International Journal of Chronic Obstructive Pulmonary Disease Dovepress

Open Access Full Text Article

ORIGINAL RESEARCH

Unravelling the Information Contained in the Single Items of the COPD Assessment Test for Different Outcomes and Smoking Status in Patients with COPD: Results from COSYCONET

Peter Alter[1], Kathrin Kahnert[2,3], Franziska C Trudzinski[4], Robert Bals[5], Henrik Watz[6], Tim Speicher[1], Sandra Söhler[1], Klaus F Rabe[7], Emiel FM Wouters[8,9], Claus F Vogelmeier[1], Rudolf A Jörres[10]

[1]Department of Medicine, Pulmonary, Critical Care and Sleep Medicine, Philipps University of Marburg (UMR), German Center for Lung Research (DZL), Marburg, Germany; [2]Department of Internal Medicine V, University Hospital, LMU Munich, Comprehensive Pneumology Center Munich (CPC-M), German Center for Lung Research (DZL), Munich, Germany; [3]MediCenterGermering, Germering, Germany; [4]Department of Pneumology and Critical Care Medicine, Thoraxklinik, University of Heidelberg, Translational Lung Research Center Heidelberg (TLRC-H), Center for Lung Research (DZL), Heidelberg, Germany; [5]Department of Internal Medicine V - Pulmonology, Allergology, Intensive Care Medicine, Saarland University Hospital, Homburg, Germany; [6]Pulmonary Research Institute at LungenClinic Grosshansdorf, Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshansdorf, Germany; [7]LungenClinic Grosshansdorf and Department of Medicine, Christian-Albrechts University, Kiel, Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshansdorf, Germany; [8]Department of Respiratory Medicine, Maastricht University Medical Centre, Maastricht, Netherlands; [9]Sigmund Freud Private University, Medical Faculty, Vienna, Austria; [10]Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, University Hospital, LMU Munich, Comprehensive Pneumology Center Munich (CPC-M), German Center for Lung Research (DZL), Munich, Germany

Correspondence: Peter Alter, Department of Medicine, Pulmonary, Critical Care and Sleep Medicine, Philipps University of Marburg (UMR), German Center for Lung Research (DZL), Baldingerstrasse 1, Marburg, Germany, Tel +49 6421 5866140, Email Alter@uni-marburg.de

Background: The COPD Assessment Test (CAT) comprises eight questions. We evaluated the information that each of the questions and the total score contributed to outcomes and characteristics of chronic obstructive lung disease (COPD), including their dependence on smoking status.

Methods: Patients with COPD of the COSYCONET cohort with Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades 1–4 and the former grade 0 were included. The evaluated outcomes included mortality, exacerbation risk, the comorbidities asthma, cardiac disease (coronary artery disease/heart failure), osteoporosis, and emphysema, for which a reduction in carbon monoxide transfer coefficient (KCO) <55% predicted was considered as marker. Analyses were performed by Cox proportional hazard or logistic multiple regression analyses separately for smokers and nonsmokers.

Results: In total, 2509 patients had complete data, among them 1884 nonsmokers (ex or never; 38.4% female; mean age±SD 66.1±8.5 years) and 625 current smokers (45.1% female, 61.6±7.9 years). The pattern of responses to the single questions of the CAT differed between outcome variables, as well as between smokers and nonsmokers, but in most cases the total score was superior to the single items. The CAT total score was associated with mortality ($p<0.05$) only in nonsmokers, while for exacerbation frequency/severity, it was of about equal importance in smokers and nonsmokers. Regarding KCO, the total score was indicative ($p<0.05$) only in nonsmokers. Particularly in smokers, single items could show opposite signs of their coefficients which therefore largely cancelled in the total score.

Conclusion: Our results show in detail for which outcomes single items are informative in nonsmokers and current smokers with COPD, overall being more informative in nonsmokers. Only regarding exacerbation risk, the predictive value was similar in both groups. These results might be helpful to extract as much as possible information from a COPD questionnaire that is often part of routine assessment.

Trial Registration: NCT01245933.

Keywords: COPD, COPD assessment test CAT, clinical questionnaire, smoking status, mortality, exacerbation

Received: 23 April 2024
Accepted: 9 October 2024
Published: 5 December 2024

Introduction

Since its introduction in 2009,[1] the COPD Assessment Test (CAT) has proved to be extremely valuable for the assessment and treatment guidance of patients with chronic obstructive pulmonary disease (COPD). The instrument has been validated and utilized in numerous studies.[2,3] It comprises eight questions with each scored from 0 (minimum impact) to 5 (maximum impact). These scores are summed to a total score (0–40) that is commonly used in studies and clinical practice. Although this summation has been validated,[1] a later analysis suggested that the first two questions (cough and phlegm) could be considered statistically independent from the last six questions.[4] Since these two symptoms are likely to be related to active smoking, and given the high number of patients with COPD who still smoke,[5] the question arises as to whether the results of CAT depend on smoking status. In addition, analyses of the single CAT items have already indicated that they carry a different amount of information with regard to different outcomes;[4,6,7] for specific purposes single questions might even be superior to the sum score. Since single items could be affected in opposite directions by a specific disease condition, this may lead to cancellation of their changes when summed. The published papers addressing single CAT items until now did not specifically analyze these questions.[8–10]

Given these considerations, we addressed two study questions. First, we considered how the pattern of responses to the single CAT items depended on major COPD characteristics, such as exacerbation risk, mortality risk, and comorbidities. These comorbidities included asthma and emphysema, and chronic cardiac disease and osteoporosis, as important components of the pulmorbidome and comorbidome, respectively.[11] Differences in the pattern of responses could potentially be of particular interest to the general practitioner in terms of a pre-test probability assessment of comorbidities in which no single biomarker or criterion is available or indicative. Even slight hints from this simple, well-established questionnaire might help to make decisions on specific but costly diagnostic approaches. The second question was whether the pattern of responses to the single items depended on smoking status, potentially suggesting stratification of the analysis according to this status. To answer the two questions, we used data from the COPD cohort COSYCONET (COPD and Systemic Consequences – Comorbidities Network)[12] that is capable of providing comprehensive, high-quality data. By using the approach as described above we hope to increase the potential of the CAT to provide clinically useful information via a more differentiated analysis of its results.

Materials and Methods

Study Population

Patients from the German observational multi-center cohort COSYCONET were included. This cohort includes patients with post-bronchodilatation spirometric COPD grades 1 to 4 according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD),[13,14] as well as patients with the former GOLD grade 0,[15,16] ie, individuals with chronic bronchitis not fulfilling the spirometric criterion of forced expiratory volume in 1 sec (FEV_1) to forced vital capacity (FVC) ratio <0.7. This latter subgroup of patients is termed "preserved ratio impaired spirometry" (PRISm), which may precede COPD.[16,17] Inclusion and exclusion criteria, study protocol, and assessments performed at each study visit have been described elsewhere.[12] The present analysis was based on data from the recruitment visit, with the determination of mortality using follow-up data over a period of 6 years. The study was approved by the ethics committees of all participating study centers and was performed according to the Declaration of Helsinki. All participants gave their written informed consent. ClinicalTrials.gov NCT01245933.

Assessments

In addition to CAT (Supplemental Table S1), we used the modified Medical Research Council (mMRC) dyspnea score[18] for the categorization of patients into GOLD groups A/B/E,[14] with exacerbation risk evaluated as proposed by GOLD and utilized in previous analyses of COSYCONET data.[5,19–21] Accordingly, patients with at least two moderate or one severe exacerbation were allocated to GOLD group E. Comorbidities were assessed from patients' reports of physician-based diagnoses, and lung function was determined according to current recommendations,[13,14] comprising forced expiratory volume in 1 sec (FEV_1), forced vital capacity (FVC), and FEV_1/FVC.[22,23] In addition, diffusing capacity for carbon monoxide was determined from single-breath maneuvers and quantified in terms of transfer factor (TLCO)

and transfer coefficient (KCO),[24] while functional residual capacity (FRC) was measured by body plethysmography.[22,25,26] The 6-min walk distance (6MWD) was assessed following a standard protocol[12] and expressed relative to reference values.[27] Chest computed tomography (CT) scans that had previously been evaluated for the presence of lung emphysema[4,6,28] were available in 316 of the patients. This information was used to check the adequacy of a predefined reduction of KCO as indicator of lung emphysema. Patients were stratified in accordance to their cigarette smoking habit: current smokers vs not-current smokers, the latter group consisting of ex- and never-smokers. Packyears were calculated in standard manner.

Statistical Analysis

Data are presented as means and standard deviations (SD) or numbers and percentages. Regression analyses included the eight single CAT items as predictors or the CAT total score divided by 8 to achieve the same scale as for the single items, and thus comparability of regression coefficients. The relationship between mortality and predictors was determined by Cox proportional hazard regression analysis and that regarding the other binary outcomes by multiple logistic regression analyses. Therefore, receiver operating characteristics (ROC) has been applied, and the chosen cut-off value of KCO of 55% predicted, as potential indicator of lung emphysema, was compared with the optimal cut-off value (Youden criterion) in a subsample of patients with a CT-based emphysema diagnosis, which was again 55% predicted (AUC, 0.781; 95% CI: 0.730, 0.832). Thus, GOLD group E, KCO < 55% pred, presence of asthma, coronary artery disease (CAD) or heart failure (HF), and osteoporosis were all used as dichotomous variables. Statistical significance was assumed for $p<0.05$. All analyses were performed using SPSS Version 29 (IBM Corporation, Armonk, NJ, USA).

Results

Study Population

Of the 2741 enrolled patients, 2509 had full data on GOLD groups, spirometric lung function, diffusing capacity, the comorbidities asthma, cardiac diseases and osteoporosis, and smoking status. Among these, 625 were current smokers (282 female, 343 male) and 1884 were non-smokers (724 female, 1160 male), among them 1682 ex-smokers and 202 never-smokers. The clinical characteristics of the two groups are given in Table 1. There were significant differences regarding the distribution of sex, age, body-mass index (BMI), FEV_1 and FVC % predicted, the ratio FEV_1/FVC, FRC %

Table 1 Patient Characteristics of the Two Groups. The Table Shows Numbers (Percentages), Means (Standard Deviations), or Medians (Quartiles). Comparisons Between Groups Were Performed with Fisher's Exact Test, Chi-Square Statistics, the Unpaired *t*-Test, or the Mann–Whitney *U*-Test (for CAT), as Appropriate

Variable	Non Smokers	Current Smokers	p value
n	1884	625	–
Sex (m/f)	1160/724 (61.6/38.4%)	343/282 (54.9/45.1%)	0.003
Age (years)	66.1 ± 8.5	61.6 ± 7.9	<0.001
BMI (kg/m^2)	27.4 ± 5.2	26.3 ± 5.6	<0.001
Pack-years	50.8 ± 41.6	42.8 ± 23.5	0.002
FEV_1 % predicted	57.2 ± 21.0	60.1 ± 19.8	0.003
FVC % predicted	78.8 ± 18.7	81.6 ± 18.2	<0.001
FEV_1/FVC	0.554 ± 0.139	0.569 ± 0.127	0.017
FEV_1/FVC Z-score	−2.51 ± 1.50	−2.52 ± 1.35	0.823
FRC % predicted	141.3 ± 37.6	147.9 ± 33.1	<0.001

(*Continued*)

Table 1 (Continued).

Variable	Non Smokers	Current Smokers	p value
TLCO % predicted	59.9 ± 23.3	59.0 ± 20.5	0.065
KCO % predicted	68.4 ± 24.7	61.6 ± 20.8	<0.001
6MWD % predicted	66.5 ± 16.5	66.7 ± 16.2	0.867
GOLD 0/1/2/3/4	16.2/7.3/35.1/33.1/8.3%	14.9/9.6/42.1/28.6/4.8%	<0.001
PRISm	147 (7.8%)	35 (5.6%)	0.075
GOLD A/B/E	39.8/24.7/35.5%	48.3/21.1/30.6%	<0.001
Asthma	362 (19.2%)	91 (14.6%)	0.008
KCO<55 % predicted	598 (31.7%)	231 (37.0%)	0.018
CAD and/or HF	360 (19.1%)	109 (17.4%)	0.375
Osteoporosis	289 (15.3%)	79 (12.6%)	0.103
Mortality within 6 years	181 (9.6%)	58 (9.3%)	0.875
CAT total score	17.0 (12.0, 23.0)	18.0 (13.0, 23.0)	0.211
CAT 1	2.0 (1.0, 3.0)	3.0 (2.0, 3.0)	<0.001
CAT 2	2.0 (1.0, 3.0)	3.0 (2.0, 3.0)	<0.001
CAT 3	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.595
CAT 4	4.0 (3.0, 5.0)	4.0 (3.0, 4.0)	<0.001
CAT 5	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	<0.001
CAT 6	0.0 (0.0, 2.0)	0.0 (0.0, 1.0)	0.002
CAT 7	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.407
CAT 8	3.0 (2.0, 3.0)	2.0 (3.0, 3.0)	0.143

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity; FRC, functional residual capacity; TLCO, transfer factor for carbon monoxide; KCO, transfer coefficient for carbon monoxide; 6MWD, 6-minute walk distance; GOLD, Global Initiative for Chronic Obstructive Lung Disease; PRISm, preserved ratio impaired spirometry; CAD, coronary artery disease; HF, heart failure; CAT, COPD Assessment Test.

predicted, TLCO % predicted, KCO % predicted, GOLD grades 0–4, GOLD groups ABE, the prevalence of asthma and reduced KCO ($p<0.05$ each). In current smokers, the male/female ratio was lower, spirometric obstruction was less severe, but diffusing capacity in terms of the transfer coefficient more reduced, while the number of pack-years was smaller and the duration of smoking longer, indicating a lower intensity of smoking.[5] Moreover, CAT items 1, 2, 4, 5 and 6 differed significantly between the two groups ($p\leq0.002$ each), but the CAT total score did not. There was no difference between the two groups in the proportion dying over the follow-up period (9.6 and 9.3% in non-smokers and smokers, respectively).

Analysis of the Single CAT Items and Total Score

The regression coefficients for the relationships between CAT (total score and individual items) and the clinical parameters are illustrated in Figure 1 and summarized in Supplemental Table S2.

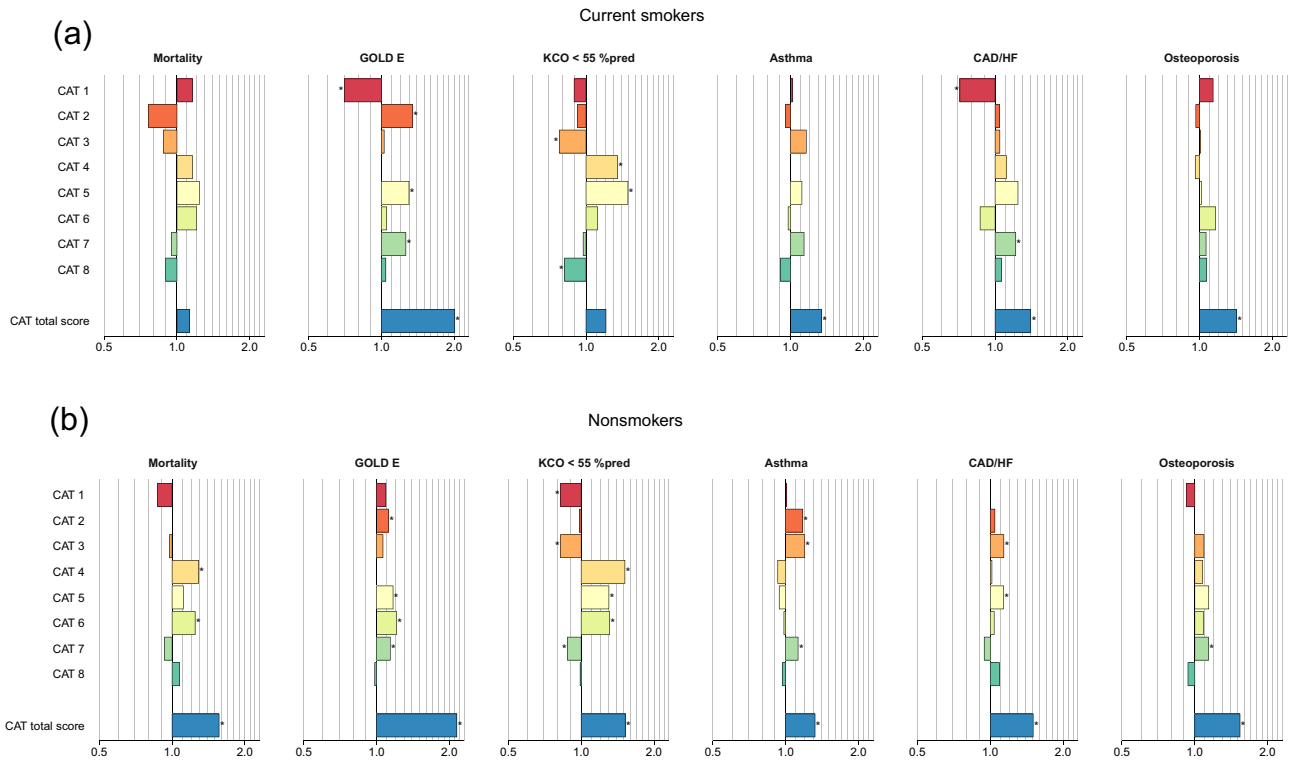

Figure 1 Odds ratios and their 95% confidence intervals for the relationships between CAT (total score and individual items) and the different outcome measures from multiple Cox or logistic regression analyses, as well as for the total score. The upper line of graphs (**a**) refers to the group of current smokers, the lower (**b**) to the nonsmokers. To achieve comparable scales and regression coefficients between the single items and the total score, the total score was divided by 8. Supporting data are in Supplemental Table S2.
Abbreviations: GOLD, Global Initiative for Chronic Obstructive Lung Disease; KCO, transfer coefficient of the lung for carbon monoxide; CAD, coronary artery disease; HF, heart failure.

Mortality Risk

In nonsmokers, CAT items 4 and 6 were significantly associated with subsequent mortality, as was the total score ($p<0.01$ each), while in current smokers there were no significant associations.

Exacerbation Risk (GOLD E)

In nonsmokers, CAT items 2, 5, 6 and 7 were positively linked to subsequent exacerbation risk, as was the total score ($p<0.05$ each). In current smokers, in addition to the total score, CAT items 2, 5 and 7 were positively associated with exacerbation risk ($p<0.05$ each). In addition, CAT item 1 (cough) was negatively associated with subsequent exacerbation risk in current smokers ($p=0.006$).

Emphysema, as Indicated by Transfer Coefficient (KCO) <55% Predicted

In nonsmokers, CAT items 1, 3 and 7 were negatively associated with presence of emphysema; items 4, 5, 6 and the total score had a positive association ($p<0.01$ each). In smokers, CAT items 3 and 8 were negatively associated with emphysema, with items 4 and 5 positively associated. There was no correlation between CAT total score and emphysema in current smokers.

Asthma

In nonsmokers, the comorbidity asthma was positively associated with CAT items 2, 3 and 7 and the total score ($p<0.05$ each). In current smokers, only the total score was positively associated with asthma ($p<0.05$ each), and none of the single items.

Cardiac Disease (Coronary Artery Disease and/or Heart Failure)

In nonsmokers, cardiac disease was positively associated with CAT items 3 and 5 and the total score ($p<0.05$). In current smokers, CAT item 1 was negatively associated with cardiac disease; item 7 and the total score were positively associated ($p<0.05$ each).

Osteoporosis

In nonsmokers, osteoporosis was positively associated with CAT item 7 and the total score ($p<0.05$ each). In current smokers, only the total score ($p=0.012$) was linked to this outcome, with a positive association.

Discussion

In the present work, answers to the eight single items of the CAT questionnaire in patients with COPD differed in their relationship to several clinical outcome variables, as well as between current smokers and nonsmokers. Previous analyses have shown that the single CAT items carry different information regarding specific characteristics of COPD, but these were obtained in different subsets of data.[4,7] In contrast, the current analyses were performed in the same set of data using similar methods, thereby ensuring the comparability of results. We also compared the single CAT items with the total score, which is commonly used in studies and clinical practice.

The total score was significantly associated with mortality and KCO (as a marker of emphysema) only in nonsmokers. In smokers, the KCO data highlight the importance of the single items, since although a number showed a strong, statistically significant correlation with baseline KCO, the total score did not due to opposite changes in individual items cancelling when summed. In contrast, the total score correlated with exacerbation risk (in terms of GOLD E), asthma, cardiac comorbidities in both smokers and non-smokers, with the size of the odds ratios similar, and with most individual items trending in the same direction as the total score. Taken together, the findings suggest that acute effects of smoking that vary between subjects can obscure the relationship between symptoms and functional alterations, which is consistent with the observation of rapid-onset changes after smoking cessation[29] and the interindividual variability in xenobiotic metabolism.[30]

Smokers with COPD were overall younger, with a higher proportion female, and a lower smoking history (in pack-years) than nonsmokers.[5] Importantly, the analysis of the single items of the CAT demonstrated a number of differences between the two groups. It seems reasonable that smokers had higher scores in cough and phlegm, while their lower scores in dyspnea, home activity and confidence leaving home indicated, on average, their better clinical state compared to nonsmokers, although most differences were small compared with the range of possible score values.

In clinical practice and in scientific studies, the CAT total score is typically used to quantify the impact of COPD on a patient's clinical state, and to assess improvements due to therapeutic interventions.[1,2,31] It has also been introduced into the recommendations for therapy by GOLD,[13,14] as an alternative to the mMRC.[32] We found the CAT total score to be relevant as indicator of exacerbation risk in both nonsmokers and smokers, with the individual CAT items regarding phlegm, confidence home activity, leaving home and sleep disturbance significantly associated with this risk in both groups, with the item regarding confidence leaving home was associated with exacerbation risk only in nonsmokers. Although the CAT was not specifically developed as a tool for the assessment of exacerbation risk, our data suggest that the total score could be used for this. In smokers, there was a negative association between the cough item and exacerbation risk, possibly due the fact that active smokers may be more likely to cough on a regular basis regardless of overall exacerbation risk.

Regarding asthma, cardiac diseases and osteoporosis, the odds ratios for the relationship with the CAT total score were similar in smokers and nonsmokers. It seems reasonable that the single items phlegm, chest tightness, and sleep disturbance were relevant only in nonsmokers with comorbid asthma, given these three symptoms might be affected by acute irritation in current smokers. A finding that seems more difficult to explain was the negative relationship between cough and cardiac disease in smokers which might be due to a selection effect reflected in a better overall health status of smokers.[5]

An important phenotype of COPD is that of lung emphysema[14] for which we used a reduction in KCO as a proxy as we did not have CT scans in the cohort to confirm the diagnosis. However, routine CT scans were obtained prior to

inclusion in a subgroup of patients,[33] verifying the validity of the chosen cut-off value of 55% predicted. The KCO data showed two aspects: First, cough and chest tightness were inversely related to this indicator particularly in nonsmokers, while emphysema was positively associated with dyspnea and limitation in home activity in both groups, and with confidence leaving home in nonsmokers. As a result of the opposite directions of these associations, some of the item scores mitigated or cancelled the correlation with the total score. Of note, in nonsmokers the odds ratio for dyspnea (item 4) was as high as that for the total score comprising all eight questions.

In contrast to the other endpoints, which were evaluated on a cross-sectional basis, mortality was evaluated over the 6-year follow-up period so far achieved in COSYCONET. Again, differences were apparent between the importance of single items, and between nonsmokers and smokers. In current smokers, as a result of associations with opposite sign, the total score was not significant as a predictor of mortality. In contrast, mortality was significantly associated with the total score in nonsmokers, as were the individual items dyspnea and confidence leaving home. We cannot exclude the possibility that the relatively low numbers of deceased patients decreased the statistical power, but it is unlikely that this explains the difference between these two groups in the total score. Of note, the proportion of patients dying did not differ between nonsmokers and smokers.

A limitation of the analyses is that, with the exception of mortality, the data are cross-sectional, do not allow for causal inferences. Moreover, they were obtained in a single population, which, however, in all respects was similar to typical COPD populations described in other studies. In addition, the analyses use mean data, so provide information about the performance of CAT at a group level, rather than individual patients. It was, however, our objective to describe the associations between the CAT items and various characteristics of COPD that are of clinical interest. As we did not have sufficient information on the presence of emphysema from chest CT scans, we relied on a surrogate marker, KCO, although this was validated in a subset of patients with CT scans. Finally, the presence of comorbidities was based on patients' reports of physicians' diagnoses, although all previous analyses of the COSYCONET data set that depended on these data yielded plausible and consistent results. In the total population of patients, the results were similar to those obtained for the (current) nonsmokers who provided the largest group of participants; we thus omitted these data. In addition, it turned out to be non-informative to summarize the CAT items into groups, such as 1–4 ("respiratory") versus 5–8 ("non-respiratory"),[8] as can already be seen by inspection of the contributions of the single items in Figure 1.

Conclusions

Our observations suggest that it is worthwhile to consider the CAT single items when using this questionnaire in clinical practice. The reason was that the single items showed different contributions to different clinical outcomes. These outcomes comprised mortality and exacerbation risk, as well as the comorbidities asthma, cardiac disease and osteoporosis, together with a surrogate marker of lung emphysema. The predictive value of the CAT was highest regarding mortality and exacerbation risk in nonsmokers. Only for exacerbation risk, current smokers showed a similarly strong relationship between the CAT and its single items as nonsmokers, while for the other outcomes the associations were weaker or absent. These findings might be of value in order to extract as much information as possible from a questionnaire that is well known and in widespread use.

Data Sharing Statement

COSYCONET is an ongoing, long-term, multi-center observational study the data of which are not intended to be available without demand. If there is interest in the analysis of specific questions, however, there is a formalized procedure for submitting an application to the study office (Competence Network on Asthma and COPD, Philipps-University Marburg, Baldingerstrasse 1, 35043 Marburg), which will be evaluated by the steering committee on scientific grounds. There is no limitation for this application except proven expertise in COPD studies.

Ethics Approval and Consent to Participate

The study protocol was approved by the central ethical committee in Marburg (Ethikkommission FB Medizin Marburg) and the respective local ethical committees: Bad Reichenhall (Ethikkommission Bayerische Landesärztekammer); Berlin

(Ethikkommission Ärztekammer Berlin); Bochum (Ethikkommission Medizinische Fakultät der RUB); Borstel (Ethikkommission Universität Lübeck); Coswig (Ethikkommission TU Dresden); Donaustauf (Ethikkommission Universitätsklinikum Regensburg); Essen (Ethikkommission Medizinische Fakultät Duisburg-Essen); Gießen (Ethikkommission Fachbereich Medizin); Greifswald (Ethikkommission Universitätsmedizin Greifswald); Großhansdorf (Ethikkommission Ärztekammer Schleswig-Holstein); Hamburg (Ethikkommission Ärztekammer Hamburg); MHH Hannover/Coppenbrügge (MHH Ethikkommission); Heidelberg Thorax/Uniklinik (Ethikkommission Universität Heidelberg); Homburg (Ethikkommission Saarbrücken); Immenhausen (Ethikkommission Landesärztekammer Hessen); Kiel (Ethikkommission Christian-Albrechts-Universität zu Kiel); Leipzig (Ethikkommission Universität Leipzig); Löwenstein (Ethikkommission Landesärztekammer Baden-Württemberg); Mainz (Ethikkommission Landesärztekammer Rheinland-Pfalz); München LMU/Gauting (Ethikkommission Klinikum Universität München); Nürnberg (Ethikkommission Friedrich-Alexander-Universität Erlangen Nürnberg); Rostock (Ethikkommission Universität Rostock); Berchtesgadener Land (Ethikkommission Land Salzburg); Schmallenberg (Ethikkommission Ärztekammer Westfalen-Lippe); Solingen (Ethikkommission Universität Witten-Herdecke); Ulm (Ethikkommission Universität Ulm); Würzburg (Ethikkommission Universität Würzburg). The study was performed in accordance with the declaration of Helsinki, and all participants gave their written informed consent.

Acknowledgments

We are grateful to all COSYCONET study centers, especially to all study nurses, for their excellent and enduring work in data collection, as well as to all patients who were willing to participate in this study over an extended period of time. We also thank David Young for helpful comments on the manuscript.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

COSYCONET is supported by the German Federal Ministry of Education and Research (BMBF) Competence Network Asthma and COPD (ASCONET) and performed in collaboration with the German Center for Lung Research (DZL). The project is funded by the BMBF with grant number 01 GI 0881, and by DZL with grant-number 82DZLI05B2. It is furthermore supported by unrestricted grants from AstraZeneca GmbH, Bayer Schering Pharma AG, Boehringer Ingelheim Pharma GmbH & Co. KG, Chiesi GmbH, GlaxoSmithKline, Grifols Deutschland GmbH, MSD Sharp & Dohme GmbH, Mundipharma GmbH, Novartis Deutschland GmbH, Pfizer Pharma GmbH, Takeda Pharma Vertrieb GmbH & Co. KG, Teva GmbH for patient investigations and laboratory measurements. For the present study, an additional grant for data management was given by Novartis Pharma GmbH. The funding body had no involvement in the design of the study, or the collection, analysis or interpretation of the data.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD assessment test. *Eur Respir J*. 2009;34(3):648–654. doi:10.1183/09031936.00102509
2. Karloh M, Fleig Mayer A, Maurici R, Pizzichini MMM, Jones PW, Pizzichini E. The COPD assessment test: what do we know so far?: A systematic review and meta-analysis about clinical outcomes prediction and classification of patients into GOLD stages. *Chest*. 2016;149(2):413–425. doi:10.1378/chest.15-1752
3. Tomaszewski EL, Atkinson MJ, Janson C, et al. Chronic airways assessment test: psychometric properties in patients with asthma and/or COPD. *Respir Res*. 2023;24(1):106. doi:10.1186/s12931-023-02394-6

4. Marietta von Siemens S, Alter P, Lutter JI, et al. CAT score single item analysis in patients with COPD: results from COSYCONET. *Respir Med*. 2019;159:105810. doi:10.1016/j.rmed.2019.105810
5. Alter P, Stoleriu C, Kahnert K, et al. Characteristics of current smokers versus former smokers with COPD and their associations with smoking cessation within 4.5 years: results from COSYCONET. *Int J Chronic Obstr*. 2023;18:2911–2923. doi:10.2147/Copd.S436669
6. Kellerer C, Jorres RA, Schneider A, et al. Prediction of lung emphysema in COPD by spirometry and clinical symptoms: results from COSYCONET. *Respir Res*. 2021;22(1):242. doi:10.1186/s12931-021-01837-2
7. Trudzinski FC, Kellerer C, Jorres RA, et al. Gender-specific differences in COPD symptoms and their impact for the diagnosis of cardiac comorbidities. *Clin Res Cardiol*. 2023;112(2):177–186. doi:10.1007/s00392-021-01915-x
8. Houben-Wilke S, Janssen DJA, Franssen FME, Vanfleteren L, Wouters EFM, Spruit MA. Contribution of individual COPD assessment test (CAT) items to CAT total score and effects of pulmonary rehabilitation on CAT scores. *Health Qual Life Outcomes*. 2018;16(1):205. doi:10.1186/s12955-018-1034-4
9. Miyazaki M, Nakamura H, Chubachi S, et al. Analysis of comorbid factors that increase the COPD assessment test scores. *Respir Res*. 2014;15(1):13. doi:10.1186/1465-9921-15-13
10. Raghavan N, Lam YM, Webb KA, et al. Components of the COPD Assessment Test (CAT) associated with a diagnosis of COPD in a random population sample. *COPD*. 2012;9(2):175–183. doi:10.3109/15412555.2011.650802
11. Trudzinski FC, Jorres RA, Alter P, et al. Sex-specific associations of comorbidome and pulmorbidome with mortality in chronic obstructive pulmonary disease: results from COSYCONET. *Sci Rep*. 2022;12(1):8790. doi:10.1038/s41598-022-12828-8
12. Karch A, Vogelmeier C, Welte T, et al. The German COPD cohort COSYCONET: aims, methods and descriptive analysis of the study population at baseline. *Respir Med*. 2016;114:27–37. doi:10.1016/j.rmed.2016.03.008
13. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med*. 2017;195(5):557–582. doi:10.1164/rccm.201701-0218PP
14. Agusti A, Celli BR, Criner GJ, et al. Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. *Am J Respir Crit Care Med*. 2023;207(7):819–837. doi:10.1164/rccm.202301-0106PP
15. Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS, Committee GS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: national heart, lung, and blood institute and world health organization global initiative for chronic obstructive lung disease (GOLD): executive summary. *Respir Care*. 2001;46(8):798–825.
16. Wan ES, Fortis S, Regan EA, et al. Longitudinal phenotypes and mortality in preserved ratio impaired spirometry in the COPDGene study. *Am J Respir Crit Care Med*. 2018;198(11):1397–1405. doi:10.1164/rccm.201804-0663OC
17. Han MK, Agusti A, Celli BR, et al. From GOLD 0 to Pre-COPD. *Am J Respir Crit Care Med*. 2021;203(4):414–423. doi:10.1164/rccm.202008-3328PP
18. Fletcher CM. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the aetiology of chronic bronchitis (MRC breathlessness score). *BMJ*. 1960;2:1662.
19. Trudzinski FC, Kahnert K, Vogelmeier CF, et al. Combined effects of lung function, blood gases and kidney function on the exacerbation risk in stable COPD: results from the COSYCONET cohort. *Respir Med*. 2019;154:18–26. doi:10.1016/j.rmed.2019.06.007
20. Alter P, Lucke T, Watz H, et al. Cardiovascular predictors of mortality and exacerbations in patients with COPD. *Sci Rep*. 2022;12(1):21882. doi:10.1038/s41598-022-25938-0
21. Alter P, Kahnert K, Trudzinski FC, et al. Disease progression and age as factors underlying multimorbidity in patients with COPD: results from COSYCONET. *Int J Chron Obstruct Pulmon Dis*. 2022;17:1703–1713. doi:10.2147/COPD.S364812
22. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report working party standardization of lung function tests, European community for steel and coal. official statement of the European respiratory society. *Eur Respir J Suppl*. 1993;16:5–40. doi:10.1183/09041950.005s1693
23. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J*. 2012;40(6):1324–1343. doi:10.1183/09031936.00080312
24. Stanojevic S, Graham BL, Cooper BG, et al. Official ERS technical standards: global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians. *Eur Respir J*. 2017;50(3):1700010. doi:10.1183/13993003.00010-2017
25. Criee CP, Sorichter S, Smith HJ, et al. Body plethysmography--its principles and clinical use. *Respir Med*. 2011;105(7):959–971. doi:10.1016/j.rmed.2011.02.006
26. Criee CP, Baur X, Berdel D, et al. [Standardization of spirometry: 2015 update. Published by German Atemwegsliga, German respiratory society and German society of occupational and environmental medicine]. *Pneumologie*. 2015;69(3):147–164. Leitlinie zur Spirometrie. Leitlinie der Deutschen Atemwegsliga, der Deutschen Gesellschaft fur Pneumologie und Beatmungsmedizin und der Deutschen Gesellschaft fur Arbeitsmedizin und Umweltmedizin zur Spirometrie. doi:10.1055/s-0034-1391345
27. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. *Eur Respir J*. 1999;14(2):270–274. doi:10.1034/j.1399-3003.1999.14b06.x
28. Kahnert K, Andreas S, Kellerer C, et al. Reduced decline of lung diffusing capacity in COPD patients with diabetes and metformin treatment. *Sci Rep*. 2022;12(1):1435. doi:10.1038/s41598-022-05276-x
29. Pezzuto A, Ricci A, D'Ascanio M, et al. Short-term benefits of smoking cessation improve respiratory function and metabolism in smokers. *Int J Chron Obstruct Pulmon Dis*. 2023;18:2861–2865. doi:10.2147/copd.S423148
30. Pezzuto A, Lionetto L, Ricci A, Simmaco M, Borro M. Inter-individual variation in CYP2A6 activity and chronic obstructive pulmonary disease in smokers: perspectives for an early predictive marker. *Biochim Biophys Acta Mol Basis Dis*. 2021;1867(1):165990. doi:10.1016/j.bbadis.2020.165990
31. Jones PW, Tabberer M, Chen WH. Creating scenarios of the impact of COPD and their relationship to COPD assessment test (CAT) scores. *BMC Pulm Med*. 2011;11:42. doi:10.1186/1471-2466-11-42
32. Pisi R, Aiello M, Calzetta L, et al. The COPD assessment test and the modified medical research council scale are not equivalent when related to the maximal exercise capacity in COPD patients. *Pulmonology*. 2023;29(3):194–199. doi:10.1016/j.pulmoe.2021.06.001
33. Kahnert K, Jobst B, Biertz F, et al. Relationship of spirometric, body plethysmographic, and diffusing capacity parameters to emphysema scores derived from CT scans. *Chron Respir Dis*. 2019;16:1479972318775423. doi:10.1177/1479972318775423