

The COPD assessment test correlates well with the computed tomography measurements in COPD patients in China

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Background: The chronic obstructive pulmonary disease (COPD) assessment test (CAT) is a validated simple instrument to assess health status, and it correlates well with the severity of airway obstruction in COPD patients. However, little is known about the relationships between CAT scores and quantitative computed tomography (CT) measurements of emphysema and airway wall thickness in COPD patients in the People's Republic of China.

Methods: One hundred and twelve participants including 63 COPD patients and 49 normal control subjects were recruited. All participants were examined with high-resolution CT to get the measurements of emphysema (percentage of pixels below -950 HU [%LAA-950]) and airway wall thickness (wall area percentage and the ratio of airway wall thickness to total diameter). Meanwhile, they completed the CAT and modified Medical Research Council questionnaire independently.

Results: Significantly higher CAT scores and CT measurements were found in COPD patients compared with normal control subjects ($P < 0.05$), and there was a tendency of higher CAT scores and CT measurements with increasing disease severity measured by GOLD staging system. Positive correlations were found between CAT scores and CT measurements ($P < 0.01$). Using multiple linear stepwise regression, CAT score = $-46.38 + 0.778 \times (\text{wall area percentage}) + 0.203 \times (\% \text{LAA}-950)$ ($P < 0.001$). Meanwhile, CAT scores and CT measurements in COPD patients all positively correlated with the modified Medical Research Council grades and negatively correlated with $\text{FEV}_1\%$ ($P < 0.01$).

Conclusion: CAT scores correlate well with the quantitative CT measurements in COPD patients, which may provide an imaging evidence that the structural changes of the lungs in this disease are associated with the health status measured by CAT.

Keywords: chronic obstructive pulmonary disease, pulmonary function, quantitative computed tomography

Introduction

The chronic obstructive pulmonary disease (COPD) assessment test (CAT) is a simple, validated, patient-completed questionnaire to assess and quantify health status and symptoms burden in COPD patients.^{1,2} It comprises eight questions, each presented as a semantic six-point (0–5) differential scale, providing a total score out of 40. Scores of 0–10, 11–20, 21–30, and 31–40 represent mild, moderate, severe, or very severe clinical impact, respectively.³ The CAT has good internal consistency and test-retest reliability;¹ previous studies have shown its significance in diagnosis, response to therapies, and management both in stable and exacerbating COPD patients.^{4–8} CAT scores correlate well with important parameters of the disease, such as dyspnea grades, pulmonary function parameters, etc.^{7–9} Nowadays, it is widely used in clinical practice all over the world.

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COPD is a chronic lung disease, and it can lead to certain irreversible structural changes in the lungs, including airway wall remodeling and emphysematous lung destruction.¹⁰ With the advances both in computed tomography (CT) technology and computer software, the multi-slice spiral CT has not only improved the early diagnosis of pulmonary microstructures and morphologic changes, but also made the quantitative measurements of structural changes in the lungs possible.^{11–13} Since the high-resolution CT (HRCT) technology has a good spatial resolution, it is currently a better imaging technology to observe small airway and lung tissue disease.¹⁴ Studies have demonstrated that –950 Hounsfield units (HU) in the inspiratory phase is a suitable threshold for the measurements of retention volume in emphysema,^{15,16} and the ratio of airway wall thickness to total diameter (WT/D) and wall area percentage (%WA) from CT scans can represent the airway dimensions in COPD patients.^{17,18} Moreover, researchers have conducted a series of studies on the relationships between disease-specific parameters and quantitative CT measurements.^{18–20} As far as we know, little is known about the relationships between CAT scores and quantitative CT measurements of emphysema and airway wall thickness in COPD patients in the People's Republic of China.

In the present study, we hypothesized that CAT scores might be related to the extent of emphysema and airway wall thickness in COPD patients. By measuring the extent of emphysema and airway wall thickness with HRCT, and investigating the relationships between CAT scores and quantitative CT measurements, we explored if there is any

association of CAT scores and structural changes of the lungs in COPD patients.

Materials and methods

Subjects

One hundred and twelve participants including 63 COPD patients and 49 normal control subjects (inclusion and exclusion criteria shown in Tables 1 and 2, respectively) were recruited. The COPD patients came from the Pulmonary Department, First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, People's Republic of China, and the normal control subjects were all volunteers. Demographic information such as height, weight, age, and smoking history were recorded at recruitment. The study was approved by the ethics committee of the First Affiliated Hospital of Anhui Medical University. All participants had given written informed consent to participate in the study and were informed of the possible risks of the study. The study was performed from July 1, 2013 to February 28, 2014.

Assessment of health status and dyspnea

The health status was evaluated by CAT, which can also provide an assessment of symptoms burden. The degree of dyspnea was evaluated with the modified Medical Research Council (mMRC) questionnaire. All subjects completed CAT and mMRC questionnaires independently on the day of taking HRCT scans. The effect of COPD on health status was measured by the CAT scores, and the COPD patients

Table 1 Inclusion and exclusion criteria for COPD patients

Inclusion criteria	Exclusion criteria
1. Age 40–80 years	Common exclusion criteria
2. Male or female	1. Unstable cardiovascular disease, such as uncontrolled high blood pressure, congestive heart failure, angina, etc
3. COPD diagnosed according the GOLD guidelines	2. Severe hepatic and renal dysfunction, malnutrition, malignant tumor, and severe anemia
4. Stable clinically, without change of medication or acute exacerbation within the past 6 weeks	3. Mental illness
5. No use of β 2-receptor agonist or anticholinergic drugs at least 12 hours before attending the study	4. History of taking regular corticosteroids or other immunosuppressive agents
6. Forced expiratory volume in 1 second to forced vital capacity ratio <70% after use of bronchodilator	5. Participation in other studies within the past 6 weeks
7. ≥ 10 pack-years history of smoking now or in the past	Exclusion criteria related to lung
8. Capable of completing CAT and mMRC questionnaires	1. Arterial oxygen saturation <90% at rest
9. Informed consent obtained	2. Acute exacerbation of COPD or pneumonia within the past 6 weeks
	3. Diagnosis of other chronic lung disease (such as bronchiectasis, cystic fibrosis, asthma, interstitial lung disease, lung cancer, etc), a history of pulmonary bulla, or pneumonectomy or other lung surgery
	4. Active pulmonary tuberculosis
	5. History of chest radiation therapy, pulmonary rehabilitation therapy, or other therapies before attending this study

Abbreviations: CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; mMRC, modified Medical Research Council.

Table 2 Inclusion and exclusion criteria for normal control subjects

Inclusion criteria	Exclusion criteria
1. Age 40–80 years	1. History of pulmonary disease or other system diseases (acute or chronic)
2. Male or female	2. Mental illness
3. No illness, symptoms, or other discomfort	3. History of taking corticosteroids or immunosuppressive agents
4. Capable of completing CAT and mMRC questionnaires	4. Have ever participated or participating in any health care activities
5. Informed consent obtained	

were classified into group I (mild), II (moderate), III (severe), and IV (very severe) according to their CAT scores.³

HRCT scans and analysis

We measured emphysema and airway wall thickness using HRCT scans, which was performed using a 64-slice spiral CT scanner (Discovery HD750; GE, USA) at full inspiration without receiving contrast medium. Images were obtained at 120 kVp and 30–60 mAs. The exposure time was 1 second and the matrix size was 512×512 pixels. Images were contiguously reconstructed using a standard algorithm with a slice thickness of 0.625 mm and a slice interval of 5 mm. In transverse reconstructed images with a window width of 1,500 HU and window level of –600 HU on the workstation monitor. Reconstructed data were transferred to advantage workstation, and measurements of CT metrics were obtained with commercial software (Pulmonary Workstation; Vida Diagnostics, Coralville, IA, USA). All CT scans were reviewed by two experienced chest radiologists. Airway measurements were collected in the apical bronchus of the right upper lobe. %WA was calculated as (total airway area – airway lumen)/total airway area ×100, and WT/D was calculated as airway wall thickness/outer diameter.¹⁸ Emphysema was defined as low attenuation areas using the HU threshold of –950;^{15,16} we calculated the percentage of pixels below this threshold (%LAA–950) from the total number within lung parenchyma.

Pulmonary function test

Post-bronchodilator FEV₁ was measured at 15 minutes after inhaling salbutamol (Ventolin; GlaxoSmithKline plc, London, UK) 400 µg, and the pulmonary function test was performed using a dry spirometer device (Erich Jaeger GmbH, Hoechberg, Germany). Subjects with FEV₁/FVC <0.70 were defined as having COPD, and FEV₁ higher than 50% predicted were classified as GOLD I–II group; subjects with FEV₁ lower than 50% predicted were classified as GOLD III–IV group according to the GOLD staging system.¹⁰

Statistical analysis

Demographic and clinical characteristics of all subjects were summarized descriptively. Data were expressed as mean ± standard deviation. Data of CT measurements were all expressed as percentages. SPSS Statistics version 17.0 was used for statistical analysis. Group comparisons were tested using one-way analysis of variance. Differences between sex ratios were compared with the chi-square test. Pearson's correlation test was used to verify the relationship between numerical variables with normal distributions. The Spearman's rank correlation test was applied to nonparametric variables. Multiple linear stepwise regression analysis was used to explore the relationship between CAT scores and quantitative CT measurements. Values of $P < 0.05$ were considered to be significant.

Results

Demographic characteristics of all subjects

One hundred and twelve participants were recruited, and the average age was 66.97±10.46 years. The subjects were classified into three groups: GOLD I–II group (n=30), GOLD III–IV group (n=33), and control group (n=49). Table 3 shows the clinical characteristics of each group. The three groups were statistically similar with respect to age, sex, and body mass index (BMI) ($P > 0.05$), but the smoking index and mMRC grades were significantly higher in the COPD groups compared to the control subjects ($P < 0.01$), the pulmonary function parameters (FEV₁% and FEV₁/FVC) were significantly lower in the COPD groups ($P < 0.01$). Moreover, mMRC grade was significantly higher in the GOLD III–IV group compared to the GOLD I–II group ($P < 0.01$), and the pulmonary function parameters were significantly lower in the GOLD III–IV group compared to the GOLD I–II group ($P < 0.01$).

Relationships between CAT scores and CT measurements in COPD patients

The CAT scores and CT measurements of emphysema and airway wall thickness in COPD patients were all

Table 3 Characteristics of all subjects

Characteristic	Control group n=49	GOLD I-II group n=30	GOLD III-IV group n=33	P
Age, years	65.1±10.3	68.6±10.1*	68.8±11.2*+	0.20 ^a
Sex, female/male	21/28	13/17	11/22	0.35 ^b
BMI (kg/m ²)	23.6±2.9	23.2±3.2*	22.9±3.4*+	0.52 ^a
Smoking index	6.7±10.9	17.6±18.4***	22.8±28.2***+	0.000 ^a
mMRC grade	0.1±0.2	1.4±0.9**	2.6±0.7***++	0.000 ^a
FEV ₁ %	100.3±13.7	63.1±7.2**	35.4±6.5***++	0.000 ^a
FEV ₁ /FVC (%)	82.4±4.8	63.9±4.0**	45.3±7.4***++	0.000 ^a

Notes: Data are presented as means ± standard deviation. *P*-values were calculated by one-way analysis of variance, except where indicated otherwise. **P*>0.05, ***P*<0.01, ****P*<0.05 versus control group; +*P*>0.05, ++*P*<0.01 versus GOLD I-II group. *One-way analysis of variance. ^aAnalysis of chi-square test.

Abbreviations: BMI, body mass index; mMRC, modified Medical Research Council.

significantly higher than in control subjects (*P*<0.05), as shown in Table 4. There was a tendency of higher CAT scores and CT measurements with increasing disease severity measured by GOLD staging system. CAT scores were taken as a dependent variable, while quantitative CT measurements, age, sex, and BMI were taken as independent variables in multiple linear stepwise regression analysis. Age, sex, BMI, and WT/D were not retained, but %LAA–950 and %WA were independent predictors of CAT score, giving the equation:

$$\text{CAT score} = -46.38 + 0.778 (\% \text{WA}) + 0.203 (\% \text{LAA-950}) \quad (1)$$

(*r*²=0.38, *P*=0.000). With the Pearson's correlation analysis, positive correlations were found between the CAT scores and %LAA–950 (*r*=0.46, *P*=0.000, Figure 1), %WA (*r*=0.48, *P*=0.000, Figure 2), and WT/D (*r*=0.37, *P*=0.003, Figure 3).

After classifying the COPD patients into four groups according to their CAT scores, 12 patients were group I (mild), 17 patients were group II (moderate), 25 patients were group III (severe), and nine patients were group IV (very severe). Table 5 shows the CT measurements in different CAT groups,

and significant differences were found in %LAA–950 and %WA between group I and other groups (*P*<0.05), but no difference was found in WT/D among CAT groups (*P*>0.05).

Relationships between pulmonary function and CT measurements, CAT scores in COPD patients

The mean value of pulmonary function parameters (FEV₁% and FEV₁/FVC) in each group are shown in Table 3. The FEV₁% predicted was inversely correlated with %LAA–950 (*r*=−0.65, *P*=0.000), %WA (*r*=−0.54, *P*=0.000), and WT/D (*r*=−0.44, *P*=0.000). Similar relationships were also found between FEV₁/FVC and %LAA–950, %WA, and WT/D (*r*=−0.60, −0.45, and −0.37, respectively, all *P*=0.000). CAT scores were inversely correlated with FEV₁% (*r*=−0.63, *P*=0.000) and FEV₁/FVC (*r*=−0.47, *P*=0.000).

Relationships between mMRC grades and CT measurements, CAT scores in COPD patients

With the Spearman's correlation analysis, the mMRC grades were positively correlated with %LAA–950 (*r*_s=0.58, *P*=0.000), %WA (*r*_s=0.40, *P*=0.001), and WT/D (*r*_s=0.33, *P*=0.008), as well as the CAT scores (*r*_s=0.66, *P*=0.000).

Table 4 CAT score and CT measurements in the total subjects

	Control group	GOLD I-II group	GOLD III-IV group	P
CAT score	0.1±0.3	15.1±8.8**	24.9±7.0***++	0.000
%WA (%)	75.3±3.6	77.9±5.6*	81.9±3.3***++	0.000
WT/D (%)	25.8±2.5	27.1±2.9**	29.0±2.3***+	0.000
%LAA (%)	2.2±1.3	7.0±2.8*	34.4±16.2***++	0.000

Notes: Data are presented as means ± standard deviation. *P*-values were calculated by analysis of variance. **P*<0.05, ***P*<0.01 versus control group; +*P*<0.05, ++*P*<0.01 versus GOLD I-II group.

Abbreviations: %LAA, percentage of low attenuation areas; %WA, wall area percentage; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; CT, computed tomography; WT/D, ratio of airway wall thickness to total diameter.

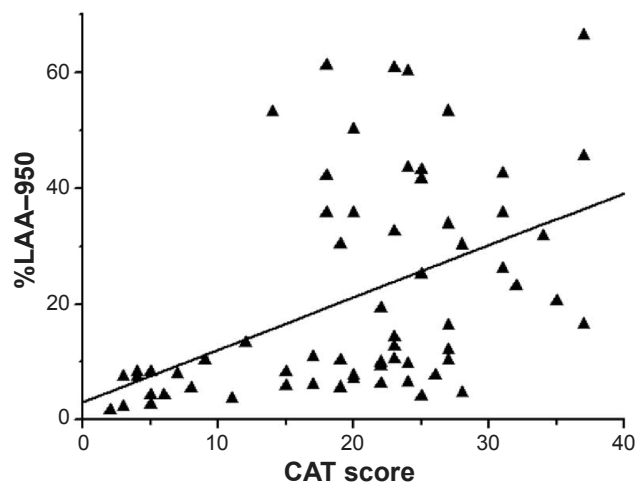


Figure 1 Positive correlation between the CAT score and %LAA-950.

Notes: $r=0.46$, $P=0.000$.

Abbreviations: %LAA-950, percentage of pixels below -950 HU; CAT, chronic obstructive pulmonary disease assessment test.

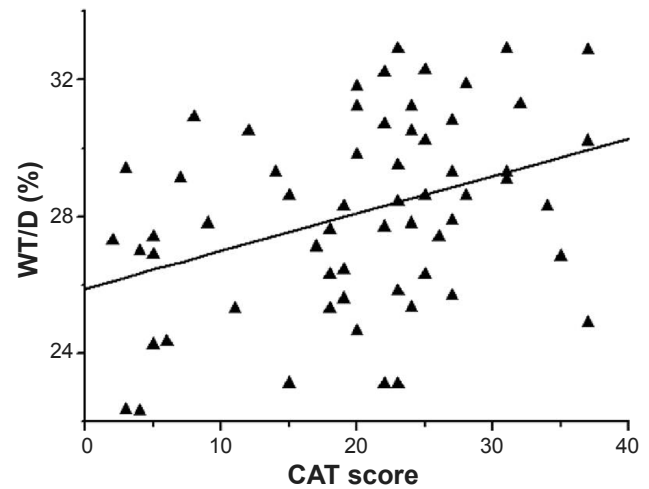


Figure 3 Positive correlation between the CAT score and WT/D.

Notes: $r=0.37$, $P=0.003$.

Abbreviations: CAT, chronic obstructive pulmonary disease assessment test; WT/D, ratio of airway wall thickness to total diameter.

Discussion

In the present study, we have demonstrated that the CAT scores and quantitative CT measurements of emphysema and airway wall thickness were significantly higher in COPD patients, which were consistent with the increasing disease severity measured by GOLD staging system. The CAT scores were significantly and positively correlated with the quantitative CT measurements in COPD patients. With a multiple linear stepwise regression analysis, both %LAA-950 and %WA were independent predictors of CAT scores. Meanwhile, both CAT scores and CT measurements were positively correlated to mMRC grades and inversely correlated to FEV₁%. After

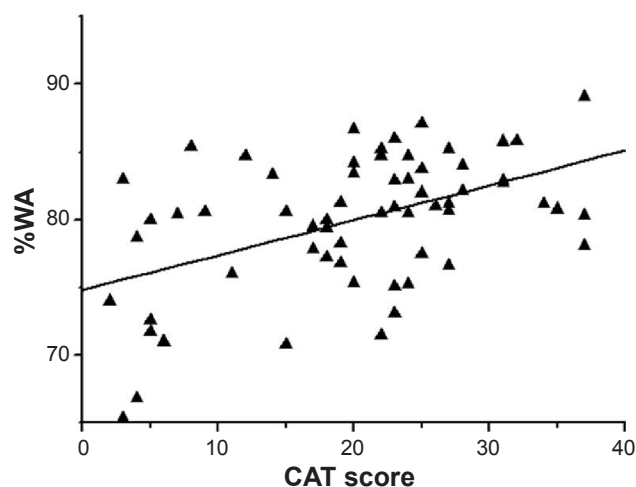


Figure 2 Positive correlation between the CAT score and %WA.

Notes: $r=0.48$, $P=0.000$.

Abbreviations: %WA, wall area percentage; CAT, chronic obstructive pulmonary disease assessment test.

classifying the COPD patients according to the CAT scores, significant differences were found in %WA and %LAA-950 between group I and other groups.

COPD is a chronic inflammatory disease, and the chronic inflammatory responses can induce parenchymal tissue destruction (resulting in emphysema) and disrupt normal repair and defense mechanisms (resulting in small airway fibrosis).²¹ These pathological changes can lead to air trapping and progressive airflow limitation, which may directly cause dyspnea and other characteristic symptoms, as well as impaired health status.¹⁰ The CAT is a good measurement of health status and symptoms burden in COPD patients.¹ Considering the CAT is a questionnaire completed by the patients, some problems such as subjectivity and being unilateral are inevitable during the examinations. While previous studies have shown the validated correlations between CAT scores and some other important parameters of COPD – such as dyspnea grades, pulmonary function parameters, and systemic inflammatory markers,^{7–9} which provided functional, physiologic, and serologic evidences for clinical practice of CAT – to our knowledge, correlation between CAT scores and the imaging parameters in COPD patients has not yet been carried out in the People's Republic of China.

Chest CT is the most prevalent examination to characterize the structural changes and offer various imaging parameters of lungs in clinic. The chest HRCT can not only give a more accurate quantification of airway dimensions and emphysema, but also allows for the phenotypic stratification of patients who have COPD into parenchymal- and

Table 5 CT measurements in different CAT groups

CAT group	%WA (%)		WT/D (%)		%LAA (%)	
	Mean \pm SD	P	Mean \pm SD	P	Mean \pm SD	P
I (0–10)	75.8 \pm 6.4	0.026	26.6 \pm 2.7	NS	5.8 \pm 2.8	0.009
II (11–20)	79.7 \pm 4.0		27.5 \pm 2.4		22.8 \pm 19.7	
III (21–30)	81.2 \pm 4.2	NS	28.7 \pm 2.7	NS	23.1 \pm 18.1	NS
IV (31–40)	83.0 \pm 3.4		29.5 \pm 2.7		24.3 \pm 15.6	

Notes: Data are presented as means \pm SD. P-values were calculated by one-way analysis of variance.

Abbreviations: %LAA, percentage of low attenuation areas; %WA, wall area percentage; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; CT, computed tomography; NS, nonsignificant; SD, standard deviation; WT/D, ratio of airway wall thickness to total diameter.

airway-predominant categories.^{11–14,18} In COPD, the small airways (2 mm or less in diameter) are the site of major air-flow resistance.¹⁰ Former studies have established that %WA of the segment bronchus of the right upper lobe is a surrogate for the dimensions of those small airways measured by histological means,²² and that is also why the apical bronchus of the right upper lobe was chosen as our target measuring site in the present study. Madani et al reported that the best correlation between CT measurements and macroscopic and microscopic measures of emphysema can be obtained using a density mask technique with a threshold level of –960 or –970 HU.²³ In our study we chose the threshold of –950 HU in the inspiratory phase since we concerned that a threshold of –960 or –970 HU might exclude milder degrees of emphysema.

Previous studies have shown the relationships between quantitative CT measurements and respiratory symptoms in COPD patients.^{24–26} Grydeland et al found that both emphysema and airway wall thickness were independently and significantly related to the symptoms burden in COPD patients.²⁴ A report from the COPDGene trial found that the extent of airway wall thickness was more strongly related to the symptoms burden than was emphysema.²⁶ CAT is also a good instrument to assess the symptoms burden. In the present study, we demonstrated that the CAT scores in COPD patients increased with the increasing level of emphysema and airway wall thickness measured by HRCT. Positive correlations were found between CAT scores and %LAA–950, %WA, and WT/D, which might indicate that the change of symptoms burden correspond with the changes of quantitative CT measurements in COPD patients. Regression analysis showed that the independent predictors of CAT scores were %LAA–950 and %WA, but not WT/D; the specific reason for this difference is unknown, and further studies are needed to gain much more insight into answering this

question. Interestingly, after classifying the COPD patients into four groups according to the CAT scores, significant differences were found only in %WA and %LAA–950 between group I (mild) and other groups. According to the GOLD guidelines, a CAT score <10 indicates a low level of symptoms, and a CAT score \geq 10 indicates a high level symptoms.¹⁰ A potential explanation for the differences in %WA and %LAA–950 between group I and other groups is that patients with a high level of symptoms may experience more serious destruction of lung parenchymal tissue and airway remodeling than the ones with less severe symptoms. While the WT/D is the ratio of airway wall thickness to total diameter, the differences might have been counterbalanced and caused the non-significant difference in WT/D between COPD patients with different levels of symptoms. However, more studies with large sample sizes are needed to gain more insight into these questions.

Dyspnea is usually the most prominent and distressing symptom of COPD patients.¹⁰ The correlations between dyspnea and imaging parameters in COPD patients were presented in several studies,^{20,24} as well as the association of dyspnea and CAT scores.^{9,27} Our study showed that both CT measurements and CAT scores were positively correlated with mMRC grades. Several explanations for these independent associations of the CT indices with dyspnea were discussed in previous studies.^{28,29} A number of studies have testified to the relationships between CT measurements and pulmonary function in COPD patients.^{18,19,30} Here we found that CT measurements and CAT scores were all negatively correlated with pulmonary function parameters; furthermore, the CT measurements and CAT scores all correspond well with the increasing disease severity measured by GOLD staging system, indicating that greater air trapping or thicker airway walls correlates with lower lung function, as well as more symptoms and worse health status. We speculate that

both CAT and quantitative CT measurements might be used to partially reflect the extent of airflow limitation in COPD patients.

There are some limitations in this study. Firstly, only the apical bronchus of the right upper lobe was measured in this study, although previous studies have demonstrated that the apical bronchus of the right upper lobe can be a surrogate for the dimensions of the small airways.²² In the future, we need to collect more data for each lung lobe of COPD patients to obtain more accurate relationships between CAT scores and quantitative CT measurements. Secondly, the sample size in our study was relatively small, which may partially account for the weak correlations between some measurements in our results. Further prospective studies involving multicenter and large sample size of COPD patients are needed.

Conclusion

In conclusion, this study shows that CAT scores in COPD patients in the People's Republic of China correlate well with the quantitative CT measurements. Not only can it give assessments of health status or symptoms burden, but it can also be associated with the extent of emphysema and airway thickening in COPD patients. For the first time in the People's Republic of China, we provide an imaging evidence that the structural changes in lungs in COPD correlate with the health status measured by CAT. We suggest that a wide use of CAT may be performed in COPD patients in the People's Republic of China.

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Disclosure

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