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**Joint Annual Meeting of the
Schweizerische Gesellschaft für Kardiologie /
Société Suisse de Cardiologie
Schweizerische Gesellschaft für Herz- und
thorakale Gefässchirurgie / Société Suisse de
Chirurgie Cardiaque et Vasculaire Thoracique
Schweizerische Gesellschaft für Pneumologie /
Société Suisse de Pneumologie**

June 15–17, 2016, Lausanne

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June 15–17, 2016, Lausanne**

**Oral Session 7: Clinical Studies in COPD
and Related Obstructive Disorders**

OR32

**Lung Function in Patients with Primary Ciliary
Dyskinesia (PCD): A Multinational Study**

F. Halbeisen^{*1}, M. Goutaki¹, E. Maurer¹, M. Boon², C. Casaulta³,
A. Clement⁴, S. Crowley⁵, E. Haarman⁶, B. Karadag⁷,
C. Koerner-Rettberg⁸, H. Mazurek⁹, L. Morgan¹⁰, K. Nielsen¹¹,
F. Santamaria¹², N. Schwerk¹³, P. Yiallourou¹⁴, P. Latzin¹⁵, J. Lucas¹⁶,
C. Kuehni¹

¹Institute of Social and Preventive Medicine, Bern, Switzerland;

²Department of Paediatrics, University Hospital Gasthuisberg
Leuven, Leuven, Barbados; ³Department of Paediatrics,
University Children's Hospital of Bern, Bern, Switzerland;

⁴Paediatric Pulmonary Department, Université Pierre et
Marie Curie, Paris, France; ⁵Section for Paediatric Heart, Lung,
Allergic Diseases, Rikshospitalet, Oslo, Norway; ⁶Department of
Pulmonary Diseases, VU University Medical Center, Amsterdam,
Netherlands; ⁷Department of Pediatric Pulmonology, Marmara
University, School of Medicine, Istanbul, Turkey; ⁸Department of
Paediatric Pneumology, University Children's Hospital of Ruhr
University Bochum, Bochum, Germany; ⁹Klinika Pneumonologii
i Mukowiscydozy, Instytut Gruźlicy i Chorób Płuc, Rabka-Zdrój,
Poland; ¹⁰Department of Respiratory Medicine, Concord
Hospital Clinical School, University of Sydney, Sydney, Australia;

¹¹Danish PCD Centre Copenhagen, Paediatric Pulmonary
Service, Copenhagen University Hospital, Copenhagen, Curaçao;

¹²Department of Translational Medical Sciences, Federico II
University, Napoli, Italy; ¹³Clinic for Paediatric Pulmonology,
Allergiology and Neonatology, Hannover Medical School,

Hannover, South Georgia and the South Sandwich Islands;

¹⁴Cyprus International Institute for Environmental and Public,
Cyprus University of Technology, Limassol, Cyprus; ¹⁵University
Children's Hospital Basel, Basel, Switzerland; ¹⁶PCD Centre,
University Hospital Southampton, NHS Foundation Trust and
University of Southampton, Southampton

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 regres-
sion 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 %pre-
dicted (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 spi-
rometry 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 func-
tion, particularly age at diagnosis, time since diagnosis, and diag-
nostic certainty.

Funding: FP7 grant 305404, SNF32003B-144068.

Disclosure of Interest: None declared.

OR33

Altitude Related Adverse Health Effects in Lowlanders with COPD Travelling to 3,200 m. Randomized Trial of Preventive Dexamethasone Treatment

M. Furian^{*1}, M. Lichtblau¹, S.S. Aeschbacher¹, M. Bisang¹, S.E. Hartmann², M. Poulin², T.D. Latshang¹, S. Ulrich¹, A. Aldashev³, T. Sooronbaev⁴, K.E. Bloch¹

¹Pulmonary Division and Sleep Disorders Center, University Hospital of Zurich, Zurich, Switzerland; ²Department of Physiology and Pharmacology and Hotchkiss Brain Institute, Faculty of Medicine, Calgary, Canada; ³Research Institute for Molecular Biology and Medicine, ⁴National Center for Cardiology and Internal Medicine, Bishkek, Kyrgyzstan

Introduction: We investigated the incidence of altitude related adverse health effects (AAHE) in lowlanders with COPD during a stay at 3200 m, 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 ± 9.3 y, FEV1 85 ± 21 %pred, SpO₂ 95 ± 2%) were studied in Bishkek (760 m), Kyrgyz Republic, and after travelling within 6 h to Tuja Ashu clinic (3200 m) and staying there for 3 days. Patients received dexamethasone (2x4 mg/d, p.o.) or placebo before ascent and during stay at 3200 m according to a double-blind randomized, placebo-controlled trial. Main outcome assessed during 3 days at 3200 m was the cumulative incidence of one of the following AAHEs: AMS (AMSc environmental symptom cerebral score ≥0.7), severe hypoxemia (SpO₂ <75% for >30 min) or discomfort requiring descent to low altitude. ClinicalTrials.com NCT02450968.

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

Conclusion: In lowlanders with COPD, GOLD grade 1–2, staying 3 days at 3200 m 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 12 h at 3200 m.

Disclosure of Interest: None declared.

OR34

Hyaluronic Acid and Its Degrading Enzyme Hyaluronidase as Systemic Biomarkers to Predict COPD Progression and Severity

E. Papakonstantinou^{1,2}, I. Bonovolias², M. Roth¹, M. Tamm¹, L. Boeck¹, A. Scherr¹, J. Rakic¹, D. Stolz^{*1} and Working group, The PROMISE study

¹Pneumology, Pulmonary Cell Research, University Hospital Basel, Basel, Switzerland; ²Pharmacology, Aristotle University of Thessaloniki, Thessaloniki, Greece

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 exacer-

Table 1. Altitude related adverse health effects in COPD patients (for Abstract OR33)

Altitude	Altitude exposure, h	Placebo group (n = 55)					Dexamethasone group (n = 57)				
		cumulative incidence, %			mean ± SD		cumulative incidence, %			mean ± SD	
		AAHE	AMSc score ≥0.7	H or D	AMSc score	SpO ₂ , %	AAHE	AMSc score	H or D	AMSc score	SpO ₂ , %
760 m	–	0	0	0	0.06±0.12	95.1±1.8	0	0	0	0.08±0.12	95.0±1.4
3,200 m	0	7	5	5	0.15±0.28*	90.7±3.5*	12	11	0	0.25±0.44*	90.7±2.6*
3,200 m	12	18	7	15	0.12±0.26 [†]	89.2±3.4*	14	11	4 [†]	0.09±0.15 [†]	89.9±2.9*
3,200 m	24	18	7	15	0.07±0.14 [†]	91.4±2.6*	16	11	5	0.09±0.16 [†]	91.4±2.6*
3,200 m	36	20	9	15	0.05±0.14 [†]	90.0±3.4*	18	12	9	0.09±0.24 [†]	90.7±2.3*

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. 760 m; [†] p < 0.05 vs. day 1 at 3,200 m; [‡] p < 0.05 vs. placebo at the same time of altitude exposure.

bation 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

A Multicentre Validation of the 1-Minute Sit-to-Stand Test in Patients with Chronic Obstructive Pulmonary Disease

S. Crook^{*1}, K. Schultz², N. Leibert², G. Büsching³, D. Jelusic², S. Keusch⁴, M. Wittmann², M. Schuler⁵, T. Radtke¹, M. Puhan¹, A. Frei¹

¹Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland; ²Klinik Bad Reichenhall, Bad Reichenhall, Germany; ³Klinik Barmelweid, Barmelweid, ⁴Zürcher Höhenklinik Wald, Wald, Switzerland; ⁵University of Wuerzburg, Wuerzburg, Germany

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

Longitudinal Assessment of Physical Activity in Patients with COPD

C.F. Clarenbach^{*1}, N.A. Sievi¹, T. Brack², M. Brutsche³, M. Frey⁴, S. Irani⁵, J. Leuppi⁶, R. Thurnheer⁷, M. Kohler¹

¹Klinik für Pneumologie, UniversitätsSpital Zürich, Zürich, ²Pulmonary Division, Cantonal Hospital of Glarus, Glarus, ³Pulmonary Division, Cantonal Hospital of St. Gallen, St. Gallen, ⁴Pulmonary Division, Clinic Barmelweid, Barmelweid, ⁵Pulmonary Division, Cantonal Hospital of Aarau, Aarau, ⁶University Clinic of Internal Medicine, Cantonal Hospital Baselland, Basel, ⁷Pulmonary Division, Cantonal Hospital of Münsterlingen, Münsterlingen, Switzerland

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 (min/max) observation time in 198 patients (137 male) 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 associ-

ated 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.

OR37

Therapy with Proton-Pump Inhibitors for Gastroesophageal Reflux Disease Does Not Reduce the Risk of Severe Exacerbations in COPD

L. Baumeler¹, E. Papakonstantinou¹, B. Milenkovic², A. Lacoma³, R. Louis⁴, J.G. Aerts⁵, T. Welte⁶, K. Kostikas⁷, F. Blasi⁸, W. Boersma⁹, A. Torres¹⁰, G.G. Rohde¹¹, L. Boeck¹², J. Rakic¹², A. Scherr¹², M. Tamm¹, D. Stolz^{*1}

¹Pneumology, University Hospital Basel, Basel, Switzerland;

²Faculty of Medicine, University of Belgrad, Belgrad, Serbia;

³Department of Microbiology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; ⁴Pneumology, University of Liege, Liege, Belgium; ⁵Department of Pneumology, Amphia Hospital/Erasmus MC, Breda, Netherlands; ⁶Department of Pneumology, Medizinische Hochschule Hannover, Hannover, Germany;

⁷Department of Pneumology, University of Thessaly, Medical School, Larissa, Greece; ⁸Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milano, Italy; ⁹Department of Pneumology, Medisch Centrum Alkmaar, Alkmaar, Netherlands; ¹⁰Department of Pneumology, Hospital Clinic, Barcelona, Spain; ¹¹Department of Respiratory Medicine, Maastricht University Medical Center, Maastricht, Netherlands;

¹²Department of Pneumology, University Hospital Basel, Basel, Switzerland

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.

Oral Session 8: Pulmonary Cell Biology

OR38

The Disease Specific Effect of Adrenomedullin on Epithelial Cells in Chronic Inflammatory Lung Disease Patients: A System Biological Approach

J. Mandal^{*1}, M. Roth¹, E. Papakonstantinou¹, L. Bubendorf², S. Savic², M. Tamm¹, D. Stolz¹

¹Pneumologie, ²Pathologie, Universitätsspital Basel, Basel, Switzerland

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 TNF α 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, TNF α). 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.

OR39

Cell-Specific Interactions between the Novel Myokine Irisin and Hyaluronic Acid in Chronic Obstructive Pulmonary Disease

E. Papakonstantinou, M. Roth, J. Mandal, M. Tamm, D. Stolz*

Pneumology, Pulmonary Cell Research, University Hospital Basel, Basel, Switzerland

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 ($1480 \pm 121 \mu\text{g/ml}$ vs. $1265 \pm 88 \mu\text{g/ml}$ $p = 0.009$). Furthermore, there was a significant ($p = 0.002$) correlation ($\rho = 0.142$) between HA and iri-

sin 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

Bacterial Endotoxin Fine-Tunes Macrophage-Fibroblast Tissue Remodeling Activity

S. Mouraux*, E. Bernasconi, J.-D. Aubert, B. Marsland, L. Nicod

Département de Médecine, CHUV, Service de Pneumologie, CHUV, Lausanne, Switzerland

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 (TGF β and immunosuppressive drugs).

Results: In monocultures, macrophages and fibroblasts presented a range of pro-remodeling activation states that culminated under immunosuppressive conditions combined with TGF β 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.

OR41**Mesenchymal Stem Cells Isolated from Human Lung Tissue Inhibit Proliferation and Collagen Expression by Lung Fibroblasts**

P. Khan¹, A. Gazdhar², S. Savic³, M. Tamm¹, D. Lardinois⁴, M. Roth¹, T. Geiser², K.E. Hostettler^{*1} and Interstitial and rare lung diseases

¹Department of Biomedicine and Clinics of Respiratory Medicine, University Hospital Basel, Basel, ²Department of Pulmonary Medicine, University Hospital Bern, Bern, ³Institute for Pathology, ⁴Division of Thoracic Surgery, University Hospital Basel, Basel, Switzerland

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 administered 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.

OR42**Virosomes Coupled to Antigen Induce Enhanced Specific CD4+ T Cell Activation Compared to Liposomes in an *in vitro* Model of Pulmonary Dendritic Cells**

R.A.M. Blom^{*1}, M. Amacker², C. Moser³, R.M. van Dijk⁴, F. Blank¹, C. von Garnier¹

¹Departement für Klinische Forschung, University of Bern, Bern, ²Mymetics SA, Epalinges, ³Swiss Federal Institute of Intellectual Property, Berne, ⁴Functional Neuroanatomy, Institute of Anatomy, University of Zürich, Zürich, Switzerland

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-treated 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- γ 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 up-regulation 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.

OR43

Metabolite Profile Differences in Exhaled Breath Condensate from Patients with Idiopathic Pulmonary Fibrosis Compared to Healthy Individuals Analyzed by Mass Spectrometry – A Pilot Study

C. Strebel^{*1}, B. Rindlisbacher², S. Guler³, T. Geiser³, C. Bovet², M. Funke³

¹Internal Medicine, Spital STS AG, Zweisimmen, ²Clinical Metabolomics Facility, ³Pulmonary Medicine, Inselspital, Bern, Switzerland

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.

Reference

Montesi SB, et al: Docosatetraenoyl LPA is elevated in exhaled breath condensate in idiopathic pulmonary fibrosis. *BMC Pulm Med* 2014;14:5.

Oral Session 11: Hysiopathology and Mechanisms of Diseases

OR60

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

O.D. Schoch¹, G. Benz^{*1}, F. Baty², J. Niedermann¹, M.H. Brutsche²

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 $<4 h$ or if excessive leakage was present for 2 consecutive nights.

Results: 240 patients were randomized. According to the pre-defined 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 be-

Table 1. (for Abstract OR60)

	With telemedicine	Without telemedicine	p value
N	109	114	–
Sex ratio (M/F)	83.5%	83.3%	1
Age	55.1 (44.1–63.9)	57.3 (47–65.3)	0.597
BMI	30.8 (27.3–35.2)	31 (28–34.9)	0.614
ODI	31 (18–58)	36 (21.5–59.5)	0.216
AHI	37 (23–68)	49.9 (27–67.5)	0.0891
ESS	10 (6–13.5)	10 (8–13)	0.704

Table 2. (for Abstract OR60)

	With telemedicine	Without telemedicine	p value
n	109	114	–
Daily usage (h)	5.23 (3.66–6.45)	4.93 (3.69–6.56)	0.868
Prop. night with CPAP used	0.967 (0.8–1)	0.967 (0.8–1)	0.876
Prop. night with efficient CPAP use	0.767 (0.467–0.933)	0.733 (0.5–0.933)	0.906

tween 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.

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References

- 1 Schoch OD, Baty F, Niedermann J, Ruediger JJ, Brutsche MH: Baseline predictors of adherence to positive airway pressure therapy for sleep apnea: a 10-year single centre observational cohort study. *Respiration* 2014;87:121–128.
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Table 1. (for Abstract OR61)

	Dexamethasone (n = 58)		Placebo (n = 51)		Treatment effect
	760 m	3,200 m	760 m	3,200 m	
TPG, mm Hg	18±5	26±6*	20±5	31±9*	4 (2; 7) ^{##}
Systolic PAP, mm Hg	31±6	39±8*	32±6	45±11*	–5 (–8; –1) ^{##}
CO, l/min	4.7±0.9	5.7±1.0**	4.9±0.7	5.7±1.1**	0.1 (–0.3; 0.6)
Pressure/flow ratio, mm Hg/l/m	4.0±1.2	4.6±1.1**	4.1±1.1	5.6±1.6	–1.0 (–1.5; –0.5) ^{##}
6 MWT, m	500±76	486±93	502±77	483±84	–20.0 (–42.4; 2.4)
SpO ₂ peak walk, %	95.0±2.5	85.1±4.2*	95.0±1.5	87.9±3.1*	2.9 (1.5; 4.3) [#]

TPG = Tricuspid pressure gradient; PAP = pulmonary artery pressure; CO = cardiac output. * p < 0.05 resp; ** p < 0.01 altitude vs. lowland; # p < 0.05; ## p < 0.01 dexamethasone vs. placebo.

OR61

Dexamethasone Reduces Pulmonary Artery Pressure in Lowlanders with COPD Travelling to 3,200 m. Randomized, Placebo-Controlled Trial

M. Lichtblau^{*,1}, M. Furian¹, S. Aeschbacher¹, M. Bisang¹, S. Hartmann², S. Ulrich¹, T. Latsang¹, A. Aldashev³, E. Mirrakhimov⁴, T. Soronbaev⁴, K.E. Bloch¹, S. Ulrich¹

¹Pneumology, University Hospital Zürich, Zürich, Switzerland;

²Departments of Physiology and Pharmacology, University of Calgary, Calgary, Canada; ³Research Institute for Molecular Biology and Medicine, ⁴National Centers for Cardiology and

Internal Medicine, Bishkek, Kyrgyzstan

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 altitude 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 800 m, SpO₂ >93%, in stable condition were included. Participants were randomized to receive dexamethasone (4 mg, bid) or placebo one day before ascent from 760 m and during a sojourn to 3,200 m in Tuja Ashu, Kyrgyz Republic. Echocardiography was performed at 760 m and after the first night at 3,200 m. 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 3,200 m, 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).

Conclusion: In lowlanders with COPD, GOLD 1–2, travelling to 3,200 m 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.

Reference

- 1 Maggiorini M, Brunner-La Rocca HP, et al: Both tadalafil and dexamethasone may reduce the incidence of high-altitude pulmonary edema: a randomized trial. *Ann Intern Med* 2006;145:497–506.

OR62

Exercise Pulmonary Hemodynamics in Systemic Sclerosis Patients – Implications for Outcome

A. Stamm^{*1}, S. Saxer¹, M. Lichtblau¹, L.C. Huber¹, O. Distler², R. Speich¹, K.E. Bloch¹, S. Ulrich¹

¹Pneumologie, ²Rheumatologie, Universitätsspital Zürich, Zürich, Switzerland

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 ≥ 25 mm Hg). From the 65 without resting PH, 28 had exercise precapillary PH (Δ mPAP/ Δ CO > 3 mm Hg/l/min & mPAP > 30 mm Hg) and 10 exercise postcapillary PH (Wedge > 20 mm Hg). 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) mm Hg/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 $\pm$ 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

ASA Score and Preoperative ICU Admission are the Only Predictors of Mortality after Surgical Biopsy for Interstitial Lung Disease

K. Furrer^{*1}, C. Nebiker², L. Junker³, S. Lazdinyte¹, S. Savic⁴, K. Hostettler³, D. Schumann¹, J. Halter⁵, M. Tamm³, D. Lardinois¹

¹Thoracic Surgery, ²Visceral Surgery, ³Pneumology, ⁴Pathology, ⁵Haematology, University Hospital Basel, Basel, Switzerland

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.

OR64**Online Bronchoscopy Atlas: An Open Access Educational Tool for Pulmonologists**

A. Koutsokera*, N. Liechti, C. Daccord, M. Bernasconi, V. Garelli, A. Valenti, D. Keller, S. Lahzami, N. Leslie, A. Ognà, A. Pasche, N. Petitpierre, D. Hinchliffe, S. Perret Bakhouy, M. Prella, R. Manzoni, A. Lenoir, J.-D. Aubert, L.P. Nicod, J.-W. Fitting, A. Lovis

Division of Respiratory Medicine, University Hospital of Lausanne, Lausanne, Switzerland

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.

OR65**Recurrent Hypercapnia and Hypoxemia in Congenital Central Hypoventilation Syndrome (Undine Syndrome) Likely Acts as Endothelial Preconditioning**

D. Hutter*,¹ L. Rovina², S. Rimoldi¹, C. Sartori³, R. Chetany¹, R. Soria¹, U. Scherrer¹, E. Rexhaj¹

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 recurrent 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 550 m and at 3883 m 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 550 m above sea level while no relevant RV/PA gradient was found in the controls (25.8 ± 8.0 vs. 20 ± 4.3 mm Hg, $P = 0.03$). In 3883 m above sea level all US subjects showed only mild increase in RV/PA gradients similar to the controls (33.5 ± 17.8 mm Hg vs. 29 ± 21 mm Hg). 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 μ m, $P < 0.01$, 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.

Poster Walk SSC/SSCS 1: COPD

PP-118

Flexible Bronchoscopy in COPD – A Case-Control Study

P. Grendelmeier, M. Tamm, K. Jahn, E. Pfimlin, D. Stolz*

Pneumology, University Hospital Basel, Basel, Switzerland

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 $\leq 90\%$ was did not differ between

COPD and non-COPD ($p = 0.125$), patients with COPD had a lower median and lowest SO_2 and persisted hypoxemic ($SO_2 < 88\%$) longer than patients without COPD. Both peak pCO_2 and time on $pCO_2 > 45$ mm Hg were higher in COPD, but increase in $paCO_2$ 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

Effect of Hyperoxia on Exercise Performance in Patients with COPD: A Randomized Trial

S. Ulrich*, S. Saxer, E. Hasler, M. Furian, K.E. Bloch

Pneumologie, Universitätsspital Zürich, Zürich, Switzerland

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 ± 6 y, FEV1 $64 \pm 19\%$ 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% W_{max} , FiO_2 0.21) bicycle protocols, according to a randomized, cross-over design. Pulmonary gas-exchange, oxygen saturation (SpO_2), cerebral and muscle tissue oxygenation (CTO and MTO) and hyperinflation by respiratory inductance plethysmography were monitored.

Table 1. (for Abstract PP-119)

	End of progressive ramp		End of constant load	
	FiO_2 0.21	FiO_2 0.50	FiO_2 0.21	FiO_2 0.50
Endurance, s	422±78	455±94*	605±274	963±444*
Work rate, watts	96±21	104±28*	72±16	72±16
$V'O_2$, l/min	1.34±0.28	1.96±0.46*	1.4±0.3	1.7±0.3*
Heart rate, l/min	125±19	126±18	130±18	122±18*
$V'E$, l/min	45±11	45±13	46±10	42±9*
$V'E/V'CO_2$	36±6	32±5*	37±7	34±5*
Breathing reserve, %	24±22	23±21	54±9	58±9*
SpO_2 , %	95±4	98±3*	94±5	98±3*
CTO, %	64±7	74±6*	61±10	67±11*
MTO, %	64±10	66±11*	61±10	67±11*
Dynamic hyperinflation, ml	1±551	232±617	478±585	141±675
Borg CR10, dyspnea	6±2	6±2	6.5±2.4	5.6±1.9*

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; $V'E/V'CO_2$ = ventilatory equivalent for CO_2 ; SpO_2 , CTO and MTO = arterial, cerebral and muscle tissue oxygenation. ERV = Expiratory reserve volume; dynamic hyperinflation = exercise induced increase in end-expiratory lung volume.

Results: In progressive ramp tests with FiO_2 0.50, mean maximal work rate was significantly increased to 108%, and oxygen uptake, SpO_2 , CTO and MTO exceed values during FiO_2 0.21, while the ventilatory equivalent for CO_2 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 1). 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 ($r = -0.54$, $p = 0.002$). At isotime corresponding to end of tests with FiO_2 0.21, heart rate, breathing frequency and minute ventilation were lower and breathing reserve, SpO_2 , CTO and MTO higher when patients were breathing FiO_2 0.5.

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.

PP-120

Mortality of Patients with Long Term Oxygen Therapy Due to Chronic Obstructive Pulmonary Disease – A Population Based Cohort Study

N. Pavlov^{*1}, A. Haynes², A.-K. Brill¹, A. Stucki³, P. Jüni⁴, S.R. Ott¹

¹Universitätsklinik für Pneumologie, Inselspital Bern, ²Institute for Social and Preventive Medicine, Bern, ³Department of Internal Medicine, Spital Thun, Thun, Switzerland; ⁴Applied Health Research Centre, St. Michael's Hospital, Toronto, Canada

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 ($\text{HR} = 1.66$, 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.

PP-121

Postural Control in COPD Patients Travelling from 760 m to 3,200 m; A Randomized Trial Evaluating Effect of Dexamethasone

L. Muralt^{*1}, M. Furian¹, M. Lichtblau¹, S.S. Aeschbacher¹, M. Bisang¹, T.D. Latshang¹, R. Clark², A. Aldashev³, T. Sooronbaev⁴, S. Ulrich¹, K.E. Bloch¹

¹Pulmonary Division and Sleep Disorders Center, University Hospital of Zurich, Zürich, Switzerland; ²School of Exercise Science, Australian Catholic University, Melbourne, Australia;

³Research Institute for Molecular Biology and Medicine,

⁴National Center for Cardiology and Internal Medicine, Bishkek, Kyrgyzstan

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 (3,200 m), Kyrgyzstan. Postural control was assessed with a Wii Balance BoardTM at 760 m and one day after arrival at 3,200 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 3,200 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 30.8, $P = 0.03$) 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 [1].

Conclusion: Lowlanders with COPD travelling from 760 to 3200 m revealed postural instability 24 h 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.

Reference

- 1 Kwok, Clark, et al: Clin Biomech 2015;30:481.

PP-122

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

C. Steurer-Stey^{*1}, J. Braun², V. Gaveikaite², S. Markun¹, K. DallaLana¹, M. Puhon²

¹Institute of primary care, ²Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zürich, Switzerland

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. Puhon: None declared.

PP-123

The Impact of Case Finding on the Recruitment Yield for COPD Research in General Practice: An Observational Study

S. Markun^{*}, T. Rosemann, K. DallaLana, C. Steurer-Stey

Institute of Primary Care, University of Zurich, Zürich, Switzerland

Introduction: Recruiting patients for research in general practice is particularly difficult in diseases that tend to remain under-diagnosed 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% ($p \leq 0.002$) 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.

Dyspnea Is an Independent Predictor of Readmission and Death in Chronic Obstructive Pulmonary Disease Patients Surviving Acute Hypercapnic Respiratory Failure

E. Dupuis¹, P.M. Social², J.P. Janssens³, T. Similowski⁴, D. Adler^{*3}

¹Service de Pneumologie, HUG, Geneva, ²HUG, Genève, ³Service de Pneumologie, HUG, Genève, Switzerland; ⁴Pitié-Salpêtrière, APHP, Paris, France

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. 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. 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.

Modeling of Oxygen Uptake Kinetics during Exercise Testing in Patients with Chronic Obstructive Pulmonary Diseases (COPD)

F. Baty^{*1}, C. Ritz², A. van Gestel¹, M. Brutsche¹, D. Gerhard³

¹Pneumologie, Kantonsspital St. Gallen, St. Gallen, Switzerland;

²Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark; ³School of Mathematics and Statistics, University of Canterbury, Christchurch, New Zealand

Introduction: The 6-Minute Walk Test (6MWT) is routinely used to quantify exercise capacity in patients with chronic cardiopulmonary 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.

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.

Fig. 1. (for Abstract PP-125).

PP-126

Mannose-Binding Lectin Protein and Its Association to Clinical Outcomes in COPD: A Longitudinal Study

J. Mandal¹, B. Malla¹, R. Steffensen², L. Costa¹, A. Egli³, M. Trendelenburg⁴, F. Blasi⁵, K. Kostikas⁶, T. Welte⁷, A. Torres⁸, R. Louis⁹, W. Boersma¹⁰, B. Milenkovic¹¹, J. Aerts¹², G.G. Rohde¹³, A. Lacoma¹⁴, K. Rentsch¹⁵, M. Roth¹, D. Stolz^{*,16}, M. Tamm¹

¹Clinic for Pulmonary Medicine and Respiratory Cell Research, University Hospital Basel, Basel, Switzerland; ²Department of Clinical Immunology, Aalborg University Hospital, Aalborg, Denmark; ³Infection Disease Department, ⁴Department of Biomedicine and Division of Internal Medicine, University Hospital Basel, Basel, Switzerland; ⁵Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milano, Italy; ⁶Pneumology, Thessaly Medical School, Thessaloniki, Greece; ⁷Pneumology, Medical School Hannover, Hannover, South Georgia and the South Sandwich Islands; ⁸Pneumology, Hospital Clinic, Barcelona, Spain; ⁹Pneumology, University of Liege, Liege, Belgium; ¹⁰Pneumology, Medisch Centrum Alkmaar, Alkmaar, Netherlands; ¹¹Faculty of Medicine, University of Belgrade, Clinic of Pulmonary Disease, Belgrade, Serbia; ¹²Pneumology, Amphia Hospital/Erasmus MC, Breda; ¹³Department of Respiratory Medicine, Maastricht University Medical Center, Maastricht, Netherlands; ¹⁴Department of Microbiology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; ¹⁵Department of Laboratorial Medicine, ¹⁶Pneumology, University Hospital Basel, Basel, Switzerland

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 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.

PP-127

On-Line Breath Analysis of COPD Patients Reveals Altered Metabolic Signatures between Frequent and Non-Frequent Exacerbators

M.T. Gaugg^{*1}, Y. Nussbaumer-Ochsner^{*2}, L. Bregy¹, A. Engler², N. Stebler², T. Gaisl², Y. Suter¹, P. Martinez-Lozano Sinues¹, R. Zenobi¹, M. Kohler^{2,3,4}

¹D-CHAB, ETH Zürich, ²Department of Pulmonology, ³Centre for Integrative Human Physiology, ⁴Zurich Centre for Interdisciplinary Sleep Research, UZH, Zürich, Switzerland

* These authors contributed equally to this work

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.

Disclosure of Interest: None declared.

PP-128

Cerebral Tissue Oxygenation in Lowlanders with COPD Spending a Night at 2,590 m

M. Furian^{*1}, D. Flueck¹, P.M. Scheiwiller¹, S. Mueller-Mottet¹, S.E. Hartmann², M. Poulin², B. Osmonov³, L. Urner¹, A. Steiner¹, M. Kohler¹, T.D. Latshang¹, S. Ulrich¹, K.E. Bloch¹

¹Pulmonary Division and Sleep Disorders Center, University Hospital of Zurich, Zurich, Switzerland; ²Department of Physiology and Pharmacology and Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Canada; ³National Center for Cardiology and Internal Medicine, Bishkek, Kyrgyzstan

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 2,590 m.

Methods: 37 COPD patients living below 800 m (mean age $\pm$ SD, 62.4 ± 12.3 y, 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 490 m and in the first night after arrival at 2,590 m.

Results: At 2,590 m, both mean SpO₂ and CTO were significantly decreased compared to 490 m 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 1).

Fig. 1. Heatmap for the most significant compounds detected on-line in exhaled breath of frequent and non-frequent exacerbators (for Abstract PP-127).

Table 1. Effect of altitude on nocturnal arterial and cerebral tissue oxygen saturation (for Abstract PP-128)

	490 m, means $\pm$ SD	2,590 m, means $\pm$ SD	Mean difference (95% CI)
Mean nocturnal SpO ₂ , %	92.0 $\pm$ 2.2	83.6 $\pm$ 4.7	-8.4 (-9.7; -7.0)*
Mean nocturnal CTO, %	65.3 $\pm$ 5.6	61.7 $\pm$ 5.4	-3.6 (-5.6; -1.5)*, †
SpO ₂ -OD, 1/h	8.2 $\pm$ 9.3	41.6 $\pm$ 34.1	33.5 (23.3; 43.7)*
CTO-OD, 1/h	0.9 $\pm$ 1.5	4.0 $\pm$ 5.8	3.1 (1.3; 4.9)*, †
CTO-OD/SpO ₂ -OD	0.14 $\pm$ 0.15	0.11 $\pm$ 0.16	-0.03 (-0.10; 0.05)

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 2,590 m 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.

PP-129

A Human *in vitro* Airway Epithelial Model to Study the Effects of Aerosolized Multi-Walled Carbon Nanotubes in Chronic Obstructive Pulmonary Diseased Cells

S. Beyeler^{*1}, S. Chortarea², B. Rothen-Rutishauser², A. Petri-Fink², S. Tschanz³, C. Von Garnier¹, F. Blank¹

¹Respiratory Medicine, University Hospital, Bern, ²Adolphe Merkle Institute, University of Fribourg, Fribourg, ³Institute of Anatomy, University of Bern, Bern, Switzerland

Introduction: The risks of occupational exposures at working places where engineered nanomaterials (one dimension below 100 nm) 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 (0.12 µg/ml; 0.4 µg/ml). Differentiation, integrity, pro-inflammatory status and viability of cultures were monitored 24 h 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 $\pm$ 2.29 Hz.

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.

PP-130

Exhaled Breath Analysis Identifies Altered Metabolic Signature in Chronic Obstructive Pulmonary Disease

L. Bregy^{*1}, Y. Nussbaumer-Ochsner^{*2}, D. García-Gómez¹, Y. Suter¹, T. Gaisl², N. Stebler², M. Gaugg¹, P. Martinez-Lozano Sinues¹, M. Kohler², R. Zenobi¹

¹Department of Chemistry and Applied Biosciences, ETH Zurich,

²Department of Pulmonology, University Hospital Zurich, Zurich, Switzerland

* These authors contributed equally to this work

Introduction: Diagnosis of chronic obstructive pulmonary disease (COPD) is currently based on fixed airflow limitation in spirometry, respiratory symptoms and an appropriate history of ex-

Fig. 1. Real-time breath analysis (left boxes): time traces of a selected feature (m/z 105.1) for a healthy 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 ($p_{FDR} = 0.02$) (for Abstract PP-130).

posure 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, FEV_1 $58.5 \pm 19.9\%$ predicted, 32.4 ± 19.2 pack years) and 14 controls (mean age 58.1 ± 8.1 years, FEV_1 $102.5 \pm 11.3\%$ 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.

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.

Disclosure of Interest: None declared.

PP-131

Management of Acute Exacerbated COPD in Three Swiss Public Hospitals: Room for Improvement in Key Elements of Care

D.P. Franzen^{*1}, S. Markun², S. Beyer³, S. Wieser⁴, K. DellaLana², T. Hess³, M. Kohler¹, C. Steurer-Stey²

¹Klinik für Pneumologie, UniversitätsSpital Zürich, ²Institut für Hausarztmedizin, Universität Zürich, Zürich, ³Pneumologie, Kantonsspital Winterthur, Winterthur, ⁴Pneumologie, Stadtsptal Waid, Zürich, Switzerland

Introduction: Hospitalizations because of acute exacerbated COPD (AECOPD) are a major burden to patients and the health-care 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 ap-

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.

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.

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.

PP-132

Physical Activity in COPD and Its Relationship to Exercise Performance and Sleep

S. Saxer*, E.D. Hasler, M. Furian, K.E. Bloch, S. Ulrich

Pneumologie, UniversitätsSpital Zürich, Zürich, Switzerland

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. Sensewear™ derived activity was quantified by the mean count of steps/day, daily estimated energy expenditure (EE) over 24 h 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 ± 6 y, FEV1 64 ± 19%pred) were recruited. Patients were moderately active (7120 ± 3492 steps/day), estimated EE was 9166 ± 1085 kJ 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 < 0.05) but not with the 6MWD. The EE

PP-133

Insights into the Recently Launched Alpha-1 Antitrypsin Registry in Switzerland

C.F. Clarenbach, N.A. Sievi, M. Kohler

Klinik für Pneumologie, UniversitätsSpital Zürich, Zürich, Switzerland

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 1) 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

Table 1. (for Abstract PP-132)

	Maximal workload	6 minute walk distance	Apnea/hypopnea index	Nocturnal SpO ₂	Number of desaturations	Oxygen desaturation index
Energy expenditure per day	0.70*	-0.07	0.50*	0.11	0.33	0.33
Average metabolic equivalents per day	0.18	0.39	-0.18	0.52*	-0.48*	-0.51*
Steps/day	0.39	0.14	0.28	0.28	0.10	0.00

Numbers represent Pearson correlation coefficients. * p < 0.05.

Fig. 1. Total number of patients in the Swiss registry (for Abstract PP-133).

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.

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.

PP-134

Cardiopulmonary- and Hemodynamic Responses during Non-Invasive Positive Airway Pressure Ventilation in Patients with Chronic Obstructive Pulmonary Disease

A. Van Gestel, M. Hörner, M. Brutsche, G. Benz, F. Baty
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, Finapres 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 mm Hg/IBI. In 9 healthy controls (5 females) with a mean (SD) age 69 (9) years, the observed mean vSBP at rest of 3.06 mm Hg/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.

PP-135

Telehealthcare in COPD – A Feasibility Trial

F. Rassouli*, M. Pfister, F. Baty, S. Schlotter, M. Brutsche

Klinik für Pneumologie und Schlafmedizin, Kantonsspital St. Gallen, St. Gallen, Switzerland

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.

PP-136

Interferon-Lambda-Genotype GG and IgG2 Predict Frequent COPD Exacerbations in a Swiss Multicenter COPD Cohort Study (TOPDOCS)

S. Henny^{*1}, T. Dieterle¹, T. Brack², M. Brutsche³, C. Clarenbach⁴, A. Egli⁵, I. Heijnen⁶, S. Irani⁷, M. Frey⁸, N. Sievi⁴, R. Thurnheer⁹, M. Trendelenburg¹⁰, M. Kohler⁴, J. Leuppi¹

¹University Clinic of Medicine, Kantonsspital Baselland, Liestal, and Medical Faculty University of Basel, Liestal, ²Internal Medicine, Kantonsspital Glarus, Glarus, ³Respiratory Medicine, Kantonsspital St. Gallen, St. Gallen, ⁴Respiratory Medicine, University Hospital Zurich, Zurich, ⁵Clinical Microbiology, University Hospital Basel, University of Basel, Basel, ⁶Division of Medical Immunology, Department of Laboratory Medicine, University Hospital Basel, Basel, ⁷Respiratory Medicine, Kantonsspital Aarau, Aarau, ⁸Respiratory Medicine, Klinik Barmelweid, Barmelweid, ⁹Respiratory Medicine, Kantonsspital Münsterlingen, Münsterlingen, ¹⁰Division of Internal Medicine and Department of Laboratory Medicine, University Hospital Basel, Basel, Switzerland

Introduction: 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

Table 1. (for Abstract PP-136)

Parameter	0 exacerbations	1 exacerbations	2 exacerbations	p (ANOVA)
MBL (µg/ml)	1.62 (±1.46)	1.85 (±1.58)	1.78 (±1.80)	0.570
IgG (g/l)	9.7 (±3.0)	8.9 (±2.2)	8.6 (±2.4)	0.018
IgA (g/l)	2.4 (±1.0)	2.6 (±1.3)	2.3 (±2.0)	0.245
IgM (g/l)	1.0 (±0.6)	1.1 (±0.8)	1.1 (±2.0)	0.875
IgE (IU/ml)	117.8 (±317.5)	285.1 (±929.2)	143.3 (±560.9)	0.149
IgG1 (g/l)	6.2 (±2.2)	5.8 (±1.1)	5.9 (±1.8)	0.237
IgG2 (g/l)	3.1 (±1.6)	2.8 (±1.1)	2.4 (±1.0)	0.001
IgG3 (g/l)	0.4 (±0.2)	0.4 (±2)	0.4 (±0.2)	0.394
IgG4 (g/l)	0.5 (±0.5)	0.6 (±0.6)	0.5 (±0.5)	0.557

Table 2. (for Abstract PP-136)

Parameter	0 exacerbations	1 exacerbations	2 exacerbations	p (Chi-square of Pearson)
Gemotype TT yes/no	33/98	28/46	18/47	0.153
Gemotype TG yes/no	42/89	28/46	27/38	0.395
Gemotype GG yes/no	0/131	1/73	3/62	0.042

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 $\pm$ standard deviation, the ANOVA-p-value of the measured biomarkers and the Chi-square of Pearson of the genotypes are shown in the following tables 1, 2.

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.

PP-137

Value of Clinical Characteristics as Predictors of Frequent Exacerbations in a Swiss Multicenter COPD Cohort Study (TOPDOCS)

S. Henny^{*1}, T. Dieterle¹, T. Brack², M. Brutsche³, C. Clarenbach⁴, S. Iran⁵, M. Frey⁶, N. Sievi⁴, R. Thurnheer⁷, M. Kohler⁴, J. Leuppi¹

¹University Clinic of Medicine, Kantonsspital Baselland, Liestal, and Medical Faculty University of Basel, Liestal, ²Internal Medicine, Kantonsspital Glarus, Glarus, ³Respiratory Medicine, Kantonsspital St. Gallen, St. Gallen, ⁴Respiratory Medicine, University Hospital Zurich, Zurich, ⁵Respiratory Medicine, Kantonsspital Aarau, Aarau, ⁶Respiratory Medicine, Klinik Barmelweid, Barmelweid, ⁷Respiratory Medicine, Kantonsspital Münsterlingen, Münsterlingen, Switzerland

Introduction: 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 $\pm$ 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 $\pm$ standard deviation and the ANOVA-p-value of different clinical parameters are shown in the following table 1.

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 1. (for Abstract PP-137)

Parameter	0 exacerbations	1 exacerbations	2 exacerbations	p (ANOVA)
COPD assessment test	13.9 (± 7.1)	16.3 (± 6.7)	19.3 (± 6.9)	0.000
Short from-6 dimension V1 questionnaire	0.7 (± 0.1)	0.7 (± 0.1)	0.6 (± 0.1)	0.000
Short from-6 dimension V2 questionnaire	0.7 (± 0.1)	0.7 (± 0.1)	0.6 (± 0.1)	0.000
GOLD (Global Initiative for Obstructive Lung Disease)	2.3 (± 0.9)	3.0 (± 0.8)	3.2 (± 0.8)	0.000
MMRC (Modified Medical Research Council dyspneascale)	1.4 (± 1.1)	2.0 (± 1.0)	2.2 (± 0.9)	0.000
Weight (kg)	80.3 (± 20.0)	75.2 (± 18.8)	70.6 (± 19.2)	0.004
Heart rate (bpm)	74.6 (± 13.5)	80.6 (± 11.5)	84.7 (± 13.6)	0.000
SO ₂ (%)	94.3 (± 3.0)	92.8 (± 4.1)	93.6 (± 3.7)	0.023
FEV1/FVCex posr % soll	66.0 (± 20.1)	53.2 (± 15.5)	48.1 (± 16.1)	0.000
Thrombocytes ($\times 10^9/l$)	248.8 (± 68.0)	267.0 (± 74.1)	287.2 (± 70.9)	0.002
Bilirubin ($\mu mol/l$)	8.7 (± 4.5)	9.4 (± 4.6)	6.6 (± 2.5)	0.007

Poster Walk SSC/SSCS 2: Sleep Rehab Physiology

PP-138

Sleep Disordered Breathing in Morbidly Obese Patients Prior to Bariatric Surgery – A Retrospective Analysis of a Single Centre Cohort

C.M. Horvath^{*,1,2}, J. Jossen¹, A.-K. Brill¹, P. Nett³, S.R. Ott¹

¹Pulmonary Medicine, Inselspital, University Hospital of Berne, Berne, ²Sleep Medicine and Pneumology, Kantonsspital St. Gallen, St. Gallen, ³Visceral Surgery and Medicine, Inselspital, University Hospital of Berne, Berne, Switzerland

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.

PP-139

How Do Patients Adhere to Chronic Treatment of Pulmonary Diseases? Preliminary Data from a Randomized Controlled Trial

C. Gregoriano^{*,1,2}, S. Henny-Reinalter¹, S. Maier¹, A.-L. Flamm¹, T. Dieterle^{1,3}, I. Arnet², K.E. Hersberger², J.D. Leuppi¹

¹University Department of Medecine, Cantonal Hospital Baselland, Liestal, ²Pharmaceutical Care Research Group, ³Faculty of Medicine, University of Basel, Basel, Switzerland

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 ($80\% \pm 19\%$ versus $51\% \pm 21\%$; $p < 0.001$). Regarding powder capsules, no difference was found between intervention and control group ($92\% \pm 9\%$ versus $88\% \pm 14\%$; $p = 0.239$). Overall, more days with correct dosing were observed for powder capsules compared to puff inhalers ($88\% \pm 12\%$ versus $66\% \pm 27\%$; $p < 0.001$) and for therapy plans with once-daily dosage compared to plans with multiple doses per day ($89\% \pm 13\%$ versus $66 \pm 27\%$; $p < 0.001$).

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.

Determination of Coordination Patterns in Preterm Infants by Esophageal Signal Recording

K. Jost¹, M. Thomet², L. Suter¹, S. Schulzke¹, A. Haeberlin^{3,4}, T. Niederhauser^{*2}

¹Department of Neonatology, University of Basel Children's Hospital (UKBB), Basel, ²Institute for Human Centered Engineering HuCE, Bern University of Applied Sciences, Biel, ³Department of Cardiology, Inselspital, Bern University Hospital, ⁴ARTORG Center for Biomedical Engineering Research, University of Bern, Bern, Switzerland

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 500 g 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.

Fig. 1. (for Abstract PP-140).

Fig. 2. (for Abstract PP-140).

PP-141

Effect of Continuous Positive Airway Pressure on Circadian Patterns of Cardiac Repolarization in Obstructive Sleep Apnoea: Data from a Randomized Controlled Trial

C. Schlatzer^{*1}, D.J. Bratton¹, E.I. Schwarz¹, T. Gaisl¹, J.C. Pepperell², J.R. Stradling², M. Kohler¹

¹Klinik für Pneumologie, UniversitätsSpital Zürich, Zürich, Switzerland; ²Oxford Centre for Respiratory Medicine and NIHR Oxford Biomedical Research Centre, Churchill Hospital, Oxford, United Kingdom

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 24 h-Holter monitoring data. Weighted means of all QTc-intervals were analysed over 24 h, during four time-periods (12 pm–6 am, 6 am–12 am, 12 am–6 pm, 6 pm–12 pm) as well as during each hour.

Results: QTc-intervals at baseline were highest from 6 pm–12 pm (411.7 ms) and shortest from 6 am–12 am (405.4 ms). Overall 24 h CPAP treatment effect on QTc was –11.3 ms ($p = 0.039$) and was estimated to be greater from 6 pm–12 pm than from 12 pm–6 am ($p = 0.068$). The CPAP treatment effect on QTc was driven by those patients in the highest QTc decile at baseline (all >430 ms). In these patients, CPAP allowed reclassification into lower risk associated values of QTc <430 ms.

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 >430 ms.

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PP-142

Resistive Work of Breathing as Target Parameter Evaluating Methacholine Challenge to Assess Airway Hyperreactivity in Comparison to Other Lung Function Parameters

R. Kraemer^{*1,2}, J. Salomon², M. Gürtler², S. Minder²

¹Department of Clinical Research, Faculty of Medicine, University of Berne, ²Centre of Pulmonary Medicine, Hirslanden Private Hospital Group, Berne, Switzerland

Introduction: We have recently shown, that effective specific airway conductance ($sG_{eff} = 1/sR_{eff}$) features a sensitive target parameter differentiating severity of airway hyperreactivity (AHR), performed by methacholine (MCH) challenge tests using a plethysmograph. sG_{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_{eff} , FEV₁ and MEF₅₀, computing sensitivity and specificity by the ROCCT software (<http://www.rocct.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 (PD₁₅₀sWOB, PD₄₀sG_{eff}, PD₂₀FEV₁, PD₂₀MEF₅₀).

Results: Best sensitivity (s) and corresponding PD for MCH was found for PD₁₅₀sWOB ($s = 85.9\%$ at 1.26 mg), followed by PD₄₀sG_{eff} ($s = 79.7\%$ at PD 0.64 mg), PD₂₀FEV₁ ($s = 70.9\%$ at 1.42 mg), and PD₂₀MEF₅₀ ($s = 65.2\%$ at 0.52 mg). Noteworthy, lowest PD were need for PD₂₀MEF₅₀, highest for PD₂₀FEV₁. Best response to MCH, and hence discrimination between mild, moderate or severe AHR, was detected by PD₄₀sG_{eff} (67.2%), followed by PD₂₀MEF₅₀ (51.4%), PD₁₅₀sWOB (47.7%), and PD₂₀FEV₁ (25.8%).

Conclusion: In comparison to standard lung function parameters sWOB features 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.

PP-143

Metabolic Effects of Inhaled Salbutamol Determined by Exhaled Breath Analysis

P.M.-L. Sinues^{*1}, Y. Nussbaumer-Ochsner^{*2}, L. Bregy¹, A. Engler², T. Gaisl², M.T. Gaugg², D. Garcia Gomez¹, Y. Suter¹, R. Zenobi¹, M. Kohler²

¹ETH Zurich, ²University Hospital Zurich, Zurich, Switzerland

* Equal contribution

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 µg 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

Fig. 1. (for Abstract PP-143).

unknown metabolite displaying a decreasing trend upon salbutamol inhalation. The average decrease after 10 and 30 min was -5.2 and -7.8%, respectively.

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.

Disclosure of Interest: None declared.

Reference

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PP-144

Comparison of Ventilator-Integrated End-Tidal CO2 and Transcutaneous CO2 Monitoring in Home-Ventilated Neuromuscular Patients

D. Orlikowski^{1,2}, H. Prigent³, F. Lofaso³, A. Ogna^{*2,4}

¹INSERM CIC 14.29, ²Service de Réanimation Médicale et Unité de Ventilation à Domicile, ³Service de Physiologie-Explorations Fonctionnelles, CHU Raymond Poincaré, Garches, France;

⁴Service de Pneumologie, CHUV, Lausanne, Switzerland

Introduction: Non-invasive transcutaneous capnometry (TcCO₂) is increasingly used to assess the home ventilation's efficiency, allowing to detect episodes of transient hypoventilation,

Fig. 2. (for Abstract PP-143).

that are not detected by punctual blood gases. 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 mm Hg and 0.6 mm Hg, respectively) and a similar critical difference (6.8 mm Hg and 7.3 mm Hg, respectively).

We found a good correlation between ETCO₂ and TcCO₂, both considering the mean nocturnal PCO₂ ($r = 0.897$, $p < 0.001$; bias −1.1 [−9.0; 6.9] mm Hg) and the maximal PCO₂ value over the night ($r = 0.905$, $p < 0.001$; bias 3.1 [−4.5; 10.8] mm Hg). 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 mm Hg and $r = 0.943$ ($p < 0.001$) for the time with PCO₂ >50 mm Hg.

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.

PP-145

The Prevalence of Airway Hyperresponsiveness to Mannitol Challenge Test among Water Pipe Smoking Young Adults in Switzerland

A. Scherr, J. Schmidlin, S. Albisser, A. Meyer, M. Tamm, D. Stolz

Pneumology, Universitätsspital Basel, Basel, Switzerland

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 (AridolTM, 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 (PD₁₅), 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.

PP-146

Short-Term Effects of Adaptive Servo Ventilation Withdrawal on Sleep Disordered Breathing in Stable Congestive Heart Failure Patients after the SERVE-HF Safety Warning

A.-K. Brill, J. Pichler Hefti, T. Geiser, S.R. Ott

Pulmonary Medicine, University Hospital (Inselspital) and University Bern, Bern, Switzerland

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% (IQR 25.45)) 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 them-

selves 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.

PP-147

A Descriptive Analysis of Pulmonary Rehabilitation Trends in Switzerland

P.-O. Bridevaux^{*,1,2}, M. Frey³, A. Turk⁴ and Working Group on Pulmonary Rehabilitation and Patient Education of the Swiss Respiratory Society

¹Service de Pneumologie, Hôpital du Valais, Sion, ²Service de Pneumologie, Hôpitaux Universitaires de Genève, Geneva, ³Reha Klinik, Barmelweid, Barmelweid, ⁴Pneumologie, Universitätsspital Zurich, Wald, Switzerland

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.

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.

PP-148

Prognostic Value of Nocturnal Hypoventilation in Unventilated Neuromuscular Disease Patients

A. Ogna^{*,1,2}, H. Prigent³, M.A. Quera Salva⁴, F. Lofaso³, D. Orlikowski^{1,5}

¹Service de réanimation médicale et Unité de ventilation à domicile, CHU Raymond Poincaré, Garches, France; ²Service de Pneumologie, CHUV, Lausanne, Switzerland; ³Service de Physiologie-Explorations Fonctionnelles, ⁴Unité du sommeil, ⁵INSERM CIC 14.29, CHU Raymond Poincaré, Garches, France

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 capno-oxymetry (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

Table 1. (for Abstract PP-147)

	Inpatient PR			Outpatient PR		
	2005	2010	2014	2005	2010	2014
Active programs	10	10	10	58	58	55
Enrolled patients	4,773	5,090	5,542	1,353	1,537	2,060
COPD, n (%)	2,052 (43.0%)	1,776 (34.9%)	2,006 (36.2%)	596 (44.1%)	956 (62.2%)	1,157 (56.2%)
Asthma, n (%)	1,427 (29.9%)	1,527 (30.0%)	1,003 (18.1%)	269 (19.9%)	170 (11.1%)	86 (4.2%)
Interstitial lung disease, n (%)	91 (1.9%)	203 (4.0%)	310 (5.6%)	48 (3.6%)	64 (4.2%)	119 (5.8%)
Pre or post thoracic surgery, n (%)	195 (4.1%)	447 (8.8%)	393 (7.1%)	58 (4.3%)	58 (3.8%)	82 (4.0%)

excluded. Nocturnal hypoventilation was defined as (1) TcCO₂ >55 mm Hg for ≥10 minutes or increase in TcCO₂ ≥10 mm Hg (in comparison to an awake supine value) to a value exceeding 50 mm Hg for ≥10 minutes, (2) peak TcCO₂ ≥49 mm Hg, and (3) mean TcCO₂ >50 mm Hg. Onset of mechanical ventilation and mortality were collected as outcomes of interest.

Results: 124 patients with normal daytime blood gases 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 mm Hg 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 capno-oxymetry 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.

PP-149

Use of Home Ventilators for Ventilatory Support during Magnetic Resonance Imaging

A. Ogn^a*,^{1,2}, X. Ambrosi¹, H. Prigent³, D. Orlikowski^{1,4}, F. Lofaso³

¹Service de réanimation médicale et Unité de ventilation à domicile, CHU Raymond Poincaré, Garches, France; ²Service de Pneumologie, CHUV, Lausanne, Switzerland; ³Service de Physiologie-Explorations Fonctionnelles, ⁴INSERM CIC 14.29, CHU Raymond Poincaré, Garches, France

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 Bennett 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.

PP-150

Severe Asthma – 5 Years of Phenotyping Patients

V. Seif^a*,¹, T. Rothe¹, L. Grize²

¹Zürcher RehaZentrum Davos, Davos Clavadel, ²Swiss TPH Basel, Basel, Switzerland

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 atopic (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.

PP-151

Think Primary Ciliary Dyskinesia in Adult Patients with Bronchiectasis

S. Filippi^{*1}, A. Jung², M. Hofer¹, T. Hess¹

¹Pneumologie, Kantonsspital Winterthur, Winterthur,

²Pneumologie, Universitäts Kinderspital, Zürich, Switzerland

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 AerocrineTM). In case of nNO levels <100 ppb or clinically high suspicion for PCB we conducted a HVMA (SAVATM 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.

Table 1. (for Abstract PP-151)

	P1 (60 years)	P2 (20 years)
FeNO	<5 ppb	<5 ppb
nNO (right/left)	8/15 ppb	109/116 ppb
HSVMA (2x)	+/+	+/pending
TEM	-	-
Chr. productive cough	+	+
Chr. rhinosinusitis	+	+
Otitis media	-	+
Bronchiectasis	tubular	cystic
Sputum microbiology	mucoïd P. aeruginosa	H. influenzae
Lung function		
FEV1/VC	71%	85%
FEV1	1.47L (76%)	3.67L (84%)
VC	2.07L (89%)	4.29L (80%)
TLC	3.78L (89%)	5.96L (85%)
RV	1.71L (101%)	1.67L (103%)
RV/TLC	45%	28%

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.

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.

Disclosure of Interest: None declared.

PP-152

Light Chain Deposition Disease: A Rare Cause of Multiple Cystic Lung Disease

A. Lenoir^{*1}, E. Clottu¹, J. Mazza-Stalder¹, A. Cairolì², I. Letovanec³, S. Rotman³, R. Lazor¹

¹Service de Pneumologie, ²Service d'Hématologie, ³Institut Universitaire de Pathologie, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

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 k 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 bendamustine 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.

PP-153

High-Altitude Climate-Therapy in Hochgebirgsklinik Davos – An Important Therapeutical Option to Treat Asthma!

H.-W. Duchna*

Hochgebirgsklinik Davos, SGP, Davos, Switzerland

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.

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PP-154

Raclette-Induced Dyspnea – A Swiss Case Report

S.P. Descombes^{*1}, S. Jegerlehner², T. Geiser¹, M. Funke¹

¹Universitätsklinik für Pneumologie, ²Universitätsklinik für Allgemeine Innere Medizin, Inselspital Bern, Bern, Switzerland

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.

PP-155

When Sleep Medicine Meets Cardiology – Unusual First Manifestation of an Arrhythmogenic Right Ventricular Dysplasia (ARVC)

C.M. Horvath^{*1}, S. Zbinden², S.R. Ott¹, A.-K. Brill¹

¹Department of Pulmonary Medicine, ²Cardiology, University Hospital and University of Berne, Berne, Switzerland

Introduction: 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: 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 hypop-

neas, 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: 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 (ARVC). 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.

PP-156

Oxygen Transport at High Altitude and Effects of Acclimatization

J. Pichler Hefti^{1,*}, T. Merz²

¹Department of Pulmonary Medicine, University and University Hospital, ²Department of Intensive Care Medicine, Inselspital, University and University Hospital Bern, Bern, Switzerland

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 24.6 mm Hg and oxygen content (CaO₂) of 145.8 ml/L at 8400 m 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 7000 m.

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 (7126 m) at baseline 550 m (before/after the expedition), twice at 4800 m (day 5 and day 17/18), at 6050 m (day 11) and 7050 m (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 7050 m (n = 12; 2 female) was evaluated. SaO₂ decreased significantly with increasing altitude from mean 97.3% at baseline to 68.8% at 7050 m and paO₂ decreased from mean 93.1 mm Hg to 42.7 mm Hg at 4800 m and to 30.4 mm Hg at 7050 m (p < 0.0001). There was no significant difference in hb levels at baseline and 4800 m (day 5), but a significant increase was found when comparing baseline levels with measurements on day 17/18 at 4800 m (p < 0.0001) and on day 21/22 at 7050 m (p < 0.0001). Compared to baseline CaO₂ decreased significantly from a mean of 198.7 ml/L at baseline to 170.7 ml/L (-14.1%, p < 0.01) at 4800 m, and to 161.7 ml/L (-18.7%, p < 0.001) at 7050 m. After acclimatization CaO₂ increased significantly by 18.1% from 170.7 to 202.9 ml/L when comparing the two measurements at 4800 m on day 5 and day 17/18 (p < 0.001). Levels of DO₂ showed normal values throughout. Compared to baseline (1093 ml/min) even increased values of 1325 ml/min were found at 7050 m (p < 0.05).

Conclusion: Hypobaric hypoxia at extreme altitude leads to a significant fall in SaO₂ and paO₂. Acclimatization assures normal CaO₂ values at 4800 m. Additional increase in cardiac output can provide normal oxygen delivery even at an altitude of 7050 m.

Disclosure of Interest: None declared.

Poster Walk SSC/SSCS 1: PAH-Tx

PP-157

Composite Clinical Worsening Endpoint in Paediatric PAH – Clinically Meaningful and Feasible for Clinical Research

M. Beghetti^{1,*}, M. Brand², R. Berger³, T. Humpf⁴, J. Wheeler⁵, D. Ivy⁶, D. Bonnet⁷ and on behalf of the TOPP investigators

¹Pediatric Cardiology, University Hospital, Geneva, ²Global Clinical Science, Actelion, Basel, Switzerland; ³Paediatric Cardiology, University of Groningen, Groningen, Netherlands; ⁴Pediatric Cardiology and Critical Care Medicine, University of Toronto, Toronto, Canada; ⁵Quanticate, London, United Kingdom; ⁶Paediatric Cardiology, University of Colorado School of Medicine, Aurora, United States; ⁷Paediatric Cardiology, Necker Hospital for Sick Children, Paris, France

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-Paediatric-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 ($\pm$ 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 parenteral 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.

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PP-158

In-Hospital Disease Burden of Sarcoidosis in Switzerland from 2002 to 2012

S. Pohle, F. Baty, M. Brutsche

Kantonsspital St. Gallen, St. Gallen, Switzerland

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.

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.

¹Pneumology, University Hospital Basel, ²Department of Paediatric Pneumology, University Childrens Hospital Basel (UKBB), Basel, ³Division of Respiratory Medicine, Department of Paediatrics, University Children's Hospital of Bern, Bern, ⁴Division of Hematology, ⁵Institute of Pathology, University Hospital Basel, Basel, Switzerland

(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

Fig. 1. (for Abstract PP-158).

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 N_2 -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 ($p = 0.001$). 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 $FEV_1\%VC_{max}$ was elevated only in 57% of patients. In general, and independent of the clinical group, a high proportion of patients with normal values in $FEV_1\%VC_{max}$ showed elevated LCI results.

Conclusion: LCI seems more sensitive compared to $FEV_1\%VC_{max}$ to detect small airway disease in patients after alloSCT. It is therefore tempting to hypothesize that N_2 -MBW may also be helpful for early diagnosis of BO in asymptomatic patients following alloSCT.

Disclosure of Interest: None declared.

PP-160

Evaluation of Comorbid Conditions in Lung Transplant Recipients

O. Bilat^{*,1}, A. Koutsokera², J.-P. Antonietti¹, M.-F. Derkenne², P.M. Soccia³, A.-K. Brill⁴, P. Grendelmeier⁵, L.P. Nicod², J.-D. Aubert²

¹Faculté de Biologie et Médecine, Université de Lausanne,

²Service de Pneumologie, CHUV, Lausanne, ³Service de Pneumologie, HUG, Genève, ⁴Pneumologie Abteilung, Inselspital, Bern, ⁵Pneumologie Abteilung, Unispital, Basel, Switzerland

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,

Fig. 1. (for Abstract PP-160).

others for 8. Comorbid conditions before and at one year after lung transplantation are shown in figure 1. 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.

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

Hyperoxia Enhances Exercise Performance in Pulmonary Arterial and Chronic Thromboembolic Pulmonary Hypertension: Randomized Trial

S. Ulrich*, H.D. Elisabeth, S. Saxer, M. Furian, S. Müller-Mottet, S. Keusch, K.E. Bloch

Pneumologie, Universitätsspital Zürich, Zürich, Switzerland

Introduction: Pulmonary hypertension impairs cardiac output, oxygen delivery and thus exercise capacity.

Methods: 22 stable PAH/CTEPH patients (8 women, 61 ± 14 y, mPAP 35 ± 10 mm Hg) underwent 4 bicycle ergospirometries 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%W_{max}, 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 1), 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.

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.

PP-162

Heart Rate Variability in Lung Transplant Recipients

T. Fontolliet*,¹, P. Gianella², V. Pichot³, P.M. Soccia², G. Ferretti¹, F. Lador²

¹APSI, UNIGE, ²Pneumologie, HUG, Genève, Switzerland; ³UJM, Saint-Etienne, France

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

Table 1. (for Abstract PP-161)

	End of progressive ramp		End of constant load	
	FiO ₂ 0.21	FiO ₂ 0.50	FiO ₂ 0.21	FiO ₂ 0.50
Endurance, s	552±111	645±136*	617±440	1,257±503*
Work rate, watts	113±38	132±48*	85±29	85±29
V'O ₂ , l/min	1.4±0.4	2.2±0.5*	1.4±0.4	1.8±0.5*
Heart rate, 1/min	130±18	137±21*	138±17	132±16
V'E, l/min	62±17	65±18*	65±19	60±14
V'E/V'CO ₂	41±9	37±7*	46±9	40±7*
SpO ₂ , %	90±6	98±2*	89±7	99±1*
CTO, %	61±9	71±7*	62±9	69±8*
MTO, %	61±8	65±11*	61±9	66±10*
Borg CR10, dyspnea	6±2	5±2	6±2	4±2*

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.

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 (0.25 Hz) 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.

PP-163

Kinetics of Cardiac Output at the Onset of Exercise in Pre-Capillary Pulmonary Hypertension

F. Lador^{*1,2}, A. Bringard³, S. Bengueddache², G. Ferretti³, K. Bendjelid^{1,3}, P.M. Soccia^{1,2}, S. Noble^{1,4}, M. Beghetti^{1,5}, D. Chemla⁶, P. Hervé⁶, O. Sitbon⁶

¹Programme Hypertension Pulmonaire, ²Pneumologie, ³APSI, ⁴Cardiologie, ⁵Cardiologie Pédiatrique, HUG, Genève, Switzerland; ⁶Pneumologie, Hôpital de Bicêtre, Paris, France

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.

PP-164

Platelet-Derived Growth Factor-BB Induced Fibroblast Remodeling Depends on Erk1/2 and Stat1 Activation Which Controls Protein Arginine Methyltransferase-1 Expression

Q. Sun^{*1,2}, L. Liu², J. Mandal³, A. Molino⁴, D. Stolz³, M. Tamm³, S. Lu², M. Roth^{1,3}

¹Biomedicine, University of Basel, Basel, Switzerland;

²Biochemistry and Molecular Biology, Jiaotong University Health Science Center, Xi'an, China; ³Pneumology, University Hospital Basel, Basel, Switzerland; ⁴Respiratory Diseases, University of Naples, Federico II, Naples, Italy

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

Spontaneous Flow Increase from Implantable Pump for Intravenous Treprostinil Delivery

G. Kopp^{*1,2}, A.-L. Hachulla^{3,4}, S. Noble^{4,5}, P.M. Soccà^{1,4}, M. Beghetti^{4,6}, F. Lador^{1,4}

¹Pneumologie, ²Médecine Interne Générale, ³Radiologie,

⁴Programme Hypertension Pulmonaire, ⁵Cardiologie,

⁶Cardiologie Pédiatrique, HUG, Genève, Switzerland

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 20 ml, Tri-cumed, 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 $\pm$ 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 40 ml). Similarly, we observed a progressive increase in the flow rate up to 1.52 ml/day (+20%) while theoretically calibrated at 1.27 ml/day ($\pm$ 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 Lenus-Pro pump, without significant complications. Nevertheless, follow-up length was limited and studies included only small collec-

tives. 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

Acute Complications after Lung Transplantation: Radio-Pathological Correlation

C. Habre¹, A.-L. Hachulla^{*1,2}, J. Gariani¹, S. Martin¹, L. Lücker³, F. Lador^{2,3}, J.-C. Pache⁴, P.M. Soccà^{2,3}, X. Montet^{1,2}

¹Division of Radiology, ²Pulmonary Hypertension Program,

³Department of Pneumology, ⁴Department of Pathology, Hôpitaux Universitaires de Genève, Genève, Switzerland

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.

Generation of an Immortalized Functional Alveolar Epithelial Cell Line from Human Induced Pluripotent Stem Cells

A. Gazdhar^{*1}, L. Tamo¹, Y. Hibaoui², S. Kallol³, M. Alves⁴,
C. Albrecht³, A. Feki⁵, T. Geiser¹

¹Department of Pulmonary Medicine, University Hospital Bern, Bern, Switzerland; ²Department of Gynecology, University Hospital Geneva, Geneva, South Sudan; ³Department of Molecular Medicine, University of Bern, ⁴Department of Pediatric Pneumology, University Hospital Bern, Bern, ⁵Department of Gynecology, Kanton Spital Fribourg, Fribourg, Switzerland

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 reprogramed 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, more-over 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 and 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.

Functional Pulmonary Perfusion with Dual-Energy CT in Children with Pulmonary Hypertension, Preliminary Results

A.-L. Hachulla^{*1,2}, F. Lador^{1,3}, S. Noble^{1,4}, J. Gariani², M. Laurent²,
X. Montet^{1,2}, Y. Aggoun⁵, M. Beghetti^{1,5}, J.-P. Vallée^{1,2}

¹Pulmonary Hypertension Program, ²Division of Radiology, ³Department of Pneumology, ⁴Department of Cardiology, ⁵Department of Pediatric Cardiology, Hôpitaux Universitaires de Genève, Genève, Switzerland

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 1.3 mSv 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_{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 ($C_{lung} = 2.0$); surrounded by normal morphological areas with normal ($C_{lung} = 5.3$) or moderate hypoperfusion ($C_{lung} = 2.9$).

1 patient had right pulmonary artery hypoplasia responsible for extensive and severe right lung hypoperfusion ($C_{lung} = 1.2$) but normal left lung perfusion ($C_{lung} = 3.8$). The last patient had chronic pulmonary embolism due to tricuspid endocarditis with severe systematized hypoperfusion defects ($C_{lung} = 0.8$).

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.

Use of Macitentan (Endothelin Receptor Antagonist) in Children

D. Hutter*, J.-P. Pfammatter

Cardiology, Inselspital, Bern, Switzerland

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 10 mg 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 5 mg is achieved.

Disclosure of Interest: None declared.

Dual Energy CT – The New V/Q Scan for the Diagnosis of CTEPH?

T. Frauenfelder¹, S. Baumüller¹, T. Pfammatter¹, S. Ulrich², R. Speich², M. Kohler², W. Weder³, I. Opitz^{*,3}

¹Institute of Diagnostic and Interventional Radiology,

²Department of Pulmonology, ³Division of Thoracic Surgery, University Hospital Zurich, Zurich, Switzerland

Introduction: The present case demonstrates the diagnostic accuracy of computed tomography imaging for the diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH).

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 mm Hg and PVR of 305 dynes.

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.

Fig. 1. Good correspondence between dual-energy-CT (left) and V/Q scan, fused with CT (right) (for Abstract PP-170).

PP-171

Dual-Energy CT Imaging of Pulmonary Hypertension

A.-L. Hachulla^{*,1,2}, F. Lador^{2,3}, J. Gariani¹, P.M. Soccia^{2,3},
M. Beghetti^{2,4}, X. Montet^{1,2}

¹Division of Radiology, ²Pulmonary Hypertension Program,

³Department of Pneumology, ⁴Department of Pediatric Cardiology, Hôpitaux Universitaires de Genève, Genève, Switzerland

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.

Poster Walk SSC/SSCS 2: Bronchoscopy-Cancer

PP-172

Electrospray: A Novel Method for Targeted Drug Delivery

P. Ruzgys¹, S. Bohringer², S. Satkauskas³, D. Hradetzky⁴, T. Geiser¹,
A. Gazdhar^{*,1}

¹Department of Pulmonary Medicine, University Hospital Bern, Bern, Switzerland; ²Institut für Medizinal-und Analysetechnologie, FHNW, Muttensz, South Sudan;

³Department of Biophysics, University of Kaunas, Kaunas, Lithuania; ⁴Institut für Medizinal-und Analysetechnologie, FHNW, Muttensz, Switzerland

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 relieving the airway obstruction.

Methods: C57BL mice were injected with 2×10^5 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 $22.46 \text{ mm}^3 \pm 12.14 \text{ mm}^3$. Similar effect was observed after Cisplatin spray $43.01 \text{ mm}^3 \pm 16.92 \text{ mm}^3$ while control tumour growth at same day was $514.30 \pm 104.50 \text{ mm}^3$.

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.

Endobronchial Coil-Spring Fiducial Markers Guiding Cyberknife® Stereotactic Radiosurgery for Medically Inoperable Early Stage Non-Small Cell Lung Cancer Patients

A. Casutt^{*1}, M. Bernasconi¹, A. Durham², M. Ozsahin², L. Nicod¹, A. Lovis¹

¹Pneumology, ²Radiation Oncology, CHUV, Lausanne, Switzerland

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.

Immunocompromised Status Is Not a Risk Factor for Surgical Lung Biopsy

K. Furrer^{*1}, C. Nebiker², L. Junker³, S. Lazdinyte¹, S. Savic⁴, K. Hostettler³, D. Schumann¹, J. Halter⁵, M. Tamm³, D. Lardinois¹

¹Thoracic Surgery, ²Visceral Surgery, ³Pneumology, ⁴Pathology, ⁵Haematology, University Hospital Basel, Basel, Switzerland

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.

Reference

- 1 Fibla JJ, Brunelli A, Cassivi SD, Deschamps C: Aggregate risk score for predicting mortality after surgical lung biopsy for interstitial lung disease. *Interact Cardiovasc Thorac Surg* 2012;15:276–279.

PP-175**Multiplex Bacterial PCR in the Bronchoalveolar Lavage of Immunocompromised Patients**

K. Affolter¹, M. Tamm², K. Jahn², L. Junker², R. Frei³, A. Egli⁴, D. Stolz^{*,5}

¹Department of Respiratory Medicine, University Hospital Basel, Basel, South Sudan; ²Clinic for Pulmonary Medicine and Respiratory Cell Research, ³Department of Microbiology, ⁴Infection Disease Department, ⁵Pneumology, University Hospital Basel, Basel, Switzerland

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 Unyvero 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.

PP-176**Operative Stabilisation of Chest Wall Trauma: Single Center Report of Initial Management and Longterm Outcome**

C. Michelitsch^{*,1}, Y.P. Acklin², G. Hässig¹, C. Sommer², M. Furrer¹

¹Department of Surgery, Thoracic Unit, ²Department of Surgery, Trauma Unit, Kantonsspital Graubünden, Chur, Switzerland

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 occurred.

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.

PP-177**24 h-Blood Profile Gene Expression Biomarkers of the Response to Bevacizumab-Erlotinib (BE) in Advanced Non-Squamous Non-Small Cell Lung Cancer (NSCLC)**

F. Baty^{*,1}, M. Früh², M. Jörger², M. Brutsche¹

¹Pneumologie, ²Oncology, Kantonsspital St. Gallen, St. Gallen, Switzerland

Introduction: Combined targeted therapies represent novel therapeutic approaches simultaneously acting on several specific molecular pathways in cancer. Patients not harboring driver muta-

tions 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 24 h 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 24 h 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 24 h 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), MPAK signaling pathway (DAPK2, PLD1, MMP9), and mTOR signaling pathway (BIRC3). The magnitude of change over 24 h 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 24 h 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 24 h 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.

PP-178

Quality of Life in Octogenarians after Thoracic Surgery

W. Moersig, A. Hiebinger, S. Lazdinyte, D. Schumann, D. Lardinois

Thoracic Surgery, University Hospital Basel, Basel, Switzerland

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

Near-Infrared Fluorescence Is Useful for Identification of the Intersegmental Plane in Thoracoscopic Lung Segmentectomy

B. Bédard^{*1}, S. Guigard¹, F. Triponez¹, M. Licker², W. Karenovics¹

¹Surgery, ²Anesthesiology, Geneva University Hospitals, Geneva, Switzerland

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.

Conclusion: Fluorescence imaging provides a technical assistance for intersegmental plane identification in VATS, and facili-

Fig. 1. (for Abstract PP-179).

tates 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.

References

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PP-180

Lung Volume Reduction Therapy in CHUV: A Medico-Economical Assessment of 3 Different Modalities

A. Casutt^{*,1}, R. Bensaker¹, A. Koutsokera¹, M. Bernasconi¹,
Y. Perentes², T. Krueger², L. Nicod¹, M. Gonzalez², A. Lovis¹

¹Pneumology, ²Thoracic Surgery, CHUV, Lausanne, Switzerland

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.

PP-181

Tobacco Advertising/Sponsorship in Switzerland: Outcome of 15 Complaints Filed by Oxyromandie Provide Evidence of Ineffectiveness of Self- Regulation by Tobacco Multinationals

R.M. Kaelin^{*,1}, M. Canevascini², P. Diethelm¹

¹Oxyromandie, Geneva, ²Stratégies Marketing, Cipret Vaud, Lausanne, Switzerland

Introduction: 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 institu-

tion of the communication branch, to guarantee 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: To test the efficacy of the self-regulation agreement between LK and Swiss Cigarette (BAT, JTI, PMI). 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.

Reference

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PP-182

The First Case of an Extraskeletal Myxoid Chondrosarkoma in the Pulmonary Artery

I. Opitz*,¹, H. Klein¹, B. Bode², L. Freitag³, D. Schneiter¹, S. Ulrich³, F. Maisano⁴, W. Weder¹

¹Division of Thoracic Surgery, ²Institute of Surgical Pathology, ³Department of Pulmonology, ⁴Department of Cardiovascular Surgery, University Hospital Zurich, Zurich, Switzerland

Introduction: We present the first described case of a primary extraskeletal myxoid chondrosarkoma (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.

Fig. 1. 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) (for Abstract PP-182).

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.

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.

PP-183

First Experience with a Biodegradable Endobronchial Stent in a Case of Bronchomalacia

T. Schneider, F. Baty, M. Brutsche

Pneumologie, Kantonsspital St. Gallen, St. Gallen, Switzerland

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 oropharyngeal carcinoma in 2003 treated with radiation of 50 Gy of the cervical and supraclavicular region followed by laryngectomy. The patient also

Fig. 1. (for Abstract PP-183).

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 larynxectomy. 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.

PP-184

Safairway: An Airway Training for Pulmonologists Performing Flexible Bronchoscopy with Non-Anaesthesiologist Administered Propofol Sedation. A Prospective Evaluation

D.P. Franzen^{*1}, M. Schulze², B. Grande², M. Kolbe^{2,3}, S. Kriech^{3,4}, C.B. Nöthiger², D.R. Spahn², M. Kohler¹

¹Klinik für Pneumologie, ²Institut für Anästhesiologie,

³Simulationszentrum, UniversitätsSpital Zürich, ⁴ETH Zürich, Zürich, Switzerland

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 1, 2). 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 ($p = 0.005$

Fig. 1. (for Abstract PP-184).

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.

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.

Fig. 2. (for Abstract PP-184).

PP-185

Hypersensitivity Pneumonitis after Bronchoscopic Lung Volume Reduction with Endobronchial Valves in a Patient with Nickel Allergy. Coincidence or Causality?

D.P. Franzen^{*1}, L. Freitag¹, M. Kohler¹, P. Schmid-Grendelmeier²

¹Klinik für Pneumologie, ²Allergiestation, Klinik für Dermatologie, UniversitätsSpital Zürich, Zürich, Switzerland

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.

PP-186

Multimodal Screening of Respiratory Disease Related to Tobacco Consumption: Results from a Screening Day at a Tertiary Center

P. Gianella^{*1}, D. Adler¹, F. Lador¹, X. Montet², P.M. Soccia¹

¹Pneumologie, ²Radiologie, HUG, Genève, Switzerland

Introduction: Chronic obstructive pulmonary disease (COPD) and pulmonary lung cancer are the most feared consequences of smoking. Smoking cessation is the intervention with de greatest capacity to influence the natural history of COPD. Lung cancer screening by thorax CT scan have shown to reduce mortality in selected patient. 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 à pulmonologist. Smoke cessation, lung specialist consultation and tobaccologist visit status were evaluated at three month.

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.

Fig. 1. (for Abstract PP-186).

PP-187

A 25-Year Follow-Up of 2 Airways Stents (Gianturco Z-Stents) Placed During Childhood

L.M. Lücker, P. Soccal, F. Lador, J. Plojoux

Pneumologie, Hôpitaux Universitaires de Genève, Genève, Switzerland

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 outward 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 ar-

rest. 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 1). 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

Fig. 1. (for Abstract PP-187).

stent in the lumen, which diameter remained above 50%. The left bronchus stent was completely covered by the bronchial mucosa.

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.

Reference

Bugmann P, et al: Chest 1994;106:1580–1582.

PP-188

Instrumentalisation of Academic Research by the Industry to Influence Swiss Tobacco Control Policies, 1962–2015

R.M. Kaelin^{*1}, P. Diethelm²

¹Oxyromandie, Geneva, Switzerland; ²Oxyromandie, Geneva, South Sudan

Introduction: 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: 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.

– **3/2001:** Diethelm/Rielle accused **Pr. Rylander** UNIGE, of fraud; paid by Philip Morris (PM) 1972–2001, 80 000.- 150 000 USD/y 'regardless what we ask him to do for us'. **11/2001:** UNIGE rectorate's advised to refuse tobacco money. **10/2004:** 6 mths after verdict UNIGE states: 'Prof. R cannot be considered independent researcher'.

– **2005 Pr. A. Auer's**, UNIGE, expert opinion: 'La constitutionnalité 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 disproportionately 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.

- Acklin, Y.P. PP-176
 Adler, D. PP-124, PP-186
 Aerts, J. PP-126
 Aerts, J.G. OR37
 Aeschbacher, S. OR61
 Aeschbacher, S.S. OR33, PP-121
 Affolter, K. PP-175
 Aggoun, Y. PP-168
 Albisser, S. PP-145
 Albrecht, C. PP-167
 Aldashev, A. OR33, OR61, PP-121
 Alves, M. PP-167
 Amacker, M. OR42
 Ambrosi, X. PP-149
 Antonietti, J.-P. PP-160
 Arnet, I. PP-139
 Aubert, J.-D. OR40, OR64, PP-160
 Baty, F. OR60, PP-125, PP-134, PP-135, PP-158, PP-177, PP-183
 Baumeler, L. OR37, PP-159
 Baumüller, S. PP-170
 Bédat, B. PP-179
 Beghetti, M. PP-157, PP-163, PP-165, PP-168, PP-171
 Bendjelid, K. PP-163
 Bengueddache, S. PP-163
 Bensaker, R. PP-180
 Benz, G. OR60, PP-134
 Berger, R. PP-157
 Bernasconi, E. OR40
 Bernasconi, M. OR64, PP-173, PP-180
 Beyeler, S. PP-129
 Beyer, S. PP-131
 Bilat, O. PP-160
 Bisang, M. OR33, OR61, PP-121
 Blank, F. OR42, PP-129
 Blasi, F. OR37, PP-126
 Bloch, K.E. OR33, OR61, OR62, PP-119, PP-121, PP-128, PP-132, PP-161
 Blom, R.A.M. OR42
 Bode, B. PP-182
 Boeck, L. OR34, OR37
 Boersma, W. OR37, PP-126
 Bohringer, S. PP-172
 Bonnet, D. PP-157
 Bonovolias, I. OR34
 Boon, M. OR32
 Bovet, C. OR43
 Brack, T. OR36, PP-136, PP-137
 Brand, M. PP-157
 Bratton, D.J. PP-141
 Braun, J. PP-122
 Bregy, L. PP-127, PP-130, PP-143
 Bridevaux, P.-O. PP-147
 Brill, A.-K. PP-120, PP-138, PP-146, PP-155, PP-160
 Bringard, A. PP-163
 Brutsche, M. OR36, PP-125, PP-134, PP-135, PP-136, PP-137, PP-158, PP-177, PP-183
 Brutsche, M.H. OR60
 Bubendorf, L. OR38
 Büsching, G. OR35
 Cairolì, A. PP-152
 Canevascini, M. PP-181
 Casaulta, C. OR32
 Casutt, A. PP-173, PP-180
 Chemla, D. PP-163
 Chetany, R. OR65
 Chortarea, S. PP-129
 Clarenbach, C. PP-136, PP-137
 Clarenbach, C.F. OR36, PP-133
 Clark, R. PP-121
 Clement, A. OR32
 Clottu, E. PP-152
 Costa, L. PP-126
 Crook, S. OR35
 Crowley, S. OR32
 Daccord, C. OR64
 DallaLana, K. PP-122, PP-123
 DellaLana, K. PP-131
 Derkenne, M.-F. PP-160
 Descombes, S.P. PP-154
 Dieterle, T. PP-136, PP-137, PP-139
 Diethelm, P. PP-181, PP-188
 Distler, O. OR62
 Duchna, H.-W. PP-153
 Dupuis, E. PP-124
 Durham, A. PP-173
 Egli, A. PP-126, PP-136, PP-175
 Elisabeth, H.D. PP-161
 Engler, A. PP-127, PP-143
 Feki, A. PP-167
 Ferretti, G. PP-162, PP-163
 Filippi, S. PP-151
 Fitting, J.-W. OR64
 Flamm, A.-L. PP-139
 Flueck, D. PP-128
 Fontolliet, T. PP-162
 Franzen, D.P. PP-131, PP-184, PP-185
 Frauenfelder, T. PP-170
 Frei, A. OR35
 Frei, R. PP-175
 Freitag, L. PP-182, PP-185
 Frey, M. OR36, PP-136, PP-137, PP-147
 Früh, M. PP-177
 Funke, M. OR43, PP-154
 Furian, M. OR33, OR61, PP-119, PP-121, PP-128, PP-132, PP-161
 Furrer, K. OR63, PP-174
 Furrer, M. PP-176
 Gaisl, T. PP-127, PP-130, PP-141, PP-143
 García Gomez, D. PP-143
 García-Gómez, D. PP-130
 Garelli, V. OR64
 Gariani, J. PP-166, PP-168, PP-171
 Gaugg, M. PP-130
 Gaugg, M.T. PP-127, PP-143
 Gaveikaite, V. PP-122
 Gazdhar, A. OR41, PP-167, PP-172
 Geiser, T. OR41, OR43, PP-146, PP-154, PP-167, PP-172
 Gerhard, D. PP-125
 Gianella, P. PP-162, PP-186
 Gonzalez, M. PP-180
 Goutaki, M. OR32
 Grande, B. PP-184
 Gregoriano, C. PP-139
 Grendelmeier, P. PP-118, PP-160
 Grize, L. PP-150
 Guigard, S. PP-179
 Guler, S. OR43
 Gürtler, M. PP-142
 Haarman, E. OR32
 Habre, C. PP-166
 Hachulla, A.-L. PP-165, PP-166, PP-168, PP-171
 Haeberlin, A. PP-140
 Halbeisen, F. OR32
 Halter, J. OR63, PP-159, PP-174
 Hartmann, S. OR61
 Hartmann, S.E. OR33, PP-128
 Hasler, E. PP-119
 Hasler, E.D. PP-132
 Hässig, G. PP-176
 Haynes, A. PP-120
 Heijnen, I. PP-136
 Henny, S. PP-136, PP-137
 Henny-Reinalter, S. PP-139
 Hersberger, K.E. PP-139
 Hervé, P. PP-163
 Hess, T. PP-131, PP-151
 Hibaoui, Y. PP-167
 Hiebinger, A. PP-178
 Hinchliffe, D. OR64
 Hofer, M. PP-151
 Hörner, M. PP-134
 Horvath, C.M. PP-138, PP-155
 Hostettler, K. OR63, PP-174
 Hostettler, K.E. OR41
 Hradetzky, D. PP-172
 Huber, L.C. OR62
 Humpl, T. PP-157
 Hutter, D. OR65, PP-169
 Interstitial and rare lung diseases OR41
 Irani, S. OR36, PP-136, PP-137
 Ivy, D. PP-157
 Jahn, K. PP-118, PP-175
 Janssens, J.P. PP-124
 Jegerlehner, S. PP-154
 Jelusic, D. OR35
 Jörger, M. PP-177
 Jossen, J. PP-138
 Jost, K. PP-140
 Jung, A. PP-151
 Jüni, P. PP-120

- Junker, L. OR63, PP-174, PP-175
- Kaelin, R.M. PP-181, PP-188
- Kallol, S. PP-167
- Karadag, B. OR32
- Karenovics, W. PP-179
- Keller, D. OR64
- Keusch, S. OR35, PP-161
- Khan, P. OR41
- Klein, H. PP-182
- Koerner-Rettberg, C. OR32
- Kohler, M. OR36, PP-127, PP-128, PP-130, PP-131, PP-133, PP-136, PP-137, PP-141, PP-143, PP-170, PP-184, PP-185
- Kolbe, M. PP-184
- Kopp, G. PP-165
- Kostikas, K. OR37, PP-126
- Koutsokera, A. OR64, PP-160, PP-180
- Kraemer, R. PP-142
- Kriech, S. PP-184
- Krueger, T. PP-180
- Kuehni, C. OR32
- Lacoma, A. OR37, PP-126
- Lador, F. PP-162, PP-163, PP-165, PP-166, PP-168, PP-171, PP-186, PP-187
- Lahzami, S. OR64
- Lardinois, D. OR41, OR63, PP-174, PP-178
- Latsang, T. OR61
- Latshang, T.D. OR33, PP-121, PP-128
- Latzin, P. OR32, PP-159
- Laurent, M. PP-168
- Lazdinyte, S. OR63, PP-174, PP-178
- Lazor, R. PP-152
- Lehbert, N. OR35
- Lenoir, A. OR64, PP-152
- Leslie, N. OR64
- Letovanec, I. PP-152
- Leuppi, J. OR36, PP-136, PP-137
- Leuppi, J.D. PP-139
- Lichtblau, M. OR33, OR61, OR62, PP-121
- Licker, M. PP-179
- Liechti, N. OR64
- Liu, L. PP-164
- Lofaso, F. PP-144, PP-148, PP-149
- Louis, R. OR37, PP-126
- Lovis, A. OR64, PP-173, PP-180
- Lu, S. PP-164
- Lucas, J. OR32
- Lücker, L. PP-166
- Lücker, L.M. PP-187
- Maier, S. PP-139
- Maisano, F. PP-182
- Malla, B. PP-126
- Mandal, J. OR38, OR39, PP-126, PP-164
- Manzoni, R. OR64
- Markun, S. PP-122, PP-123, PP-131
- Marsland, B. OR40
- Martin, S. PP-166
- Martinez-Lozano Sinues, P. PP-127, PP-130
- Maurer, E. OR32
- Mazurek, H. OR32
- Mazza-Stalder, J. PP-152
- Merz, T. PP-156
- Meyer, A. PP-145, PP-159
- Michelitsch, C. PP-176
- Milenkovic, B. OR37, PP-126
- Minder, S. PP-142
- Mirrakhimov, E. OR61
- Moersig, W. PP-178
- Molino, A. PP-164
- Montet, X. PP-166, PP-168, PP-171, PP-186
- Morgan, L. OR32
- Moser, C. OR42
- Mouraux, S. OR40
- Mueller-Mottet, S. PP-128
- Müller-Mottet, S. PP-161
- Muralt, L. PP-121
- Nebiker, C. OR63, PP-174
- Nett, P. PP-138
- Nicod, L. OR40, PP-173, PP-180
- Nicod, L.P. OR64, PP-160
- Niederhauser, T. PP-140
- Niedermann, J. OR60
- Nielsen, K. OR32
- Noble, S. PP-163, PP-165, PP-168
- Nöthiger, C.B. PP-184
- Nussbaumer-Ochsner, Y. PP-127, PP-130, PP-143
- Nyilas, S. PP-159
- Ogna, A. OR64, PP-144, PP-148, PP-149
- Opitz, I. PP-170, PP-182
- Orlikowski, D. PP-144, PP-148, PP-149
- Osmonov, B. PP-128
- Ott, S.R. PP-120, PP-138, PP-146, PP-155
- Ozsahin, M. PP-173
- Pache, J.-C. PP-166
- Papakonstantinou, E. OR34, OR37, OR38, OR39
- Pasche, A. OR64
- Passweg, J. PP-159
- Pavlov, N. PP-120
- Pepperell, J.C. PP-141
- Perentes, Y. PP-180
- Perret Bakhouy, S. OR64
- Petitpierre, N. OR64
- Petri-Fink, A. PP-129
- Pfammatter, J.-P. PP-169
- Pfammatter, T. PP-170
- Pfimlin, E. PP-118
- Pfister, M. PP-135
- Pichler Hefti, J. PP-146, PP-156
- Pichot, V. PP-162
- Plojoux, J. PP-187
- Pohle, S. PP-158
- Poulin, M. OR33, PP-128
- Prella, M. OR64
- Prigent, H. PP-144, PP-148, PP-149
- Puhan, M. OR35, PP-122
- Quera Salva, M.A. PP-148
- Radtke, T. OR35
- Rakic, J. OR34, OR37
- Rassouli, F. PP-135
- Rentsch, K. PP-126
- Rexhaj, E. OR65
- Rimoldi, S. OR65
- Rindlisbacher, B. OR43
- Ritz, C. PP-125
- Rohde, G.G. OR37, PP-126
- Rosemann, T. PP-123
- Roth, M. OR34, OR38, OR39, OR41, PP-126, PP-164
- Rothe, T. PP-150
- Rothen-Rutishauser, B. PP-129
- Rotman, S. PP-152
- Rovina, L. OR65
- Ruzgys, P. PP-172
- Salomon, J. PP-142
- Santamaria, F. OR32
- Santori, C. OR65
- Satkauskas, S. PP-172
- Savic, S. OR38, OR41, OR63, PP-159, PP-174
- Saxer, S. OR62, PP-119, PP-132, PP-161
- Scheiwiller, P.M. PP-128
- Scherr, A. OR34, OR37, PP-145
- Scherrer, U. OR65
- Schlatzer, C. PP-141
- Schlotter, S. PP-135
- Schmid-Grendelmeier, P. PP-185
- Schmidlin, J. PP-145
- Schneider, T. PP-183
- Schneiter, D. PP-182
- Schoch, O.D. OR60
- Schuler, M. OR35
- Schultz, K. OR35
- Schulze, M. PP-184
- Schulzke, S. PP-140
- Schumann, D. OR63, PP-174, PP-178
- Schwarz, E.I. PP-141
- Schwerk, N. OR32
- Seif, V. PP-150
- Sievi, N. PP-136, PP-137
- Sievi, N.A. OR36, PP-133
- Similowski, T. PP-124
- Sinues, P.M.-L. PP-143
- Sitbon, O. PP-163
- Soccal, P. PP-187
- Soccal, P.M. PP-160, PP-162, PP-163, PP-165, PP-166, PP-171, PP-186
- Social, P.M. PP-124
- Sommer, C. PP-176
- Sooronbaev, T. OR33, PP-121
- Soria, R. OR65
- Soronbaev, T. OR61
- Spahn, D.R. PP-184
- Speich, R. OR62, PP-170
- Stamm, A. OR62
- Stebler, N. PP-127, PP-130
- Steffensen, R. PP-126
- Steiner, A. PP-128
- Steuere-Stey, C. PP-122, PP-123, PP-131
- Stolz, D. OR34, OR37, OR38, OR39, PP-118, PP-126, PP-145, PP-159, PP-164, PP-175
- Stradling, J.R. PP-141
- Strebel, C. OR43
- Stucki, A. PP-120
- Sun, Q. PP-164
- Suter, L. PP-140
- Suter, Y. PP-127, PP-130, PP-143
- Tamm, M. OR34, OR37, OR38, OR39, OR41, OR63, PP-118, PP-126, PP-145, PP-164, PP-174, PP-175
- Tamo, L. PP-167
- The PROMISE study OR34
- Thomet, M. PP-140
- Thurnheer, R. OR36, PP-136, PP-137

Torres, A. OR37, PP-126	Urner, L. PP-128	Welte, T. OR37, PP-126	Yiallourous, P. OR32
Trendelenburg, M. PP-136	Valenti, A. OR64	Wheeler, J. PP-157	Zbinden, S. PP-155
Trendelenburg, M. PP-126	Vallée, J.-P. PP-168	Wieser, S. PP-131	Zenobi, R. PP-127, PP-130,
Triponez, F. PP-179	van Dijk, R.M. OR42	Wittmann, M. OR35	PP-143
Tschanz, S. PP-129	van Gestel, A. PP-125	Working group, The	
Turk, A. PP-147	Van Gestel, A. PP-134	PROMISE study OR34	
Ulrich, S. OR33, OR61, OR62,	von Garnier, C. OR42	Working Group on	
PP-119, PP-121, PP-128,	Von Garnier, C. PP-129	Pulmonary Rehabilitation	
PP-132, PP-161, PP-170,	Weder, W. PP-170, PP-182	and Patient Education	
PP-182		of the Swiss Respiratory	
		Society PP-147	