the CRMS and CF groups (p = 0.32). Similarly, there was insufficient evidence to conclude that mean percentage predicted (FEV1pp) differed between the CRMS (102.2 ± 6.4%) and CF (96.6 ± 11.6%) groups (p = 0.23).

Conclusions: There were no significant differences in LCI or FEV1pp between the CF and CRMS groups, although we identified one child with CRMS with an abnormal LCI, suggesting the potential utility of MBW to stratify children with CRMS at risk of developing CF. Ongoing EBC analysis and correlation with lung function tests may be an additional way to assess lower airway inflammation in children with CRMS and risk of progression to CF.

Acknowledgements: This work was supported by a Warshaw Fellows Research Grant.

Oxygen-enhanced magnetic resonance imaging and multiple-breath washout with or without short extension as novel assessment tools of cystic fibrosis lung health

C. Short1,2, T. Semple1,2, M. Abkir1,2, M. Tibiletti3, M. Rosenthal3, S. Fadley1,2, G. Parker4,6, J. Davies3,5, Royal Brompton and Harefield Hospitals, Guys and St Thomas’ Trust, London, UK; 2National Heart and Lung Institute, Imperial College London, London, UK; 3European Cystic Fibrosis Society, Lung Clearance Index Core Facility, London, UK; 4Biotechyn Ltd, Manchester, UK; 5Department of Pediatric Respiratory Medicine, Royal Brompton Hospital, Guys and St Thomas’s NHS Foundation Trust; 6Centre for Medical Image Computing, Department of Medical Physics and Biomedical Engineering, University College London, London, UK

Background: Poor sensitivity of spirometry and forced expiratory volume in 1 second (FEV1) means that the gold standard for lung function testing in cystic fibrosis (CF) is suboptimal. The lung clearance index (LCI2.5) derived from multiple-breath washout (MBW) is considered a good alternative but also has limitations. We recently developed an extension to MBW (MBWShX) to capture signal from previously overlooked under- and unventilated lung tissue (UVLU) [1], although any MBW protocol will lack spatial information. Oxygen-enhanced magnetic resonance imaging (OE-MRI) provides a functional assessment of the lung on a spatial level, without the use of hyperpolarized gas or ionizing radiation. The parameter reported here, R2* enhancement, originates from the influence on the proton MRI signal of oxygen in the airways and dissolved within alveolar water and capillary blood. It thus represents a surrogate outcome combining ventilation, gas exchange, and perfusion, with lower enhancement indicative of worse disease. We are conducting a longitudinal study to establish climetries of these techniques; early cross-sectional data are reported here.

Methods: Twenty people with CF underwent spirometry, MBWShX (Eco-medics Exhalizer D, Spiroware software 3.3.1) and OE-MRI on one day. MBWShX protocol: After the standard MBW end of test, subjects performed a slow vital capacity (SVC), followed by tidal breathing until end-of-test criteria were re-met. Quantification of UVLU is calculated by change in percentage of nitrogen resulting from the SVC, standardized for lung size. LCI2.5 (LCL2.5 + UVLU) is a measure of global lung health, whereas UVLU is a standalone marker. The MRI protocol consisted of a dynamic series of multislice two-dimensional dual-echo radio frequency–spoiled T1-fast field echo sequences acquired with a temporal resolution of approximately 1.5 seconds during free breathing using a Siemens Aera 1.5 T scanner. The initial 60 acquisitions were obtained with medical air; the gas supply was then switched to 100% oxygen for 150 acquisitions and then returned to medical air for a final 150 acquisitions. Dynamic quantitative R2* maps were calculated, and the lung parenchyma, excluding central major vasculature, was manually segmented. Normally distributed parameters are presented as mean ± SD and nonparametric parameters as median (range). Pearson (R) and Spearman (r) tests were used to assess correlations. P < 0.05 was considered significant.

Results: All 20 participants completed MBWShX, and the OE-MRI protocol. Subjects were aged 13 ± 5.3, with FEV1pp of 92.2 ± 12.3%, predicted forced vital capacity (FVCpp) of 98.8 ± 11.2%, LCI of 7.5 (6.3–15.6), LCI2.5 of 9.0 (6.1–31.0), and UVLU of 1.2 (−0.3–15.3). R2* enhancement (0.087 ± 0.017/mS) did not correlate with FEV1pp or FVCpp, but significant positive correlations were seen with LCI2.5 (r = −0.47, p < 0.05), LCIShX (r = −0.64, p = 0.01), and UVLU (r = −0.67, p = 0.001).

Conclusions: OE-MRI is feasible and tolerated by children as young as 7. Unlike spirometric values, LCI2.5 correlated significantly with OE-MRI R2*, again highlighting the superior sensitivity of MBW over FEV1 in mild to moderate CF lung disease. Novel MBWShX values also performed well; correlations with OE-MRI were numerically greater than with LCI2.5 although at this stage, we are not powered for statistical comparison. This ongoing project will assess short- and long-term repeatability of these novel assays, create a normative range, assess spatial heterogeneity, and optimize MBW and OE-MRI parameters for use as future clinical and research outputs.

Acknowledgements: This project was funded by Cystic Fibrosis Foundation Grant ID- 0208A120.

Reference


The Streamlined Treatment of Pulmonary exacerbations in Pediatrics pilot study of oral antibiotic timing in pediatric cystic fibrosis pulmonary exacerbations

D. Sanders1, J. Hoppe2, E. Zemanick2, W. Morgan3, T. Bartz4, N. Kime5, K. Hinckley Stukovskiy4, K. Kronmal6, M. Rosenfeld6,7, STOP PEDS Study Group,8 Pediatrics, Indiana University, Indianapolis, IN; 2Pediatrics, Children’s Hospital Colorado, Denver, CO; 3Pediatrics, University of Arizona, Tucson, AZ; 4Biostatistics, University of Washington, Seattle, WA; 5Pediatrics, School of Medicine, University of Washington Seattle, WA; 6Epidemiology, School of Medicine, University of Washington, Seattle, WA

Background: Optimizing pulmonary exacerbations (PEX) management is a top research priority for the cystic fibrosis (CF) community. Several reports support more aggressive use of oral antibiotics for the treatment of PEX symptoms, although particularly in children with relatively preserved lung health, milder exacerbations are frequently virally driven and self-limited and may not always require oral antibiotics, particularly in the era of highly effective modulator therapy. Streamlined Treatment of Pulmonary exacerbations in Pediatrics (STOP PEDS) was a multicenter, pilot study evaluating feasibility and acceptability of randomization to one of two arms for management of mild PEX within 1 to 7 days of symptom onset: early oral antibiotics (initiation at randomization plus airway clearance) versus tailored therapy (airway clearance alone at randomization, with oral antibiotics initiated for worsening cough, cough not improving within 7 days, or cough not resolved by 14 days).

Methods: STOP PEDS was a prospective, multicenter, randomized, unblinded study that enrolled children with CF aged 6 to 18 at a time of clinical stability and followed them through one randomized PEX or up to 18 months. Parents received a text message weekly to report new cough. For mild PEX meeting prespecified criteria, children were eligible for randomization to the early antibiotics or tailored therapy arm. Participants with a randomized PEX were followed for 28 days and then exited the study. The study team contacted the participant at defined intervals following randomization, and treatment was escalated (i.e. antibiotics were started for the “tailored therapy” arm, and participants returned to clinical care in the “early antibiotic” arm) for prespecified criteria or upon request of the participant or family. All study procedures could be conducted remotely. The primary objective was to estimate the proportion of participants randomized to the tailored therapy arm that avoided antibiotics during the 28-day PEX period.

Results: One hundred twenty-one children were enrolled at 10 study sites between November 2020 and December 2021; 65% were on highly effective modulators, 55% were aged 12 to 18, 48% were male, and 50% between November 2020 and December 2021; 65% were on highly effective modulators, 55% were aged 12 to 18, 48% were male, and 50% had grown methicillin-susceptible Staphylococcus aureus (MSSA) and 12% Pseudomonas aeruginosa isolated from their most recent culture. The mean (SD) baseline FEV1, at enrollment was 98 (16%). Ninety-four participants had reported at least one PEX, and 63 (goal 80) PEX were randomized after a mean (SD) of 102 (87) days of enrollment. All but 3 were reported remotely, unrelated to a clinic visit. Thirteen participants reported only PEX that met criteria for being too severe that were not randomized. Eighteen
participants had 29 PEx that met criteria for randomization but were not randomized; parent or participant discomfort with randomization was the most common reason (45% of eligible PEx that were not randomized).

Among the 33 participants randomized to the "tailored therapy" arm, 23 (70%) were not treated with oral antibiotics within 28 days of randomization. Across both arms, 35% returned to clinical care: 13 (43%) in the "early antibiotic" arm and 9 (27%) of the "tailored therapy" arm. Failure to improve within 7 days and incomplete recovery within 14 days of randomization were the most common reasons. Nineteen participants reported 31 adverse events (AEs). The majority were mild and unrelated to study procedures.

**Conclusions:** The STOP PEDS pilot study met its primary objectives by demonstrating that a single mild PEx in a selected population could resolve without oral antibiotics in 70% of the cases, and by demonstrating the feasibility of enrollment, identification of PEx through weekly texts, randomization of PEx treatment, and adherence to study measures. A definitive clinical trial is necessary to evaluate the short- and long-term safety and efficacy of this approach for repeated PEx events.

**Acknowledgements:** This work was supported by the Cystic Fibrosis Foundation. The authors thank study sites, participants, and families.

**TRANSPORTATION**

**143 Bronchoalveolar lavage proteome identifies pathways of disease that segregate lung transplant recipients with and without bronchiolitis obliterans syndrome**

E. Skala1, N. Sharma2,3, D. Hayes4,5, A. Ziady5,6 1Division of Bone Marrow Transplantation and Immune Deficiency, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2Transplant Program, Brigham & Women’s Hospital, Boston, MA; 3Department of Medicine, Harvard Medical School, Boston, MA; 4Division of Pulmonary Medicine, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 5Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH; 6Division of Bone Marrow Transplantation and Immune Deficiency, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

**Background:** Lung transplantation (LTx) is a treatment option for many end-stage lung diseases, including cystic fibrosis (CF). Proteomic analysis of bronchoalveolar lavage (BAL) fluid from LTx recipients has not been performed to identify potential biomarkers or pathways associated with bronchiolitis obliterans syndrome (BOS). We hypothesized that determining the differences between patients with and without BOS might shed light on the molecular underpinnings of disease.

**Methods:** We analyzed BAL fluid from 31 adult LTx recipients with (n = 15, 2 female) and without (n = 16, 3 female) BOS. Samples were collected from patients who underwent LTx for idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, or alpha 1 antitrypsin deficiency. Whole BAL protein was precipitated with acetone, resolubilized, fractionated using sodium dodecyl sulfate gel electrophoresis, in-gel trypsin digested, and subjected to mass spectrometry–based proteomic analysis.

**Results:** Our liquid chromatography mass spectrometry proteomic approach identified 4908 protein isoforms that were present in at least half of either cohort, with 227 isoforms (p < 0.01, false discovery rate (FDR) <0.1) distinguishing LTx recipients with and without BOS. Pathway analysis of differentially expressed proteins revealed vascular permeability (p = 0.003), proliferation and migration (p < 0.06), protein localization to ciliary membrane (p < 0.001), and prostaglandin E2 immune response (p = 0.049) (Figure 1). A more stringent percolator-decay analysis identified 9 isoform differences and reveals changes in platelet degranulation (p < 0.001, FDR = 6.09e-6), kallikrein-kinin driven inflammation (p < 0.001, FDR = 3.37e-3), lectin-induced complement pathway (p < 0.001, FDR = 6.09e-6), blood coagulation (p < 0.001, FDR = 4.567e-5), and IL-6 mediated inflammation (p < 0.004, FDR = 9.96e-3). Disease associations of identified differences included connective tissue diseases (p < 0.001, FDR = 3.26e-3), wounds and injuries (p < 0.001, FDR = 3.26e-3), and autoimmune disease (p < 0.001, FDR = 3.26e-3). Strong signals antigen presentation and immunoglobulin mediated immune response (p < 0.001) and viral transcription (p < 0.001) were also observed in the BOS cohort.

**Conclusions:** The data suggest that antiviral, antimicrobial, complement inhibition, and antigen presentation are features of disease in LTx patients who developed BOS. Therapies that target these pathways may be of benefit. Furthermore, our proteomic approach may offer an additional tool for the diagnosis of BOS in LTx recipients.

**Acknowledgements:** National Heart, Lung, and Blood Institute R01HL142210 (Ziady).

**144 Computed tomography body composition and clinical outcomes after lung transplantation in cystic fibrosis**

A. Jennerich1, L. Downey1, C. Goss1,2, S. Kapnadak1, J. Pryor3, K. Ramos1 1Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Washington, Seattle, WA; 2Division of Pulmonary and Sleep Medicine, Department of Pediatrics, University of Washington, Seattle, WA; 3Division of General Internal Medicine, University of Washington, Seattle, WA

**Background:** Low muscle mass is common in patients undergoing lung transplantation and may be linked to worse post-transplantation outcomes, but existing studies assessing muscle mass and post-transplantation outcomes include few patients with cystic fibrosis (CF). To address this limitation, we identified a cohort of people with CF and examined the relationship between pre-transplantation muscle mass measured using computed tomography (CT) and post-transplantation outcomes.

**Methods:** Between May 1993 and December 2018, of 152 adults with CF who underwent lung transplantation at our institution, 83 met inclusion criteria and had usable CT scans. Using Cox proportional hazards regression, we evaluated the association between pre-transplantation thoracic skeletal muscle index (SMI) and our primary outcome of death after lung transplantation. Secondary outcomes, including days to post-transplantation extubation and post-transplantation hospital and intensive care unit (ICU) length of stay, were assessed using linear regression. We also examined associations between thoracic SMI and pre-transplantation pulmonary function and 6-minute walk distance.

**Results:** There was no association between pre-transplantation thoracic SMI and death after lung transplantation (HR 1.025; 95% CI, 0.948–1.099), days to post-transplantation extubation, or post-transplantation hospital