

ABSTRACTS

Physical Activity Limitation as Measured by Accelerometry in Pulmonary Arterial Hypertension

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Background: The 6-min walk test, commonly used to assess exercise capacity and response to therapy in pulmonary arterial hypertension (PAH), has many well-described limitations. Sedentary time is associated with adverse cardiovascular outcomes and reduced quality of life, and measuring sedentary time and physical activity using accelerometry is another potential way to quantify exercise capacity in PAH. Whether sedentary time is different in patients with PAH vs control subjects is unknown.

Methods: Physical activity was measured in 20 patients with PAH and 30 matched healthy control subjects using accelerometry for 7 consecutive days. Patients with PAH completed standard 6-min walk testing, and baseline demographics were recorded for all study participants. Total daily activity counts, sedentary time, and proportion of time at various activity levels were compared between groups.

Results: Sedentary time was significantly higher in patients with PAH (mean, 92.1% daily activity; 95% CI, 89.5-94.8%) than in control subjects (mean, 79.9% daily activity; 95% CI, 76.4%-83.5%; $P < .001$), and all levels of physical activity were reduced in the PAH group compared with the control group ($P < .01$ for all). Daily moderate to vigorous physical activity was reduced in the PAH group (7.5 min; 95% CI; 0.8-15.6 min) compared with the control group (mean, 64.7 min; 95% CI, 51.1-78.2 min; $P < .001$). Activity counts correlated with 6-min walk distance in the PAH group (Spearman rank correlation = 0.72, $P < .001$).

Conclusions: Sedentary time is increased in patients with PAH and may lead to increased risk for metabolic and cardiovascular morbidity. Quantitation of daily activity and sedentary time using accelerometry may be a novel end point for PAH management and clinical trials.

Brachial Artery Diameter and the Right Ventricle: The Multi-Ethnic Study of Atherosclerosis-Right Ventricle Study

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Background: Endothelial dysfunction is associated with left ventricular morphology and long-term cardiovascular outcomes. The purpose of this study was to assess the relationship between both baseline brachial artery diameter and peripheral endothelial function (assessed by brachial artery ultrasonography) and right ventricular (RV) mass, RV end-diastolic volume (RVEDV), and RV ejection fraction (RVEF).

Methods: The Multi-Ethnic Study of Atherosclerosis (MESA) performed cardiac MRI and brachial artery ultrasonography on participants without clinical cardiovascular disease. Baseline brachial artery diameter and flow-mediated dilation were assessed.

Results: The mean age was 60.9 years, and 49.4% of subjects were men ($n = 2,425$). In adjusted models, larger brachial artery diameter was strongly associated with greater RV mass ($\beta = 0.55$ g, $P < .001$), larger RVEDV ($\beta = 3.99$ mL, $P < .001$), and decreased RVEF ($\beta = 0.46\%$, $P = .03$). These relationships persisted after further adjustment for the respective left ventricular parameters. Flow-mediated dilation was not associated with RV mass or RVEF and was only weakly associated with RVEDV.

Conclusions: Brachial artery diameter is associated with greater RV mass and RVEDV, as well as lower RVEF. Changes in the systemic arterial circulation may have pathophysiologic links to pulmonary vascular dysfunction or abnormalities in RV perfusion.

Multidetector CT Scan for Acute Pulmonary Embolism: Embolic Burden and Clinical Outcome

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Background: In patients with acute pulmonary embolism (PE), the correlation between the embolic burden assessed by multidetector CT (MDCT) scan and clinical outcomes remains unclear. Patients with symptomatic acute PE diagnosed based on MDCT angiography were included in a multicenter study aimed at assessing the prognostic role of the embolic burden evaluated with MDCT scan.

Methods: Embolic burden was assessed as (1) localization of the emboli as central (saddle or at least one main pulmonary artery), lobar, or distal (segmental or subsegmental arteries) and (2) the obstruction index by the scoring system of Qanadli. The primary outcome was 30-day all-cause death or clinical deterioration. Predictors of all-cause death or clinical deterioration were identified by Cox regression statistics.

Results: Overall, 579 patients were included in the study; 60 (10.4%) died or had clinical deterioration at 30 days. Central localization of emboli was not associated with all-cause death or clinical deterioration (hazard ratio [HR], 2.42; 95% CI, 0.77-7.59; $P = .13$). However, in 516 hemodynamically stable patients, central localization of emboli (HR, 8.3; 95% CI, 1.0-67; $P = .047$) was an independent predictor of all-cause death or clinical deterioration, whereas distal emboli were inversely associated with these outcome events (HR, 0.12; 95% CI, 0.015-0.97; $P = .047$). No correlation was found between obstruction index (evaluated in 448 patients) and all-cause death or clinical deterioration in the overall study population and in the hemodynamically stable patients.

Conclusions: In hemodynamically stable patients with acute PE, central emboli are associated with an increased risk for all-cause death or clinical deterioration. This risk is low in patients with segmental or subsegmental PE.

Diaphragm Muscle Thinning in Patients Who Are Mechanically Ventilated

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Background: Approximately 40% of patients in medical ICUs require mechanical ventilation (MV). Approximately 20% to 25% of these patients will encounter difficulties in discontinuing MV. Multiple studies have suggested that MV has an unloading effect on the respiratory muscles that leads to diaphragmatic atrophy and dysfunction, a process called ventilator-induced diaphragmatic dysfunction (VIDD). VIDD may be an important factor affecting when and if MV can be discontinued. A sensitive and specific diagnostic test for VIDD could provide the physician with valuable information that might influence decisions regarding extubation or tracheostomy. The purpose of this study was to quantify, using daily sonographic assessments, the rate and degree of diaphragm thinning during MV.

Methods: Seven intubated patients receiving MV during acute care were included. Using sonography, diaphragm muscle thickness was measured daily from the day of intubation until the patient underwent extubation or tracheostomy or died. We analyzed our data using standard descriptive statistics, linear regression, and mixed-model effects.

Results: The overall rate of decrease in the diaphragm thickness of all seven patients over time averaged 6% per day of MV, which differed significantly from zero. Similarly, the diaphragm thickness decreased for each patient over time.

Conclusion: Sonographic assessment of the diaphragm provides noninvasive measurement of diaphragmatic thickness and the degree of diaphragm thinning in patients receiving MV. Our data show that diaphragm muscle thinning starts within 48 h after initiation of MV. However, it is unclear if diaphragmatic thinning correlates with diaphragmatic atrophy or pulmonary function. The relationship between diaphragm thinning and diaphragm strength remains to be elucidated.

Clinical Significance of the Differentiation Between *Mycobacterium avium* and *Mycobacterium intracellulare* in M avium Complex Lung Disease

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Background: *Mycobacterium avium* and *Mycobacterium intracellulare* are grouped together as the M avium complex; however, little is known about the clinical impact of this species differentiation. This study compared the clinical features and prognoses of patients with M avium and M intracellulare lung disease.

Methods: From 2000 to 2009, 590 patients were given a new diagnosis of M avium complex lung disease; 323 (55%) had M avium lung disease, and 267 (45%) had M intracellulare lung disease.

Results: Compared with the patients with M avium lung disease, the patients with M intracellulare lung disease were more likely to have the following characteristics: older age (64 vs 59 years, $P = .002$), a lower BMI (19.5 kg/m² vs 20.6 kg/m², $P < .001$), respiratory symptoms such as cough (84% vs 74%, $P = .005$), a history of previous treatment for TB (51% vs 31%, $P < .001$), the fibrocavitary form of the disease (26% vs 13%, $P < .001$), smear-positive sputum (56% vs 38%, $P < .001$), antibiotic therapy during the 24 months of follow-up (58% vs 42%, $P < .001$), and an unfavorable microbiologic response after combination antibiotic treatment (56% vs 74%, $P = .001$).

Conclusions: Patients with M intracellulare lung disease exhibited a more severe presentation and had a worse prognosis than patients with M avium lung disease in terms of disease progression and treatment response. Therefore, species differentiation between M avium and M intracellulare may have prognostic and therapeutic implications.

Inhaled Corticosteroid Dose Response Using Domiciliary Exhaled Nitric Oxide in Persistent Asthma: The FENOtype Trial

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Background: International guidelines advocate a standard approach to asthma management for all, despite its heterogeneity. "Personalized" treatment of inflammatory asthma phenotypes confers superior benefits. We wished to evaluate dose response to inhaled corticosteroids (ICSs) in patients with asthma with an elevated fractional exhaled nitric oxide (FENO) phenotype using domiciliary measurements.

Methods: We performed a randomized, crossover trial in 21 patients with mild to moderate persistent asthma receiving ICSs with elevated FENO (>30 parts per billion [ppb]) that increased further (>10 ppb) after ICS washout. Patients were randomized to 2 weeks of either fluticasone propionate 50 µg bid (FP100) or 250 µg bid (FP500). The primary outcome was response in diurnal domiciliary FENO levels. Secondary outcomes included mannitol challenge, serum eosinophilic cationic protein (ECP), blood eosinophil count, and asthma control questionnaire.

Results: We found significant dose-related reductions of diurnal FENO compared with baseline µ morning FENO: baseline = 71 ppb (95% CI, 61-83 ppb); FP100 = 34 ppb (95% CI, 29-40 ppb), $P < .001$; FP500 = 27 ppb (95% CI, 22-33 ppb), $P < .001$; and significant dose separation for morning, $P < .05$, and evening, $P < .001$. Time-series FENO displayed exponential decay: FP100 $R^2 = 0.913$, half-life = 69 h (95% CI, 50-114 h); FP500 $R^2 = 0.966$, half-life = 55 h (95% CI, 45-69 h), as well as diurnal variation. The Asthma Control Questionnaire showed significant improvements exceeding the minimal important difference (>0.5) with values in keeping with controlled asthma (<0.75) after each dose: FP100 = 0.48 (95% CI, 0.24-0.71), $P = .004$; FP500 = 0.37 (95% CI, 0.18-0.57), $P = .001$. All other secondary inflammatory related outcomes (mannitol, ECP, and eosinophils) showed significant improvements from baseline but no dose separation.

Conclusions: There is a significant dose response of diurnal FENO to ICS in patients with asthma with an elevated FENO phenotype, which translates into well-controlled asthma. Further interventional studies are warranted using domiciliary FENO in this specific phenotype.

Prediction of peak flow values followed by feedback improves perception of lung function and adherence to inhaled corticosteroids in children with asthma

Feldman JM, Kutner H, Matte L, Lupkin M, Steinberg D, Arcoleo SA, Thorax 2012;67:1040-1045

Background: Failure to detect respiratory compromise can lead to emergency healthcare use and fatal asthma attacks. The purpose of this study was to examine the effect of predicting peak expiratory flow (PEF) and receiving feedback on perception of pulmonary function and adherence to inhaled corticosteroids (ICS).

Methods : The sample consisted of 192 ethnic minority, inner-city children (100 Puerto Rican, 54 African-American, 38 Afro-Caribbean) with asthma and their primary caregivers recruited from outpatient clinics in Bronx, New York. Children's PEF predictions were entered into an electronic spirometer and compared with actual PEF across 6 weeks. Children in one study were blinded to PEF (n=88; no feedback) and children in a separate study were able to see PEF (n=104; feedback) after predictions were locked in. Dosers were attached to asthma medications to monitor use.

Results: Children in the feedback condition displayed greater accuracy ($p<0.001$), less under-perception ($p<0.001$) and greater over-perception ($p<0.001$) of respiratory compromise than children in the no feedback condition. This between-group difference was evident soon after baseline training and maintained across 6 weeks. The feedback condition displayed greater adherence to ICS ($p<0.01$) and greater quick-relief medication use ($p<0.01$) than the no feedback condition.

Conclusions: Feedback on PEF predictions for ethnic minority, inner-city children may decrease under-perception of respiratory compromise and increase adherence to controller medications. Children and their families may shift their attention to asthma perception and management as a result of this intervention.

Changes in prevalence and load of airway bacteria using quantitative PCR in stable and exacerbated COPD

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Background: Prevalence and load of airway bacteria in stable and exacerbated chronic obstructive pulmonary disease (COPD) has been previously studied using microbiological culture. Molecular techniques, such as quantitative PCR (qPCR), may be more informative.

Methods: In this study, 373 sputum samples from 134 COPD outpatients were assessed for prevalence and load of typical airway bacteria (*Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*) by multiplex qPCR, with 176 samples analysed for atypical bacteria. Paired stable and exacerbation typical bacteria data were compared in 52 patients. We compared routine culture with qPCR in 177/373 samples.

Results: Typical bacteria were more prevalent in exacerbation than stable-state paired samples: 30/52 (57.7%) vs. 14/52 (26.9%); $p=0.001$. In patients who were bacteria-positive at both time points, mean (± 1 SEM) load was significantly higher at exacerbation than stable state (108.5(± 0.3) vs. 107.2(± 0.5) cfu/ml), constituting a 20-fold increase ($p=0.011$). qPCR was more discriminatory at detecting typical bacteria than microbiological culture (prevalence 59.3% vs. 24.3%; $p<0.001$). At stable state, higher airway bacterial load correlated with more severe airflow limitation (FEV₁%predicted) ($r=-0.299$; $p=0.033$) and higher inhaled corticosteroid dosage ($r=0.382$; $p=0.008$). Mean C-reactive protein was higher in bacterial-associated exacerbations (35.0 Vs 25.1 mg/L; $p=0.032$).

Conclusions: Airway bacterial prevalence and load increase at COPD exacerbations and are an aetiological factor. qPCR is more discriminatory than culture, identifying higher airway bacterial prevalence. Exacerbations associated with bacterial detection showed a higher mean C-reactive protein level. In the stable state, airway bacterial load is related to more severe airflow limitation and higher inhaled corticosteroid dosage used.

Continuous positive airway pressure improves sleepiness but not calculated vascular risk in patients with minimally symptomatic obstructive sleep apnoea: the MOSAIC randomized controlled trial

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Background: Continuous positive airway pressure (CPAP) for symptomatic obstructive sleep apnea (OSA) improves sleepiness and reduces vascular risk, but such treatment for the more prevalent, minimally symptomatic disease is contentious.

Methods: This multicenter, randomized controlled, parallel, hospital-based trial across the UK and Canada, recruited 391 patients with confirmed OSA (oxygen desaturation index >7.5/h) but insufficient symptoms to warrant CPAP therapy. Patients were randomized to 6 months of auto-adjusting CPAP therapy, or standard care. Primary endpoints were change in Epworth Sleepiness Score (ESS) and predicted 5-year mortality using a cardiovascular risk score (components: age, sex, height, systolic blood pressure, smoking, diabetes, cholesterol, creatinine, left ventricular hypertrophy, previous myocardial infarction or stroke). Secondary endpoints included some of the individual components of the vascular risk score, objectively measured sleepiness and self-assessed health status.

Results: Of 391 patients randomized, 14 withdrew, 347 attended for their follow-up visit at 6 months within the predefined time window, of which 341 had complete ESS data (baseline mean 8.0, SD 4.3) and 310 had complete risk score data. 22% of patients in the CPAP group reported stopping treatment and overall median CPAP use was 2:39 h per night. CPAP significantly improved subjective daytime sleepiness (adjusted treatment effect on ESS -2.0 (95% CI -2.6 to -1.4), $p < 0.0001$), objectively measured sleepiness and self-assessed health status. CPAP did not improve the 5-year calculated vascular risk or any of its components.

Conclusions: In patients with minimally symptomatic OSA, CPAP can reduce subjective and objective daytime sleepiness, and improve self-assessed health status, but does not appear to improve calculated vascular risk.

Air travel and chronic obstructive pulmonary disease: a new algorithm for pre-flight evaluation

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Background: The reduced pressure in the aircraft cabin may cause significant hypoxaemia and respiratory distress in patients with chronic obstructive pulmonary disease (COPD). Simple and reliable methods for predicting the need for supplemental oxygen during air travel have been requested.

Objective: To construct a pre-flight evaluation algorithm for patients with COPD.

Methods: In this prospective, cross-sectional study of 100 patients with COPD referred to hypoxia-altitude simulation test (HAST), sea level pulse oximetry at rest (SpO_{2SL}) and exercise desaturation (SpO_{26MWT}) were used to evaluate whether the patient is fit to fly without further assessment, needs further evaluation with HAST or should receive in-flight supplemental oxygen without further evaluation. HAST was used as the reference method.

Results An algorithm was constructed using a combination of SpO_{2SL} and SpO_{26MWT} . Categories for SpO_{2SL} were >95%, 92-95% and <92%, the cut-off value for SpO_{26MWT} was calculated as 84%. Arterial oxygen pressure (PaO_{2HAST}) <6.6 kPa was the criterion for recommending supplemental oxygen. This algorithm had a sensitivity of 100% and a specificity of 80% when tested prospectively on an independent sample of patients with COPD (n=50). Patients with $SpO_{2SL} > 95\%$ combined with $SpO_{26MWT} \geq 84\%$ may travel by air without further assessment. In-flight supplemental oxygen is recommended if $SpO_{2SL} = 92-95\%$ combined with $SpO_{26MWT} < 84\%$ or if $SpO_{2SL} < 92\%$. Otherwise, HAST should be performed.

Conclusions The presented algorithm is simple and appears to be a reliable tool for pre-flight evaluation of patients with COPD.

Association between β -blocker therapy and outcomes in patients hospitalised with acute exacerbations of chronic obstructive lung disease with underlying ischaemic heart disease, heart failure or hypertension

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Background: β -Blocker therapy has been shown to improve survival among patients with ischaemic heart disease (IHD) and congestive heart failure (CHF) and is underused among patients with chronic obstructive pulmonary disease (COPD). Evidence regarding the optimal use of β -blocker therapy during an acute exacerbation of COPD is particularly weak.

Methods: We conducted a retrospective cohort study of patients aged ≥ 40 years with IHD, CHF or hypertension who were hospitalised for an acute exacerbation of COPD from 1 January 2006 to 1 December 2007 at 404 acute care hospitals throughout the USA. We examined the association between β -blocker therapy and in-hospital mortality, initiation of mechanical ventilation after day 2 of hospitalisation, 30-day all-cause readmission and length of stay.

Results: Of 353082 patients who met the inclusion criteria, 29% were treated with β blockers in the first two hospital days, including 22% with β_1 -selective and 7% with non-selective β blockers. In a propensity-matched analysis, there was no association between β -blocker therapy and in-hospital mortality (OR 0.88, 95% CI 0.71 to 1.09), 30-day readmission (OR 0.96, 95% CI 0.89 to 1.03) or late mechanical ventilation (OR 0.98, 95% CI 0.77 to 1.24). However, when compared with β_1 selective β blockers, receipt of non-selective β blockers was associated with an increased risk of 30-day readmission (OR 1.25, 95% CI 1.08 to 1.44).

Conclusions: Among patients with IHD, CHF or hypertension, continuing β_1 -selective β blockers during hospitalisation for COPD appears to be safe. Until additional evidence becomes available, β_1 -selective β blockers may be superior to treatment with a non-selective β blockers.

Utility of overnight pulse oximetry and heart rate variability analysis to screen for sleep-disordered breathing in chronic heart failure

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Background: Sleep-disordered breathing (SDB) is under diagnosed in chronic heart failure (CHF). Screening with simple monitors may increase detection of SDB in a cardiology setting. This study aimed to evaluate the accuracy of heart rate variability analysis and overnight pulse oximetry for diagnosis of SDB in patients with CHF.

Methods: 180 patients with CHF underwent simultaneous polysomnography, ambulatory electrocardiography and wrist-worn overnight pulse oximetry. SDB was defined as an apnoea-hypopnoea index ≥ 15 /h. To identify SDB from the screening tests, the per cent very low frequency increment (%VLFI) component of heart rate variability was measured with a pre-specified cutoff $\geq 2.23\%$, and the 3% oxygen desaturation index was measured with a pre-specified cutoff >7.5 desaturations/h.

Results: 173 patients with CHF had adequate sleep study data; SDB occurred in 77 (45%) patients. Heart rate variability was measurable in 78 (45%) patients with area under the %VLFI receiver operating characteristic curve of 0.50. At the $\geq 2.23\%$ cutoff, %VLFI sensitivity was 58% and specificity was 48%. The 3% oxygen desaturation index was measurable in 171 (99%) patients with area under the curve of 0.92. At the pre-specified cutoff of >7.5 desaturations/h, the 3% oxygen desaturation index had a sensitivity of 97%, specificity of 32%, negative likelihood ratio of 0.08 and positive likelihood ratio of 1.42. Diagnostic accuracy was increased using a cutoff of 12.5 desaturations, with sensitivity of 93% and specificity of 73%.

Conclusions: The high sensitivity and low negative likelihood ratio of the 3% oxygen desaturation index indicates that pulse oximetry would be of use as a simple screening test to rule out SDB in patients with CHF in a cardiology setting. The %VLFI component of heart rate variability is not suitable for detection of SDB in CHF.