# 2020 California Research Forum on Lung Health
## Abstract Submissions
### *Emerging Technologies and Treatment in Pulmonary Medicine*

**Presenting Author: Asghar Abbasi, PhD**
**Institute: Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center**
T**itle:** COPD attenuates NK and TReg cell mobilization following high-intensity interval exercise

Introduction. COPD causes inflammation and alters circulating immune cell populations. In health, exercise mobilizes immune cells and promotes anti-inflammation. Aim. To determine the change in circulating immune cell subtypes in response to exercise in COPD and controls. Methods. Age- and sex- matched ex-smokers with (n=5) and without (n=4) COPD performed a single bout of high-intensity interval exercise (10x 1 min at 120% peak work rate, 2 min recovery). Venous blood was collected at baseline (BSL) and post-exercise (0, 30 and 120 min) to quantify 12 immune cell subtypes using multicolor flow cytometry. Two-way ANOVA (Dunnett's posthoc) assessed the effects of time x group. Results. Leukocytes were increased ($p<0.002$) by exercise in CON (65±15%) and COPD (44±21%). Main effects of time ($p<0.01$) on immune cell subtypes in all subjects are shown in Table 1. Time x group interaction ($p<0.0001$) showed that exercise increased CD56+ NK (Cohen's d=0.97, at 0 min post-exercise) and CD3+CD25hiCD127+ TRegs (d=0.25, at 120 min post-exercise) more in CON than COPD. Conclusion. Exercise-induced leukocytosis was not different between COPD and controls. Exercise predominantly altered lymphoid cell fractions in both groups. However, exercise-induced increases in NK and TReg subtypes were absent in COPD. These data suggest that the potentially beneficial effects of exercise on immunosurveilance are attenuated in COPD.

Support: This project was supported by funds provided by The Regents of the University of California, Tobacco-Related Diseases Research Program, Grant Number No. 28FT-0017.

**Table 1.** Main effects of time ($p<0.01$) and effect size vs. baseline on immune cell subtypes in all subjects

| Subtype | Direction of change | Time point | Effect size (Cohen's d) |
|---|---|---|---|
| CD4+ T cells | Decrease | 0 min post-exercise | -0.74 |
| $CD56^{hi}$ NK cells | Decrease | 0 min post-exercise | -0.43 |
| CD8+ T cells | Increase | 0 min post-exercise | 0.58 |
| $CD56^{lo}CD16+$ NK cells | Increase | 0 min post-exercise | 1.55 |
| CD16+ neutrophils | Increase | 120 min post-exercise | 0.77 |
| CD3+ lymphocytes | Increase | 120 min post-exercise | 0.85 |

**Presenting Author: Robert Calmelat**
**Institute: Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center**
**Title:** Bronchodilator acutely reduces expiratory flow limitation during exercise in COPD demonstrated by dynamic hyperinflation, flow-volume curve analysis and impulse oscillometry.

Purpose: We sought to identify expiratory flow limitation during exercise in COPD by establishing associations among dynamic hyperinflation (DH; by inspiratory capacity, IC), concavity of spontaneous expiratory flow-volume curves (by rectangular area ratio, RAR) and airway resistance and reactance (by impulse oscillometry, IOS) pre- and post-albuterol administration.

Methods: 15 patients volunteered (66.0 8.2 yrs; 8 male; GOLD PRISM/1/2/3/4: 1/4/4/4/2). IC and IOS were measured every 2 min during incremental cycling. RAR was measured breath-by-breath.

Results: Albuterol increased FEV1%pred. at rest (61[31,72] vs 67[38,81]%, p=0.001) and IC at peak exercise (1.99[1.19,2.25] vs 2.16[1.27,2.37] L, p=0.012). Albuterol did not change RAR at peak exercise (0.50[0.45,0.60] vs 0.57[0.45,0.61], p=0.156), but reduced resistance (R5, 0.69[0.54,0.80] vs 0.51[0.48,0.58] cmH2O/L/s, p=0.018), reactance (AX, 2.68[1.19,5.32] vs 1.81[1.11,2.70] cmH2O/L/s, p=0.017) and resonant frequency (Fres, 27.7[22.1,34.1] vs 25.3[22.1,27.7] Hz, p=0.012). FEV1%pred., IC and RAR were significantly associated with AX at peak exercise (Figure).

Conclusions: Albuterol reduces airway resistance and reactance during exercise in COPD, which are associated with reductions in dynamic hyperinflation and expiratory flow limitation.

Support: Pulmonary Education and Research Foundation

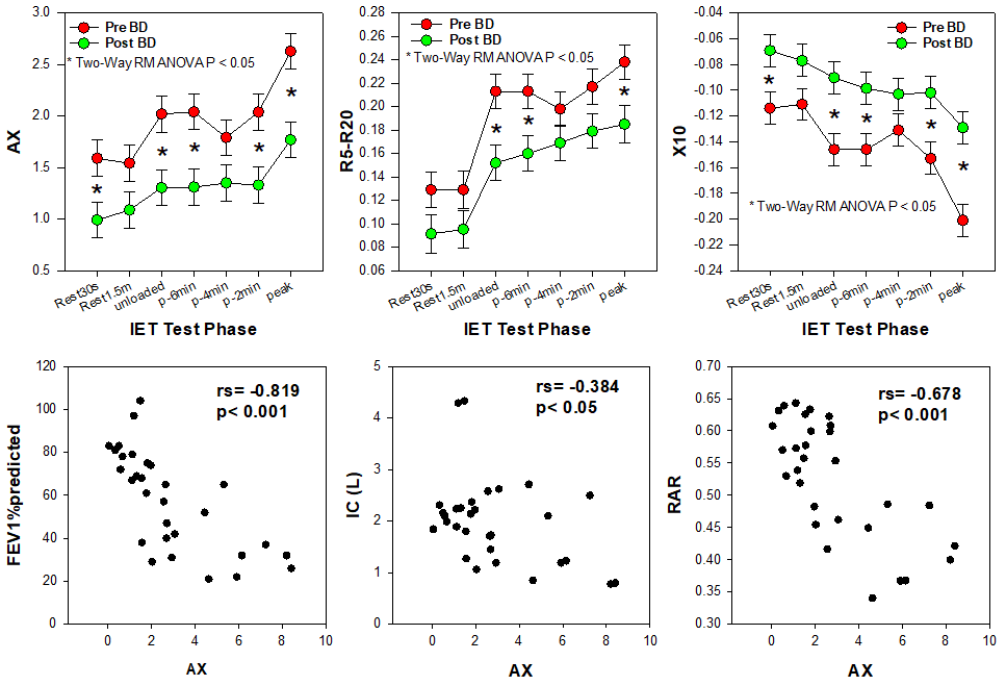



**Figure 1. Top Row: Changes in reactance (AX, X10) and resistance (R5-R20) during rest and exercise in COPD pre- and post-albuterol bronchodilator (BD). Repeated measures two-way ANOVA includes all tests and test phases from both pre- and post-bronchodilator incremental tests. Bottom Row: Spearman correlation between reactance (AX) and resting pulmonary function (FEV1%pred), inspiratory capacity (IC) and rectangular area ratio (RAR) at peak exercise. Regressions include both pre- and post-BD data.**

**Presenting Author: Daniel J. da Costa, MD**
**Institute: Harbor-UCLA Medical Center**
**Title:** Tunneled Indwelling Pleural Catheters: A County Experience

Introduction: Tunneled pleural catheters (TPC) are an important option for outpatient management of malignant pleural effusions. However, optimal management requires strategic self-care, health literacy, and social support which may be more challenging for socioeconomically disadvantaged patients. Studies validating efficacy of TPCs have primarily included patients in higher socioeconomic settings [1]. The objective of our study was to characterize the utilization of TPCs in an indigent population from a large academic public hospital.

Methods: This was a retrospective study of patients who received TPCs at Harbor-UCLA Medical Center between 2014 to 2018. Patient characteristics, procedural outcomes, and complications were collected from the electronic health record using a standardized data collection form.

Results: There were 53 patients who received TIPCs during the study period. Of these, 27 (50%) of patients were Hispanic/Latino, 9 (17%) were Black, 9 (17%) were White, and 8 (15%) were Asian. 24 (45%) patients were non-English speakers. The majority of patients had Medi-Cal insurance, emergency insurance, or were uninsured (31, 12, and 4, patients respectively).

The most common primary cancers were lung 16 (30%), breast 12 (23%), and gynecologic 8 (15%). Patients frequently presented to healthcare settings with advanced cancer; 37 (70%) of patients had stage IV disease and 32 (60%) had malignant pleural effusions at the time of diagnosis. TIPCs were placed in-hospital for 44 (83%) of patients. A total of 39 (74%) patients managed their TPCs without in- home assistance from medical personnel. Complications included 2 (4%) pleural space infections, 2 (4%) soft tissue infections, and 11 (21%) catheter malfunctions.

Conclusion: Despite differences in insurance status, primary language, and in-home support complication rates for primarily indigent patients at an academic public hospital were similar to the published literature and should not deter use of TPC in this population.

[1] Iyer NP et al. Annals ATS 2019;6(1)124-131

**Presenting Author: Sheryl Flynn PT, PhD**
**Institute: Blue Marble Health**
**Title:** Usability and Feasibility of a Digital Home-based Pulmonary Rehab Program for COPD

Introduction: COPD negatively impacts quality of life, and functional capabilities, while also being an expensive personal and societal burden. Pulmonary rehabilitation (PR) improves quality of life, functional capacity and lowers healthcare utilization, however many are unable to access PR due to travel, mobility limitations, and cost. Home-based PR is a cost effective alternative that improves quality of life, exercise capacity, and dyspnea in some adults with COPD. We developed the Health in Motion- Inspiration Point (HiM-IP) Platform to support home-based PR. HiM-IP a downloadable, mobile app that contains self-guided standardized assessments, educational modules, exercise routines tailored to the client's needs, a health diary, a physician-assigned COPD Action Plan, and personalized goals that connects patients with care providers. A care-provider webapp uses a dashboard through which they assign activities and review data to inform care. Completing usability and feasibility studies are the first step in validating HiM-IP.

Methods: For usability, n=11 adults with COPD completed two rounds of use of HiM-IP to measure learning, requests for help, and time to complete.

Results: Participants were GOLD-2 (n=7) or GOLD-3 (n=3), and 54% were female, with ages 72.6 (7.8) with St. George's Questionnaire scores of 48.6 (11.4) and Lung Needs Questionnaire 4.5 (2.0). Participants rated the platform with high usability (SUS scores in 90%ile). Participants took statistically significantly less time to complete the second round for all activities including downloading the app ($p<.005$), completing the Timed Up and Go Test (TUG) ($p<.004$), completing an exercise routine ($p<.003$) and completing a Breathing Technique lesson ($p<.004$), as well as statistically significantly fewer requests for help across all activities ($p<.01$), indicating a quick learning curve. Participants reliably performed the TUG ($r=.846$ compared with video-based scores) and reported an increase in self- perceived breathlessness and exertion from pre-exercise to post-exercise routine suggesting that HiM-IP can track exertion and breathlessness during an exercise routine. In a subgroup (n=5) adults, we explored adherence to a 3x/wk home exercise program during a 2-week in-home trial. We found that participants with COPD completed an average of 6.4 exercise sessions/week (range 5-8x/wk).

Conclusion: HiM-IP is usable and feasible for home use, and participants enjoyed using it. A clinical trial is currently comparing use of home-based HiM-IP with traditional clinic-based PR. If the outcomes are positive, HiM-IP may offer a lower-cost alternative for adults who lack access to PR.

**Presenting Author: Gregory Grandio, MD**
**Institute: USC**
**Title:** Pulmonary rehabilitation improves quadriceps muscle strength in patients with chronic respiratory disorders: Relating quadriceps peak torque to its peak electromyographic signal

Rationale: Skeletal muscle dysfunction is an important factor in reduced exercise capacity, impaired quality of life and higher health-care utilization in COPD. Reduced quadriceps function is associated with decreased survival, functional status, and quality of life. Relating quadriceps peak torque (Tq) to its peak electromyographic (EMG) signal (Eq) is an index that may predict fatigue during active contraction. It has not been investigated in patients with chronic respiratory disorders. We hypothesized that the ratio Eq/Tq in such patients should be increased in comparison to healthy control subjects.

Objectives: To assess changes in skeletal (limb) muscle strength in patients undergoing a standard 8-week outpatient pulmonary rehabilitation (PR) program.

Methods: Peak Tq as measured by dynamometry and its corresponding peak Eq were recorded using surface sensors and electrodes placed over the vastus lateralis in stable patients undergoing PR. Signals were averaged for a train of 5 knee extensions from the knee bent at 90 degrees to the horizontal plane against a graded resistance adjusted on the dynamometer (isokinetic contractions). Maneuvers were performed at beginning, midway through, and at completion of PR. The ratio Eq/Tq was used as an index of muscle fatigue. Results were compared to those of healthy control subjects who had previously testd the equipment for accuracy and reproducibility.

Results: Nine patients (F6/M3, mean age 52 y; diagnoses: 5 interstitial lung disease, 2 bronchiectasis, 2 COPD) were tested and their results compared to 10 healthy individuals (F8/M2, mean age 49 y). Their mean Eq/Tq ratio was 3.1 times as high as that of the control subjects ($p < 0.01$). Mean Eq/Tq in patients decreased from baseline by 37% midway through PR, and by 36% at the end of PR (ANOVA, $p<0.05$).

Conclusions: Baseline skeletal muscle contraction in patients with chronic respiratory disorders requires greater neural stimulation to generate a force equivalent to that in healthy individuals, as shown by an increased Eq/Tq. The ratio decreases with PR, indicating improvement in skeletal muscle strength. Use of Eq/Tq has the potential to assess skeletal muscle fatigue and its reversal in patients undergoing PR.

**Presenting Author: Charles Lanks, MD**
**Institute: Harbor-UCLA Medical Center**
**Title:** Cortical Oxygenation by Time-Resolved Near-Infrared Spectroscopy is Greater in Survivors Than Non- Survivors of Septic Shock

Introduction: The ability to assess the adequacy of regional tissue O2 delivery in sepsis and septic shock holds the potential to inform clinical management. Time-resolved near-infrared spectroscopy (TRS-NIRS) measures tissue oxygen saturation (StO2) and hemoglobin concentration ([tHb]) in real time. TRS-NIRS differs from traditional NIRS by quantifying absorption, scattering and the time-of-flight of individual photons, allowing oxygenated and deoxygenated hemoglobin to be quantified using diffusion theory. This pilot study examined whether cortical StO2 or [tHb] were associated with standard clinical assessment of risk, markers of perfusion adequacy or responsive to fluid resuscitation in patients with sepsis or septic shock.

Methods: 15 patients with sepsis or septic shock and 15 healthy controls were enrolled. Cerebral cortex (frontal lobe) StO2 and [tHb] were assessed at 0.2Hz using TRS-NIRS (TRS-NIRO, Hamamatsu Photonics, Japan) for up to 48 hours after ICU admission. Test-retest reliability was assessed using coefficient of variation (CV) by re-initializing and reapplying the NIRS probes on 5 different occasions. Clinical measurements included central venous pressure (CVP), mean arterial pressure (MAP), venous blood [lactate] and [hemoglobin], severity of illness by SOFA score and volume and timing of intravenous fluid boli. Relationships between StO2, [tHb] and clinical measurements were investigated by linear regression. Differences between groups (sepsis vs. control; survivors vs. non-survivors) and effect of receiving at least 500 mL of intravenous fluids (pre vs. post) were assessed by t-test.

Results: There was strong test-retest reliability for cortical StO2 and [tHb] (CV=3.9±4.1% and 6.2±5.0%). Cortical StO2 was lower in septic patients than controls (46.3±11.1% vs. 60.8±3.6%; p=0.003) despite most having satisfactory systemic indices of tissue perfusion (CVP, 11.3±6.0 mmHg; MAP, 77.5±8.8 mmHg; [lactate], 2.0±1.6 mmol/L). Cortical StO2 was negatively correlated with SOFA score (r2=0.71) and [lactate] (r2=0.32). Cortical [tHb] was positively correlated with cortical StO2 (r2=0.41) and peripheral blood [Hb] (r2=0.35). Cortical StO2 was greater in surviving patients (50.8±10.4%; n=11) than non-survivors (37.2±14.4%; n=4; p=0.03). Cortical StO2 was not different after fluid resuscitation (51.9±10.7% vs 50.2±13.4%; n=15; p=0.34).

Conclusion: Sepsis and septic shock was associated with a low cortical StO2. Furthermore, StO2 was strongly associated with severity of illness (SOFA score) and was lower in non-survivors, despite adequate perfusion using standard clinical measurements. Cortical StO2 was not significantly affected by fluid resuscitation. This pilot study suggests that TRS-NIRS may have utility to assess severity, the real- time adequacy of cortical O2 delivery to utilization, and even the risk of death, in critically ill patients.

**Presenting Author: Harrison Ngue**
**Institute: USC**
**Title:** The Value of Cardiopulmonary Exercise Testing in Patients with Cancer: Occult Pulmonary Vascular Limitation Is the Major Cause of Dyspnea

Hypothesis : Patients with cancer commonly experience dyspnea of unclear etiology. Cardiopulmonary exercise testing (CPET) can provide an objective way of diagnosing the causes for more accurate treatment.

Objectives: In this retrospective study, we evaluated patients with hematologic and solid-organ malignancies who underwent CPET between the years of 2008-2013 to determine which kind of exercise limitation (cardiac, ventilatory, pulmonary-vascular, or neuromuscular) was the primary cause of their dyspnea.

Methods: Subjects were exercised on a stationary cycle ergometer with increasing workloads at increments of 5-15 Watts. Measurements of minute ventilation (V'E), heart rate (HR), breathing reserve (V'E/MVV), oxygen uptake (V'O2), O2-pulse (V'O2/HR), and ventilatory equivalents for carbon dioxide and oxygen (V'E/V'CO2 and V'E/V'O2) were collected. A peak V'O2 <80% predicted indicated a circulatory or ventilatory limitation. Normal lung function with ventilatory equivalents of >120% predicted at anaerobic threshold or peak exercise (or failure of elevated values to normalize with exercise) indicated circulatory limitation with a prominent pulmonary vascular component.

Results: Complete clinical and physiological data were available for 36 patients (M/F 20/16). Thirty-two (89%) exhibited ventilatory or circulatory limitation as shown by a reduced peak V'O2. The largest cohort comprised patients with pulmonary vascular limitation (n=18) and exhibited either normal spirometry or mild restrictive changes. Their mean ± SD peak V'O2 was 61 ± 17% predicted. Four patients exhibited normal physiologic findings. The lowest mean peak V'O2 was in the cardiovascular cohort (45% predicted, n=5). The lowest mean breathing reserve was in the ventilatory cohort (26% predicted, n=10). The mean peak V'E/O2 and V'E/CO2 were highest in the cardiovascular and ventilatory cohorts. Six of 10 patients with ventilatory limitation (V'E/MVV >70% and normal peak O2-pulse) exhibited an obstructive spirometric pattern, with the remainder showing a restrictive deficit.

Conclusion: Oncologic patients with dyspnea primarily exhibited a circulatory cause for exercise limitation, with a prominent pulmonary vascular component. Potential factors include effects of chemo- and radiation therapy on cardiac function and the pulmonary vascular endothelium, or pulmonary thromboembolic disease. All patients, regardless of ventilatory, cardiovascular or pulmonary vascular limitation, exhibit an increase in dead space breathing.

| Table : Physiologic Variables at Peak Exercise | | | | | | |
|---|---|---|---|---|---|---|
| | Normal | CV | Ventilatory | Pulmon Vasc | Musculoskeletal | P† |
| N | 4 | 3 | 10 | 18 | 1 | -- |
| duration exercise (min) | 10.8 ± 1.8 | 10.8 ± 1.8 | 11.4 ± 5.6 | 10.2 ± 2.6 | 6.5 | -- |
| $V'_E$ (L/min) | 48.2 ± 9.3 | 37.3 ± 10.4 | 52.4 ± 16.8 | 57.4 ± 15.3 | 19.3 | 0.051 |
| $V'_E$/MVV (%) | 45.7 ±7.9 | 47.3 ± 17.6 | 74.3 ± 10.6 | 54.2 ± 10.8 | 43 | **0.0001** |
| $V'O_2$ (mL/min) | 1385.3 ± 291.3 | 892.7 ± 250.8 | 1108.3 ± 217.8 | 1185.8 ± 424.9 | 594 | 0.104 |
| $V'O_2$ (% pred) | 84.3 ± 13.9 | 44.7 ± 24.3 | 68.1 ± 13.3 | 61.3 ± 17.3 | 70 | 0.07 |
| $V'O_2$/HR (mL/beat) | 10.5 ± 4.4 | 6.3 ± 1.3 | 9.5 ± 2.2 | 9.3 ± 2.9 | 5 | 0.235 |
| $V'O_2$/HR (% pred) | 99 ± 14.3 | 47 ± 19.1 | 84.3 ± 15.8 | 74.3 ± 17.3 | 83 | **0.018** |
| $V'_E/V'O_2$ (%) | 35 ± 2.4 | 42 | 47.5 ± 12.5 | 50.5 ± 10.6 | 33 | **0.012** |
| $V'_E/V'O_2$ (% pred) | 77.2 ± 16.1 | 182.2 ± 100.1 | 148.3 ± 47.8 | 137 ± 44.1 | 89.2 | 0.142 |
| $V'CO_2$ (mL/min) | 1646.8 ± 404.3 | 1060.7 ± 310.5 | 1274.3 ± 287.9 | 1460.4 ± 569.9 | 623 | 0.137 |
| $V'_E/V'CO_2$ (%) | 29.5 ± 2.6 | 35.7 ± 1.7 | 41.0 ± 6.6 | 41.7 ± 8.86 | 31 | **0.017** |
| $V'_E/V'CO_2$ (% pred) | 79.9 ± 17.4 | 189 ± 111 | 156.3 ± 51.5 | 136.5 ± 43.5 | 100 | 0.163 |

Values represent mean ± SD.

†Comparisons amongst cohorts by ANOVA.

CV, cardiovascular; HR, heart rate; MS, musculoskeletal; $V'_E$, minute ventilation; $V'O_2$, oxygen consumption; $V'CO_2$, carbon dioxide output

**Presenting Author: Billy Peng**
**Institute: USC**
**Title:** Tidal expiratory flow limitation (tEFL) and its relation to lung hyperinflation in patients with chronic airflow obstruction (CAO)

Background/Introduction: Tidal expiratory flow limitation (tEFL) is defined as absence of increase in air flow during forced expiration effort compared to tidal breathing as recorded by forced expiratory flow-volume curves. Air trapping is expected to worsen with increase in tEFL. Tidal EFL is also influenced by increase in BMI. The relation between tEFL and lung hyperinflation has not been systematically investigated.

Objective: To evaluate the relation of magnitude of tEFL to the degree of air trapping as assessed by measurement of lung volumes by body plethysmography in patients with chronic airflow limitation (CAO).

Methods: Records of patients with chronic airflow obstruction (CAO) and complete lung function data were retrospectively reviewed. Lung function testing, including post-bronchodilator spirometry, was conducted according to American Thoracic Society guidelines. Tidal EFL was computed as a percent of the tidal volume spanned (intersected) by the forced expiratory-volume curve. Study received IRB approval (HS-17-00120).

Results: The records of 344 patients with CAO were reviewed; complete lung function data for 272 (158 M, 114 F) were available for analysis. Characteristics of subjects were (mean +/- SD): Age 58±11 years, BMI 28 ± 7, FVC (% pred) 85 ± 21, FEV1 (% pred) of 67 ± 22, FEV1/ FVC of 57 ± 11, TLC (% pred) of 107 ± 19, RV (% pred) of 143 ± 43, FRC (% pred) 120 ± 29, and IC (% pred) 91± 25 (abbreviations below table). One hundred ninety two (71%) patients exhibited tEFL; their mean (±SD) tEFL was 74%±23. Their mean FEV1/FVC and FEV1 was 55±11% and 62±21% predicted, respectively. Using univariate analysis, we found strongest correlations between tEFL and FEV1 in patients with BMI <30 ($p < 7.8$ E10-13), and between tEFL and RV in patients with BMI≥30 ($p < 4.9$ E10-5). Mean MMRC for patients with tEFL <50% was 2.2±1.5; for those with tEFL ≥50% was 3.1±1.1.

Conclusions: Increased air trapping and obesity (a chest wall disorder) are strongly associated with expiratory flow limitation in patients with chronic airflow limitation.

**Table:** Anthropometric and physiologic data for 272 patients

| tEFL (%) | 0 | <50 | ≥50 | P† |
|---|---|---|---|---|
| n | 80 | 31 | 161 | |
| $FEV_1$ (% pred) | 80.2±18.9 | 74.8±20.6 | 59.4±19.8 | <0.001 |
| FVC (% pred) | 95.4±17 | 90.8±19.5 | 79.4±20.6 | <0.001 |
| $FEV_1$/FVC (%) | 61±8.1 | 59.3±8.9 | 54±11.3 | <0.01 |
| IC (% pred) | 89±20.6 | 100.4±28.2 | 89.6±25.5 | <0.01 |
| TLC (% pred) | 108.5±16.3 | 108.8±16 | 105.5±21.4 | NS |
| FRC (% pred) | 122.5±25.2 | 112.6±23.9 | 120.6±31.5 | <0.02 |
| RV (% pred) | 132.8±37.6 | 135.4±30.6 | 149.2±45.9 | <0.01 |
| RV/TLC (%) | 42.1±10.4 | 44.6±10.4 | 50.2±10.2 | <0.01 |
| FRC/TLC (%) | 63.2±8 | 58.4±10.7 | 62.3±9.4 | <0.05 |
| IC/TLC (%) | 36.8±8 | 41.5±10.7 | 37.9±9.7 | <0.01 |

†comparisons between cohorts by ANOVA

tEFL, tidal expiratory flow limitation; FVC, forced vital capacity; $FEV_1$, forced expiratory volume in one second; IC, inspiratory capacity; TLC, total lung capacity; FRC, functional residual capacity; RV residual volume.

**Presenting Author: Harry Rossiter, PhD**
**Institute: Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center**
**Title:** Longitudinal follow-up of older former smokers reveals rapid decline in muscle oxidative capacity and physical activity

Introduction: Locomotor muscle oxidative capacity and daily physical activity are low in chronic obstructive pulmonary disease (COPD), and associate with mortality. The longitudinal rate of decline in these variables is unknown.

Aim: To determine the rate of decline in muscle oxidative capacity, physical activity and pulmonary function over 5-years in former smokers, with and without COPD.

Methods: 17 COPD (GOLD 1/2/3/4 = 3/6/4/4) and 6 smokers with normalspirometry (CON) volunteered. Assessments at baseline and follow-up included: calf muscle oxidative capacity from the O2 consumption recovery rate constant (k) using
near-infrared spectroscopy; 7-day physical activity (PA) by triaxial accelerometry (vector magnitude units, VMU/min; steps/day); pulmonary function by spirometry.

Results: Mean follow-up was 4.6±0.6 years. There was no difference in smokinghistory (ATS pack-years: CON 38±19; COPD 37±15; p=0.41), or age (p=0.51) between COPD and CON. Annualized rates of decline in k and PA were rapid, but did not differ among groups (Table). Relative 5-year decline in k (-30±17%), VMU/min (-31±23%) and steps/day (-32±30%) were double that of FEV1 (-16±11%) (N.S.).

Conclusion: 5-year follow-up in former smokers with and without COPD revealed rapid decline in muscle oxidative capacity and physical activity.

Support: ATS-2018-11; U01HL089856; U01HL08989; R01HL151452.
Table: See attachment

**Table**. Five-year decline in pulmonary function, skeletal muscle oxidative capacity and physical activity in former smokers with and without COPD.

| | | **Age** years | **$FEV_1$** L/min | ***k*** 1/min | **Vector Magnitude Unit** VMU/min | **Step/day** count |
|---|---|---|---|---|---|---|
| **CON** (n=6) | Baseline | 67.6(10.9) | 2.43(0.45) | 1.61(0.52) | 384.5(192.1) | 6844(3249) |
| | Follow-up | 72.3(10.7) | 2.09(0.37) * | 1.09(0.39) * | 251.4(143.0) | 4126(2300) $ |
| | Rate of decline/year | - | -0.07(0.04) | -0.11(0.09) | -29.3(34.0) | -587(575) |
| **GOLD 1-2** (n=9) | Baseline | 66.8(9.3) | 2.44(0.46) | 1.34(0.18) | 473.4(260.2) | 5080(3627) |
| | Follow-up | 73.5(9.6) | 2.11(0.37) * | 0.96(0.18) * | 291.3(131.7) * | 4329(2287) |
| | Rate of decline/year | - | -0.08(0.05) | -0.09(0.05) | -35.4(30.5) | -46(196) |
| **GOLD 3-4** (n=8) | Baseline | 63.7(10.0) | 1.08(0.71) | 1.17(0.38) | 252.3(153.3) | 3720(3063) |
| | Follow-up | 68.3(10.6) | 0.81(0.45) $ | 0.76(0.18) * | 135.3(82.4) * | 1900(1528) * |
| | Rate of decline/year | - | -0.05(0.06) | -0.08(0.09) | -28.7(20.7) | -41(26) |

Data are mean(SD). CON, smokers with normal spirometry. GOLD, Global Initiative for Chronic Obstructive Pulmonary Disease. FEV1, forced expiratory volume in the first second. *k*, recovery rate constant, index of muscle oxidative capacity. * $p \leq .05$ and $ $p = .06$ vs. Baseline (T-test).

**Presenting Author: Alexander Sherman, MD**
**Institute: UCLA**
**Title:** Endobronchial Ultrasound Assessment of Central Pulmonary Vasculature in Critically Ill Intubated Adults: A Case Series

Introduction:

Standard of care in assessing critically ill intubated patients with suspicion for pulmonary embolism is imaging with computed tomography pulmonary angiography (CTPA). When CTPA cannot be obtained due to clinical instability or renal dysfunction precluding use of intravenous contrast, physicians must decide if risk of pulmonary embolism is high enough to warrant empiric therapy. Endobronchial ultrasound (EBUS) may allow clinicians to visualize thrombi in the central pulmonary arteries (PA) to help guide treatment decisions.

Methods:

Endobronchial ultrasound was used to visualize thrombi in the central pulmonary arteries (PA) in intubated patients with suspected or confirmed pulmonary embolism.

Results:

Case 1: 22-year old female presented after syncope with hypoxemia and obstructive shock. CTPA showed pulmonary embolism. She developed cardiac arrest and was administered 100mg intravenous alteplase. She was hypotensive despite therapeutic anticoagulation. EBUS demonstrated persistent thrombus in the distal right PA, right lower lobe PA, left basal trunk, and bilateral interlobar PA. Figure 1 demonstrates thrombus in the distal right PA on (A) CTPA and (B) EBUS. She underwent suction thrombectomy, was extubated within 24 hours, and discharged on room air.

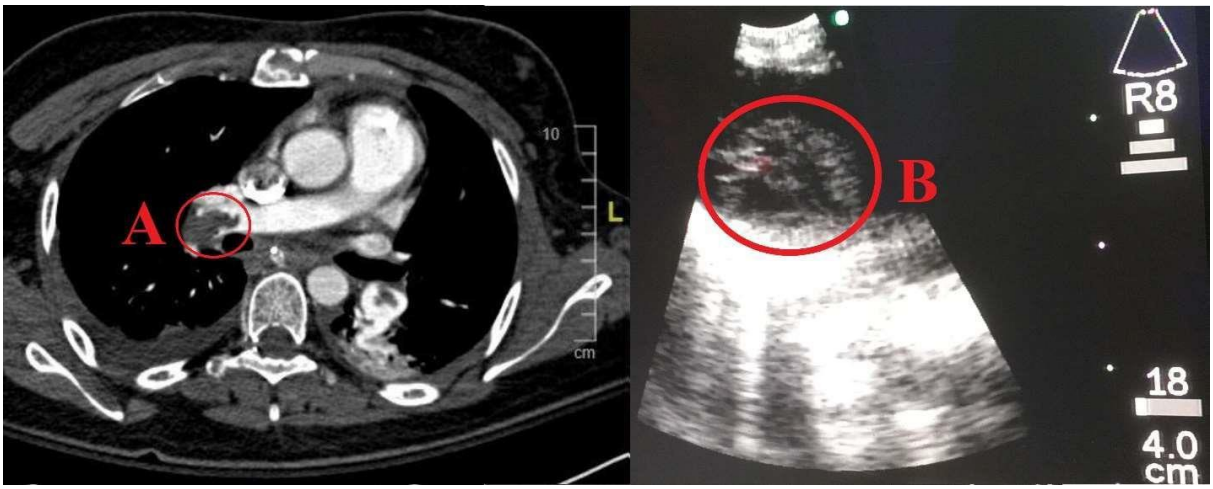
Case 2: 60-year old female with interstitial pneumonia presented with exertional dyspnea while awaiting bilateral orthotopic lung transplantation (BOLT). After donor lung acceptance but before transplantation, she developed tachycardia to 140s and refractory hypoxemia. She developed acute right ventricular failure peri-intubation and required cannulation to veno-arterial extracorporeal membrane oxygenation (VA ECMO). EBUS showed no proximal pulmonary embolism and sheunderwent successful BOLT. Pathology of explanted lungs showed no evidence ofthrombus.

Case 3: 65-year old male with malignant pleural effusion from pulmonary adenocarcinoma and chronic kidney disease was admitted for video-assisted thoracoscopic pleurodesis. Procedure was aborted due to respiratory and renal failure, then he developed shock and hypoxia requiring intubation. Transesophageal echocardiography showed right ventricular strain and right PA thrombus with poor visualization of left PA. EBUS showed bilateral interlobar and basal trunk thrombi. He was placed on VA-ECMO for peri-procedural support and underwent suction thrombectomy with improvement in mean PA pressure from 33mmHg to 13mmHg. Despite therapeutic anticoagulation, he decompensated two days later and CTPA showed extensive bilateral pulmonary emboli. His respiratory status worsened and he chose to pursue comfort-oriented care and died.

Conclusion:

This case series suggests that EBUS may play a role in assessing proximal pulmonary vasculature. This technique obviates the need for patient transportation or use of intravenous contrast in diagnosing proximal pulmonary embolism.

Figure 1. Thrombus in the distal right pulmonary artery seen on both (A) computed tomography pulmonary angiography and (B) endobronchial ultrasound



**Presenting Author: Nicholas Tiller, PhD**
**Institute: Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center**
**Title:** Relationships among muscle oxidative capacity, coronary artery calcium, and hepatic steatosis in COPD: A pilot study

Introduction. COPD is characterized by inactivity and muscle deconditioning. We recently showed a negative association between muscle oxidative capacity and serum triglycerides in severe COPD. It is unclear whether these maladaptations contribute to increased cardiometabolic disease risk.

Aim. To assess relationships among muscle oxidative capacity, coronary artery calcium (CAC), and hepatic steatosis (liver-to-spleen Hounsfield Unit ratio; L/S) in smokers with and without COPD. Methods. Data from 90 COPDGene subjects (GOLD 1/2/3/4=10/12/6/7; 55 controls) were retrospectively analyzed. Coronary artery calcium (CAC) and L/S were assessed from chest CT. Muscle oxidative capacity was estimated from the O2 consumption recovery rate constant (k) using near-infrared spectroscopy.

Results. k was lower in COPD than controls (1.67±0.45 vs 1.31±0.44 min-1; $p<0.001$, $d=0.81$). Total CAC (452±694 vs 707±1503; $p>0.05$) and calcification in the independent coronary arteries were not different between groups ($p>0.05$). L/S was greater in COPD (1.45±0.49 vs 1.31±0.26 HU; $p=0.038$, $d=0.36$), and the threshold for fatty liver disease (L/S<1.0) was met by 9% and 7% of COPD patients and controls, respectively. Age-adjusted regressions showed no correlation between k and L/S ($r[88]=-0.14$, $p=0.189$) or CAC ($r[88]=-0.05$, $p=0.648$).

Conclusions. CAC was not different between COPD patients and controls and was not associated with muscle k, suggesting that factors other than muscle oxidative capacity contribute to CAC formation in COPD. The hypothesis that COPD patients with low k may have more echolucent (less calcified) plaque, and thus increased CVD risk, remains to be tested.

**Presenting Author: Clay Wu, MD**
**Institute: USC**
**Title:** The Effects Of Pregnancy On Spirometric Changes In Patients With Cystic Fibrosis.

Rationale: Pregnancy is a viable option for cystic fibrosis (CF) patients as their life expectancy has continued to improve with the advent of new therapies. Pregnant CF patients often complain of increasing dyspnea during the latter stages of pregnancy. We therefore sought to elucidate the effect of lung function before and after delivery. Specifically, we assessed the effects of pregnancy on spirometric values.

Methods: The records of 23 patients with CF were reviewed for data analysis. A retrospective analysis was then performed on 11 of these patients (13 pregnancies) who had complete data sets at pre-specified time intervals between 2009 and 2017. Spirometry was measured pre-pregnancy, at first and third trimesters, and every three months post-partum up to one year. We also adjusted for confounding factors of age and pre-gestational BMI (ANOVA). We used a BMI of 22 kg/m2 as the pre-defined cut-off, the recommended pre-gestational BMI by the CF Foundation.

Results: The cohort data showed a significant decline in FEV1 and FVC from pre-pregnancy to third trimester of pregnancy (by 8.1%, $p < 0.043$ and 9.3%, $p < 0.013$, respectively). There were no statistically significant differences amongst spirometric values when adjusted for BMI and age over the entire time course. The decrease in FEV1 recovered at six months postpartum, while the FVC returned to baseline values by one year post-partum.

Conclusions: The reduction in FEV1 and FVC seen in our population of pregnant patients cannot fully be explained by cephalad displacement of the diaphragm because there was no association when corrected for BMI. These changes, however, can be explained by an increase in intravascular blood volume and lung water during third trimester. The FEV1 recovers by 6 months postpartum, however the FVC does not recover until 12 months. During these last six months, the FEV1/FVC increases, likely because of a reversal of bronchiolar narrowing with elimination of lung water. These findings would also explain the reduction in dyspnea experienced by CF patients following delivery.

**Presenting Author: Wei Yuan, MD**
**Institute: Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center**

Introduction. Impulse oscillometry (IOS) is a simple, non-invasive means of assessing resistance and reactance in the large and small peripheral airways. The technique has the advantage of being effort-independent, requiring only basic training to perform. While IOS has traditionally been used to assess airway function at rest, this study presents preliminary data on the test-retest reproducibility of IOS measurements made during dynamic, incremental exercise (CPET).

Methods. Five healthy subjects (3 male, 2 female) volunteered for the study (stature = 1.71 ± 0.02 m; mass = 75.7 ± 8.4 kg; age = 57 ± 12 y). Following baseline measures of pulmonary function (spirometry, body plethysmography, diffusing capacity, impulse oscillometry), subjects performed an incremental exercise test on an electromagnetically-braked cycle ergometer. Exercise commenced unloaded (0 W) for 3 min, after which the work rate was increased in a ramp fashion by 10 W·min−1 to volitional fatigue. Impulse oscillometry (pressure oscillations 5 – 35 Hz) was performed for 20 s every second minute during incremental exercise, without interrupting the pedal duty cycle. After at least 90 min passive rest, an identical protocol was repeated, with IOS values of resistance at 5 Hz (R5), reactance at 5 Hz (X5), reactance area (AX), resonant frequency (FRes), and small airway resistance (R5-R20) compared between tests.

Results. Subjects had healthy baseline pulmonary function (FEV1 = 92 ± 10%Pred). One-sample t-test showed no systematic differences in R5, X5, AX, FRes, or R5-R20 ($p > 0.05$). Bland Altman plots and linear regression showed no systematic bias in R5, X5, AX, FRes, or R5-R20, but Fres showed at higher frequencies a lower value on the second test indicative of lasting exercise-induced bronchodilation. Intra-class correlation (ICC) showed strong test-retest reproducibility with R5 (ICC = 0.68, $p = 0.002$), Fres (ICC = 0.82, $p < 0.001$) and R5-R20 (ICC = 0.69, $p = 0.002$).

Conclusions. Our preliminary analyses suggest that IOS may be a valid means of assessing airway function during exercise.

**Presenting Author: Dongxing Zhao, MD**
**Institute: Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center**
**Title:** Serum Amyloid A (SAA) in Stable COPD Patients is Associated with the Frequent Exacerbator Phenotype

INTRODUCTION: Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with rapid decline in lung function, deterioration of quality of life and increased mortality. These effects are worsened in those with frequent exacerbations (≥ 2 exacerbations per year). Serum amyloid A (SAA) is increased during the acute phase of a COPD exacerbation (Bozinovski et al. Am J Respir Crit Care Med 177:269-278, 2008), induced by inflammatory mediators such as TNFa. SAA can be modestly elevated in the stable phase of COPD. The aim of this study was to determine whether serum amyloid A (SAA) concentration in stable COPD was associated with the frequent exacerbator phenotype. We hypothesized that SAA would be greater in stable COPD patients with ≥ 2 exacerbations in the previous year.

METHODS: In a single visit, 88 stable patients (4 female) with severe COPD were assessed for demographics, medical and smoking history, exacerbation frequency, pulmonary function and fraction of expired nitric oxide (FeNO). Venous blood was collected and serum was assessed for inflammatory variables. SAA was measured by ELISA (R&D, #DY3019-05). Logistic regression was used to assess the associations between the frequent exacerbator phenotype and inflammatory variables.

RESULTS: Patients were 64.2±7.3 years old with FEV1 37.8±9.4% predicted. Ten (11.4%) patients were classified as frequent exacerbators. Serum concentration of SAA (129.7±67.7 vs. 80.7±51.9 mg/L; P=0.008; mean±SD) and surfactant protein D (SP-D; 16.5±11.5 vs. 10.5±8.5 mg/L; P=0.048) were greater in frequent exacerbators compared to those with 1 or fewer exacerbations in the previous year. SAA was not associated with FEV1 %predicted or FVC %predicted. After adjusting for sex, age, BMI, FEV1/FVC and smoking pack-years, SAA remained independently associated with the frequent exacerbator phenotype (OR 1.49; 95%CI 1.09-2.04; P=0.012; Figure). After adjustment, SP-D and other inflammatory variables including IL-1β, IL-4, IL-6, IL-8, CRP, LTB4, GMCSF, FeNO, MMP8, MMP9, PRG4 were not associated with the frequent exacerbator phenotype.

CONCLUSION: In the stable phase of COPD, SAA is greater in frequent exacerbators than those with 1 or fewer exacerbations in the previous year.
FIGURE: See attachment.