Original paper

Chronic Respiratory Disease

Chronic Respiratory Disease
Volume 16: 1–8

DOI: 10.1177/1479972318775422
journals.sagepub.com/home/crd

SAGE

Depression is a major determinant of both disease-specific and generic health-related quality of life in people with severe COPD

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Abstract

The quality of life of patients with chronic obstructive pulmonary disease (COPD) decreases significantly as the disease progresses; those with severe COPD are affected most. This article investigates predictors of the disease-specific and generic health-related quality of life (HRQL) in patients with severe COPD. This multicentre prospective cross-sectional study enrolled 80 patients with severe COPD. At enrolment, all patients completed a disease-specific instrument, the St George's Respiratory Questionnaire (SGRQ), and a generic instrument, the Short Form 36 Health Survey Questionnaire (SF-36). The data were analyzed by Pearson's correlation and multiple linear regression. The mean age of the patients was 66 $\pm$ 8 years; 93% were males. The SGRQ and SF-36 scores were not influenced by age or sex. Depression, dyspnea, the number of exacerbations, and exercise capacity significantly predicted the total SGRQ score ($p < 0.05$). Depression was the strongest determinant of the total SGRQ score. The SF-36 physical component summary scores were related to depression, dyspnea, and the number of exacerbations ($p < 0.05$). In comparison, the SF-36 mental component summary scores were related to depression and anxiety ($p < 0.05$). Depression is a significant determinant of both the disease-specific and generic HRQL in patients with severe COPD. Screening and early intervention for depression in patients with severe COPD could improve the HRQL.

Keywords

Quality of life, chronic obstructive pulmonary disease, depression, dyspnea, severe

Date received: 8 January 2018; accepted: 4 April 2018

Introduction

Noncommunicable diseases (NCDs) including chronic lung disease, heart disease, stroke, cancer, and diabetes kill over 35 million people each year, representing nearly two-thirds of the world's deaths. Chronic obstructive pulmonary disease (COPD) is a major respiratory NCD that is currently the third leading cause of death worldwide.[1] COPD is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic

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inflammatory response in the airways and the lungs. Health-related quality of life (HRQL) is perceived as an important outcome of treatment in subjects with COPD.[2–4]

Recent population-based studies of HRQL found that patients with COPD had worse physical function and mental health compared with the general population.[5–7] Impaired HRQL in patients with COPD is known to be associated with increased dyspnea,[8–10] physical impairment,[10] depression and anxiety,[10,11] readmission,[12] and mortality.[13] As disease progresses, patients with COPD experience increasing deterioration of their HRQL, with greater limitations to their basic daily life activities and declining participation in social activities.[14] In fact, the severity of airflow limitation as an indicator of disease progression, based on post-bronchodilator forced expiratory volume in 1 second (FEV_1) percentage predicted, is considered an important factor influencing HRQL.[15–17] According to Kim et al.,[18] HRQL in COPD patients worsened with the COPD severity measured by FEV_1.

However, little is known about the factors influencing HRQL in patient with severe COPD patients ($FEV_1 < 50\%$),[19] although some literature shows that they have overall symptom burden and a poor HRQL comparable to that of advanced cancer patients.[20–22]

In order to help people with severe COPD cope better with a poor HRQL, the factors that contribute to HRQL need to be identified and understood. HRQL encompass disease-specific aspects and more generic health-related issues.[23] Disease-specific HRQL instruments such as the St George's Respiratory Questionnaire (SGRQ) are designed to assess the health impact associated with a respiratory disease,[24] while generic instruments such as the Short Form 36 Health Survey Questionnaire (SF-36) measure overall health status to compare other population groups.[25]

To the best of our knowledge, this is the first study to investigate factors influencing disease-specific and generic HRQL in an Asian population with severe COPD. Therefore, the aim of the study was to investigate the predictors of disease-specific and generic HRQL in Korean population with severe COPD.

Methods

Subjects and study design

This cross-sectional study was conducted between March 2010 and November 2010. A total of 80 patients with severe COPD (post-bronchodilator $FEV_1 < 50\%$ predicted) were enrolled from the pulmonology outpatient clinics of six institutions in Korea.[19] A diagnosis of COPD was established based on medical history, current symptoms, pulmonary function tests (PFTs), and a post-bronchodilator FEV_1 to forced vital capacity (FVC) ratio (FEV_1/FVC) of < 0.7. Patients with an illness other than COPD that was likely to result in death within 6 months or an inability to perform the PFT and 6-min walk test (6MWT) were excluded; such conditions included myocardial infarction within the preceding 4 months, unstable angina, and congestive heart failure (New York Heart Association class III or IV). Patients considered clinically unstable were also excluded; this was defined as significant changes in medication including treatment with systemic corticosteroid or antibiotics, disease exacerbation, or hospital admissions in the preceding 6 weeks.

General characteristics—including age, sex, cumulative smoking (pack years), education level, monthly income, employment status, marital status, and comorbidities (hypertension, diabetic mellitus, arthritis, osteoporosis, angina, incontinence, gastritis, and other diseases)—were assessed by a questionnaire.

The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all patients.

Clinical and physiological measurements

Body mass index (BMI) was obtained by the following equation: $BMI = weight/height^2$ and was measured before the PFT. The modified Medical Research Council (mMRC) scale, which is the most commonly used validated scale to assess dyspnea in daily living in chronic lung disease, uses the following five-point grading scale[26]: 0 = *Not troubled with breathlessness except with strenuous exercise*; 1 = *Troubled by shortness of breath when hurrying on the level or walking (WK) up a slight hill*; 2 = *Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when WK at own pace on the level*; 3 = *Stops for breath after walking about 100 yards or after a few minutes on the level*; and 4 = *Too breathless to leave the house or breathless when dressing or undressing*.

Acute exacerbations were defined as an unscheduled visit to a health-care provider, an emergency department visit, or hospitalization.

Functional exercise capacity was measured by 6MWT, expressed as an absolute value, as per the American Thoracic Society (ATS) guidelines.[27] The

6MWT was conducted in an enclosed corridor on a measured course 30 m in length, and subjects were instructed to walk from one end to the other, covering as much distance as possible during a 6-min period. Patients were verbally encouraged and allowed to rest if needed, and the time remaining was called out after every elapsed minute. Spirometry was performed according to the ATS/European respiratory society (ERS) recommendations using a standard PFT unit (Sensor Medics Vmax 22; Viasys Healthcare Inc., Conshohocken, Pennsylvania, USA).[28] Physical activity was determined using the self-administered short form 2.0 version of the International Physical Activity Questionnaire (IPAQ).[29] The IPAQ requires respondents to estimate time spent in various levels of physical activity during the previous week. Scores for WK and moderate (MPA) and vigorous (VPA) activities are calculated as durations and frequencies multiplied by known metabolic equivalents per activity (METs/minutes/week); VPA = 8.0 METs; MPA = 4.0 METs; and WK = 3.3 METs. The total physical activity score is an index of the sum of the values reported for VPA, MPA, and WK. An item pertaining to time spent sitting is not included in the total physical activity score.

Anxiety and depression

The Korean version of the Hospital Anxiety and Depression Scale (HADS) was used to evaluate the patients' anxiety and depression status.[30] The HADS consists of 14 items, 7 of which score for anxiety and 7 for depression. The theoretical scores for anxiety and depression on the HADS range from 0 to 21; scores of 0–7 in respective subscales are considered normal, with 8–10 borderline and 11 or over indicating clinical anxiety or depression.

Health-related quality of life

The SGRQ is a disease-specific questionnaire used extensively for patients with COPD and several other chronic pulmonary diseases.[24] The questionnaire consists of 50 items classified into three domains that measure symptom score, activity limitations, and the psychosocial impact of the disease; and scores for each domain and the total score range from 0 to 100, with high scores indicating poor health status. Part I covers patients' recollections of their symptoms over a period of 1 month, to assess their perception of any recent respiratory problems, including with respect to frequency and severity; part II addresses patients' current state and the activity score measures disturbances to daily physical activity that cause or are limited by breathlessness. The total score summarizes the impact of the disease on overall health status. The Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) is the most frequently utilized generic HRQL measure for both patients with COPD and the general population.[25] The SF-36 includes eight health indices: physical functioning, role of physical, bodily pain, general health perceptions, vitality, social functioning, role of emotional, and mental health. The questionnaire has well-documented reliability and validity and provides physical component summary (PCS) and mental component summary (MCS) scores—higher scores indicate a better health status.

Statistical analysis

Data are expressed as frequencies (n, %) for categorical variables and means $\pm$ standard deviation for continuous variables. Pearson's correlation coefficient (r) was used to assess the relationships between physiological and psychosocial factors and HRQL. For the multivariate logistic regression to identify the predictors of disease-specific and generic HRQL in patients with severe COPD, we included variables that were significant in the Pearson's correlation analysis.

The SPSS for Windows software (version 22.0; SPSS Inc., Chicago, Illinois, USA) was used for all calculations. The level of significance was set at $p < 0.05$.

Results

Characteristics of subjects

A total of 80 patients were included in the study; Baseline characteristics of patients with severe COPD are shown in Table 1. The mean age was 66 $\pm$ 8.3 years and 74 (92.5%) were male. On average, patients had a disease duration of 9.3 years, mMRC dyspnea grade of 2.33, and 6MWD of 309 m. The SGRQ (total), SF-36 PCS, and SF-36 MCS scores were 45.1 $\pm$ 17.6, 56.7 $\pm$ 20.7, and 69.5 $\pm$ 18.5, respectively.

The relationships between clinical factors and HRQL

Table 2 shows the Pearson's correlation coefficients between the SGRQ, SF-36, and clinical factors. Being in paid work, increased exercise capacity (6MWD),

Table 1. Baseline characteristics of the patients with severe COPD ($n = 80$).[a]

Characteristic	Value
Sex (male)	74 (92.5%)
Age (years)	66 ($\pm$8.3)
Smoking (pack years)	37.2 ($\pm$28.8)
Education level	
Basic ($\leq$6 years)	23 (28.8%)
Secondary (7–11 years)	29 (36.3%)
Higher ($\geq$12 years)	28 (35%)
Monthly income (US$)	
Very low (<1000)	51 (63.8%)
Low (1000 to <2000)	17 (21.3%)
Middle (2000 to <3000)	1 (1.3%)
High (>3000)	11 (13.8%)
Marital status	
Currently married	67 (83.8%)
Single, divorced, widowed	13 (16.3%)
Employment status (paid work)	68 (85%)
COPD duration (years)	9.3 ($\pm$9.2)
Dyspnea (MMRC scale)	
Grade 0	3 (3.8%)
Grade 1	19 (23.8%)
Grade 2	23 (28.8%)
Grade 3	19 (23.8%)
Grade 4	16 (20%)
6MWD (m)	309 ($\pm$85.7)
Spirometry FEV_1% predicted	37.6 ($\pm$7.3)
Spirometry FEV1/FVC%	45.9 ($\pm$10.8)
BMI (kg/m^2)	21.4 ($\pm$3.3)
Physical activity (MET/minutes/week)	2271.1 ($\pm$3198)
Number of comorbidities	
0	40 (50%)
1	28 (35%)
2	8 (10%)
>=3	4 (5%)
Exacerbations in the past year	
No	52 (65%)
Yes	28 (35%)
HADS-A	3.5 ($\pm$3.9)
HADS-D	6.3 ($\pm$4)
SGRQ (total)	45.1 ($\pm$17.6)
SF-36 (PCS)	56.7 ($\pm$20.7)
SF-36 (MCS)	69.5 ($\pm$18.5)

COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; BMI: body mass index; MET: metabolic equivalent of task; MMRC: Modified Medical Research Council; 6MWD: 6-min walk distance; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; SGRQ: St. George's Respiratory Questionnaire; SF-36: Short Form 36 Health Survey Questionnaire; PCS: physical component summary; MCS: mental component summary; SD: standard deviation.

[a] Data are presented as mean $\pm$ SD or numbers with percentages in parentheses unless otherwise indicated.

and physical activity were related to better disease-specific health status, as indicated by a lower SGRQ (total) score (Pearson's correlation coefficient (r) = -0.263, $r = -0.495$, and $r = -0.300$, respectively). Increased dyspnea, HADS-A, and HADS-D scores were related to poor disease-specific health status ($r = 0.603$, $r = 0.451$, and $r = 0.573$, respectively). Regarding generic physical HRQL, as indicated by SF-36 PCS score, higher education level, being in paid work, increased 6MWD, and physical activity were related to higher SF-36 PCS score, indicating better generic physical health status ($r = 0.249$, $r = 0.266$, $r = 0.422$, and $r = 0.272$, respectively). Similar to SGRQ, increased dyspnea, HADS-A, and HADS-D scores were related to a lower SF-36 PCS score ($r = -0.501$, $r = -0.420$, and $r = -0.589$, respectively). In terms of generic mental HRQL, higher education level, being in paid work, increased 6MWD, and physical activity were related to a higher SF-36 MCS score, indicating better generic mental health status ($r = 0.253$, $r= 0.234$, $r = 0.305$, and $r = 0.233$, respectively). Similar to the SF-36 PCS score, increased dyspnea, HADS-A, and HADS-D scores were related to lower SF-36 MCS score ($r = -0.367$, $r = -0.610$, and $r= -0.678$, respectively). Dyspnea and depression had strong correlations with both the SGRQ total score and SF-36 PCS score in severe COPD patients. Anxiety and depression had strong correlations with SF-36 MCS score.

The significant factors associated with HRQL in patients with severe COPD

We investigated the significant factors influencing the disease-specific and generic HRQL in patients with severe COPD, using multiple linear regression model (Table 3). The multivariate analysis showed that depression, dyspnea, and 6MWD were significant predictors of both SGRQ (model $R^2 = 0.540$) and SF-36 PCS score (model $R^2 = 0.453$). Depression and anxiety were significant predictors of SF-36 MCS score (model $R^2 = 0.474$). Depression was a significant predictor of both disease-specific and generic HRQL in patients with severe COPD.

Discussion

The present study revealed that HRQL in patients with severe COPD was associated with several factors including depression, anxiety, dyspnea, and exercise capacity. In terms of the disease-specific HRQL, the

Table 2. Pearson's correlation between HRQL (SGRQ, SF-36 PCS, and SF-36 MCS) and other clinical variables.[a]

	SGRQ (total)		SF36 (PCS)		SF36 (MCS)	
Variable	*r*	*p* Values	*r*	*p* Values	*r*	*p* Values
Education level		—	0.249	0.025	0.253	0.023
Employment status	−0.263	0.018	0.266	0.017	0.234	0.036
Dyspnea (MMRC)	0.603	< 0.001	−0.501	< 0.001	−0.367	<0.001
6MWD	−0.495	< 0.001	0.422	< 0.001	0.305	0.005
Physical activity	−0.300	0.006	0.272	0.014	0.233	0.037
HADS-A	0.451	< 0.001	−0.420	< 0.001	−0.610	< 0.001
HADS-D	0.573	< 0.001	−0.589	< 0.001	−0.678	< 0.001

MMRC: Modified Medical Research Council; 6MWD: 6-min walk distance; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; SGRQ: St. George's Respiratory Questionnaire; SF-36: Short Form 36 Health Survey Questionnaire; PCS: physical component summary; MCS: mental component summary; HRQL: health-related quality of life; r = Pearson correlation coefficient.

[a]All correlations are statistically significant.

SGRQ is used extensively for patients with chronic pulmonary diseases. Our study found that depression, dyspnea, and exercise capacity were significantly associated with the SGRQ in patients with severe COPD. However, FEV_1 was not correlated with the SGRQ in this population. This is consistent with previous data from the National Emphysema Treatment Trial.[31] In contrast, according to Hajiro et al., FEV_1 significantly influenced SGRQ in patients with severe COPD.[15] Sundh et al.[32] also found that a lower FEV_1% predicted was related to a lower HRQL in severe COPD patients as assessed by COPD Assessment Test, which was shown to have a good correlation with the SGRQ in patients with COPD.[33] In addition, this study revealed that exacerbations in the previous year were not correlated with the SGRQ.

A comprehensive assessment of HRQL in patients with COPD requires instruments that not only evaluate the disease-specific effects but also the overall burden of the disease on functioning and emotional well-being in daily life.[34] We found that depression had a considerable influence on both the SF-36 PCS and MCS scores. Dyspnea and exercise capacity were also significant predictors of the SF-36 PCS score, and anxiety was significantly associated with the SF-36 MCS scores. In a comparative survey study of COPD patients with the healthy general population using the SF-36, patients with very severe COPD had a lower HRQL than the general population or those with MPA or severe COPD.[7] Moy et al. showed that exercise capacity, dyspnea, age, and self-report of being disabled were significant determinants of the SF-36 PCS score, and dyspnea, depression, antidepressant use, daytime sleepiness, and education were significant determinants of the SF-36 MCS score in severe COPD patients.[31]

The present study is the first to show that depression is a strong determinant of both SF-36 PCS score and MSC score in addition to disease-specific HRQL in patients with severe COPD. Recent studies have reported that the prevalence of depression in COPD patients is 10–40% and that the patients with more severe COPD stages had a higher prevalence.[35–37] Evidence suggests that COPD patients with coexisting depression or anxiety have an increased risk of experiencing further exacerbations, frequent hospital admissions, impaired quality of life, and mortality compared with those without these conditions. Atlantis et al. reported that depression and anxiety adversely affect the prognosis of COPD, conferring an increased risk of exacerbation and possibly death, while COPD increased the risk of developing depression.[38] Ng et al. reported that 44.1% of inpatients with COPD exacerbations had depression, and depression was associated with a poorer quality of life, greater number of respiratory symptoms, longer hospital stay, and higher mortality rate.[39] Fan et al. reported that 41% of the patients with severe COPD were depressed, and depressed patients had a higher mortality.[40] Given the association of depression with greater prevalence, poorer HRQL, and increased mortality,[41] screening and early intervention for depression in patients with severe COPD may be a therapeutic option. A retrospective cohort study of US veterans showed that COPD patients with depression who accessed specialist mental health clinics had a 30% reduction in mortality.[42]

Table 3. Multivariate logistic regression: Significant determinants of HRQL (SGRQ, SF-36 PCS, and SF-36 MCS) in patients with severe COPD ($n = 80$).

Determinant	SGRQ (total; model $R^2 = 0.53$)		SF36 (PCS; model $R^2 = 0.45$)		SF36 (MCS; model $R^2 = 0.47$)	
	Coef (95% CI)	*p* Values	Coef (95% CI)	*p* Values	Coef (95% CI)	*p* Values
Dyspnea (MMRC)	0.371 (3.021 to 8.293)	< 0.001	−0.265 (−8.133 to −1.370)	0.006		
HADS-A					−0.246 (−2.330 to −0.042)	0.042
HADS-D	0.372 (0.915 to 2.369)	< 0.001	−0.440 (−3.216 to −1.352)	< 0.001	−0.497 (−3.412 to −1.204)	< 0.001
6MWD	−0.241 (−0.084 to −0.015)	0.005	0.193 (0.002 to 0.091)	0.039		

HRQL: health-related quality of life; George's Respiratory Questionnaire; SF-36: Short Form 36 Health Survey Questionnaire; COPD: chronic obstructive pulmonary disease; PCS: physical component summary; MCS: mental component summary; HRQL: health-related quality of life; MMRC: Modified Medical Research Council; 6MWD: 6-min walk distance; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; Coef: adjusted coefficient; CI: confidence interval.

The etiology and mechanisms of the increased prevalence of depression in patients with COPD are not well understood. Dantzer et al. proposed that when activation of the peripheral immune system continues unabated, such as during systemic infections, cancer, or autoimmune diseases, the ensuing immune signaling to the brain can lead to an exacerbation of sickness and the development of symptoms of depression in vulnerable individuals.[43] However, using data from a large cohort, Hanania et al. demonstrated that clinical and biological measures were less important determinants of depression in patients with COPD than disease symptoms and quality of life.[36] Other studies have also suggested associations with depression and COPD; the irreversible airflow limitation caused a decrease in the oxygen supply to the brain and loss of regional gray matter accompanied by impairment of white matter microstructural integrity, which was associated with disease severity and may underlie the psychological and mood changes of COPD.[44] COPD-related fears contributed incrementally to disease-specific disability.[45]

There were several limitations to our study. First, because the subjects were recruited during outpatient visits, the number of patients with severe COPD is relatively small. The subjects were also predominantly males. As a result, generalization of the results to females with COPD may be unwarranted. Second, our definition of depression was based on the score of a self-reported questionnaire (HADS), and we did not seek a physician-based diagnosis of depression. Finally, we could not assess any possible etiological or causal links between COPD and depression, and COPD-related changes in HRQL over time, because of the cross-sectional nature of this analysis.

Conclusion

HRQL in patients with severe COPD was associated with several factors including depression, anxiety, dyspnea, and exercise capacity. Among these, depression was the strongest predictor of both disease-specific and generic HRQL. Further studies should identify psychological predictors of poor HRQL in COPD patients using well-designed prospective cohorts to isolate the mediating role played by depression. In addition, clinicians should pay attention to a number of physiological and psychosocial factors to optimize HRQL in patients with severe COPD.

Authors' note

The contents of this manuscript have not been copyrighted or published previously. There are no directly related manuscripts or abstracts, published or unpublished, by any authors of this paper. Informed consent was obtained from all individual participants included in the study.

Authors' contribution

Sun Mi Jang and Ki Uk Kim contributed equally to this work.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by 2-year Research Grant of Pusan National University.

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