Paired Inspiratory/Expiratory Volumetric CT and Deformable Image Registration for Quantitative and Qualitative Evaluation of Airflow Limitation in Smokers with or without COPD

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Rationale and Objectives: To evaluate paired inspiratory/expiratory computed tomography (CT; iCT/eCT) and deformable image registration for quantitative and qualitative assessment of airflow limitation in smokers.

Materials and Methods: Paired iCT/eCT images acquired from 35 smokers (30 men and 5 women) were coregistered and subtraction images (air trapping CT images [aCT]) generated. To evaluate emphysema quantitatively, the percentage of low-attenuation volume (LAV%) on iCT was calculated at −950 HU, as were mean and kurtosis on aCT for quantitative assessment of air trapping. Parametric response maps of emphysema (PRMe) and of functional small airways disease (PRMs) were also obtained. For qualitative evaluation of emphysema, low-attenuation areas on iCT were scored by consensus of two radiologists using Goddard classification. To assess air trapping qualitatively, the degree of air trapping on aCT was scored. For each quantitative and qualitative index, the Spearman rank correlation coefficient for forced expiratory flow in 1 second was calculated, and differences in correlation coefficients were statistically tested.

Results: The correlation coefficients for the indices were as follows: mean on aCT, 0.800; kurtosis on aCT, −0.726; LAV%, −0.472; PRMe, −0.570; PRMs, −0.565; addition of PRMe and PRMs, −0.653; emphysema score, −0.502; air trapping score, −0.793. The indices showing significant differences were as follows: mean on aCT and addition of PRMe and PRMs ($P = 1.43 \times 10^{-8}$); air trapping score and emphysema score ($P = .0169$).

Conclusions: Air trapping images yielded more accurate quantitative and qualitative evaluation of airflow limitation than did LAV%, PRMe, PRMs, and Goddard classification.

Key Words: COPD; emphysema; airflow limitation; image registration.

Chronic obstructive pulmonary disease (COPD) is characterized by chronic and progressive airflow limitation that is not fully reversible (1). According to a projection made in 2002, COPD is expected to become the fourth leading cause of death in the world by 2030 (2). Moreover, COPD is the only one with a steadily rising prevalence among the four major causes of mortality: cardiovascular disease, malignant neoplasm, cerebrovascular disease, and COPD (3).

Airflow limitation in COPD is caused by lung parenchymal destruction (emphysema) and small airways disease. Contributions of these two components to airflow limitation vary substantially from patient to patient, thus potentially affecting clinical presentation, disease severity, and therapeutic response (1). Furthermore, separate assessment of emphysema and small airways disease provides valuable information regarding disease heterogeneity for identification of COPD phenotypes (4).

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For quantification of emphysema with computed tomography (CT), percentage of low-attenuation volume (LAV%) is most widely accepted and highly efficacious (5). On the other hand, accurate evaluation of small airways disease has been difficult because small airways cannot be directly visualized by clinical CT scanners because of limited spatial resolution (6). Recently, therefore, several studies have focused on quantification of air trapping on paired inspiratory/expiratory CT scans to determine the extent of small airways disease (6–13). In addition, the parametric response map (PRM) has been developed as a versatile imaging biomarker capable of assessing the extent of emphysema and small airways disease and providing detailed spatial information on disease distribution in COPD (13). To the best of our knowledge, however, there has been no study to compare PRM to other types of quantification of air trapping.

We hypothesized that the extent of emphysema and small airways disease in COPD patients could be evaluated quantitatively and qualitatively with the aid of paired inspiratory/expiratory volumetric CT images and deformable image registration (12,13). Thus, the aims of our study were as follows: 1) to develop a new methodology for evaluating airflow limitation caused by small airways disease, 2) to correlate quantitative and qualitative indices made possible by the new methodology with airflow limitation measured by pulmonary function test, and 3) to compare the usefulness of these indices obtained with our methodology to that of other quantitative and qualitative indices, including LAV% (5), PRM (13), and Goddard classification (14).

MATERIALS AND METHODS

The review board of our institution approved this retrospective study. Written informed consent was obtained from all patients for the use of their data for research.

Patients

Thirty-five patients were included in this retrospective study, comprising 30 men and five women aged 70.5 ± 11.5 years (mean ± standard deviation) with a smoking history of 51.0 ± 40.6 pack years. Twenty-nine patients were diagnosed with COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (1). Their GOLD classification was as follows: stage I, 3; stage II, 19; and stage III and IV, 7. These patients visited our hospital because of smoking cessation or COPD treatment. Patients with active pneumonia, lung tumor, or mediastinal tumor were excluded. All the patients underwent the pulmonary function test and paired inspiratory/expiratory CT scans, and the mean interval between the two procedures was 13.5 ± 16.9 days.

Pulmonary Function Test

The pulmonary function test was performed with an automated spirometer (System 9 or 21; Minato Ikagaku, Osaka, Japan). Data were obtained for vital capacity, residual volume, forced expiratory flow in 1 second (FEV_1), forced vital capacity, ratio of FEV_1 to forced vital capacity (FEV_1/FVC), and diffusing capacity of the lung for carbon monoxide. The results of the pulmonary function test, except for FEV_1/FVC, were expressed as percentages of the standard predicted values established by the Japanese Respiratory Society (15).

CT Scan Acquisition

All the patients were scanned with a 320-detector-row scanner (Aquilion ONE; Toshiba Medical Systems, Otawara, Japan), which was calibrated regularly with a standard water and air phantom. Noncontrast helical CT scans were acquired from the lung apices through the lung bases. After having been given careful instruction for breathing, the patients were scanned at full inspiration and full expiration. The same parameters were used for both CT scans: tube current, 250–270 mA; tube potential, 120 kV; gantry rotation time, 0.5 seconds; and pitch, 0.869. Spirometric gating was not used for this study. Raw CT data were reconstructed into contiguous 1-mm thick images with a standard kernel (FC 13).

Deformable Image Registration

The Open Source software Advanced Normalization Tools (ANTS; available at http://www.picsl.upenn.edu/ANTS) was used for deformable image registration (12,16). Evaluation of Methods for Pulmonary Image Registration 2010 ranked ANTS-based image registration as the highest among 34 algorithms (17). For this study, the parameters of ANTS were adjusted as previously reported (18). The image registration was performed using antsIntroduciton.sh, which was included in ANTS.

The previously obtained paired inspiratory/expiratory volumetric CT images were downsized to reduce the amount of computation required. The downsized images were then sent to a computational pipeline that automatically coregistered the two sets of CT images and generated a voxel-by-voxel correspondence between them. In the present study, the inspiratory CT images were reference, and the downsized expiratory CT images were deformed. Finally, voxel-by-voxel subtraction between the downsized coregistered inspiratory/expiratory CT images yielded downsized subtraction CT images. Eventually, five sets of CT images for each patient were obtained for quantitative and qualitative evaluation: acquired paired inspiratory/expiratory CT images, downsized coregistered inspiratory/expiratory CT images, and downsized subtraction CT images. A schematic diagram of the procedure for image preparation is shown in Figure 1.