Computational Analysis of Thoracic Multidetector Row HRCT for Segmentation and Quantification of Small Airway Air Trapping and Emphysema in Obstructive Pulmonary Disease

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Rationale and Objectives: Obstructive pulmonary disease phenotypes are related to variable combinations of emphysema and small-airway disease, the latter manifested as air trapping (AT) on imaging. The investigators propose a method to extract AT information quantitatively from thoracic multi–detector row high-resolution computed tomography (HRCT), validated by pulmonary function testing (PFT) correlation.

Materials and Methods: Seventeen patients with obstructive pulmonary disease who underwent HRCT and PFT within a 3-day interval were retrospectively identified. Thin-section volumetric HRCT in inspiration and expiration was registered and analyzed using custom-made software. Nonaerated regions of lung were segmented through exclusion of voxels > −50 Hounsfield units (HU); emphysematous areas were segmented as voxels < −950 HU on inspiratory images. Small-airway AT volume (ATV) was segmented as regions of lung voxels whose attenuation values increased by less than a specified change threshold (set from 5 to 300 HU in 25-HU increments) between inspiration and expiration. Inspiratory and expiratory total segmented lung volumes, emphysema volume (EV), and ATV for each threshold were subsequently calculated and correlated with PFT parameters.

Results: A strong positive correlation was obtained between total segmented lung volume in inspiration and total lung capacity ($r = 0.83$). A strong negative correlation ($r = -0.80$) was obtained between EV and the ratio between forced expiratory volume in 1 second and forced vital capacity. Stronger negative correlation with forced expiratory volume in 1 second/forced vital capacity ($r = -0.85$) was demonstrated when ATV (threshold, 50 HU) was added to EV, indicating improved quantification of total AT to predict obstructive disease severity. A moderately strong positive correlation between ATV and residual volume was observed, with a maximum r value of 0.72 (threshold, 25 HU), greater than that between EV and residual volume ($r = 0.58$). The benefit of ATV quantification was greater in a subgroup of patients with negligible emphysema compared to patients with moderate to severe emphysema.

Conclusions: Small-airway AT segmentation in conjunction with emphysema segmentation through computer-assisted methodologies may provide better correlations with key PFT parameters, suggesting that the quantification of emphysema-related and small airway–related components of AT from thoracic HRCT has great potential to elucidate phenotypic differences in patients with chronic obstructive pulmonary disease.

Key Words: Air trapping; COPD; emphysema; quantification; deformable registration.

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Obstructive pulmonary disease is most often due to chronic obstructive pulmonary disease (COPD), which is a major global public health problem. It is the fourth leading cause of chronic morbidity and mortality in the United States and is anticipated to rank fifth in 2020 in burden of disease caused worldwide (1,2). Moreover, among the four major causes of mortality, namely, cardiovascular disease, malignant neoplasm, cerebrovascular disease, and COPD, the last is the only one that has been steadily rising in prevalence (2).

COPD is defined as chronic, progressive airflow limitation that is not fully reversible, associated with a range of pathologic changes in the lungs with significant extrapulmonary effects, caused by chronic inflammation and structural changes (1). The chronic airflow limitation is caused by a mixture of small-airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). The relative contributions of these two components vary substantially from patient to patient. The presence and extent of each component has the potential to affect clinical presentation, disease severity, prognosis, and therapeutic response (1).

The concept of COPD phenotyping addresses this variability in pathophysiologic presentation by attempting to separate emphysema (which we designate as static air trapping [AT]) from small-airway disease (which we designate as dynamic AT) and to quantify their relative contributions to each individual patient's clinical presentation (3,4). Currently, the diagnosis, classification of severity, and clinical follow-up of COPD patients rely on pulmonary function testing (PFT), which includes spirometry, gas diffusion testing, and lung volumes by body plethysmography (1). On the basis of spirometric parameters, patients are then categorized in normal, restrictive, obstructive, or combined patterns of disease, with the obstructive pattern typically associated with COPD (1). Furthermore, the degree of obstruction can be assessed quantitatively. Nevertheless, PFT parameters have a fundamental limitation, as they provide a global assessment of pulmonary function but cannot provide information regarding the regional heterogeneity of disease nor quantification of the relative contributions of emphysema and small-airway disease.

Imaging plays a secondary but increasingly important role in patients with COPD, particularly in the evaluation of emphysema (5). Most pulmonary imaging used clinically currently assesses anatomic changes and provides qualitative or gross semiquantitative estimates of disease severity. However, functional assessment is limited, and quantitative assessment is rarely used outside the research setting. Small-airway disease is often difficult to diagnose directly. Nonetheless, through the detection of regions of pulmonary AT as a surrogate marker for small-airway disease, paired inspiratory and expiratory thoracic high-resolution computed tomography (HRCT) may provide a means for quantitative COPD phenotyping.

On HRCT, the volume of emphysema is typically measured through application of an attenuation threshold mask (which may vary from −890 to −980 Hounsfield units [HU]) on inspiratory images (6–8). This is equivalent to static AT, in the sense that emphysematous areas of the lung lose elastic recoil and therefore do not change appreciably in volume between inspiration and expiration. In contradistinction, small-airway AT is characterized by lung parenchymal areas that are not emphysematous but that fail to increase in attenuation (or to decrease in volume) beyond a certain level between full inspiration and end-expiration (7). In clinical practice, the presence of small-airway AT is typically determined qualitatively through visual detection of persistent areas of low attenuation on expiratory HRCT images relative to inspiratory HRCT images, and the degree of small-airway AT is assessed semiquantitatively (none, mild, moderate, or severe) (9,10). An inability to objectively quantify the amount of small-airway AT limits the ability to phenotype COPD and to accurately assess response following therapeutic intervention, particularly in the setting of new drug development.

The goals of this preliminary study were to propose a computer-assisted methodology to extract quantitative data about emphysema and small-airway AT via a deformable registration model between paired inspiratory and expiratory HRCT image data sets with automatic segmentation of pulmonary volumes and to study their correlations with PFT parameters. We hypothesized that small-airway AT quantification in addition to emphysema quantification would provide better functional correlation between HRCT and PFT compared to emphysema quantification alone.

MATERIALS AND METHODS

Approval from our institutional review board and a Health Insurance Portability and Accountability Act waiver were obtained prior to study initiation for retrospective analysis of patient image data sets and PFT results.

Patient Selection

The selection criteria for inclusion in the study were an obstructive pattern on PFT, as measured by a ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) < 0.7 (indicating an obstructive pulmonary disease) and available paired inspiratory and expiratory thoracic HRCT studies within 3 days of PFT. Seventeen patients were chosen (11 women, 6 men; mean age, 56.76 years; range, 39–86 years). The severity of obstruction on PFT was classified following the 2005 American Thoracic Society and European Respiratory Society guidelines as mild (three patients), moderate (three patients), severe (five patients), and very severe (six patients). Eleven patients had primary clinical or radiologic diagnoses of COPD, whereas three patients had nontuberculous mycobacterial infection, one patient had cystic fibrosis, one patient had lymphangioleiomyomatosis, and one patient had granulomatous-lymphocytic interstitial lung disease.

Image Acquisition and Reconstruction

All patients were scanned using 64-slice multi–detector row computed tomography (Siemens Medical Systems, Malvern, PA). Images were acquired with 120 kVp, variable tube current–time products because of automatic tube current modulation, 64 × 0.75 mm collimation, pitch of 0.8, and