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Original Research

Change in individual chronic obstructive pulmonary disease assessment test item scores after short-term bronchodilator therapy and its impact on exacerbation in treatment-naïve patients with chronic obstructive pulmonary disease

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Abstract

Background: The chronic obstructive pulmonary disease (COPD) assessment test (CAT) measures the health status of patients with COPD. We aimed to investigate the change in individual CAT scores after short-term bronchodilator therapy among treatment-naïve patients with COPD.

Methods: Data from 148 patients newly diagnosed with COPD between January 2016 and April 2020 were retrospectively analyzed. We compared the CAT score, modified Medical Research Council (mMRC) dyspnea grade, and forced expiratory volume in 1 s (FEV_1) before and after short-term (6 ± 2 months) bronchodilator therapy. We analyzed the change trends using generalized estimating equations.

Results: The mean patient age was 70.9 years, and 92.6% were male. The total CAT score did not significantly improve. However, among the CAT items, phlegm [adjusted difference: −0.22 (−0.48, −0.002)], chest tightness [−0.30 (−0.56, −0.05)], and breathlessness [−0.45 (−0.66, −0.23)] scores significantly improved after bronchodilator therapy. The patients were divided into two groups: CAT score improved ($n = 69$) and not improved group ($n = 79$). The development of moderate-to-severe exacerbations during follow-up was significantly lower (2.9% *versus* 17.7%, $p = 0.004$) in the CAT score improved group.

Conclusion: The improvement in CAT items indicating respiratory symptoms was more evident than the CAT total score after short-term bronchodilator therapy. Despite the significant increase in FEV_1 after bronchodilator therapy, fewer than half of the patients achieved meaningful improvement in CAT, and this group showed significantly lower development of exacerbation during follow-up.

Keywords: COPD, COPD assessment test, modified Medical Research Council dyspnea grade, patient-reported outcome

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide.[1–3] It is characterized by persistent airflow limitations and symptoms. The diagnosis, assessment of disease severity, and treatment recommendations for COPD have been guided by the degree of airflow limitation based on spirometry

findings for many years.[4] However, as the degree of symptoms and exacerbations vary across patients with the same degree of airflow limitation,[5,6] the 'ABCD' assessment tool for COPD was first proposed in 2011 and revised in 2017 by combining symptom burden and history of exacerbation with the future risk of exacerbation.[7] Regarding evaluation of symptoms, the COPD assessment test (CAT) or modified Medical Research Council (mMRC) dyspnea scale are widely used.[8–11]

While the mMRC dyspnea scale is a simple self-rating tool that only measures the degree of dyspnea,[10] the CAT consists of eight items, including cough, phlegm, chest tightness, breathlessness, activities, confidence, sleep, and energy, reflecting the impact of both pulmonary and extra-pulmonary symptoms on health status.[8] In addition, the total CAT score is associated with various clinical parameters of disease severity, such as shortness of breath, exercise capacity, exacerbation history, and comorbidities.[12–14] Furthermore, changes in the total CAT score are associated with the degree of improvement in symptoms after pulmonary rehabilitation (PR), pharmacologic treatment, and treatment for patients with acute exacerbation of COPD.[15–17] Recent studies have shown that each CAT item contains additional information and contributes differently to the total score.[18–20] However, to the best of our knowledge, there are a few data primarily focusing on changes in each CAT item after bronchodilator therapy initiation and its association with other clinical factors. Thus, we investigated changes in individual CAT scores after short-term bronchodilator therapy among treatment-naïve patients with COPD and compared lung function, mMRC dyspnea, and exacerbations between patients whose CAT scores improved and those whose CAT scores did not.

Material and methods

Study population

This was a retrospective cohort study. From electronic medical records, we obtained the data of 211 newly diagnosed COPD patients whose post-bronchodilator forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) was less than 70% and who were treatment naïve from January 2016 to April 2020 at the Samsung Medical Center in Seoul, South Korea. We excluded patients with asthma ($n = 6$) or patients with lung cancer who underwent surgical resection ($n = 4$). In addition, 43 patients were excluded because they did not have CAT scores, resulting in 148 patients in the final study population (Supplementary Figure 1). This study was approved by the Samsung Medical Center Institutional Review Board (no. 2020-11-101), and the need for informed consent was waived, as we only used de-identified patient information.

Variables and methods

Bronchodilator therapy was confined to the use of long-acting muscarinic antagonists (LAMAs), long-acting beta-2 agonists (LABAs), or combined LAMA/LABA, with or without inhaled corticosteroids. Initial inhalers were prescribed according to clinical practice guidelines.[11,21] We defined short-term bronchodilator therapy as 6 months of treatment, as COPD patients are expected to exhibit some improvement in their outcome after approximately 6 months of initial therapy according to the previous literature.[22,23]

For lung function and patient-reported outcomes (PROs), data from two different time points were included: initial outpatient visit (baseline) and visit after 6 months of bronchodilator therapy (follow-up). As this was a retrospective study, we allowed a margin of ± 2 months for the follow-up visit to take place to accommodate the patients' individual circumstances. Spirometry was used to assess lung function both at baseline and at follow-up using a Vmax 22 system (SensorMedics, Yorba Linda, CA, USA) following the recommendations of the American Thoracic Society and European Respiratory Society guidelines. The predicted percentage values for FEV_1, FVC, and lung for carbon monoxide were calculated using the equation developed for the Korean population.[24,25] The severity of airflow limitation was classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) grading system as follows: GOLD grade I (predicted $FEV_1 \geq 80\%$), GOLD grade II (predicted FEV_1, 50–80%), GOLD grade III (predicted FEV_1, 30–50%), or GOLD grade IV (predicted $FEV_1 < 30\%$).

Both CAT scores and mMRC dyspnea scales were assessed at baseline and at follow-up visits to

evaluate changes in PROs after short-term bronchodilator use.

The CAT consists of eight items (cough, phlegm, chest tightness, breathlessness, activities, confidence, sleep, and energy) defined by contrasting adjectives.[8] Each item score ranges from 0 to 5 points, resulting in a total CAT score ranging from 0 to 40 points, with higher scores representing worse health status. Based on a minimum clinically important difference (MCID) of 2 points for the total CAT score,[26] patients who exhibited a decrease of 2 points or more were classified into an 'improved' group and those that failed to exhibit such a decrease into a 'not improved' group. The mMRC dyspnea scale is scored from grades 0 to 4, depending on the severity of the dyspnea.[10] Patients were asked to complete the CAT and mMRC questionnaires, which were validated in Korean before the outpatient visit.[27,28]

Moderate exacerbation was defined as an outpatient clinic visit for additional treatment, such as antibiotics or systemic corticosteroid, and severe exacerbation was defined as hospitalization or an emergency room visit owing to one or more of the following reasons: worsening of dyspnea, increased sputum volume, and purulent sputum.[11,29] Demographic and clinical information, including age, sex, smoking history, body mass index, comorbidities (pulmonary and extra-pulmonary), and a history of moderate or severe exacerbation in the previous year at baseline were also included.

Statistical analysis

Normally distributed continuous variables were expressed as mean (SD) and compared using Student's *t*-test. Variables with skewed distributions were expressed as median (interquartile range) and compared using the nonparametric Wilcoxon rank-sum test. Categorical variables were expressed as percentage (%) and compared using the chi-square test or Fisher's exact test.

We used a generalized estimating equation model for longitudinal data analysis to model changes in CAT score, FEV_1, and the proportion of patients with mMRC dyspnea grade ≥ 2, using the data obtained at the two time points: at the initial visit and after 6 (± 2) months of treatment with a bronchodilator. For the CAT score and FEV_1 as a continuous variable, we modeled the change in each value after treatment with a bronchodilator with respect to baseline. For the mMRC dyspnea grade, we calculated the odds ratios (ORs) and 95% confidence interval (CI) for changes in the proportion of patients with mMRC grade ≥ 2 after 6 (± 2) months of treatment with bronchodilators compared with baseline. All models were adjusted for age, smoking history, GOLD grade, pulmonary comorbidity, other comorbidities, and acute exacerbation history in the previous year. To estimate which area is associated with changes in total CAT improvement, we also performed stratified analyses according to baseline CAT scores (≤ 20 and > 20) following the CAT user's guide (http://www.catestonline.org).[30]

To estimate the association between FEV_1 as an objective measure, and CAT score and mMRC dyspnea grade as PROs, we used a Spearman rank correlation.

When we performed longitudinal data analysis to detect 2 points change as minimal clinical difference of CAT between the initial visit and after 6 months of treatment, under 5% level of significance with 148 patients (SD of change was 8), the power of the study was 0.86.

All reported *p*-values were two-sided, and the significance level was set at $p = 0.05$. Statistical analyses were performed using the SPSS software (IBM SPSS Statistics ver. 25, Chicago, IL, USA).

Results

Baseline characteristics

A total of 148 patients were included in the study. Patients were followed up for a median of 5.8 (5.1–6.5) months (Table 1). The mean age of the patients was 70.9 years (SD, 8.3), and 92.6% of them were male. Forty-six patients (31.1%) were current smokers. There were 48 patients (32.4%) with acute exacerbations in the previous year, five (3.4%) of whom had a history of severe acute exacerbation. Most patients ($n = 107$, 72.3%) were classified as GOLD grade II. The number of patients who first started bronchodilator therapy with LAMA and LABA combination was 98 (66.2%), followed by 20 patients (13.5%) who started bronchodilator therapy with LAMA alone.

Table 1. Characteristics of the study patients (*N* = 148).

Variables	Total (*N* = 148)
Age, years [mean (SD)]	70.9 (8.3)
Sex, male	137 (92.6)
Body mass index, kg/m^2	23.2 (21.1–25.5)
Smoking history	
Never-smoker	11 (7.4)
Ex-smoker	91 (61.5)
Current smoker	46 (31.1)
Pack-year (*n* = 137)	40 (30–50)
History of pulmonary disease	
Tuberculosis	15 (10.1)
Bronchiectasis	8 (5.4)
Lung cancer	4 (2.7)
Comorbidities	
No	36 (24.3)
Yes[a]	112 (75.7)
Diabetes mellitus	33 (22.3)
Hypertension	57 (38.5)
Chronic heart failure	21 (14.2)
Cardiovascular disease	35 (23.6)
Chronic liver disease	3 (2.0)
Chronic kidney disease	12 (8.1)
Other malignancies[b]	44 (29.7)
Exacerbation in the previous year	
Moderate-to-severe exacerbation	48 (32.4)
Severe exacerbation	5 (3.4)
Lung function	
Post-BD FEV_1, L	1.97 (1.63–2.12)
Post-BD FEV_1, % predicted	66 (56–75)
Post-BD FEV_1/FVC	57 (47–65)
DLco, % (*n* = 122)	64 (53–75)
GOLD grade	
Grade I	24 (16.2)
Grade II	107 (72.3)
Grade III	15 (10.1)
Grade IV	2 (1.4)
GOLD group	
Group A	33 (22.3)
Group B	89 (60.1)
Group C	6 (4.1)
Group D	20 (13.5)
Initial bronchodilator prescribed	
LAMA	20 (13.5)
LAMA + LABA	98 (66.2)
ICS + LAMA or ICS + LABA	15 (10.1)
ICS + LAMA + LABA	15 (10.1)

BD, bronchodilator; CAT, COPD assessment test; DLco, diffusing capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroids; LABA, long-acting beta-2 agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council; *SD*, st andard deviation.
Data are presented as *n* (%) or medians (interquartile ranges), except for the age category.
[a]Patients might have more than one comorbidity.
[b]Gastric cancer (*n* = 7), prostate cancer (*n* = 7), bladder cancer (*n* = 6), esophageal cancer (*n* = 6), hepatic cell carcinoma (*n* = 4), colon and rectal cancer (*n* = 3), laryngeal cancer (*n* = 3), breast cancer (*n* = 2), lymphoma (*n* = 1), malignant thymoma (*n* = 1), ureter cancer (*n* = 1), and renal cell carcinoma (*n* = 1).

Correlation between the CAT score, mMRC dyspnea grade, and FEV_1

The total CAT score was weakly correlated with FEV_1 (% predicted) at baseline and after bronchodilator therapy (rs, baseline = –0.236; rs, after bronchodilator therapy = –0.251). There was no correlation between change in total CAT score and change in FEV_1 (% predicted) (rs = –0.002, $p = 0.810$) (Figure 1). The proportion of

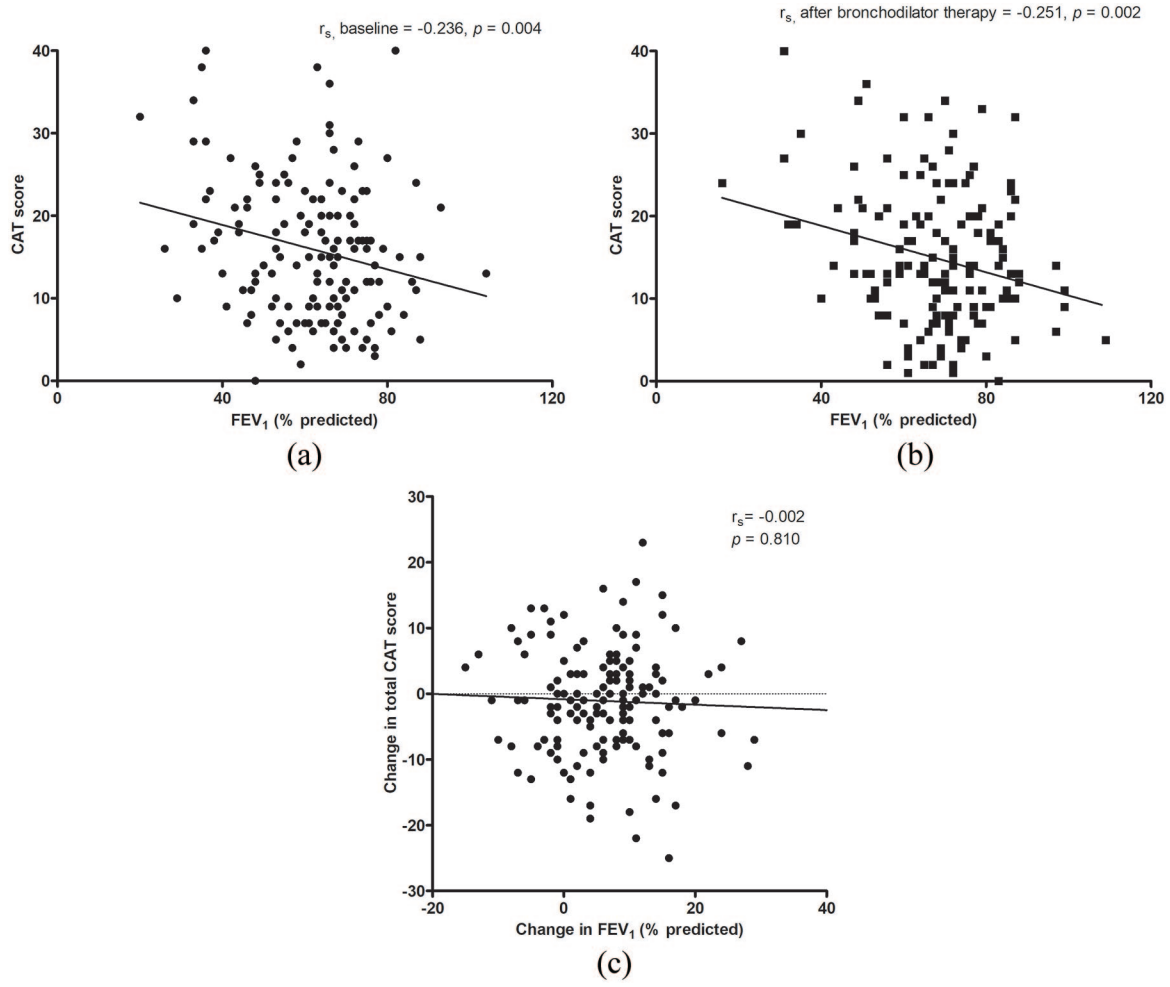

Figure 1. Correlation between the total CAT score and FEV1. (a) Baseline, (b) after short-term (6 ± 2 months) bronchodilator therapy. (c) Correlation between the change in total CAT score and change in FEV1 at baseline and after short-term (6 ± 2 months) bronchodilator therapy.
CAT, COPD assessment test; FEV_1, forced expiratory volume in 1 s.

patients with mMRC dyspnea grade ⩾ 2 was moderately correlated with the total CAT score ($rs_{baseline}$ = 0.434; $rs_{after\ bronchodilator\ therapy}$ = 0.450). In particular, mMRC dyspnea grade ⩾ 2 showed a moderate correlation with breathlessness ($rs_{baseline}$ = 0.561; $rs_{after\ bronchodilator\ therapy}$ = 0.443) in the CAT (Supplementary Table 1).

Changes in the CAT scores after bronchodilator therapy

Overall, during a median of 5.8 months of initial bronchodilator therapy, CAT total scores did not improve (16.0 ± 8.4 at baseline *versus* 14.9 ± 8.3 after bronchodilator therapy, p = 0.13). However, individual item scores for chest tightness (1.8 ± 1.5 *versus* 1.5 ± 1.3, p = 0.02) and breathlessness (3.2 ± 1.5 *versus* 2.8 ± 1.4, $p < 0.001$) were significantly improved after bronchodilator therapy. In addition, FEV_1 (1810 ± 490 mL/s *versus* 1990 ± 490 mL/s, $p < 0.001$) was increased, and the proportion of patients with mMRC dyspnea grade ⩾ 2 [64 ([43.2%) *versus* 47 (31.8), p = 0.041] was significantly decreased after bronchodilator therapy. After adjustment for age, smoking history, GOLD stage, pulmonary comorbidity, other comorbidities, and history of exacerbation, individual item scores for phlegm [–0.22 (–0.48, –0.002)], chest tightness [–0.30 (–0.56, –0.05)], and breathlessness [–0.45 (–0.66, –0.23)] were significantly improved after bronchodilator therapy. The FEV_1 increased [adjusted

Table 2. Change of CAT scores, lung function, and mMRC dyspnea grade in total patients (*N* = 148).

	Baseline	After bronchodilator therapy	*p*-value	Adjusted difference[a]
CAT total scores	16.0 ± 8.4	14.9 ± 8.3	0.13	−1.10 (−2.40, 0.20)
CAT individual item score				
Cough	1.9 ± 1.5	1.7 ± 1.3	0.13	−0.22 (−0.48, 0.04)
Phlegm	2.1 ± 1.4	1.9 ± 1.4	0.07	**−0.22 (−0.44, −0.002)**
Chest tightness	**1.8 ± 1.5**	**1.5 ± 1.3**	**0.02**	**−0.30 (−0.56, −0.05)**
Breathlessness	**3.2 ± 1.5**	**2.8 ± 1.4**	**< 0.001**	**−0.45 (−0.66, −0.23)**
Activities	1.4 ± 1.6	1.4 ± 1.4	0.34	−0.09 (−0.32, 0.14)
Confidence	1.5 ± 1.5	1.5 ± 1.6	0.90	0.03 (−0.22, 0.28)
Sleep	1.6 ± 1.5	1.8 ± 1.5	0.20	0.17 (−0.11, 0.45)
Energy	2.4 ± 1.4	2.4 ± 1.4	0.64	−0.20 (−0.26, 0.22)
CAT pulmonary item score	9.1 ± 4.5	7.9 ± 4.1	0.003	−1.19 (−1.92, −0.46)
CAT extra-pulmonary item score	6.9 ± 4.9	7.0 ± 4.9	0.74	0.09 (−0.66, 0.84)
Lung function[b]				
FEV_1, mL	**1810 ± 490**	**1990 ± 490**	**< 0.001**	**170 (130, 220)**
FEV_1, % predicted	**61.8 ± 14.8**	**68.2 ± 14.9**	**< 0.001**	**6.43 (5.01, 7.85)**
mMRC dyspnea grade ⩾ 2	64 (43.2)	47 (31.8)	0.041	**0.58 (0.39, 0.85)**

CAT, COPD assessment test; mMRC, modified Medical Research Council; FEV1, forced expiratory volume in 1 s.
Data presented as mean (SD) or *n* (%). Data were collected at two points in 'Baseline' and 'After Bronchodilator therapy [after median 5.8 (5.1–6.5) months]'.
Bold values mean statistically significant values.
[a]Adjusted for age, smoking history, Global Initiative for Chronic Obstructive Lung Disease grade, pulmonary comorbidity, other comorbidities, and acute exacerbation history.
[b]Adjusted for age, smoking history, pulmonary comorbidity, other comorbidities, and acute exacerbation history.

difference: 170 (95% CI: 130, 220) mL], and the proportion of patients with mMRC dyspnea grade ⩾ 2 decreased [OR, 0.58 (0.39, 0.85)] (Table 2).

Characteristics of patients with improved or unchanged total CAT score

After the initial bronchodilator therapy, 69 patients (46.6%) showed improved CAT scores. Within the group with an improved CAT score, the total CAT score showed a decline both in patients with a baseline CAT score of > 20 [–9.71 (11.82, 7.60)] and in those with a baseline CAT score of ⩽ 20 [–6.32 (–7.56, –5.08)] (Supplementary Table 2).

There were no significant differences in age, sex, body mass index, smoking status, pulmonary comorbidities, or extra-pulmonary comorbidities between the two groups. In addition, there were no differences in baseline pulmonary function, GOLD grade, and type of initially prescribed bronchodilator between the two groups (Supplementary Table 3). Total CAT score [–7.80 (–903, –6.58)] and scores for each of the eight individual items significantly improved in the group showing improved CAT score, whereas those for each item, with the exception of breathlessness [0.12 (–0.16, 0.40)], worsened in the group that exhibited no improvement. The FEV_1 [190 (140, 240) mL] improved and the proportion of patients with mMRC dyspnea grade ⩾ 2

Table 3. Adjusted changes in the CAT score, lung function, and mMRC dyspnea grade before and after treatment in CAT improved or not improved patients.

CAT score	Improved[a] (*N* = 69)	Not improved (*N* = 79)
CAT total scores	**−7.80 (−9.03, −6.58)**	**4.76 (3.64, 5.88)**
CAT individual item score		
Cough	**−1.10 (−1.44, −0.77)**	**0.56 (0.26, 0.86)**
Phlegm	**−1.06 (−1.34, −0.78)**	**0.51 (0.28, 0.74)**
Chest tightness	**−1.31 (−1.62, −0.99)**	**0.57 (0.30, 0.84)**
Breathlessness	**−1.09 (−1.36, −0.82)**	0.12 (−0.16, 0.40)
Activities	**−1.01 (−1.28, −0.73)**	**0.71 (0.47, 0.96)**
Confidence	**−0.80 (−1.12, −0.50)**	**0.75 (0.45, 1.06)**
Sleep	**−0.60 (−0.97, −0.22)**	**0.84 (0.49, 1.20)**
Energy	**−0.84 (−1.12, −0.56)**	**0.70 (0.41, 1.00)**
CAT pulmonary item score	**−4.57 (−5.33, −3.79)**	**1.75 (1.04, 2.47)**
CAT extra-pulmonary item score	**−3.25 (−4.06, −2.44)**	**3.01 (2.26, 3.76)**
Lung function[b]		
FEV_1, mL	**190 (140, 240)**	**150 (80, 230)**
FEV_1, % predicted	**6.78 (4.93, 8.64)**	**6.12 (4.02, 8.23)**
mMRC dyspnea grade ⩾ 2[c]	**0.36 (0.20, 0.64)**	0.85 (0.52, 1.40)

CAT, COPD assessment test; FEV_1, forced expiratory volume in 1 s; mMRC, modified Medical Research Council.
Data are presented as adjusted differences (95% confidence intervals).
Adjusted for age, smoking history, Global Initiative for Chronic Obstructive Lung Disease grade, pulmonary comorbidity, other comorbidities, and acute exacerbation history.
Bold values mean statistically significant values.
[a]A decrease of 2 points or more.
[b]Adjusted for age, smoking history, pulmonary comorbidity, other comorbidities, and acute exacerbation history.
[c]Changes in the number of persons belonging to the mMRC grade ⩾ 2 group before and after treatment were indicated, and the data were presented as odds ratio (95% confidence intervals).

significantly decreased [OR, 0.36 (0.20, 0.64)] in the group with improved CAT score. In the other group, FEV_1 [150 (80, 230) mL] improved significantly, but the proportion of patients with mMRC dyspnea grade ⩾ 2 did not decrease [OR, 0.85 (0.52, 1.40)] (Table 3).

Regarding the occurrence of exacerbation during follow-up, all patients were stable without COPD exacerbation at the time of initial and follow-up CAT score measurement and 10.8% experienced exacerbations during follow-up. Prior to bronchodilator therapy, there was no significant difference in moderate-to-severe exacerbation history in the previous year between the groups (36.2% *versus* 29.1%, $p = 0.356$). However, during the short-term follow-up after bronchodilator therapy, the group with improved CAT score had significantly fewer moderate-to-severe exacerbations than the other group (2.9% *versus* 17.7%, $p = 0.004$) (Figure 2) and there was no significance difference in follow-up duration between two groups ($p = 0.979$).

Discussion

In our study, the average total CAT score did not significantly improve in newly diagnosed COPD patients who were treatment naïve after 6 months of bronchodilator therapy. However, among the

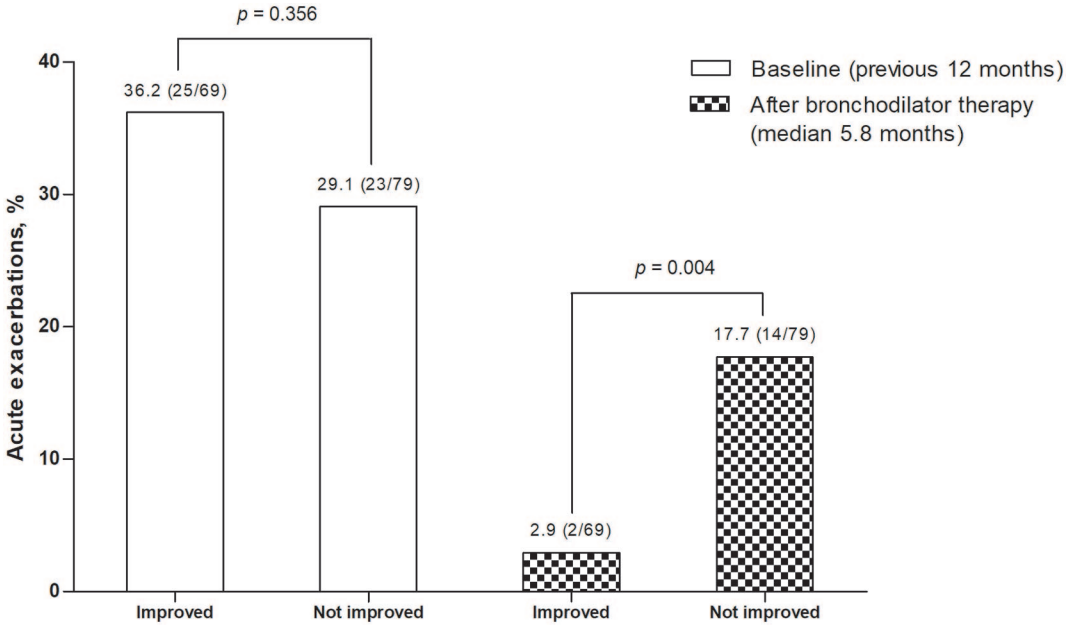

Figure 2. Comparison of moderate-to-severe exacerbations at baseline (previous 12 months) and after short-term (6 ± 2 months) bronchodilator therapy between the CAT score improved and not improved groups.
CAT, COPD test.

individual CAT items, phlegm, chest tightness, and breathlessness significantly improved, suggesting an impact of bronchodilator therapy on the improvement of respiratory symptoms. Approximately, half of the patients showed an improvement in the CAT score exceeding the MCID (⩾2 points), and they showed a significant improvement across all items of the CAT, irrespective of the baseline CAT score (⩽20 or >20). In the group with improved CAT score, the proportion of patients with mMRC dyspnea grade ⩾2 also decreased. While the FEV_1 was improved after short-term bronchodilator therapy in both groups regardless of CAT score improvement, development of moderate-to-severe exacerbation during follow-up was significantly lower in the group with improved CAT score despite the similar baseline exacerbation history in the two groups.

Although the CAT was developed to be unidimensional and without subdomains,[8] the items can be pragmatically grouped into two groups based on their content: cough, phlegm, chest tightness, and breathlessness as 'pulmonary items'; and activities, confidence, sleep, and energy as 'extra-pulmonary items'.[18,20] In our study, scores for phlegm, chest tightness, and breathlessness items of the CAT remarkably improved after short-term bronchodilator therapy in all patients. Scores for items five through eight (activities, confidence, sleep, and energy), classified as 'extra-pulmonary', did not show any change. Previous studies have typically used the total CAT score to determine the correlation with patients' symptoms, clinical course, lung function, and other PROs.[15–17] However, a recent study reported that single items of the CAT contain additional information regarding COPD phenotypes,[31] presence of emphysema,[19] comorbidities,[32] and fatigue,[33] which is not discernible from the total score. Another study suggested that the CAT items contribute differently to the total score.[18] A substantial number of patients classified into the high impact group (CAT score >18) did not report a high level of respiratory symptoms, indicating that non-respiratory symptoms can impact disease burden. In particular, when the impact of PR on the scores of each CAT item and total CAT score was analyzed, the response to PR varied by individual item; however, the item 'energy' showed the largest effect size for PR. Similarly, the type of item that shows a significant response may depend on the type of intervention that was applied for chronic respiratory diseases. This cannot be determined only by changes in total CAT score. Thus, while the total score captures the overall impact of COPD,

focusing on each item might be helpful when evaluating CAT score changes over time or in response to a specific treatment.

Many studies have shown that lung function does not fully represent the current health status of patients with COPD and that PRO tools might improve the clinicians' understanding of the patient's condition.[13,34,35] Similar to previous studies, our study also showed that the correlation between lung function and CAT score is weak.[16,35] In particular, lung function parameters, such as FEV_1, increased significantly for all study patients and even in the group that showed no improvement in the CAT score, but none of the eight individual items of the CAT score improved in this group after treatment initiation. In addition, the development of moderate-to-severe exacerbation during follow-up markedly differed between the two groups, although there was no such difference at baseline, which is consistent with a previous study showing that COPD patients with stable or improved health status had a lower likelihood of exacerbation.[36] This is also in line with the finding that a significant increase in the total CAT score could help detect COPD exacerbation.[13,37] Thus, without PROs, clinicians might misinterpret the patient's clinical status solely based on lung function, while worsening symptoms and exacerbations may be overlooked. Therefore, a comprehensive assessment that involves tracking CAT score changes and exacerbations in addition to lung function is necessary.

Both the CAT and mMRC dyspnea scales are frequently used PRO measurement tools in clinical practice. From the results that lung function alone cannot explain all the heterogeneous features of COPD, the 2011 GOLD report recommended that the CAT and mMRC dyspnea scale be used to evaluate patients' symptoms.[7] Cheng *et al.*[38] reported that the CAT score is more effective than the mMRC dyspnea grade in indicating the severity of clinical symptoms and comorbidity consequences. In addition, the mMRC dyspnea scale is limited in its ability to evaluate dyspnea, as several studies have demonstrated the dissociation of the mMRC dyspnea grade with other PROs and clinical symptoms. However, in our study, the proportion of patients with mMRC dyspnea grade ≥ 2 significantly decreased in all patients and in the group with CAT score improvement, while it remained similar even after bronchodilator therapy in the group that showed no improvement in the CAT score. Therefore, we suggest that it might be helpful to use both the CAT and the mMRC dyspnea grade together to assess the symptom burden in COPD patients.

Certain limitations of our study must be acknowledged. First, this was a relatively small retrospective study conducted at a single institution in South Korea, which limits its generalizability to other populations. In particular, 93% of the patients who participated were male and the mean age was 70.9 years, which is consistent with the characteristics of Korean COPD patients recruited from tertiary hospitals.[39] This is partly attributable to a selection bias, given the lower predominance of male individuals in the national survey.[40] Second, due to the nature of study design we were not able to include important confounders, such as exposure history other than smoking, such as biomass. Third, no other PRO measurement tools, aside from the CAT score and mMRC dyspnea grade were used. If measurement tools, such as the Saint George's Respiratory Questionnaire and the clinical COPD questionnaire had been used, they might have provided additional information. In addition, there was a difference in baseline CAT scores between the groups with and without improvement in CAT scores. In the group with improved CAT score, it is possible that the observed improvement was due to the baseline CAT score being high, providing room for further improvement. However, in the analysis in which the patients were subdivided according to their baseline CAT score, the CAT score still exhibited improvement regardless of whether the baseline CAT score was high or low (Supplementary Table 2). From this result, it could be concluded that improvements in the CAT score after bronchodilator therapy cannot simply be explained by high basal scores.

Conclusion

In conclusion, individual CAT items corresponding to respiratory symptoms was more improved after short-term bronchodilator therapy in newly diagnosed and treatment-naïve COPD patients. In addition, the change in the CAT total score can provide a simple estimate of the patient's health status and exacerbation risk, which was not fully captured by FEV_1 measurements in patients with COPD. Therefore, measuring the

patients' lung function by repeatedly measuring the CAT score and tracking the changes might help to understand their condition. In addition, when evaluating patients using CAT score changes, it might be useful to evaluate each item together with the overall score.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Samsung Medical Center, and the requirement for informed consent was waived because of the retrospective nature of the study.

Consent for publication

Not applicable.

Author contributions

Bo-Guen Kim: Data curation; Formal analysis; Investigation; Methodology; Writing – original draft; Writing – review & editing.
Sun Hye Shin: Data curation; Investigation; Methodology; Writing – original draft; Writing – review & editing.
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Juhee Cho: Conceptualization; Formal analysis; Methodology; Supervision; Writing – review & editing.
Hye Yun Park: Conceptualization; Methodology; Supervision; Writing – review & editing.

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Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and materials

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

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Supplemental material

Supplemental material for this article is available online.

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