hypopnea index</th>
<th>Nocturnal SpO2</th>
<th>Number of desaturations</th>
<th>Oxygen desaturation index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy expenditure per day</td>
<td>0.70*</td>
<td>-0.07</td>
<td>0.50*</td>
<td>0.11</td>
<td>0.33</td>
<td>0.33</td>
</tr>
<tr>
<td>Average metabolic equivalents per day</td>
<td>0.18</td>
<td>0.39</td>
<td>-0.18</td>
<td>0.52*</td>
<td>-0.48*</td>
<td>-0.51*</td>
</tr>
<tr>
<td>Steps/day</td>
<td>0.39</td>
<td>0.14</td>
<td>0.28</td>
<td>0.28</td>
<td>0.10</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Numbers represent Pearson correlation coefficients; *p<0.05.

Conclusion: Patients with less severe airflow obstructions show higher daily activity. Daily activity measurements recorded in COPD patients with an arm sensor provide important information that is complementary to lung function, ergometry and walk tests since activity recordings estimate EE over several days in the setting of the patients’ everyday life. Daytime and nocturnal ventilation and oxygenation differently affect activity derived estimates of EE.

Disclosure of Interest: None Declared
Introduction: Since 2013 the Federal Office of Public Health in Switzerland (BAG) requires that all patients receiving replacement therapy for alpha 1-antitrypsin deficiency (AAT deficiency) are centrally registered by the Swiss Society of Pneumology. Moreover, patients should be biannually controlled by pulmonary A clinics (Genf, Lausanne, Bern, Basel, Zürich or St. Gallen). The registry allows insights about care of people with AAT deficiency and helps to better understand outcomes and disease progression.

Methods: The registry collects data from patients with AAT deficiency who receive replacement therapy (mandatory registry inclusion) and from patients without replacement therapy (facultative inclusion). Data include information from face to face interview (eg smoking, exacerbations), lung function and symptom scores. The preliminary data of the first 2 years (read out end 2015) are presented with general descriptive statistics and illustration for individual cases.

Results: Until read out 48 patients were registered (figure) of whom 42 had a complete baseline evaluation and 28 had at least one follow-up visit. Their mean (SD) age was 52 (12) years and BMI 24.7 (4.0) kg/m2. Twelve patients were already under replacement therapy at baseline evaluation while in 15 patients replacement therapy was started in the follow-up period. Mean (SD) FEV1 %pred. and DLCO % in the replacement group was 35.7(13.1)% and 35(11)% vs. 54.4(24.2)% (p=0.016) and 59(24)% (p= 0.003) in the group without substitution. Of 12 patients under replacement therapy at baseline, 58% had at least one exacerbation in the year prior to inclusion compared to 53% in the group without replacement (p=0.76). Mean CAT score under substitution was 16(9) vs 14(7) in patients without replacement therapy.

Picture/Graph:
Conclusion: Since relaunch of the registry in 2013 the initial results shed light on characteristics of “real-world” patients with AAT deficiency living in Switzerland. Nearly 60% of patients in the registry receive a replacement therapy and usually present with severely reduced lung function at time of inclusion. The goal of the registry will be to improve understanding of AAT deficiency by studying the disease course in a real world setting.

Disclosure of Interest: None Declared
Cardiopulmonary- and hemodynamic responses during non-invasive positive airway pressure ventilation in patients with chronic obstructive pulmonary disease
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Pneumology, KSSG, St. Gallen, Switzerland

Introduction: In order to decrease the work of breathing and improve lung mechanics in patients with acute and chronic respiratory failure, non-invasive positive pressure ventilation (NPPV) seems to be the treatment of choice. However, data reflecting cardiopulmonary- and hemodynamic responses during NPPV in patients with COPD are mostly lacking. The overall aim of the present study was to investigate if NPPV influences cardiopulmonary- and hemodynamic responses by conducting three different levels of positive pressure throughout the entire breathing cycle in patients with COPD and in age-gender matched controls.

Methods: Non-invasively obtained continuous hemodynamic measurements of beat-to-beat arterial blood pressure was recorded with the FinometerTM device (FMS, Finapress Measurement Systems, Amsterdam, Netherlands) using of a photoplethysmographic-arterial/ volume clamp applied at the level of the right index finger. Measurements were conducted during a resting period of five minutes as well as during 3 minutes of 3 different levels of NPPV. The variable of choice was the speed of beat-to-beat changes in systolic blood pressure (vSBP). vSBP was assessed by calculating the mean of absolute successive interbeat-interval differences of oscillatory fluctuations in SBP.

Results: In 9 patients with COPD (6 females) with a mean (SD) age 67 (6) years, forced expiratory volume in one second (FEV1) was 43 (10) % predicted, and mean vSBP at rest was 4.06 mmHg/ IBI. In 9 healthy controls (5 females) with a mean (SD) age 69 (9) years, the observed mean vSBP at rest of 3.06 mmHg/ IBI was not significantly different (p=0.18) from that of the patients. In addition, by using linear regression with mixed effects we demonstrated that there was no difference of vSBP between the patients and the healthy controls among the 3 different levels of NPPV. However, there was a significant positive association between the level of NPPV (mbar) and vSBP in both groups (patients estimates= 0.120, SE= 0.040, p=0.005, healthy controls estimates= 0.102, SE= 0.021, p<0.001).

Conclusion: Patients with COPD do not have steeper blood pressure changes than healthy controls. By conducting positive airway pressure the speed of fluctuations in SBP increases both in patients with COPD and in healthy controls.

Disclosure of Interest: None Declared
Introduction: Consultation intervals of COPD patients are currently based on personal judgement of the treating physicians, disease severity and patient preference. By this routine, important disease events (e.g. acute exacerbations of COPD (AECOPD)) are recognised belatedly. By earlier detection of these, emergency admissions and emergency hospitalisations could possibly be reduced. Different studies investigating multidisciplinary COPD-management programs supported by telehealthcare have shown conflicting results. The objective of the present study is to test the feasibility and establish telehealthcare to optimise care for COPD patients.

Methods: COPD patients daily entered their perception regarding the disease answering a structured questionnaire, which is focused on the detection of AECOPD using the electronic health care platform “Evita” by Swisscom, which has been adapted for this project by the study team and Swisscom. All entered data were daily analysed by the study team (pulmonologist and nurse), who called the patient by phone in case of suspected AECOPD for further evaluation.

Results: Of 339 screened patients, 48 (14.2%) were included. Main reasons for exclusion were missing technical equipment (27%) and not being interested in participating (23%). Mean age was 63 years; mean follow up was 231 days. Primary endpoints: data completeness was 87.6% (9819/11083 patient days); 93.8% (45/48 patients) completed the study. Secondary endpoints: with the current “alarming” system, we identified 60 AECOPD in 22 patients. 2 AECOPD were not detected by this algorithm. The sensitivity of the procedure in detecting AECOPD was 96.8%; specificity was 98.3%, positive predictive value 26.1% and negative predictive value 99.9%. No patient died. We conducted 230 telephone calls in 38 patients with a mean duration of 3.8 minutes.

Conclusion: Telehealthcare for COPD is feasible in a selected subgroup of COPD patients, missing technical equipment being the main exclusion criterion. Eligible patients show an excellent compliance of 88% completely entered data and a high acceptance with 94% of patients completing the study. The current telehealthcare procedure has a very high sensitivity and negative predictive value for detecting or excluding AECOPD, while the positive predictive value is low. The last aspect can lead to a disproportional expenditure of time and has to be improved by refining the intervention algorithm.

Disclosure of Interest: None Declared
8. Pneumology and Thoracic Surgery

Interferon-lambda-genotype gg and IgG2 predict frequent COPD exacerbations in a Swiss multicenter COPD cohort study (TOPDOCS)

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Introduction: Background and Importance

Chronic obstructive pulmonary disease (COPD) exacerbations are associated with disease progression, worsening health status, more hospitalizations and COPD-related mortality. During stable COPD, the identification of patients at high risk for exacerbations has a high impact for clinical management. Several biomarkers hold promise to predict exacerbation episodes, however, the assessment of the individual risk of exacerbation is challenging.

Objective

The goal of this study was to investigate the impact of different biomarkers and genetic single nucleotide polymorphisms (SNPs) as predictors of frequent exacerbations (≥2/y).

Methods: In 270 patients (mean age 63 years; 67% male) with COPD enrolled in The Obstructive Pulmonary Disease Outcomes Cohort of Switzerland (TOPDOCS) biomarkers such as concentrations of serum mannose-binding lectin (MBL), immunoglobulins and IgG subclasses were quantified, and IFN-lambda-genotypes (rs8099917) were determined. Biomarkers and genotypes were associated in COPD patients with frequent (≥2 per year) and less frequent (0-1 per year) exacerbations.

Results: The mean value ± standard deviation, the ANOVA-p-value of the measured biomarkers and the Chi-square of Pearson of the genotypes are shown in the following table

Picture/Graph:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0 exacerbations</th>
<th>1 exacerbation</th>
<th>2 exacerbations</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBL (µg/ml)</td>
<td>1.62 (± 1.46)</td>
<td>1.85 (± 1.58)</td>
<td>1.78 (± 1.80)</td>
<td>0.570</td>
</tr>
<tr>
<td>IgG (g/l)</td>
<td>9.7 (± 3.0)</td>
<td>8.9 (± 2.2)</td>
<td>8.6 (± 2.4)</td>
<td>0.018</td>
</tr>
<tr>
<td>IgA (g/l)</td>
<td>2.4 (± 1.0)</td>
<td>2.6 (± 1.3)</td>
<td>2.3 (± 1.0)</td>
<td>0.245</td>
</tr>
<tr>
<td>IgM (g/l)</td>
<td>1.0 (± 0.6)</td>
<td>1.1 (± 0.8)</td>
<td>1.1 (± 2.0)</td>
<td>0.875</td>
</tr>
<tr>
<td>IgE (IU/ml)</td>
<td>117.8 (± 317.5)</td>
<td>285.1 (± 929.2)</td>
<td>143.3 (± 560.9)</td>
<td>0.149</td>
</tr>
<tr>
<td>IgG1 (g/l)</td>
<td>6.2 (± 2.2)</td>
<td>5.8 (± 1.6)</td>
<td>5.9 (± 1.8)</td>
<td>0.237</td>
</tr>
<tr>
<td>IgG2 (g/l)</td>
<td>3.1 (± 1.6)</td>
<td>2.8 (± 1.1)</td>
<td>2.4 (± 1.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>IgG3 (g/l)</td>
<td>0.4 (± 0.3)</td>
<td>0.4 (± 0.2)</td>
<td>0.5 (± 0.5)</td>
<td>0.394</td>
</tr>
<tr>
<td>IgG4 (g/l)</td>
<td>0.5 (± 0.5)</td>
<td>0.6 (± 0.6)</td>
<td>0.5 (± 0.5)</td>
<td>0.557</td>
</tr>
</tbody>
</table>

Picture/Graph 2:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0 exacerbations</th>
<th>1 exacerbation</th>
<th>2 exacerbations</th>
<th>P (Chi-square of Pearson)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype TT</td>
<td>33/ 98</td>
<td>28/ 46</td>
<td>18/ 47</td>
<td>0.153</td>
</tr>
<tr>
<td>Genotype TG</td>
<td>42/ 89</td>
<td>28/ 46</td>
<td>27/ 38</td>
<td>0.395</td>
</tr>
<tr>
<td>Genotype GG</td>
<td>0/ 131</td>
<td>1/ 73</td>
<td>3/ 62</td>
<td>0.042</td>
</tr>
</tbody>
</table>
**Conclusion:** We observed that IgG, in particular IgG2 subclass concentrations but not serum MBL levels are associated with an increased risk of COPD exacerbations. Genotyping of the IFN-lambda-gen showed that GG-genotype may be linked to higher exacerbation risk as well. Therefore, measuring IgG2 and determining the IFN-lambda-genotype may be helpful to predict the risk of exacerbation in patients with COPD and thus to prevent complications and disease progression in these patients.

**Disclosure of Interest:** None Declared
Introduction: Background and Importance
Chronic obstructive pulmonary disease (COPD) exacerbations may be linked to serious consequences. They contribute to disease progression, worsening health status, more hospitalization and are directly linked to COPD-related mortality. Some patients are at particularly high risk. However, the individual risk of exacerbation is difficult to determine.

Objective
The goal of this study was to investigate the value of clinical characteristics as predictors of frequent exacerbations (≥2/y).

Methods: In 270 patients (mean age 63 ± years; 67% male) with COPD enrolled in The Obstructive Pulmonary Disease Outcomes Cohort of Switzerland (TOPDOCS) different clinical parameters were measured. Differences between COPD patients with frequent (≥2 per year) and less frequent (0-1 per year) exacerbations were assessed.

Results: The mean value ± standard deviation and the ANOVA-p-value of different clinical parameters are shown in the following table:

Picture/Graph:
**Conclusion:** CAT-score, the GOLD-classification, MMRC-score and the SF-6D V1 and V2 are significantly associated with exacerbation risk. Also the weight, heart rate, O2-saturation, lung function parameters, the thrombocytes and bilirubin-value appear to contribute further to the prediction of frequent exacerbations.

**Disclosure of Interest:** None Declared

<table>
<thead>
<tr>
<th>parameter</th>
<th>0 exacerbations</th>
<th>1 exacerbation</th>
<th>2 exacerbations</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD Assessment Test</td>
<td>13.9 (± 7.1)</td>
<td>16.3 (± 6.7)</td>
<td>19.3 ± 6.9</td>
<td>0.000</td>
</tr>
<tr>
<td>Short Form-6 dimension V1 questionnaire</td>
<td>0.7 (± 0.1)</td>
<td>0.7 (± 0.1)</td>
<td>0.6 (± 0.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>Short Form-6 dimension V2 questionnaire</td>
<td>0.7 (± 0.1)</td>
<td>0.7 (± 0.1)</td>
<td>0.6 (± 0.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>GOLD (Global Initiative for Chronic Obstructive Lung Disease)</td>
<td>2.3 (± 0.9)</td>
<td>3.0 (± 0.8)</td>
<td>3.2 ± 0.8</td>
<td>0.000</td>
</tr>
<tr>
<td>MMRC (Modified Medical Research Council dyspnea scale)</td>
<td>1.4 (± 1.1)</td>
<td>2.0 (± 1.0)</td>
<td>2.2 (± 0.9)</td>
<td>0.000</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.3 (± 20.0)</td>
<td>75.2 (± 18.8)</td>
<td>70.6 (± 19.2)</td>
<td>0.004</td>
</tr>
<tr>
<td>heart rate (bpm)</td>
<td>74.6 (± 13.5)</td>
<td>80.6 (± 11.5)</td>
<td>84.7 (± 13.6)</td>
<td>0.000</td>
</tr>
<tr>
<td>sO2 (%)</td>
<td>94.3 (± 3.0)</td>
<td>92.8 (± 4.1)</td>
<td>93.6 (± 3.7)</td>
<td>0.023</td>
</tr>
<tr>
<td>FEV1/FVC (%) Post % Soll</td>
<td>66.0 (± 20.1)</td>
<td>53.2 (± 15.5)</td>
<td>48.1 (± 16.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>Thrombocytes (x10^9/l)</td>
<td>248.8 (± 68.0)</td>
<td>267.0 (± 74.1)</td>
<td>287.2 (± 70.9)</td>
<td>0.002</td>
</tr>
<tr>
<td>Bilirubin (μmol/l)</td>
<td>8.7 (±4.5)</td>
<td>9.4 (±4.6)</td>
<td>6.6 (±2.5)</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Introduction: Obstructive sleep apnea (OSA) is a common disease in the general population. Obesity is a strong risk factor of OSA and its prevalence is continuously increasing with an estimated number of 1.1 billion obese individuals (BMI>30 kg/m²) by 2030. Bariatric surgery is an intervention that produces substantial and sustained weight loss in adults. Due to the increased peri- and postoperative risk in these patients an assessment for sleep apnoea prior to bariatric surgery is recommended. The aim of this retrospective cohort study was to investigate the prevalence and independent predictive factors of OSA (AHI>5/h) in obese patients prior to bariatric surgery in a single university centre.

Methods: We analysed data of all morbidly obese patients (BMI>35 kg/m²) who underwent a home respiratory polygraphy prior to bariatric surgery between January 2012 to July 2015. Additional demographic data, laboratory values, pulmonary function testing and data from sleep questionnaires (STOPBang, Epworth Sleepiness Scale, Fatigue Severity Scale) were analysed. Statistics were performed using descriptive and multiple linear regression analysis.

Results: 265 patients were included in the analysis (76% female; median age 39 years (IQR 29-48); BMI 42.1 kg/m² (IQR 38.5-46.7)). Overall OSA (AHI>5/h) was present in 43% of patients (females 35%, males 68%, p<0.001), moderately to severe OSA (AHI>15/h) was detected in 21% (females 13%, males 48%, p=0.002). Only age (p<0.05) remained as a statistically predictive risk factor for OSA in the multiple linear regression analysis.

Conclusion: In our cohort of morbidly obese patients prevalence of OSA is relatively low compared to other studies, probably due to the younger and predominately female cohort. Routine screening for OSA prior to bariatric surgery should be performed, especially in males and older females. Better screening algorithms are needed to identify patients at risk.

Disclosure of Interest: None Declared
Introduction: Poor adherence to long-term therapies may result in poor health outcomes and increased health care costs. The objective of this study is to investigate the effects of an acoustic reminder on adherence in patients with asthma or COPD with long-term inhalative medications.

Methods: In this on-going prospective single-blind randomized controlled trial, in- and outpatients from several hospitals in the Basel region diagnosed with asthma or COPD and with prescribed inhalative medication were recruited. Moreover, they must have experienced at least one exacerbation in the previous 12 months. The intervention group is provided with an acoustic reminder for inhalation and receives support calls when the medication is not taken as prescribed. Objective adherence was measured in both groups with the electronic devices “Smartinhalers” for puff inhalators and punch cards mounted with a “Polymedication Electronic Monitoring System” for powder capsules, which record date and time of each actuation. We present preliminary data on adherence patterns of the first 54 patients (154 patients are planned to enroll) recruited since January 2014 and who completed the study. Adherence was defined as percentage of days with correct dosing (correct number of prescribed inhalations).

Results: Of the 54 (76% male, age: 67.9 ± 9.1 yrs) investigated patients, 42 (78%) had COPD, 8 (15%) asthma and 4 (7%) asthma-COPD overlap syndrome. Adherence to puff inhalers was significantly higher in the intervention group compared to the control group (80% ± 19% versus 51% ± 21%; p<0.001). Regarding powder capsules, no difference was found between intervention and control group (92% ± 9% versus 88% ± 14%; p=0.239). Overall, more days with correct dosing were observed for powder capsules compared to puff inhalers (88% ± 12% versus 66% ± 27%; p<0.001) and for therapy plans with once-daily dosage compared to plans with multiple doses per day (89% ± 13% versus 66 ± 27%; p<0.001).

Conclusion: These preliminary results suggest a beneficial effect of regular reminder on the adherence of asthma and COPD patients. Moreover, adherence with once-daily dosage regimens and with devices allowing the administration of predefined doses appears to be higher compared to treatment plans with multiple doses per day and devices that have to be loaded by the patient. The higher adherence rate obtained with electronic punch cards containing powder capsules might be due to their function as visual reminder.

Disclosure of Interest: None Declared
Introduction: Preterm birth accounts for more than 10% of births worldwide. In Switzerland, about 800 are born very preterm, meaning before 32 weeks gestational age. This population suffers from autonomic dysregulation, manifesting as temperature instability and poor control of the heart rate and breathing that necessitates intensive monitoring. Along the way, successful coordination of swallowing and breathing, reflecting a higher neurological function, represents a milestone in overall child development. Unfortunately, accurate diagnostic tools that objectively assess coordination patterns of these functions in neonates are lacking. This study presents a novel approach on esophageal signal recording to derive the desired signal modalities.

Methods: The esophageal measurement setup consists of two main components: a gastric feeding tube equipped with multiple electrodes, which can be used for infants down to 500g of body weight (Edi®-tube, Maquet, Getinge Group, Sweden), is connected to a high-resolution biopotential recorder (g.USBamp, g.tec, Austria). The recorder features multichannel signal acquisition with a sampling rate up to 38.4 kHz and 24 bit resolution. The high signal-to-noise ratio in combination with DC coupling allows the simultaneous recording of esophageal ECG, diaphragm EMG, and motion-induced baseline wander arising from respiration and esophageal peristalsis. The setup together with custom-build software was used in a clinical trial of preterm and term infants of 32 to 42 weeks gestational age.

Results: Primary analysis of the 8-lead recordings in 9 of 15 newborns shows promising results. Diaphragm EMG acquired during inspiration triggers a mechanical response seen as pseudo-periodic, baseline wander (figure 1). In contrast, esophageal peristaltic superimposing the ECG and EMG signals is acquired as stationary wave with all esophageal leads (electrode 1 = most proximal) during oral feeding (figure 2).
Conclusion: Preliminary results in infants indicate the feasibility to extract the coordination of heart rate, breathing and swallowing from high-resolution esophageal signals. This would allow an objective assessment of maturational processes in preterm infants and might support the introduction of oral feeds and decision of discharge from the intensive care. Ongoing investigations focus on automatic pattern recognition applied to the esophageal signals.

Disclosure of Interest: None Declared
Effect of continuous positive airway pressure on circadian patterns of cardiac repolarization in obstructive sleep apnoea: data from a randomized controlled trial.

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Introduction: Obstructive sleep apnoea (OSA) has been proposed as an independent risk factor for sudden cardiac death (SCD). This study takes advantage of a previous randomized trial, evaluating circadian patterns of the QTc-interval, a marker of cardiac repolarization and biomarker for SCD, in patients with OSA. We hypothesized that patients with OSA exhibit longest QTc during the nighttime and that continuous positive airway pressure (CPAP) therapy would reverse this.

Methods: 118 patients diagnosed with moderate-to-severe OSA were randomized to receive therapeutic or subtherapeutic CPAP for four weeks. Of these, 84 had full 24h-Holter monitoring data. Weighted means of all QTc-intervals were analysed over 24h, during four time-periods (12pm-6am, 6am-12am, 12am-6pm, 6pm-12pm) as well as during each hour.

Results: QTc-intervals at baseline were highest from 6pm-12pm (411.7ms) and shortest from 6am-12am (405.4ms). Overall 24h CPAP treatment effect on QTc was -11.3ms (p=0.039) and was estimated to be greater from 6pm-12pm than from 12pm-6am (p=0.068). The CPAP treatment effect on QTc was driven by those patients in the highest QTc decile at baseline (all>430ms). In these patients, CPAP allowed reclassification into lower risk associated values of QTc<430ms.

Conclusion: CPAP treatment led to an overall reduction in the QTc-interval. This reduction seems more pronounced during evening hours and in patients with a QTc>430ms.

Disclosure of Interest: C. Schlatzer: None Declared, D. Bratton: None Declared, E. Schwarz: None Declared, T. Gaisl: None Declared, J. Pepperell: None Declared, J. Stradling Conflict with: Prof Stradling reports personal fees from ResMed UK, outside the submitted work., M. Kohler Grant/ research support from: Prof Kohler reports grants from University of Zurich during the conduct of the study.
Introduction: We have recently shown, that effective specific airway conductance \( (sG_{\text{eff}} = 1/sR_{\text{eff}}) \) features a sensitive target parameter differentiating severity of airway hyperreactivity (AHR), performed by methacholine (MCH) challenge tests using a plethysmograph. \( sG_{\text{eff}} \) is computed as ratio between the integral of the tidal flow/volume loop, and the integral of the resistive work of breathing \( (sWOB) \). The aim was to assess AHR by \( sWOB \) in comparison to \( sG_{\text{eff}} \), \( FEV_1 \) and \( MEF_{50} \), computing sensitivity and specificity by the ROCET software (http://www.roccet.ca)

Methods: From the database of our centre 348 subjects (141 males; 207 females; aged 14.7 to 88.4 ys) were selected, in order to differentiate asthmatic patients (121, 34.8%) from non-asthmatic subjects (227, 65.2%). \( sWOB \) was computed as integral of the plethysmographic box-shift-volume versus tidal-flow loop. MCH (5%) was administered as aerosol in 3 consecutive cumulative provocation levels (P1: 0.2 mg; P2: 1.0 mg; P3: 2.2 mg), using the Jaeger aerosol provocation system (APS). Provocation doses (PD) were calculated for each parameter specifically (PD\(_{150sWOB}\), PD\(_{40sG_{\text{eff}}}\), PD\(_{20FEV_1}\), PD\(_{20MEF_{50}}\)).

Results: Best sensitivity \((s)\) and corresponding PD for MCH was found for PD\(_{150sWOB}\) \((s=85.9\text{\% at 1.26 mg})\), followed by PD\(_{40sG_{\text{eff}}}\) \((s=79.7\text{\% at 0.64 mg})\), PD\(_{20FEV_1}\) \((s=70.9\text{\% at 1.42 mg})\), and PD\(_{20MEF_{50}}\) \((s=65.2\text{\% at 0.52 mg})\). Noteworthy, lowest PD were need for PD\(_{20MEF_{50}}\), highest for PD\(_{20FEV_1}\). Best response to MCH, and hence discrimination between mild, moderate or severe AHR, was detected by PD\(_{40sG_{\text{eff}}}\) (67.2\%), followed by PD\(_{20MEF_{50}}\) (51.4\%), PD\(_{150sWOB}\) (47.7%), and PD\(_{20FEV_1}\) (25.8\%)

Conclusion: In comparison to standard lung function parameters \( sWOB \) feathers a highly sensitive, and discriminating parameter in the assessment of AHR. Moreover, it offers insight into underlying mechanisms of lung physiology of MCH challenge tests,

Disclosure of Interest: None Declared
Introduction: Salbutamol is a short-acting bronchodilator and is widely used in the treatment of obstructive lung disease. The metabolic mechanisms by which salbutamol influences the airways and may produce side effects remains to be fully elucidated. Metabolic profiling of body fluids is a possible approach to address this lack of knowledge. However, inhaled salbutamol acts quickly, with an onset of action < 15 min, which makes it difficult to capture rapid metabolic changes induced by salbutamol. In this study we used a real time mass spectrometric breath analysis technique to study changes in endogenous metabolites in response to salbutamol inhalation.

Methods: 35 patients with moderate to severe chronic obstructive pulmonary disease participated in this study. Exhaled breath analysis was performed at baseline, 10 and 30 min after the inhalation of 200 ug salbutamol. Significant differences in exhaled metabolite levels in response to salbutamol inhalation were sought. A paired t-test followed by estimation of false discovery rate (FDR) in multiple comparisons was used for this purpose. Statistical significance was set at p < 0.01 and FDR < 0.01.

Results: A total of 115 mass spectral features were found to be significantly altered as a result of salbutamol inhalation. Figure 1 shows an example of one metabolite (i.e. dodecanoic acid) that significantly increased after drug inhalation. The average increase after 10 and 30 min was 8.1 and 9.5%, respectively. A complete series of fatty acids showed a similar response. Figure 2 shows an unknown metabolite displaying a decreasing trend upon salbutamol inhalation. The average decrease after 10 and 30 min was -5.2 and -7.8%, respectively.

Picture/Graph:

![Dodecanoic acid](image1)

![Signal intensity](image2)
Conclusion: Analysis of exhaled breath by real time mass spectrometry allows to capture rapid metabolic changes induced by inhaled medication. Alterations of fatty acid profiles are consistent with previous blood-based studies [1]. Further in depth identification of altered metabolic routes is likely to provide insights on the mechanisms by which activation of beta-adrenergic receptors lead to relaxation of smooth muscles in the airways.


*Equal contribution

Disclosure of Interest: None Declared
PP-144
8. Pneumology and Thoracic Surgery
Comparison of ventilator-integrated end-tidal co2 and transcutaneous co2 monitoring in home-ventilated neuromuscular patients.
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Introduction: Non-invasive transcutaneous capnometry (TcCO2) is increasingly used to assess the home ventilation’s efficiency, allowing to detect episodes of transient hypoventilation, that are not detected by punctual blood gazes. Recently, end-tidal CO2 (ETCO2) sensors have been integrated in life-support home ventilators. The purpose of this study was to compare the ventilator-integrated ETCO2 with TcCO2, in home-ventilated neuromuscular disease patients.

Methods: ETCO2 and TcCO2 were simultaneously measured during one night in 28 patients. Daytime blood gases were drawn on the following morning to measure arterial PCO2 (PaCO2).

Results: Compared to PaCO2 values, both ETCO2 and TcCO2 showed a small bias (-0.1 mmHg and 0.6 mmHg, respectively) and a similar critical difference (6.8 mmHg and 7.3 mmHg, respectively).

The concordance of the two techniques in detecting overnight PCO2 fluctuations was high, with r=0.919 (p<0.001) for the time spent with PCO2 >45 mmHg and r=0.943 (p<0.001) for the time with PCO2 >50 mmHg.

Conclusion: The ventilator-integrated end-tidal CO2 monitoring is as reliable as the currently used transcutaneous measurement, resulting to be a valuable proxy of the overnight PCO2 evolution. This result opens the possibility of a simplification in the monitoring of home ventilated patients, since ETCO2 measurement can be performed directly and repeated at home, with a low additional cost. However, the accuracy of both these measurement techniques is not sufficient to replace blood gases, which remain the reference examination to determine absolute PCO2 value.

Disclosure of Interest: None Declared
Introduction: In contrast to conventional cigarette smoking the association between water pipe exposure and its consecutive inflammatory bronchial changes remains widely unknown. We aimed to determine whether water pipe smoking is associated with the development of airway hyperresponsiveness.

Methods: Airway reactivity was measured in a population of 74 students recruited from University of Basel, Switzerland, by using mannitol challenge test (Aridol™, Pharmaxis LTD). Depending on their individual smoking behaviour subjects were categorized in four subgroups (acute and chronic water pipe consumers, cigarette smokers and never smokers). Primary endpoint was the prevalence of airway hyperresponsiveness in water pipe smokers. Thereby, a distinction between acute water pipe exposition, defined as a single episode of smoking after a minimal abstinence of 14 days, and chronic water pipe exposition, characterized by weekly consumption over at least the last four weeks, was made.

Results: Data of 74 students have been analysed (15 acute, 9 chronic water pipe smokers, 18 cigarette smokers and 32 life-long non-smokers). Baseline characteristics including age, lung function and atopy status were similar between subgroups. Airway hyperresponsiveness to mannitol was more common in chronic smokers (26.3%) as compared to the other groups (p= 0.028). The provoking dose to induce a 15% fall in FEV₁ (PD 15), a measure of sensitivity, was 155 mg [115-395] in cigarette smokers as compared 315 mg [155-475 mg) in non-smokers. The Response dose ratio (RDR), a measure of reactivity, was highest in cigarette smokers (0.023 [0.011-0.051]) followed by chronic (0.010 [0.007-0.015]) and acute water-pipe consumers (0.011 [0.006-0.015] and non-smokers (0.007 [0.005-0.017]). In contrast to non-smokers (p=0.007) RDR between chronic cigarette and chronic water pipe smokers differed not significantly (p=0.11).

Conclusion: Airway reactivity to mannitol challenge test is similarly increased in water pipe users as compared to cigarette smokers. This observation might be helpful in future, to understand the impact of water pipe smoking on lung health more precisely.

Disclosure of Interest: None Declared
**Introduction:** In May 2015, preliminary results of a randomized controlled trial (SERVE-HF) addressing adaptive servoventilation (ASV) in chronic congestive heart failure (CHF) patients with central sleep apnea (CSA) prompted safety warnings by the manufacturer, sleep and respiratory societies. It was recommended to identify and discuss ASV discontinuation with CHF patients with reduced cardiac function and CSA currently treated with ResMed ASV devices.

The aim of this study was to analyze the short-term effects of ASV withdrawal in those patients.

**Methods:** After the safety warning patients fulfilling the risk criteria were identified and invited for urgent visits. If all criteria were still met after the reassessment, a monitored ASV withdrawal was offered. This included a respiratory polygraphy (PG) in the first night and after 14 days if no alternative treatment was started. We retrospectively analyzed clinical symptoms, course of SDB and decisions on further SDB treatment after ASV withdrawal.

**Results:** 24 out of 212 patients on ResMed ASV devices were classified as being at risk. 22 patients (median LV-EF 32.5% (IQR25.45)) were available for reassessment (1 died, 1 cancelled appointments). After reassessment and exclusion of patients who were no longer at risk (n=5) and patients who declined ASV withdrawal (n=2), 15 patients remained for the analysis. 11 patients agreed to discontinue ASV and 4 had already stopped ASV themselves before the visit. Compared to the diagnostic AHI 11/11 patients had similar severity of SDB (median AHI 36.7/h [IQR 25.3,50.5]) in night 1 after ASV withdrawal with CSA in n=10. Subjective intolerance of the ASV withdrawal was seen in four patients (bad sleep quality, n=3; severe nocturnal dyspnea leading to hospitalization, n=1). 8 patients and the 4 who had already stopped ASV treatment before the visit continued the withdrawal without subjective clinical worsening. The PG at night 14 showed relevant SDB in 11/12 patients with a median AHI of 24/h [IQR 14.7,30.3]. Following the ASV withdrawal trial, 12 patients permanently discontinued ASV (without substitution n=4; CPAP titration n=3, nocturnal oxygen n=5). 3 patients continued ASV.

**Conclusion:** ASV withdrawal in patients with stable chronic CHF and CSA leads to a return of sleep disordered breathing by the first night. The treatment effect of ASV does not seem to be prolonged. Treatment options for affected patients have to be adapted to the patient’s individual needs.

**Disclosure of Interest:** None Declared
Introduction: Pulmonary rehabilitation (PR) has been shown efficient to improve dyspnea, reduce exacerbation rate and enhance quality of life in patients with chronic respiratory disease. Reports suggest underuse of PR in Switzerland. We report here on the most recent available data on PR in Switzerland.

Methods: In 2015, standardized questionnaires were addressed to pulmonologists in charge of accredited inpatient (IPR) or outpatient pulmonary rehabilitation (OPR) programs in Switzerland. We studied the trends in PR practice over 9 years.

Results: Data were available for all accredited 10 inpatient and 55 (out of 58) outpatient PR centers. Total number of patients enrolled in PR programs increased from 2005 (n = 6126) to 2014 (n = 7602, + 24.1%). Outpatient PR had faster growth compared to inpatient PR (+52.2% vs +16.1%). Overall, enrollment was larger in all diagnostic categories but more so for patients with interstitial lung disease (+208%). Proportion of COPD patients decreased in IPR programs (43.0% in 2005 to 36.2% in 2014) and increased in OPR programs over the study period, alongside with a growing proportion of patients referred before or after thoracic surgery.

<table>
<thead>
<tr>
<th></th>
<th>Inpatient PR</th>
<th>Outpatient PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active programs</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Enrolled patients</td>
<td>4773</td>
<td>5090</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>2052(43.0%)</td>
<td>1776(34.9%)</td>
</tr>
<tr>
<td>Asthma, n (%)</td>
<td>1427(29.9%)</td>
<td>1527(30.0%)</td>
</tr>
<tr>
<td>Interstitial lung disease, n (%)</td>
<td>91(1.9%)</td>
<td>203(4.0%)</td>
</tr>
<tr>
<td>Pre or post thoracic surgery, n (%)</td>
<td>195(4.1%)</td>
<td>447(8.8%)</td>
</tr>
</tbody>
</table>

Conclusion: In Switzerland, Pulmonary Rehabilitation growth appears steady over the years and faster for ambulatory programs. However, our data also suggest that most patients with chronic pulmonary disease are not offered PR, despite clinical evidence.

Disclosure of Interest: None Declared
**Introduction:** In neuromuscular diseases (NMD), guidelines recommend initiation of home mechanical ventilation (HMV) in case of daytime hypercapnia or nocturnal desaturation as an indirect sign of hypoventilation. Transcutaneous capnometry (TcCO2) enables the direct assessment of nocturnal hypercapnia, however the best cut-off values to be used remain to be defined.

We aimed to compare the prognostic value of different definitions of nocturnal hypoventilation issued from the literature, in the NMD cohort followed at our reference center.

**Methods:** All consecutive TcCO2 recordings performed between 2010 and 2014 in non-ventilated adult NMD patients were retrospectively collected. Patients with daytime hypercapnia were excluded. Nocturnal hypoventilation was defined as (1) TcCO2 >55 mmHg for ≥10 minutes or increase in TcCO2 ≥10 mmHg (in comparison to an awake supine value) to a value exceeding 50 mmHg for ≥10 minutes, (2) peak TcCO2 ≥49 mmHg, and (3) mean TcCO2 >50 mmHg. Onset of mechanical ventilation and mortality were collected as outcomes of interest.

**Results:** 124 patients with normal daytime blood gazes were analysed (age 39 [IQR 31-55] years; vital capacity 61% [43-82] of predicted).

The prevalence of hypoventilation ranged from 3% to 44%, depending on the definition used. Over a median follow-up of 2.8 years, 55 patients (44%) were started on HMV and 4 died. Nocturnal peak TcCO2 ≥49 mmHg was the best predictor of HMV onset during follow-up, identifying patients with a hazard ratio of 2.1 [95%CI 1.2-3.7] in multivariate analysis adjusting for lung function parameters.

**Conclusion:** Nocturnal hypercapnia with daytime normocapnia seems to predict the need for HMV over the following few years. This may have practical consequences for the decision to start HMV in NMD patients. Nocturnal capnometry should be included in the consensus guidelines, and peak TcCO2 should be considered as a criterion to start HMV both in clinical practice and in future prospective studies.

**Disclosure of Interest:** None Declared
Use of home ventilators for ventilatory support during magnetic resonance imaging.

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Introduction: Magnetic resonance imaging (MRI) represents a valuable diagnostic tool in acute and chronic pathologies affecting the neurologic system. Its use may however be limited in acute and chronic neurological and neuro-muscular disease patients, who cannot maintain the supine position in spontaneous breathing for the duration required for the procedure. The use of mechanical ventilation during the MRI exam may allow to overcome this problem, but very few ventilators are MRI-compatible. A possible alternative may consist in leaving the ventilator in the MRI control room, where non-MRI-specific devices are allowed, and to ventilate the patient by the means of a longer circuit.

We aimed to evaluate the performance of home life support ventilators used with a longer circuit, allowing the application of ventilatory support during MRI.

Methods: Four life-support home ventilators were tested on a bench using 3 circuits of 4.8 m length and 3 ventilation settings: Breas VIVO 60, ResMed Astral 150, Covidien Puritan Bennet PB 560 and Philips Respironics Trilogy 100.

Results: We found measurable differences in the efficacy of the ventilation effectively delivered to the test lung, which was influenced from the used ventilator, the type of circuit and the ventilation parameters. In the volumetric setting with unvented circuit, the difference between set VT and delivered VT ranged between -10% and +3%. In the barometric setting, only the ventilators providing automatic compensation for circuit compliance and resistance were reliable in the delivery of the set inspiratory and end-expiratory pressures.

Conclusion: The use of home ventilators during MRI may represent a valuable alternative when a MRI-compatible ventilator is not available, but may require an adjustment of the ventilatory setting, and a systematic verification of the parameters effectively delivered to the patient.

Disclosure of Interest: None Declared
Introduction: For the last years the Zürcher RehaZentrum Davos has been focussing on caring for severe asthma patients. Various study groups have undertaken efforts to categorise asthma into different phenotype clusters to better predict treatment outcomes. Especially in allergic asthma, diagnostic and therapeutic allergen avoidance facilitates phenotyping and treatment. Our study intends to analyse distribution of asthma phenotypes and characteristics of our patients.

Methods: All patients referred with asthma symptoms refractory to treatment from 2010-2014 were included. For statistical analysis we used Mann-Whitney-U test and Fisher’s exact test. P<0.05 was deemed as statistically significant.

Results: In 5 cases asthma could not be confirmed. 9 patients suffered from difficult-to-control asthma. 71 patients had severe asthma. They predominantly suffered from late-onset asthma (n=57 vs n=14 early-onset). Late-onset asthmatics had a significantly higher mean FeNO level (57.06 vs 25.92, p=0.0286) and tendency to a higher eosinophil count in white blood cells compared to their early-onset counterparts (6.36% vs 4.07%, p=0.0929). With adequate treatment these levels decreased and a trend towards better FEV1 levels (89.31% vs 75.55%, p=0.0837) could be seen which shows that FeNO and eosinophilic count are markers of good response to corticosteroids. Of the late-onset asthmatics, 21 patients (36.84%) were considered atopics (positive reaction to either skin prick-test allergen or CAP-test) and of the early-onset group, 12 were atopic (85.71%, p<0.001). Sensitisations were clinically relevant in 11 atopic early-onset patients (78.57%) but only in 9 late-onset patients (15.79%, p<0.001). This supports the thesis that late-onset asthma, unlike early-onset asthma, is most often not triggered by exogenous airborne allergens and that atopy plays a less important role in the course of the disease.

Conclusion: In severe asthma, modern treatment options like Mepolizumab and Omalizumab should be chosen depending on eosinophil count and the relevance of sensitisations, respectively. These differences reveal the importance of properly phenotyping specific asthma types to set patients on the right treatment path.

Disclosure of Interest: None Declared
Introduction: Bronchiectasis is a common manifestation of different diseases with similar clinical presentation. One of the underlying disorders is Primary Ciliary Dyskinesia (PCD), an autosomal recessive genetic disorder with mutation in one of many genes with primary manifestation of bronchiectasis, paranasal sinus and ear disorders. Nasal exhaled NO (nNO) testing with a cutoff < 100 ppb has a good sensitivity (91%) and specificity (96%) for PCD. High-speed video microscopy analysis (HVMA) has excellent sensitivity (100%) and specificity (93%). Transmission electron microscopy (TEM) is 100% specific but with low sensitivity. Immunofluorescence staining (IF) has a better sensitivity compared to TEM with equal specificity.

Methods: Since 2015 we introduced systematic screening for PCD in the workup of bronchiectasis in adults with nNO (NIOX MINO Aerocrine™). In case of nNO levels <100 ppb or clinically high suspicion for PCB we conducted a HVMA (SAVA™ software) and a TEM. Diagnosis is confirmed by at least two independent pathological HVMA results and typical clinical symptoms and/or pathological TEM result and/or repetitive low nNO. IF is done in all confirmed cases for determination of ciliary protein defect.

Results: 2015 we diagnosed two cases of PCD. Both patient had low FeNO and nNO concentration. The results of the HVMA confirmed the diagnosis in both cases. In both cases TEM was negative for PCD. IF results are pending.

Patient’s characteristics and results are summarized in table 1

<table>
<thead>
<tr>
<th></th>
<th>P1 (60 years)</th>
<th>P2 (20 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FeNO</td>
<td>&lt; 5 ppb</td>
<td>&lt; 5 ppb</td>
</tr>
<tr>
<td>nNO (right/left)</td>
<td>8/15 ppb</td>
<td>109/116 ppb</td>
</tr>
<tr>
<td>HVMA (2 x)</td>
<td>+/-</td>
<td>+/pending</td>
</tr>
<tr>
<td>TEM</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chr. productive cough</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chr. rhinosinusitis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Otitis media</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>tubular</td>
<td>cystic</td>
</tr>
<tr>
<td>Sputum microbiology</td>
<td>mucoid P. aeruginosa</td>
<td>H. influenzae</td>
</tr>
<tr>
<td>Lung function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1/VC</td>
<td>71%</td>
<td>85%</td>
</tr>
<tr>
<td>FEV1</td>
<td>1.47L (76%)</td>
<td>3.67L (84%)</td>
</tr>
<tr>
<td>VC</td>
<td>2.07L (89%)</td>
<td>4.29L (80%)</td>
</tr>
<tr>
<td>TLC</td>
<td>3.78L (89%)</td>
<td>5.96L (85%)</td>
</tr>
<tr>
<td>RV</td>
<td>1.71L (101%)</td>
<td>1.67L (103%)</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>45%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Conclusion: Since the introduction of systematic screening for PCD with nNO in the workup of bronchiectasis in adults we found two cases with late diagnosed PCD. Both diagnoses were confirmed by HVMA. PCD should be taken into consideration in cases of unclear bronchiectasis in adults. Confirmation of PCD by HVMA and not TEM in cases with positive nNO screening is crucial. Early diagnosis and managing of PCD is important to prevent further complications and deterioration of pulmonary function.

References:

Disclosure of Interest: None Declared
Light chain deposition disease: a rare cause of multiple cystic lung disease
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Introduction: Light chain deposition disease (LCDD) is a rare disorder characterized by clonal production of immunoglobulin light chains and their deposition in various organs. Renal involvement is the most frequent. Pulmonary involvement is extremely rare, and may present as lung nodules or multiple cystic lung disease which may be misdiagnosed as emphysema, lymphangioleiomyomatosis (LAM), Langerhans cell histiocytosis (LCH), or Birt-Hogg-Dubé syndrome (BHD).

Methods: Case presentation: A 58-year-old man, with a remote 10 pack-year smoking history, developed mild exertional dyspnoea over a 2-year period. Lung function tests showed obstructive ventilatory defect (FEV1/FVC 66%, FEV1 107%, DLCO 61%). Chest CT-scan was interpreted as showing pulmonary emphysema and bronchiectasis. Over the next 2 years, FEV1 decreased by 490 ml. A second chest CT-scan showed a worsening of parenchymal changes, and the patient was referred to our clinic. Review of chest imaging led to the hypothesis of a multiple cystic lung disease distinct from LAM, LCH, and BHD.

Results: Serum protein electrophoresis found a monoclonal IgM κ gammopathy, with IgM increased to 13.44 g/l, free IgM κ light chains increased to 45.10 mg/l (N=3.3-19.4), and a κ/λ ratio increased to 7.982 (N=0.26-1.65). Bronchial biopsies showed interstitial and perivascular amorphous eosinophilic deposits in the submucosa, without apple-green birefringence at Congo red dye. Immunohistochemical staining was positive for both κ and λ chains, with predominant κ staining. Electron microscopy showed subepithelial dense fibrillar deposits, non consistent with amyloid. Surgical lung biopsy showed the same patterns. Bone marrow smear showed lymphoplasmocytic lymphoma. Pulmonary LCDD secondary to IgM κ lymphoplasmocytic lymphoma was diagnosed. There was no renal involvement. Because of rapidly progressive pulmonary involvement, rituximab was started. IgM and Ig κ-chains decreased after 6 cycles, but without normalisation, so bendamustin was added. Stability of lung function and chest imaging was then observed over the next year.

Conclusion: LCDD is a rare cause of multiple cystic lung disease, but should be considered in the differential diagnosis of patients presenting with multiple lung cysts at chest imaging. Treatment aims at suppressing clonal light chain production and organ deposition, but its efficacy is unknown. Further deterioration has been reported, eventually leading to respiratory insufficiency, lung transplantation, and death.

Disclosure of Interest: None Declared
8. Pneumology and Thoracic Surgery

High-altitude climate-therapy in hochgebirgsklinik davos – an important therapeutical option to treat asthma!

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Introduction: An important therapeutical aim in asthma-therapy is to achieve symptom-control and a risk-reduction concerning exacerbations, airway obstruction, and side-effects of medication (GINA 2015).

Methods: In GINA 2015, high-altitude climate-therapy and even allergene-avoidance is not clearly recommended as a therapeutical option, although high-altitude climate-therapy is beneficial for many asthmatic patients due to less air pollution, less air humidity, a significant reduction of aero-allergens, and a lack of house-dust mite allergens (Schuh, Nowak 2011).

Results: Former studies showing beneficial effects of high-altitude climate-therapy show limitations due to a lack of controls or a limited number of patients studied. Thus scientific evidence of these studies is low (Fieten et al. 2015). Nevertheless, many patients with difficult-to-treat asthma show massive improvement of their asthma-symptoms. As an example, a simple peak-flow-test in a patient with allergic asthma due to house-dust-mite allergy shows a quick improvement from 300 to more than 700 l/min while being on rehabilitation-therapy in the Hochgebirgsklinik Davos (1600 m above sea-level).

Conclusion: Climate-therapy in high-altitude as practised in the Hochgebirgsklinik Davos is a beneficial and sustained therapeutical option for patients especially with difficult-to-treat asthma. Randomized controlled studies are needed to further prove beneficial effects of high-altitude climate-therapy.


Disclosure of Interest: None Declared
Introduction: We report on a 48 year-old overweight female patient, known for well controlled allergic asthma since childhood and binge eating disorder. She had gastric banding in 1998 for severe obesity.

Methods: At admission, she presented with acute dyspnea and respiratory failure with acute respiratory acidosis (pH 7.08) and hypoxemia (oxygen saturation of 80%). The clinical status showed prolonged expiration with wheezing. Initial standard therapy with inhalation of corticosteroids and bronchodilators in addition to systemic corticosteroids failed and oral intubation was necessary due to respiratory exhaustion. Chest CT-scan excluded pulmonary embolism, but showed severe achalasia. The patient gradually improved and was extubated. Afterwards detailed history revealed that preceding her symptoms she had raclette for dinner. She later complained about abdominal fullness and reflux.

Results: Acute exacerbation of our patient's asthma can have several trigger factors. Since achalasia is a rare but a known long-term complication of a gastric banding, the eating disorder with binge eating might be causative. Ingestion of a large portion of raclette possibly provoked acute reflux and/or increased pressure on the lung by the cheese-filled esophagus and led to acute asthma exacerbation. She had no indices for allergic reaction against cheese. And last but not least obesity might also be a trigger factor.

Conclusion: Our case illustrates the importance of thorough history taking and clinical examination of patients with acute asthma exacerbation. It is of utmost importance to search for trigger factors, which can be surprising as in our case and needs to be addressed in treatment strategy.

Disclosure of Interest: None Declared
Introduction: Background: While obstructive sleep apnea is a distinct sleep related breathing disorder, central sleep apnea (CSA) is usually secondary to an underlying disease or due to medication. Primary CSA is rare.

Methods: Case report: A 43 year-old accountant was diagnosed with sleep disordered breathing in another hospital. The external sleep study report stated an AHI of 18.6/h consisting predominantly of hypopneas, which were classified mainly as obstructive, but also some central events and episodes with periodic breathing were scored. A trial of continuous positive airway pressure (CPAP) was initiated, but it was not tolerated due to feeling “lightheaded”. At referral to our sleep center, the patient complained about fatigue, excessive daytime sleepiness (falling asleep in front of the computer in the afternoon) and decreasing physical fitness (not being able to perform long cross country runs). A repeat polysomnography at our sleep lab revealed predominantly central sleep apnea with an intermittent pattern of Hunter-Cheyne-Stokes breathing (AHI 22/h).

Results: Treatment and course: The patient was started on adaptive servo-ventilation but despite a good suppression of the AHI to 2.4/h the treatment was not tolerated. A search for an underlying morbidity as cause of the central sleep apnea was performed and an echocardiography revealed severe right heart failure with a dilated right ventricle. A perfusion/ventilation scintigraphy showed peripheral pulmonary embolism in both upper lobes, ECG showed T-inversions and an epsilon wave. Right heart catheterization ruled out pulmonary hypertension. Cardiac MRI showed typical features confirming the diagnosis of an arrhythmogenic right ventricular cardiomyopathy (AVRC). Heart failure and antiarrhythmic medication were started, a prophylactic cardioverter defibrillator (ICD) was implanted, and the patient was advised to avoid strenuous exercises. An evaluation for heart transplantation was initiated and the patient and his family were offered genetic counselling. Nocturnal oxygen was offered as alternative treatment for CSA.

Conclusion: In patients with central sleep apnea the evaluation of underlying causes (eg neurologic disease, cardiac disease, end stage renal disease and opioid-analgesics) is strongly recommended, especially if no circumstances are known that may explain sufficiently the presence of central sleep apnea or Hunter-Cheyne-Stokes respiration.

Disclosure of Interest: None Declared
Introduction: Mountaineering at high altitude is on the edge of the physiological capacity. Data on blood oxygen content and oxygen transport of mountaineers at extreme altitude is scarce. Values as low as a mean arterial partial pressure (paO2) of 24.6mmHg and oxygen content (CaO2) of 145.8ml/L at 8400m asl have been reported in 4 subjects using intermittent oxygen supply. The aim of our study was to assess oxygen content and oxygen transport capacity as well as effects of acclimatization in a large group of volunteers during an expedition to altitudes above 7000m.

Methods: Arterial blood gas sampling (paO2, oxygen saturation (SaO2), haemoglobin (hb)) and transthoracic echocardiography were performed in 39 subjects (female/male: 18/21) during an expedition to Mt. Himlung Himal (7126m) at baseline 550m (before/after the expedition), twice at 4800m (day 5 and day 17/18), at 6050m (day 11) and 7050m (day 21/22). Cardiac output at rest was determined by measurement of stroke volume (left ventricular outflow tract diameter, velocity time integral) and heart rate. Based on these values CaO2 and oxygen delivery (DO2) were calculated.

Results: The data of a subgroup with a complete dataset at 7050m (n = 12; 2 female) was evaluated. SaO2 decreased significantly with increasing altitude from mean 97.3% at baseline to 68.8% at 7050m and paO2 decreased from mean 93.1mmHg to 42.7mmHg at 4800m and to 30.4mmHg at 7050m (p<0.0001). There was no significant difference in hb levels at baseline and 4800m (day 5), but a significant increase was found when comparing baseline levels with measurements on day 17/18 at 4800m (p<0.0001) and on day 21/22 at 7050m (p<0.0001). Compared to baseline CaO2 decreased significantly from a mean of 198.7ml/L at baseline to 170.7ml/L (-14.1%, p< 0.01) at 4800m, and to 161.7ml/L (-18.7%, p<0.001) at 7050m. After acclimatization CaO2 increased significantly by 18.1% from 170.7 to 202.9ml/L when comparing the two measurements at 4800m on day 5 and day 17/18 (p<0.001). Levels of DO2 showed normal values throughout. Compared to baseline (1093ml/min) even increased values of 1325ml/min were found at 7050m (p<0.05).

Conclusion: Hypobaric hypoxia at extreme altitude leads to a significant fall in SaO2 and paO2. Acclimatization assures normal CaO2 values at 4800m. Additional increase in cardiac output can provide normal oxygen delivery even at an altitude of 7050m.

Disclosure of Interest: None Declared
Composite clinical worsening endpoint in paediatric pah - clinically meaningful and feasible for clinical research

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Introduction: Clinical worsening (CW) composites are used in adult Pulmonary Arterial Hypertension (PAH) clinical research and is in discussion for future use in paediatric PAH research across all age ranges.

Methods: This study, using data from the Tracking-Outcomes-in-Pediatric-Pulmonary-Hypertension (TOPP) registry, describes the occurrence of individual outcomes and its CW composite: death, lung transplantation (LT), PAH-related hospitalisation (i.e. increased right heart failure, hemoptysis), atrial septostomy, deterioration in WHO functional class (FC) (change in 1 FC), initiation of parenteral prostanoids, syncope, PAH worsening (i.e. occurrence/progression of at least 2 symptoms: dyspnea, cyanosis, cough, fatigue, chest pain, dizziness). Predictive Cox proportional hazards models of time to death/LT were conducted for the aforementioned individual outcomes and CW composite (excl. death/transplantation).

Results: 255 incident (diagnosed ≤3 months) patients (i.e. idiopathicPAH/familialPAH, PAH associated with congenital heart disease) were included in the analysis. 155 (60%) were female and the mean (±SD) age at diagnosis was 7.5 (±5.2) years; 159 (62%) had iPAH/fPAH; 109 (43%) were in WHO FC II and 87 (34%) in class III. The highest incident rates per 100 person-years (95% CI) were observed for deterioration in WHO FC 24.8 (20.8, 29.5) and PAH related hospitalisation 18.3 (15.0, 22.4). In univariate models, first event of deterioration in WHO FC,(hazard ratio (HR)=6.7; 95% CI 3.1,14.4), and first occurrence of PAH worsening (HR=4.8; 95% CI 2.5 , 9.0) were highly predictive of time to death/lung transplantation. PAH related hospitalisation and initiation of parental prostanoids had similar HRs. The predictive value of the occurrence of syncope did not reach statistical significance. The HR of the CW composite was 2.7 (95% CI 1.4, 5.3). The multivariate predictive models which included all individual variables (all univariate p-values <0.15) revealed deterioration of WHO FC (HR=3.5; 95% CI 1.5, 8.3), PAH related hospitalisation (HR=2.6; 95% CI 1.3, 5.2) and occurrence of PAH worsening (HR=2.1, 95% CI 1.0, 4.4) to be significant independent predictors of death/LT.

Conclusion: The chosen CW composite as well as the individual components (except syncope) occurred to be predictive for death/LT, thus supports the usefulness for clinical research but also for risk assessment during follow-up in paediatric PAH.

Disclosure of Interest: M. Beghetti Grant/ research support from: Actelion, Bayer, Consultant for: Actelion, Bayer, EliLilly, GSK, Speakers bureau: Actelion, M. Brand Employee for: Actelion, R. Berger Grant/ research support from: Actelion, Consultant for: Actelion, GSK, EliLilly, Bayer, United therapeutics, Speakers bureau: Actelion, T. Humpl Consultant for: Actelion, J. Wheeler: None Declared, D. Ivy Grant/ research support from: Actelion, EliLilly, United Therapeutics, Consultant for: Actelion, Bayer, EliLilly, United therapeutics, Speakers bureau: Actelion, D. Bonnet Grant/ research support from: Actelion, Consultant for: Actelion, Bayer, EliLilly
**Introduction:** Sarcoidosis is a multisystem disease with an unpredictable and sometimes fatal course while the underlying pathomechanism is still unclear. Reasons of the increasing hospitalization rate and mortality in the United States remain in dispute. Incriminated are a number of distinct comorbidities and risk factors as well as the application of more aggressive therapeutic agents. Our aim was to investigate the recent mortality and hospitalization rates as well as the underlying comorbidities of hospitalized sarcoidosis patients in Switzerland.

**Methods:** In this nested case-control study, a nation-wide database provided by the Swiss Federal Office for Statistics enclosing every hospital entry covering the years 2002-2012 (n = 15,627,573) was analyzed. Cases, defined as any hospitalization with the diagnosis of sarcoidosis either as main or concomitant diagnosis, were compared with age- and sex-matched controls without the diagnosis of sarcoidosis.

**Results:** There were 8,385 cases with a diagnosis of sarcoidosis representing 0.054% (8,385 / 15,627,573) of all hospitalizations in Switzerland. Hospitalization and mortality rates remained stable over the observed time period. Sarcoidosis patients had significantly higher medication-related comorbidities compared to matched controls. Also, they were more frequently re-hospitalized (median annual hospitalization rate 0.28 [IQR 0.15–0.65] vs. 0.19 [IQR 0.13–0.36] per year), had a longer hospital stay (6 [IQR 2–13] vs. 4 [IQR 1–8] days), had more comorbidities (4 [IQR 2–7] vs. 2 [IQR 1–5]), and had a significantly higher in-hospital mortality (2.6% [95% CI 2.3%–2.9%] vs. 1.8% [95% CI 1.5%–2.1%]; p<0.001 respectively). A worse outcome was observed among sarcoidosis patients having co-occurrence of associated respiratory diseases (see Graph). Moreover, age was an important risk factor for re-hospitalization.

**Picture/Graph:**
Conclusion: Our analysis revealed stable mortality and hospitalization rates among sarcoidosis patients over the observed time period. However, patients with sarcoidosis showed a significantly worse outcome compared to matched controls. This could be due to the disease itself as well as to a cluster of specific comorbidities and complications namely associated respiratory diseases. Moreover, there is evidence that side effects of more aggressive treatment approaches could contribute to this poorer outcome.

Disclosure of Interest: None Declared
Nitrogen multiple breath washout for diagnosis of bronchiolitis obliterans in patients after allogeneic stem cell transplantation

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Introduction: Chronic lung allograft dysfunction (CLAD) is the main cause of deaths after allogeneic stem cell transplantation (alloSCT). Bronchiolitis obliterans syndrome or Bronchiolitis obliterans (BO) are the leading causes of CLAD. In addition to chronic Graft-versus-Host Disease (cGvHD), risk factors for development of BO are increasing recipient age, pre-transplantation status and reduction in the FEV1/%VC ratio. Commonly used bodyplethysmography however fails to detect early signs of BO. Sensitive lung function tests like the nitrogen multiple breath washout (N₂-MBW) measure ventilation in-homogeneity especially in the small airways and thus seem promising for early diagnosis of BO. The aim of this study was to compare N₂-MBW and bodyplethysmography data with post alloSCT pulmonary outcome.

Methods: This is a monocentric, cross-sectional cohort study. Consecutive, unselected alloSCT recipients underwent bodyplethysmography and N₂-MBW. Patients were divided into five groups based on FEV1/%VCmax, histology and cGvHD overall score and were categorized as: 1) low risk (FEV1/%VCmax ≥70, low risk cGvHD overall score (=0), 2) high risk (FEV1/%VCmax ≥70, high risk cGvHD overall score (1-3), 3) BOS (FEV1/%VCmax <70, if performed no BO in histology), 4) BO (histological proven lymphocytic or constrictive bronchiolitis obliterans), 5) other (histological diagnosis other than BO). Main outcome was the Lung clearance index (LCI) as a measure of overall ventilation inhomogeneity.

Results: 225 adults, mean age 52.8±12.3 years, underwent bodyplethysmography and N₂-MBW within 0.2-34 years following alloSCT during routine visits. Good quality data for at least two LCI examinations could be obtained in 151 (67.1%) cases. As compared to normal, mean LCI differed significantly across the groups (p= 0.001), see table 1). In the BO group (4), LCI was clearly elevated above the upper limit of normal (8 units lung turnover) in 94% of all patients, whereas FEV1/%VCmax was elevated only in 57% of patients. In general, and independent of the clinical group, a high proportion of patients with normal values in FEV1/%VCmax showed elevated LCI results.

Conclusion: LCI seems more sensitive compared to FEV1/%VCmax to detect small airway disease in patients after alloSCT. It is therefore tempting to hypothesize that N₂-MBW may also be helpful for early diagnosis of BO in asymptomatic patients following alloSCT.

Disclosure of Interest: None Declared
Introduction: Besides their main respiratory diagnosis, lung transplant recipients are susceptible to several general comorbid conditions that may affect their survival and their quality of life.

Methods: The aim of this retrospective study was to evaluate the prevalence of several definite comorbid conditions at the time of listing and one year after transplant. The outcome at 3 years, including, survival, functional status, and 6 minute walking distance were collected and compared to those from the International Registry (ISHLT).

Results: Between 17.08.2008 and 02.08.2014, 110 patients underwent lung transplantation in the Centre Universitaire Romand de Transplantation. After exclusion of multiorgan transplants (1), retransplantation (11), absence of consent (13), too short follow-up (7), 78 patients remained for the analysis. COPD was the main diagnosis for 33 patients, lung fibrosis for 20, Cystic fibrosis for 17, others for 8. Comorbid conditions before and at one year after lung transplantation are shown in the table. Overall survival at 3 years was 82%. Among survivors, 88% were in functional class NYHA < 2 and 96% were entirely autonomous. Chronic allograft dysfunction was diagnosed in 11% and suspected in 9%. Despite some positive trends, no comorbidity was statistically associated with mortality, mainly due to the overall high prevalence of comorbid conditions and low number of deaths.

Picture/Graph:
Conclusion: We conclude that comorbid conditions, especially of the cardiovascular and renal system are highly prevalent in lung transplant candidates and further increase after surgery. Even if no statistical correlation with survival could be established in this single cohort study, a pre-emptive management may improve the quality and the long term survival of these patients.

Disclosure of Interest: None Declared
PP-161
8. Pneumology and Thoracic Surgery
Hyperoxia enhances exercise performance in pulmonary arterial and chronic thromboembolic pulmonary hypertension: randomized trial
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Introduction: Pulmonary hypertension impairs cardiac output, oxygen delivery and thus exercise capacity.

Methods: 22 stable PAH/CTEPH patients (8 women, 61±14y, mPAP 35±10mmHg) underwent 4 bicycle ergospirometies to exhaustion on different days breathing oxygen enriched (FiO₂ 0.50) or ambient air (FiO₂ 0.21) and using progressively increased or constant load (75%Wmax, FiO₂ 0.21) protocols, respectively, according to a randomized, balanced cross-over design. ECG, pulmonary gas-exchange, oxygen saturation by pulse oximetry (SpO₂), cerebral (CTO) and muscle (MTO) tissue oxygenation by near-infrared spectroscopy were monitored.

Results: In progressive ramp tests under FiO₂ 0.50, maximal work rate, oxygen uptake, SpO₂, CTO and MTO exceed values during FiO₂ 0.21 at end-exercise (table), while ventilatory equivalent for CO₂ and heart rate were reduced at isotime. In constant load tests with FiO₂ 0.50 endurance was increased by 210±223% vs. FiO₂ 0.21.

<table>
<thead>
<tr>
<th></th>
<th>End of progressive ramp</th>
<th>End of constant load</th>
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</thead>
<tbody>
<tr>
<td>Endurance, s</td>
<td>FiO₂ 0.21</td>
<td>FiO₂ 0.50</td>
</tr>
<tr>
<td>Work rate, watts</td>
<td>552 ± 111</td>
<td>645 ± 136*</td>
</tr>
<tr>
<td>V'O₂, l/min</td>
<td>113 ± 38</td>
<td>132 ± 48*</td>
</tr>
<tr>
<td>Heart rate, 1/min</td>
<td>130±18</td>
<td>137±21*</td>
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<tr>
<td>V'E, l/min</td>
<td>62±17</td>
<td>65±18*</td>
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<tr>
<td>V'E/V'CO₂</td>
<td>41±9</td>
<td>37±7*</td>
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<tr>
<td>SpO₂, %</td>
<td>90±6</td>
<td>98±2*</td>
</tr>
<tr>
<td>CTO, %</td>
<td>61±9</td>
<td>71±7*</td>
</tr>
<tr>
<td>MTO, %</td>
<td>61±8</td>
<td>65±11*</td>
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<tr>
<td>Borg CR10, dyspnea</td>
<td>6 ± 2</td>
<td>5 ± 2</td>
</tr>
</tbody>
</table>

Mean±SD values during final 30 sec of exercise; * P<0.05 vs. FiO₂ 0.21; V'O₂: oxygen uptake; V'E: minute ventilation; V'E/V'CO₂: ventilatory equivalent for CO₂; SpO₂, CTO and MTO: arterial, cerebral and muscle tissue oxygenation

Conclusion: In patients with PAH/CTEPH, breathing oxygen enriched air increases exercise performance by improving ventilatory efficiency and arterial oxygenation thereby enhancing oxygen availability in muscles and brain. Therefore, hyperoxia holds promise to improve efficacy of exercise training in PAH/CTEPH patients undergoing rehabilitation.

Disclosure of Interest: None Declared
Introduction: Bilateral lung transplantation (BLT) implies complete lung denervation. So BLT is an excellent model for testing cardiovascular regulation in absence of modulation of heart activity by lung afferents. The high frequency (HF) component of heart rate variability (HRV) is synchronous with breathing frequency (BF). If this comes from neural modulation of the heart beat by BF, HF of HRV should disappear after BLT. The aim of this study was to analyse HRV in BLT as compared with healthy controls (C).

Methods: Eleven BLT (6 women and 5 men), aged 49.0±14.5 yrs and eleven sex- and age-matched healthy controls (C), aged 47.3±14.5 were studied. We continuously recorded heart rate (HR, by electrocardiography), arterial blood pressure (Portapres) and BF (ultrasonic device) during 10 min of free breathing at rest, 10 min of cadenced breathing (0.25Hz) at rest and 5 min with handgrip, in supine posture. We evaluated spontaneous variability of R-R interval (RR), systolic, diastolic and mean pressure (SAP, DAP and MAP respectively), by power spectral analysis, and baroreflex sensitivity (BRS), by the sequence method, using the BRSanalysis® software. 2-way ANOVA and Tukey post-hoc test were used.

Results: BLT, compared to C, had higher HR, but the same SAP, DAP and MAP. BF was higher in BLT than in C during free breathing. BLT showed lower BRS, total power (PTOT), low-frequency peak (LF) and HF, in all conditions. The LF/HF ratio was higher in BLT than in C. In normalised units, BLT had higher LF (LFnu) and lower HF (HFnu) than C. Concerning blood pressure, BLT had higher PTOT, LF and HF powers for SAP; higher HF and lower LF/HF for DAP; lower LF/HF for MAP.

Conclusion: Lung denervation carried along a remarkable reduction of HRV. The higher LF/HF ratio implies that the PTOT drop was mostly due to the HF component. The reverse was the case for SAP. Thus, the results of this study are compatible with the hypothesis that a neural modulation from lung afferents contributes to the HF component of HRV.

Disclosure of Interest: None Declared
Introduction: Cardiac output (CO) is a cornerstone parameter in pre-capillary pulmonary hypertension (PH). The Modelflow (MF) method offers a reliable non-invasive determination of beat-by-beat changes of this parameter. So MF makes it possible to explore CO adjustment with the best temporal resolution, allowing description of cardiovascular adjustments upon exercise onset in PH patients.

Methods: Fifteen subjects (5 PH patients, 10 healthy controls) performed a submaximal constant supine exercise on a cycle ergometer after 5 min of rest. CO was continuously determined by MF (CO$_{MF}$). Kinetics of heart rate (HR), stroke volume (SV) and CO were determined with 3 monoexponential models suiting to the characteristics of the tested parameters.

Results: In PH patients but not in healthy controls, we observed a sudden drop of SV upon exercise onset followed by a progressive increase to reach baseline. SV kinetics implied a transitory drop of CO whose adjustment to a new steady level was dependent of HR increase. The kinetics of HR and CO at exercise onset for PH patients was slower than that of controls for all models. This was also the case for SV on-kinetics in model-1. For model-2 and -3, SV kinetics was faster for PH patients than for controls.

Conclusion: This is the first description of beat-by-beat cardiovascular adjustments upon exercise onset in PH patients. The overall kinetics of HR and CO appeared slower than those of healthy controls and there was a transitory drop of CO upon exercise onset in PH due to a sudden drop of SV.

Disclosure of Interest: None Declared
Introduction: Tissue remodeling of sub-epithelial mesenchymal cells is a prominent pathology of chronic obstructive pulmonary disease (COPD) and asthma. The increased airway wall thickness reduces the airway lumen and limits breathing. Airway wall remodeling occurs independent of inflammation, which may explain why none of the asthma/COPD drugs reduces remodeling. Therefore, novel therapeutic targets have to be identified. We have shown that allergen inhalation increased airway remodeling in sub-epithelial fibroblasts through a novel class of proteins the protein arginine methyltransferases (PRMT) in a rat asthma model.

Methods: Human primary airway fibroblasts obtained from patients with severe asthma or COPD or controls (tumors) were stimulated with 10 ng/ml platelet-derived growth factor (PDGF)-BB for 0 – 48 hours. Protein and mRNA were isolated by standard procedures. Protein expression was determined by Western-blot and mRNA by RT-PCR. Signal transduction was inhibited by specific chemicals for Erk1/2 mitogen activated protein kinase (MAPK). PRMT1 expression in tissue was determined by immuno-histochemistry.

Results: In tissue sections of asthma patients PRMT1 was expressed in epithelial and sub-epithelial cells. In isolated bronchial fibroblasts PDGF-BB up-regulated PRMT1 expression within 1 hour, lasting up to 48 hours. The sequence of the regulatory signaling pathway was: Erk1/2 MAPK – Stat1 – PRMT1. The activity of PRMT1 was reduced by pre-incubation with either: (i) the pan-PRMT inhibitor AMI1, (ii) PD98059 (Erk1/2 MAPK inhibitor), or (iii) by Stat1 small interference RNA. The inhibition of PRMT1 activity also decreased PDGF-BB induced fibroblast proliferation, COX2 production, collagen-1A1 secretion, and fibronectin production, thus it reduced remodeling on several levels.

Conclusion: Our findings suggest that PRMT1 is a novel and central regulator for tissue remodeling of sub-epithelial fibroblasts in asthma and presents a novel therapeutic and diagnostic target for airway wall remodeling.

Disclosure of Interest: None Declared
PP-165
8. Pneumology and Thoracic Surgery
Spontaneous flow increase from implantable pump for intravenous treprostinil delivery

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Introduction: Prostacyclin pathway represents a major target in the treatment of pulmonary arterial hypertension (PAH). Due to its longer half-life and thermostability, treprostinil allows the development of implantable devices for its IV administration. This approach is appealing as it may offer less restrictive use for patients, reducing manipulation of central venous and associated infectious risk.

Methods: We would like to share our experience with two cases receiving intravenous treprostinil by subcutaneous implantable pump.

Results: The first case is a 46 year-old female suffering from drug-induced PAH. Due to clinical and hemodynamic deterioration, treatment of subcutaneous treprostinil was introduced 4 years after diagnosis. The tolerance of the latter quickly becomes limited, an implantable pump was proposed (LenusPro 20ml, Tricumed, Germany). We observed during the next 4-years follow-up a gradual decrease in the residual volume of treprostinil present in the device before the refilling, causing it to shorten the time between them. While the pump is theoretically calibrated to a constant flow rate (1.04 ml/day ±10%), the flow increased up to 1.64 ml/day (+58%). The second case is a 22 year-old man, followed for idiopathic PAH, diagnosed at age 4. Since age 15, the patient developed numerous catheter-related infections, requiring hospitalization and central line replacement. At age 19, an intravenous implantable pump was proposed (LenusPro 40ml). Similarly, we observed a progressive increase in the flow rate up to 1.52ml/day (+20%) while theoretically calibrated at 1.27 ml/day (±10%).

Conclusion: The flow rate delivered by the implantable pump in these two patients exceeded the upper tolerated limit within 2 year and continued to increase to reach +58 and +20% respectively. Only few published case series are actually available but has legitimately drawn attention, reporting good results with the LenusPro pump, without significant complications. Nevertheless, follow-up length was limited and studies included only small collectives. The use of an implantable pump in PAH management is attractive. However, systematic clinical validation with a proper clinical trial is needed to assess its safety and justify potentially additional costs induced by its use.

Disclosure of Interest: None Declared
PP-166
8. Pneumology and Thoracic Surgery
Acute complications after lung transplantation: radio-pathological correlation
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Introduction: To recognize acute complications following lung transplantation on chest CT scan confirmed by broncho-alveolar lavage or pathology obtained by transbronchial biopsies.

Methods: Lung transplantation for end-stage pulmonary diseases prompts regular assessment by CT scan for graft dysfunction. Acute pathologies may induce non-specific clinical signs regardless of their nature. Radiologists should be aware of specific signs and their time of occurrence to improve medical management and bronchoscopic procedures.

Results: Acute lung transplantation-associated complications with radiological expression could be classified into 3 major categories:
Post-surgical issues– Primary graft dysfunction is transient and appears as pulmonary edema of noncardiogenic origin. Vascular complications may involve pulmonary artery stenosis, with right ventricle or pulmonary dilatation and decreased perfusion of the ipsilateral lung. Bronchial anastomosis dehiscence manifests as focal parietal defect, adjacent air collection and persistent pneumothorax.
Alloimmune responses - Acute rejection episodes occurs in up to 30% of recipient within the first year after transplant, but also later and should be emphasized with new or persistent pleural effusions, lung volume loss and septal thickening. Chronic allograft lung dysfunction occurs in up to 50% of patients after surgery. Constrictive bronchiolitis might appear with typical air-trapping on expiratory chest CT scan.
Infections - Gram-negative bacilli, such as Pseudomonas aeruginosa, may manifest as disseminated patchy consolidations and centrilobular nodules. Angioinvasive aspergillosis typically demonstrates solid nodules and ground glass halo sign. Cytomegalovirus pneumonia may be suggested by consolidation or ground glass opacities and reticular interstitial pattern.

Conclusion: Chest CT scan is an important tool in the follow-up of lung transplantation allowing the identification of complications and aiding in the guidance of transbronchial biopsies and broncho-alveolar lavage for pathologic diagnosis.

Disclosure of Interest: None Declared
PP-167
8. Pneumology and Thoracic Surgery
Generation of an immortalized functional alveolar epithelial cell line from human induced pluripotent stem cells
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Introduction: The establishment of an alveolar epithelial cell (AEC) line derived from induced pluripotent stem cells (iPSC), represents a novel opportunity in lung disease modelling and tissue engineering. In the present study, we succeeded in generating type II AECs from iPSCs. To ensure homogeneous and long term propagation of these cells, iPSC-derived type II AECs, were immortalized by human telomerase reverse transcriptase and polycomb complex protein BMI-1 lentiviral vectors.

Methods: Human Fibroblasts were reprogrammed into induced pluripotent stem cells (iPSC). iPSC were characterized by immunostainings and differentiated towards definitive endoderm. After 5 day the definitive endoderm was grown in alveolar epithelial specific medium to generate alveolar epithelial cells. The cells were characterized by electron microscopy, immunofluorescence, moreover ELISA and invitro wound healing was performed to assess the biological function of these cells.

Results: The generated type II AEC line displayed morphological characteristics of type II AECs including growing as a cobble stone monolayer. Thus, electron microscopy analysis of this cell line confirmed the presence of lamellar body and microvilli. Also this cell line expressed type II AEC proteins such as cytokeratin, surfactant protein C and lysotracker DND 26 (marker for lamellar body). Furthermore, the type II AEC line exhibited functional properties of type II AECs including an increase of their transepithelial electrical resistance over time and an improved wound closure in presence of serum in the invitro wound healing assay. Upon TNF-α stimulation, these cells released IL-6 an IL-8 cytokines. Consistent with type II AEC phenotype, the cell line showed the ability to uptake and release of surfactant protein B and to differentiate towards type I AECs.

Conclusion: Altogether, this study established immortalized type II AECs derived from iPSCs as a novel cellular model for lung disease modelling and tissue engineering.

Disclosure of Interest: None Declared
Introduction: To assess pulmonary perfusion with dual-energy CT in order to better understand morphological pulmonary or vascular abnormalities and their functional consequences in the pediatric population.

Methods: Four children with severe pulmonary hypertension confirmed by right heart catheterism underwent a dual-energy chest CT scan for parenchymal and vascular assessment. 2 patients (2 and 8 months old) had bronchopulmonary dysplasia, 1 patient (1 month-old) a patent ductus arteriosus with treated right diaphragmatic hernia, and 1 patient (13 years-old) with tricuspid endocarditis. Each CT-scan corresponded to an irradiation dose of 0.38, 0.49, 0.28 and 1.3mSv respectively. Parenchymal and pulmonary arteries or aortic abnormalities were noted. Perfusion maps were reconstructed for functional lung analysis. Pulmonary perfusion was also rated qualitatively as severe hypoperfusion, moderate hypoperfusion or normal perfusion using a color-scale map. Iodine parenchymal lung concentrations ($C_{\text{lung}}$, mg/mL) were measured and normalized by the left atrial concentration. Then, a morphological and functional correlation was realized.

Results: 2 patients had pulmonary fibrosis with honeycombing, cysts and bronchiectasis responsible for severe hypoperfusion ($C_{\text{lung}}=2.0$); surrounded by normal morphological areas with normal ($C_{\text{lung}}=5.3$) or moderate hypoperfusion ($C_{\text{lung}}=2.9$).

1 patient had right pulmonary artery hypoplasia responsible for extensive and severe right lung hypoperfusion ($C_{\text{lung}}=1.2$) but normal left lung perfusion ($C_{\text{lung}}=3.8$). The last patient had chronic pulmonary embolism due to tricuspid endocarditis with severe systematized hypoperfusion defects ($C_{\text{lung}}=0.8$).

Conclusion: Chest DE-CT can allow complete assessment of vascular anatomy, parenchymal morphology and functional pulmonary imaging in different pediatric pathologies, particularly when the lung seems morphologically normal.

Disclosure of Interest: None Declared
Introduction: Since February 2014 Macitentan (ERA) is licensed by swissmedic. For the pediatric population the medication is only available as off label use. At the time of market introduction in Switzerland we had one patient who was not eligible for Bosentan treatment due to accompanying liver disorder. In a well controlled setting we therefore decided to switch to Macitentan instead. As this patient was doing well under treatment with this new generation ERA we started to switch our Bosentan or Sildenafil patients to Macitentan. At the same time we initiated eligible new patients immediately on Macitentan.

Methods: Retrospective observational analysis of patients treated with Macitentan. The initiation of therapy is established by a simple protocol and last 10 days. Newborns and young children remain in hospital for initiation of therapy. All patients have been registered and reported to the drug selling company Actelion.

Results: n=11 patients, 3.1±7.8 years of age, 9 male, 2 female, 4 switched from Sildenafil, 3 switched from Bosentan, treatment duration 11.8±10.5 months. All patients have been treated with 10mg per day. 10 patients received in addition diuretics and/or ACE inhibitor treatment. 1 patient died under treatment due to genetic disorder. In 1 patient treatment could be ceased after 1 year without any complications. All patients did not show any signs for liver disorder or other side effects.

Conclusion: Our data indicate that the use of Macitentan in children for all age groups is safe. Initiation of therapy should be established in young children in hospital at least until a dose of 5mg is achieved.

Disclosure of Interest: None Declared
Introduction: The present case demonstrates the diagnostic accuracy of computed tomography imaging for the diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: -

Results: A 63 year old patient with a history of repeated pulmonary embolism presented with persistent dyspnoea on exertion (NYHA III). The V/Q scan revealed multiple perfusion defects which were illustrated with equal accuracy in dual-energy-CT. The diagnosis of CTEPH was confirmed in right heart catheter with a precapillary pulmonary hypertension with mean pulmonary artery pressures of 34 mmHg and PVR of 305 dynes.

Figure 1: good correspondence between dual-energy-CT (left) and V/Q scan, fused with CT (right).

Conclusion: In conclusion, dual-energy CT is a favorable method to rule out CTEPH versus essential pulmonary hypertension and to identify candidates for pulmonary endarterectomy (PEA). Furthermore, dual-energy and 320-slices CT might be a similarly accurate screening method for CTEPH as the reference standard ventilation/perfusion (V/Q) scintigraphy. In the near future, CT could position itself as the key for screening consideration and for surgical operability with the distinct patient advantage of 1-stop-shop.

Disclosure of Interest: None Declared
Introduction: To recognize signs of pulmonary hypertension (PH) on chest CT, appreciate the severity and allow follow-up under treatment.
To diagnose and characterize a potential underlying disease.
To assess lung perfusion using iodine maps provided by Dual-Energy CT (DE-CT).

Methods: PH is a life-threatening condition with an insidious onset. Patients have non-specific symptoms and always undergo a chest CT as part of their work-up.
Dual-Energy Chest CT is also an essential tool to characterize the cardiovascular and parenchymal changes of PH.

Results: Morphological signs of PH on enhanced chest CT include a) an increased diameter of the proximal pulmonary arteries with diminished peripheral vessels, b) mosaic lung perfusion, c) dilatation of bronchi, d) systemic arterial hypertrophy and shunts, and e) right cardiac changes.
Chronic thromboembolic pulmonary hypertension, or lung diseases such as pulmonary fibrosis or chronic obstructive pulmonary disease are important underlying causes of PH, identifiable on CT.
Dual-energy CT with functional analysis allows additional qualitative and quantitative insights of pulmonary perfusion by implementation of iodine maps, especially in the depiction of systematized perfusion defects or perfusion heterogeneity.

Conclusion: Chest DE-CT enables the simultaneous assessment of vascular anatomy, parenchymal morphology, cardiac changes and functional pulmonary imaging in PH.

Disclosure of Interest: None Declared
Introduction: Invasive bronchogenic carcinoma is very fatal due to airway obstruction which leads to sudden death. Surgical removal of such tumours remains the treatment of choice. However, large numbers of patients with microscopic residual tumours (R1-resection) have recurrence and bad prognosis. Also currently used radio and chemo therapy options are associated with complications, and severe side effects. In the current study, we report the development of a novel therapeutic procedure to deliver approved chemotherapeutics directly at the tumour using novel non-invasive electrospray technique. Electrospray mediated local chemotherapy will act as an adjuvant offering palliative care by local administration of higher concentration of chemotherapeutic drugs in the tumour while reducing side effects and reliving the airway obstruction.

Methods: C57BL mice were injected with 2x10^5 Lewis lung carcinoma LLC cells (ATCC; USA) subcutaneously. After 15 days the animals were anesthetized and the tumours were exposed after skin incision. Tumours were electrosprayed with Methotrexate or Cisplatin both with dose of 100 µg at 1 mg/ml concentration. Electrospray was performed at day 1 and day 4. Tumour volume was measured every day for 8 days after electrospray. The animals were sacrificed on 8th day.

Results: 7 days after beginning of two electrospray procedures with Methotrexate the tumour size was reduced and the growth was retarded to 22.46 mm^3 ± 12.14 mm^3. Similar effect was observed after Cisplatin spray 43.01 mm^3 ± 16.92 mm^3 while control tumour growth at same day was 514.30 ± 104.50 mm^3.

Conclusion: We successfully demonstrated the feasibility of targeted drug delivery in the subcutaneous tumour by electrospray in mice model. A miniaturized device has been developed that requires only a single port access, therefore the concept is suitable for application through a bronchoscope and offers a novel and promising tool to target invasive tumours.

Disclosure of Interest: None Declared
Introduction: Radiosurgery has been developed as a curative treatment option for early stage non-small cell lung cancer (NSCLC) patients who are not candidates for surgical resection. CyberKnife® radiosurgery allows high dose radiation delivery to tumours with better accuracy than conventional stereotactic radiation therapy. Respiratory-related movements may, however, reduce the doses to the tumour and increase the doses administered to healthy tissues. Tumour tracking with fiducial markers is a known technique to overcome this problem. Fiducial markers placement close to the tumour has been reported by the transcutaneous, intravascular or endobronchial route. We report our experience with coil-spring fiducial marker (CsFM) bronchoscopic deployment under radial-endobronchial ultrasound (R-EBUS) probe and fluoroscopy guidance.

Methods: Medically inoperable early stage NSCLC patients were evaluated for CsFM placement (Terumo AZUR-CX®) and CyberKnife® radiosurgery guidance in our tertiary care center. Flexible bronchoscopies (4.2 mm Olympus® BFP180) were performed under moderate sedation in association with an ultrathin R-EBUS probe (1.7 mm Olympus® UM-S20-17S). After the CT-scan reading, the airways in the target zone were scanned with R-EBUS probe looking for the typical signal. This point was visualised by fluoroscopy and samplings were performed in case of non-diagnostic lesion. Afterwards, the CsFMs were deployed under fluoroscopy guidance in the subsegmental bronchi around (2-3 cm radius) the tumour/s. Chest radiography was obtained to confirm CsFM placement and to rule out any pneumothorax. The patients were then admitted one night for monitoring.

Results: In a 6-months period, 3 patients underwent CsFM placement. No complications were recorded. One patient had 2 synchronous NSCLCs. Therefore, 4 tumours were assessed with the R-EBUS probe. 14 CsFMs were placed. The mean duration for the procedure was 29 minutes (range 27-31). On the CT-scan for radiosurgery programming performed during the week after the CsFMs deployment, 12 out of 14 were still in the deployed position, and were used for tracking. The tumour lesions were treated at a dose of 55 Gy in 5 fractions administered over 10 days. No patients developed radiation-induced pneumonitis requiring a treatment.

Conclusion: Endobronchial deployment of CsFMs guiding Cyberknife® radiosurgery was well tolerated, rapidly performed and safe. It allowed precise and lung sparing irradiation of early stage NSCLC patients.

Disclosure of Interest: None Declared
Introduction: Current guidelines for interstitial lung disease (ILD) recommend surgical lung biopsy (SLB) as a powerful method for specific diagnosis. An aggregate risk score for predicting outcome after SLB for ILD[1] includes immunosuppressive treatment and open lung biopsy as important predictors of mortality. Therefore, we performed an independent retrospective study to validate immunosuppression as a predictor of increased mortality after SLB for ILD.

Methods: All patients with ILD who underwent diagnostic SLB between 2000 and 2014 were included. The patients were classified as: immunocompromised or immunocompetent. ROC-curve and multivariate analyses were performed to determine predictors of mortality. Variables included were age, surgery (VATS vs. open), number of biopsies, American Society of Anaesthesiologist (ASA) score, smoking history, pre-operative ICU admission, preoperative lung function and coronary artery disease. Statistical significance was set at p<0.05.

Results: 161 immunocompromised patients (87 males, 74 females), mean age 51.8 years (±14.15, range 19-79) and 133 immunocompetent patients (86 males, 47 females), mean age 60.4 years (±14.51, range 22-85) were included in this study. The ASA-score distribution was 17 with II (10.6%), 110 with III (68.3%) and 33 with IV (20.5%) immunocompromised vs. 31 with II (23.3%), 90 with III (67.7%) and 11 with IV (8.3%) immunocompetent patients and 25 vs. 14 were admitted to the ICU pre-operatively, respectively. 30- and 90-day mortality in immunocompromised patients were 9.9% (n=16) and 15.5% (n=25) vs. 5 (3.8%) and 8 (6%) in immunocompetent patients, respectively. Surgery (VATS vs. open), age, smoking history, number of biopsies, lung function and coronary artery disease were not independent predictors. ROC-Curve analysis for 30-day mortality revealed ASA score (area under the curve 0.799, p=0.014) and pre-op ICU admission (area under the curve 0.903, p=0.001) as the only significant predictors for mortality.

Conclusion: In our experience immunocompromised patients had no increased risk of morbidity and mortality after surgical lung biopsy. Pre-operative ICU admission and ASA score were the only independent significant predictors.


Disclosure of Interest: None Declared
Introduction: Rapid, accurate microbiological results may allow appropriate antibiotic therapy, withholding or adapting antibiotics, and thus reducing risks and costs of empirical antibiotic therapy. The objective of this study was to investigate the diagnostic performance of a new molecular diagnostic assay (Curetis Unyvero – p55) in the bronchoalveolar lavage of immunocompromised patients.

Methods: Prospective, non-interventional, controlled study including 522 immunocompromised patients undergoing diagnostic bronchoalveolar lavage for suspicion of lower respiratory tract infection. Results of Curetis Unvyero Application, a test intended to detect and to identify genes of 21 microorganisms and 19 genes associated with antibiotic resistance in 4 hours, were compared to results of conventional microbiology cultures and/or PCR-based reference methods (for atypical microorganisms).

Results: Patients had a mean age of 57.63 ± 14.73 years, 58.6% were male. The most common symptoms were cough (57.5%), dyspnea (23.8%), phlegm (22.6%), fever (20.7%) and decreased FEV1 (11.3%). Most common causes of immunosuppression were allogenic stem cell transplantation (20.3%), lung transplantation (14.6%) and hematological malignancies (38.1%). Curetis Unyvero - p55 in bronchoalveolar lavage provided 68.35% sensitivity, 86.00% specificity, 46.55% positive predictive value, 93.12% negative predictive value, 5.16 PLR and 0.37 NLR compared to conventional culture. The sensitivity of the multiplex PCR improved regarding only gram negative pathogens about 10% (68.35% vs. 76.19%).

Conclusion: The Unyvero application – p55 detects more potentially pathogenic bacteria than conventional methods in the BAL of immunocompromised patients and is useful in narrowing antibiotic therapy particularly for lower respiratory tract infections caused by gram negative pathogens.

Disclosure of Interest: None Declared
Operative stabilisation of chest wall trauma: single center report of initial management and longterm outcome
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Introduction: Conservative treatment of even severe thoracic trauma including flail chest was traditionally the standard of care. Recently we reported possible benefits of surgical chest wall stabilization in accordance with other groups. The aim of this study was to critically review our indications and results of internal fixation of rib fractures after blunt thoracic trauma also in the longterm course.

Methods: We analysed the prospectively collected data of a consecutive series of patients having had internal rib fracture fixation at our institution from 8/2009 until 12/2014 and we retrospectively studied the late outcome by clinical examination or personal interview.

Results: From 1398 patients with a thoracic trauma treated at our institution during that time period 235 sustained a severe thoracic trauma (AIS ≥3). In 23 of these patients 102 internal rib fixation were performed using the MatrixRIB® system. The mean age of these patients with chest wall stabilization was 49.3 years with a mean ISS of 22.9. Operation time was 115±51 minutes. From 18 local resident patients follow up could be obtained after an average time period of 27.6 (12-68) months. All of these patients were free of pain and had no limitations in their daily routine. Of all implants, 5 splint tips perforated the rib in the postoperative course but all patients remained clinically asymptomatic. Plate osteosynthesis showed no loss of reduction in the postoperative course. No case of hardware prominence, wound infection or non-union occured.

Conclusion: In our carefully selected thoracic trauma patients, locked plate rib fixation seems to be safe and beneficial not only in the early posttraumatic course but also after months and years patients remain asymptomatic and complete recovery is the rule.

Disclosure of Interest: None Declared
Introduction: Combined targeted therapies represent novel therapeutic approaches simultaneously acting on several specific molecular pathways in cancer. Patients not harboring driver mutations may benefit from such therapies, but identifying predictive biomarkers is paramount for proper patient selection.

Methods: The phase II clinical trial SAKK 19/05 investigated the safety and efficacy of combined first-line treatment with bevacizumab and erlotinib in unselected patients with NSCLC. Blood samples were taken in 43 non-squamous NSCLC patients at baseline and 24h after the beginning of initiation of the combined bevacizumab/erlotinib targeted therapy. Messenger RNA was extracted and hybridized on Affymetrix GeneChip Human Exon 1.0 ST arrays. The gene expression levels at baseline and 24h were investigated using dually constrained correspondence analysis. The gene expression prognostic and predictive value was assessed using Cox proportional hazards regression and linear regression. Validation of our putative biomarkers was done using the online survival analysis software in NSCLC (KM-Plotter).

Results: Blood gene expression variations measured 24h after initiation of targeted therapy indicate a direct effect on genes that belong to the KEGG pathway "Pathways in cancer". More specifically, a significant down-regulation was found in genes that are part of the cytokine-cytokine receptor interaction (IGF1R, IGF2R), MAPK signaling pathway (DAPK2, PLD1, MMP9), and mTOR signaling pathway (BIRC3). The magnitude of change over 24h was not predicting patient's outcome. Gene expression makers at baseline included Cancer susceptibility candidate 1 and 18, regarding overall survival and time-to-progression under BE, respectively. Predictive markers at 24h included genes belonging to the "Pathways in cancer" which were predictive of time-to-progression under BE, whereas a series of genes encoding for immunoglobulins were predictive of overall survival. These results were adjusted for the patients' EGFR mutational status and independently validated using the KM-Plotter webtool.

Conclusion: Blood gene expression levels at baseline and 24h after the initiation of bevacizumab/erlotinib provide potential novel biomarkers of the response to combined targeted therapy in unselected patients with advanced non-squamous NSCLC.

Disclosure of Interest: None Declared
Introduction: Surgery in octogenarians is performed with acceptable morbidity and mortality. However, little is known about the quality of life (QoL) after surgery especially in octogenarians. The goal of this study was to retrospectively examine quality of life in octogenarian patients.

Methods: Patients aged 80 years and older who had thoracic surgery between June 2013 and November 2015 were asked to recall their QoL before surgery and their present QoL by completing the EORTC QLQ-C30 questionnaire. The questionnaires and the medical history of the patients were analysed in SPSS. A statistical significance between pre- and post-operative scores was set at \( p < 0.05 \).

Results: 79 patients (40 male and 39 female) with a mean age of 84 years (range 80 to 98) were included in the study. 24 patients (30.4%) had undergone a thoracotomy, and 55 patients (69.6%) minimally invasive procedures. 59 (75%) of the patients were ASA III. The average hospitalization time was 14 days (SD ±9.4 days) and 30-day mortality was 12/79 (15%). 30 patients answered the questionnaire, of which 21 were male and 9 were female. The average time between surgery and receipt of the questionnaire was 8.4 months (SD ±4.8 months). There was no significant difference in age, hospitalization time, and ASA between the patients who answered the questionnaire and those who did not answer. There was no significant difference in overall QoL before and after the surgery \( (p=0.157) \). There were significant differences in physical functioning \( (p=0.000) \), role functioning \( (p=0.032) \), cognitive functioning \( (p=0.002) \), fatigue \( (p=0.009) \), and appetite loss \( (p=0.048) \).

Conclusion: Our results suggest that QoL after thoracic surgery in octogenarians is comparable to preoperative QoL. Since health in elderly people is the most important factor to maintain a good QoL, denial of surgical treatment only due to advanced age should no longer be acceptable.

Disclosure of Interest: None Declared
PP-179

8. Pneumology and Thoracic Surgery

Near-infrared fluorescence is useful for identification of the intersegmental plane in thoracoscopic lung segmentectomy

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Introduction: The aim was to evaluate the fluorescence imaging during lung segmentectomy by Video-Assisted Thoracic Surgery (VATS).

Methods: Study of VATS segmentectomies assisted by fluorescence imaging (PINPOINT® Novadaq, Canada) in the University Hospitals of Geneva from November 2014 to August 2015. Analysis of technical input, pathological findings, postoperative course and cTNM / pTNM correlation.

Results: Intersegmental plane identification was perfect in all 17 consecutive segmentectomies, providing additional assistance in case of difficulty with anatomical vascular segmentation. Due to fluorescence imaging, an additional arterial or parenchyma section was performed in two patients (12%). One patient was converted to lobectomy by thoracotomy because of oncological reasons. The postoperative course was uneventful except in one patient who developed pneumonia and prolonged air leak (10 days). The drain was removed on POD1 or POD2 in 16 patients with a mean hospital stay of 4.9 +/- 2.3 days. Resections were complete for 4 benign lesions and 13 lung cancers.

Picture/Graph:

Conclusion: Fluorescence imaging provides a technical assistance for intersegmental plane identification in VATS, and facilitates vascular identification. It contributes to the quality of diagnostic and therapeutic excisions of small nodules which are often not visible and not palpable during VATS.


Disclosure of Interest: None Declared
Introduction: Therapeutic options for severe emphysema are limited. Lung volume reduction (LVR) treatment by endobronchial valves, coils or surgery are palliative procedures. All these therapies are available in Switzerland, however, direct clinical and medico-economical comparison is currently not available. In our institution all candidates are assessed by a monthly multidisciplinary board. We reviewed our data to evaluate the efficacy, safety and the cost of these 3 procedures.

Methods: Between 2005-15 all patients treated in our center with LVR were included in this retrospective analysis. Costs included only the resources of the initial hospitalization (devices, staff, stay). The reimbursement based on the DRG system was collected for each patient. Changes in the lung function, quality of life and dyspnea were recorded at 6 and 12 months. Valves were deployed only in a lobe without collateral ventilation. An average of 10 coils were inserted unilaterally in the most severely affected lobe. Surgery was performed by unilateral mini-invasive thoracoscopy.

Results: 7 patients were treated by valves, median cost (MC) 16,501 Frs and median DRG reimbursement (MDRGR) 18,612 Frs. 2 patients developed severe pneumothorax requiring definitive removal of valves, 2 patients had no benefit (valves were removed and coils inserted) and 3 had subjective benefit. At 12 months, the mean change of these 3 patients was a 26% gain in FEV1 and a 0.53L decrease in RV. 13 patients were treated by coils, MC 21,373 Frs and MDRGR 8,456 Frs. 1 patient had severe pneumonia with septic shock, 3 presented COPD exacerbation and 1 pneumothorax. 5 patients had major subjective benefit. At 12 months, the mean change was a 15.8% gain in FEV1 and a 1.33L reduction in RV. 13 patients were treated by surgery, MC 31,279 Frs and MDRGR 26,431 Frs. 3 patients had prolonged air leak, 2 had transient auricular fibrillation. 5 had major subjective benefit. At 12 months, the mean change was a 10.7% gain in FEV1 and a 17.4% reduction in RV.

Conclusion: Comparisons of the three LVR modalities are difficult due to differences in patient selection (e.g. type of emphysema, exclusion criteria). However, at 12 months, the efficacy of these modalities seems similar. Pneumothorax is frequent with valves. Financial losses are clearly identified with the coils, costs of these devices should be lowered and specific reimbursements created to improve the implementation of these 3 techniques.

Disclosure of Interest: None Declared
Introduction: Background: Since 80% of current smokers have started smoking before adulthood, tobacco smoking is considered a paediatric disease. Tobacco advertising mostly targets young people, as the industry critically needs them as “replacement smokers”. The WHO/FCTC requires a total ban of advertising, promotion and sponsorship (art. 13 and its guidelines). In Switzerland, the industry opposes such ban, arguing that self-regulation offers sufficient protection. Since 1966, the Swiss tobacco industry has adopted an advertising code. In 1974, it has obtained the support of the Swiss “Lauterkeits-kommission” (LK - “neutral and independent institution of the communication branch, to garantee self-regulation of advertising”) to supervise its application. To defeat the 1993 twin initiatives, it redrafted the code “to sanitize the industry's image”.

Methods: Aim: To test the efficacy of the self-regulation agreement between LK and Swiss Cigarette (BAT, JTI, PMI)

Method: Potential violations of the voluntary code between 2013 and 2014 were identified and 15 complaints were submitted to LK by OxyRomandie

Results: Of the 15 complaints filed; 4 (warnings <10% surface, no warning) were accepted, 3 (outside ashtrays) resulted in corrective action, i.e. 47% success rate. The procedure was characterized by long delays, 13-21 months, rendering action superfluous. Despite acceptance of the complaint, violations continued. Decisions by LK were not made public but were simply referred to Swiss Cigarette for internal consideration. A campaign aggressively targeting young people, the Marlboro “Maybe” campaign, was considered to be in conformity of the code. Legalistic arguments of dubious value by the tobacco companies were uncritically accepted and repeated by LK.

Conclusion: Self-regulation of tobacco advertising is ineffective and only produces a misleading impression of protection, allowing tobacco companies in Switzerland to use a wide array of sophisticated advertising, sponsorship and marketing techniques to target young people without any real obstacle.


Disclosure of Interest: None Declared
The first case of an extraskeletal myxoid chondrosarcoma in the pulmonary artery

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Introduction: We present the first described case of a primary extraskeletal myxoid chondrosarcoma (EMC) in the pulmonary artery.

Methods: We report the case of a 21-year old female who presented herself with progressive dyspnea. The diagnostic work up with CT scan showed a mass in the main trunk of the pulmonary artery. Complete work up included a fine needle aspiration via EBUS, echocardiography, positron-emission tomography, computed tomography, a heart MRI and V/Q scan of the lung and an immunological screen. The cytology of EBUS FNA showed myxoid proliferations, suggestive of a mesenchymal neoplasia.

Results: We performed a pulmonary tumor endarterectomy with partial reconstruction of the right pulmonary artery in deep hypothermia without circulatory arrest. The postoperative course was uneventful and she was discharged at day 6. The definitive histological examination revealed an EMC, usually found in the lower proximal extremities. A translocation of the EWSR1-gen in the q22;q12 locus was found as well as S100 negativity. Microscopic complete resection was proven in the distality of the endarterectomy specimen. Because of the low proliferation rate of the tumor under 10 % and a complete resection no adjuvant therapy was performed. 10 months after surgery the patient is free of recurrence in follow-up CT scan and back to her normal work life and sports activity.

Figure: Contrast enhanced CT scan of the chest (A), PET/CT scan shows a limited FDG uptake (B), Tumor is located in the main PA (C) extending into the left and right trunk (D), where it is attached to the wall and was completely resected and right PA partially reconstructed (E).

Conclusion: EMC are a rarity within the mesenchymal tumors with an incidence of 2-3 % of all soft-tissue sarcoma and most likely occur in the proximal lower extremities, but also limb girdles and trunk. Prognosis is good with 5 year survival rate of about 90 % after complete resection. Localization in the PA has not been described so far, and only rarely in the heart.

Disclosure of Interest: None Declared
First experience with a biodegradable endobronchial stent in a case of bronchomalacia

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Introduction: Stents are widely used therapeutic modality to preserve airways from obstruction. Stents are categorized according to the following materials: silicone or other polymer stents, self-expandable metal stents, and hybrid polymer-metal stents. Among possible drawbacks, stents may disturb airway clearance and may be prone to migration. In addition, complications may occur including formation of granuloma and obstruction due to trapped secretions. In this context, the use of biodegradable stents might be an attractive alternative.

Methods: A 72 years old patient suffering from dyspnea especially on exercise was referred to our Department of Pulmonary Medicine. The patient’s history included a liver-transplantation related to a cryptogenic cirrhosis in 1994, an oropharyngial carcinoma in 2003 treated with radiation of 50 Gy of the cervical and supraclavicular region followed by laryngectomy. The patient also suffered from normofrequent atrial fibrillation. Endoscopically there was a breath dependent subtotal stenosis of the left main bronchus (under conscious sedation and awake). The right side only showed a small narrowing of the main bronchus. The FEV1 was 0.94 l (37%) and VC 2.17 l (67%).

Results: The patient had a history of granulomas in the area of laryngectomy. He also had a tracheostomy, therefore a silicon stent was difficult to implant. As a consequence, in this case of benign stenosis we decided to implant a 14 x 30 mm biodegradable polydioxanone stent. The wall tension seemed to be less than with silicon or nitinol stent. In situ, the stent did not expand fully and was longer than calculated, spanning from the main carina to the partially open ostium of the left upper lob. Fifty days later, the stent was partially bioabsorbed and the in- and expiratory functionality were reverted with the left main bronchus open (Figure 1). There were no problem of mucus. The lung functions improved regarding FEV1 1.40 l (55%) and VC 2.79 l (87%).

Conclusion: Biodegradable stents are a promising alternative option for the maintenance of the endobronchial lumen.

Disclosure of Interest: None Declared
Introduction: Non-anaesthesiologist administered propofol sedation (NAAPS) for flexible bronchoscopy (FB) is controversial, since there is no standardised training program in airway management (AM) for pulmonologists. The aim of this study was to investigate the clinical performance and acceptance of an AM algorithm and training program for pulmonologists performing NAAPS.

Methods: An AM algorithm for pulmonologists applying 3 manoeuvres including bag mask ventilation (BMV), laryngeal tube (LT), and needle cricothyrotomy (NCT) was established at our institution (Figures). AM trainings consisted of a detailed demonstration and four consecutive attempts to succeed with each of these devices. The trainings were scheduled in 2 training sessions with a break of 8 weeks in between. The primary outcome was the improvement of completion time needed for a competent airway. Secondary outcomes were the trainees’ overall reactions to the training and the established algorithm, and the perceptions of psychological safety (PS) during the training using standardised scales.

Results: 23 staff members of the Department of Pulmonology performed 184 standardised AM procedures, and returned 42 questionnaires. Median completion times of LT placement and NCT improved significantly between session 1 and 2 (p=0.005 and p=0.040, respectively), whereas BMV was only marginally significant (p=0.050). Trainees perceived that training is useful and expressed contentment with this training and the algorithm. The perception of PS increased after training.

Picture/Graph:
PROBLEM: O2-DESATURATION ≥ 4% OR < 90% OR APNEA > 30 SEC

STEP 1

Problem solved?

YES

STEP 2

Problem solved?

YES

STEP 3

PROBLEM SOLVED: O2 Saturation >90% OR increase > 4% + spontaneous Ventilation

Picture/Graph 2:
**Conclusion:** An AM algorithm and training for pulmonologists leads to improved technical airway management skills, and is considered useful by trainees and raised their perception of PS during training. It thus represents a promising program.

**Disclosure of Interest:** None Declared
Introduction: Endobronchial valve (EBV) placement is an established lung volume reduction procedure aiming to improve lung function and exercise capacity in patients with severe emphysema. As EBVs consist of silicone and Nitinol (metal alloy of nickel and titanium), there are concerns that nickel ions might be released which could have a clinical impact in patients allergic to nickel.

Methods: To the best of our knowledge, this is the first case of a typical hypersensitivity pneumonitis (HP) after treatment with EBVs in a patient with a known nickel allergy.

Results: Following EBV implantation our patient developed all clinical symptoms and radiological signs of an allergic reaction including positive response to steroid treatment. While a marked skin reaction after nickel scratching was detectable, he did not show a positive skin reaction to a scratch test with the Nitinol-containing EBV. Also nickel release in an EBV eluate measured by inductively coupled plasma mass spectrometry was not detectable.

Conclusion: Thus, it remains a matter of debate, if the reported HP is associated with the EBV treatment. The mechanism, how nickel ions would find their way through the silicone membrane into bronchial mucosa is elusive. Anyhow, the patient had a radiologically successful procedure with evidence of complete RUL atelectasis after EBV treatment leading to decreased hyperinflation and improvement of lung function. In the end, HP and EBV treatment may have occurred coincidentally.

Disclosure of Interest: None Declared
Multimodal screening of respiratory disease related to tobacco consumption: results from a screening day at a tertiary center.
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Introduction: Chronic obstructive pulmonary disease (COPD) and pulmonary lung cancer are the most feared consequences of smoking. Smoking cessation is the intervention with the greatest capacity to influence the natural history of COPD. Lung cancer screening by thorax CT scan have shown to reduce mortality in selected patients. Prevention and early care is the cornerstone of treatment of COPD and lung cancer.

Methods: We offered a respiratory disease multimodal screening day to the Geneva smoker’s population. A spirometry and a specialized medical consultation were proposed. A thorax CT scan was performed in selected participants. All smokers were advised to quit tobacco consumption and consult a tobaccologist. People with lung disease were suggested to consult a pulmonologist. Smoke cessation, lung specialist consultation and tobaccologist visit status were evaluated at three months.

Results: 232 subjects intended to participate to the screening day. 180 participated actively (Fig. 1). 11 active smokers (8.3%) quitted tobacco consumption during the three month following the screening day. 10 persons (34.5%) report having had a lung specialist consultation. 3 smokers (2.2%) contact a tobaccologist as suggested. 26 people have had thorax CT scan. We found 2 oncologic advanced lung diseases and 4 patients with lung nodule stable on 3 months radiological follow up.

Conclusion: Such multimodal screening day for tobacco-related respiratory diseases is an interesting approach. Its impact as still to be evaluated, but consideration should be given to the potential positive impact of this kind of initiative on the population awareness about smoking consequences and paramount importance of smoking cessation.

Disclosure of Interest: None Declared
A 25-year follow-up of 2 airways stents (gianturco z-stents) placed during childhood.

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Introduction: Transposition of great vessels in infants is treated by a switch operation, which may be complicated by life-threatening vascular-driven tracheobronchial compression. The use of non-absorbable stents for benign airways compression in children is not the optimal treatment but can be an alternative in case of surgical failure.

Methods: A 25-year old man was referred to our Pulmonary Medicine outpatient because of a 6 weeks cough, which improved after an antibiotic course. He didn’t complain of dyspnoea. Clinical examination was unremarkable. He was born with a D-transposition of great vessels, operated at 6 days of life. Three months later, he presented with a stridor complicated by a respiratory arrest. Bronchoscopy showed a 70% narrowing of the trachea and a subtotal obstruction of the left main bronchus. Computed tomography-scan revealed a tracheal compression by the ascending aorta and a left main bronchus compression by the innominate artery. Because failure of 2 surgical innominate artery’s suspensions, 2 Gianturco metallic Z stents were inserted in the trachea and the main left bronchus with a good result. During following years, physicians observed several strut’s rupture of the tracheal stent, and barb’s fragmentations, followed by a rupture of the left main bronchus stent, without migration. These stents ruptures were found incidentally. For the management of the recent cough, work-up included pulmonary function tests, revealing a restrictive pattern, a flattening of the inspiratory curve and a chest computed tomography-scan showing a posterior rupture of tracheal stent. One fragment had migrated through the posterior tracheal wall and reached the anterior part of a vertebral body, next to the oesophagus (Figure). The left main bronchus stent seemed broken at its distal inferior part but did not migrate outside the bronchus.

Results: The patient underwent a bronchoscopy, which confirmed the posterior rupture of the tracheal stent. Stitches of the stent could not be visualized in the posterior wall of the trachea. There was a protrusion of the distal anterior part of the tracheal stent in the lumen, which diameter remained above 50%. The left bronchus stent was completely covered by the bronchial mucosa.

Picture/Graph:
Conclusion: This case shows a 25-years follow-up of a patient with 2 stents placed in his airways as an infant. Despite several fractures of the stents, the patient remained pauci-symptomatic and did not suffer of severe complication so far.


Disclosure of Interest: None Declared
Introduction: Background: Tobacco (TBCO) multinationals use “independent” academics to fuel their policy of denial and of manufactured doubt about TBCO toxicity and effectiveness of TBCO control measures. Thus influencing political decision makers, media and public opinion, they aim at blocking/delaying TBCO control measures, or replacing them with favourable legislation.

Methods: Aim/Methods: Search for TBCO funded studies in Swiss institutions and actions taken by academic authorities to protect their integrity.

Results: - 1962 up to 2000 ASFC (Association Suisse Fabricants Cigarettes – now Swiss Cigarette) funded research in CHUV, ETHZ, UNIBAS, UNIFR, UNIGE, UNIL, USZ. Many were basic biological projects, including respiratory physiology. Specifically, e.g.: Pr. Grandjean and Dr Weber, ETHZ, on passive smoke exposure of humans funded 1962-77 (stopped by “unfavourable” results); Pr. Baettig’s, ETHZ, on psychopharmacology of nicotine, 1967-94; Pr. Dauwalder’s, UNIL, psycho-social study on tolerance, used against public smoking bans 1992-98. No action.
- 10/2004: 6 mths after verdict UNIGE states: “Prof. R cannot be considered independent researcher”.
- 2005 Pr. A. Auer’s, UNIGE, expert opinion : “La constitutionalité de l’initiative populaire genevoise Fumée passive et santé” paid for by JapanTBCO. Published during the popular vote campaign, it concluded that “it’s all but proven, that the smoking ban is efficient for health protection” arguing disproportionally restricted liberty. It relied on a flawed study of older cohorts funded by PM, ignored other data and WHO statements. No action by UNIGE.
- 2014 Prof. Wolf und Kaul’s, UNIZH: “...The (possible) effects of plain packaging on smoking prevalence in Australia”. Data and funding by PM, with the right to influence on publication and control over how results are communicated. Since the applied statistical method is not adequate to the issue, UNIZH was urged to retract the study. No action, notwithstanding, that re-analysis of data by other methods comes to the opposite conclusion.

Conclusion: TBCO money influences experts by funding wide array of research. Institutions are either denying and pretext academic freedom to justify inaction, or slow in taking action against misuse of the scientific process.

Disclosure of Interest: None Declared