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Quantitative computed tomography measurements to evaluate airway disease in chronic obstructive pulmonary disease: Relationship to physiological measurements, clinical index and visual assessment of airway disease

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ABSTRACT

Purpose: To correlate currently available quantitative CT measurements for airway disease with physiological indices and the body-mass index, airflow obstruction, dyspnea, and exercise capacity (BODE) index in patients with chronic obstructive pulmonary disease (COPD).

Materials and methods: This study was approved by our institutional review board (IRB number 2778). Written informed consent was obtained from all subjects. The subjects included 188 current and former cigarette smokers from the COPDGene cohort who underwent inspiratory and expiratory CT and also had physiological measurements for the evaluation of airflow limitation, including FEF25-75%, airway resistance (Raw), and specific airway conductance (sGaw). The BODE index was used as the index of clinical symptoms. Quantitative CT measures included % low attenuation areas [% voxels ≤ 950 Hounsfield unit (HU) on inspiratory CT, $\%LAA_{-950ins}$], percent gas trapping (% voxels ≤ −856 HU on expiratory CT, $\%LAA_{-856exp}$), relative inspiratory to expiratory volume change of voxels with attenuation values from −856 to −950 HU [Relative Volume Change $(RVC)_{-856\ to\ -950}$], expiratory to inspiratory ratio of mean lung density ($E/I\text{-ratio}_{MLD}$), Pi10, and airway wall thickness (WT), luminal diameter (LD) and airway wall area percent (WA%) in the segmental, subsegmental and subsubsegmental bronchi on inspiratory CT. Correlation coefficients were calculated between the QCT measurements and physiological measurements in all subjects and in the subjects with mild emphysema ($\%LAA_{-950ins}$ <10%). Univariate and multiple variable analysis for the BODE index were also performed. Adjustments were made for age, gender, smoking pack years, FEF25-75%, Raw, and sGaw.

Results: Quantitative CT measurements had significant correlations with physiological indices. Among them, $E/I\text{-ratio}_{MLD}$ had the strongest correlations with FEF25-75% (r = −0.648, <0.001) and sGaw (r = −0.624, <0.001) while in the subjects with mild emphysema subsegmental WA% and segmental WA% had the strongest correlation with FEF25-75% (r = −0.669, <0.001) and sGaw (r = −0.638, <0.001), respectively. The multiple variable analyses showed that $RVC_{-856\ to\ -950}$ was an independent predictor of the BODE index showing the highest R^2 (0.468) as an independent variable among the QCT measurements.

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Conclusion: Quantitative CT measurements of gas trapping such as E/I-ratio $_{MLD}$, correlate better with physiological indices for airway disease than those of airway such as WA% or LD. In mild emphysema, however, quantitative CT measurements of airway correlate better with the physiological indices. $RVC_{-856\ to\ -950}$ is a predictor of the BODE index.

1. Introduction

Quantitative CT (QCT) analysis has emerged as a new approach to measure the disease severity of chronic obstructive lung disease (COPD). QCT assessment of emphysema, using the density mask technique, correlates quite well with spirometric measurements and with pathologic severity of emphysema [1,2] and spirometric evaluation [3–7] with the clinical status of COPD patients [8–13]. QCT may also estimate the degree of small airway disease of COPD indirectly by using the percent of low attenuation area less than or equal to −856 Hounsfield unit (HU) on expiratory CT ($\%LAA_{-856exp}$) or directly by using airway measurements, such as airway wall thickness (WT), luminal diameter (LD) and airway wall area percent (WA%). Several reports have already documented the feasibility of these airway measurements from multidetector CT acquisitions, which may reflect the severity of small airway disease [8–10,12–20]. However, it is not still fully understood which QCT measurements will better represent the severity of airway disease in COPD. Especially, our concern was whether indirect measurements (i.e. measurements of gas trapping) or direct measurements (i.e. measurements of airway) are better to reflect the severity of airway disease. Thus, this study aimed to determine which of currently available measurements is most feasible to represent the clinical severity of airway disease of COPD by evaluating the relationship between airway QCT parameters and physiological indices of airway disease, and clinical severity of COPD. We also tried to visually grade the severity of airway disease of COPD and correlated the grading system with the clinical indices and compared with airway QCT parameters.

2. Materials and methods

This study was approved by our institutional review board (IRB number 2778). Written informed consent was obtained from all subjects, and the study was compliant with the Health Insurance Portability and Affordability Act. This study was retrospectively conducted in a single institution using part of the COPDGene study data, which has prospectively been being gathered.

2.1. Study population

The study subjects consisted of 188 current and former cigarette smokers who had complete sets of QCT measurements obtained by CT according to the study protocol [21] and also had physiological airway measurements, including Raw, sGaw and FEF25-75%, measured within 90 days of CT examination between February, 2008 and December, 2010. The physiological measurements were performed according to the ATS guidelines [22,23].

2.2. Clinical parameter to estimate the severity of COPD

The body-mass index, airflow obstruction, dyspnea, and exercise capacity index (BODE) [24] was used to estimate the clinical severity of COPD. The BODE index was available in all the study subjects. The BODE index was calculated as previously reported [24].

2.3. CT examination

CT examination was performed according to the standardized COPDGene study protocol [21]. In brief, all subjects underwent volumetric CT at full inspiration and at the end of a normal expiration. All CT scans were performed with a tube potential peak of 120 kVp with a fixed mAs of 200 for inspiratory CT and 50 for expiratory CT at a gantry rotation time of 0.5 s. The reconstructed slice thicknesses were 0.625 mm and 0.60 mm for General Electric Medical Systems and Siemens scanners, respectively. Scans were acquired on LS-16 (General Electric Medical Systems) (n = 15), Definition-64(Siemens Medical Solutions) (n = 121) or Definition-AS-128 (Siemens Medical Solutions) (n = 52) scanner.

2.4. CT quantification

All CT images were analyzed using the Pulmonary Workstation 2 software (VIDA Diagnostics, Inc, Coralville, IA). Soft tissue algorithms were used for CT quantification. Both lungs as well as each lung lobe were automatically segmented with manual edits as necessary by professional technologists. Proximal vasculature and bronchi were automatically removed. Percent low attenuation areas were defined as percent lung tissue ≤ −950HU on inspiratory CT ($\%LAA_{-950ins}$) (Fig. 1A). Percent gas trapping areas were defined as percent lung tissue ≤ −856HU on expiratory CT ($\%LAA_{-856exp}$). This definition of gas trapping is based on the concept that the attenuation of normal lung parenchyma is usually around −856 HU on inspiratory CT and thus areas with CT attenuation less than −856HU on expiratory CT can be regarded as showing inadequate gas emptying (i.e. gas trapping). In addition, we measured the relative inspiratory to expiratory volume change of voxels with attenuation values from −856 to −950 HU ($RVC_{-856\ to\ -950}$) which was proposed by Matsuoka et al. as a measurement of gas trapping [25]. This measure is calculated by the following formula: $RVC_{-856\ to\ -950}$ = relative lung volume −856 HU to −950 HU on expiratory CT% −relative lung volume −856 HU to −950 HU on inspiratory CT% [relative lung volume −856 HU to −950 HU% = (lung volume between −856 HU and −950HU in voxel CT value) × 100/lung volume ≥ −950HU in voxel CT value] [25]. We also calculated the expiratory to inspiratory ratio of mean lung density (E/I-ratio $_{MLD}$) [26]: the expiratory mean lung density in HU is divided by the inspiratory mean lung density, and presented as percentage. Thus, increase in gas trapping results in a higher E/I-ratio $_{MLD}$.

The airway tree was generated using an automated region-growing technique (Fig. 1B). Detailed airway analysis was completed for the segmental bronchi in six selected airway pathways (RB1, RB4, and RB10 of the right lung and LB1, LB4 and LB10 of the left lung), as well as two generations distally. Airway wall disease was evaluated using measures of airway wall thickness, luminal diameter and airway wall area percent (% wall area/total bronchial area) (Fig. 1C).These measurements were quantified in each of 6 segmental, subsegmental and subsubsegmental bronchi. Airway measurements were obtained as averages across the middle third of each segment. We calculated mean values of airway wall thikness (WT), luminal diameter (LD) and airway wall area percent