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# Relationship of emphysema and airway disease assessed by CT to exercise capacity in COPD

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**KEYWORDS**
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**Summary**
*Objective:* To assess the association of emphysema and airway disease assessed by volumetric computed tomography (CT) with exercise capacity in subjects with chronic obstructive pulmonary disease (COPD).
*Methods:* We studied 93 subjects with COPD (Forced Expiratory Volume in 1 s [$FEV_1$] %predicted mean ± SD 57.1 ± 24.3%, female gender = 40) enrolled in the Lung Tissue Research Consortium. Emphysema was defined as percentage of low attenuation areas less than a threshold of −950 Hounsfield units (%LAA-950) on CT scan. The wall area percentage (WA%) of the 3rd to 6th generations of the apical bronchus of right upper lobe (RB1) were analyzed. The 6-min walk distance (6MWD) test was used as a measure of exercise capacity.
*Results:* The 6MWD was inversely associated with %LAA-950 ($r = -0.53$, $p < 0.0001$) and with the WA% of 6th generation of RB1 only ($r = -0.28$, $p = 0.009$). In a multivariate regression model including CT indices of emphysema and airway disease that were adjusted for demographic and physiologic variables as well as brand of CT scanner, only the %LAA-950 remained significantly associated with exercise performance. Holding other covariates fixed, this model

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showed that a 10% increase of CT emphysema reduced the distance walked in 6 min 28.6 m (95% Confidence Interval = −51.2, −6.0, $p = 0.01$).
*Conclusion:* These results suggest that the extent of emphysema but not airway disease measured by volumetric CT contributes independently to exercise limitation in subjects with COPD.


## Introduction

A reduction in exercise capacity is frequent in subjects with chronic obstructive pulmonary disease (COPD)[1] and is traditionally associated with impaired lung function.[2–6] There is, however, increasing recognition that spirometric measures of lung function alone do not explain all the variance found in clinical measures of disease. As detailed by Reilly in his editorial to the UPLIFT study, COPD appears to be an aggregate of several unique subtypes.[7] Given this heterogeneous population, new measures of disease such as computed tomography (CT) assessment of emphysema and airway disease are of great interest in helping to understand disease pathophysiology and standard clinical measures such as exercise capacity.

The 6-min walk distance test (6MWD) is a commonly used measure of exercise capacity in subjects with COPD. It requires minimal equipment to perform and is widely available.[8] While CT is increasingly used to quantitatively assess both the emphysema and airway disease in COPD,[9–18] studies of their contribution to exercise capacity are more limited.[19–21] Gould et al[20] and Lee et al[21] reported an association between emphysema assessed by CT and exercise capacity assessed by walking tests, but the relation of airway disease to exercise capacity, however, has not been demonstrated.

Based on prior studies revealing the inverse correlation between CT airway disease and lung function,[12,14] we hypothesize that CT measures of airway disease would provide complimentary information to CT measures of emphysema in predicting exercise capacity measured by 6MWD independent of lung function. We undertook this study using data from Lung Tissue Research Consortium (LTRC), a National Heart, Lung and Blood Institute initiative to characterize subjects with chronic pulmonary diseases such as COPD.

## Methods

### Subjects selection

The data used in this study were collected as part of the LTRC and included measures of lung function, exercise testing, and volumetric CT scanning of the chest performed prior to lung volume reduction surgery, transplantation, and resection for suspected malignancy (www.ltrcpublic.com). Subjects were evaluated for inclusion in our study if they had a diagnosis of COPD (postbronchodilator forced expiratory volume in 1 s to forced expiratory vital capacity ratio [$FEV_1$/FVC] $<0.7$) and a high resolution volumetric CT scan available for quantitative analysis. Five out of the 99 patients that met the two above criteria were eliminated because of a history of chronic heart failure which has been demonstrated to influence exercise performance.[22] A sixth subject was excluded because of a giant bulla in the right lung which resulted in mediastinal displacement. The final study cohort consisted of 93 subjects and informed consent was obtained from each participant. The study was approved by the Institutional Review Board of Brigham and Women's Hospital (BWH).

### Physiologic assessment

All subjects underwent standardized spirometric measures of lung function according to American Thoracic Society (ATS) guidelines.[23] The postbronchodilator $FEV_1$ and FVC were recorded in liters and expressed as percentages of predictive values ($FEV_1$%P and FVC%P) using standardized prediction equations.[24] Lung volume measurements were performed by body plethysmography. The residual volume, total lung capacity, and the residual volume to total lung capacity ratio were expressed as percentages of predicted values (RV%P, TLC%P and RV/TLC%P, respectively).[25] The 6MWD was performed in a standardized manner following ATS recommendations.[26] This test was typically performed once prior to a subject undergoing surgery. In four patients more than one walk test was taken while they were awaiting transplantation. In these cases, the walk test in closest proximity to the surgery was evaluated. Oxygen saturation ($SO_2$) was measured before and at the end of the walk test. Oxygen supplementation was titrated to achieve a resting $SO_2$ level of at least 88% prior to starting the test. The walking distance was recorded in meters.

### Imaging assessment

The radiology core laboratory defined CT protocols for LTRC.[27] CT scanners follow the American College of Radiology guidelines for accreditation (www.acr.org/accreditation/computed). Computed tomographic images were acquired in the supine position at full inflation using both General Electric (GE) and Siemens scanners. GE Protocol: 55 subjects underwent CT scanning using a GE CT scanner. Images were acquired using a 30 cm field of view (FOV) in a GE LightSpeed 16 multislice scanner using a tube voltage of 140 kVp, a tube current of 300 or 375 mA for most subjects ($n = 48$) and variable doses for the remaining subjects. Images were reconstructed using the bone algorithm at 1.25 mm slice thickness and 0.625 mm interval. Siemens Protocol: 38 subjects underwent CT scanning by using Siemens Sensation 10 or 64 multislice scanners. Images were similarly acquired using a 30 cm FOV at 140 kVp with an automated dose modulation. Images were reconstructed