Dyspnea in COPD: Beyond the modified Medical Research Council scale*

Dispneia em DPOC: Além da escala *modified Medical Research Council*

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Abstract

Objective: To determine the correlations among various dyspnea scales, spirometric data, exercise tolerance data, and the Body mass index, airway Obstruction, Dyspnea, and Exercise capacity (BODE) index in patients with COPD. **Methods:** Between March of 2008 and July of 2009, 79 patients with COPD were recruited, and 50 of those patients were included in the study. After being regularly treated with formoterol for one month, the patients completed the modified Medical Research Council (mMRC, dyspnea scale), Baseline Dyspnea Index (BDI), Oxygen Cost Diagram (OCD), and Shortness Of Breath Questionnaire (SOBQ). Subsequently, the patients underwent spirometry and six-minute walk tests (6MWTs), with determination of the six-minute walk distance (6MWD), as well as initial and final SpO_2. All patients also completed the Visual Analogue Scale (VAS) and the Borg scale. **Results:** The best correlations were between the Borg scale and the VAS (r_s = 0.79) and between the BDI and the SOBQ (r_s = –0.73). Among the one-dimensional scales (the VAS, mMRC, OCD, and Borg scale), only the VAS correlated with the spirometric parameters, whereas the multidimensional scales BDI and SOBQ did correlate, but poorly. The MRC, BDI, and SOBQ correlated well with 6MWD. Among the spirometric data, inspiratory capacity (IC) and FVC had the strongest correlations with 6MWD. In the multivariate analysis, BDI and IC were selected as the best predictors of 6MWD. **Conclusions:** Multidimensional dyspnea scales should be applied in the evaluation of COPD patients.

Keywords: Pulmonary disease, chronic obstructive; Spirometry; Dyspnea; Exercise tolerance.

Resumo

Objetivo: Avaliar as correlações entre diversos instrumentos de avaliação de dispneia, dados espirométricos e de tolerância ao exercício e índice *Body mass index, airway Obstruction, Dyspnea, and Exercise capacity* (BODE) em pacientes com DPOC. **Métodos:** Entre março de 2008 e julho de 2009, de 79 pacientes com DPOC recrutados, 50 foram selecionados. Esses pacientes retornaram após um mês de tratamento regular com formoterol e responderam aos seguintes instrumentos: escala *modified Medical Research Council* (mMRC), *Baseline Dyspnea Index* (BDI), *Oxygen Cost Diagram* (OCD) e *Shortness Of Breath Questionnaire* (SOBQ). Em seguida, realizaram espirometria e teste de caminhada de seis minutos (TC6), com a medição da distância percorrida no TC6 (DTC6), medida de SpO_2 inicial e final, e graduação da dispneia pela escala analógica visual (EAV) e escala de Borg. **Resultados:** As melhores correlações entre os instrumentos foram entre Borg e EAV (r_s = 0,79) e BDI e SOBQ (r_s = –0,73). Entre as escalas unidimensionais (VAS, mMRC, OCD e de Borg), apenas VAS se correlacionou com os parâmetros de espirometria, ao passo que as escalas multidimensionais BDI e SOBQ apresentaram fraca correlação. Houve boas correlações entre mMRC, BDI e SOBQ com DTC6. Entre os parâmetros espirométricos, a capacidade inspiratória (CI) e CVF tiveram as melhores correlações com DTC6. Na análise multivariada, BDI e CI foram selecionados como os melhores preditores para DTC6. **Conclusões:** Escalas multidimensionais de dispneia devem ser aplicadas para avaliar pacientes com DPOC.

Descritores: Doença pulmonar obstrutiva crônica; Espirometria; Dispneia; Tolerância ao exercício.

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Introduction

Worldwide, COPD is the fourth leading cause of death.[1] The disease is characterized by airflow obstruction that is not fully reversible. It is clinically characterized by cough, expectoration, wheezing, dyspnea, and exercise intolerance.

Dyspnea is a symptom associated with exercise performance and, therefore, quality of life. One of the major goals of COPD treatment is a reduction in dyspnea. The severity of the disease can be determined by the intensity of dyspnea.[2]

The severity of COPD is habitually classified by FEV_1 after bronchodilator use.[1] However, there is only a weak correlation between FEV_1 and dyspnea. Inspiratory capacity is related to lung hyperinflation, which is a basic mechanism of dyspnea in COPD, and therefore correlates with dyspnea.[3] The six-minute walk test (6MWT) is used in order to determine the six-minute walk distance (6MWD), which correlates with the performance of activities of daily living in patients with COPD.[4]

Various instruments are available to measure dyspnea. To measure the degree of dyspnea during exercise, the visual analogue scale (VAS) and the Borg scale are used,[5,6] whereas the modified Medical Research Council (mMRC) dyspnea scale,[7] Oxygen Cost Diagram (OCD),[8] and Baseline Dyspnea Index (BDI),[9] as well as the Shortness Of Breath Questionnaire (SOBQ, developed at the University of California),[10] are used in order to measure the degree of dyspnea during activities of daily living. Each of these instruments has its strong points and weak points.[11] With the exception of the SOBQ, all of these instruments have previously been used in studies conducted in Brazil.[12-15]

In order to gain a better understanding of the relationships between the various dyspnea scales, pulmonary function, and exercise tolerance, we determined the correlations among various dyspnea scales, spirometric data, and 6MWT data in a group of symptomatic patients with COPD.

Methods

We consecutively evaluated 79 COPD patients (≥ 40 years of age) treated between March of 2008 and July of 2009 at the Pulmonology Outpatient Clinic of the São Paulo Hospital for State Civil Servants, located in the city of São Paulo, Brazil.

The inclusion criteria were as follows: presenting with symptomatic COPD, defined as any degree of dyspnea reported on the medical chart; presenting with a postbronchodilator FEV_1/FVC ratio below the lower limit of the reference range; having had a postbronchodilator $FEV_1 \leq 65\%$ of the predicted value, documented through pulmonary function testing, within the last twelve months; and having a smoking history of ≥ 10 pack-years.

The exclusion criteria were as follows: presenting with dyspnea due to any cause other than COPD; using supplemental oxygen, since these patients have difficulty in performing the 6MWT; being unable to perform the 6MWT; being unable to answer the dyspnea questionnaires and scales; being unable to perform the pulmonary function tests; presenting with exacerbation in the last three months; and presenting with radiological abnormalities indicative of other conditions. A total of 29 patients were excluded for various reasons.

The 50 eligible patients were instructed to use only formoterol (12 µg every 12 h) for one month and then return to the outpatient clinic. When patients returned, they underwent the following:

1) Formoterol inhalation—The recommended dose of formoterol was inhaled in the presence of the researcher.
2) Completion of the dyspnea scales and questionnaires—The SOBQ was translated to Portuguese with the aid of English teachers and Brazilians residing in English-speaking countries.
3) Spirometry—At least 20 min after formoterol use, slow vital capacity and FVC maneuvers were performed. Prebronchodilator tests were not performed then. The tests were performed with a spirometer (Koko Pneumotach; PDS Instrumentation Inc., Louisville, CO, USA), in accordance with the Brazilian Spirometry Guidelines, and the predicted values were those derived for the Brazilian population.[16]
4) 6MWT—Two 6MWTs were performed, with a 30-min interval between the two, in accordance with the protocol suggested by the American Thoracic Society (ATS).[17] We included the following parameters,

obtained before and after the 6MWT with the greatest 6MWD: SpO_2; HR; the VAS score; and the Borg scale score.

After data collection, the Body mass index, airway Obstruction, Dyspnea, and Exercise capacity (BODE) index was calculated.[18]

The present study was reviewed and approved by the local research ethics committee, and all participants gave written informed consent.

Nonparametric Spearman's correlation coefficients were used in order to express the relationships between the pairs of variables. An anterograde multivariate regression model was applied in order to determine which dyspnea scales and functional parameters correlated better with the 6MWD. The 6MWD values were expressed in absolute values, since several of the predicted values tested presented residuals that correlated with the anthropometric data. Values of $p \leq 0.05$ were considered significant.

Results

Most of the patients were male (70%), White (84%), and former smokers (80%). Of the 50 patients evaluated, 35 (70%) had had ≤ 9 years of schooling. Dyspnea, measured by the mMRC scale, was classified as grade 3 in 16% of the patients; grade 2 in 46%; grade 1 in 34%; and grade 0 in 4%. The two patients who presented with grade 0 dyspnea (as assessed by the mMRC scale) had reported dyspnea before the treatment given during the study.

The mean values for the postbronchodilator spirometric data, obtained up to 1 year before the study outset, were as follows: FVC = 83 ± 18%; FEV_1 = 50 ± 12%; and FEV_1/FVC ratio = 47 ± 10%. In 12 patients, there was a significant variation in postbronchodilator FVC. In 15 patients, there was a significant variation in FEV_1, and, in the spirometric test performed before the study, 11 patients showed a postbronchodilator FEV_1 > 10% higher than the predicted value.

The general and functional data of the patients are shown in Table 1. The values of FEV_1 and FEV_1% after formoterol use were higher than those obtained through the spirometry performed up to 1 year before the inclusion of the patients in the present study.

The measurements obtained with the dyspnea scales and questionnaires, as well as those derived from the 6MWT, are shown in Table 2. The mean 6MWD was greater in males than in females (447 ± 67 m vs. 408 ± 51 m; t = 2.03, p = 0.048).

The correlation matrix between the BODE index, the dyspnea scale scores, and the dyspnea questionnaire scores is shown in Table 3.

The correlation coefficients (r_s) between the various measurements of dyspnea ranged from 0.31 to 0.79, and all correlations were in the expected direction. The strongest correlation was between the post-6MWT Borg scale score and the post-6MWT VAS score (r_s = 0.79). There was also a strong correlation between the BDI and the SOBQ score (r_s = −0.73). Weaker but significant correlations were observed among the scores on the remaining dyspnea scales.

The BODE index correlated with the mMRC dyspnea scale score (scale included in the BODE index; r_s = 0.60), the SOBQ score (r_s = 0.62), the BDI (r_s = −0.59), and the VAS score (r_s = 0.50). The BODE index also correlated with the Borg scale and OCD scores, although these correlations were weaker (r_s = 0.41 and r_s = −0.29, respectively).

Table 1 - Characteristics of the 50 patients under study and results of the pulmonary function tests after the use of formoterol.

Characteristic	Results*
Gender (M/F), n	35/15
Age, years	69 ± 8
Smoking history (pack-years)	46 ± 22
Smoking status (current/former smokers), n	10/40
Exposure to smoke from wood stoves, n	37
mMRC grade (0/1/2/3/4), n	2/17/23/8/0
BMI, kg/m^2	27 ± 5
FVC, L	2.7 ± 0,7
FVC, % of predicted	85 ± 14
FEV_1, L	1.3 ± 0.4
FEV_1, % of predicted	52 ± 12
FEV_1/FVC	46 ± 9
IC, L	2.1 ± 0.6
SVC, L	3.0 ± 0.9
BODE index, median (range)	3 (0-5)

mMRC: modified Medical Research Council scale; BMI: body mass index; IC: inspiratory capacity; SVC: slow vital capacity; and BODE: Body mass index, airway Obstruction, Dyspnea, and Exercise capacity. *Results expressed as mean ± SD, except where otherwise indicated.

Table 2 - Dyspnea scale scores, dyspnea questionnaire scores, and six-minute walk test results.

Characteristic	Results
mMRC*	2 (0-3)
OCD*	41 (6-95)
BDI*	7 (3-11)
SOBQ*	38 (3-106)
6MWD, m**	435 ± 64.7 (192-570)
Post-6MWT VAS*	53 (3-100)
Post-6MWT Borg scale*	4 (0-7)
Pre-6MWT SpO_2**	94 ± 3.4 (85-99)
Post-6MWT SpO_2**	89 ± 5.8 (71-96)
Post-6MWT SpO_2 – Pre-6MWT SpO_2*	5.5 (0-15)
Post-6MWT HR**	110 ± 17.5 (75-142)
Maximum HR, %**	73.0 ± 11.6 (49-92)

mMRC: modified Medical Research Council scale; OCD: Oxygen Cost Diagram; BDI: Baseline Dyspnea Index; SOBQ: Shortness Of Breath Questionnaire; 6MWT: six-minute walk test; 6MWD: six-minute walk distance; and VAS: visual analogue scale. *Results expressed as median (range). **Results expressed as mean ± SD (range).

The correlations among dyspnea scales, dyspnea questionnaires, pulmonary function tests, and 6MWT parameters are shown in Table 4.

The post-6MWT FEV_1 and post-6MWT SpO_2 correlated best with the BDI and the SOBQ score. The scores on these scales, as well as on the mMRC scale, showed the best correlations with 6MWD.

Inspiratory capacity, expressed in absolute values, did not correlate with any of the dyspnea scales evaluated. The same occurred when inspiratory capacity was expressed as a percentage of the predicted value (data not shown).

There were significant correlations between the 6MWD and inspiratory capacity, as well as between the 6MWD and FVC (r_s = 0.57 and r_s = 0.54, respectively). Significant but weaker correlations were observed between the 6MWD and FEV_1, between the 6MWD and VC, and between the 6MWD and post-6MWT SpO_2.

The anthropometric data (age and height) correlated with the 6MWD. These data were included, together with the various dyspnea scales, in an anterograde multivariate regression model in order to determine their effect on the 6MWD. The final model selected three variables. The first variable that was selected was the BDI, with a coefficient of determination of 0.23, and the inclusion of the variables "age" and "height" increased the coefficient to 0.43. Other dyspnea scales were not selected.

A similar procedure was used in order to correlate the 6MWD with the anthropometric variables, the functional variables (in absolute values), and the post-6MWT SpO_2. Only inspiratory capacity was selected by the model, with a coefficient of determination of 0.32.

Discussion

The results of the present study indicate that the evaluation of symptomatic patients with COPD should take into account multiple variables, which, although interrelated, express different aspects of the disease.

In pulmonary function tests performed prior to the study outset, many of our patients presented a postbronchodilator increase in FEV_1 > 10% higher than the predicted value. Cases such as these should not be excluded from COPD studies.[19]

Table 3 - Spearman's correlations among dyspnea scale scores, dyspnea questionnaire scores, and the Body mass index, airway Obstruction, Dyspnea, and Exercise capacity index.

Parameter	mMRC	OCD	BDI	SOBQ	VAS[a]	Borg[a]	BODE
mMRC	1.00						
OCD	–0.31*	1.00					
BDI	–0.60**	0.50**	1.00				
SOBQ	0.53**	–0.49**	–0.73**	1.00			
VAS[a]	0.40**	–0.40**	–0.40**	0.59**	1.00		
Borg[a]	0.48**	–0.36**	–0.36**	0.53**	0.79**	1.00	
BODE index	0.65**	–0.29*	–0.59**	0.62**	0.50**	0.41**	1.00

mMRC: modified Medical Research Council scale; OCD: Oxygen Cost Diagram; BDI: Baseline Dyspnea Index; SOBQ: Shortness Of Breath Questionnaire; VAS: visual analogue scale; and BODE: Body mass index, airway Obstruction, Dyspnea, and Exercise capacity index. [a]At the end of the six-minute walk test. *$p < 0.05$. **$p < 0.01$.

Table 4 - Correlations among dyspnea scale scores, dyspnea questionnaire scores, pulmonary function test results, and six-minute walk test results.

Parameters	mMRC	OCD	BDI	SOBQ	VAS[a]	Borg[a]	6MWD
FVC, L	−0.13	0.00	0.28*	−0.22	−0.09	0.03	0.54**
FEV_1, L	−0.16	0.10	0.37**	−0.37**	−0.29*	−0.16	0.44**
FEV_1, %	−0.12	0.11	0.31*	−0.39**	−0.43**	−0.24	0.18
FEV_1/FVC	−0.03	0.17	0.20	−0.29*	−0.28*	−0.26	−0.05
IC, L	−0.12	−0.02	0.23	−0.21	−0.10	0.01	0.57**
SVC, L	−0.05	−0.03	0.20	−0.11	0.07	0.13	0.49**
SpO_2	−0.20	0.10	0.34*	0.35*	−0.25	−0.29	0.31*
Maximum HR	0.04	0.13	−0.03	0.14	0.16	0.24	0.15
Maximum HR, %	0.05	0.13	−0.05	0.10	0.11	0.17	0.03
6MWD	−0.51**	0.25	0.47**	−0.46**	−0.28*	−0.17	1.00

mMRC: modified Medical Research Council scale; OCD: Oxygen Cost Diagram; BDI: Baseline Dyspnea Index; SOBQ: Shortness Of Breath Questionnaire; VAS: visual analogue scale; 6MWD: six-minute walk distance; IC: inspiratory capacity; and SVC: slow vital capacity. [a]At the end of the six-minute walk test. *$p < 0.05$. **$p < 0.01$.

The mean 6MWD was 432 m. The BODE index guidelines define an extremely short 6MWD as < 350 m.[18] In the present study, the 6MWD was < 350 m in only 4 individuals (8%). In the present study, the 6MWT was clearly a submaximal test, as evidenced by the maximum HR attained at the end of the test (72% of the predicted value).

Dyspnea is a sensation of respiratory discomfort and is therefore a symptom. The evaluation of the degree of dyspnea provides an independent dimension that is not provided by pulmonary function tests or by measuring dyspnea in an exercise laboratory. The degree of dyspnea influences and predicts health-related quality of life, as well as survival, more broadly than do physiological measurements.[20,21] The pathophysiology of dyspnea varies according to the disease in question. In patients with COPD, dyspnea can occur due to dynamic hyperinflation, neuromechanical dissociation, gas exchange abnormalities, and inspiratory muscle weakness, as well as to cognitive and psychological influences. None of the instruments that are currently available to evaluate dyspnea address all aspects of this symptom. There are unidimensional scales, such as the VAS and the Borg scale, which take into account only one aspect of dyspnea, activity-based unidimensional scales (the mMRC scale and the OCD), and indirect, multidimensional scales, such as the BDI and the SOBQ, which are also activity-based but address various other aspects of dyspnea. The dyspnea scales are validated (i.e., considered to have construct validity) when their scores are shown to correlate with other variables that reflect correlated phenomena, such as the degree of pulmonary dysfunction and exercise capacity. The various dyspnea scales were developed in order to quantify limitations in the activities of daily living due to dyspnea, and interrelations among the scales are therefore expected.[22]

In the present study, the best interscale correlations were between the two scales that were used at the end of the 6MWT (the Borg scale and the VAS) and between the two multidimensional scales (the BDI and the SOBQ). These findings are not surprising. The Borg scale and the VAS are useful for measuring dyspnea after a certain task, such as an exercise test. These instruments are useful in measuring dyspnea at a given time point. However, they play a limited role in longitudinal measurements.

The MRC scale has been used for decades. Patients were originally categorized into 5 grades, ranging from 1 ("normal") to 5 ("too dyspneic to leave the house"). Subsequently, the ATS published a revised version, designated the mMRC scale, in which dyspnea grades range from 0 to 4.[7] The revised scale focuses primarily on dyspnea that occurs during walks. Because it evaluates only the dyspnea that is related to specific activities, the scale does not allow a multidimensional evaluation of dyspnea. In addition, the mMRC scale does not readily detect changes in the degree of dyspnea after a therapeutic intervention.[11] The mMRC scale is widely used in patients with COPD because it is simple and easy to use, as well as correlating with quality of life and prognosis.[21] The OCD

is similar to the mMRC scale in that it is a unidimensional scale related to activities of daily living.

One group of authors developed a dyspnea scale divided into two parts: baseline dyspnea (the BDI) and transition dyspnea.[9] The objective of the BDI is to provide a cross-sectional measure of dyspnea, whereas that of the transition dyspnea index is to measure the variation in dyspnea in relation to the baseline value. The scale is divided into three categories: functional impairment; magnitude of task; and magnitude of effort. The category "functional impairment" evaluates whether dyspnea has resulted in limitations or incapacity related to activities of daily living or work. Similarly to the mMRC scale, the category "magnitude of task" evaluates the types of tasks that provoke dyspnea. The category "magnitude of effort" evaluates to what degree patients can exert themselves without experiencing dyspnea, including whether they must frequently interrupt a habitual activity that involves repeated effort. The Transition Dyspnea Index ranges from 0 (severe) to 4 (no impairment) in each category, and the total score therefore ranges from 0 to 12 points.

The SOBQ was developed by researchers at the University of California at San Diego.[10] This questionnaire requires patients to indicate how often they develop dyspnea in 21 activities of daily living, associated with various levels of exertion, on a 6-point scale, which ranges from 0 (never) to 5 (maximum dyspnea or inability to perform the activity due to dyspnea). Three additional questions, also on a 6-point scale (limitations in daily living due to dyspnea, fear of becoming ill during excessive effort, and fear of dyspnea), are included, totaling 24 items. The total score ranges from 0 to 120. To our knowledge, the present study is the first to use the SOBQ in Brazil, and the correlations we found between this questionnaire and the remaining dyspnea scales were similar to those reported in a study conducted in the United States,[10] suggesting that the SOBQ is valid for use in Brazil. In the aforementioned study,[10] 143 patients with COPD and airflow obstruction ranging from mild to severe were evaluated. The results showed that, of the various dyspnea scales evaluated, the SOBQ and the BDI presented the highest levels of reliability and validity. In the present study, there was a strong correlation between these two instruments, and both showed better correlations with FEV_1, SpO_2, and 6MWD than did the remaining scales. Based on the multivariate analysis, the BDI was selected as the scale that best correlated with the 6MWD.

The 6MWD correlates with the efforts expended in the activities of daily living and complements the evaluation of COPD.[4] We found that the 6MWD correlated well with the mMRC scale score, the BDI, and the SOBQ score, as well as with the various spirometric parameters. Neither the OCD score nor the Borg scale score correlated with the 6MWD.

In the present study, SpO_2 was significantly, albeit weakly, correlated with the 6MWD, the BDI, and the SOBQ score. However, SpO_2 did not correlate with the mMRC scale score. Post-6MWT SpO_2 has prognostic value in COPD.[23]

The correlation between dyspnea and airflow obstruction in COPD is weak or nonexistent.[3,24] With the exception of the VAS score, the unidimensional scale scores did not correlate well with the spirometric parameters. However, the BDI, SOBQ score, and VAS score showed weak, but significant, correlations.

Inspiratory capacity at rest (in absolute values) did not correlate with any of the dyspnea scale scores. In COPD patients, inspiratory capacity decreases during exertion, such as that occurring during walk tests,[25] even in patients with mild obstruction.[26] When anthropometric variables, functional variables, and SpO_2 were included in the multivariate model with the 6MWD, only inspiratory capacity was selected. In another study conducted in Brazil,[27] inspiratory capacity was the best predictor of 6MWD.

One group of authors[28] divided COPD, according to the dyspnea scores obtained with the SOBQ, BDI, and mMRC scale, into three categories: category 1 (SOBQ, 0-40; BDI, 9-12; mMRC, 0-1); category 2 (SOBQ, 41-80; BDI, 5-8; mMRC, 2); and category 3 (SOBQ, 81-120; BDI, 1-4; mMRC, 3-4). If we adopted this categorization, most of our patients would fit into category 2 (based on the BDI and the SOBQ scores) or category 1 (based on the mMRC scale scores).

In a review of the application of dyspnea and quality of life scales in COPD,[29] it was concluded that a unidimensional scale can be used if applied in conjunction with specific quality of life scales. Alternatively, a multidimensional scale, which

correlates better with quality of life, can be used. The BDI can be used for that purpose. The BDI correlates well with quality of life scores in COPD, and the changes in quality of life after rehabilitation correlate with the variations in the Transition Dyspnea Index.[30]

The limitations of the present study include the relatively narrow spectrum of disease severity and the fact that only one observer administered the questionnaires, reproducibility therefore not being evaluated.

The SOBQ was evaluated for the first time in Brazil, and the questionnaire proved useful in the evaluation of patients with COPD. The advantage of this questionnaire is that it evaluates the emotional aspect of dyspnea, which the other instruments do not address.

The results of the present study underscore the fact that the correlations between functional parameters and dyspnea are weak. The results also indicate that the VAS is superior to the Borg scale and that the OCD is of little use. In addition, we can conclude that multidimensional instruments are required in order to quantify dyspnea during the monitoring of outpatients with COPD and chronic dyspnea. The use of such instruments can guide decisions regarding the treatment of these patients and thereby improve the prognosis.

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