Pulmonary Function Parameters in High-resolution Computed Tomography Phenotypes of Chronic Obstructive Pulmonary Disease

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Abstract: *Background:* Heterogeneity of clinical presentation of chronic obstructive pulmonary disease (COPD) attributes to different pathological basis. High-resolution computed tomography (HRCT) phenotypes of COPD may reflex the pathological basis of COPD indirectly by evaluating the small airway inflammation and emphysema. How the pulmonary function related with different HRCT phenotypes has not been well known. The aim was to explore the features of pulmonary function parameters in the 3 phenotypes. *Methods:* Sixty-three stable COPD patients were allocated in 3 groups based on HRCT findings: phenotype A (absence of emphysema, with minimal evidence of emphysema with or without bronchial wall thickening [BWT]), phenotype E (emphysema without BWT) and phenotype M (emphysema with BWT). The pulmonary function testing was also analyzed. *Results:* The values of forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC%), FEV_1% and maximum expiratory flows $(MEF)_{50}$% were the highest in phenotype A ($P < 0.05$), so was residual volume (RV)/total lung capacity (TLC%) in phenotype E ($P < 0.05$). Those with MEF_{50}/MEF_{25} ratio >4.0 were more prevalence in phenotype A than in E and M (odds ratio = 2.214; $P < 0.05$). The occurrences of RV/TLC% >40% were higher in phenotype E than in A and M (odds ratio = 3.906; $P < 0.05$). Receiver operating characteristic analysis showed that the cutoff value of MEF_{50}/MEF_{25} ratio for identifying phenotype A was 2.5, with sensitivity 66.7% and specificity 92.9%. The cutoff value of RV/TLC% for identifying phenotype E was 57.4%, with sensitivity 75.0% and specificity 79.1%. *Conclusions:* The different features of pulmonary function parameters were found in various HRCT phenotypes; MEF_{50}/MEF_{25} ratio could imply phenotype A, whereas RV/TLC% may be the indicator of phenotype E.

Key Indexing Terms: Chronic obstructive pulmonary disease; High-resolution computed tomography; Pulmonary function parameters; MEF_{50}/MEF_{25} ratio; RV/TLC%. **[Am J Med Sci 2015;349(3):228–233.]**

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease both in its clinical presentation and pathologic basis.[1] Although forced expiratory volume in 1 second (FEV_1) acts as the major index for diagnosis and evaluation of COPD, it cannot provide a comprehensive evaluation of the complexity of COPD by itself.[2,3]

For better evaluation of COPD, it is essential to find the underline pathological basis, even with the same FEV_1 grade.[4] However, it is hard to get pathological evidence without biopsy. Developed advances in high-resolution computed tomography (HRCT) have allowed direct radiographic assessment of luminal caliber and wall thickness of small airways.[5,6] Morphologically, the HRCT of some patients with COPD could show severe emphysema with apparent low attenuation areas (LAA), accompanied with or without inflammation of bronchial wall thickening (BWT).[7–9] Based on above, HRCT phenotypes were concerned to reflect the pathologic changes indirectly, that is, phenotype A, which means absence or minimal evidence of emphysema, with or without BWT; phenotype E means emphysema without BWT, and phenotype M shows emphysema with BWT.

As for the pulmonary function, reductions in expiratory flow are generally appreciated as the relatively sensitive measurements of small airway obstruction.[10] Maximum expiratory flows (MEF) at forced vital capacity (FVC) impairments can reflect various pathological changes of small airway.[11] The ratio of MEF_{50} to MEF_{25} (MEF_{50}/MEF_{25} ratio) greater than 4.0 is used as an index of injury to the small airways in subjects even without airflow limitation in Japan.[12] MEF_{50}/MEF_{25} ratio depends on the elastic recoil pressure in the alveoli, airway resistance and bronchial collapsibility instead of emphysema. In small airway disease, MEF_{25} is thought to decrease more than MEF_{50}, resulting in the elevation of MEF_{50}/MEF_{25} ratio, even with no abnormality in FVC or FEV_1.[13] Residual volume (RV) increases greater than total lung capacity (TLC) and leads to an increase in lung volume with COPD. The increased lung volumes may allow increased radial traction from the reduced numbers of parenchymal attachments that distend the airways with further inspiration. It is important to note RV/TLC% to assess the severity of emphysema (SE).

Until recently, few studies have been carried out to clarify the morphological changes correlated with pulmonary function.[14,15] Thus, it aimed to investigate the features of pulmonary function parameters in different HRCT phenotypes.

MATERIALS AND METHODS

Study Population

A total of 63 stable COPD patients presenting beyond 40 years old were recruited from the outpatient clinic of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, from October 2012 to September 2013. Diagnosis was made according to the Global Initiative for Chronic Obstructive Lung Disease Guidelines (GOLD).[9] The study was approved by the Ethics Boards of Ruijin Hospital, and all subjects gave written informed consent before participating. Patients were excluded if

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they had a history of asthma and/or cystic fibrosis, any relevant cardiovascular disorders or events. In addition, patients who had suffered from either a respiratory tract infection or exacerbation of an airway disease in the previous 3 weeks or had other disorders that may have influenced the results of the study were also excluded.

Age, body mass index (BMI, kg/m^2), history of smoking and morning pulmonary function testing were documented for all patients. Postbronchodilator ratio of FEV_1 to FVC (FEV_1/FVC %), FEV_1 in percent of predicted (FEV_1%), maximal expiratory flow at 25% (MEF_{25}%), 50% (MEF_{50}%) and 75% (MEF_{75}%) of the FVC, RV/TLC% were analyzed.

HRCT Phenotypes

HRCT scanning (SomAToM; Siemens, Germany) at full inspiration (at TLC level with 140 KVp, 200 mA and pitch of 1.375) were performed. Three slices (1 mm thick) were obtained at 3 anatomical levels: upper (1 cm above the superior margin of the aortic arch), middle (1 cm below the carina) and lower lung field level (3 cm above the right diaphragm) (Figure 1).

Evaluation of Emphysema

The HRCT images were photographed with a window setting appropriate for the lungs (window level from −700 to −900 HU; width from 800 to 1000 HU). Emphysema was scored visually by LAA in the bilateral upper, middle and lower lung fields according to the method of National Emphysema Treatment Trial.[16] The score in each dimension was calculated as the percentage of LAA to the total lung field area,[8] that is, score 0: LAA $<$ 5%; 1:5% $\leq$ LAA $<$ 25%; 2:25% $\leq$ LAA $<$ 50%; 3:50% $\leq$ LAA $<$ 75% and 4:LAA $\geq$ 75%. The SE was graded in accordance with the sum of scores taken from 6 dimensions as follows: grade 0, total score = 0; grade 1, total score = 1 to 3; grade 2, total score = 4 to 6; grade 3, total score = 7 to 9 and grade 4, total score = 10 to 12.

Evaluation of Bronchitis

HRCT images were obtained at the window levels appropriate for bronchi (airways ranged from 2 to 4 mm in diameter) (window width: 1500 HU; window level: −450 HU) and mediastina (window width: 400 HU; window level: 63 HU).[17] BWT in all lung fields was graded as reported automatically by software[18]: grade 0, BWT $<$30% of adjacent pulmonary artery diameter; grade 1, 30% $\leq$ BWT $<$ 50% of adjacent pulmonary artery diameter and grade 2, BWT $\geq$50% of adjacent pulmonary artery diameter.

Confirmation of HRCT Phenotypes

HRCT images were analyzed independently by 1 chest radiologist and 1 pulmonary physician. Three phenotypes according to the visual HRCT findings were defined as follows,[8] phenotype A (SE $\leq$1 regardless of BWT), phenotype E (SE $\geq$grade 2 without BWT) and phenotype M (SE $\geq$grade 2 and BWT $\geq$grade 1).

Statistical Analysis

The data were expressed as mean ± SD. The distributions of the HRCT phenotypes were compared using Pearson's χ^2 test. Differences among HRCT phenotypes were analyzed by 1-way analysis of variance followed by least significant difference post hoc tests. Multiple logistic regression analysis was used to calculate odds ratio (OR) with 95% confidence interval (CI) for association of clinical characteristics, pulmonary function and HRCT phenotypes. The sensitivity and specificity for MEF_{50}/MEF_{25} ratio and RV/TLC% cutoff values were calculated by constructing receiver operating characteristic (ROC) curves. The data were analyzed using computer programs: SPSS (13.0; Chicago, IL). Statistical trends were considered to be significant at $P < 0.05$.

RESULTS

Demographics and HRCT Phenotypes

A total of 63 patients with COPD (average age: 69 years; 43 male/20 female) were classified into 3 groups based on the HRCT findings, that is, phenotype A group (21 cases), phenotype E (20 cases) and phenotype M (22 cases) (Table 1).

Ages were not significantly different among the 3 phenotypes ($P > 0.05$). As for gender difference, there was a higher proportion of females (13/21) in phenotype A than phenotype E (3/20) and phenotype M (4/22) ($P = 0.002$). Higher BMI was found in patients in phenotype A than phenotype E or M (25.2 ± 3.5 vs. 21.6 ± 3.9 and 21.2 ± 2.9 kg/m^2; $P < 0.01$). The smoke rate was lower in phenotype A than in the other 2 phenotypes ($P = 0.014$).

The FEV_1/FVC%, FEV_1%, MEF_{50}% and MEF_{50}/MEF_{25} ratio were significantly higher in phenotype A than in the other 2 phenotypes ($P < 0.05$). However, the RV/TLC% was significantly higher in phenotype E than in phenotype A ($P < 0.05$). MEF_{25}% and MEF_{75}% did not show any differences among 3 phenotypes ($P > 0.05$).

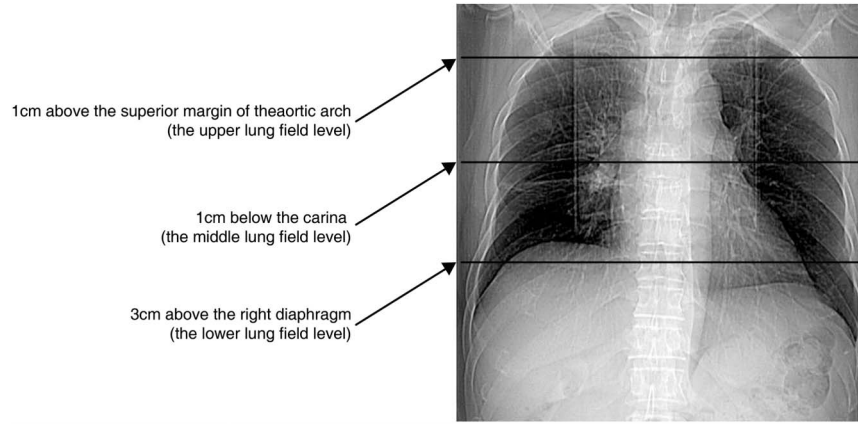

FIGURE 1. Evaluation of HRCT scanning at 3 anatomical levels.