Respiration

Respiration 2022;101:500–528
DOI: 10.1159/000524018

Published online: March 30, 2022

Abstracts are available online only, free of charge,
at www.karger.com/doi/10.1159/000524018

SSP/SSTS – SSSSC Joint Annual Meeting 2022

Lucerne, Switzerland, March 30–April 1, 2022

SCHWEIZERISCHE GESELLSCHAFT FÜR PNEUMOLOGIE
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SSP/SSTS – SSSSC Joint Annual Meeting 2022
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Conflict of Interest Statement

The reviewing and selection of the Abstracts included herein were overseen by Prof. Dr. med. Silvia Ulrich, Klinik für Pneumologie, Universitätshospital Zurich. Prof. Ulrich has no conflicts of interest in connection with the selection of these Abstracts to report.

Program

Respiration

SSP Oral Communication - Physiology, Exercise, Sleep

O01

Effect of Acetazolamide on Walk Distance in Patients with Precapillary Pulmonary Hypertension: Randomized, Placebo-Controlled, Cross-Over Trial

M. Lichtblau[1], *S. Saxer*[2], *P. Appenzeller*[2], *J. Müller*[2], *C. Berlier*[2], *S.R Schneider*[2], *M. Furian*[2], *K.E. Bloch*[2], *S. Ulrich*[2]

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Aims: Acetazolamide for 1 week improved oxygenation in patients with pulmonary arterial or distal chronic thromboembolic pulmonary hypertension (PH, PAH/CTEPH). We investigated whether longer-term acetazolamide therapy improves the 6-min walk distance (6MWD).

Methods: 28 patients stable on therapy (15 PAH, 13 women, mean±SD age 62±15 y, 6MWD 551±92m, SpO_2 95±3%) were randomised to each 5 weeks of acetazolamide (250mg capsules bid) and placebo separated by ≥2 weeks washout in a double-blind crossover protocol. Primary outcome was the 6MWD with missing data replaced by last measures. Secondary outcomes were blood gases and side effects.

Results: 25 patients completed the trial per protocol, 3 stopped in phase 1 (2 acetazolamide, 1 placebo). 6MWD changed by a mean (95%CI) of -25m(-46 to -3), p=0.025 resp. -5m(-7 to 18), p=0.400, in response to acetazolamide resp. placebo (treatment-effect -19m(-42 to 4), p=0.100). With acetazolamide vs. placebo, PaO_2 was higher (11.0±0.3 vs. 9.6±0.3 kPa; difference 1.4(1.8 to 1.0)), arterial pH lower (7.37 vs. 7.44; -0.07(-0.06 to 0.08)), and $PaCO_2$ lower (3.9±0.1 vs. 4.5±0.1 kPa; -0.6(-0.4 to -0.7)), all p<0.001. Side effects were mild but more common during acetazolamide (paraesthesia 37 vs. 4%, taste-change 22 vs. 0%, dyspnoea 26 vs. 4%, all p<0.05).

Conclusions: In PH-patients, acetazolamide for 5 weeks did not improve 6MWD despite improved oxygenation. Therefore, our data do not support acetazolamide for improving exercise in PH, also in regard of increased dyspnea due to acidosis-induced hyperventilation.

ClinicalTrials.gov Identifier: NCT02755298

Conflict of interest to declare?: No

O02

Prediction of Peak Oxygen Uptake from 6-Minute Walk Test in Pulmonary Hypertension

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Introduction: Maximal oxygen consumption (VO2max) assessed by cardiopulmonary exercise training (CPET), is an important parameter for risk assessment in patients with pulmonary hypertension (PH). However, CPET may not be available for all PH-patients. Thus, we aimed to test previously published predictive models of VO2max from the 6-minute walk distance (6MWD) for their accuracy and to create a new model.

Methods: We tested four models (Ross(2010), Miyamoto(2000) and Zapico et al.(2019)). To derive a new model, data was split into a training and testing dataset (70:30) and step-wise linear regression was performed. To compare the different models standard error of estimate (SEE) was calculated and the models have been graphically compared by Bland-Altman plots. Sensitivity and specificity for correct prediction into low risk classification (VO2max > 15 ml/min/kg) was calculated for all models.

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Results: 276 observations were included in the analysis (194/82 training/testing dataset). 6MWD and VO2max significantly correlated ($r = 0.65$, $p < 0.001$). Linear regression showed significant correlation of 6MWD, weight and heart rate response (HRR) with VO2max and the best fitting prediction equation was: VO2max = 1.83 + 0.031x6MWD(m) – 0.023xweight(kg) – 0.015xHRR(bpm). SEE for the different models were 3.03, 3.22, 4.36 and 3.08ml/min/kg for Ross, Miyamoto, Zapico et al. and the new model respectively. Predicted mean VO2max was 16.5ml/min/kg (vs. observed 16.1ml/min/kg).

Conclusion: 6MWD and VO2max reveal good correlation in all models. However, the accuracy of all models is inadequate for clinical use. Thus, CPET and 6MWD measures both remain valuable risk assessment tools in the management of PH.

Conflict of interest to declare?: No

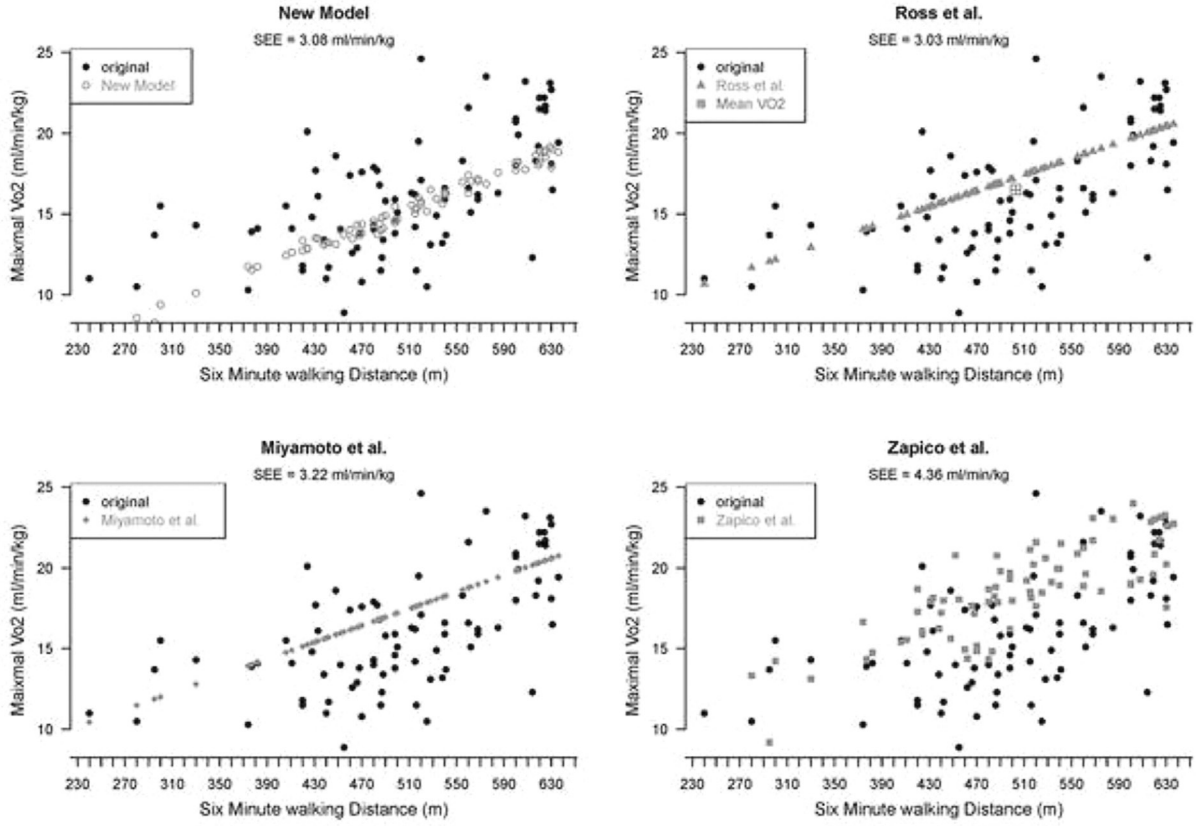

Fig. 1. Comparison of predictive models. The panels show the predicted values for maximal oxygen uptake (maximal VO2) against the 6-minute walk distance for each model separately. In each panel, the original data from the testing dataset is depicted for comparison. Standard error of estimate (SEE) for each model is shown below the panel headers. Mean VO2 as determined by the generalized equation by Ross et al. is shown in the corresponding panel.

O03

Predictors of Survival in Adults with Duchenne Muscular Dystrophy

A.-C. Stoewhas[1], M. Furian[1], B. Kindler[2], M. Rosche[3], F. Habersatter[3], H. Arndt[1], E.I. Schwarz[1], K.E. Bloch[1]

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Introduction: In patient with Duchenne Muscular Dystrophy (DMD) life expectancy has significantly improved by implementation of supportive care, including mechanical ventilation and nutritional support. We analyzed causes of death and factors associated with survival in patients with DMD.

Methods: We prospectively followed patients with DMD treated at the University Hospital Zurich between 1993-2020. Clinical data, lung function and echocardiography were analyzed in patients living at home and in a specialized care facility, the Mathilde Escher Stiftung (MEH).

Results: We included 81 patients (36 living at home, 45 in the MEH) in our study. Median (quartiles) age at initial presentation was 17y (14;19), forced expiratory volume (FEV1) 40 %predicted (21;58), left ventricular ejection fraction (LVEF) 49% (40;55), body mass index 20.1 kg/m2 (17.3;24.4). The individual observation period was 9y (6 to 14). 33 (41%) deaths occurred from respiratory, cardiac or other causes (1/3 each). 66 patients received noninvasive ventilation (NIV) initiated at age 20y (17;23). Of these 17 were subsequently switched to ventilation via tracheostomy at age 27y (23;28). 27 patients received nutritional support via PEG after age 21y (19;26). In Kaplan-Meier analysis, median age at death was 33.5y (26.7;37.0). In univariable Cox regression analysis, low FEV1 and LVEF predicted reduced survival; living in a specialized care facility was associated with earlier need of NIV, tracheostomy and PEG but similar survival compared to the patients living at home.

Conclusions: The survival in DMD patients receiving comprehensive interdisciplinary care at our reference center was similar to that reported internationally. Most deaths were respiratory and cardiac related. Living in a specialized facility may have contributed to the similar survival of patients living in the MEH and those at home despite more advanced disease in the former requiring earlier ventilatory assistance and nutritional support via PEG.

Conflict of interest to declare?: No

O04

Sleep Apnea in School-Age Children Living at High and Low Altitude

M. Grimm[1,2], A. Seglias[1,2], L. Ziegler[1,2], M. Mademilov[3,2], E. Isaeva[4,2], K. Tynybekov[4,2], A. Tilebalieva[4,2], N. Osmonbekova[4,2], G. Mirzalieva[3,2], K. Magdieva[3,2], A. Taalaibekova[3,2], S. Buenzli[1,2], M. Furian[1,2], T. Sooronbaev[3,2], S. Ulrich[1,2], K.E. Bloch[1,2]

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Introduction: In adult highlanders, sleep apnea is more common than in lowlanders (Latshang et al. Eur Respir J 2017). We evaluated the prevalence of sleep apnea in children living at high altitude in comparison to age-matched controls living at low altitude.

Methods: Healthy children, 7-14 y of age, living at 2500-3500m in the Tien Shan mountains, Kyrgyzstan, were prospectively studied in a health post at 3250m. Healthy controls of similar age living at 700-800m were studied in a University Hospital at 760m in Bishkek. Assessments included a clinical examination, medical history, the pediatric sleep questionnaire (PSQ, range 0 to 1 with increasing symptoms) and respiratory sleep studies scored according to pediatric standard criteria.

Results: In children living at high altitude (n = 37, 17 girls, median [quartiles] age 10.8y [9.6;13.0]), sleep studies revealed: mean nocturnal pulse oximetry 90% (89;91), oxygen desaturation index (>3%) 4.6/h (2.8;7.2), apnea/hypopnea index, total 1.2/h (0.6;1.7), central 1.1/h (0.5;1.3), PSQ 0.27 (0.18;0.45). In low-altitude controls (n=41, 17 girls, age 11.6y [9.5;13.0], P between-groups comparison 0.69), sleep studies revealed: pulse oximetry 97% (96;97), oxygen desaturation index 0.8/h (0.2;1.3), apnea-hypopnea index, total 0.1 (0.0;0.4), central 0.0 (0.0;0.3), PSQ 0.18 (0.14;0.31), P<0.05 all between-group comparisons.

Conclusions: In school-aged children living at high altitude, nocturnal oxygen saturation was lower, and the total and central apnea/hypopnea index were higher compared to children living at low altitude. The greater score of sleep symptoms in children residing at high altitude suggests a potential clinical relevance of the nocturnal hypoxemia and subtle sleep-related breathing disturbances.

Conflict of interest to declare?: No

O05

Self-Monitoring to Detect Early Signs of Altitude Illness in COPD: A Diagnostic Accuracy Study

M. Furian[1,2], M. Mademilov[2,3], K. Bitos[1,2], S. Buenzli[1,2], A. Abdraeva[2,3], B. Champigneulle[4], A. Carta[1,2], M. Bauer[1,2], T. Ulrich[1,2], P.M. Scheiwiller[1,2], J. Müller[1,2], A. Sevik[1,2], S. Ulrich[1,2], L. Mayer[1,2], M. Grimm[1,2], S. Schneider[1,2], U. Sheraliev[2,3], A Alymbekova[3], N Shakiev[3], A Taalaibekova[3], A Ozonova[3], K Magdieva[3], G Mirzalieva[3], A Akylbekov[3], S. Ulrich[1,2], T. Sooronbaev[2,3], K.E. Bloch[1,2]

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Background: There are no reliable means to identify patients with COPD at risk of altitude-related adverse health effects (ARAHE) during altitude travel. Therefore, diagnostic tests that predict ARAHE in COPD would be desirable.

Methods: This prospective diagnostic accuracy study included patients with COPD (FEV_1 40-80%pred.), living <800m, SpO_2 ≥92% and $PaCO_2$ <6kPa. After baseline evaluation at 760m, patients traveled by bus to a clinic at 3100m and stayed there for 2 days. During this period, they performed structured self-monitoring (SSM) using a symptom checklist and pulse oximetry. They reported occurrence of at least moderate symptoms of acute mountain sickness (AMS) and/or SpO_2 ≤84% (=positive index test). Patients remained at 3100m to observe whether ARAHE (=positive reference test), i.e. severe AMS symptoms, SpO_2 <80% for >30min or any condition requiring medical intervention subsequently developed or not. Measures of diagnostic accuracy were computed. ClinicalTrials.gov NCT03957759.

Results: 150 COPD patients (77 women), mean±SD age 56.9±9.5yrs, participated. At 3100m, 85(57%) remained SSM negative, 60(40%) became SSM positive, 5(3%) were indeterminate; ARAHE occurred in 107 of 145 (74%). Most common ARAHE were severe hypoxemia (59%) and AMS (13%). Diagnostic accuracy of SSM quantified by C-statistic (95%CI) was 0.69 (0.62 to 0.76), sensitivity 51%, specificity 87% and positive and negative predictive value 92% and 39%, respectively.

Conclusion: In patients with moderate to severe COPD ascending to 3100m, ARAHE are common. SSM of symptoms and pulse oximetry is highly positive predictive of imminent ARAHE. Therefore, testing positive in SSM may allow COPD patients to timely descend or take preventive treatment thereby reducing the risk of ARAHE.

Conflict of interest to declare?: No

O06

The Effects of Intermittent Hypoxic Training Strategies on Maximal Oxygen Uptake: A Meta-Analysis with Meta-Regression

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Introduction: Intermittent hypoxic stimuli can be applied nocturnally, at rest during wakening hours, and during exercise. The effectiveness of these strategies on maximal oxygen uptake (VO_2max) remains debated. In addition, factors influencing this effect remain to be determined.

Methods: We performed a series of random effect meta-analysis including controlled and non-controlled studies for the three types of hypoxic exposure (i.e., nocturnal, rest, exercise). Studies investigating VO_2max before and after exposure of healthy participants to intermittent hypoxia (i.e., <24 hours/day) for more than one session were included. The weighted mean change from baseline (MC) for non-controlled studies and the mean difference (MD) for controlled studies were calculated. We also performed multiple meta-regressions on variables of interest (i.e., age, sex, FiO_2, duration of exposure, exercise intensity). For VO_2max, results are ml/min/kg.

Results: We retrieved 2166 studies, 111 were included. Nocturnal hypoxia increased VO_2max significantly (MC=1.51, 95% confidence interval [95%CI]=0.36; 2.66) within hypoxic groups but not compared to controls (MD=1.30, 95%CI=-0.21; 2.81). Meta-regression did not identify factors associated with the VO_2max change. Resting hypoxia significantly increased VO_2max within hypoxic groups (MC=1.03, 95%CI=0.31; 1.74) but not compared to controls (MD=0.94, 95%CI=-0.56; 2.44). Meta-regression identified FiO_2 and total hypoxia duration as potential effect modifiers in the hypoxic groups. In comparison with control, meta-regression identified age as a potential effect modifier. Hypoxic exercise training significantly increased VO_2max within the hypoxic groups (MC=2.65, 95%CI=2.02; 3.28) but not compared to controls (MD=0.57, 95%CI=-0.40; 1.55). Meta-regression identified age as a potential effect modifier in the hypoxic groups. In comparison to control, no significant effect modifiers were identified.

Conclusion: Intermittent hypoxia during sleep, rest and exercise does not seem to increase VO_2max more than control. The meta-regression identified higher age to enhance the effects of hypoxic exposure. In addition, longer exposure and lower FiO_2 seem to increase impacts at rest.

Conflict of interest to declare?: No

SSP Oral Communication - Infection, Lung Cancer, Intervention

O07

Smartphone-Enabled Detection of Cough in Covid-19 Pneumonia – Results of an Exploratory, Observational Cohort Study

M. Boesch[1], *F. Rassouli*[1], *F. Baty*[1], *F. Barata*[2,3], *D. Cleres*[2,3], *P. Tinschert*[2,3,4], *I. Shih*[2,3,4], *E. Fleisch*[2,3], *M.H. Brutsche*[1]

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Introduction: COVID-19-associated upper and lower respiratory tract infection is caused by SARS-CoV-2 and is characterized by dry cough, dyspnea and an exaggerated inflammatory response. This study profiled cough trajectories in hospitalized, non-critically ill patients with COVID-19 and non-COVID-19 pneumonia using mobile technology.

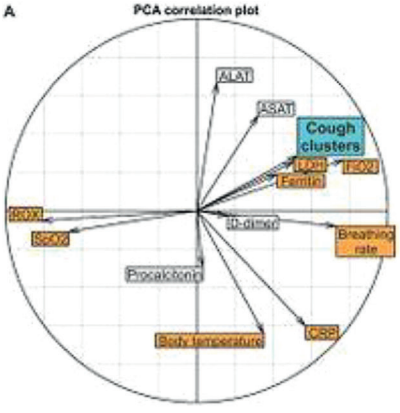
Methods: In this single-center, exploratory, observational cohort study conducted at the Cantonal Hospital St.Gallen, we employed an automated, near real-time, contact-free, smartphone-enabled cough counter based on a convolutional neural network to detect cough occurrences in 45 pneumonia patients in a non-ICU setting, 33 of which were infected with SARS-CoV-2 in the pre-Delta variant period (Apr-Nov 2020). Cough frequencies were correlated to various laboratory and clinical parameters.

Results: Cough frequencies declined steadily over time and were negatively associated with the length of hospital stay irrespective of the underlying type of pneumonia. Exploratory analyses showed distinct patterns of cough evolution in patient subgroups stratified for age and sex. Emanating from a higher initial cough count, COVID-19 patients showed a trend towards a steeper decline in cough frequencies compared to non-COVID-19 patients. In COVID-19, linear mixed models showed that cough levels were significantly associated with markers of inflammation (ferritin, CRP, body temperature), the degree of oxygenation/the requirement for oxygen supplementation (SpO2, FiO2, ROX score, breathing rate), and LDH indicating cell damage; in contrast, no association with a marker of hemostasis (D-dimer) was found (**Figure 1**).

Conclusion: Mobile technology might leverage cough counting in hospitalized patients with a lower respiratory tract infection and suggests cough frequency as a surrogate marker for disease activity and response to treatment in COVID-19 and other types of pneumonia. Planned future investigations target the suitability of this novel potential digital biomarker for predicting clinical improvement vs. deterioration in pneumonia patients to personalize treatment interventions by digitally-informed decisions.

Conflict of interest to declare?: Yes

If you have a conflict, please specify: Dr. Peter Tinschert and Dr. Iris Shih are co-founders of Resmonics AG.



B

Linear mixed model for cough count associations in COVID-19

Correlation parameter	p-value
SpO2	**0.015**
FiO2	**<0.001**
Breathing rate	**<0.001**
ROX index	**0.002**
LDH	**<0.001**
CRP	**0.001**
Ferritin	**<0.001**
Body temperature	**0.009**

Correlation parameter	p-value
ALAT	>0.05
ASAT	>0.05
D-dimer	>0.05
Procalcitonin	>0.05

Fig. 1.

O08

Antibiotic Killing Predicts Clinical Outcomes Independent of Drug Resistance

F.K. Bright[1], A. Jovanovic[1], B. Wicki[1], L. Sauteur[1], A. Wuest[1], D.M Grogono[2], F. Geier[1], M. Tamm[3], P. Dehio[1], J. Nemeth[4], M. Abanto[1], R. Thomson[5], S. Bell[6], A.R Floto[2,7], L. Boeck[1,3]

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Introduction: Antimicrobial susceptibility testing (AST) is critical for guiding treatment in infectious diseases. However, in chronic pulmonary infections, AST often correlates poorly with treatment success. AST evaluates growth across different antibiotic concentrations, but not bacterial killing, which may be required to efficiently clear long-lasting infections. By overcoming the poor scalability and reproducibility of killing assessments, we establish the clinical relevance of sterilising antimicrobial treatment in *Mycobacterium abscessus*, a particularly difficult-to-treat pathogen causing increasing rates of chronic pulmonary infections globally.

Method: We assessed drug susceptibility (MICs) and bacterial killing in regard to clinical outcomes in an international cohort of 142 cystic fibrosis patients with *M. abscessus* lung disease. To evaluate bacterial killing, we developed a live-cell imaging platform that allowed testing thousands of conditions.

Results: Using our imaging approach, we analysed bacterial killing in 142 *M. abscessus* isolates using 11 drugs. We observed various time-kill profiles across and within drugs tested, indicating that bacterial killing is a drug property and a fundamental bacterial phenotype. Cefoxitin and imipenem kill-kinetics were predictive for clearing infections independent of MICs. Poor killing with cefoxitin was also associated with a faster lung function decline. In contrast, MICs were not predictive for lung function, and only azithromycin MICs were related to bacterial clearance. Finally, we demonstrate that time-kill kinetics of drugs with a similar mode of action correlate, emphasising a common underlying killing mechanism unrelated to specific drug targets.

Conclusion: We present a novel method for assessing bacterial killing, demonstrate highly diverse killing kinetics in *M. abscessus* and validate its importance via predicting clinical outcomes; thereby challenging current drug susceptibility measures and the concept of bacteriostatic vs bactericidal drugs. Our findings highlight the relevance of mechanisms underlying antimicrobial killing, potentially improve clinical guidance, and enforce sterilising drug development.

Conflict of interest to declare?: No

O09

Effects of Transient Heat Stress during Ex-Vivo Lung Perfusion EVLP on Damaged Donor Lungs in Small and Large Animal Models

A. Ojanguren[1], A. Hasenauer[1], A. Debonneville[1], R. Parapanov[1], J. Lugrin[1], M. Gonzalez[1], J.Y. Perentes[1], L. Liaudet[2], T. Krueger[1]

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Introduction: Ex-vivo lung perfusion (EVLP) is a technique allowing evaluation of potential donor lungs before transplantation. The heat shock response (HSR) is a highly conserved adaptive response to stress, related to the induction of heat shock proteins (HSPs) which promote significant cytoprotection. We hypothesized that a moderate heat stress applied during EVLP elicits a HSR and improves lung graft function by interfering with immune inflammation and oxidative stress pathways.

Methods: Rats were assigned either to Control group (Ctrl, n=5) or to 4 Heat Stress groups (HS, n=5, each group). After 1h of *in situ* warm ischemia, Perfadex flushing, and hypothermic preservation (1h), lungs were mounted on normothermic EVLP (37°C, 3h, Ctrl) or HS EVLP with (41.5°; 42.0°; 42.5° and 43.5°C for 30 min), then normotermic EVLP (37°C).

Donor pigs lungs (n=12) were submitted to organ procurement and subjected to extended hypothermic preservation (16h). Lungs were randomly assigned into two groups: Control, n=6: 4h EVLP at 37°C; and (HS), n=6: normothermic EVLP (37°C, 2h), then HS EVLP (42°, 30min), then normothermic EVLP (37°C, 1.5h). Lung mechanics were measured during EVLP. In both experiments, Steen solution, Bronchoalveolar lavage (BAL) fluid, and lung tissue were kept at -80°C for further analysis.

Results: Functional analysis showed that moderate HS (41.5°-42°C) improved lung functions during EVLP in rat and pig experiments. HS groups (rat and pig) had significant increase of HSPs mRNA and protein (Hspa1a, Hsc70 and Hmox-1); decreased expression of IL-1α, IL-1β and TNFa in rat model as well, IL6/IL10 ratio in pig model; reduction of nitrotyrosative stress (3-NT), and lung edema (proteins in BAL).

Conclusion: Moderate heat stress during EVLP induced HSR, reduced nitroxidative stress, decreased lung edema, and inhibited inflammatory response. EVLP HS preconditioning could be a way to recondition damaged donor lungs.

Conflict of interest to declare?: No

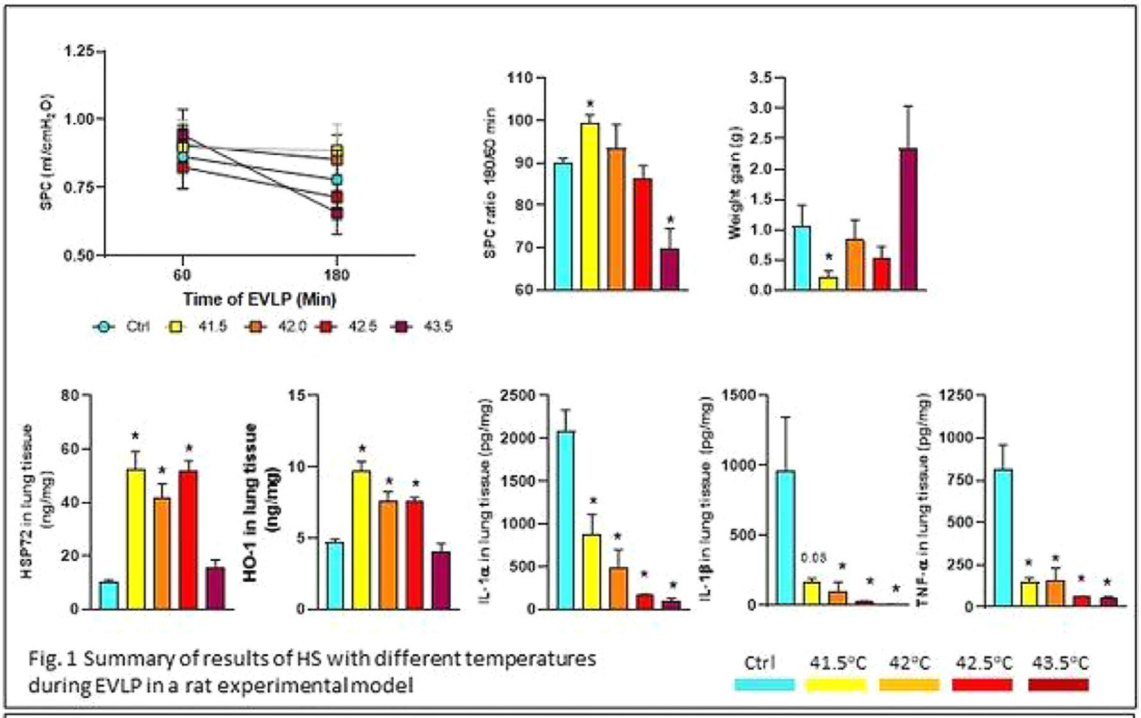

Fig. 1 Summary of results of HS with different temperatures during EVLP in a rat experimental model

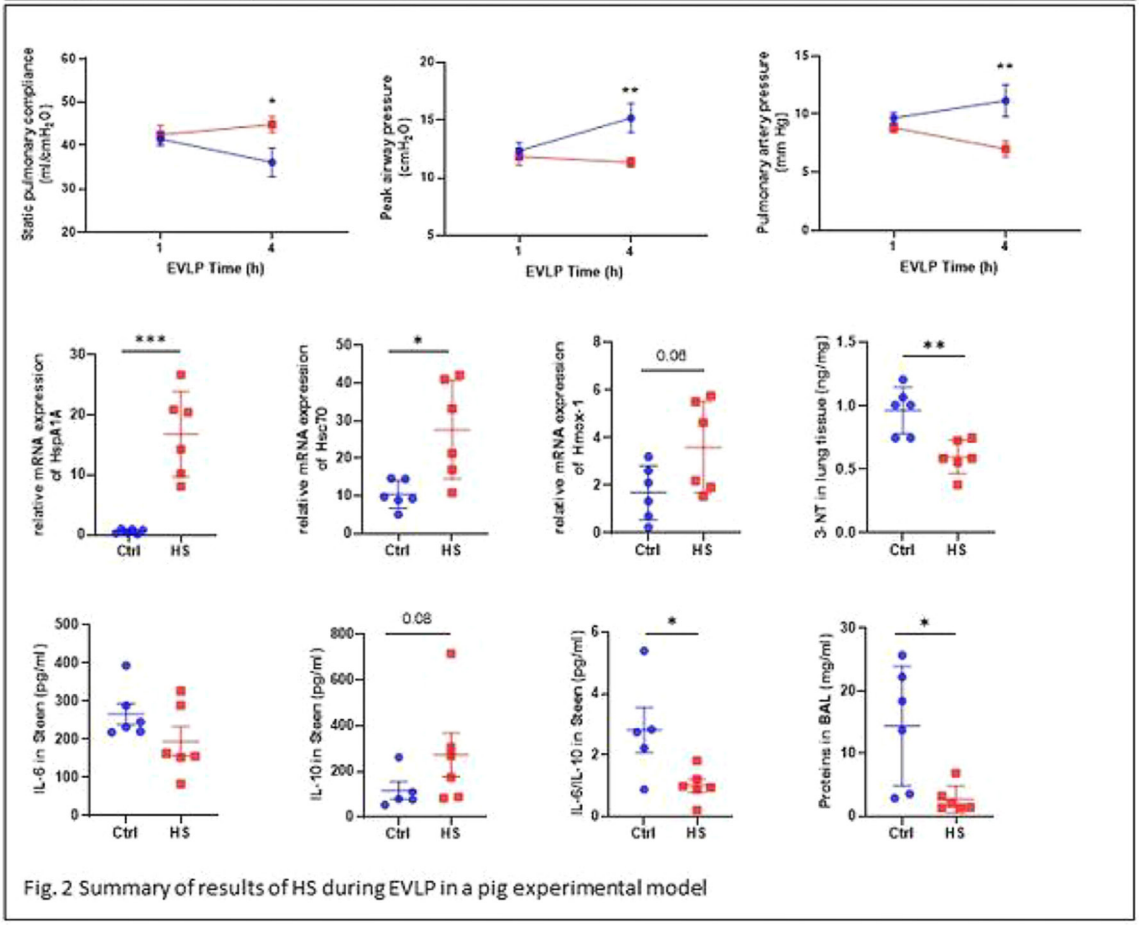

Fig. 2 Summary of results of HS during EVLP in a pig experimental model

Fig. 1.

O10

Smoking Prevention Intervention with School Classes in University Hospital by Thoracic Surgeon und Pulmonologist. The Zurich Prevention Project

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Introduction: Smoking prevention in schoolchildren to inform and prevent smoking initiation has been widely studied, however the potential effect of interventions provided in a hospital scenario is unknown. An intervention program named "Schoolchildren smoking prevention in the hospital" was developed in which the health aspects of smoking and its individual consequences were presented in an interactive informational event provided by a thoracic surgeon and a pulmonologist. We aimed to assess the feasibility and the short-term effect of smoking-related knowledge improvement in schoolchildren in a hospital setting.

Methods: 45 school-classes in Canton of Zurich in Switzerland were provided with an anonymous survey using a 5-item questionnaire with questions on general knowledge about smoking and included in this prospective observational cohort study. The primary endpoint was to compare the knowledge improvement by interpretation of answers before-and-after the smoking prevention intervention. Additionally, the performance of children was compared after setting up an overall score and specific subgroups according to gender and school-level.

Results: Between Jan 2010, and Oct 2019, 1267 schoolchildren aged 10 to 16 years; participated in this intervention program and completed of the questionnaire before and after intervention. The amount of correctly answered questions increased from 40%(±20) before to 81%(±17), p< 0·0001 after the educational session.

Conclusion: An intervention program on health effects of smoking provided by lung specialists in the hospital is feasible, well received, leads to a substantial increase of knowledge and hopefully can be further explored in the development of smoking prevention programs for schoolchildren.

Conflict of interest to declare?: No

O11

Swiss Pilot Low-Dose Computed Tomography Lung Cancer Screening Study

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Introduction: Low-dose computed tomography (LDCT) lung cancer screening is endorsed by US guidelines and has recently been shown effective in a large European randomized controlled trial. Nevertheless, actual realization of a lung cancer screening program is challenging and depends on country-specific factors. This pilot study aimed to evaluate implementation, execution, and performance of LDCT lung cancer screening in Switzerland.

Methods: Since October 2018, asymptomatic participants aged 55-74 years with more than 30 pack-years smoking history were enrolled at a tertiary hospital in Switzerland. Participants with history of lung cancer, major (palliative) health problems or those that had a thorax CT scan 18 months prior to enrollment were excluded. First, we evaluated lung cancer risk according to NLST guidelines. Second, we estimated lung cancer risk using the PLCOm2012 model risk calculator with threshold of 5%. Lung nodules were assessed according to Lung-RADS (Version 1.1. 2019). Participants were recruited through flyers, a newspaper article and pulmonary specialists. Screening consisted of one LDCT-scan, follow-up was recommended for suspicious nodules only. LDCT assessment was performed by two radiologists, one of them a board certified chest radiologist. Enrollment and follow-up are currently ongoing.

Results: To date, 75 participants (25 (33%) females) with a median age of 62 years (interquartile range [IQR] 56-67 years) were included. Median number of pack years smoked was 49 (IQR 41-58 pack years). Median PLCOm2012 6-year lung cancer probability was 2.7% (IQR 2.6-2.9%), 19 (26%) participants had stopped smoking before enrollment. 6 participants required follow up imaging of suspect nodules, resulting in a recall rate of 8%. At baseline, lung cancer was found in 2 (2.7%, one squamous cell (stage IIIA) and one adenocarcinoma (stage IV)) participants.

Conclusion: In this Swiss LDCT lung cancer screening pilot study using modified inclusion criteria, 2.7 % were diagnosed with lung cancer to date.

Conflict of interest to declare?: No

SSPP Free Communications

O12

Sinonasal Features in Patients with Primary Ciliary Dyskinesia - An EPIC-PCD Study

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Introduction: Most patients with primary ciliary dyskinesia (PCD) have sinonasal symptoms, but yet little is known on their frequency and severity. We aimed to describe sinonasal features in PCD patients using data from the Ear-nose-throat (ENT) Prospective International Cohort of PCD patients (EPIC-PCD), a multicentre observational clinical cohort.

Method: We included patients who had a routine ENT clinical examination and completed the FOLLOW-PCD standardised symptoms questionnaire at the same visit. We compared reported symptoms and clinical findings in children and adults.

Results: We included 208 patients (108 males) with median age 16 years (range 0-63). 178 (86%) patients reported chronic nasal symptoms that in 73 (35%) persisted. Specifically, 116 (56%) reported blocked nose, and 129 (62%) rhinorrhoea. 18 of 72 adults reported anosmia compared to only 3 of 136 children. 133 (64%) patients reported headaches, which in 26 appeared when bending down. Clinical examination showed blocked nose in 88 (42%) patients. Nasal mucosa was evaluated in 190 patients and showed erythema in 64 and oedema in 61. 32 of 182 patients had nasal polyps (19 adults and 13 children) and 66 of 174 had hypertrophic turbinates. The Sinonasal Outcome Test-22 was available for 57 patients with a moderate median score of 39 (range 4-86), that did not differ by age.

Conclusion: The EPIC-PCD is the largest prospective cohort describing sinonasal features in PCD patients. Sinonasal symptoms are common in PCD patients, which underlines the need of ENT input in the multidisciplinary care. Sinonasal disease worsens with age as more adults present with nasal polyps and have impaired sense of smell.

Funding: SNF PZ00P3_185923

Conflict of interest to declare?: No

O13

Do Face Masks Cause Abnormal Gas Exchange during Exercise Testing in Children?

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Introduction: Parents fear that face masks may impair gas exchange in children with respiratory problems during physical activity but data are lacking. We therefore studied if wearing a surgical face mask during physical exercise leads to abnormal gas exchange in children with exercise-induced symptoms (EIS).

Methods: This cross-sectional study was nested in the Swiss Paediatric Airway Cohort (SPAC), a clinical cohort study of children referred to respiratory outpatient clinics. We recruited children with EIS performing an exercise-induced asthma (EIA) test on a treadmill at the Lucerne Children's Hospital. The EIA test was performed according to the American Thoracic Society guidelines. FEV1 was measured before and at 2, 5, 10 and 15 minutes after exercise. Oxygen saturation (SpO2) was measured before and after exercise with an oximeter. Capillary blood gases were analysed immediately after exercise to assess gas exchange. We assessed differences between medians with the Wilcoxon signed rank test.

Results: We included 25 children (age 9-16 years, 76% girls). FEV1 was significantly reduced after exercise (2.83 L vs. 2.27 L, $p<0.001$). There were no episodes of oxygen desaturation after exercise. The lowest SpO2 value was 93%. We found no difference in SpO2 before and after exercise ($p=0.096$). Capillary blood gas analysis did not show CO2 retention in any of the children. The highest pCO2 value (5.67 kPa) was well below the upper limit of normal (6.0 kPa).

Conclusion: There was no evidence of abnormal gas exchange in children with EIS wearing a surgical face mask during an EIA test. These findings may help promote the use of surgical masks among children during the COVID-19 pandemic.

Conflict of interest to declare?: No

O14

Research Priorities for Primary Ciliary Dyskinesia - Experts´ Perspective

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Introduction: Despite advances in primary ciliary dyskinesia (PCD) research, many open questions remain. Due to limited resources to address them, we aimed to identify the current knowledge gaps and priorities for clinical and epidemiological PCD research using mixed-methods approaches.

Method: We performed in-depth semi-structured interviews with specialists involved in PCD research and clinical care, selected using purposive sampling in order to have rich, relevant and diverse data. We transcribed, coded, and analysed the interview data using thematic analysis.

Results: We interviewed 28 participants from 15 countries including paediatric and adult pulmonologists, Ear-Nose-Throat (ENT) specialists, nurses, physiotherapists, epidemiologists, and diagnostic scientists. We included interviewees from settings with different research resources and varying research experience. Main themes identified as important focus areas for PCD research were evaluation of treatments, endpoints for clinical trials, quality of life, ENT and fertility problems, research in adults and minority groups, infections and antimicrobial agents, early diagnosis, and phenotypic variability. Other themes covered were availability of resources and difficulties in performing PCD research, and the importance of research collaborations and patients' involvement in research.

Conclusion: The use of qualitative approaches improves in-depth understanding of participants' perspective. These results will be used to develop an online survey which will be circulated among specialists from the BEAT-PCD clinical research collaboration network. FIndings from this study can help prioritize research needs and suggest studies to address them.

Funding: European Respiratory Society

Conflict of interest to declare?: No

SSSSC Poster Walks

P01

Comparison of AI-Driven Scoring with Manual Scoring of Lab-Based Polysomnography Data

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Introduction: Polysomnography (PSG) with manual sleep scoring is the gold standard in diagnosing sleep pathologies. Since manual scoring is time consuming and prone to inter-/intra-patient variability, alternative AI-driven automatic procedures were developed. The aim of this study was to compare AI-driven sleep scoring using two different approaches with manual scoring.

Methods: 24 consecutive PSGs were scored manually by one experienced sleep technician and were compared with two different AI-driven scoring systems - Michele Sleep Scoring software (MSS, Cerebra Medical Ltd. in Winnipeg, MB, Canada) and ASEEGA® software (Physip© SA in Paris) / Embla® Remlogic™ software (Version 4.0.1). The automatic scoring of the EEG was performed with ASEEGA, that of respiratory events with Remlogic. The scoring criteria of AASM guidelines 2014 were applied. The analysis of differences between AI-driven scoring and manual scoring was performed using Bland-Altman methodology.

Results: PSGs of 24 patients (15 men) with a mean age of 55 ±14years, a mean body mass index (BMI) of 32.7 ±7.2 kg/m2 and mean Epworth Sleepiness Scale 8.4 ±4 were assessed. Overall, there was a good consistency between AI-driven and manually scored records. However, compared to the reference, MSS overestimated sleep stages 1&2 and unterestimated sleep stage 3, while all NREM

sleep stages were scored more accurately with ASEEGA/Remlogic (see Table 1 and Figure 1). REM sleep using MSS was in good agreement with manual scoring, while ASSEGA/Remlogic tended to overestimate REM Sleep. AHI was underestimated in both AI-driven methods, while ODI was scored more accurately in MSS, compared to manual scoring.

Conclusion: In our study comparing AI-driven sleep scoring with manual scoring, sleep stages were scored more accurately using ASEEGA/Remlogic, while AHI was underestimated in both AI-driven scoring methods. In summary, taking into account certain limits AI-driven scoring of PSGs is a useful tool in diagnosing sleep disturbances.

Conflict of interest to declare?: No

Table 1.

	MSS vs. manual		ASEEGA/Remlogic vs. manual	
	Bias (CI)	LLA to ULA (range)	Bias (CI)	LLA to ULA (range)
Sleep latency	7.3 (-0.1 to 14.7)	-27.2 to 41.8 (69.0)	**11.6 (3.4 to 20.0) ***	-26.7 to 49.9 (76.6)
Sleep efficiency	**-10.8 (-16.5 to -5.1) ***	-37.2 to 15.6 (42.8)	-3.5 (-8.8 to 1.7)	-28.1 to 21.0 (49.1)
Sleep stage N1+N2	**11.7 (5.4 to 18.0) ***	-17.4 to 40.8 (58.2)	-4.5 (-9.5 to 0.4)	-27.7 to 18.6 (46.3)
Sleep stage N3	**-13.0 (-18.2 to -8.0) ***	-36.3 to 10.2 (46.5)	0.6 (-2.9 to 4.1)	-15.5 to 16.8 (32.3)
Sleep Stage REM	-0.6 (-3.1 to 2.0)	-12.5 to 11.3 (23.8)	**4.1 (0.9 to 7.3) ***	-10.9 to 19.1 (30.0)
Arousal Index	4.8 (-3.3 to 12.8)	-32.5 to 42.0 (74.5)	1.8 (-5.7 to 9.3)	- 32.9 to 36.5 (69.4)
AHI	**-10.1 (-14.6 to -5.6) ***	-30.8 to 10.7 (41.5)	**-4.2 (-7.4 to -0.9) ***	-19.2 to 10.8 (30.0)
ODI	-0.2 (-3.1 to 3.1)	- 15.7 to 15.2 (30.7)	**-3.2 (-5.6 to -0.8) ***	-14.3 to 8.0 (22.3)

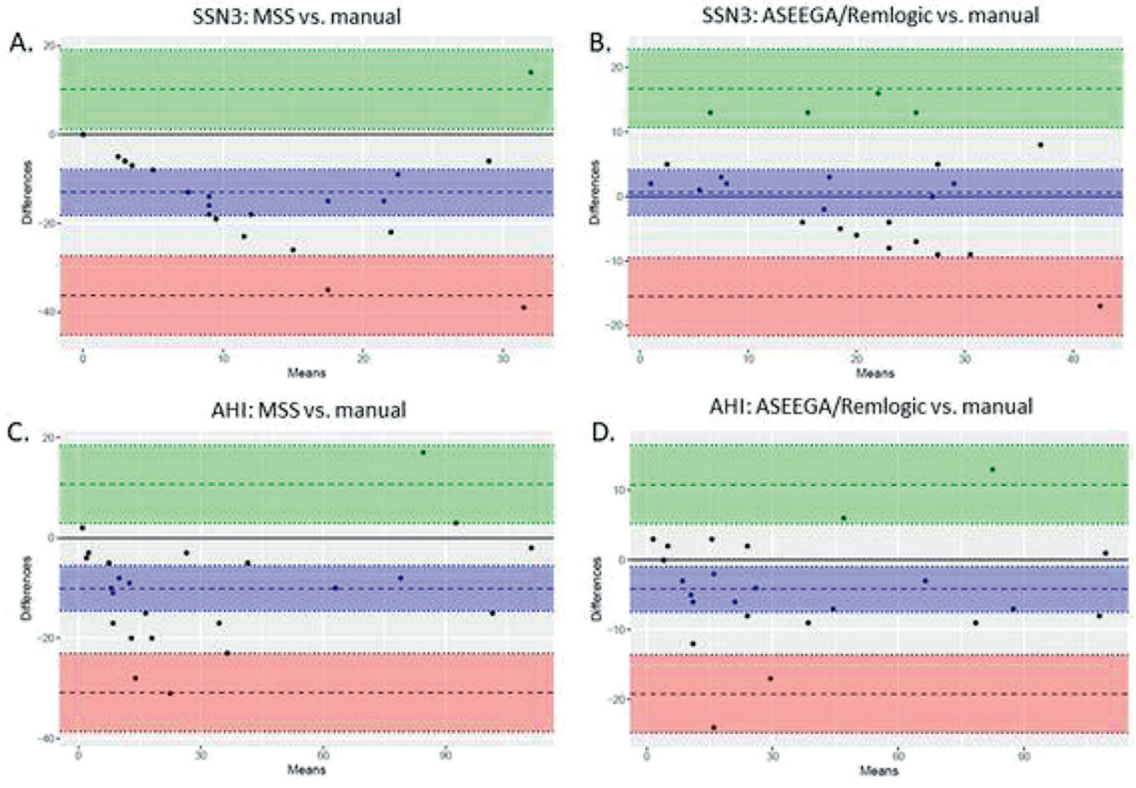

Fig. 1.

P02

Robotic Beds for the Treatment of Positional Obstructive Sleep Apnoea - A Randomised Cross-Over Pilot Trial

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Introduction: Positional interventions may affect patency of the upper airway during sleep. Such interventions might be beneficial for patients with positional sleep apnoea (POSA). The aim was to assess the effect of two actuated beds (trunk-elevation and sideward-turning) on OSA severity and sleep fragmentation.

Method: Adults with POSA and an apnoea-hypopnoea-index (AHI) ≥10/h were eligible. Following a baseline polysomnography, patients were allocated to intervention nights in the intelligent sleep apnoea bed (ISABel) 1 and ISABel2 in random order. In case of an apnoea or hypopnoea, ISABel1 elevated the upper body by 50° and ISABel2 induced a one-side bed-inclination of 30°, both interventions lasting for 10 minutes. Sustained trunk elevations (ISABel1) and position change from supine to non-supine (ISABel2) were defined as successful interventions.

Results: Six adult men (57±11y, BMI 28±4 kg/m2, AHI 39±15/h) with POSA were included. Neither trunk elevation (ISABel1) nor side-inclination (ISABel2) – about 10 interventions per night – resulted in a significant reduction in supine or overall AHI. Respiratory-related arousals increased in ISABel2 compared to baseline while non-respiratory arousals did not significantly change and were comparable between the beds (1/3 of movements induced arousals). Sleep efficiency was not affected by the actuated beds. However, only 13% of side inclinations in ISABel2 resulted in successful change into a non-supine position. The time to the next respiratory event following bed movements was longer in ISABel1 than in ISABel2, and when ISABel2 that resulted in a position change to non-supine position. See table 1.

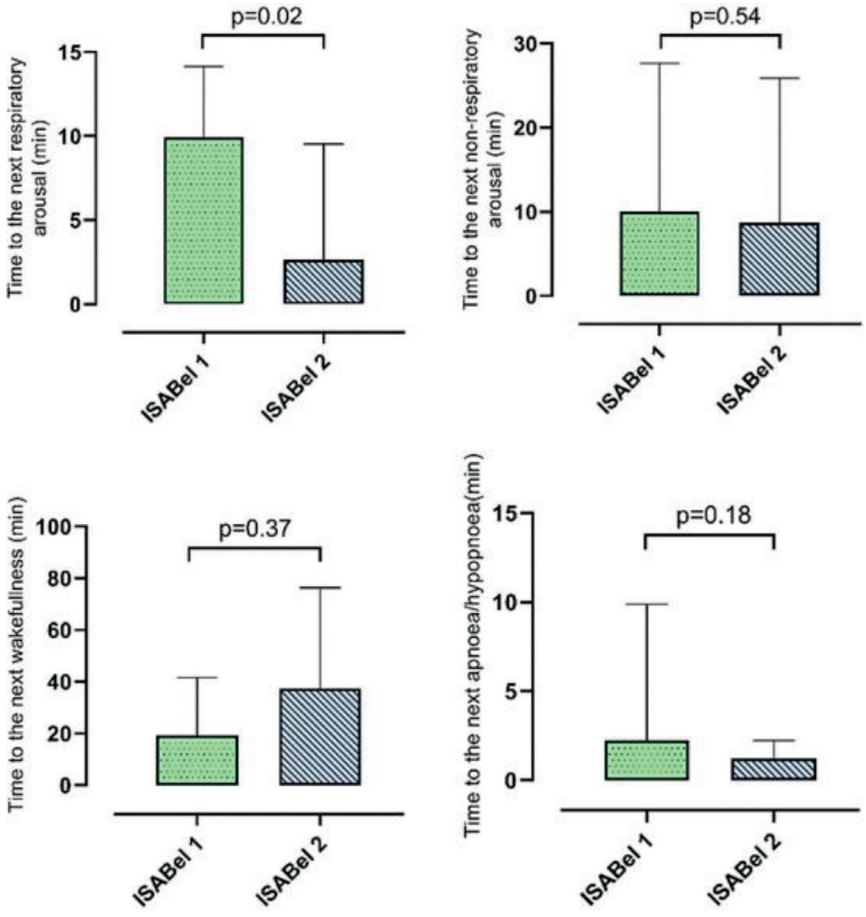

Fig. 1.

Table 1.

	Baseline	ISABel 1	ISABel 2	p ISABel 1 – ISABel 2	p Baseline – ISABel 1	p Baseline- ISABel 2	Overall p
AHI (/h)	38.60 (14.80)	29.60 (8.35)	58.55 (21.88)	**0.03**	0.56	**0.03**	**<0.01**
AHI supine (/h)	72.10 (18.28)	57.75 (10.85)	72.70 (18.88)	**0.03**	0.06	0.31	**0.02**
ODI (/h)	27.90 (14.50)	21.90 (9.78)	45.20 (21.68)	**0.03**	0.06	0.06	**0.04**
ODI supine (/h)	59.60 (27.63)	43.30 (32.48)	67.75 (12.85)	**0.03**	0.16	0.16	**0.01**
Sleep efficacy	85.45 (3.73)	80.20 (12.63)	85.10 (2.50)	0.09	0.56	0.79	0.31
Respiratory AI (/H)	6.35 (5.83)	9.75 (8.18)	19.40 (7.10)	0.06	0.69	**0.03**	**0.02**
Non-respiratory AI (/h)	8.10 (7.95)	7.05 (4.08)	7.10 (6.85)	0.84	0.84	0.56	0.61
Bed AI (/h)	-	1.40 (1.75)	1.45 (0.40)	0.84	-	-	-

Table 1. Values of POSA severity measures and arousals. Data are reported as median ± interquartile range.

Conclusion: Tilting beds might reduce supine AHI (trunk elevation) and prolong the time to the next apnoea or hypopnoea (trunk elevation and side inclination). However, side inclination might not necessarily change supine position and some bed movements might induce arousals. Improvements on the beds to reduce movement-induced arousals and increase successful interventions are needed.

Conflict of interest to declare?: No

SSP/SSTS Poster Walk: Infections, Interstitial and Obstructive Lung Diseases

P03

Health-Related Quality of Life in Covid-19 Long-Haaulers

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Background: Out of the SARS-CoV-2 pandemic, a growing number of infected people experience long-lasting symptoms. Even patients, who suffered from a mild acute infection, show a variety of persisting and debilitating neurocognitive, respiratory and/or cardiac symptoms, consequently leading to severe limitations in everyday living. This study aims to characterize the impact of Post-Covid symptoms regarding health-related quality of life (HRQOL).

Method: In this observational study, outpatients seeking counseling in the interdisciplinary Post-Covid consultation of the University Hospital of Zurich with symptoms persisting for more than 4 weeks were included. Patients who received an alternative diagnosis or suffered from a severe acute Covid-19 infection were excluded. Patient characteristics were extracted out of medical reports. To assess HRQOL, a total of three questionnaires were distributed: St. George's Respiratory Questionnaire (SGRQ), Euroquol-5D-5L (EQ-5D-5L) and the Short form 36 (SF-36).

Results: 112 participants were included, 86 (76.8%) were female, median (IQR) age was 43 (32, 52.5) years with 126 (91, 180) days under symptoms. Most frequently, patients suffered from fatigue (81%), concentration difficulties (60%), and dyspnea (60%). The median (IQR) SGRQ total score was 39.58 (26.65, 54.26). Predictors for low SGRQ activity scores were female sex (p= 0.005), for SGRQ symptom score living alone (p = 0.031) and having more than 6 symptoms (p = 0.001). Patients stated mostly having trouble to perform usual activities, having pain/discomfort or anxiety out of the EQ-5D-5L (figure 1). EQ index value was significantly lower in females, participants with a reduced employment status and experiencing more than 6 symptoms. Regarding health domains in the SF-36, Post-Covid patients showed remarkably lower scores in all domains compared to the Swiss population in 2015/2016 (table 1).

Conclusion: Post-Covid symptoms significantly affect health-related quality of life. This demonstrates that developing therapeutic strategies and long-term management of patients is of paramount importance.

Conflict of interest to declare?: No

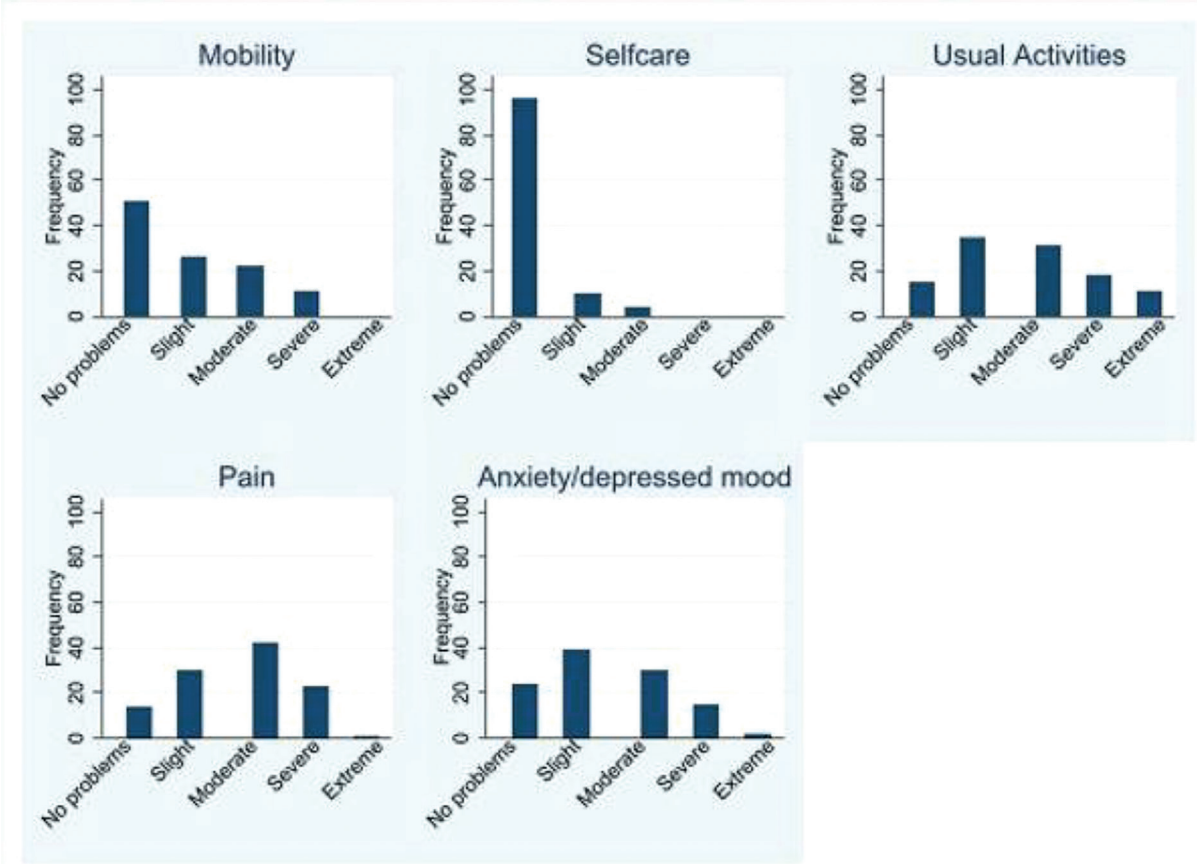

Fig. 1.

Table 1.

Health domain	Long-Covid cohort (n=112), mean (SD)	Prepandemic Swiss population 2015–2016 (n=1209), mean (SD)(1)
Physical functioning	64.50 (24.97)	91.16 (17.01)
Role limitations (physical)	28.60 (37.43)	86.41 (20.60)
Bodily pain	62.08 (28.95)	74.58 (26.03)
General health	50.86 (18.76)	75.64 (17.35)
Vitality/Energy	29.77 (19.47)	63.24 (17.22)
Social role functioning	56.36 (30.20)	85.84 (20.02)
Emotional role functioning	51.35 (43.76)	87.64 (19.22)
Emotional well-being	60.04 (18.98)	75.02 (16.18)
Physical health	47.07 (19.33)	NA
Mental health	49.68 (19.49)	NA
Total SF-36 score	50.22 (19.29)	NA

P04

Personal Experience of the First COVID-19 Wave and the Lockdown and Its Impact on Respiratory Health of Cystic Fibrosis Patients

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Introduction: During the first COVID-19 wave in Switzerland, the authorities ordered a 3-month lockdown during which elective medical procedures were postponed and protective measures were proposed to protect vulnerable persons. They were encouraged to stay at home and employers were required to adapt to the new requirements. The aim of our study was to determine the impact of this period on respiratory health of cystic fibrosis patients (pwCF), and their personal experience, whether psychological or in terms of interactions with their family, or their professional or health care environment.

Methods: Non-lung transplanted pwCF from 7 Swiss centers were included. Subjects with previous or active COVID-19 infection were excluded. Co-primary outcomes included 1/ a comparison of FEV1 before and after lockdown and 2/ results of a 44-item self-administered questionnaire developed to assess the impact of the first COVID-19 wave and the lockdown on pwCF. Secondary outcomes were other functional and weight comparisons and follow-up of COVID-19 serological status.

Results: Among 127 screened pwCF, 99 (78%) were included (n=69 adults and n=30 children). One patient was excluded due to COVID-19 infection. Baseline characteristics are reported in table 1a. There was no significant difference between FEV1 before and after lockdown. Table 1b reports quantitative items showing the impact of this period on the private sphere, medical care and health status. Results of Lickert scales are heterogeneous (table 2). In particular, fear of contracting COVID-19 was more pronounced among adults. Patients felt strongly supported by their close relatives and health care teams. The professional world showed understanding with patients even if it was sometimes difficult to assume the position of "vulnerable person".

Conclusion: Despite delayed medical elective management, this period did not have a significant impact on pwCF' respiratory health. Personal experience showed an important variability, with an overall high resilience.

Conflict of interest to declare?: No

Table 1.

Table 1a Baseline characteristics	Age <16 N=30	Age >=16 N=69	Missing values Age < 16/ age > 16
Male gender (n,%)	17 (56.7)	35 (50.7)	-
Age, years (Mean, SD)	7.1(4.6)	31.8 (13.5)	-
FEV1 L (Mean, SD)	1.72 (0.63)	2.41 (0.96)	12/2
FEV1 %	93.6 (16.7)	66.8 (20.9)	12/2
FVC L	2.11 (0.73)	3.52 (1.12)	12/2
FVC %	98.7 (13.8)	82.3 (17.4)	12/2
Weight, kg	27.3 (14.3)	60.8 (9.3)	7/2
Exacerbation rate per year, (Mean, SD)	1.6 (1.4)	2.5 (2.0)	1/3
Occupation			-
• School, training, n (%)	21 (70%)	21 (30.4%)	-
• Looking for a job	-	8 (11.6%)	-
• Actively employed	-	29 (42.0%)	-
• Housewife/homemaker	-	4 (0.6%)	-
• Absence from school or work for health reasons	-	7 (10.1%)	-
• Not working for other reasons	9 (30%)	5 (7.2%)	-
CFTR modulator, n (%)	1 (3.3)	16 (23.9%)	-

Table 1b Quantitative results from questionnaire			
Working/studying from home during lockdown (N,%)	16 (59.3%)	28 (43.8%)	3/5
Need to announce CF diagnosis to employer or school due to COVID 19 (N,%)	4 (14.8%)	21 (33.3%)	3/6
Any postponed face-to-face medical contact (N,%)	9 (33.3%)	43 (70.5%)	5/8
Consultation postponed (N,%)	9 (33.3%)	43 (65.2%)	3/3
Annual review postponed (N,%)	2 (7.1%)	15 (22.7)	2/3
Lung transplant assessment postponed (N,%)	0 (0%)	2 (3.3%)	4/10
PEX* (N/%)	14 (46.7%)	24 (34.8%)	0/0
AB for PEX during lockdown (N,%)	7 (24.1%)	16 (24.2%)	0/3
Hospitalization for PEX during lockdown (N/%)	1 (3.4%)	3 (4.5%)	1/3
COVID PCR performed during lockdown (N/%)	6 (22.2%)	13 (19.6%)	3/3
COVID PCR positive (N/%)	0	0	-
Positive COVID IgG after lockdown (N,%)	0	1 (2.3%)	23/25

*PEX= Acute pulmonary exacerbation

Table 2.

Question	Adult with CF n=67 (%)			Children with CF n=12 (%)			All CF patients n=84 (%)			Missing data (%)
	More	No change	Less	More	No change	Less	More	No change	Less	
Have you changed the number of physiotherapy sessions with a professional?	1.39	89.21	89.21	3.45	48.28	48.28	2.17	88.91	88.91	7.07
Have you changed your respiratory drainage practices at home (without professional support)?	28.62	67.69	7.69	20.69	75.86	3.45	23.4	70.21	6.38	5.03
Have you changed the time spent participating in a physical activity (walking, running, cycling, fitness, etc.)?	41.54	18.46	40	34.48	48.28	17.24	39.36	27.66	32.98	5.03
	YES	Neither Y or N	NO	YES	Neither Y or N	NO	YES	Neither Y or N	NO	
I was very scared of catching COVID 19 during this time	16.46	16.46	23.08	31.03	13.79	55.17	50	17.02	32.98	5.03
I was afraid of dying from COVID 19 during this time	13.85	13.38	30.77	6.9	17.24	75.86	25.53	15.96	58.51	5.03
I was afraid of having serious consequences if I caught COVID 19	53.95	20	26.15	27.59	6.9	65.52	45.74	15.96	38.3	5.03
I was worried that I would have to go to the hospital during this time because of the risk of catching COVID 19	69.23	10.77	20	48.28	13.79	37.93	62.77	11.7	25.53	5.03
I completely cut off my social contacts (friends, family not living with me) during this time to avoid catching COVID 19	71.88	9.38	18.75	72.41	6.9	20.69	72.04	8.6	19.35	6.06
It was difficult to come to an agreement with the people living in my house on what protective measures to take	20.31	14.06	65.63	6.9	3.45	89.66	16.13	10.75	73.12	6.06
If I had fallen ill with COVID 19, I would have been afraid of infecting my loved ones, especially those who help me on a daily basis with my respiratory disease	72.31	15.92	10.77	68.97	18.32	14.81	70.63	17.39	11.96	7.07
I felt very isolated during this time	16.92	13.85	29.23	31.71	17.86	46.43	20.54	15.05	34.41	6.06
I had more conversations than usual with other CF patients on social media	10.94	17.19	71.88	3.7	25.93	70.37	8.79	19.78	71.43	4.08
I felt supported by my friends and relatives during this time	78.46	20	1.54	75.86	17.24	6.9	77.66	19.15	3.19	5.03
I feel that I have been less protected by my relatives (friends, family, colleagues)	32.31	27.69	40	34.48	13.79	51.72	32.98	23.4	43.62	5.03
I found the official COVID 19 information regarding my medical condition to be clear enough	49.23	12.31	38.46	35.71	17.86	46.43	45.16	13.98	40.86	6.06
I felt more excluded from society than usual due to my respiratory illness	34.09	18.06	31.25	28.57	21.43	50	46.74	16.3	36.96	7.07
I had difficulty facing the eyes of others due to my usual CF related cough	65.63	13.63	18.75	21.43	35.71	67.86	32.17	14.13	53.7	7.07
If I had fallen ill and had been suspected of COVID 19, I would not have wanted to go to the hospital so as not to overload the medical system and caregivers	14.06	15.63	70.31	7.69	23.08	69.23	12.22	17.78	70	7.07
I felt like I was left out of the health care system	9.23	12.31	78.46	0	22.22	77.78	6.52	15.22	78.26	9.09
I was afraid that I would not be entitled to necessary treatment in the hospital because of my respiratory disease	14.06	9.38	76.56	0	3.27	96.43	9.78	7.61	82.61	7.07
I felt supported by the caregivers who usually take care of me	72.02	25.4	1.59	72.41	24.14	3.45	72.83	25	2.17	7.07
During the period of lockdown, I felt sadder than usual	46.15	15.38	38.46	34.24	17.24	58.62	39.36	15.96	44.68	7.07
During the period of lockdown, I felt more anxious than usual	16.92	3.08	40	34.48	6.9	58.62	30	4.26	65.74	5.03
During the lockdown period, I got poorer quality sleep than usual	25.15	23.08	50.77	3.45	17.24	79.31	19.15	21.28	59.57	5.03
During the lockdown period, I was more motivated to follow my treatment	32.31	41.54	26.15	34.24	41.38	34.48	29.79	41.49	28.72	5.03
Due to my respiratory illness, I am afraid that I will have less chances than others in the world of work since the COVID 19 epidemic	36.51	28.57	34.92	11.11	51.85	37.04	28.89	35.56	35.56	9.09
My employer / teacher has been sympathetic with my health problem during this period	57.89	31.58	10.53	76.67	23.33	0	63.1	29.76	7.14	13.33
I feel that I have been over-protected, due to my state of health, by my employer / my teacher during this period	22.81	40.35	36.84	13.33	34.62	50	20.48	38.55	40.96	10.38
I felt uncomfortable with my colleagues or comrades because of the specific measures needed to protect my health from others during this time	31.58	36.84	31.58	17.86	28.57	53.57	27.06	34.12	38.82	14.14

Table 2 : detailed responses to Likert questions

P06

Induced Pluripotent Stem Cell Derived Alveolar Lung Organoids

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Introduction: Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease with high morbidity and mortality for which novel therapeutic options are urgently needed. Lack of representative *in vitro* and *in vivo* models and shortage of patient material, specifically alveolar epithelial cells are the major limitations to identify new drug candidates. Induced pluripotent stem cells (iPSCs) are a promising novel technology that can be used to generate patient and disease-specific cells. iPSCs can be differentiated and grown in 3D culture to organoids that can be further used for basic research, disease modelling and drug screening. We aim to recapitulate the complex microenvironment of the alveoli *in vitro* by combining alveolar epithelial cells and endothelial cells to form alveolar lung organoids.

Methods: iPSCs were grown and differentiated into Alveolar Lung Organoids (ALO) in a sequential manner with ALOs maturing after ~40 days. iPSCs were separately differentiated into endothelial cells by chemical induction. Each stage of differentiation was validated via qPCR, Flow Cytometry and microscopy.

Results: iPSCs cultured in defined media were first differentiated into Definitive Endoderm; media was changed directing the cells towards Anterior Foregut Endoderm(AFE). AFE were differentiated into Alveolar Lung Organoids in two stages with branching structures emerging in matrigel after ~d35, and maturing after ~d40. Mature ALOs had AECI and AECII markers with multiple cell types. iPSC were separately differentiated via chemical induction into endothelial cells which was validated by CD31 staining.

Conclusion: iPSC differentiate into mature ALOs and endothelial cells; different factors affect the efficiency of self organization of ALOs that are comprised of multiple cell types. Further complexity will be achieved by combined culture with endothelial cells.

Conflict of interest to declare?: No

P07

Long-Term Azithromycin Disturbs the Richness and Composition of the Lower and Upper Airway Microbiota in Idiopathic Pulmonary Fibrosis

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Introduction: Interaction between the lung and the environment is involved in the pathogenesis of idiopathic pulmonary fibrosis (IPF). Environmental disturbance in the lower airways is identifiable through changes in microbiota composition and increase in bacterial burden. Azithromycin (AZT) is a multifunctional agent with anti-inflammatory and antibiotic properties. Preclinical studies provided evidence for anti-fibrotic effects and observational studies showed a benefit on mortality and hospitalization rate in IPF patients.

However, it is currently unknown what effect AZT has on the respiratory microbiota in IPF, including the carriage of antibiotic resistance genes previously reported in the context of other respiratory diseases.

Method: In a double-blind randomized controlled crossover trial, 24 IPF patients underwent two 12-week interventions (AZT 500mg or placebo 3 times per week), separated by a 4-week washout (NCT02173145). Paired sputum and oropharyngeal swab samples were analyzed by 16S ribosomal RNA gene sequencing. Bacterial burden and the carriage of macrolide and tetracycline resistance genes were determined by real-time quantitative PCR.

Results: AZT treatment reduced microbiota richness and phylogenetic diversity in both lower and upper airways but with a stronger and more persistent effect, still present 5 months after treatment, in lower airways. Four of five patients with increased

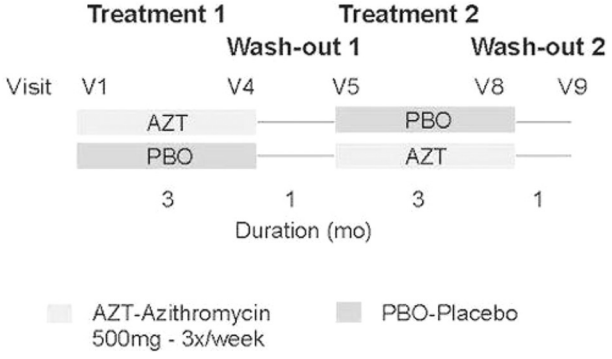

Fig. 1. Study Design

antibiotic resistance during treatment had a decrease in bacterial load and enrichment of the genus *Streptococcus* in the lower airways. In contrast, five patients without increase in resistance showed an unchanged bacterial load and enrichment of *Prevotella*. Changes in respiratory microbiota were not correlated with changes in lung function over the study period.

Conclusion: AZT leads to sustained changes in the richness and composition of the lower and upper airway microbiota in IPF patients. While these changes are not correlated to short-term changes in lung function or clinical status, longer-term follow-up studies are required.

Conflict of interest to declare?: No

P08

Prevalence of Exertion-Induced Laryngeal Obstruction in Elite Athletes – Results of a Cross-Sectional Surveillance

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Introduction: Breathing problems during physical exercise is a common problem among elite athletes. Often treatable pathologies are detected late. A literature review from 2017 reported a prevalence of 7% in the normal population and 35% among athletes. The study aims to provide an overview and better understanding of upper airway dysfunction in Swiss elite athletes. The current substudy presented here concentrates on the findings of exertion-induced laryngeal obstruction (EILO).

Method: The prevalence of EILO diagnosed with a continuous laryngeal examination during exercise (CLE) was evaluated in 28 consecutive elite athletes suffering from exertional respiratory symptoms (15 male and 13 females aged 15 up to 34 years). All athletes were members of the Swiss Olympic Team or a national elite sport association and were examined between May 2019 and November 2021. Data from patient history, lung function, bronchial provocation tests, exercise tests (CPET/CLE) as well as laryngeal pH-metry were collected.

Results: The prevalence of EILO in symptomatic elite athletes was 60% with a relevant gender difference - more women than men had EILO (81% vs. 43%, p=0.12). The characteristics of reported symptoms were not associated with presence or absence of EILO.

Conclusion: EILO is very prevalent in elite athletes with exertional respiratory symptoms. It should, therefore, actively be ruled out in symptomatic elite athletes to allow for an early diagnosis and therapeutic intervention. The next step consists of integrating these findings in the overall features of upper airway dysfunction in the study population.

Conflict of interest to declare?: No

P09

Validation of a Small Cough Detector in Clinical Practice

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Introduction: The assessment of cough frequency in clinical practice relies predominantly on the patient's history. Up to now objective evaluation of cough was feasible but by bulky equipment and during a relatively brief time (i.e., hours up to one day). Hence, cough recording was not performed outside clinical studies.

Method: We recorded cough epochs and explosive cough phases with a novel cough detector (SIVA-P3) over 8 days in outpatients suffering from chronic cough. During the first 24 hours, the system was validated against cough events counted by a trained human listener. The comfort to wear and use the device was assessed by a questionnaire.

Results: In total, 27 patients (51±14 y) with either chronic unexplained cough (n=13), COPD (n=4), asthma (n=4) or interstitial lung disease (n=6) were studied. The comfort of wearing and using the device was rated as very high by most of the patients. When patients were asked if SIVA-P3 was disturbing, 32% answered never or almost never, 40% answered rarely, 16% answered occasionally, 8% answered often and 4% answered always.

	cough epochs	explosive cough
Sensitivity	85.7% ± 14.1%	79.1% ± 15.9%
Specificity	99.9% ± 0.1%	99.9% ±0.1 %
Positive predictive value	87.1% ± 10.3%	90.8% ± 8.3%
Negative predictive value	99.9% ± 0.1%	99.8% ± 0.3%
False positives/hr	0.3 ± 0.3	0.4 ± 0.4
False negatives/hr	0.6 ± 0.9	2.2 ± 3.4

Preliminary summary of algorithm measures: cough epochs (counting continuous coughing with pauses smaller than 2 s between explosive cough phases as individual events) and explosive cough (counting single explosive cough phases as individual events) detection (n=27) with standard error.

Conclusion: SIVA-P3 monitors coughing for a longer time period than the state-of-the-art solution mostly used in clinical trials (which involves human listeners) and shows comparable or higher sensitivity than other devices with fully automatic cough counting described in literature. Due to its wearing comfort and its deep learning trained algorithm, it has the potential to be used in clinical practice.

SIVA-P3 Prototype

Conflict of interest to declare?: Yes

If you have a conflict, please specify: The Department of Pneumology at the University Hospital received research funding to conduct the SIVA-P3 study.

P10

Arterial Oxygen Partial Pressure and Adverse Health Effects in COPD at Altitude

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Importance: Patients with chronic obstructive pulmonary disease (COPD) experience low partial pressure of arterial oxygen (PaO_2) and altitude-related adverse health effects (ARAHE) when travelling to high altitude. We analyzed altitude-related PaO_2 and ARAHE in patients with COPD.

Objective: To estimate PaO_2 in relation to altitude and ARAHE in COPD.

Data sources: A systematic search of PubMed and Embase from inception to May 2021.

Study selection: Peer-reviewed prospective studies in COPD providing arterial blood gases within <3 days at altitude >1500m.

Data extraction and synthesis: Study characteristics were extracted and risk estimates calculated from individual data. Estimates were pooled using random-effects meta-analysis.

Main outcomes and measures: Relative risk estimates and 95% confidence intervals for the association between PaO_2 and altitude in patients with COPD.

Results: Seven studies suitable for quantitative analysis were identified. Data from 233 (45.2% female) patients with COPD exposed altitudes up to altitude 3100 m were available. A 1000m altitude gain was associated with a mean PaO_2–decrease of 0.81kPa (95%CI, 0.73 to 0.89; X^2=25.61, I^2=84.4%, P<0.001). In multivariate regression analysis, COPD severity and baseline PaO_2 were independent predictors of PaO_2 at altitude, whereas age and gender were not. 37.8% of patients experienced ARAHE, and older age, female sex, COPD severity, baseline PaO_2 and altitude reached were independent predictors of ARAHE (area under the curve: 0.9275, P<0.001).

Conclusions and relevance: This study provides estimates of PaO_2 and risk of ARAHE in patients with COPD at altitudes of many tourist destinations. The findings may contribute to improve patient care.

Conflict of interest to declare?: No

P11

Alleviating Effects of Bio-Mimetic Nanocarriers with Toll-Like Receptor Agonists in the Course of Allergic Airways Disease

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Allergic Asthma is characterized by airway hyperresponsiveness due to a maladaptive Th2/Th9/Th17 immune response against innocuous environmental substances. Current treatments manage to reduce symptoms but do not alter the course of disease. Therefore, there is urgent need for more efficacious treatment approaches, aiming at the cause of the disease.

We have designed bio-mimetic nanoparticles and characterised their effects in a mouse model of experimental allergic inflammatory airways disease (EAIAD) to skew the Th2/Th9/Th17-biased immune response towards Th1.

We established a EAIAD mouse model to treat allergic response with liposomes or virosomes conjugated with ovalbumin (OVA) and a TLR7/8 agonist, followed by monitoring the specific immune response. Immune cells in different lung compartments (flow cytometry), as well as lung function (Flexivent System™), immunoglobulins and cytokine levels (ELISA) were monitored before and after treatment.

Our model showed an enhanced level of eosinophils in lung and lymph nodes of EAIAD mice (sensitized with OVA) compared to negative controls (saline). Treatment with OVA-liposomes reduced eosinophil levels in allergic animals.

Lung function data revealed that treatment with OVA-liposomes rescued animals from impaired lung function, such as enhanced airway resistance, increased forced expiratory volume in 0.1 second (FEV0.1) and reduced peak expiratory flow (PEF) as found in non-treated OVA-sensitized and challenged positive controls. Serum IgE measurements showed enhanced levels in non-treated sensitised and challenged animals when compared to the non-sensitised control group, while treatment with

OVA-virosomes and OVA-liposomes rescued animals from enhanced IgE levels. Cytokine analysis showed an alleviating effect of "naked" liposomes and virosomes on the release of Th2 cytokines in particular.

Our findings show that allergen and adjuvant-modified virosomes and liposomes ameliorate hallmarks of EAIAD and some alleviating effects were observed independent of allergen. Bio-mimetic nanoparticles employed as carriers for antigen and adjuvant show great potential as therapeutic approach for re-programming allergic airways disease.

Conflict of interest to declare?: No

P12

Impact of Phenotypes and Comorbidities on Intra-Hospital Outcomes of Hospitalized Patients with an Exacerbation of COPD: A Retrospective Observational Study

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Introduction: Exacerbations in COPD (AECOPD) range in severity from mild increase in symptoms to hypercapnic respiratory failure (HRF). Identification of the risks of severe AECOPD is important given its prognostic impact.

We analyzed the characteristics of hospitalized patients with AECOPD to understand the factors associated with noninvasive ventilation (NIV) needs, prolonged hospital stay and mortality.

Method: We conducted a single-center, retrospective study on AECOPD occurring during hospitalization or leading to hospitalization at the CHUV between July 1, 2017 and December 31, 2019. Data collection was made possible thanks to the CIM10-GM code. Co-morbidities were assessed using the Charlson Comorbidity Index (CCI). The use of NIV, the length of hospital stay as well as the intra-hospital survival were used to define the intra-hospital outcome.

Results: We considered 512 episodes of AECOPD. Hypercapnic AECOPD requiring NIV was strongly associated with underweight (BMI <18.5kg/m2), OR 2.5 (95% CI [1.3-5.0]), CCI greater than 3, OR 2.0 (95% CI [1.1-3.5]) and the concomitant presence of obstructive sleep apnea (OSA) with OR 3.9 (95% CI [1.9-7.7]. Female sex (3.2 days longer (95% CI [1.3 - 5.1] p = 0.001), concomitant acute heart failure (3.2 days (p = 0.006) 95% CI [0.96-5.6]), intensive care stay (8.8 days 95% CI [5.8-11.84]) p <0.001) and CCI >3 (3 days, 95%CI [1.0-5.1] p = 0.004) increased the mean length of stay. 5.1% of EA-COPD ended in in-hospital death. NIV (OR 2.82, 95% CI [1.2-6.6]) and CCI greater than 3 (OR 3.2, 95% CI [1.2-8.2]) showed a significant positive relationship with the presence of in-hospital death.

Conclusion: HRF requiring NIV in hospitalized patients with AECOPD was more frequent in the presence of OSA, underweight and a polymorbid condition. These results underline the importance of a multidisciplinary management of COPD patients and can help physicians in implementing better standard of care.

Conflict of interest to declare?: No

SSP/SSTS Poster Walk: Thoracic Surgery/Interventions and Pulmonary Vascular Disease

P13

The Impact of Breathing Hypoxic Gas and Oxygen on Pulmonary Hemodynamics in Patients with Pulmonary Hypertension

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Background: Pure oxygen breathing (hyperoxia) may improve hemodynamics in patients with pulmonary hypertension (PH) and allows to calculate right-to-left shunt fraction (Qs/Qt), whereas breathing normobaric hypoxia may accelerate hypoxic pulmonary vasoconstriction (HPV). This study investigates how hyperoxia and hypoxia affect mean pulmonary artery pressure (mPAP) and pulmonary vascular resistance (PVR) in patients with PH and whether Qs/Qt influences the changes of mPAP and PVR.

Study design and methods: Adults with pulmonary arterial or chronic thromboembolic PH (PAH/CTEPH) underwent repetitive hemodynamic and blood gas measurements during right heart catheterization under normoxia (FiO_2 0.21), hypoxia (FiO_2 0.15) and hyperoxia (FiO_2 1.0) for at least 10 minutes.

Results: We included 149 patients (79/70 PAH/CTEPH, 59% women, mean±SD 60±17 years). Multivariable regressions (mean change, confidence interval) showed that hypoxia did not affect mPAP and cardiac index, but increased PVR (0.4 (0.1 to 0.7) WU, p=0.021) due to decreased pulmonary artery wedge pressure (-0.54 (-0.92 to -0.162, p=0.005). Hyperoxia significantly decreased mPAP (4.4 (-5.5 to -3.3) mmHg, p<0.001) and PVR (-0.4 (-0.7 to -0.1) WU, p=0.006) compared to normoxia. Qs/Qt (14±6%) was >10% in 75% of subjects but changes of mPAP and PVR under hyperoxia and hypoxia were independent of Qs/Qt.

Conclusion: Acute exposure to hypoxia did not relevantly alter pulmonary hemodynamics indicating a blunted HPV-response in PH. In contrast, hyperoxia remarkably reduced mPAP and PVR, indicating a preserved vasodilator response to oxygen and possibly

supporting oxygen therapy in patients with PH. A high proportion of PH-patients showed elevated Qs/Qt, which however was not associated with changes in pulmonary hemodynamics in response to changes in FiO_2.

Conflict of interest to declare?: No

P14

Can High Altitude Simulation Testing Predict Physiological and Clinical Changes at Real Altitude in Patients with Pulmonary Vascular Diseases?

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Introduction: Annually, millions of people expose themselves to hypobaric hypoxia (HH) while traveling to touristic mountain areas or by plane, among them patients with pulmonary arterial or chronic thromboembolic pulmonary hypertension (PAH/CTEPH, PH). We tested whether high altitude simulation testing (HAST) using normobaric hypoxia (NH) at low altitude correlates with changes in blood gases and right heart function in PH patients under HH conditions.

Method: 21 stable PH-patients (64±15y, 10 female, 12 PAH) participated the trial. Arterial blood gas analysis and echocardiography during NH (FiO_2 15%) at low altitude and within 20-45 min after arrival at 2500m (HH condition) were assessed.

Results: During NH, 12/21 revealed SpO_2<92% corresponding to a positive HAST according to BTS-recommendations. At 2500m, 3/21 received oxygen due to safety criteria (SpO_2 <80% for >30min), of which 2 were HAST-negative. During HH vs. NH, patients revealed significantly lower $PaCO_2$ 4.4±0.1 vs. 4.9±0.1kPa, mean difference (95%CI) -0.5kPa (-0.7 to -0.3), PaO_2 6.7±0.2 vs. 8.1±0.2kPa, -1.3kPa (-1.9 to -0.8) and oxygen content 16.9±0.4 vs.17.6±0.4ml/dl, -0.6ml/dl (-1.2 to 0) and higher tricuspid regurgitation pressure gradient 55±4 vs. 45±4mmHg, 10mmHg (3 to 17).

Conclusion: A comparable exposure time to NH and HH both equivalent to ≈2500m revealed several significant physiological differences, which may be attributed to lower barometric pressure at real altitude, or different adaptive mechanisms. The use of HAST to predict physiological changes at altitude remains questionable.

(ClinicalTrials.gov: NCT03592927 & NCT03637153).

Conflict of interest to declare?: No

P15

Characteristics and Management of Chronic Thromboembolic Pulmonary Disease Patients without Pulmonary Hypertension in an Expert Centre

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Introduction: Chronic thromboembolic pulmonary disease (CTEPD) without pulmonary hypertension (PH) is a recent entity referring to patients with exercise limitation caused by obstruction of pulmonary arteries by unresolved fibrotic clots, but without PH at rest. Data regarding this entity and its appropriate management are scarce.

Method: This retrospective study describes the characteristics and outcome of a cohort of CTEPD patients without PH in the French PH referral centre, from 2015 to 2020. Demographics were compared to a cohort of CTEPH patients treated during the same period.

Results: Thirty-nine CTEPD without PH patients and 426 CTEPH patients were treated from 2015 to 2020 (Characteristics of both groups are detailed in Table). Twenty-two out of 39 CTEPD without PH patients (56%) were deemed operable and 12 underwent pulmonary endarterectomy (PEA). PEA significantly improved symptoms and hemodynamics with a mean PVR reduction from 171 (±38) to 118 (±43) dyn.s.cm^{-5} (p=0.015). Surgery was associated with a complication rate of 33% (infectious, cardiovascular or renal events). No deaths occurred and patients remained clinically stable after a median follow-up of 47 months. Among the 17 inoperable patients (44%), 4 underwent balloon pulmonary angioplasty. Nineteen of 39 patients (49%) were followed without intervention. This subgroup was less symptomatic (p=0.01), had a higher cardiac index (p=0.04), when compared to the interventional subgroup. The nineteen untreated patients remained clinically stable after a median follow-up of 41 months.

Conclusions: CTEPD without PH patients are younger and more likely to have previous pulmonary embolism, when compared to CTEPH patients. PEA improves symptoms and hemodynamics but is associated with a significant rate of complications. A subgroup of CTEPD without PH patients appears clinically stable when treated conservatively. Therefore, these patients should be thoroughly assessed prior to instrumental treatment (particularly PEA), seeking for clear signs of exercise limitation.

Conflict of interest to declare?: No

Table 1.

Table. Comparison of the baseline characteristics of CTEPD patients, with or without pulmonary hypertension (PH), followed in the French National Referral Centre, from 2015 to 2020. Data are presented in mean (±SD), or n (%). PE: pulmonary embolism; NYHA FC: functional class; 6MWD: 6-minute walking distance; mPAP: mean pulmonary arterial pressure; PVR: pulmonary vascular resistance.

	CTEPD without PH (n=39)	CTEPH cases (n=426)	*p* value
Age at diagnosis	49 (±12)	67 (±14)	<0.0001*
Female	16 (39%)	218 (51%)	0.2
History of PE	37 (95%)	339 (79.6%)	0.02 *
Operable	22 (56%)	243 (57%)	>0.9
NYHA FC I-II/III-IV	0-26/13-0		
6MWD (m)	490 (±106)		
Hemodynamics			
mPAP (mmHg)	20.6 (±3.3)		
Cardiac index (l/mn/m^2)	3.1 (±0.5)		
PVR (dyn.s.cm^{-5})	153 (±48)		

P16

Comparison of Cardiac Output Measurements by Direct Fick using Pulse Oximetry vs. Blood Gases in Pulmonary Hypertension

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Background: Exact and simultaneous measurements of mean pulmonary artery pressure (mPAP) and cardiac output (CO) is crucial to calculate pulmonary vascular resistance (PVR), which is essential to define pulmonary hypertension (PH). Simultaneous measurements of mPAP and CO are not feasible using the direct Fick (DF) method, due to the necessity to sample blood from the catheter-tip. We evaluated a modified DF method, which allows simultaneous measurement of mPAP and CO without needing repetitive blood samples.

Methods: 24 patients with pulmonary arterial or chronic thromboembolic PH had repetitive measurements of CO at rest and end-exercise during three phases of a crossover trial. CO was assessed by the original DF method using oxygen uptake, measured by a metabolic unit, and arterial and mixed venous oxygen saturations from co-oximetry of respective blood gases served as reference. These CO-measurements were then compared with a modified DF method using pulse oximetry at the catheter- and fingertip.

Results: The bias among CO measurements by the two DF methods at rest was -0.26 L/min with limits of agreement of ± 1.66 L/min. The percentage error was 28.6%. At end-exercise, the bias between methods was 0.29 L/min with limits of agreement of ± 1.54 L/min and percentage error 16.1%.

Conclusion: DF using catheter- and fingertip pulse oximetry is a practicable and reliable method for assessing CO in PH-patients. This method has the advantage of allowing simultaneous measurement of PAP and CO, and frequent repetitive measurements such as needed during exercise.

Conflict of interest to declare?: No

P18

Clinical and Lung Function Outcomes in Lung Transplant Recipients Receiving Extracorporeal Photopheresis for Chronic or Recurrent Acute Lung Allograft Dysfunction

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Introduction: Despite advances in recent years, the prognosis for patients undergoing lung transplantation (LTx) remains worse than for other solid organ transplant recipients. The main reason for poor prognosis is development of chronic lung allograft dysfunction (CLAD). Treatment options for progressing CLAD are scarce, with extracorporeal photopheresis (ECP) as an established rescue therapy.

Methods: We performed a retrospective data analysis of all LTx recipients commencing ECP for CLAD, acute cellular rejection

(ACR) or other reasons (post transplant lymphatic disease with consecutive ACR) in the time period from 01/2010 – 09/2020. Patients were followed-up for a max. time period of 5 years. Mortality and lung function development were assessed by CLAD stage and by CLAD subtype before initiation of ECP treatment.

Results: Overall, 105 patients (mean age 50.3 years) received at least one ECP following LTx. 57 patients (61.3%) died within the study period, with a median of 15 months survival. Mortality was 57% for patients who started ECP at CLAD1, 39% for CLAD2, 93% for CLAD3, and 90% for CLAD4 ($p<0.001$). 8 out of 37 (22%) of patients who started therapy with CLAD1 survived five years without disease progression. 19% of patients were classified as ECP responders Response to ECP treatment was lower in patients with CLAD-RAS / mixed subtype (14.3%) and patients with ECP onset in CLAD stages 3 (7.1%) and 4 (11.1%)

Discussion: In this retrospective analysis of a large group of CLAD patients treated with ECP after LTx, early onset of ECP was associated with better long-term survival. Patients with the CLAD subtype CLAD/BOS responded best. It showed a slower decline and in some cases an intermittent improvement of lung function. ECP might therefore prevent long-term disease progression without the need for re-transplantation even in patients refractory to first-line treatment options for CLAD.

Conflict of interest to declare?: No

P19

Cytosolic DNA Sensors as Potential New Pharmacological Targets in *Ex Vivo* Lung Perfusion and Lung Transplantation

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Introduction: Cell damage caused by ischemia/reperfusion (I/R) promotes the release of danger-associated molecular patterns triggering inflammatory responses. DNA released from injured cells activate cytosolic DNA (cDNA) sensors cGAS and AIM2. The cGAS-STING pathway induces the production of type I interferons (IFNs) and IFN stimulated genes (ISGs). The present study aims at the identification of a potential role of cDNA sensors in early inflammation of reperfused lung using the rat *ex vivo* lung perfusion (EVLP) and lung transplantation (LTx) models.

Methods: Heart-lung blocks from male Sprague-Dawley rats cannulated in the pulmonary artery and left atrium were assigned to four groups (n=5/6). Cold ischemia (CI): lungs were flushed with 4°C Perfadex and stored inflated (FiO_2 0.5) for 7h in 4°C Perfadex. Warm ischemia (WI): lungs were deflated for 1h at room temperature, flushed and stored for 6h in 4°C Perfadex. CI+EVLP: lungs were stored at 4°C for 2h, followed by 3h EVLP, and 2h in 4°C Perfadex. WI+EVLP: after 1h WI, lungs were flushed and stored at 4°C for 1h, followed by 3h EVLP and 2h cold preservation. Right lungs were used as controls, left lungs were transplanted and sampled 2h after LTx. We analyzed by RT-PCR and western blot the expression of the cytosolic DNA sensors cGAS, STING and AIM2 and by RT-PCR the expression of the downstream gene *Ifnb*, and the ISGs *Ifit1* and *Isg15* in whole lung tissue.

Results: cGAS, STING and AIM2 proteins are expressed in lung after the ischemic period. mRNA of *Cgas*, *Sting*, *Aim2*, *Ifnb* and the ISGs *Ifit1* and *Isg15* were induced by the reperfusion regardless of the conditions of preservation (CI or WI).

Conclusion: These preliminary data provide evidence that cDNA sensors, especially the cGAS-STING axis, may play a role in the early inflammation of the reperfused lung.

Conflict of interest to declare?: No

P20

Efficacy of Concomitant Diagnosis and Correct Surgical Therapy for Early Stage Lung Cancer in a Hybrid Theatre

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Objective: Due to emergent lung cancer screening programs, detection of small pulmonary nodules increased. Anatomical resection in case of lung cancer with only one intervention becomes increasingly desirable. Literature lacks of interventions including both diagnosis and correct resection. We review our patients for the efficacy of an one-step approach with detection, diagnosis and therapy of early-stage lung cancer.

Methods: Undiagnosed pulmonary nodules suspicious of lung cancer, which were not detectable by conventional video-assisted thoracoscopic surgery (VATS) due to depth and seize, were scheduled for a hybrid procedure consisting of a cone-beam CT-guided hook wire insertion and a C-arm assisted thoracoscopic wedge resection for frozen section. All procedures were analyzed for outcomes including success rate of image-guided nodule resection and rate of concomitant correct anatomical resection.

Results: Twenty-three patients with 25 pulmonary nodules underwent image-guided VATS (iVATS) in the hybrid theatre (HT). Twenty-two nodules were successfully marked by hook wire, one lesion was found by ultrasound and two lesions by palpation. In 16 patients (70%) wedge resection for frozen section showed malignancy. Five patients with previous history of lung cancer received only a diagnostic wedge resection, as frozen section could not differentiate between primary or secondary lung cancer. Eleven patients (48%) had early-stage primary lung cancer (8 adenocarcinoma, one typical carcinoid, one small-cell lung cancer and one squamous-cell lung cancer). 10 of them (91%) received a completion anatomical resection during the same intervention (7 lobectomies, 3 segmentectomies). In one patient, malignancy was only confirmed in final histology.

Conclusions: Almost all patients with diagnosis of primary early-stage lung cancer in the HT received definitive treatment during the same operation. One-step diagnosis by iVATS with frozen section and concomitant completion anatomical resection in a HT for otherwise non-well approachable lung cancer might be advisable for the current increasing detection of pulmonary nodules.

Conflict of interest to declare?: No

P21

Role of Postoperative Follow-Up with 18F-FDG PET/CT in Asymptomatic NSCLC Patients - A Retrospective Single-Institution Study

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Introduction: The optimal surveillance strategy in patients with resected non-small cell lung cancer (NSCLC) is unknown. Early detection of recurrences by intense imaging follow-up may improve survival and whole-body fluorine-18-deoxyglucose positron emission tomography-computed tomography (FDG-PET/CT) might be the optimal imaging modality given its high accuracy in preoperative staging. However, the role of FDG-PET/CT during postoperative surveillance remains controversial.

Methods: Data from a single-center cohort of 205 patients with resected stage I-III NSCLC and FDG-PET/CT surveillance was retrospectively collected, and patterns of recurrence and secondary primary lung cancer (SPLC) analyzed. All patients had preoperative FDG-positive tumor lesions and regular follow-up imaging with at least one postoperative FDG-PET/CT.

Results: With a median follow-up time of 26.3 months (range, 4.1-60.6), the rate for recurrence and secondary primary lung cancer (SPLC) was 22% and 8%, respectively. Approximately half of patients with recurrences presented with possibly associated pulmonary or general symptoms. However, this was the case only in 18% of patients with SPLC. Overall, 83% of all recurrences, and 65% of SPLC were detected on FDG PET/CT. Secondary curative-intent treatment was possible in 37% of patients with recurrences and in all patients with SPLC. For patients who had secondary curative-intent treatment for recurrence, the 1- and 2-year recurrence-free survival rates were 63% [42%, 96%] and 53% [31%, 91%], respectively. Incidental FDG-positive PET/CT findings occurred in 25% of all patients, mostly infections (71%).

Conclusion: In our cohort of patients with resected stage I-III NSCLC, recurrence was identified in more than 80% of all cases in one of the standardized three PET/CTs performed as part of our follow-up imaging protocol during the first two years after resection. Nearly all patients with non-distant recurrence qualified for a second curatively intended treatment. Further studies are necessary to identify patients who might benefit from an even more intensive surveillance strategy.

Conflict of interest to declare?: No

P22

Influence of Mycophenolate Mofetil Dosage and Plasma Levels on the Occurrence of Chronic Lung Allograft Dysfunction in Lung Transplants

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Introduction: Development of chronic lung allograft dysfunction (CLAD) is a limiting factor for post-lung transplant survival. We evaluated, whether the dose of the immunosuppressant mycophenolate mofetil (MMF) or the active metabolite of MMF, mycophenolic acid (MPA) plasma concentrations, affect the development of CLAD in patients with lung transplantation.

Methods: In this retrospective, controlled cohort study we recruited 71 patients with a lung transplantation between 2010 and 2014 who provided a consent and did not develop complications within a year after transplantation. The observation period ranged to July 01, 2021. An event-time-analytical Cox proportional-hazards regression model with time-dependent covariates was used to estimate the association of MMF dose, MPA plasma concentrations and CLAD, with adjustment for sociodemographic factors and coexisting conditions.

Results: 37 patients did not develop CLAD (41.3±15.6 years, FEV1 95.5±19.1% predicted) and 34 patients developed CLAD (age 50.9±13.3 years, FEV1 102.2±25.4% predicted). The mean plasma MPA concentration did not differ significantly between the groups without and with CLAD (2.8±1.7 mg/L and 3.0±2.3mg/L; p=.724). While there was a dose-effect relationship between MMF dosage, plasma MPA concentrations, as well as lymphocyte levels, traditional risk factors (age, lung-function, radiological features) predicted CLAD. Continuously measured MPA plasma concentration did not predict CLAD (period of 382.97 patient-years) nor death (period of 472.8 patient-years).

Conclusion: MMF dosage and MPA plasma concentration were not associated with CLAD development or death. CLAD may be influenced by other components of immunosuppression or other factors.

Conflict of interest to declare?: No

Table 1. No association could be established between MPA or MMF dosage and the occurrence of CLAD.

Variables	Patients without CLAD (n=37)	Patients with CLAD (n=34)	p-value
Average MPA-level, mg/l	2.8 ± 1.7	3.0 ± 2.3	0.724
Average MMF-dosage, mg	1828 ± 533	1731 ± 676	0.511

Values are displayed as median ± SD

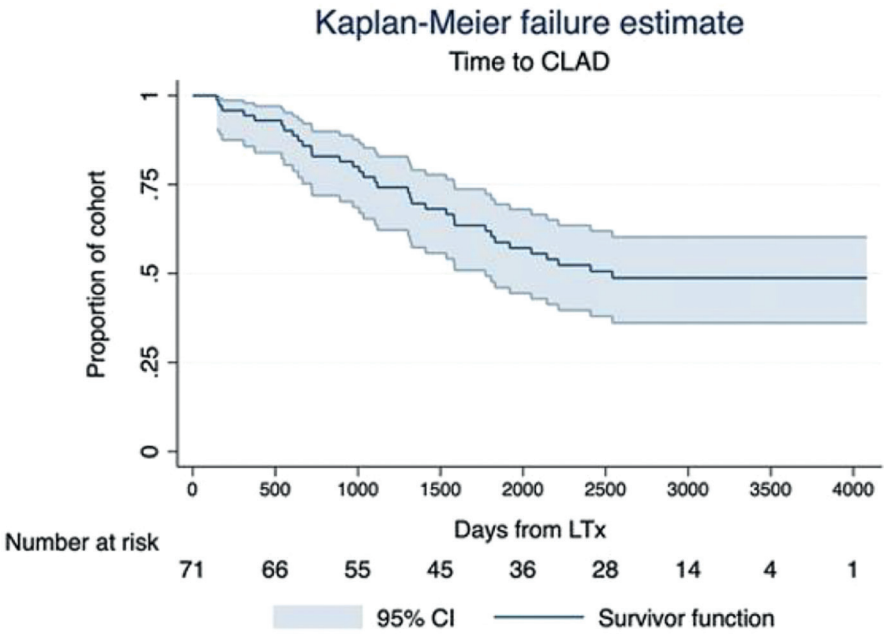

Fig. 1. Almost 50% of the patients developed CLAD by the 5th post-transplant year.

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