Original Article

PREDICTORS OF QUALITY OF LIFE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH DIFFERENT FREQUENCY OF EXACERBATIONS

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ABSTRACT

Objective: The health related quality of life (HRQL) is influenced by exacerbation of chronic obstructive pulmonary disease (COPD) and physiological factors can alter heath status. The aims of this study were to evaluate the consequences of exacerbation on HRQL and to examine the predictive factors associated with HRQL.

Methodology: One hundred and eighty eight patients were recruited from respiratory clinics of two hospitals. We used St. George's Respiratory Questionnaire (SGRQ) to assess health status. Hand dynamometer was used to measure muscle strength and vitalograph spirometer to measure lung function. Body mass index (BMI) was also calculated. Dyspnoea status was measured with baseline dyspnoea index (BDI) and Medical Research Council (MRC) grades.

Results: The SGRQ total and component scores were significantly worse in the group that had frequent exacerbation. Age and hand grip strength were the most significant predictors of HRQL scores in stable and unstable group. BDI is significant only for stable and MRC for unstable patients.

Conclusion: The present study illustrates that COPD patients with high exacerbations have lower health status than stable COPD patients.

KEY WORDS: Chronic obstructive pulmonary disease, Exacerbations, Quality of Life.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is characterized by reduced maximal expiratory flow and slow forced emptying of the lungs; features that do not change markedly over several months.[1] COPD is a frequent cause of morbidity and disability.[2]

In patients with COPD, an acute worsening of respiratory symptoms is often described as an exacerbation. Along with the physical deterioration, exacerbations have a major impact on patients' feelings of well-being and health-related quality of life (HRQL).[3] Furthermore, an increased number of past exacerbations is one of the best predictors for the risk of future recurrent exacerbation[4] and also the decline in health status.[5] The effect of exacerbations on HRQL and the long term impact of exacerbations has only been assessed in two previous studies[5,6] but did not explain the effect of physi-

ological factors such as body mass index (BMI) and hand grip strength on HRQL in COPD patients with exacerbations and in order to improve health status in COPD, it is very crucial to identify factors that are essentially associated with HRQL in patients with COPD.

The aims of this study were to examine the effect of exacerbation on HRQL and the role of factors that could predict health status in patients with COPD exacerbations. This research has also examined the impact of disease on HRQL in follow up visits scheduled 5-6 months apart.

PATIENTS AND METHODS

From June 2004 to July 2006, we recruited patients with clinical diagnosis of COPD who were attending outpatient respiratory clinics of participating centres in the region of North-east of England. Inclusion criteria were chronic airflow impairment confirmed by spirometry and according to the GOLD criteria, not have any upper limb disability that could alter the hand grip measurements and no history of stroke or dementia. The ethical approval was gained from all relevant institutional ethical committees and written informed consent was obtained from all study participants.

To compare and explore association between exacerbation and health status, we categorized our data into groups. The group of patients who had > 3 exacerbation in last six months, categorized as unstable group (with more frequent exacerbations) whereas patients with ≤ 3 exacerbations as stable group (with less frequent exacerbations).

Patients in an unstable phase were identified by the attending physician during the scheduled follow up visits. The follow up visits were rescheduled at the time of enrolment. We measured body weight and standing height to calculate body mass index (BMI). Muscle strength was measured by using hand dynamometer and lung functions by dry spirometer (Vitalograph) according to ATS criteria.[7] The St. George's Respiratory Questionnaire (SGRQ) was completed by all study participants.

The SGRQ is a standardized questionnaire designed to be completed without assistance.[8,9] It measures health status and perceived well-being in persons with obstructive airway diseases. It contains 50 items (76 levels) divided into three sections: "Symptoms" deals with the frequency and severity of respiratory manifestations, "activity" relates to activities that cause or are limited by breathlessness, and "impact" covers aspects of social function and psychosocial disturbances that result from respiratory diseases. Scores on the SGRQ range from 0 (no disturbance of HRQL) to 100 (worst HRQL).

Dyspnoea was assessed by using Mahler' Dyspnoea Indices (MDI) and Medical Research Council Scale (MRC). The MDI consists of two parts. The BDI that rated the severity of dyspnoea at a single state and was filled at initial visit and a transition dyspnoea index (TDI) that denoted changes from baseline and was filled on follow-up by the researcher. The scores in both indices depend on ratings for three different categories: functional impairment; magnitude of task, and magnitude of effort. At the baseline state, dyspnoea was rated in five grades from 0 (severe) to 4 (unimpaired) for each category. The ratings for each of the three categories were added to form a baseline focal score (range, 0 to 12). At the transition period, changes in dyspnoea were rated by seven grades, ranging from -3 (major deterioration), to +3 (major improvement). The ratings for each of the three categories were added to form a transition focal score (range, -9 to +9).[10] The usefulness of MRC scale in COPD patients was documented by Bestall et al.[11] that MRC dyspnea Scale showed a significant relationship to exercise performance, being independent of lung function data. The scores ranges from 1 to 5. Patients with MRC grade 5 represents maximum disability due to shortness of breath. The follow up visits were scheduled in clinics after six months. All research protocols were same as of initial visit except BDI which was replaced by TDI in follow up visits.

The difference between groups were tested using unpaired t test and X^2 depending on the nature of variables. The Spearman correlation coefficient (r) was calculated to assess the association between HRQL and clinical and functional variables. Ordinal regression was

used to identify the association of Physiological variables with SGRQ score. Data analyses were performed using the statistical Package for the Social Sciences (SPSS) Version 14.0.

RESULTS

The mean age, height, weight and BMI in overall population was 72.5±8.3, 1.6±0.1, 70.7±18.2 and 26.6±7.1 respectively. The mean pack year history was 40.5±20.3. (Table-I)

The unstable COPD patients with high exacerbations (>3) had significantly lower muscle strength than stable COPD patients (Table-II). Patients with high frequency of exacerbations (>3) had significantly ($p<0.001$) higher symptoms, impacts and activity scores than stable patients (Table-III). The distribution of SGRQ scores in different exacerbation groups are shown in Figure-1.

The predictors for overall population (including all patients with exacerbation (0-5), stable patients (frequency of exacerbation 0-3) and unstable patients (frequency of exacerbation >3) as shown in Table-IV.

For overall population; age, frequency of exacerbation, FEV1/FVCx100, dominant hand grip, dominant hand grip % predicted, BMI, BDI and MRC are the significant predictors for HRQL as assessed by SGRQ. For stable group; age, dominant hand grip % predicted, dominant hand grip and BDI are significant predictors of health related quality of life scores (Symptoms, Activity, impact and total SGRQ scores). For unstable COPD group, all predictors are same as stable group except BDI, which is replaced by MRC.

Changes in HRQL in COPD after Six Months Interval: Patients with frequent exacerbation had a greater change in SGRQ components than infrequent exacerbations, although the improvement was not clinically significant in terms of HRQL. Table-V shows the scores of health related quality of life by means SGRQ and scores in patients with stable and unstable COPD at baseline and follow up indicates that at follow up, difference between two study groups is approximately same as at baseline.

Table-II: Baseline physiological measurements in stable and unstable Patients.

Physiological Measurements	*Stable (n=77)*	*Unstable (n=111)*	
	Mean ± SD	Mean ± SD	p-value
FEV1(L)	1.1 ± 0.5	1.09 ± 0.5	NS
FEV1/ FVCx100	51.0 ± 14.2	53.5 ± 14.0	NS
FEV1 (% Pred)	47.6 ± 22.6	50.3 ± 20.0	NS
Dominant Hand Grip(kg)	27.7 ± 9.5	23.4 ± 9.4	0.002
Total Hand Grip(Kg)	49.5 ± 17.2	42.6 ± 16.2	0.006

Definition of abbreviations: BMI=body mass index; total hand grip=Right hand +left hand grip;NS=not significant; Data presented as mean ± SD; p=<0.05 as assessed by unpaired t test

DISCUSSION

The results of this study confirms that stable patients (less frequent exacerbators) have significantly better HRQL than patients with unstable (frequent exacerbators) COPD. Hand grip strength and age are very effective predictors of HRQL in these patients.

In general, this study demonstrates that HRQL could be explained by the following variables; age, frequency of exacerbations, FEV1(%), hand grip strength (% Pred) and dominant hand grip, BMI, MRC score and BDI dyspnea index. Although the significant level

Table-I: Patient characteristics at baseline for overall study population who completed the follow up.

Variables	*Overall lN=188(100%)*	*Males N= 93(49.4%)*	*Females N= 95(50.6%)*	*stable N= 77(41%)*	*unstable N= 111(51%)*
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Age	72.5 ± 8.3	71.9 ± 8.2	73.1 ± 8.5	73.0 ± 8.7	72.4 ± 8.1
Male/Female	93/95	----	----	43/34	51/56
Height (m)	1.7 ± 0.1	1.7 ± 0.08	1.5 ± 0.1	1.6 ± 0.1	1.6 ± 0.1
Weight(kg)	70.7 ± 18.2	75.3 ± 18.1	66.3 ± 17.3	69.3 ± 17.8	72.0 ± 18.5
BMI(kg/m^2)	26.6 ± 7.1	26.1 ± 6.3	27.1 ± 7.8	26.3 ± 7.2	27.0 ± 7.1
Pack year History	40.5 ± 20.3	40.6 ± 20.5	40.4 ± 20.2	42.5 ± 17.0	48.0 ± 13.7

Table-III: The components of SGRQ and total score in stable and unstable groups.

QOL COMPONENTS	*Stable*	*Unstable*	
	Mean ± SD	Mean ± SD	p-value
SYMPTOMS%	67.5 ± 19.0	82.0 ± 12.3	<0.001
ACTIVITY%	83.2 ± 16.3	90.1 ± 14.0	0.002
IMPACT%	56.0 ± 20.3	67.5 ± 19.0	<0.001
SGRQ%	66.0 ± 16.2	77.02 ± 13.4	<0.001

Definition of abbreviations: QOL=Quality of life; Data presented as mean±SD; p<0.05 by unpaired t test

of these factors were distinguishable when we divided our study groups into frequent (unstable) and infrequent (stable) exacerbators of COPD.

Finally this study reveals that there is no significant difference in terms of improvement in HRQL in COPD patients and the level of improvement were almost same in stable and unstable COPD patients after six months follow up.

To our knowledge, this is the third follow up study to evaluate the effect of exacerbation on health related quality of life using SGRQ as a disease specific questionnaire and first study considered grip strength as a physiological variable and to find its relationship with HRQL in addition to BMI, lung functions and dyspnea indices.

The present study shows that age is an important predictor of HRQL. In support, Ferrer et al. reported that age is independently associated with HRQL.[12] The reason for this similarity would be the wider range of the subjects' age. The age range of Ferrer et al study was 40-69 while the age range of present study was from 47-96 with mean age of 72.5. This age range is substantially wider than that of Ferrer

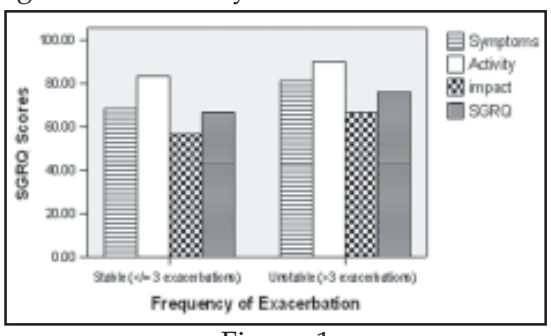

Figure-1

Table-IV: The significant predictors for SGRQ domains in COPD patients

Independent Variables	*Overall (N=188) p value*	*Stable (N=77) p value*	*Unstable (N=111) p value*
Age			
Symptoms	NS	NS	0.03
Activity	NS	NS	NS
Impact	0.001	<0.01	0.02
Total SGRQ	<0.001	0.04	0.002
Frequency of exacerbation			
Symptoms	<0.001	NS	NS
Activity	0.02	NS	NS
Impact	<0.001	NS	NS
Total SGRQ	<0.001	NS	NS
FEV1/FVCx100			
Symptoms	0.04	NS	NS
Activity	NS	NS	NS
Impact	NS	NS	NS
Total SGRQ	0.03	NS	NS
Hand Grip (% Predicted)			
Symptoms	NS	NS	NS
Activity	0.03	NS	0.02
Impact	0.01	NS	0.02
Total SGRQ	0.003	<0.001	0.01
Dominant Hand Grip(kg)			
Symptoms	NS	NS	NS
Activity	NS	NS	0.01
Impact	<0.001	0.05	0.01
Total SGRQ	<0.001	NS	0.002
BMI(kg/m²)			
Symptoms	NS	NS	NS
Activity	NS	NS	NS
Impact	0.01	NS	NS
Total SGRQ	0.02	NS	NS
MRC			
Symptoms	NS	NS	0.01
Activity	NS	NS	0.05
Impact	0.01	NS	NS
Total SGRQ	0.02	NS	NS
BDI			
Symptoms	NS	NS	NS
Activity	0.01	NS	NS
Impact	0.01	0.02	NS
Total SGRQ	0.003	0.005	NS

p<0.05 are significant predictors of HRQL assessed by Regression Analysis

et al and this difference could be a factor which makes our result more promising. The advanced and retired age in our study population seems to be a strong factor known to cause a modified life style regardless of

Table-V: HRQL scores by SGRQ in COPD patients at baseline and follow ups.

HRQL Components %	*Frequent Exacerbations >3/ six months N=111 Mean ± SD*	*Infrequent exacerbations ≤3/ six months N=77Mean ± SD*	*p value*
Baseline Symptoms	81.8 ± 12.3	67.6 ± 18.7	<0.001
Followup Symptoms	80.5 ± 13.7	67.0 ± 18.6	<0.001
Baseline Activity	90.6 ± 13.0	82.6 ± 16.8	<0.001
Followup Activity	88.8 ± 15.1	81.6 ± 16.8	0.003
Baseline Impact	68.0 ± 18.3	55.3 ± 20.5	<0.001
Followup Impact	68.0 ± 18.1	55.2 ± 20.4	<0.001
Baseline SGRQ	77.1 ± 13.0	65.6 ± 16.4	<0.001
Followup SGRQ	76.2 ± 14.0	65.1 ± 16.2	<0.001

SGRQ=St.George's Respiratory Questionnaire; data presented as mean ± SD

whether or not patients suffers from COPD. Smoking status did not appear to play an important role; neither in developing exacerbations nor in improving health status.

In our study population, females showed little bit worse HRQL scores than males but the data was not statistically significant. Our study is supported by few research studies.[13,14] On the other hand, in a recently published data, this has been reported that in moderate to severe COPD patents, there are gender differences in health status scores and also suggested that physiological variables are independently associated with those scores differed in men and women.[15] This contradiction of the report with respect to our study may be due to the difference in the age range of women population which was 56±11 vs 63±8 (men), whereas in our study the age range in males were 72±8.5 and 73±8.2 respectively.

The correlation between lung functions and HRQL has been shown to be weak in a number of studies.[16] The present study also suggests that the relationship is relatively weaker than BDI and MRC. In favour, various clinicians agreed that some clinical treatment in COPD does not affect by improving lung functions but HRQL, therefore improvement in HRQL does not always means improvement in lung functions. For example, newly introduced pulmonary rehabilitation including proper training for breathing methods in COPD, training of extremities, education about COPD have been successful in improving HRQL without having any effect on lung functions. Therefore dyspnoea rating scales such as MRC and Mahler's are now being taken into account in HRQL studies.

Till 2002, studies have documented that generally COPD patients lose weight and become malnourished.[17-19] However, it was unclear whether low body weight is a risk factor for COPD or consequences of established disease or impact of low body weight on HRQL. Another study reported hypercapnia during sleeping in COPD patients with high BMI.[20] Therefore, studies suggest that overweight can have a very lively role in HRQL in COPD patients. This study confirms the association of BMI with HRQL. Therefore body composition should be considered to improve disease progression and should be a part of the possible therapies for improvement of HRQL.

Peripheral weakness is commonly found in patients with COPD. It is suggested that muscle weakness in COPD is due to muscle atrophy and prolong inactivity and muscle deconditioning are the important factors in the loss in muscle mass and muscle strength in COPD.[21] As suggested by the positive relationship between muscle strength and exercise tolerance and by the improvement in QOL occurring after strength training in patients with COPD,[22] muscle weakness may contribute to alter QOL. Previous studies also indicate that muscle mass is commonly decreased in COPD patients[23] and muscle weakness in stable COPD patients does not affect all muscles in similar extent.[24] Another study revealed that hand grip strength is a powerful predictor of cause specific and total mortality.[25] Therefore, assessment of muscle strength measurements should be

included as an essential part of patients' care suffering from COPD. To the best of our knowledge, this study may be unique and new in the aspect that we considered hand grip strength (total hand grip strength, dominant hand grip strength and dominant hand grip strength % pred norms of that age and sex)[26] as a determinant of HRQL in COPD patients. The present study suggested that all aspects of hand grip strength (dominant hand grip and hand grip % pred of age and sex) have significant influence on HRQL. This study shows that hand grip strength is a very powerful predictor of HRQL in stable and unstable groups. Unfortunately no previous studies have considered hand grip strength as a measure of HRQL in these patients. Hence, present study appeared vital as it considered hand grip strength as a predictor of HRQL and results are very promising. Nonetheless more research is needed to evaluate this association which would really be a beneficial with respect to health status in COPD patients.

The severity of dyspnea in COPD patients and its correlation with various pulmonary physiological tests have been published.[27] This study aimed at exploring dyspnoea scores measured with two different clinical rating tools in stable and unstable COPD group and its relationship with quality of life. This study suggests that both MRC and BDI are significant tools which can predicts health status. However their effects are different in two study groups. BDI appeared to be a better predictor of HRQL in stable COPD whereas MRC scores appeared better in unstable patients.

This study also confirms that frequency of exacerbation is inversely proportional to HRQL; health status decreases as frequency of exacerbation increases. However we are able to find the impact of disease on HRQL in follow up visits scheduled within 5-6 months. It shows that patients with high frequency of exacerbations had higher symptoms, impacts and activity scores than stable patients. The present study also suggests that COPD patients with high exacerbations have lower muscle strength than stable patients. It also indicates that patients with stable COPD have low value of SGRQ scores; they have better quality of life than unstable COPD.

In these COPD patients, exacerbations were associated with a long term effect on HRQL. After controlling for baseline characteristics among patients with moderate COPD, those with frequent exacerbation had a greater change in SGRQ components than those with infrequent exacerbation, although the improvement was not clinically significant in terms of HRQL which may lead to a conclusion that 5-6 months duration is not ideal to detect changes in HRQL in COPD patients.

This study supports the hypothesis that the acute negative impact of exacerbations could accumulate overtime and consequently patients experiencing a great number of exacerbations can eventually exhibit a marked deterioration in HRQL.[28] However, time interval probability, which exhibits such deteriorations in health status in patients with frequent exacerbation, has not been mentioned. This may be an objective contradiction as our follow-ups were 5-6 months and this interval between follow-ups may not be adequate to execute any improvement or decline in HRQL. The study shows that frequent and non frequent exacerbators have similar extent of improvement in HRQL which cannot be explained.

This study has encountered certain limitations that need to be mentioned. Firstly, the drop outs. The most important reason was feeling too ill. Consequently, the most ill COPD patients have not been compared with each other. However, since the COPD patients included in this study had a wide range of airway obstruction, we expect the data to be valid for the majority. Secondly, may be the grip strength values which were based on a subjective measure of comorbidity (especially, associated chronic/acute joint diseases). However, these diseases may reflect symptoms rather than physician-diagnosed disease. Despite anything, the data we obtained are expected to be valid for assessing symptoms and grip strength, because in medical science patients are considered to be the best experts in reporting their symptoms. In addition; comorbidities were differently and randomly distributed

among patients which may alter the responses on HRQL questionnaire, COPD perception and the effect of COPD on health status. Consequently it might be concluded that the effect of COPD on HRQL could have been over estimated. The influence of COPD on HRQL independent of comorbidity. Comorbidity contributed significantly to the HRQL in all domains.[29] Furthermore, Doll et al highlights the fact that deterioration of QOL is most strongly associated with reports of both increasing numbers of AECB during the previous year and the presence of environmental air pollution[30] and this study does not consider environmental air pollutants as a determinant of HRQL.

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