Complete Reference Ranges for Pulmonary Function Tests from a Single Population

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Rationale: Reference ranges are a prerequisite for interpreting pulmonary function tests and are important in diagnosis, assessment and management of respiratory disease. Although intuitively advantageous in terms of consistency few reference equations for all commonly measured aspects of pulmonary function have been derived from single populations. Approaches to the selection of variables for inclusion in equations may not always be based on biological reasoning and equations for static lung volumes have not undergone recent review. **Methods:** A cohort of 212 Caucasian never smokers with no respiratory disease or symptoms underwent detailed pulmonary function testing (spirometry, plethysmographic lung volumes, airway resistance and gas transfer). Equations were developed by linear regression including gender as an explanatory variable. Other candidate variables were based on prior univariate analysis. Comparisons with European Community for Steel and Coal (European) and NHANES III (American) reference equations were by quantiles of difference and plots of difference vs. predicted values. **Main results:** Reference equations were produced for all commonly used pulmonary function tests. Previous equations resulted in significantly lower predicted vs. measured values for spirometry with the greatest difference seen with the European equations (mean bias FEV_1 European: male 0.48L, female 0.36L, American: male 0.30L, female 0.14L). Most static lung volumes were significantly under predicted by European equations (mean bias TLC males 1.14L, females 0.89L, SVC males and females 0.66L). **Conclusions:** This study provides contemporary equations for a Caucasian population including newer spirometric parameters of increasing clinical relevance. Their implementation has the potential to overcome many of the problems associated with currently used equations.

Biomarker Profiles Accurately Predict Patients with COPD

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Objective: We sought to examine whether inflammatory biomarker profiles accurately discriminate between subjects with and without COPD. **Methods:** We used samples collected from a previously published case-control study of lung cancer. Using a high throughput multiplex assay (Luminex), 17 cytokines described to be associated with COPD were simultaneously measured in 25 µL of serum. The cytokines included TNF-α, IL-1β, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-8, ENA-78, IL-10, IL-17, GM-CSF, RANTES, FGF, MIP1-β, MCP-1 and IFN-γ. The outcome variable was a subject-reported physician diagnosis of COPD that has a specificity of 93.8% for a FEV_1/FVC ratio less than 0.70. We used logistic regression modelling to ascertain a parimonious model. Model discrimination was estimated using the area under the receiver operator chacteristic curve (AUC). An AUC of 0.5 is not better than chance alone while an AUC 1.0 discriminates perfectly. **Results:** Cytokines were measured in 185 current smokers, of whom 60 reported a physician's diagnosis of COPD. Both forward and backwards stepwise modeling retained IL-17, IL-2 and MCP-1. Backwards stepwise modeling added IL1-beta and IL1ra. Using these 5 cytokines to predict COPD, we calculated an AUC of 0.72 (95%CI: 0.64-0.80). Forcing all cytokines in the model had a small effect (AUC 0.74 (95%CI 0.67-0.82)). Restricting to subjects without lung cancer and repeating the analyses (n=123) improved the model's performance (AUC 0.81 (95%CI: 0.71-0.92)) and demonstrated an 88.6% accuracy for a subject-reported physician diagnosis of COPD. **Conclusion:** These results suggest that modeling biologic constituents of host response has potential to identify biomarker profiles that accurately identify and discriminate among smokers with and without COPD.

✱ Excessive Lung Function Declines and Risk of Death: Implications for Medical Monitoring

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Rationale: Rate of decline in lung function has been found to predict all-cause mortality, but detailed quantitative relationships have not yet been derived for this outcome. This study investigates the predictive effect of certain numeric indices of excessive lung function decline and implications for subsequent medical monitoring. **Methods:** Spirometry results were available for 2,467 US white male coal miners who had performed two spirometry tests at least 7 years apart (mean 13.4 yrs) and whose vital status was followed up to 20 years (mean 12.1 yrs) from the last test. A nonparametric locally weighted regression (LOESS) method was used to describe the relationship between rate of decline and mortality. Rates of decline were then categorized based on commonly used cutoff points (30, 60, and 90 mL/yr). A Cox proportional hazard model was used to estimate the adjusted relative risk of all-cause mortality (RR) by decline. Covariates included age, change in body mass index (BMI), smoking (pack-years), and height-adjusted initial FEV_1. The adjusted RR was also calculated for never smokers and for those whose initial FEV_1 was above the lower limit of normal ($FEV_1 > LLN$). **Conclusion:** FEV_1 declines exceeding 60 mL/yr were associated with increasing risk of all-cause mortality in the overall cohort, and declines exceeding 90 mL/yr were associated with increased mortality in two subgroups—those who had an initial normal FEV_1 and, importantly, those who had never smoked.

Results:

Group	<30 mL/yr (reference)	60-90 mL/yr	>90 mL/yr
Adjusted RR (95% CI)			
Total cohort	1	1.54 (1.10, 2.15)	1.99 (1.37, 2.87)
$FEV_1 > LLN$	1	1.41 (0.95, 2.10)	1.70 (1.07, 2.69)
Never smokers	1	2.48 (0.94, 6.53)	3.07 (1.06, 8.86)

The findings and conclusions in this abstract have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.

Assessment of the Prevalence and Impact of Bronchiectasis in α_1-Antitrypsin Deficiency

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INTRODUCTION: It has been recognised that evaluation is needed of the prevalence and clinical impact of bronchiectasis in subjects with α_1-antitrypsin deficiency[1]. **METHODS:** 66 randomly selected PiZ subjects were characterised with high resolution CT, lung function and health status questionnaire (St George's Respiratory Questionnaire). Bronchiectasis severity was assessed from CT using a modified visual scoring system[2] and emphysema assessed both visually and by CT densitometry (15th percentile point) using the Pulmo CMS software. **RESULTS:** Basal panlobular emphysema was visualized in 50 subjects and 30 of these also had co-existing apical centrilobular emphysema. Bronchiectasis was identified in 64 subjects. Total bronchiectasis score correlated with FEV_1 (% predicted) (rs=-0.223, p=0.03), CT densitometry (rs=-0.37, p=0.001) and health status (Total, rs=0.36, p=0.001; Symptoms, rs=0.35, p=0.001; Activity, rs=0.32, p=0.003; Impacts, rs=0.34, p=0.002). Bronchial wall thickening correlated with FEV_1 (% predicted) (rs=-0.49, p<0.001). **CONCLUSIONS:** The prevalence of bronchiectasis in α_1-antitrypsin deficiency is greater than currently recognised and may be a feature of disease progression. Bronchiectasis severity relates to health status, emphysema severity and physiological impairment.

[1]ATS/ERS Statement *Am J Respir Crit Care Med* 2003; 168:818-900

[2]Bhalla M et al *Radiology* 1991; 8: 213-229

FEV_6: Behaviour and Correlates in the Elderly

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The achievement of an acceptable FVC in elderly can be difficult, needing as much as 15-20 seconds of exhalation. FEV_6 has been proposed as a valid alternative for FVC in functional diagnosis of airway obstruction and restriction in order to reduce patients effort during spirometry. The aims of this study were to estimate FEV_6 reproducibility, to identify correlates of a good quality FEV_6 and factors affecting volumetric differences between FEV_6 and FVC in elderly patients. Retrospective study based on data collected within the multicenter Sa.R.A project, involving 24 Italian pulmonary and geriatric institutions. 1971 subjects aged 65-100 yrs were examined; among them 1870 spirometric tests were performed. We analysed the volume-times curves to calculate FEV_6 in patients that achieved a good start of test (Vext < 150 ml) and a good end of test (FET ≥ 6 seconds). Demographic, anthropometric, clinical and respiratory function correlates of FEV_6 and FVC achievements were assessed by logistic regression. FEV_6 was obtained in 88.9% of spirometries with acceptable start of test, while FVC only in 60.6%. A 150ml-reproducibility was found in 92.4% cases for FEV_6, 86% for FVC. Male sex, lower age, airway obstruction, higher educational level, lack of depression and better cognitive function were independent determinants of an easier achievement of FEV_6. Independent factors affecting the achievement of an acceptable FVC were female sex, younger age, absence of airway obstruction, higher FEV_1 and lack of depression. Factors related to higher volumetric differences between FEV_6 and FVC were male sex, smoke habit and higher FVC. In elderly patients FEV_6 is more easily achievable and more reproducible than FVC. Different factors affect its achievement. Age and depression are major determinants for a poorer quality of spirometry, affecting both FEV_6 and FVC.

Potential Consequences of Not Reaching the Minimum Daily Physical Activity as Recommended by Guidelines in Stable COPD Patients

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Objective: The present study investigated whether patients with Chronic Obstructive Pulmonary Disease (COPD) reach the minimum recommendation of daily physical activity according to the American College of Sports Medicine (ACSM) guidelines, and what are the consequences of non-compliance with these guidelines. **Methods:** Activity monitoring, pulmonary function, muscle force, exercise capacity, quality of life, functional status and different disease severity indexes (GOLD, BODE and MRC) were assessed in 23 COPD patients (61[59-69] years; FEV_1 39[34-53]%pred; median [25-75% interquartile range]). **Results:** According to compliance with the guidelines (>30 minutes of walking per day), 12 patients were considered active and 11 were considered inactive. The inactive group had worse airflow obstruction, exercise capacity, MRC and BODE (p<0.05 for all). In addition, they had lower walking time in daily life and intensity during walking (p<0.05 for both). MRC and BODE were superior to the GOLD in predicting compliance to the guidelines (specificity 0.83 for MRC and BODE versus 0.50 for the GOLD). The BODE was significantly increased with each day of inactivity. **Conclusions:** A large number of COPD patients do not walk more than 30 minutes per day and hence can not be compliant with the minimum recommended daily physical activity. Each day of inactivity per week increases the BODE. To predict whether a patient is capable of reaching the ACSM guidelines, both BODE and MRC may be more useful than the GOLD.

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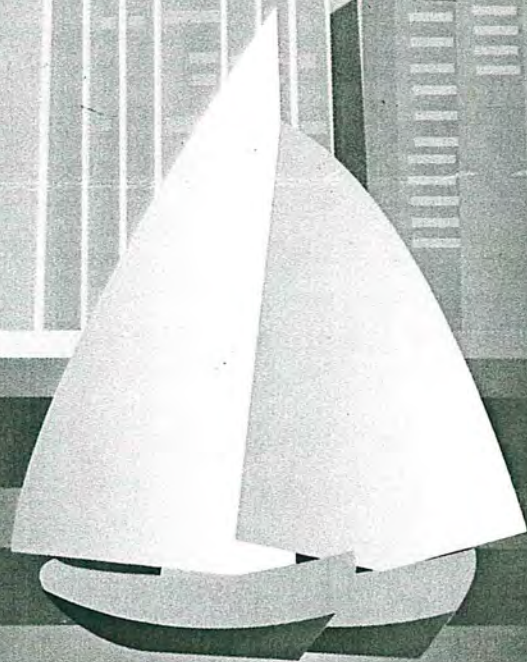
ABSTRACTS
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