

Correlation of CAT, CCQ and mMRC Scores in Patients of COPD with Exacerbation and after Treatment

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD), a globally prevalent disease holds a huge stake among all pulmonary patients being admitted throughout the year. Various disease specific and health related quality of life questionnaires such as the Constructed Response Question (CRQ) and St. George's Respiratory Questionnaire (SGRQ) are readily available, although, attributing to their complex structure, they can't be used in a widespread manner. Some new scores like COPD Assessment Test (CAT), Clinical COPD Questionnaire (CCQ) were developed to ease-off this dilemma. However, there is a need to justify usage of these patient-friendly simplified scores by objectifying their inter-score reliability and correlation with disease severity and progression using statistical analysis.

Aim: To analyse efficacious use of CAT, CCQ score and modified Medical Research Council (mMRC) scale in assessing health status of COPD with exacerbation. Additionally, it was also targeted to assess the inter-score correlation and reliability.

Materials and Methods: A total of 180 confirmed cases of COPD with exacerbation were included in this study and subjected to requisite biochemical parameters, assessment scores at their admission, after 1 week and then after 4-6 week (at stabilisation)

and spirometry. 136 patients were followed-up to 4-6 weeks and studied. Quantitative and qualitative variables thus obtained were compared statistically to find out correlation, if any. A p-value of <0.05 was considered significant.

Results: Mean difference between CAT score at exacerbation and at 1 week and CAT score at exacerbation and at 4-6 weeks were statistically significant. The changes in CCQ scores from exacerbation to 1 week and 6 weeks were also found to be statistically significant. Similar pattern was also observed in assessing timescale variability of mMRC score. There was good correlation between CAT, CCQ and mMRC scores at exacerbation, 1 week and it continually intensified as patients progressed towards a more stable state (4-6 weeks). Similar pattern was also observed with significant progressive positive correlation between change in CAT, CCQ and mMRC scores from exacerbation to 1 week and from exacerbation to 4-6 weeks.

Conclusion: These score have a high correlative reliability when used to assess health status among various stages of disease from exacerbation towards a stable state. Similarly, correlation between change of individual score from exacerbation towards recovery state was also high.

Keywords: COPD assessment test, Clinical COPD questionnaire, Forced expiratory volume, Global initiative for chronic obstructive lung disease, Modified medical research council scale, St. George's respiratory questionnaire

INTRODUCTION

The COPD is characterised by a persistent and progressive limitation of airflow in the airways resulting from an increased inflammatory response to noxious particles or gases [1]. Repeated exacerbations accentuate overall morbidity and mortality.

The global prevalence of physiologically defined COPD in adults aged >40 years is approximately 9-10% [2]. A recent study [3] suggested that in India, the overall prevalence of chronic bronchitis in adults >35 years is 3.49%. Based on this study, the national burden has estimated as 14.84 million [3]. Recently, updated Global initiative for chronic Obstructive Lung Disease (GOLD) guidelines 2017, divides patients diagnosed with COPD into categories based on annual number of exacerbations, mMRC score and health status as assessed with the CAT [4]. The grading of airflow limitation is not included in the new ABCD categorisation.

Some most comprehensive disease specific and health related quality of life questionnaires such as the CRQ [5] and SGRQ [6] are too complex to use in routine practice. Later, two shorter questionnaire CAT and CCQ have been developed. CAT is a questionnaire made of eight components which can be easily self-administered by the patient and it aids in assessing the COPD severity and its effect on daily activities (quality of life) [7]. CCQ benefits are from comprising only ten items that makes it particularly

suitable for routine use to measure clinical health status [7]. These scores have the advantage of simplicity over other questionnaires and both have very good correlation with the SGRQ [6-8], which is considered as GOLD standard of all questionnaires. However, their usefulness to assess the clinical course of exacerbations has not been investigated adequately. mMRC scale, which measures the severity of breathlessness, cannot be equivalent to questionnaires related to quality of life. The use of mMRC is still widespread due to early applicability and correlates with clinical parameters and FEV1. The great majority of patients with an SGRQ of 25 or more will have an mMRC of 2 or more, hence it can still be considered an effective tool for assessing health status in COPD patients [9].

Therefore, this study was designed with an aim to assess the course of health status and change in quality of life during exacerbation in patients with COPD and after stabilisation up to 6 weeks, using CAT score, CCQ score and mMRC grading.

MATERIALS AND METHODS

This institutional based, observational prospective study was undertaken in Department of Medicine, Maulana Azad Medical College, Lok Nayak hospital, New Delhi.

Inclusion criteria: The diagnosed cases of COPD patients who presented in acute exacerbation i.e., acute worsening of respiratory symptoms that results in dire need of additional therapy as per

GOLD Guideline, to the Medicine Emergency as well in Outpatient Department of the institute were included in this study.

The study data was compiled over duration of 6-8 months in the year 2013-14. Index study was conducted after prior approval no F.11/IEC/MAMC/2013-14/53 of Institution Ethics Committee Maulana Azad Medical College.

The sample size was calculated using standard formula: $n = Z^2 P (1-P) / d^2$ (Where, n =sample size, z =z statistic for the level of confidence, P =expected prevalence of COPD i.e., 9% [2] and d =allowable error). The study projected a 95% confidence level with $\pm 5\%$ allowable error, for the study. The sample size needed was ~140 but, taking into consideration forthcoming losses in participants' number; a total of 180 patients of COPD were enrolled in the study.

Informed consent was taken from all the patients. All the patients were subjected to complete history and physical examination and particulars of the patients such as name, age, sex, pack years of smoking, duration of COPD (if previously diagnosed), medications being used, number and frequency of past ICU/In-patient admissions, treatment compliance, etc., were noted in a pre-structured proforma and a compiled data extended excel-sheet was made.

A series of basic biochemical investigations and cx-ray, ECG were carried out. Body mass index was calculated. Spirometry test was performed after stabilisation.

CAT [7] and CCQ questionnaires [8] were filled-up within 48 hours of admission, after 1 week and at 4-6 weeks. mMRC grading was done based on patient's symptoms at admission, 1 week and after 4-6 weeks.

Exclusion criteria: Patients who were having some pre-existing non-respiratory illnesses such as anaemia, cardiac illness, chronic kidney disease and chronic liver disease were excluded from this study. Patients having previously diagnosed respiratory entities such as pneumonia, diffuse bronchiectasis, and interstitial lung disease were also excluded.

Of the 180 Inpatient COPD patients enrolled in the study, 21 patients died due to the severity of their illness during in-hospital stay; 23 patients were lost to follow-up as they never visited centre again once discharged [Table/Fig-1]. Thus, 136 patients were followed-up to 4-6 weeks and the change in CAT, CCQ and mMRC scores were analysed.

Smoking habits*	Frequency (%)	Gender distribution (N=180)			
		Male		Female	
		N	%	N	%
Bidi smokers	133 (74%)	141	78.3	39	21.6
Cigarette smokers	23 (13%)	23		--	
Chullah/Biomass fuel	37 (21%)	14		23	
No smoking/exposure	07 (4%)	02		05	
During study period (from admission to 6 weeks) (effective, N=136)					
Number of patients lost follow-up		23			
Number of patients died		21			

[Table/Fig-1]: Gender distribution and Smoking habits in the study group.

STATISTICAL ANALYSIS

The absolute frequencies and percentages were used to describe the quantitative variables. Furthermore, cumulative frequencies and percentages were used for ordinal qualitative variables. The description of quantitative variables was performed using the mean, standard deviation, median and quartiles. The correlation between quantitative variables was performed using the Spearman's correlation coefficient. A p -value of <0.05 was considered significant. The Pearson's correlation coefficient (r) has the values starting from -1 to 1. The relationship between two variables is strong when value are >0.7 .

RESULTS

The mean age of the index study group was 59.68 years (range: 32-82 years). The mean age of males was 58.61 years and the females was 63.05 years. 78% of the COPD patients were male as shown in [Table/Fig-1]. Out of 180 patients, majority had exposure to bidi smoke. Some of the patients were smokers as well having exposure to chullah/biomass fuel combustion.

The mean \pm SD values of CAT, CCQ and mMRC scores at admission, after 1 week and after stabilisation (at 4-6 weeks) was calculated as shown in [Table/Fig-2]. These scores were calculated taking into account only the effective number of participating patients at subsequent point of time respectively i.e., at admission, 1 week and 4-6 week.

Parameters	CAT score	CCQ score	mMRC score
Mean \pm SD (at admission)	36.11 \pm 2.766	5.1657 \pm .60054	3.84 \pm .368
Mean \pm SD (at 1 week)	20.91 \pm 5.532	2.9856 \pm 0.80330	2.89 \pm 0.507
Mean \pm SD after stabilisation (at 4-6 weeks)	10.36 \pm 7.488	1.5579 \pm 0.92365	1.97 \pm 0.748

[Table/Fig-2]: CAT, CCQ and mMRC scores at admission, at 1 week and at stable COPD (4-6 weeks).
SD: Standard deviation; CAT: COPD Assessment test; CCQ: Clinical COPD Questionnaire; mMRC: modified Medical Research Council

The respective changes of CAT, CCQ and mMRC scores from admission to 1 week and from admission to 4-6 weeks were calculated along with the estimation of statistical significance, as shown in [Table/Fig-3].

Change in CAT score from admission to 1 week Mean \pm SD Sig. (2- tailed)	Change in CAT score from admission to 4-6 weeks Mean \pm SD Sig. (2- tailed)
14.91 \pm 4.935 ($p \leq 0.001$)	25.58 \pm 8.012 ($p \leq 0.05$)
Change in CCQ score from admission to 1 week	Change in CCQ score from admission to 4-6 weeks
2.15 \pm 0.723 ($p \leq 0.001$)	3.46 \pm 1.06 ($p \leq 0.05$)
Change in mMRC grade from admission to 1 week	Change in mMRC grade from admission to 4-6 weeks
0.93 \pm 0.469 ($p \leq 0.001$)	1.83 \pm 0.719 ($p \leq 0.05$)

[Table/Fig-3]: Change in CAT Scores, CCQ Scores and mMRC grading at 1st week and 4-6 weeks of follow-up.
SD: Standard deviation; CAT: COPD Assessment Test; CCQ: Clinical COPD Questionnaire (CCQ); mMRC: modified Medical Research Council

Correlations coefficient among CAT, CCQ and mMRC scores showed that correlation increases as the COPD patients improved towards a stable state (6 weeks) compared with at admission and 1 week. Correlations among change in CAT, CCQ and mMRC scores from admission to 1 week and after stabilisation (6 weeks) showed that correlation increased as the COPD patients improved to stable state compared with admission and at 1 week, respectively [Table/Fig-4].

Analysis of CAT score showed that the variation in the CAT score between exacerbation onset and recovery was not dependent on the score at exacerbation (p -value 0.629). However, there was good correlation between variation in the CCQ score from exacerbation to stabilisation with score at exacerbation (p -value of <0.001) and weak correlation between variation in the mMRC score from exacerbation to stabilisation with score at exacerbation (p -value of <0.05).

DISCUSSION

The study conducted, is one of its kind using longitudinal comparison of CAT, CCQ and mMRC scores in Indian COPD population. The authors compared the data majorly with studies conducted previously using similar parameters and methodology. The mean age of index study group was lower compared to similar studies done by Miravittles M et al., and by Lee S et al., [10,11]. In this

Scores	At the time of admission			1 st week			4 th -6 th week		
	CAT score	CCQ score	mMRC score	CAT score	CCQ score	mMRC score	CAT score	CCQ score	mMRC score
CAT score	-	0.555	0.467		0.768	0.462	-	0.875	0.774
CCQ score	0.555	-	0.564	0.768	-	0.467	0.875	-	0.78
mMRC score	0.467	0.564		0.462	0.467	-	0.774	0.78	-
Correlations among change in CAT, CCQ and mMRC scores from admission to 1 week and exacerbation to stabilisation.									
Correlation coefficient (Sig. 2- tailed)	Exacerbation to 1 st week			Exacerbation to stabilisation (6 th week)					
	CAT score	CCQ score	mMRC score	CAT score	CCQ score	mMRC score			
ΔCAT score		0.756	0.422	-	0.737		0.746		
ΔCCQ score	0.756	-	0.513	0.737		0.638			
ΔmMRC score	0.422	0.513	-	0.746	0.638	-			

[Table/Fig-4]: Correlations coefficient(r) among CAT, CCQ and mMRC score.
 CAT: COPD Assessment Test; CCQ: Clinical COPD Questionnaire (CCQ); mMRC: modified Medical Research Council

study, major stake is male participants (78%) attributing to prevalent smoking habit compared to females, as described in previous studies done by Miravittles M et al., and Jindal SK [10,12]. However, worldwide the pattern of smoking and tobacco consumption is changing as evidenced by increasing COPD prevalence among females, in various epidemiological data [13-16].

Mean BMI calculated in index study was 24.79 kg/m². Demographic data including BMI thus included, it being an independent negative determinant of COPD survival, as advocated by Chailleux E et al., and Yang L et al., [17,18]. In this study, majority of the participants were smokers (bidi, cigarette or household/occupational biomass fuel exposure) similar to study conducted by Jindal SK et al., [19].

A statistically significant change of mean CAT score at exacerbation, at 1 week and after 6 weeks was found in the index study; advocating its high predictability in assessing health status. Mean CAT score in stable COPD was much lower than in exacerbation as shown by Jones PW et al., and Agusti A et al., [20,21]. An epidemiological, prospective, multicentre study by Miravittles M et al., included 476 COPD patients with a CAT score of 22.8 points in their inpatients, which was significantly reduced to 12.4 after recovery from the acute episode [10]. The difference between CCQ score at exacerbation and at 1st week and between CCQ score at exacerbation and at 4th-6th week (after stabilisation) were found to be statistically significant.

This suggests that CCQ score is a good predictor of health status, as there was significant reduction of CCQ score after recovery at 1 week and after stabilisation at 4-6 weeks. In a study done by Miravittles M et al., in Spain, statistically significant improvement in the CCQ score from exacerbation to recovery was observed [10]. In a multicentre prospective cohort study with 121 patients done by Trappenburg JC et al., change in CCQ total scores were significantly higher during exacerbation, 3.5±0.69 compared to -0.4±0.37 in stable state (p<0.001) [22]. The mean change in CCQ-total score was decreased significantly after stabilisation (Δ-CCQ-score: -2.6, 95% CI: -4.3 to -0.9, p=0.001).

In the index study, the difference between mMRC score from exacerbation and at 1 week was 0.93±0.469 (p<0.001) and between exacerbation and at 4-6 weeks was 1.83±0.719 (p<0.05). To the best of our knowledge, the study is the first of its kind in assessing the course of health status of COPD patients from exacerbation to recovery using mMRC score. Some previous studies disregarded the frequent usage of mMRC scale in COPD classification as a surrogate to CAT score, attributing its capability of assessing only one parameter i.e., breathlessness [9,23]. However, results showed mMRC scale in good correlation with exacerbation as a well stable state.

At exacerbation, a good correlation was found between CAT and CCQ scores and CAT and mMRC scores, respectively. Similarly, correlation between CCQ and mMRC scores at exacerbation also found to be significant. There was strong correlation between CAT

and CCQ score at 1 week and at 4-6 weeks. Correlation between CAT and mMRC at 1 week was weak (p<0.001) while at 4-6 weeks was positive [Table/Fig-3,4]. Correlation between CCQ and mMRC score at 1 week was significant whereas it was much stronger at 4-6 weeks.

These results suggested that both CAT and CCQ are measuring similar factors and can be used reliably and interchangeably in this context. Though mMRC measures only breathlessness, shortness of breath is the most frequent symptom reported by patients with long lasting COPD. The presence of dyspnoea significantly reduces the quality of life, leads to inability to work in a productive manner. So, the study can use mMRC as a preliminary aid to assess the health status and clinical course in all COPD patients.

As far as CAT and CCQ are concerned, the study showed similar results with the studies done by Miravittles M et al., in Spain and by Ringbaek T et al., [10,24].

In a study done by Kim S et al., the classification of COPD on the basis of mMRC or CAT score was not identical [25]. The mMRC score is the most strongly correlated with dyspnea item of CAT. However, this study supported the use of this score in predictive analysis of COPD.

There was a good correlation between change in CAT and change in CCQ scores from exacerbation to 1 week and from exacerbation to 4-6 weeks (r=0.756 and 0.737, respectively; p<0.001). A significant correlation was observed between change in CAT and change in mMRC scores from exacerbation to 1 week and from exacerbation to 4-6 weeks (r=0.422 and 0.746, respectively; p<0.001). Correlation between change in CCQ and change in mMRC scores from exacerbation to 1 week and from exacerbation to 4-6 weeks were also significant (r=0.513 and 0.638, respectively; p<0.001 for both).

Similar study conducted by Miravittles M et al., found an acceptable correlation between the change (exacerbation-recovery) scores in both questionnaires (R=0.594; p<0.0001) [10].

Spirometric assessment was also done in the index study once the admitted patients attained a comfortable state varied from Day 3 to Day 5 to perform the test. The severity of COPD stage reported in spirometry (using FEV1 as per GOLD parameters) correlated neither with the CAT, CCQ and mMRC scores neither at admission nor with the course of recovery of the patients from exacerbation to stabilisation. This result was consistent with the study done by Jones PW et al., [23]. They illustrated that, within any given COPD category as per GOLD staging, patients may have anything between relatively well preserved to very poor health status.

In the index study, it was seen that a worse score at exacerbation onset leads to a significant improvement in CAT and CCQ after recovery in terms of absolute figures. Findings of the study conducted by Miravittles M et al., defied this study's findings probably because they enrolled both inpatients and out patients in their study but in this study only inpatients were enrolled which were having more debilitating condition [10].

Limitation(s)

Sample size of the study was in accordance with the global as well local prevalence [2,3]. However, the patients included here were of the same race; COPD patients of different races may have different outcomes. All the comparative scores have an in-built subjective component within, landing in result variability. In the index study and its statistical analysis, confounding factors as comorbidities like CAD which may have a negative impact on disease outcome were not ruled out completely. Lastly, the data thus obtained might be biased by the single medical-centre-based patients rather than population based patient inclusion.

CONCLUSION(S)

Comprehensive questionnaires such as CAT and CCQ are much detailed and suitable for prediction of outcome of acute exacerbation of COPD. Additionally, they also have advantage of simplicity for the patient. Use of mMRC scale which measures the severity of breathlessness is still widespread because of easy applicability. Therefore CAT, CCQ and mMRC scores can be used interchangeably as better objective scales, attributing to their inter-equality and reliability.

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