Impact of Baseline and Induced Dyspnea on the Quality of Life of Patients With COPD

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OBJECTIVE: Dyspnea is the main symptom of chronic obstructive pulmonary disease (COPD) and as such is an important determinant of health-related quality of life. It is, however, weakly correlated to severity of obstruction and there is little information available on how it exercises its effect on health-related quality of life. The aims of this study were to identify the determinants of baseline dyspnea and to ascertain how that factor influences the health-related quality of life of patients with COPD.

PATIENTS AND METHODS: A total of 101 patients with COPD were studied. Tests included full lung function assessment, the bronchial provocation test (n=70), and the 6-minute walk test. The following variables were measured: baseline dyspnea, bronchoconstriction-induced dyspnea, exertional dyspnea, health-related quality of life, and levels of anxiety and depression.

RESULTS: Determinants of baseline dyspnea were anxiety (explained variance, 17%), maximum inspiratory pressure (4%), and PaO_2 (4%). In patients with mild to moderate COPD (forced expiratory volume in 1 second, >50% of predicted), the main determinant of health-related quality of life was anxiety (explained variance, 43%). Other determinants were the number of meters walked in the 6-minute-walk test, age, and baseline dyspnea (variance explained by both factors, 26%). Baseline dyspnea and bronchoconstriction-induced dyspnea were both identified as independent determinants of health-related quality of life (on the activity and impact subscales of the St George's Respiratory Questionnaire, respectively). The main determinant of health-related quality of life in patients with severe COPD (forced expiratory volume in 1 second, ≤50% of predicted) was baseline dyspnea. Finally, the main determinants of anxiety were exertional dyspnea (variance, 42%) and baseline dyspnea (6%).

CONCLUSIONS: Anxiety is the main determinant of health-related quality of life in patients with COPD, and it is triggered mainly by baseline dyspnea and exertional dyspnea.

Key words: *Chronic obstructive pulmonary disease. COPD. Dyspnea. Health-related quality of life.*

Importancia de la disnea basal e inducida en la calidad de vida de los pacientes con EPOC

OBJETIVO: La disnea es el principal síntoma de la enfermedad pulmonar obstructiva crónica (EPOC), por lo que tiene un papel importante en la calidad de vida relacionada con la salud (CVRS). Sin embargo, guarda una relación débil con la gravedad de la obstrucción y hay pocos datos sobre cómo influye en la CVRS. Así pues, nuestro objetivo ha sido averiguar los determinantes de la disnea basal y cómo influye ésta en la CVRS de los pacientes con EPOC.

PACIENTES Y MÉTODOS: Se estudió a 101 pacientes con EPOC, a los que se realizaron exploración funcional completa, test de provocación bronquial (n = 70) y test de la marcha (TM). Se midieron la disnea basal, la inducida por broncoconstrictor y por esfuerzo, la CVRS y los grados de ansiedad y depresión.

RESULTADOS: La disnea basal vino determinada por la ansiedad (un 17% de la variancia explicada), la presión inspiratoria máxima (4%) y la presión arterial de oxígeno (4%). En la EPOC leve-moderada (volumen espiratorio forzado en el primer segundo > 50%) la CVRS se explicó fundamentalmente por la ansiedad (el 43% de la variancia). Los metros caminados en el TM, la edad y la disnea basal explicaron otro 26%. La disnea basal también apareció como determinante independiente de la CVRS en la subescala de Actividades, y la inducida por broncoconstricción en la subescala de Impacto. En la EPOC grave (volumen espiratorio forzado en el primer segundo ≤ 50%) la disnea basal fue el determinante fundamental de la CVRS. Los principales determinantes de la ansiedad fueron la disnea provocada por el TM (el 42% de la variancia) y la basal (6%).

CONCLUSIONES: La ansiedad es el determinante fundamental de la CVRS en la EPOC; dicha ansiedad está mediada fundamentalmente por la disnea inducida por esfuerzo y la disnea basal.

Palabras clave: *EPOC. Disnea. Calidad de vida relacionada con la salud.*

Introduction

Dyspnea is not only the most problematic of all chronic obstructive pulmonary disease (COPD) symptoms but also the most common—and sometimes the only—reason patients seek consultation. The perception of dyspnea is a subjective measure that affects medical and treatment decisions, even when there are no signs of deterioration

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during physical examination or lung function testing. Dyspnea greatly influences health-related quality of life (HRQOL) in patients with COPD[1,2] and can also interfere with emotional state. Acute dyspnea, for example, is a powerful stress trigger and chronic dyspnea can lead to depressive episodes.[3] The patient's general sensation of breathlessness in usual circumstances (baseline dyspnea), however, is also important, not only from the perspective of the patient, but also because it is a better predictor of survival than forced expiratory volume in 1 second (FEV_1).[4,5] Little has been published, however, about the determinants of such baseline dyspnea. Furthermore, patients with COPD may also have bronchial hyperresponsiveness, which, in certain circumstances, can lead to bronchoconstriction and a sudden deterioration in the patient's condition. It has been seen in other obstructive airway diseases, such as asthma, that certain patients have a low level of perception of their symptoms.[6] These patients, known as poor perceivers, tend to disregard medical advice and treatment and are therefore more likely to experience a fatal or near-fatal attack.[7,8] There is little information available, however, on how dyspnea affects HRQOL in patients with COPD. The present study had 2 aims: to identify the determinants of underlying baseline dyspnea and to study how perception of acute bronchoconstriction and baseline dyspnea can influence HRQOL in patients with COPD.

Patients and Methods

Selection of Patients

We consecutively enrolled 101 patients with COPD (as defined by the American Thoracic Society[9]) who attended the respiratory medicine outpatient clinic of Hospital Universitario La Fe in clinically stable condition (no respiratory infections or changes in regular treatment in the preceding 6 weeks). Of the 101 patients, 99 were men, 2 were women, 23 were smokers, and 78 were ex-smokers. Their ages ranged from 41 to 81 years. None of them had serious comorbidity or diseases that could cause airflow limitation. Excluded from the study were patients with asthma, conditions other than COPD that can cause dyspnea, chronic respiratory failure, psychiatric conditions, and patients in the process of applying for disability benefits. All the participants agreed to take part in the study following an explanation of its objectives and protocol.

Study Protocol

Patients were evaluated prospectively in 2 visits. In the first visit, we assessed both the patient's usual level of dyspnea (baseline) in the preceding month using a modified version of the Medical Research Council (MRC) scale[10] and the patient's perception of dyspnea during acute bronchoconstriction induced by a bronchial provocation test (performed only in the absence of contraindications). In the second visit—held within 2 weeks of the first—we tested clinical and functional stability and used the 6-minute walk test in order to record exertional dyspnea on the Borg scale[11]; oxygen saturation and heart rate were measured before and after the test. We also evaluated HRQOL and emotional state (anxiety and depression).

Assessment of Lung Function

Lung function was assessed by spirometry (with a pneumotachometer), static lung volumes (by helium dilution), and the ratio between the diffusing capacity of lung for carbon monoxide (DLCO) and alveolar volume.[12] DLCO was corrected for hemoglobin and carboxyhemoglobin saturation levels detected in arterial blood gas analysis.[13] Maximum inspiratory pressure and maximum expiratory mouth pressure were also measured.[14]

Perception of Dyspnea Induced by Acute Bronchoconstriction

The bronchial provocation test was performed on patients without contraindications (n=70).[15-16] Spirometry was performed before and after inhalation of physiological saline solution, and the results of the second test were used as the initial reference value for the purposes of calculating the percentage decrease of FEV_1. The test was stopped when a decrease of 20% or more in FEV_1 was reached. Patients were immediately administered 600 µg of salbutamol using a pressurized metered-dose inhaler and a spacer device. A third spirometry was performed 20 minutes later to check that the bronchoconstriction had disappeared.

Perception of dyspnea was evaluated as follows: 30 seconds after inhaling the saline solution and receiving each dose of histamine, patients were asked to rate their perception of dyspnea on a modified version of the Borg scale.[17] Flow-volume curves were then obtained. To rate their dyspnea, patients were instructed not to take into account any other sensations such as nasal or pharyngeal irritation, unpleasant tastes in their mouths, or coughing. They were unaware of the substance they had been administered and its possible effects on breathing. The data obtained were used to calculate the score for perception of dyspnea when FEV_1 had decreased by at least 20% with respect to the initial postsaline value (PS_{20}) and the change in Borg score[18] (difference between PS_{20} and postsaline dyspnea rating).

Evaluation of HRQOL

We used the Spanish version of the St George Respiratory Questionnaire to evaluate HRQOL.[19] This questionnaire contains 50 yes/no items divided into 3 domains, or subscales: symptoms, activity, and impacts. Each subscale is scored separately and an overall score can also be obtained. Scores range from 0% to 100% and a high score is indicative of poor HRQOL.

Evaluation of Psychological Factors

Anxiety levels were evaluated using the State-Trait Anxiety Inventory (STAI), a self-administered questionnaire used to assess state and trait anxiety.[20] The total possible score ranges from 0 to 60 points and a score of over 38 indicates a risk of developing an anxiety disorder.

Depression was evaluated using the Spanish version of the 1978 Beck Depression Inventory, a self-administered questionnaire containing 21 items relating to depression symptoms.[21] The total possible score ranges from 0 to 63 points, and a score of 10 to 16 indicates mild or subclinical depression, 17 to 29, moderate depression, and 30 to 63, severe depression.

Statistical Analysis

Spirometry, lung volume, and diffusion values were expressed as a percentage of theoretical reference values and all other parameters as absolute values. Maximum inspiratory pressure was expressed as a positive figure to facilitate calculations. Data were tested for normality using the Kolmogorov–Smirnov test and nonnormally distributed data were normalized using mathematical procedures. Analysis of variance and the Duncan post hoc test were performed to study possible intergroup differences with regards severity of airflow limitation. Correlations were assessed using the Spearman correlation coefficient, and parameters seen to be significantly correlated were analyzed by

multiple regression analysis (backward stepwise approach) to identify the determinants of dyspnea and anxiety.

Results

Of the 101 patients studied, 23 had mild COPD, 50, moderate COPD, and 28, severe COPD (according to the criteria established by the European Respiratory Society[22]). Table 1 shows the values for lung function, emotional state, and dyspnea according to COPD severity. The mean (SD) scores obtained on the STAI-state and STAI-trait scales (16.55 [11.21] and 21.33 [11.05], respectively) were at the limits of what is considered normal for the general population, and the mean trait anxiety score was significantly higher in patients with severe COPD than in those with mild or moderate disease (Table 1). Only 9 patients (8.9%) scored higher than 38 points (indicating a risk of developing an anxiety disorder). Depression scores were also significantly higher in patients with severe COPD, and unlike anxiety scores, were indicative of disease in a large proportion of patients (54/101 [53.46%]). Baseline dyspnea in the preceding month as measured in the first visit was also significantly higher in patients with severe COPD than in patients with milder forms of the disease, but there were no significant differences between those with mild and moderate disease (Table 1).

Baseline dyspnea was significantly associated with a number of lung function variables, emotional state, and exertional and bronchoconstriction-induced dyspnea (Figure 1A). On subjecting these variables to multiple regression analysis, however, we saw that only trait anxiety, maximum inspiratory pressure, and PaO_2 retained statistical significance (explained variance, 25%) (Figure 1B).

For the group as a whole, we found significant correlations between HRQOL and lung function variables (FEV_1, forced vital capacity, vital capacity, carboxyhemoglobin, maximum inspiratory pressure, maximum expiratory pressure, residual volume/total lung capacity ratio, and 6-minute walk distance), dyspnea in the preceding month (MRC score), emotional state (Beck Depression Inventory and STAI state and trait scores), perception of airway caliber changes (change in Borg score and PS_{20}), and age and active smoking (Table 2). Multivariate analysis revealed that anxiety, age, 6-minute walk distance, and depression were all associated with the overall HRQOL score (explained variance, 69%). (Figure 2). As carboxyhemoglobin scores increased, HRQOL scores decreased, but this association was not statistically significant in the multivariate analysis. On analyzing the subscales of the St George's Respiratory Questionnaire, we saw that baseline dyspnea (measured on the MRC scale) and perceived bronchoconstriction (measured by change in Borg score) explained a small proportion of the variance observed in the activity and impacts subscales, respectively. The greatest proportion of the variance in these subscales was explained by trait anxiety (Figure 2). In view of the considerable impact that anxiety had on HRQOL, we decided to investigate which COPD variables had an influence on that aspect.

TABLE 1
Lung Function, Emotional State, and Dyspnea Parameters According to COPD Severity[a]

	All Patients	Mild COPD, Stage 0[b]	Moderate COPD, Stage 1[b]	Severe COPD, Stage 2[b]	$F_{98.2}$	*P*	Post Hoc Analysis
Age, y	63.25 (7.71)	62 (7.37)	64.18 (7.36)	62.6 (8.6)	0.75	NS	
Smoking, pack-years	63.1 (32.9)	63.8 (38.4)	62 (28.7)	64.6 (36.1)	0.063	NS	
FEV_1, L	58.6 (15.7	80 (7.8)	59.2 (5.8)	39.9 (6.67)	236.2	<.0000	0≠1≠2
FVC, L	97.07 (18.2)	112.3 (12.8)	97.9 (14.3)	83 (17.74)	24.26	<.0001	0≠1≠2
TLC, L	6.79 (1.07)	6.7 (1.15)	6.7 (1.06)	7.02 (1)	0.94	NS	
RV/TLC	51.27 (7.84)	45.22 (7.18)	50.16 (5.95)	58.21 (6.16)	28.35	<.0001	0≠1≠2
DLCO/VA, $mL \cdot min^{-1} \cdot mm\ Hg^{-1}$	74.9 (22.65)	80.35 (28.9)	75.9 (21.3)	67.86 (16.31)	1.76	NS	
PImax, cm H_2O	86 (35.24)	106.2 (48.2)	83.5 (29.41)	76.1 (26.06)	5.41	.005	0≠1≠2
PEmax, cm H_2O	151 (47.73)	160.9 (44.8)	152 (51.54)	142.3 (42.6)	0.97	NS	
pH	7.43	7.43 (0.03)	7.43 (0.02)	7.42 (0.03)	0.29	NS	
$PaCO_2$, mm Hg	41.45 (3.96)	40.05 (5.06)	41.2 (3.04)	43.69 (3.57)	7.33	.001	2≠(0=1)
PaO_2, mm Hg	72.33 (8.02	72.61 (6.69)	73.3 (8.9)	70.43 (7.26)	1.16	NS	
MRC score	1	1	1	2			
STAI-S	16.55 (11.2)	15.6 (10.13)	15.18 (10.13)	19.85 (11.1)	1.92	NS	
STAI-T	21.3 (11.05)	16.87 (11.3)	20.9 (9.6)	25.93 (11.96)	4.73	.01	2≠(0=1)
Beck score	12.3 (8.67)	10.17 (7.91)	10.94 (7.96)	16.46 (9.33)	4.89	.009	2≠(0=1)
BMI, kg/m^2	27.3 (4.2)	28.17 (3.78)	26.88 (3.62)	28.16 (5.34)	1.18	NS	
HRQOL[c], total	42.49 (18.6)	35.6 (21.6)	42.4 (17.8)	48.4 (16.01)	3.061	NS	
HRQOL[c], symptoms	40.8 (20.4)	32.4 (21)	43 (19.2)	43.7 (20.9)	2.605	NS	
HRQOL[c], impacts	36.7 (21)	30.8 (23.9)	34.9 (20.2)	44.9 (18.09)	3.39	.03	2≠(0=1)
HRQOL[c], activity	54.7 (23.9)	47.9 (27.9)	53 (23.3)	63.2 (19.5)	2.94	NS	
6MWD, m	523.6 (85.6)	565 (65.8)	527.8 (73.8)	481 (101.7)	6.28	.03	0≠(1=2)

Abbreviations: 6MWD, 6-minute walk distance; Beck, Beck Depression Inventory; BMI, body mass index; DLCO, diffusing capacity of lung for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HRQOL, health-related quality of life; MRC, Medical Research Council; NS, not significant; PEmax, maximum expiratory pressure; PImax, maximum inspiratory pressure; RV/TLC; residual volume/total lung capacity ratio; VA, alveolar volume.
[a]Values are expressed as means (SD) except for dyspnea values (MRC score), which are expressed as medians.
[b]According to European Respiratory Society criteria.[21]
[c]Assessed using the St George's Respiratory Questionnaire.

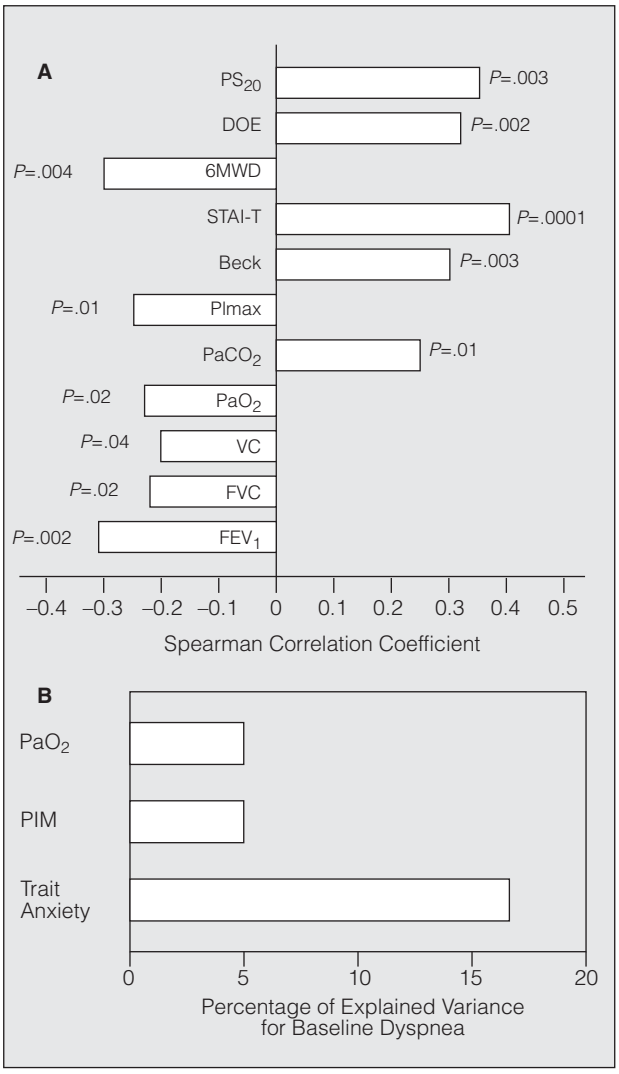

Figure 1. A: Spearman correlation coefficients between baseline dyspnea and lung function, emotional state, and induced dyspnea parameters. B: Determinants of dyspnea according to multivariate analysis (multiple regression).
PS_{20} indicates perceived dyspnea when FEV_1 has decreased by 20% during bronchial provocation test; DOE, dyspnea on exertion (6-minute walk test); 6MWD, 6-minute walk distance; STAI-T, State-Trait Anxiety Inventory, trait score; Beck, Beck Depression Inventory; PImax, maximum inspiratory pressure (expressed in positive values); VC, vital capacity; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second.

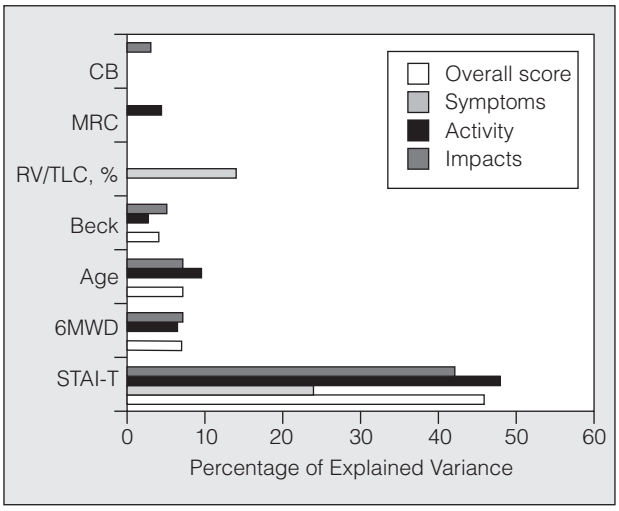

Figure 2. Determinants of health-related quality of life (St George's Respiratory Questionnaire) in COPD according to multiple regression analysis (all patients).
CB indicates change in Borg dyspnea score; MRC, Medical Research Council dyspnea score; RV/TLC, residual volume/total lung capacity ratio; Beck, Beck Depression Inventory; 6MWD, 6-minute walk distance; STAI-T, State-Trait Anxiety Inventory, trait score.

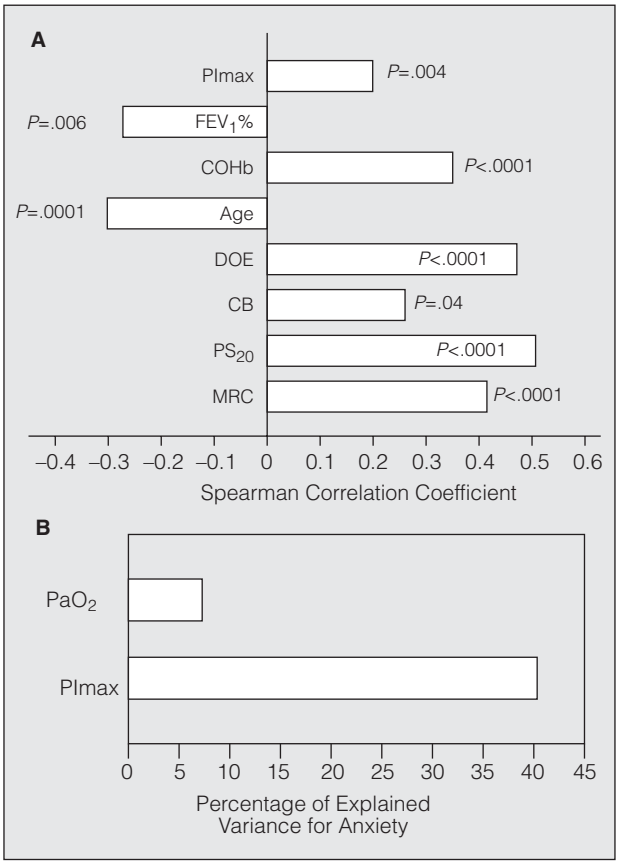

Figure 3. A: Spearman correlation coefficients between anxiety, lung function parameters, and perception of dyspnea. B: Determinants of anxiety in patients with chronic obstructive pulmonary disease according to multiple regression analysis.
PImax indicates maximum inspiratory pressure; FEV_1%, forced expiratory volume in 1 second as percentage of predicted; COHb, carboxyhemoglobin; DOE, dyspnea on exertion (6-minute walk test); CB, change in Borg score; PS_{20}, perceived dyspnea when FEV_1 has decreased by 20% during bronchial provocation test; MRC, Medical Research Council dyspnea score.

Regression analysis revealed that 50% of the variance in trait anxiety was explained by the underlying baseline and exertional dyspnea (induced during the 6-minute walk test) combined (Figure 3).

We then sought to determine if the factors related to HRQOL differed for patients with severe COPD (FEV_1 ≤50% of predicted, n=31) and for those with milder forms of the disease (FEV_1 >50% of predicted, n=70). The results for the second group of patients were similar to those described above, with trait anxiety explaining the largest proportion of variance (HRQOL questionnaire as a whole, 43%; symptoms subscale, 25%; activity subscale, 47%; impacts subscale, 40%) (Figure 4A). The results for patients

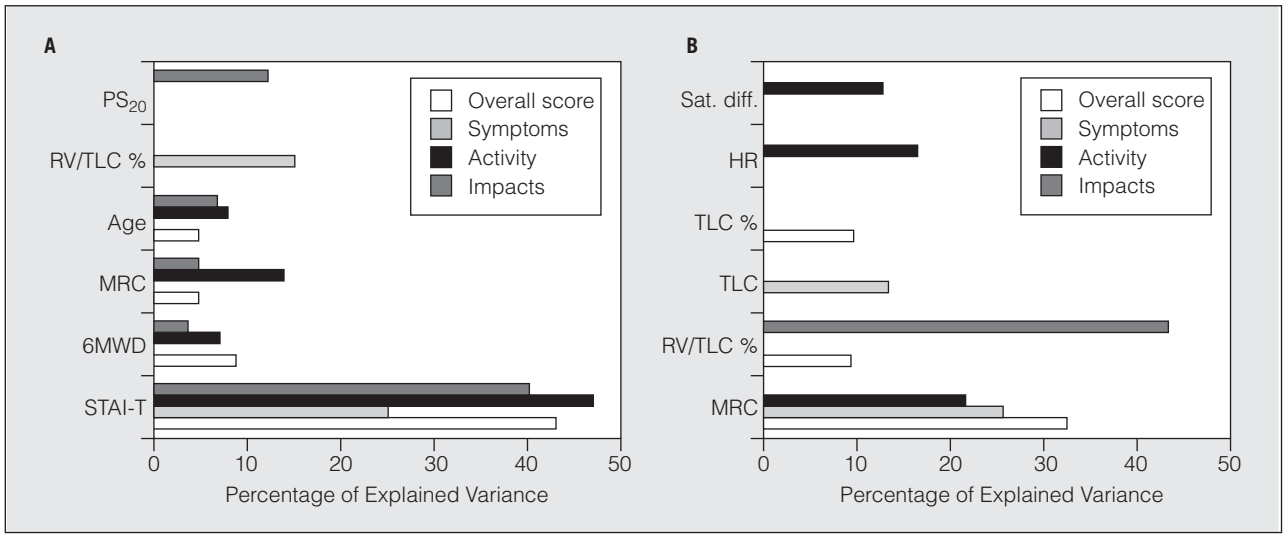

Figure 4. A: Determinants of health-related quality of life (St George's Respiratory Questionnaire) in patients with COPD and a forced expiratory volume in 1 second (FEV_1) of over 50% (multiple regression analysis). B: Determinants of health-related quality of life (St George's Respiratory Questionnaire) in patients with severe COPD (FEV_1 ≤50% of predicted), multiple regression analysis.
PS_{20} indicates perceived dyspnea when FEV_1 has decreased by 20% during bronchial provocation test; RV/TLC, residual volume/total lung capacity ratio; MRC, Medical Research Council; 6MWD, 6-minute walk distance; STAI-T, State-Trait Anxiety Inventory, trait score; Sat. diff., difference in saturation before and after 6-minute walk test; HR, heart rate on completion of 6-minute walk test.

with severe COPD, however, showed that HRQOL was primarily determined by underlying baseline dyspnea, air trapping, and saturation and heart rate on completion of the 6-minute walk test (Figure 4B).

Discussion

Patients with COPD frequently attach little importance to certain symptoms of their disease. Cough and expectoration, for example, are often attributed to smoking, and difficulty breathing, to getting old. Dyspnea alone, however, can have a major impact on activities of daily living, such as walking, getting around, socializing, and looking after oneself or one's home.[23] Furthermore, not all patients perceive dyspnea equally,[24] and not all episodes of dyspnea are triggered by the same factors. Physiological parameters provide objective information on the state of the airway in patients with COPD, but they give no indication of what impact the disease has on patients' lives. Furthermore, dyspnea intensity and lung function measurements are only weakly associated.[25] We therefore need to learn more about COPD from the perspective of the patient and to deepen our understanding of HRQOL, dyspnea, and how they are related.

As was to be expected, we found that patients with more severe forms of COPD had higher baseline dyspnea scores on the MRC scale as well as higher levels of depression and anxiety. Our results showed that baseline dyspnea was explained by level of anxiety, respiratory muscle strength (maximum inspiratory pressure), and PaO_2. Respiratory muscles are known to play an important role in dyspnea and there is probably a relation between respiratory muscle strength and air trapping.[26] Patients who had a greater perception of acute bronchoconstriction (expressed by PS_{20} and change in Borg score) scored higher on the HRQOL questionnaire.

TABLE 2
Correlations Between Health-Related Quality of Life Overall and Subscale Scores[a] and General, Lung Function, Emotional State, and Dyspnea Parameters[b]

	Overall Score	Subscales		
		Activity	Impacts	Symptoms
FEV_1%	–0.26[d]	–0.23[c]	–0.26[d]	–0.22[c]
FVC%	–0.24[c]	–0.2[c]	–0.21[c]	–0.25[c]
VC%	–0.26[d]	–0.25[d]	–0.2[c]	–0.25[c]
RV/TLC%	0.26[c]	0.21[a]	0.23[a]	0.28[c]
PImax	–0.27[c]	–0.25[c]	NS	–0.32[d]
PEmax	–0.26[d]	–0.24[c]	–0.25[c]	–0.21[c]
Carboxyhemoglobin	0.27[d]	0.22[c]	0.26[c]	0.23[c]
6MWD	–0.32[d]	–0.4[e]	–0.3[d]	NS
DOE	0.48[e]	0.51[e]	0.5[e]	0.3[d]
MRC score	0.58[e]	0.61[e]	0.53[e]	0.39[e]
Beck score	0.57[e]	0.56[e]	0.61[e]	0.37[e]
STAI-S	0.62[d]	0.61[e]	0.62[e]	0.46[e]
STAI-T	0.59[d]	0.58[e]	0.61[e]	0.36[e]
PS_{20}	0.61[d]	0.64[e]	0.67[e]	0.34[d]
CB score	0.35[c]	0.33[c]	0.46[d]	NS
Age	–0.31[d]	–0.23[d]	–0.28[d]	–0.27[d]
Smoking habit	0.24[c]	NS	NS	0.33[e]

Abbreviations: 6MWD, 6-minute walk distance; BDI, Beck Depression Inventory; CB, change in Borg score (difference between initial dyspnea and dyspnea when FEV_1 falls by 20%); DOE, dyspnea on exertion (6-minute walk test); FEV_1,% forced expiratory volume in 1 second as percentage of predicted; FVC% forced vital capacity as percentage of predicted; MRC, Medical Research Council; NS, not significant; PEmax, maximum expiratory pressure; PImax, maximum inspiratory pressure; PS_{20}, perceived dyspnea when FEV_1 has decreased by 20% during bronchial provocation test; RV/TLC, residual volume/total lung capacity ratio; STAI-S, State and Trait Inventory, state score; STAI-T, State and Trait Inventory, trait score; VC, vital capacity.
[a]Evaluated using St George's Respiratory Questionnaire.
[b]Data are expressed as Spearman correlation coefficients.
[c]$P<.05$. [d]$P<.01$. [e]$P<.001$.

Our findings seem to be similar to those reported for asthma, where patients who had a mistaken or heightened perception of dyspnea also performed worse in terms of HRQOL.[27] In the present study, patients with higher levels of dyspnea on completion of the 6-minute walk test also obtained higher scores on the HRQOL questionnaire. These findings would seem to suggest that dyspnea, whether baseline or induced by any stimulus, is, in itself, an important determinant of HRQOL. In the multivariate analysis of the group as a whole, however, we did not find this to be the case as dyspnea did not explain HRQOL for either the questionnaire as a whole or the symptoms subscale. We did, however, find dyspnea to be an independent determinant of HRQOL in terms of activity and impacts (underlying baseline and bronchoconstriction-induced dyspnea, respectively) but only to a minor extent. These findings cannot be ignored as they probably mean that dyspnea has an impact on social functioning and activities of daily living in patients with an increased sensation of acute bronchoconstriction. In any case, the most notable finding to emerge from the present study is the considerable impact that anxiety has on HRQOL. Anxiety alone explained 46% of the variance for HRQOL in general, and was also the main determinant on all the subscales of the St George's Respiratory questionnaire. If we also consider depression, another independent determinant of HRQOL, albeit to a lesser extent, emotional state explained over half of the variance of HRQOL in patients with COPD.

Considering the above, thus, it would seem that emotional state rather than dyspnea is a key determinant of HRQOL in patients with COPD. Before reaching a definitive conclusion, however, we must ask ourselves what aspects of COPD influence a patient's emotional state. To answer this question, we investigated which components of COPD were capable of influencing trait anxiety. According to our results, 60% of anxiety was explained by underlying baseline and exertional dyspnea induced by the 6-minute walk test combined. Therefore, although dyspnea may not have directly impacted HRQOL, it was a major determinant of trait anxiety, and trait anxiety, in turn, was the main determinant of HRQOL. In other words, dyspnea causes anxiety and anxiety affects quality of life. Our results seem to confirm the theoretical model proposed by Jones[1] regarding the interaction between dyspnea and psychological factors. Jones suggested that there was a vicious, self-perpetuating circle between dyspnea and emotional state and that either factor could exacerbate the other without a major deterioration of respiratory function. It should be stressed that although the STAI is a validated and widely used instrument, it is not used to 'diagnose' anxiety. We can therefore only conclude that patients with high scores on questionnaires of this type have a predisposition to a heightened perception of dyspnea. It is also noteworthy that bronchoconstriction-induced dyspnea was not an independent determinant of anxiety but, interestingly, perception of acute changes in bronchial caliber did have a negative affect on certain aspects of HRQOL. We believe that this has 2 explanations: *a)* COPD involves a chronic, underlying airflow limitation, and unlike in asthma, bronchoconstriction tends to develop progressively; and *b)* a large number of patients with COPD have a poor perception of acute changes in bronchial caliber.[18] In other words, because acute bronchoconstriction occurs less frequently than do a usual sensation of dyspnea or dyspnea induced by walking, it does not affect anxiety levels but is capable of negatively impacting HRQOL.

Our results are different in some respects to those reported by Jones et al.[28] In our study, for example, anxiety had a greater impact than dyspnea on HRQOL on all the subscales of the St George's Respiratory Questionnaire. The 2 studies, however, are not strictly comparable as different instruments were used to measure anxiety and our patients all had COPD whereas those of Jones et al were a mixed group, some with asthma and others with COPD.[28]

It has been reported that different aspects of HRQOL in COPD vary with disease severity[29] and our patients were no exception. We found that the determinants of HRQOL in patients with milder forms of the disease (FEV_1 >50%) were similar to those of the group as a whole, although this is not surprising as 70% of the patients studied had mild or moderate COPD. The main determinant of HRQOL in these patients was anxiety, followed by baseline dyspnea and bronchoconstriction-induced dyspnea to a somewhat lesser extent. Anxiety lost its importance as a determinant in patients with more severe COPD (FEV_1 ≤50%), to be replaced by baseline dyspnea, air trapping and desaturation variables, and increased heart rate during exercise. In patients with more severe obstruction, baseline dyspnea provided the best explanation for HRQOL in general and also for the activity and symptoms subscales. It has been reported that air trapping is among the pathophysiologic mechanisms that can generate dyspnea in patients with COPD,[30] and we indeed saw that it had a greater impact on HRQOL than airway limitation. It is interesting to note that anxiety did not affect HRQOL in patients with severe COPD, even though they had higher anxiety levels than those with milder forms of the disease. We believe that this is because the considerable physical deterioration that occurs in patients with advanced disease probably outweighs the emotional component.

Our study has certain limitations. We used the 6-minute walk test rather than a stress test to evaluate exertional dyspnea. Nonetheless, like other studies, we found that 6-minute walk distance was a major independent determinant of HRQOL.[31,32] This probably reflects the importance that patients attach to being able to carry out daily tasks that require walking. The 6-minute walk test has the advantage that it is a more familiar and relevant form of exercise to patients with COPD than is cycle ergometry or continuous treadmill exercise.[31,32] Accordingly, our results indicate that patients who have fewer obstacles to overcome during activities of daily living have a better quality of life. Although it has been reported that leg fatigue is a more common limiting factor in stress tests than dyspnea,[33] we believe that it does not exert quite the same effect during

submaximal exercise, which is a closer reflection of the physical effort that patients make in their everyday lives. Our results suggest that dyspnea had a greater limiting effect on walking capacity than did leg muscle fatigue, as baseline dyspnea, desaturation, and increased heart rate during exercise were all determinants of HRQOL on the activity subscale of the St George's Respiratory Questionnaire. Another possible limitation of this study is the fact that most of the patients in the study group had moderate COPD; there were only a few cases of severe obstruction and no cases of respiratory failure. This is because the patients were consecutively enrolled from our hospital's outpatient clinics. The resulting group, however, is probably more representative of the general population than if it had been selected from among hospitalized patients. Finally, there were fewer women than would be expected given the prevalence of COPD in women,[34] suggesting that the disease is probably underdiagnosed in them in our setting.

In conclusion, psychological factors, and anxiety in particular, have a major impact on HRQOL in patients with mild or moderate COPD, and a considerable amount of the anxiety felt by these patients is caused by baseline or exertional dyspnea. Dyspnea, therefore, has a substantial indirect impact on HRQOL in patients with mild to moderate COPD as breathing difficulties can affect emotional state. Furthermore, both chronic baseline and bronchoconstriction-induced dyspnea can also directly affect HRQOL. In patients with severe COPD, for example, dyspnea, together with air trapping, is a key determinant of HRQOL. Our results support a focus on reducing dyspnea when treating COPD and underline the importance of psychological factors in this disease.

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