Collapsibility of Lung Volume by Paired Inspiratory and Expiratory CT Scans:

Correlations with Lung Function and Mean Lung Density

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Rationale and Objectives: To evaluate the relationship between measurements of lung volume (LV) on inspiratory/expiratory computed tomography (CT) scans, pulmonary function tests (PFT), and CT measurements of emphysema in individuals with chronic obstructive pulmonary disease.

Materials and Methods: Forty-six smokers (20 females and 26 males; age range 46–81 years), enrolled in the Lung Tissue Research Consortium, underwent PFT and chest CT at full inspiration and expiration. Inspiratory and expiratory LV values were automatically measured by open-source software, and the expiratory/inspiratory (E/I) ratio of LV was calculated. Mean lung density (MLD) and low attenuation area percent (<−950 HU) were also measured. Correlations of LV measurements with lung function and other CT indices were evaluated by the Spearman rank correlation test.

Results: LV E/I ratio significantly correlated with the following: the percentage of predicted value of forced expiratory volume in the first second (FEV_1), the ratio of FEV_1 to forced vital capacity (FVC), and the ratio of residual volume (RV) to total lung capacity (TLC) (FEV_1%P, $R = -0.56$, $P < .0001$; FEV_1/FVC, $r = -0.59$, $P < .0001$; RV/TLC, $r = 0.57$, $P < .0001$, respectively). A higher correlation coefficient was observed between expiratory LV and expiratory MLD ($r = -0.73$, $P < .0001$) than between inspiratory LV and inspiratory MLD ($r = -0.46$, $P < .01$). LV E/I ratio showed a very strong correlation to MLD E/I ratio ($r = 0.95$, $P < .0001$).

Conclusions: LV E/I ratio can be considered to be equivalent to MLD E/I ratio and to reflect airflow limitation and air-trapping. Higher collapsibility of lung volume, observed by inspiratory/expiratory CT, indicates less severe conditions in chronic obstructive pulmonary disease.

Key Words: Lung volume; chronic obstructive pulmonary disease; computed tomography; pulmonary emphysema; airflow obstruction.

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With the development of imaging analysis using computed tomography (CT) in individuals with chronic obstructive pulmonary disease (COPD), several quantitative CT indices have been advocated and proved to be significant for predicting lung function. The more commonly used indices are the percentage of low attenuation area (LAA%) and mean lung density (MLD). Further, these indices on expiratory CT scans have been often reported to be stronger predictors for lung function than those on inspiratory scans (1–11). Regarding MLD, it is also known that the expiratory/inspiratory (E/I) ratio of MLD demonstrates significant correlations with pulmonary function tests (PFTs) (4,5,12).

In contrast, lung volume (LV) measured by CT has not been as rigorously assessed in subjects with COPD. Although inspiratory/expiratory LV and plethysmographic measures of total lung capacity (TLC) and residual volume (RV) (1,2,13), the relationship between CT-based LV measurements, including

LV E/I ratio, and airflow limitation or air-trapping is still undefined.

The relationship between MLD and LV has been gradually recognized. A recent study showed the direct relationship between inspiratory LV and MLD (14). Further, Zaporozhan and colleagues reported that the difference in MLD (ΔMLD) strongly correlated with the difference in LV (ΔLV) on paired inspiratory/expiratory CT scans, and that ΔLV correlated with forced expiratory volume in the first second (FEV_1) (2). Based on these results, it can be predicted that expiratory LV would also reflect expiratory MLD, which is a useful CT index to predict lung function, and that LV E/I ratio would be correlated to MLD E/I ratio and be a predictor of lung function.

We therefore hypothesized that LV E/I ratio would show significant correlations with PFT as well as MLD E/I ratio, and that the CT-based LV measurements would be correlated with MLD measurements. Thus, the aims of this study are to clarify the relationship between PFT and LV measurements, including LV E/I ratio, and to confirm the correlation between LV measurements and other CT indices, in particular MLD.

MATERIALS AND METHODS

The study and manuscript were reviewed and approved according to the procedures outlined by the National Heart, Lung, and Blood Institute Lung Tissue Research Consortium (LTRC). This study was also approved by the Institutional Review Board at Brigham and Women's Hospital. Further information on the LTRC is available on the website (www.ltrcpublic.com).

Subjects

All subjects gave written informed consent. A total of 46 subjects (20 females and 26 males; age range, 46 − 81 years), who were enrolled in the LTRC, were included in this study. All subjects were current or former smokers (mean pack-years, 50.8 ± 38.4). Those who had pneumothorax, lobar atelectasis, huge bulla, interstitial pneumonia, a mass in the lung (>3 cm in diameter), or a previous history of a lung operation were not included in the study. Table 1 summarizes the characteristics of the subjects.

Pulmonary Function Tests

All 46 subjects performed prebronchodilator spirometry, including FEV_1 and forced vital capacity (FVC), according to American Thoracic Society standards as described previously (15). Diffusing capacity for carbon monoxide (DLco) was measured by the single breath method. These values were expressed as the percentages of predicted values. RV and TLC were also measured using plethysmography (16). Table 1 summarizes the PFT results.

According to the Global Initiative for Chronic Obstructive Lung Disease staging (17), 46 subjects were classified as follows: smokers with normal lung function, $n = 6$; Global Initiative for Chronic Obstructive Lung Disease stage 1, $n = 7$; stage 2, $n = 19$; stage 3, $n = 9$; and stage 4, $n = 5$.

TABLE 1. Clinical Characteristics of 46 LTRC Subjects

	Mean ± SD	Range
Age (y)	67.7 ± 7.9	46–81
Smoking index (pack-years)	50.8 ± 38.4	5–180
FEV_1 (%predicted)	57.9 ± 24.6	15–114
FEV_1/FVC	0.55 ± 0.14	0.25–0.81
RV/TLC	0.50 ± 0.12	0.32–0.73
DLco (%predicted)	61.6 ± 22.2	22–103

DLco, diffusing capacity for carbon monoxide; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity; LTRC, Lung Tissue Research Consortium; TLC, total lung capacity; RV, ratio of residual volume.

Thin-section CT

All subjects were scanned with 16-detector CT (Light Speed 16 or LightSpeed Pro16, GE Medical Systems, Milwaukee, WI) at full inspiration and full expiration without receiving a contrast medium. Before CT scanning, subjects were coached to hold breaths at full inspiration and full expiration. Images were obtained using 140 kV and 300 mA. The scanning field of view ranged from 28 to 44 cm, which was based on the subject's body habitus. Exposure time was 0.53 seconds and the matrix size was 512 × 512 pixels. Images were reconstructed with a 1.25 mm slice thickness (with 0.625 mm overlapping), using the "Bone" algorithm.

Measurements of Lung Volume and other CT Indices

The analysis for LV and other CT indices was performed using free open-source software (Airway Inspector, Brigham and Women's Hospital, Boston, MA) (www.airwayinspector.org), as described previously (18,19). The software automatically measured LV, LAA% (<−950 HU), and MLD. In brief, the software executed the following process: the software segmented the lung parenchyma (−1024 to −500 HU) from the chest wall and the hilum; LV was calculated by summing the voxels in this attenuation range; MLD was obtained by averaging the CT values of the voxels in the lung parenchyma; and the volume of LAA (−1024 to −950) in the lung parenchyma was calculated and LAA% was obtained by dividing the total LAA volume by LV. In each subject, this process was performed both on inspiratory and expiratory scans. Figure 1 shows an example of the analysis done by the software. Ultimately, E/I ratios of LV and MLD, as well as the differences in LV and MLD (ΔLV and ΔMLD) between inspiratory and expiratory scans, were calculated.

Statistical Analysis

All statistical analyses were performed using JMP 7.0 software (SAS Institute, Cary, NC). Data were expressed as mean ±