Usefulness of the Chronic Obstructive Pulmonary Disease Assessment Test to Evaluate Severity of COPD Exacerbations

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Rationale: The Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) is an eight-item questionnaire designed to assess and quantify the impact of COPD symptoms on health status. COPD exacerbations impair quality of life and are characterized by worsening respiratory symptoms from the stable state. We hypothesized that CAT scores at exacerbation relate to exacerbation severity as measured by exacerbation duration, lung function impairment, and systemic inflammation.

Objectives: To evaluate the usefulness of the CAT to assess exacerbation severity.

Methods: One hundred sixty-one patients enrolled in the London COPD cohort completed the CAT at baseline (stable state), exacerbation, and during recovery between April 2010 and June 2011.

Measurements and Main Results: Frequent exacerbators had significantly higher baseline CAT scores than infrequent exacerbators (19.5 ± 6.6 vs. 16.8 ± 8.0, P = 0.025). In 152 exacerbations, CAT scores rose from an average baseline value of 19.4 ± 6.8 to 24.1 ± 7.3 (P < 0.001) at exacerbation. Change in CAT score from baseline to exacerbation onset was significantly but weakly related to change in C-reactive protein (rho = 0.26, P = 0.008) but not to change in fibrinogen (rho = 0.09, P = 0.351) from baseline to exacerbation. At exacerbation, rises in CAT score were significantly associated with falls in FEV1 (rho = −0.20, P = 0.032). Median recovery time as judged by symptom diary cards was significantly related to the time taken for the CAT score to return to baseline (rho = −0.42, P = 0.012).

Conclusions: The CAT provides a reliable score of exacerbation severity. Baseline CAT scores are elevated in frequent exacerbators. CAT scores increase at exacerbation and reflect severity as determined by lung function and exacerbation duration.

Keywords: chronic obstructive pulmonary disease; exacerbations; severity; patient-reported outcomes; symptoms

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory airway condition associated with episodes of acute deterioration termed exacerbations (1). Exacerbations are among the most common causes of medical admission to the hospital (2), and the rate at which they occur appears to reflect an independent susceptibility phenotype (3). They are also important events in the natural history of COPD that drive lung function decline (4, 5), increase risk of cardiovascular events (6), and are responsible for much of the morbidity (7) and mortality (8) associated with this highly prevalent condition.

COPD exacerbations are characterized by a worsening of respiratory symptoms from the usual stable state, especially dyspnea, increased sputum volume, and purulence. Changes in exacerbation symptoms relate to exacerbation recovery time (9), which is an index of exacerbation severity. In addition to exacerbation length, exacerbation severity influences acute treatment (9) and drives hospital admission and mortality (8).

Patient diary cards are direct measures of exacerbation symptoms that provide accurate information regarding the commencement and resolution of exacerbations (9). They can detect exacerbations that are both reported and unreported to healthcare professionals, thus allowing accurate determination of exacerbation frequency (7). However, currently there is no standardized, objective method for assessing symptom severity at exacerbation of chronic obstructive pulmonary disease (COPD) that has been universally accepted and available for use in both routine clinical practice and clinical trials.

What This Study Adds to the Field

The COPD Assessment Test (CAT) provides a reliable score of exacerbation severity, and its incorporation into assessment strategies may aid healthcare professionals to determine the severity of exacerbations and potentially assist management. The CAT may also prove useful in clinical trials to objectively assess the ability of novel interventions to reduce exacerbation severity.

(Received in original form October 17, 2011; accepted in final form January 11, 2012)


The London COPD cohort is funded by the MRC Patient Research Cohort Initiative. This work was supported by an unrestricted educational grant from GlaxoSmithKline.

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This article has an online supplement, which is accessible from this issue’s table of contents at www.atsjournals.org

Am J Respir Crit Care Med Vol 185, Iss. 11, pp 1218–1224, Jun 1, 2012
Copyright © 2012 by the American Thoracic Society
Originally Published in Press as DOI: 10.1164/rccm.201110-1843OC on January 26, 2012
Internet address: www.atsjournals.org

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Currently there is no standardized, objective method for assessing symptom severity at exacerbation of chronic obstructive pulmonary disease (COPD) that has been universally accepted and available for use in both routine clinical practice and clinical trials.

What This Study Adds to the Field

The COPD Assessment Test (CAT) provides a reliable score of exacerbation severity, and its incorporation into assessment strategies may aid healthcare professionals to determine the severity of exacerbations and potentially assist management. The CAT may also prove useful in clinical trials to objectively assess the ability of novel interventions to reduce exacerbation severity.
How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 1 2 3 4 5 I am very sad

I never cough 0 1 2 3 4 5 I cough all the time

I have no phlegm (mucus) in my chest at all 0 1 2 3 4 5 My chest is completely full of phlegm (mucus)

My chest does not feel tight at all 0 1 2 3 4 5 My chest feels very tight

When I walk up a hill or one flight of stairs I am not breathless 0 1 2 3 4 5 When I walk up a hill or one flight of stairs I am very breathless

I am not limited doing any activities at home 0 1 2 3 4 5 I am very limited doing activities at home

I am confident leaving my home despite my lung condition 0 1 2 3 4 5 I am not at all confident leaving my home because of my lung condition

I sleep soundly 0 1 2 3 4 5 I don’t sleep soundly because of my lung condition

I have lots of energy 0 1 2 3 4 5 I have no energy at all

TOTAL SCORE

Figure 1. Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT). Reprinted by permission from GlaxoSmithKline.

We hypothesized that elevated CAT scores at COPD exacerbation relate to exacerbation severity as measured by exacerbation length, lung function impairment, and systemic inflammation. Furthermore, we hypothesized that CAT scores can be used to model recovery. Therefore, well-characterized patients were prospectively assessed using the CAT in the baseline stable state, at exacerbation presentation, and thereafter for 5 weeks during the recovery period.

METHODS

Patient Recruitment

This study involved 161 patients with COPD enrolled in the London COPD cohort between January 1, 2009 and June 1, 2011. The patients form part of a rolling cohort used to prospectively investigate the mechanisms of COPD exacerbations. Patients were included if the post-bronchodilator FEV₁ was less than or equal to 80% predicted from age, height, and sex, and FEV₁/FVC ratio was less than 0.7 (12). Patients with a history of any other significant respiratory diseases were excluded, as were those unable to complete daily diary cards.

At annual review or recruitment, a full medical and smoking history was obtained, a clinical examination performed, and the SGRQ (13) completed. Comorbid diagnoses were established using clinical history and examination findings during a stable-state visit, supported where appropriate with a review of available medical records. FEV₁ and FVC were measured with a Vitalograph Gold Standard spirometer (Vitalograph Ltd., Maids Moreton, UK). Oxygen saturations were also measured (PureSAT; Nonin Medical Inc., Plymouth, MN). Body mass index (BMI) was calculated from height and weight.

Ethical approval for the study was granted from the Royal Free Hospital research ethics committee, and all patients gave written informed consent.
consent. Permission to use the CAT questionnaire was obtained from GlaxoSmithKline. The recruitment and monitoring of these patients has been previously described, and the cohort has been the subject of previous publications (7, 9, 14–16), but the current study is entirely novel and has not been reported before.

Monitoring and Definition of Exacerbations
Patients were asked to record daily peak expiratory flow rate (PEFR) measured with a mini-Wright meter (Clement-Clark International, Harlow, UK), hours spent outside the home, and any increase in respiratory symptoms on diary cards. An exacerbation was defined as an increase for two consecutive days in respiratory symptoms, with at least one major symptom (dyspnea, sputum purulence, or sputum volume) plus either another major or a minor symptom (wheeze, cold, sore throat, and cough), the first of which was defined as the day of onset of the exacerbation. Symptoms counts were obtained by summing each increased respiratory symptom recorded on diary cards per day. Exacerbation duration was defined as the number of days after onset that worsening symptoms persisted. The last day of recorded worsening symptoms before two consecutive symptom-free days defined the end of the exacerbation. Exacerbation recovery was not determinable if patients failed to record diary card symptoms or continuously recorded symptoms for more than 99 days after onset. Exacerbation frequency was calculated for each patient using diary card data obtained between January 2009 and June 2011. For recently recruited patients with less than 1 year diary data, exacerbation frequency was based on the number of exacerbations the patient recalled for the year before recruitment. Previous work has shown a good correlation between the number of exacerbations recorded on diary cards and the number of exacerbations remembered by the patient over the same 1-year period (17) and has shown that exacerbation frequency represents a stable patient phenotype (3).

Exacerbation Assessment
Exacerbations were treated according to the prevailing guidelines and clinical judgment with increased inhaled therapy, antibiotics, and/or oral steroids. Neither the magnitude of exacerbation CAT score nor the diary card symptom score played any role in treatment decisions. When patients attended for an exacerbation, venous blood samples were taken and spirometry performed before commencing exacerbation treatment. Serum C-reactive protein (CRP) was measured using Modular Analytics E 170 Module (Roche, Burgess Hill, UK) and plasma fibrinogen using theClauss method (IL ACL Top Coagulation Analyzer, Lexington, MA).

CAT Administration
Patients completed the CAT at least once under supervision in clinic and then at home, based on their symptoms experienced on the day of completion. Patients completed at least one CAT questionnaire in the stable, baseline state. Baseline occurred more than 35 days after and 21 days before exacerbation onset. If unavailable before index exacerbation, CAT scores during periods of stability postexacerbation were used to provide a baseline. No differences were seen between baseline scores obtained preindex exacerbation and baseline scores postexacerbation. Repeat scores were averaged to give a baseline CAT score. CAT questionnaires were also administered during exacerbation between April 2010 and June 2011. The exacerbation CAT score took place within 7 days of the symptomatic onset of the exacerbation as judged by diary cards, was completed before starting therapy, and was recorded on the day treatment commenced. These were mandatory study criteria. A subgroup of patients also completed CAT scores on a daily basis during their recovery. For the recovery subgroup, the first exacerbation was selected for analysis provided the patient had fully completed the questionnaire on at least 21 of 35 days post onset. CAT Recovery was the time taken from exacerbation onset for the CAT score to return to baseline value (see Figure E1 in the online supplement).

Statistical Analysis
Data were analyzed with STATA 8.2 (Stata Corporation, College Station, TX). Normally distributed data were expressed as mean and standard deviation (SD) and skewed data as median and interquartile range (IQR). Comparisons were made by paired Student t test or Wilcoxon signed-rank test. The relationship between exacerbation frequency and baseline CAT scores was examined with a negative binomial regression model, whereas Poisson regression was used to model exacerbation recovery and CAT scores. Cross-sectional regression models were used to analyze the relationship between inflammatory markers during exacerbation and CAT score as allowance could be made for repeated measures on the same patient.

RESULTS

Patient Characteristics
One hundred sixty-one patients with COPD completed at least one CAT questionnaire when stable (exacerbation free). Their baseline characteristics are reported in Table 1 alongside 75 patients who were assessed using the CAT at exacerbation and the 52 of these who completed the CAT questionnaire daily during exacerbation recovery. The patients had moderate to severe disease with a mean FEV1 % predicted of 50.3% (range, 14.0–79.7%). Patients in whom CAT was assessed at exacerbation had significantly higher exacerbation frequencies ($P < 0.001$) but differed in no other respect. Patients completed the CAT successfully when stable and when acutely unwell during an exacerbation. In total, 6,404 out of 6,514 questionnaires (98.3%) were completed fully. There was no significant difference in the percentages fully completed at baseline, 3,496 of 3,561 (98.2%), compared with those at exacerbation onset and during recovery, 2,908 of 2,953 (98.5%, $P = 0.35$).

Use of CAT at Baseline

Baseline CAT and exacerbation frequency. The 161 patients had a mean baseline CAT score of 18.1 (SD, 7.45). Frequent exacerbators ($\geq$2 exacerbations per year, $n = 80$) had a mean CAT score of 19.5 (SD, 6.6) compared with infrequent exacerbators ($<2$ exacerbations per year, $n = 81$), whose mean CAT score was 16.8 (SD, 8.0; $P = 0.025$; Figure 2). Thus, there was an average 2.7-point difference in CAT score between the frequent and infrequent exacerbators.

Relationship between CAT score and systemic inflammatory markers in the baseline state. At baseline, serum CRP was measured on the same day as a CAT was completed in 318 blood samples obtained from 150 separate patients and plasma fibrinogen in 282 blood samples from 144 patients. There was a significant relationship between systemic inflammation, as measured by log10 fibrinogen, and CAT score on the day of baseline sampling, regression coefficient $= 0.0014$ (95% CI, 0.0001–0.0027; $P = 0.035$; Figure 3), $R^2 = 0.024$ using random-effects generalized least squares regression. However, there was no statistically significant relationship between log10 CRP and CAT scores, regression coefficient $= 0.0059$ (95% CI, $-0.0016$ to 0.0133; $P = 0.122$).

No difference in baseline CAT scores was seen between patients with or without potentially confounding comorbidities (congestive heart failure, renal failure, obesity, or sleep-disordered breathing; Table 2), confirming previous work that CAT scores appear unaffected by low levels of comorbidity (18).

Use of CAT at Exacerbation

The CAT was completed at 152 treated exacerbations by 75 patients. The median interval from diary card exacerbation onset to the day of treatment was 2 days (IQR, 1–4). Figure 4 shows that the CAT score rose from an average baseline value of 19.4 (SD, 6.8) to 24.1 (SD, 7.3; $P < 0.001$) at exacerbation.

The magnitude in rise of CAT score from baseline to exacerbation was not affected by patient baseline characteristics. Patients whose change in CAT score at exacerbation was on
average greater or equal to 2 units displayed no significant difference in age (73.2 vs. 70.3 yr, \( P = 0.13 \)), FEV1, % predicted (47.6 vs. 47.3, \( P = 0.94 \)), or exacerbation frequency (2.73 vs. 2.48, \( P = 0.586 \)) from those with smaller changes in CAT score.

The symptomatic characteristics of exacerbations did not significantly affect the magnitude of CAT rise at exacerbation (see online supplement). Although patients within the London COPD cohort complete daily symptom diary cards, which allows detection of exacerbations that are unreported to healthcare professionals and untreated with extra medication (7), all 152 exacerbations included in the analyses were treated. The vast majority of exacerbations were treated with systemic treatment after clinical review by a member of the research team; 103 exacerbations were treated with antibiotics and oral corticosteroids, 22 with antibiotics alone, and 7 with oral steroids alone. Just 20 patients increased inhaled therapy (bronchodilators and/or inhaled corticosteroids) alone without systemic treatment. One hundred thirty-two exacerbations fitted this criterion. The mean change in CAT score from baseline to exacerbation was 5.2 units (SD, 6.7; \( n = 132 \)). Mean change in CAT score from baseline to exacerbation for patients who received increased inhaled therapy alone was 2.0 (4.9), although this was based on just 20 exacerbations. Further work is required to further explore the relationships between changes in CAT at exacerbation and choice of exacerbation treatment.

**Relationship between CAT score and systemic inflammatory markers at exacerbation.** CAT scores at exacerbation were significantly related to concurrent levels of systemic inflammatory markers. At exacerbation, serum CRP was measured on the same day as a CAT was completed in 114 exacerbations and plasma fibrinogen in 111 exacerbations. After log10 transformation, both inflammatory markers were significantly related to the CAT score recorded at exacerbation, and with allowance for repeated measures in the same patient, log10 CRP increased by 0.028 (95% CI, 0.013–0.043; \( P < 0.001 \)) and log10 fibrinogen by 0.003 (95% CI, 0.001–0.005; \( P = 0.015 \)), per unit increase in

**Table 1. Clinical Characteristics of Patients in the Baseline, Exacerbation, and Recovery Analyses**

<table>
<thead>
<tr>
<th>Baseline ( (n = 161) )</th>
<th>Exacerbation ( (n = 75) )</th>
<th>Recovery Subgroup ( (n = 52) )</th>
<th>( P ) Value*</th>
<th>( P ) Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>71.3 ± 9.4</td>
<td>71.3 ± 8.4</td>
<td>0.99</td>
<td>71.3 ± 7.9</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>1.22 ± 0.47</td>
<td>1.14 ± 0.41</td>
<td>0.10</td>
<td>1.14 ± 0.4</td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>50.3 ± 16.9</td>
<td>47.9 ± 16.3</td>
<td>0.10</td>
<td>47.1 ± 16.6</td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.59 ± 0.78</td>
<td>2.51 ± 0.79</td>
<td>0.09</td>
<td>2.52 ± 0.9</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>47.4 ± 12.6</td>
<td>46.5 ± 13.0</td>
<td>0.38</td>
<td>46.2 ± 13.1</td>
</tr>
<tr>
<td>Smoking pack-years</td>
<td>53.5 ± 38.9</td>
<td>52.2 ± 39.9</td>
<td>0.62</td>
<td>50.6 ± 37.3</td>
</tr>
<tr>
<td>( \text{SpO}_2 ), %</td>
<td>94.7 ± 2.0</td>
<td>94.6 ± 2.1</td>
<td>0.52</td>
<td>94.4 ± 2.1</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>26.4 ± 5.6</td>
<td>26.6 ± 5.4</td>
<td>0.36</td>
<td>27.0 ± 5.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median (IQR)</th>
<th>Median (IQR)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbation frequency</td>
<td>1.95 (0.90–3.00)</td>
<td>2.73 (1.70–4.10)</td>
</tr>
<tr>
<td>No. (%)</td>
<td>97 (60)</td>
<td>43 (57)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>49 (31)</td>
<td>20 (27)</td>
</tr>
</tbody>
</table>

**Definition of abbreviations:** BMI = body mass index; CAT = Chronic Obstructive Pulmonary Disease Assessment Test; SD = standard deviation; \( \text{SpO}_2 \) = oxygen saturation measured by pulse oximetry.

*Comparison between 52 patients with exacerbation CAT scores during recovery and 109 patients in whom a recovery time was not examined.

†Comparison between 52 patients with exacerbation CAT scores during recovery and 109 patients in whom a recovery time course was not examined.

The main analysis was repeated using a strict healthcare use definition of an exacerbation, based on physician review and increased systemic treatment. One hundred thirty-two exacerbations fitted this criterion. The mean change in CAT score from baseline to healthcare use exacerbation was 5.2 units (SD, 6.7; \( n = 132 \)). Mean change in CAT score from baseline to exacerbation for patients who received increased inhaled therapy alone was 2.0 (4.9), although this was based on just 20 exacerbations. Further work is required to further explore the relationships between changes in CAT at exacerbation and choice of exacerbation treatment.

**Figure 2.** Mean baseline Chronic Obstructive Pulmonary Disease Assessment Test (CAT) scores between frequent and infrequent exacerbators (161 patients). Vertical lines represent SEs.

**Figure 3.** Relationship between log10 fibrinogen and Chronic Obstructive Pulmonary Disease Assessment Test (CAT) score at baseline (282 samples from 144 patients).
CAT score. Change in CAT score from baseline to exacerbation onset was significantly related to change in CRP (rho = 0.26, P = 0.008) but not to change in fibrinogen (rho = 0.09, P = 0.351) from baseline to exacerbation.

**Lung function changes and CAT scores at exacerbation.** CAT scores were significantly related to contemporaneous spirometry, as measured by FEV₁. At exacerbation, spirometry was performed on the same day as a CAT was completed in 112 exacerbations. Mean paired FEV₁ measured at baseline was 1.12 L (SD, 0.44) and 1.01 L at exacerbation (SD, 0.44; P < 0.001). Rises in the CAT score recorded at exacerbation were significantly associated with falls in FEV₁ at exacerbation (rho = −0.20, P = 0.032).

**Time Course of CAT Scores during Exacerbation Recovery**

Fifty-two different patients completed the CAT questionnaire on at least 21 of 35 days during the recovery phase after an exacerbation. All of these 52 exacerbations were treated: 41 with antibiotics and oral steroids, 5 with antibiotics alone, 3 with oral steroids alone, and 3 with increased inhaled therapy alone. Figure 5 shows the time course of the CAT scores, PEFR, and diary card symptom counts (further details are available in the online supplement).

**Relationship between CAT score and symptom recovery.** CAT scores reflected symptomatic recovery after exacerbations. Among the 52 episodes, the median recovery time as judged by symptom diary cards was 12 days (IQR, 9–23; n = 47), and this was significantly related (rho = 0.42, P = 0.012) to the time taken for the CAT score to return to baseline (median, 11 d; IQR, 4.5–17; n = 40).

**DISCUSSION**

This novel study prospectively assessed the usefulness of the CAT to evaluate exacerbation severity in patients with COPD. At exacerbation, CAT scores were significantly elevated from paired baseline values, and we have uniquely demonstrated that CAT scores reflect exacerbation severity as measured by exacerbation length and reduction in lung function. A weak relationship was also found between systemic inflammatory markers and CAT scores at exacerbation. Furthermore, we have shown that baseline CAT scores are significantly elevated in patients with stable COPD with a history of frequent exacerbations.

The CAT is a validated health status questionnaire that is free to use and can be administered without prior permission for research purposes and by individual practitioners (http://www.catestonline.org). Previous studies have shown that the instrument can be successfully administered in both primary (18) and secondary care settings (11) and is responsive to a course of pulmonary rehabilitation and able to distinguish different levels of response (11). Additionally, CAT scores exhibit little variability across countries; they are not influenced by age or sex but reflect disease severity in the stable state as determined by Global Initiative for Chronic Obstructive Lung Disease spirometric staging, Medical Research Council dyspnea score, SGRO, and clinician-judged severity (10, 18).

Our study complements this existing work by demonstrating that the CAT can be used as a score of the multidimensional nature of COPD exacerbation severity. At present, the assessment of symptom severity at exacerbation and during recovery is subjective in nature, with no established scoring system in clinical practice. Exacerbation therapy is currently determined by a subjective physician assessment of exacerbation severity, and so an objective tool to determine exacerbation severity will fulfill an important unmet need. This has particular relevance as patients are increasingly seen by healthcare professionals in the community, often within their own homes, without the benefit of objective measures of exacerbation severity such as accurate spirometry or systemic inflammatory markers. PEFR is a cheap, reliable, and easy way for patients to assess lung function on a daily basis. We have shown in previous studies that PEFR decreases to a small extent but significantly at exacerbation onset and can be a useful tool to indicate exacerbation recovery in population studies. However, the changes are not large enough to use PEFR at an individual level for exacerbation detection and monitoring (9).

An objective, validated exacerbation severity score is also required for use in clinical trials. Treatments to prevent exacerbations may also reduce exacerbation severity in addition to exacerbation frequency, but at present tools to determine efficacy of this are limited, and only exacerbation rates are usually recorded in clinical studies (19, 20). Most clinical trials to date have used therapy and hospitalization rates to assess exacerbation severity, and thus an objective symptom severity score will enable the ability of novel interventions to reduce exacerbation severity to be assessed and compared across studies (21). Therapies involving either exacerbation prevention or management of the acute exacerbations may reduce exacerbation CAT scores or the time taken for scores to recover to baseline. Further evaluation of the CAT in clinical trials is now required.

The CAT provides an objective quantification of the impact of symptoms that is acceptable to patients and can be easily completed at exacerbation and during recovery. We have previously

**TABLE 2. EFFECT OF COMORBIDITIES ON BASELINE CHRONIC OBSTRUCTIVE PULMONARY DISEASE ASSESSMENT TEST SCORE**

<table>
<thead>
<tr>
<th>Comorbidity Absent</th>
<th>Comorbidity Present</th>
<th>P Value (Unpaired t Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>CAT Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>18.2 ± 7.6 (n = 143)</td>
<td>18.1 ± 6.8 (n = 16)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>17.9 ± 7.6 (n = 130)</td>
<td>19.4 ± 7.2 (n = 29)</td>
</tr>
<tr>
<td>Any cardiovascular disease (excluding hypertension)</td>
<td>17.8 ± 8.0 (n = 112)</td>
<td>18.9 ± 6.6 (n = 29)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17.7 ± 6.4 (n = 152)</td>
<td>18.6 ± 6.7 (n = 29)</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>18.0 ± 7.5 (n = 153)</td>
<td>22.9 ± 5.4 (n = 6)</td>
</tr>
<tr>
<td>Obesity (body mass index &gt; 30 kg/m²)</td>
<td>18.0 ± 7.7 (n = 122)</td>
<td>18.7 ± 6.4 (n = 36)</td>
</tr>
<tr>
<td>Chronic kidney disease (estimated glomerular filtration rate &lt; 60 ml/min)</td>
<td>18.5 ± 7.6 (n = 126)</td>
<td>16.5 ± 6.2 (n = 29)</td>
</tr>
<tr>
<td>Severe chronic kidney disease (estimated glomerular filtration rate &lt; 30 ml/min)</td>
<td>18.1 ± 7.4 (n = 152)</td>
<td>21.0 ± 4.5 (n = 3)</td>
</tr>
</tbody>
</table>

**Definition of abbreviations:** CAT = Chronic Obstructive Pulmonary Disease Assessment Test; SD = standard deviation.
shown that systemic inflammation, as measured by plasma fibrinogen and serum CRP, increases at exacerbation (22–24), and in this study we have demonstrated a weak relationship between CAT scores at exacerbation and systemic inflammatory markers. Inflammatory changes at COPD exacerbations are also related to clinical nonrecovery and recurrent exacerbations within 50 days (15). Recovery time is an index of exacerbation severity (9), and for the first time this study has evaluated use of the CAT during exacerbation recovery. We have demonstrated that CAT scores reflect recovery after exacerbations, the time taken for scores to return to baseline being significantly related to recovery time as judged by symptom diary cards. Additionally, at exacerbation, CAT scores are significantly but modestly related to contemporaneous lung function impairment, as measured by FEV₁, consistent with previous data examining the relationship between baseline CAT scores and FEV₁ (18). Thus, CAT scores provide an easily quantifiable overall score of exacerbation severity and may be useful in studies evaluating interventions for the management of acute exacerbations.

When measured in the stable state, CAT scores are highly correlated to concurrent SGRQ measurements (10). However, this study has shown a divergence between the behavior of the CAT and SGRQ during exacerbation recovery. After a study of exacerbations of chronic bronchitis, although an early improvement is seen in SGRQ scores when measured 4 weeks after an index event, improvements can also slowly continue for several months (25). In this study we found that CAT scores have returned to baseline levels more rapidly. This may be a result of the daily use of the instrument in this study and the response system in the CAT, which is based on categories of difference between two extreme statements about the same COPD impact. In contrast, the SGRQ has predominantly dichotomous yes/no responses and is administered at intervals. Thus, although we have demonstrated that the CAT can reliably assess exacerbation severity, daily CAT readings may overestimate the speed of recovery of health status postexacerbation.

This study has also added to previous data examining the use of the CAT in the baseline stable state by examining the relationship between baseline CAT scores and exacerbation frequency. Patients with a history of frequent exacerbations have worse quality of life (7), increased risk of hospitalization (26), and greater mortality (8). Frequent exacerbators also exhibit faster decline in lung function (4) and may have worse functional status, as measured by time outdoors (16). In this study we have shown that baseline CAT scores relate to exacerbation frequency. When used in the stable state, scores were significantly elevated in frequent exacerbators, defined by two or more exacerbations per year, compared with infrequent exacerbators. Also, baseline CAT scores were weakly but significantly related to concurrent fibrinogen levels. We have previously shown that plasma fibrinogen levels are elevated in patients with stable COPD (23) and that increased systemic inflammation, as measured by fibrinogen, in patients with stable COPD over time is directly linked to disease progression, as defined by lung function decline (27). Further work is required to explore whether CAT scores may potentially be a useful marker of disease progression over time in COPD.

Because our results indicate that CAT scores may reflect levels of systemic inflammatory markers, albeit weakly, this finding may have particular relevance in clinical trials of antiinflammatory therapeutic agents in COPD. The effects of antiinflammatory therapies are difficult to assess as changes in FEV₁ tend to be small (28), and exacerbation frequency as an outcome has to be assessed over at least a 12-month period. Further study is now required of CAT scores during antiinflammatory interventions in COPD.

The Exacerbations of Chronic Pulmonary Disease Tool (EXACT) is a patient-reported outcome diary specifically designed to quantify the frequency, severity, and duration of exacerbations of COPD in clinical trials (21). EXACT scores have been shown to differentiate patients who were stable from patients with mild and moderate exacerbations as judged by clinicians (21). However, to date no published data have demonstrated the relationship of EXACT scores to levels of systemic inflammation and lung function changes seen at exacerbation and during recovery. Furthermore, in published papers thus far, the
EXACT has been used in conjunction with a personal digital assistant (21, 29) or Blackberry smartphone (30), potentially limiting its widespread uptake in routine clinical practice.

We have shown that the CAT is a potentially useful, widely applicable tool that can aid assessment of exacerbation severity. The CAT can be easily and rapidly completed in many healthcare settings and could potentially be integrated into care bundles of patients with COPD without additional cost. Patient recognition of exacerbation symptoms and prompt treatment improves exacerbation recovery and reduces the risk of hospitalization in patients with COPD (31). Further evaluation is now required of the CAT within exacerbation management strategies to assess usefulness of the tool within clinical practice.

In conclusion, the CAT provides a reliable score of exacerbation severity. CAT scores increase at exacerbation and reflect exacerbation severity as determined by lung function and exacerbation length. A weak relationship was also found between systemic inflammatory markers and CAT scores at exacerbation. Thus, the CAT is a valuable instrument to enhance and standardize COPD exacerbation assessment. Incorporating this questionnaire into assessment strategies may aid healthcare professionals to determine the severity of exacerbations, particularly in situations where access to other objective measures of severity is limited. The CAT may also prove useful in clinical trials to objectively assess the ability of novel interventions to reduce exacerbation severity.

Author disclosures are available with the text of this article at www.atsjournals.org.

Acknowledgment: The authors thank Beverly Kowlessar (research nurse) for her help in CAT administration and collection. They also thank Gilbert Nadeau (GlaxoSmithKline) for facilitating use of the CAT in this study.

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