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ORIGINAL RESEARCH

Clinical Characteristics of COPD Patients According to COPD Assessment Test (CAT) Score Level: Cross-Sectional Study

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Purpose: The chronic obstructive pulmonary disease (COPD) assessment test (CAT) is widely used to assess the impact of COPD symptoms on health status. Whilst the CAT consists of eight different items, details on the distribution of each item are limited. This study aimed to investigate the distribution and clinical implication of each CAT item, stratified by CAT severity group, in stable COPD patients.

Patients and Methods: This was a cross-sectional study at a single referral hospital in South Korea. Spirometry confirmed COPD patients with CAT measured at the first clinical visit were retrospectively identified. Patients were categorized into three groups: low ($0 \leq CAT < 10$), medium ($10 \leq CAT < 20$), and high ($20 \leq CAT \leq 40$) impact group. For the purpose of this analysis, the first four items (cough, sputum, chest tightness, and dyspnea) and the remaining four items (activities, confidence, sleep and energy) were also grouped as "pulmonary" and "extra-pulmonary", respectively.

Results: A total of 815 patients were included, and mean (SD) forced expiratory volume in 1 s (FEV_1) was 62.8 (17.4) % pred. Among them, 300 patients (36.8%) were in the high impact group and had a greater exacerbation history and lower lung function. The proportion of "extra-pulmonary" items score was greater in patients with higher total CAT scores, with the activity and confidence items showing higher scores.

Conclusion: In our study, in addition to dyspnea, activity limitation is a particular problem in individual patients with higher CAT total scores, for which physicians need to pay more attention. Our study suggests that whilst CAT total score captures the overall impact of COPD, each item of the CAT contains potentially useful information in understanding the patient's symptom burden.

Keywords: COPD, COPD assessment test, patient reported outcome, symptom

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation.[1] Whilst chronic cough and sputum being the common symptoms,[2,3] exertional dyspnea is the most characteristic symptom of COPD that often restricts exercise capacity and activities of daily life of patients.[4–6] Accordingly, patients with symptomatic COPD have reduced health-related quality of life, which leads to substantial socioeconomic burden.[7] Thus, disease-specific health status questionnaires for comprehensive assessment of symptoms beyond dyspnea are recommended in COPD guidelines, including the St. George's Respiratory Questionnaire (SGRQ)[8] and the Chronic Respiratory Disease Questionnaire (CRQ).[9]

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These tools are well validated and reliable but are too complex to implement in clinical practice.

The COPD assessment test (CAT) is an easy and simple measurement with an eight-item questionnaire including severity of cough, sputum, chest tightness, dyspnea, activities, confidence, sleep, and energy.[10–12] It is widely used in daily practice to assess and quantify the impacts of COPD symptoms on the health status, and correlates well with the SGRQ score in clinically stable COPD patients.[12] It is one of the key determinants in assessing disease severity and guiding treatment in Global Initiative for Chronic Obstructive Lung Disease (GOLD) report.[1] Furthermore, a significant increase in CAT total score at a clinic visit is useful to detect worsening or exacerbation of COPD.[13,14]

Previous studies on CAT mostly focused on total score,[10–12] rather than each item of CAT. A few have investigated single CAT items with regard to COPD screening,[15] phenotypes,[16,17] comorbidities,[18,19] emphysema,[18] and fatigue.[2] However, studies on the distribution and clinical significance of single items in CAT based on CAT total scores are lacking. Therefore, we aimed to evaluate the distribution and clinical implication of each item of CAT according to the total CAT score of stable COPD patients.

Materials and Methods

Study Population

This is a cross-sectional study. Consecutive COPD patients were selected from the CLUE (COPD LUng Evolution) registry, an ongoing cohort at Samsung Medical Center (a 1979-bed referral hospital in Seoul, South Korea) that consists of the patients who have post bronchodilator forced expiratory volume in 1 second (FEV_1) over forced vital capacity (FVC) less than 0.7 with age over 40 years. Between January 2016 and April 2019, 875 COPD patients who were enrolled into the registry and measured CAT were retrospectively identified. We excluded 31 patients who experienced acute exacerbation on the day of study visit, 17 patients who had a pulmonary resection or endobronchial valve insertion and 12 patients without matchable spirometry results. The final sample included 815 patients (Figure 1). For this cross-sectional study, data of the first visit were used. The Institutional Review Board of Samsung Medical Center approved this study (No. 2019–09-071-001) and the requirement for informed consent was exempted as this study was a retrospective analysis of the de-identified data that was routinely collected during clinical practice.

COPD Assessment Test

The CAT consists of eight items including cough, sputum, chest tightness, dyspnea, activities, confidence, sleep and energy. Item scores range from 0 to 5 points resulting in a total CAT score ranging from 0 to 40 points.[11] Based on CAT total scores, patients were categorized into three groups: low ($0 \leq CAT < 10$), medium ($10 \leq CAT < 20$), and high ($20 \leq CAT \leq 40$) impact group according to CAT users guide (http://www.catestonline.org). In this study, the first four items (cough, sputum, chest tightness, and dyspnea) were grouped pragmatically, based on their content, into "pulmonary items" whilst the remaining four items (activities, confidence, sleep and energy) were grouped as "extra-pulmonary items".[20]

Data Collection and Measurements

Data obtained from the CLUE cohort database included age, sex, smoking history, body mass index (BMI), modified medical research council (mMRC) dyspnea scale, COPD assessment test (CAT) score, history of acute exacerbation, and Charlson comorbidity index (CCI).[21] Acute exacerbation was defined as an outpatient clinic visit, hospitalization or an emergency room visit owing to one or more of the following: worsening of dyspnea, increased sputum volume and purulent sputum. In this study, we collected the history of moderate to severe exacerbation in the previous year, which was routinely recorded as the structured form during clinic visit.

Spirometry, diffusing capacity of the lung for carbon monoxide (DLco), and lung volumes were performed using a Vmax 22 system (SensorMedics, Yorba Linda, CA, USA) according to American Thoracic Society/European Respiratory Society criteria.[22,23] Absolute values of FEV1 and FVC were obtained and the percentages of predicted FEV1 and FVC were calculated using a reference from a representative Korean sample.[24] Absolute DLco values (mL/mmHg/min) was obtained using the same apparatus and calculated into the percentage of predicted values using a formula based on a representative Korean sample.[25] Moderate to severe decrease in DLco was defined as DLco $\leq$ 60% pred[26] and hyperinflation was defined as residual volume (RV)/total lung capacity (TLC) > 40%.[27]

Validation Cohort

To validate the findings from the current study, data from a multicenter cohort of COPD patients were used. In brief, the Korean COPD Subgroup Study (KOCOSS) is an ongoing, multicenter observational cohort study, which has

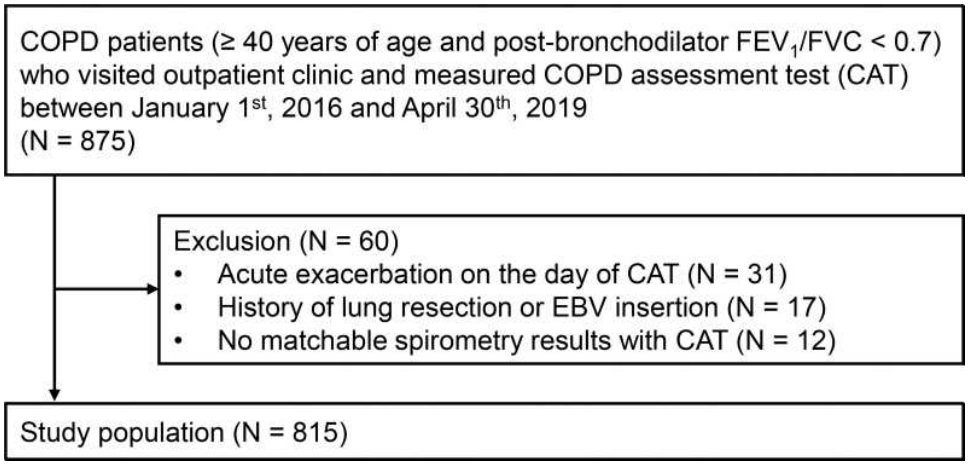

Figure 1 Flowchart of study population.

recruited COPD patients from referral hospitals in South Korea since December 2011. Patients who were diagnosed with COPD by a pulmonologist, aged ≥ 40 years, had a post-bronchodilator $FEV_1/FVC < 0.7$, and showed respiratory symptoms were included. For this study, we used the data of 2181 patients who were enrolled from January 2012 to December 2019. After excluding those who missed CAT (n = 19), a total of 2162 patients were analyzed.

Statistical Analysis

Although the CAT was developed to be unidimensional with no subdomains,[11] for the purpose of this descriptive analysis, the items were grouped into two groups based on the face-validity of items that appear to be related. In addition, to provide a continuous estimate of increasing pattern of each CAT item according to the total CAT score, we used locally weighted scatterplot smoothing (Figure 2). We then analyzed the patients grouped by overall CAT impact score using the recommended banding (http://www.catestonline.org).

All data are presented as numbers (%) for categorical variables and means (standard deviation) for continuous variables. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, whilst the Student's *t*-test was used to compare continuous variables. To test for linear trends, the group category was included as a continuous variable in the regression models. All tests were two-sided, and p-values < 0.05 were considered significant. All analyses were performed using Stata software (ver. 14.0; Stata Corporation, College Station, TX, USA).

Results

The baseline characteristics of 815 patients included in the analysis are summarized in Table 1. The mean age was 72.1 (standard deviation 8.9) years and most patients were male (90.9%). According to the baseline CAT score, 182 (22.3%), 333 (40.9%) and 300 (36.8%) patients were categorized as low, medium and high impact, respectively. The median age and male predominance were similar across the groups,

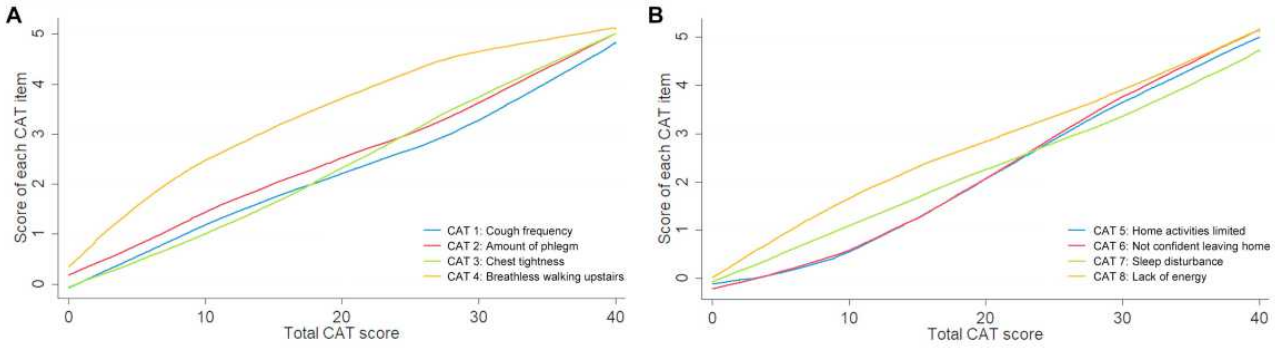

Figure 2 Different increasing pattern of each CAT items according to total CAT score. (**A**) Pulmonary items (cough, sputum, chest tightness and dyspnea) and (**B**) Extra-pulmonary items (activities, confidence, sleep and energy).

Table 1 Baseline Characteristics of Patients According to Total CAT Score Groups

	Total (N = 815)	CAT < 10 (N = 182)	10 ≤ CAT < 20 (N = 333)	CAT ≥ 20 (N = 300)	P for Trend	P for Trend*
Age, years	72.1 (8.9)	72.1 (8.9)	72.0 (9.0)	72.2 (8.8)	0.878	–
Sex, male	741 (90.9)	166 (91.2)	303 (91.0)	272 (90.7)	0.836	–
Smoking status					<0.001	<0.001
Never	85 (10.4)	27 (14.8)	31 (9.3)	27 (9.0)		
Former	544 (66.8)	128 (70.3)	228 (68.5)	188 (62.7)		
Current	186 (22.8)	27 (14.8)	74 (22.2)	85 (28.3)		
BMI (kg/m^2)+	23.5 (3.4)	24.0 (3.0)	23.2 (3.2)	22.8 (3.6)	<0.001	<0.001
Underweight	54 (6.6)	8 (4.4)	17 (5.1)	29 (9.7)		
Normal	300 (36.8)	51 (28.0)	114 (34.2)	135 (45.0)		
Overweight	202 (24.8)	63 (34.6)	86 (25.8)	53 (17.7)		
Obese	259 (31.8)	60 (33.0)	116 (34.8)	83 (27.7)		
mMRC (n = 714)						
≥ 2	328 (45.9)	36 (23.4)	102 (35.2)	190 (70.4)	<0.001	<0.001
Any previous history of acute exacerbation (n = 710)‡	228 (32.1)	337 (23.1)	79 (28.2)	112 (41.5)	<0.001	<0.001
Charlson comorbidity index	2.87 (1.95)	2.95 (1.82)	2.89 (1.99)	2.81 (1.95)	0.413	0.401
Treatment					<0.001	<0.001
None	274 (33.6)	75 (41.2)	128 (38.4)	71 (23.7)		
LAMA or LABA	119 (14.6)	31 (17.0)	60 (18.0)	28 (9.3)		
LAMA/LABA	167 (20.5)	41 (22.5)	65 (19.5)	61 (20.3)		
ICS/LABD#	107 (13.1)	22 (12.1)	35 (10.5)	50 (16.7)		
ICS/LAMA/LABA	148 (18.2)	13 (7.1)	45 (13.5)	90 (30.0)		

Notes: Data are mean (standard deviation) or number (%). *Adjusted for age and sex. +Categorized according to Asian-specific criteria into underweight (<18.5 kg/m^2), normal weight (18.5 – <23 kg/m^2), overweight (23 – <25 kg/m^2), and obese (≥25 kg/m^2). ‡ Moderate to severe exacerbation in the previous year. #Among 107 patients, 104 patients were using ICS/LABA, 2 patients were using ICS and LAMA, and 1 patient were using ICS monotherapy.

Abbreviations: CAT, COPD assessment test; BMI, Body mass index; mMRC, modified medical research council dyspnea scale; LAMA, Long-acting muscarinic antagonists; LABA, Long-acting beta agonists; ICS, Inhaled corticosteroid; LABD, Long-acting bronchodilators.

whereas prevalence of current smokers increased from less symptomatic to highly symptomatic group. The high impact group also had a lower BMI, more dyspnea and higher rate of previous exacerbations compared to the other groups. There was no significant trend in comorbidities across three groups. Table 2 shows the baseline pulmonary function of each group; post-bronchodilator FEV_1, DLco, and RV/TLC showed worsening trend with higher CAT score.

The proportional contribution of the four "pulmonary" items (cough, sputum, chest tightness and dyspnea) and four "extra-pulmonary" items (activities, confidence, sleep and energy) to the total CAT score are presented, split by impact severity group, in Figure 3. The proportion of extra-pulmonary item scores was progressively greater with higher overall CAT total score, whilst that of pulmonary symptoms decreased accordingly.

Figure 4 further demonstrates the distribution of mean score for each CAT item. Dyspnea was the most predominant symptom overall, and the rest of the "pulmonary" items were proportionately higher with total CAT scores. In contrast, the "extra-pulmonary" items, particularly activities and confidence showed sharp increment between moderate impact group and high impact group. The absolute values of each CAT item are available in Supplementary Table E1. In addition, this pattern of deterioration of extra-pulmonary impacts was similar between patients with FEV_1 < 50% pred (n = 179) and those with FEV_1 ≥ 50% pred (n =636) (Supplementary Figure 1) and between patients with DLco

Table 2 Baseline Pulmonary Function Parameters of Patients According to Total CAT Score Groups

	Total (N = 815)	CAT < 10 (N = 182)	10 ≤ CAT < 20 (N = 333)	CAT ≥ 20 (N = 300)	P value	P for Trend
Post-bronchodilator spirometry						
FVC, L	3.41 (0.85)	3.42 (0.84)	3.52 (0.77)	3.26 (0.92)	<0.001	0.011
FVC, % pred	81.9 (16.5)	81.4 (14.6)	84.5 (15.4)	79.3 (18.2)	<0.001	0.052
FEV_1, L	1.83 (0.61)	1.99 (0.55)	1.93 (0.55)	1.62 (0.65)	<0.001	<0.001
FEV_1, % pred	62.8 (17.4)	68.0 (14.9)	66.0 (15.1)	55.9 (19.1)	<0.001	<0.001
< 50%	179 (22.0)	20 (11.0)	46 (13.8)	187 (37.7)	<0.001	<0.001
FEV_1/FVC	53.5 (11.7)	58.4 (9.0)	54.8 (10.5)	49.1 (12.9)	<0.001	<0.001
DLco, % pred (n = 591)	66.3 (21.0)	73.5 (17.9)	68.9 (20.5)	58.4 (21.0)	<0.001	<0.001
≤ 60%	241 (40.8)	31 (24.2)	93 (36.1)	117 (57.1)	<0.001	<0.001
Lung volume (n = 426)						
RV/TLC	41.7 (9.7)	40.8 (9.1)	40.2 (9.0)	44.2 (10.5)	<0.001	0.003
> 40%	213 (50.0)	43 (71.8)	88 (49.2)	82 (56.9)	0.060	0.018

Notes: Data are mean (standard deviation) or number (%).
Abbreviations: CAT, COPD assessment test; FVC, Forced vital capacity; FEV_1, Forced expiratory volume in 1s; RV, Residual volume; TLC, Total lung capacity; DLco, Diffusing capacity of the lung for carbon monoxide.

≤ 60% pred (n =241) and those with DLco > 60% pred (n =350) (Supplementary Figures 2).

Discussion

In this study, we found that patients with high impact CAT scores (≥ 20) were more likely to be current smokers, have more dyspnea and previous exacerbation history and have lower lung function and BMI. In a further analysis on the distribution of each CAT item according to total CAT score categories, the proportion of "pulmonary" items score was much higher than that of "extra-pulmonary" items in patients with mild impact. However, the proportion of "extra-pulmonary" items score was markedly higher in the high impact group. We also found that CAT items about activities and confidence were most severely influenced in the high impact group, and the pattern was similar in subgroups categorized by FEV_1 50% pred or DLco 60% pred.

Beyond the total CAT score, we elaborated the distribution and clinical significance of each component of CAT. Compared to patients with lower total CAT scores, in patients with high impact (CAT scores ≥ 20), the proportional contribution of "pulmonary" items to the total score was less whilst the contribution of "extra-pulmonary" items increased up to 48.0%. When each of 8 items was analyzed separately, the "pulmonary" item scores were proportionally higher across the impact groups, whilst "extra-pulmonary" items showed a bigger step increase with higher total CAT scores. This was seen particularly with the activities and confidence items. A similar observation was made during the development of the CAT showing that "confidence" better distinguished more severe patients.[11] Our finding highlights that limitation in physical activity plays a major role in impaired quality of life in high impact group. Whilst clinicians usually focus more on patients' respiratory symptoms and pharmacological treatment during routine practice, our results suggest that CAT items can detect patients who suffer from deteriorated physical activities, particularly before they become highly symptomatic in terms of total CAT scores. In this regard, clinicians should pay more attention to "extra-pulmonary" symptoms and seek individualized and comprehensive interventions, such as pulmonary rehabilitation.

Our findings are consistent with previous studies, which reported that CAT score correlates with diverse clinical features of COPD. Several studies have reported that the increased CAT score is associated with dyspnea[28,29] and acute exacerbation state or its future risk.[11–13,29–31] Whilst it is known that FEV_1 has a weak correlation with CAT score,[12,28] several studies have shown a correlation between total CAT scores and GOLD grades.[12,29] In our study, we also found a correlation between total CAT scores and the degree of airflow limitation and DLco. However, it is of note that one third of patients with FEV_1 < 50% pred had CAT score < 20, whereas one third of patients with FEV_1 ≥ 50% pred had CAT score ≥ 20. As shown in the Supplementary

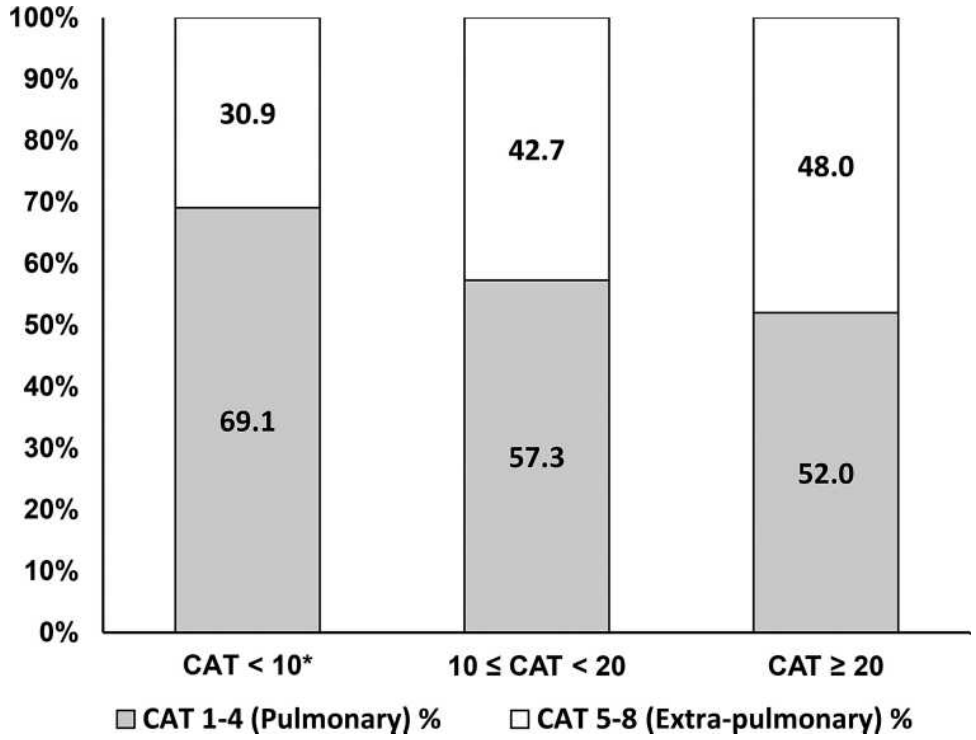

Figure 3 Proportion contribution of four pulmonary items (cough, sputum, chest tightness and dyspnea) and four extra-pulmonary items (activities, confidence, sleep and energy) to the total CAT score, according to impact severity group. *Four patients had zero score in CAT.

Figure 1, patients had different degrees of airflow limitation but showed visually similar distribution of each item of CAT when total CAT score was <20. This shows that FEV_1 does not fully reflect the impact of COPD, emphasizing that FEV_1 does not say it all.[28]

COPD is a systemic disease not only affecting the lungs but also having non-respiratory manifestations, including skeletal muscle dysfunction with atrophy and weakness, systemic inflammation and nutritional depletion.[32,33] Our study showed the association between high CAT scores and a lower BMI, which is a surrogate marker of cachexia.[34] GOLD also recommends that nutritional supports should be provided to malnourished COPD patients, which can improve overall quality of life.[1,35] Similarly, the higher prevalence of smoking exposure among subjects with high CAT score might partly explain the effect of systemic inflammation on their extra-pulmonary manifestations. These findings suggest that patient reported outcomes

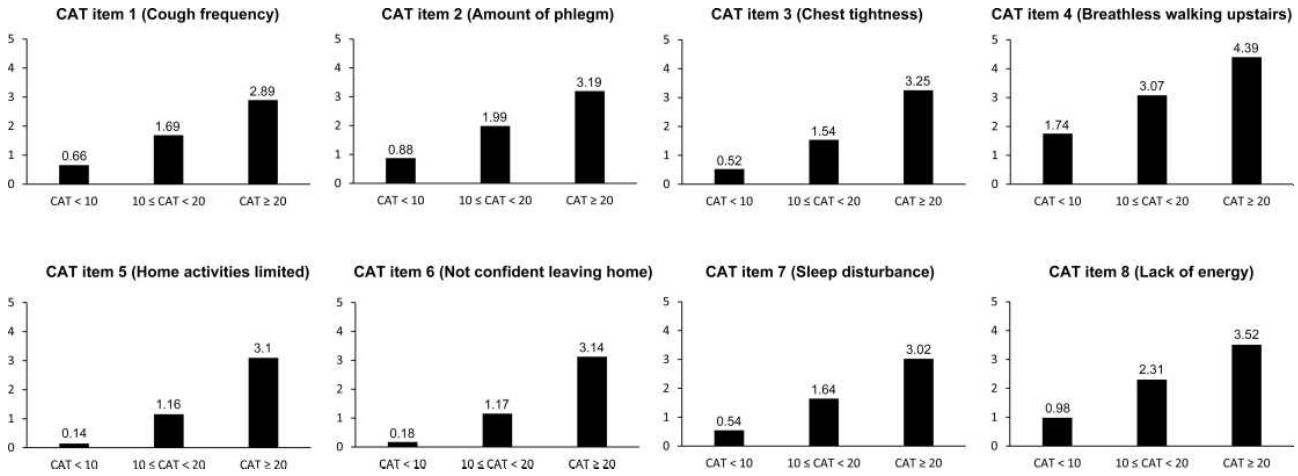

Figure 4 Distribution of mean score for each CAT items according to impact severity group (absolute values are available in supplementary table E1).

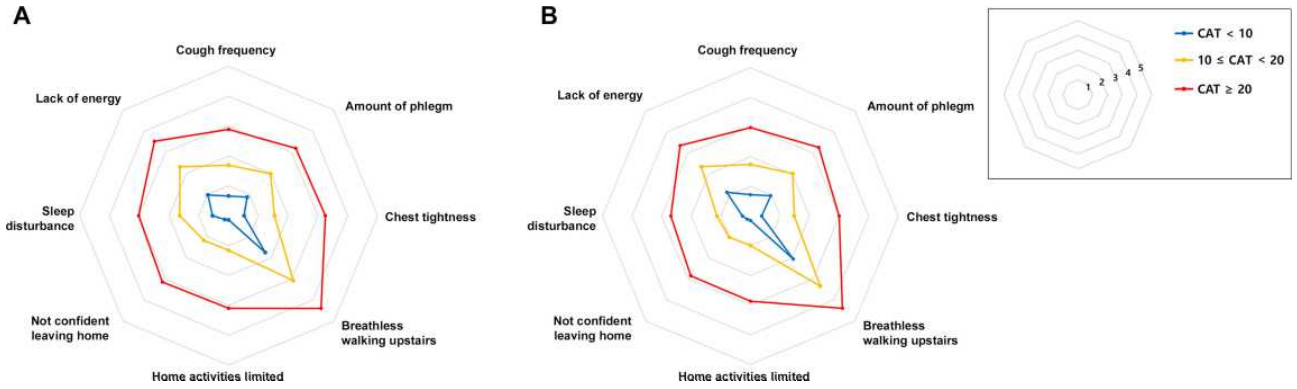

Figure 5 Distribution of mean score for each CAT items according to impact severity group in (**A**) CLUE registry (the present study, N = 815) and (**B**) KOCOSS cohort (multicenter cohort for validation, N = 2162).

are essential component in understanding this complex disease and achieving the goal of reducing symptom burden and improving quality of life, by non-pharmacological and pharmacological therapies.

Our study had several limitations. First, this is a retrospective analysis of data from a single referral center, which limits its generalizability. To address this limitation, we performed the same analysis using the data of 2162 patients from the KOCOSS cohort. As shown in Figure 5 and Supplementary Table E1, the pattern of deterioration of CAT items was very similar in both cohorts (except for sleep). The clinical characteristics of KOCOSS patients were summarized in Supplementary Table E2. Second, our patient cohort showed a marked male predominance (> 90%) which has been consistently reported in multicenter studies from Korea that are based on pulmonology clinics.[36,37] This is due to a selection bias, as the male predominance was lesser in national survey.[38] In part, this is attributable to a very low female smoking rate (3.4%) in Korea.[39] However, there was no gender difference in CAT scores in previous studies.[12,40] Third, due to the cross-sectional nature, we could not investigate the impact of each CAT items on clinical outcomes, such as future exacerbation or response to treatments. Further longitudinal studies with serially measured CAT are necessary to better understand the clinical utility of CAT in daily practice. Fourth, as we restricted the study population to stable COPD patients, we carefully reviewed and excluded patients who experienced acute exacerbation on the study visit (who were prescribed systemic steroids or referred to emergency department after clinic visit). However, co-existence of clinical instability caused by other disease could not be completely excluded. Lastly, although there was no significant association between CCI and CAT total scores in our study, we lacked information on patients' mental health. In the analysis using KOCOSS data (Supplementary Table E2), there were more patients with depressive disorder (defined as a Beck Depression Inventory ≥ 16 or more)[41] in high impact group. It is known that depression and anxiety are associated with high CAT scores, especially with the extra-pulmonary items.[19] Depression was also correlated with SGRQ score, particularly with impact and activity domain.[42] Thus, psychological problem may have contributed to the greater increase of extra-pulmonary items in high impact group, which should also be addressed as part of the integrated patient care.

Conclusion

Using the CAT total scores and distribution of individual items of CAT, we found that dyspnea is the most prominent symptom in all patient groups regardless of total impact categories. Whilst dyspnea increased proportionally with worsening impact of COPD, CAT items regarding activities and confidence showed a sharp deterioration when patients became highly impacted (CAT total score ≥ 20). This novel insight suggests a new look into CAT items such that clinicians need to pay more attention to patients' activities beyond dyspnea and seek a comprehensive intervention.

Abbreviations

BMI, body mass index; CAT, COPD assessment test; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; CRQ, Chronic Respiratory Disease Questionnaire; DLco, diffusing capacity of carbon

monoxide of the lung; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified medical research council; RV, residual volume; SGRQ, St. George's Respiratory Questionnaire; TLC, total lung capacity.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding authors (Dr Sun Hye Shin or Hye Yun Park) in response to reasonable requests.

Ethics Approval

This study was approved by the Institutional Review Board of Samsung Medical center and the requirement for informed consent was exempted given the retrospective nature of the study.

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Disclosure

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