Confirmatory Evaluation of the Modified Medical Research Council Questionnaire for Assessment of Dyspnea in Patients with Chronic Obstructive Pulmonary Disease in Portugal

Análise Confirmatória do Questionário Medical Research Council para Avaliação da Dispneia em Doentes com Doença Pulmonar Obstrutiva Crónica em Portugal

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ABSTRACT

Introduction: The Modified British Medical Research Council Questionnaire is considered an adequate and simple measure of breathlessness in chronic obstructive pulmonary disease. It is widely used in clinical practice in Portugal, but it still lacks confirmatory evaluation for the Portuguese setting. The aim of this study was to perform a cultural adaptation and validation of the Modified British Medical Research Council Questionnaire so that its most suitable version can be made available to researchers and clinicians in Portugal.

Material and Methods: We performed a cross-sectional descriptive study involving patients with chronic obstructive pulmonary disease aged 40 years or older. We applied the Modified British Medical Research Council Questionnaire and the previously validated Portuguese-language version of the clinical questionnaire for chronic obstructive pulmonary disease between January and June 2019. We determined the agreement between the two questionnaires with kappa agreement, with a 95% confidence interval, and we used Spearman correlation to find a correlation between two scores.

Results: The study included 65 patients managed in a hospital pulmonology clinic (aged 68 ± 7 years; with predicted FEV_1 of 49.86% ± 16.5%). The Modified British Medical Research Council scale correlated significantly with all the domains and the overall score of the clinical questionnaire for chronic obstructive pulmonary disease ($0.46 < r < 0.68$; $p < 0.001$). In bilingual patients, interclass correlation coefficient was 0.912 ($p < 0.001$).

Conclusion: The Portuguese version of the Modified British Medical Research Council Questionnaire is a valid instrument for measurement of breathlessness in chronic obstructive pulmonary disease.

Keywords: Portugal; Pulmonary Disease, Chronic Obstructive; Reproducibility of Results; Surveys and Questionnaires

RESUMO

Introdução: O Questionário *British Medical Research Council* (mMRC) Modificado é considerado um instrumento adequado e simples para a medição da dispneia na doença pulmonar obstrutiva crónica (DPOC). Tem sido amplamente usado na prática clínica em Portugal, mas carece de avaliação confirmatória para o cenário português. O objetivo deste estudo é realizar a adaptação cultural e validação do Questionário *British Medical Research Council* Modificado para que a versão mais adequada possa estar disponível a investigadores e clínicos em Portugal.

Material e Métodos: Realizamos um estudo descritivo e transversal com doentes com doença pulmonar obstrutiva crónica e idade ≥ 40 anos. Aplicamos o Questionário *British Medical Research Council* Modificado e o questionário clínico para a doença pulmonar obstrutiva crónica previamente validado para a língua portuguesa, entre janeiro e junho de 2019. Determinámos a concordância entre os dois questionários com *kappa agreement*, com 95% de intervalo de confiança, e usámos o coeficiente de correlação de Spearman para determinar a correlação entre os dois *scores*.

Resultados: O estudo incluiu 65 doentes seguidos em consulta hospitalar de Pneumologia (idades de 68 ± 7 anos; com FEV_1 49,86% ± 16,5% do predito). A Escala Modificada do *British Medical Research Council* correlacionou-se significativamente com todos os domínios e pontuação total do questionário clínico ($0,46 < r < 0,68$; $p < 0,001$). Nos doentes bilingues, o coeficiente de correlação interclasse foi 0,912 ($p < 0,001$).

Conclusão: A versão portuguesa do Questionário Modificado do *British Medical Research Council* é um instrumento válido para a medição da dispneia na doença pulmonar obstrutiva crónica.

Palavras-chave: Estudos Validação; Doença Pulmonar Obstrutiva Crónica; Inquéritos e Questionários; Portugal; Reprodutibilidade dos Testes

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by progressive airflow obstruction, with a consequent decrease of functional capacity. Airflow limitation and dyspnea significantly affect patients' quality of life.[1]

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This disease causes over three million deaths worldwide every year, and the World Health Organization has predicted that COPD will become the third most common cause of death in the world by 2030.[2,3] A study published in 2013 found that the estimated prevalence of COPD in the Lisbon region (Portugal) was 14.2% in adults aged 40 or older, although it is often underdiagnosed.[4]

The major risk factor for the development of COPD is cigarette smoking, but other environmental factors, such as exposure to air pollutants, may contribute as well.[5] Diagnosis requires spirometry testing in subjects with a history of exposure to known risk factors and symptoms such as dyspnea and/or chronic cough with sputum production.[6]

Chronic and progressive dyspnea is the most characteristic symptom of COPD, but cough with sputum production is also frequent.[7] Chronic respiratory symptoms may precede spirometric abnormalities, although the patients' symptoms should be adequately assessed since they can be used to develop earlier and appropriate interventions.[7]

The Modified British Medical Research Council (mMRC) Questionnaire is considered an adequate and simple measure of breathlessness in COPD, and it is easy to apply and understand.[8,9] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019 report recommends a combined COPD assessment that includes the use of mMRC in the assessment of dyspnea.[7] The tool already has an European Portuguese version, which is widely used in daily practice, but it lacks confirmatory evaluation.[10] It is important to understand whether a valid and suitable version of the questionnaire is being used in the Portuguese population.

The aim of this study was to perform a cultural adaptation and validation of the Modified British Medical Research Council Questionnaire

MATERIAL AND METHODS

We obtained the Portuguese version of the mMRC Questionnaire using a translation and back-translation carried out by a committee specially created for this purpose. The original version of the mMRC Questionnaire was translated into Portuguese by three independent translators. Another three independent translators performed the back-translation process. The final versions were merged into one by a committee whose members were fluent in English, and the final version was compared with the original version. The committee made all the adjustments, converged, and approved one final Portuguese-language version (see Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/15208/Appendix_01.pdf). The equivalence between the two versions (English and Portuguese) was also evaluated. Previously, eleven bilingual individuals completed both versions, first the original version and then the Portuguese translation after a week. We calculated correlations between the scores obtained with both versions.

We performed this cross-sectional descriptive study at the COPD clinic in Centro Hospitalar e Universitário de Coimbra from January to June 2019.

The inclusion criteria of the study were a) COPD diagnosis confirmed by spirometry (with a post-bronchodilator FEV_1/FVC *ratio* < 0.7) at least six months before the study period; b) age of 40 years or above; c) attendance at the COPD clinic of the Centro Hospitalar e Universitário de Coimbra – Hospital Geral during the study period.

We applied the following exclusion criteria: a) history of conditions that could influence the dyspnea-related disability, such as asthma, active pulmonary tuberculosis, lung cancer, or pulmonary resection; b) non-pulmonary diseases considered to be disabling, severe, or difficult to control; c) infections or hospitalization within the last three months; d) history of COPD exacerbation (defined as an acute worsening of respiratory symptoms that results in additional therapy) within the last 6 weeks; e) medication change within the last four weeks; f) cognitive deterioration with inability to understand the questionnaire.

For the purposes of the final study, we used a convenience sample, until it reached at least n = 50 of respondents. This protocol was approved by the Human Research Ethics Committee of the Portuguese Regional Health Administration of the Center and every patient provided informed consent before being enrolled in the study.

The mMRC Questionnaire comprises five items. We gave the Portuguese version to each patient and instructed him or her to read the descriptive statements and then select the number which best fit his or her shortness of breath. The Clinical Questionnaire for COPD (CCQ) for the European Portuguese language, validated in 2012, was also applied in order to analyze the correlation between the two questionnaires.[11]

We also obtained patient spirometric and socioeconomic data (age, sex, and educational level).

The mMRC dyspnea scale is a simple grading system for assessing dyspnea levels and is used for grading the impact of dyspnea on daily activities. There are five statements graded from 0 ("Not troubled by breathlessness except during strenuous exercise") to four ("Too breathless to leave the house or breathless when dressing or undressing"). Patients select the statement that most closely corresponds with their level of impairment.[12] In order to assess the severity of dyspnea, GOLD primarily recommends using the mMRC dyspnea Questionnaire.[9] The mMRC Questionnaire is a reliable measure that correlates favorably with lung function measurements, and it is a suitable tool for assessing symptoms in routine clinical practice.[1,8]

The CCQ is a clinical tool for evaluating the health status (symptoms, functional status and mental status) of people with COPD. The questionnaire comprises three domains and 10 items with an overall score consisting of symptoms (four items), functional state (four items), and mental state (two items). Participants must answer the CCQ questions, based on their experience in the last seven days, on a Likert-type scale that assumes the following values: 0) never, 1) hardly ever, 2) a few times, 3) several times, 4) many times, 5) a great many times, and 6) almost all the time.

The total score ranges from 0 to 60. The primary outcome measure of CCQ is the mean total score (divided by 10 items), with higher scores representing a worse health status and quality of life.[11]

We summarized the characteristics of the study population using descriptive statistical methods with percentage, mean, and standard deviation (SD).

The agreement between these two questionnaires was determined with kappa agreement with a 95% confidence interval. Spearman correlation was used to find a correlation between the two scores. We performed all calculations using SPSS Statistics version 26®.

The primary outcome was the concordance of GOLD classification while using mMRC and CCQ. We used the cut-off points at mMRC two and CCQ 1.5 to allocate patients into each GOLD classification.

We did not perform test-retest agreement, since the participants were patients who attended a hospital outpatient clinic and were not hospitalized.

RESULTS

We characterized the group of patients included in the present study (n = 65) with moderate to severe obstruction, as well as with a small rate of exacerbation (Table 1).

Out of all respondents, 4.62% and 12.31%, respectively, scored in the highest category (4) and the lowest category (0) on the mMRC, showing we did not reach a ceiling effect. Comparing the results from both questionnaires, 13.85% (n = 9) of the respondents who had a mMRC score < 2 had a CCQ score ≥ 2. On the other hand, 6.15% (n = 4) of the respondents who had a mMRC score ≥ 2 got a CCQ score < 2 (Table 2).

The mMRC scale correlated significantly with all the domains and the overall score of the CCQ ($0.46 < r < 0.68$; $p < 0.001$) (Table 3).

The mean administration time for mMRC was 58 ± 0.4 seconds. The bilingual patient interclass correlation coefficient was 0.912; $p < 0.001$. Cronbach's alpha was not possible to calculate due to scale characteristics. We also got no blank answers, showing that the mMRC Questionnaire seems to be adequate and feasible.

DISCUSSION

Although it has been used in various studies in different

Table 1 – Sample baseline characteristics

Characteristics	n	(%)	Mean (± SD)
Age (years)			68 (± 7)
Sex (Male)	56	86.15	
Weight (kg)			66.98 (± 9.55)
BMI (kg/m^2)			23.4 (± 3.9)
FEV$_1$% predicted			49.86 (± 16.5)
Gold A	23	35.40	
B	26	40.00	
C	7	10.80	
D	9	13.80	
Smoking history	46	70.77	
Current smoker	4	6.15	
Exacerbations in the last 12 months			
0	28	43.08	
1	21	32.31	
≥ 2	16	24.62	
mMRC dyspnea			1.77 (± 1.12)
0 - 1	30	46.15	
≥ 2	34	52.31	
CCQ total			2.13 (± 0.89)
CCQ Symptoms			2.33 (± 1.15)
CCQ Functional State			2.40 (± 1.20)
CCQ Mental State			1.20 (± 1.20)
CCQ total			2.12 (± 0.92)
Acceptable (CCQ < 1)	6	9.23	
Acceptable for moderate disease (1 ≤ CCQ < 2	19	29.23	
Instable-severe limited (2 ≤ CCQ < 3)	27	41.54	
Very instable-very severe limited (CCQ ≥ 3)	13	30.00	

Table 2 – mMRC questionnaire results and percentage of overlap between mMRC and QQC questionnaires (< 2 versus ≥ 2 scores)

mMRC	n	%
0	8	12.31
1	22	33.85
2	15	23.08
3	17	26.15
4	3	4.62
mMRC 0 - 1	30	46.15
mMRC ≥ 2	35	53.85

mMRC < 2 (n/%)		**mMRC ≥ 2** (n/%)	
CCQ < 2 (n/%)	CCQ ≥ 2 (n/%)	CCQ < 2 (n/%)	CCQ ≥ 2 (n/%)
21/32.3%	9/13.8%	4/6.15%	31/47.7%

Table 3 – Associations between mMRC and QQC scores

CCQ domains *vs* mMRC	*r*	*p*
Symptoms QQC *vs* mMRC	0.52	< 0.001
Functional state CCQ *vs* mMRC	0.46	< 0.001
Mental State CCQ *vs* mMRC	0.68	< 0.001
CCQ Total *vs* mMRC	0.66	< 0.001

languages, we found no description of the validation process or of the cultural and social adaptation of the Portuguese version of the mMRC apart from a translation and validation for the Brazilian setting.[1] This study conducted in Brazil showed that the Portuguese-language version for the Brazilian cultural and social scenario proved reproducible and valid for patients with COPD.[1]

We chose the CCQ as the validation criterion for the European Portuguese language version and cultural adaptation of the mMRC Questionnaire because it is considered as an instrument with proven validity and is widely used in scientific research.[11] There is evidence that both CCQ and mMRC scores have inter-equality and reliability.[13]

The mMRC Questionnaire correlated significantly with all the domains and with the overall score of the CCQ, showing that the translated version is valid (Table 3).

According to GOLD 2019, COPD patients should undergo assessment of either dyspnea using mMRC or symptoms using CAT™. By combining the risk of exacerbation with the score of one of these tools, patients can be grouped in the clusters “A, B, C, D”. The pharmacological approach is different for each cluster profile. Since therapy can have prognostic implications, it is important that we trust the results that are being measured, which further strengthens this validation study and paves the way to a future validation of CAT™ for European Portuguese. In addition, the importance of accurate dyspnea measurement tools, in addition to the prognostic information they provide,(whose paradigmatic example is their inclusion in the BODE index) also have significant implications for clinical practice, for example in monitoring interventions performed in patients with COPD, whether pharmacological, rehabilitation or other.

On the other hand, even though both mMRC and CAT™ are useful tools for clustering patients, they evaluate different dimensions of COPD patients. Future research could compare the performance of both tools in the different patient clusters, different care settings or even for different levels of obstruction. Different performances can lead physicians to choose the most suitable tool for the patient according to these characteristics. This hypothesis becomes even more relevant if this ‘assessment individualization model’ leads to different therapeutic strategies.

Our study only included patients with moderate to severe obstruction and with small rates of exacerbation. This limitation is comprehensive once data was collected in a hospital clinic. Nevertheless, patients with mild obstruction or patients with higher rates of exacerbation, should also be assessed because, as previously mentioned, an individualized approach can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status. In particular, patients with frequent exacerbations, due to the potential for greater symptomatic weight, are a population where the precise characterization of the degree of dyspnea variation can potentially predict important clinical declines and, therefore, it is a population of COPD patients where there is a benefit of greater inclusion in future studies. Primary care and Emergency departments can be settings of great interest for future research both with mMRC and CAT™.

We believe that further validation contributions can have major importance, with larger and more representative samples, of either patients or type of clinical setting, bearing always in mind that establishing a correlation does not imply causality.

An important limitation in this process of cultural validation and adaptation is the lack of test-retest assessment, given the clinical context in which the questionnaires were provided to patients. Test-retest reliability is important when measuring stable variables. The mMRC Questionnaire measures dyspnea, which is a variable that changes over time. Since patients could have different degrees of dyspnea on different assessments, test-retest was not performed. Despite this limitation, we believe that it is not a critical error in our methodology, and it was guaranteed that the Portuguese version of the questionnaire is an effective method for the symptomatic evaluation of the dyspnea of COPD patients. No ceiling effect was observed, like in other studies, allowing us to add validity in the evaluation of outpatients with COPD.[14]

A Portuguese study with outpatients during acute exacerbations of COPD suggests that mMRC is more sensitive to changes with interventions during acute exacerbations than in stable stages of COPD.[15]

Our study showed that the Portuguese-language version of the mMRC Questionnaire is feasible and externally valid when compared with a traditional and previously validated instrument. The confirmatory evaluation and cultural adaptation of mMRC to Portuguese patients can pave the way for future research involving patients with acute

exacerbations of COPD, even in a primary health care setting. Repeating this study with larger samples and in different locations could give more robustness to its conclusions. In future studies, the validation of the mMRC Questionnaire in palliative care may be an advantage in assessing patients with COPD in this context.

CONCLUSION

Individualization in the provision of care is increasingly both the present and future. We hypothesized that individualization, may not only be the result of an adequate evaluation, but that the evaluation itself can be improved if it becomes individualized.

Because many Portuguese COPD patients are managed in primary care, we believe it has potential for future research, both in terms of the number of potential patients, but also to assess different health care contexts. Using simple tools also has the advantage of decreasing resistance to use, especially in a scenario where there is already a high workload. Being able to have validated instruments for use in these scenarios, will be an asset in the management of patients with COPD.

The Portuguese version of the mMRC Questionnaire is a valid instrument for measurement of breathlessness in COPD patients. Although it is already widely used in clinical practice, confirmatory evaluation of this tool makes it available for use by Portuguese researchers and empowers its use by clinicians.

AUTHORS CONTRIBUTION

SAR, CSC: Design of the work, draf of the paper, final approval of the manuscript.

MV, JM, JC: Data acquisition and processing, critical review and correction of the paper, final approval of the manuscript.

CR: Critical review and correction of the paper, final approval of the manuscript.

ARM: Statistical work, critical review of the paper, final approval of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have no competing interests to report.

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