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EXPERT REVIEWS

Health status during hospitalisations for chronic obstructive pulmonary disease exacerbations: the validity of the Clinical COPD Questionnaire

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Hospitalisations for chronic obstructive pulmonary disease (COPD) exacerbations are characterised by a significant worsening of the respiratory symptoms which can impair the health status (HS). However little is known on the HS behaviour during such events. Prospective study evaluating the validity of the Clinical COPD Questionnaire (CCQ) as a HS measure in hospitalisations for COPD exacerbations. The CCQ total score (CCQ-T) correlated with EQ-VAS (-0.51, $p < 0.0001$), was able to discriminate between longer and shorter duration hospitalisation (CCQ-T 3.83 vs 3.03, respectively $p = 0.001$), had a Cronbach-α of 0.86, and improved significantly over the hospitalisation period (CCQ-T on day 7 of hospitalisation 2.55 vs 3.77 at baseline, $p < 0.0001$). CCQ is an excellent tool for the assessment of the HS dynamics in hospitalisations for COPD exacerbations.

Keywords: chronic obstructive pulmonary disease • Clinical COPD Questionnaire • exacerbations • health-related quality of life • hospitalizations for COPD exacerbations • questionnaires • respiratory • symptoms

Chronic obstructive pulmonary disease (COPD) is a prevalent chronic inflammatory disease of the lungs, which is mainly related to smoking [1]. It is characterized by progressive respiratory symptoms such as dyspnea, cough and sputum production, and by accelerated lung function decline [1].

The severity of such symptoms and that of the lung function impairment can increase on a transitory basis during disease exacerbations. Such events be of variable severity, and while the mild and moderate COPD exacerbations can be treated at primary care level or at the emergency department, the severe exacerbations usually require hospitalization. In practice, the clinical severity of COPD exacerbations is often assessed by clinical investigations and by the opinion of the clinician. Formal measurements of symptoms and disability as perceived by the patient have been reported but did not reach widespread clinical use. As in stable COPD, measurement of health status during exacerbations by properly developed questionnaires might be of pivotal importance to measure both the individual and the group impact of such events and would allow the quantification of their perceived severity [2–4].

Several questionnaires such as the Saint George Respiratory Questionnaire and the Chronic Respiratory Disease Questionnaire have been used in various settings such as pharmacological interventions, rehabilitation or advanced COPD [5,6]. However, such questionnaires are recommended in stable COPD for research purposes but are difficult to use in clinical practice due to their length and complexity. Given this focus on stable COPD and the existing paradigms of health status assessment in this disease, there is a certain degree of reticence in applying such tools during COPD exacerbations. Recently, the GOLD committee recommended the use of one of the

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Table 1. Baseline characteristics of the patients hospitalized with a diagnosis of exacerbated chronic obstructive pulmonary disease.

Characteristic	Value
Mean age (years; SD) 80	67.03 (10.12)
Gender 80	F = 18 M = 62
Smoking status (%) 80 Ex-smokers Nonsmokers Smokers	 45 (56.2) 17 (21.2) 18 (22.5)
BMI, mean (kg/m^2, SD) 64	24.85 (4.63)
Known COPD diagnosis, mean (years, SD) 23	11.23 (9.52)
WHO-5 score mean (SD) 80	19.55 (20.24)
EQ-VAS baseline score mean (SD) 80	27.91 (25.18)
BDI score mean (SD) 79	3.26 (2.67)
CCQ-S baseline score (SD) 80	3.60 (1.27)
CCQ-F baseline score, mean (SD) 80	3.50 (1.34)
(SD) CCQ-M baseline score, mean 80	3.60 (1.63)
CCQ-T baseline score, mean (SD) 80	3.57 (1.08)

BDI: Baseline dyspnea index; CCQ-F: Clinical COPD questionnaire-functional; CCQ-M: Clinical COPD questionnaire-mental; CCQ-S: Clinical COPD questionnaire-symptoms; CCQ-T: Clinical COPD questionnaire-total; COPD: Chronic obstructive pulmonary disease; EQ-VAS: Visual analogue scale of the EuroQOL-5D questionnaire; WHO-5: Well-being index.

three measures (Clinical COPD Questionnaire [CCQ], COPD Assessment Test or Medical Research Council-modified dyspnea scale) as patient reported outcome tools to assess the impact of the disease COPD on patients [1,3]. Although formal measurement of health status during an exacerbation is currently not recommended because of the lack of supportive clinical data, and is therefore avoided, it is probably wise to explore the validity of these instruments in an exacerbation in clinical practice. We therefore validated one out of the three recommended questionnaires, namely, the CCQ, during severe exacerbations requiring hospitalization [7,8].

Methods

This was a prospective study performed between March and November 2008 in the Pulmonary Disease University Hospital in Iasi, Romania. Patients with an admission diagnosis of exacerbated COPD (clinical diagnosis) and who consented to participate were included in the study. Those excluded were patients who refused to participate, were too ill to complete the questionnaires, had other respiratory acute or chronic diseases as the reason for referral, were illiterate or had altered consciousness/mental status.

Questionnaires & scales

EuroQol-5, the Baseline Dyspnea Index/Transitional Dyspnea Index (BDI/TDI), the WHO Five Well-Being Index (WHO-5) and the CCQ were used [9–13]. The EuroQoL-5 is a generic 5-item questionnaire, which also has a visual analogue scale (VAS) included in the tool's structure. EuroQoL-5D has been used in patients with different chronic diseases, including COPD [12]. In COPD, visual analogue scale of the EuroQOL-5D questionnaire (EQ-VAS) was found to correlate well with disease severity [12]. EuroQol-5 was administered at baseline (within the first 24 h of admission) and on the seventh day of hospitalization.

WHO-5, a five-item scale that was initially developed as a 10-item scale to screen depression in patients with diabetes was subsequently reduced to the current five-item scale and was validated as such in various languages and settings, including elderly people [9,10,14]. In our study, it was administered within the first 24 h of hospital admission.

Dyspnea, which is the dominant respiratory symptom in COPD in both, the stable and the exacerbated state, was evaluated with BDI/TDI [13]. This tool was chosen because it allows the evaluation of the improvement in dyspnea in a reliable manner and because the minimal clinically important difference is known and equals 1 unit of score [11].

CCQ is a 10-item disease-specific questionnaire with three domain (symptom, mental and functional) scores and a total score. This questionnaire has two versions, a 24-h version and a 7-day version, and was validated in patients with stable COPD [15]. Its MCID was calculated to 0.4 [16].

CCQ questionnaire was administered within first 24 h of admission (baseline) after further 24 h and at the seventh day of hospitalization if applicable.

Statistical analysis

MedCalc version 12 was used for data analysis. Concurrent validity was evaluated with correlations (Pearson's) among baseline CCQ scores and the scores of other questionnaires or scales used. Intraclass Correlation Coefficient of the CCQ was calculated in order to assess test–retest reliability. Questionnaire responsiveness was evaluated by calculating the improvements (and their 95% CIs) of CCQ individual and total scores on the seventh day of hospitalization. Internal consistency (Cronbach's α) was also evaluated. Divergent validity of the clinical COPD questionnaire-total (CCQ-T) was evaluated against the oxygen saturation measured on the nail bed (SpO2) at the time of admission. Discriminant validity was measured using an indirect measure of disease severity, that is, the hospitalization duration. Therefore, we compared the baseline domain scores and the total score in patients with early hospital discharge (EHD, hospitalization duration $\leq$7 day) compared with patients with late hospital discharge (LHD, hospitalization duration >7 days).

Results

Data sets from 80 patients admitted to the hospital for an exacerbation of COPD were included in the analysis. Baseline characteristics are presented in Table 1.

Table 2. Concurrent validity for baseline clinical chronic obstructive pulmonary disease questionnaire domain and total scores.

Scores of the comparator scales	CCQ-symptoms scores (significance level)	CCQ-functional scores (significance level)	CCQ-mental scores (significance level)	CCQ-total scores (significance level)
WHO-5	-0.52 (p < 0.0001)	-0.56 (p < 0.0001)	-0.41 (p = 0.002)	-0.65 (p < 0.0001)
EQ-VAS	-0.32 (p = 0.005)	-0.54 (p < 0.0001)	-0.29 (p = 0.01)	-0.51 (p < 0.0001)
BDI	-0.37 (p = 0.0008)	-0.78 (p < 0.0001)	-0.30 (p = 0.006)	-0.64 (p < 0.0001)

BDI: Baseline dyspnea index; CCQ: Clinical COPD Questionnaire; EQ-VAS: Visual Analogue Scale of the EuroQoL-5D Questionnaire; WHO-5: Well-being index.

Convergent validity

Baseline CCQ domain scores and the total score were found to correlate significantly with those of the other validated scales such as Euro-VAS score, with WHO-5 and with BDI (Table 2).

Divergent validity

The divergent validity of the baseline CCQ-T score was evaluated with data available for 54 patients, and there was no relation between the CCQ-T and SpO2: r = -0.09 (p = 0.48).

Repeatability

Intraclass correlation coefficients of the domain scores and of the total score are presented in the Table 3.

Reliability

Cronbach's α was 0.7 for clinical COPD questionnaire-symptoms (CCQ-S), 0.62 for clinical COPD questionnaire-mental (CCQ-M), 0.90 for clinical COPD questionnaire-functional (CCQ-F) and 0.86 for CCQ-T.

Responsiveness

All CCQ domains and the total score decreased at the seventh day of hospitalization and this behavior reflected an improvement of health status exceeding the minimal clinically important difference (Table 4).

Discriminant validity

We found that baseline CCQ-S, CCQ-F and CCQ-T scores differed significantly between the predefined subsets of patients, that is, patients with LHD, respectively, with EHD: CCQ-S 3.89 in LHD versus 3 in EHD, p = 0.03, CCQ-F 3.75 in LHD versus 2.99 in EHD, p = 0.02, CCQ-T 3.83 versus 3.03 in LHD, p = 0.001.

Discussion

In this study, we assessed the validity of the CCQ to measure health status during an exacerbation of COPD that required hospitalization. We found that this questionnaire was a valid measure of health status in such a setting. Most importantly, we demonstrated that CCQ was responsive to change, and that it was able to discriminate among various stages of exacerbation severity giving at day 1 of hospital admission an indication of possible early discharge. We compared the performance of the CCQ with that of a generic questionnaire (EQ-VAS), which was chosen because the VAS component was reported to be a valid measure of disease severity in stable COPD [12]. We hypothesized that, the EQ-VAS could be used in exacerbations and especially in severe ones that require hospitalization as it was previously found to be an appropriate measure of health status in patients with exacerbated COPD [17]. In our study, EQ-VAS was found to correlate well with the CCQ-T and the CCQ-F. WHO-5 was administered to assess the mood status CCQ-M, as well as based on the fact that depression was previously found to be associated with a high risk of hospitalizations for COPD exacerbations [18]. It did not correlate too strongly with this domain score probably because of the fact that the latter assesses the mood status in closer relation with the underlying disease; on the other hand, it did correlate well with CCQ-T. A symptom scale (BDI/TDI) was used as a comparison for CCQ-S, but surprisingly, the BDI did not correlate so strongly with this domain score. We explain this by the fact that CCQ-S also assesses the impact of other respiratory

Table 3. Intraclass correlation coefficients.

CCQ domain	Intraclass correlation coefficient for single measures (95% CI)	Intraclass correlation coefficient for average measures (95% CI)	Intraclass correlation coefficients in the original validating study [15]
CCQ-S	0.94 (0.90–0.96)	0.97 (0.94–0.97)	
CCQ-F	0.93 (0.90–0.96)	0.97 (0.95–0.98)	
CCQ-M	0.88 (0.81–0.92)	0.93 9 (0.9–0.96)	
CCQ-T	0.95 (0.92–0.97)	0.97 (0.96–0.98)	0.94

CCQ-F: Clinical COPD Questionnaire-functional; CCQ-M: Clinical COPD Questionnaire-mental; CCQ-S: Clinical COPD Questionnaire-symptoms; CCQ-T: Clinical COPD Questionnaire-total; COPD: Chronic obstructive pulmonary disease.

Table 4. Responsiveness.

CCQ	Baseline measurement (mean value)	Seventh day measurement (mean value)	p-value for the difference
CCQ-S	3.82	2.18	$p < 0.0001$
CCQ-F	3.73	2.71	$p < 0.0001$
CCQ-M	3.73	2.83	$p < 0.0001$
CCQ-T	3.77	2.55	$p < 0.0001$

CCQ-F: Clinical COPD Questionnaire-functional; CCQ-M: Clinical COPD Questionnaire-mental; CCQ-S: Clinical COPD Questionnaire-symptoms; CCQ-T: Clinical COPD Questionnaire-total; COPD: Chronic obstructive pulmonary disease.

symptoms such as cough or sputum production and that BDI/TDI also assesses the interference between dyspnea and daily functioning. In support of this, latter statement is the fact that in our study actually BDI correlated better with CCQ-F. BDI/TDI was previously evaluated in exacerbated COPD, and in the subsequent recovery period was found to be responsive to the acute symptoms change during exacerbations [19].

In this study, CCQ-T score was found to correlate well with all three comparison measures used, as discussed above. Furthermore, there was no correlation between CCQ-T and physiological variables such as SpO2. This finding is concordant with those reported in previous studies performed in patients with stable COPD and in which the quality of life scores did not correlate with other objective measures such as the forced expiratory volume in 1 s [20]. In our study, we did not consider forced expiratory volume in 1 s as an appropriate objective comparison item given its variability during the disease exacerbation.

In the original validating study, the discriminant validity was evaluated in the stable disease in relationship to the smoking cessation intervention, and it was found that the scores of the abstinent patients were significantly better compared with previous scores reported while still smoking [15]. In our study, which was performed in patients with severe exacerbated COPD, we considered that the most plausible way to assess this discriminative ability was to use a measure of disease severity, and the easiest way was to compare baseline CCQ scores in patients with early discharge versus late discharge. This approach was appropriate since the domain assessing the symptoms and functional status, as well as the total score at baseline were significantly worse in patients who were hospitalized for a longer period of time.

Our study found that the internal consistency was very good for each domain score and the highest for the CCQ-F domain. This means that in patients with COPD exacerbations in general and with COPD hospitalizations in particular, the functional status impairment can be evaluated with this domain.

As well as this, other questionnaires were assessed in the setting of COPD exacerbations: the short-form Chronic Respiratory Disease Questionnaire and the Saint George Respiratory Questionnaire were also found to have psychometric properties that make them suitable to assess COPD exacerbations requiring visit to the emergency department [21]. More recently, the COPD Assessment Test was used to monitor the severity of exacerbations, but the analysis of the subsequent-related recovery was hampered by the absence of a formal MCID [22]. However, a specific analysis in COPD hospitalizations was not performed in each of the mentioned studies; this is not the case of our analysis, which was performed only in such population.

Overall, CCQ was found to be a reliable measure to assess the severity of health status impairment during hospitalization for COPD exacerbation and it might be very helpful in documenting the patient perception on the severity of the acute episode.

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Key issues

- In stable chronic obstructive pulmonary disorder (COPD), health status is often evaluated as a measure of patient-perceived disease severity.
- However, health status assessment is not widely accepted for COPD exacerbations and especially for hospitalizations.
- The Clinical COPD Questionnaire is a health status tool that is recommended to be used in patients with stable COPD in secondary as well as in primary care.
- It was also evaluated in milder COPD exacerbations and found to be a valid instrument.
- In this study it was also found to be appropriate for severe COPD exacerbations requiring hospitalizations.
- Health status should be commonly used in the setting of COPD exacerbations in order to better document their severity.

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