Rev Port Pneumol. 2017;xxx(xx):xxx–xxx

revista portuguesa de
PNEUMOLOGIA
portuguese journal of pulmonology
www.revportpneumol.org

ORIGINAL ARTICLE

Agreement of different reference equations to classify patients with COPD as having reduced or preserved 6MWD

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Received 28 April 2017; accepted 31 August 2017

KEYWORDS
Pulmonary disease;
Chronic obstructive;
Exercise tolerance;
Exercise test;
Walk test;
Reference values

Abstract
Background: Interpretation of the six-minute walk distance (6MWD) is enhanced by using recommended reference equations. Whenever possible, the choice of equation should be region-specific. A potential problem is that different equations for the 6MWD may have been developed for the same population, and it may be complicated to choose the most suitable.
Objective: To verify the agreement of different reference equations in classifying patients with Chronic Obstructive Pulmonary Disease (COPD) as having reduced or preserved 6MWD.
Methods: 159 patients with COPD performed the six-minute walk test according to international standardization. They were classified as having reduced 6MWD if it was below the lower limit of normal. Five Brazilian equations (Iwama; Britto1; Britto2; Dourado; Soares) and the two non-Brazilian equations most cited worldwide (Troosters; Enright) were used. The agreement for patients classified as reduced or preserved 6MWD was verified by Cohen's Kappa (pair-to-pair) analysis. The proportion of patients classified as having reduced walked distance was compared by the Chi-squared test.
Results: Agreement between equations varied largely in classifying subjects as having reduced or preserved 6MWD (Kappa: 0.10–0.82). Brazilian equations with the highest agreement were Iwama, Britto1 and Britto2 (Kappa > 0.75). The proportion of patients classified as having reduced 6MWD was statistically similar only between equations in which the agreement was higher than 0.70.

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https://doi.org/10.1016/j.rppnen.2017.08.007

Please cite this article in press as: Machado FVC, et al. Rev Port Pneumol. 2017. https://doi.org/10.1016/j.rppnen.2017.08.007

Conclusion: Even reference equations from the same country vary considerably in the classification of reduced or preserved 6MWD, and it is recommended that the region-specific ones be used as they give with higher agreement for similar and comparable interpretation of the patients' functional exercise capacity.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is defined, according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD),[1] as ''*a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases*''. A consequence of these abnormalities is air trapping, which leads to dyspnea and lung hyperinflation.[1,2] Thus, patients are thrust into a vicious cycle of COPD symptoms and are liable to decrease their level of physical activity in daily life, adopting a predominantly sedentary lifestyle.[3,4] Furthermore, physical inactivity may lead to deconditioning as well as to systemic consequences, such as peripheral muscle weakness, impaired quality of life and functional status, body composition abnormalities, and poor exercise capacity,[1,5] resulting in an increase in the intensity of symptoms.

Exercise intolerance is a common finding in patients with COPD and is known to be multifactorial.[1,6] Hence, its evaluation is essential in research and clinical settings, since it plays an important role in disease progression.[7] Field tests, such as the six-minute walk test (6MWT), are available and have been widely used to assess functional exercise performance in these patients,[7,8] the 6MWT is easy to perform, inexpensive and highly reproducible.[7,9] Moreover, it provides the most comprehensive prognostic information available in the majority of chronic respiratory diseases.[7] In addition, it is used to prescribe training intensity[10] and to verify the effectiveness of interventions,[8] besides being a predictor of morbidity and mortality in COPD.[11]

Interpretation of the 6MWT is enhanced if reference values are obtained through the use of equations which consider anthropometric, demographic and/or physiological variables of a population. These equations predict the expected ''normal'' distance to be walked during the test for a given patient. Different authors have proposed reference values for the six-minute walk distance (6MWD, *i.e.*, the distance achieved in the test).[12–17] It is worth noting that there is a large number of available equations in Brazil[14–17] and these equations are composed of similar predictors, despite having quite variable coefficients of determination. Some related aspects still remain unknown, such as whether or not these equations agree in classifying patients as having reduced or preserved 6MWD. This information would be valuable and could help avoid differences in the clinicians and researchers' interpretation of the patient's functional exercise capacity. Thus, the aim of this study was to verify the agreement of different reference equations (five from Brazil and two from other countries) in classifying COPD patients as having reduced or preserved 6MWD.

Methods

Design and sample

A cross-sectional study was conducted with a convenience sample of patients with stable COPD enrolled at the Pulmonary Outpatient Clinic and Rehabilitation Center at the University Hospital of the State University of Londrina (HU/UEL), Londrina, Brazil. The study was approved by the Research Ethics Committee of the institution (number 123/09), and all participants gave written informed consent.

Inclusion criteria were: diagnosis of COPD according to the GOLD[1]; no exacerbation in the last three months, or any severe comorbidity which could interfere with the performance of the tests; not having attended to any formal exercise program in the preceding year. Subjects were excluded if they could not complete the research protocol due to any physical hindrance to their performance.

Assessments

Demographic (gender and age) and anthropometric (height [cm], body weight [kg] and body mass index [kg/m^2]) data were collected. Pulmonary function was evaluated by spirometry using a portable spirometer (Spirobank G®; MIR, Italy). The test procedures were performed according to American Thoracic Society (ATS)/European Respiratory Society (ERS) standardization.[18] Reference values used were proposed by Pereira et al.[19] for the Brazilian population.

The 6MWT, used to evaluate the functional exercise capacity, was performed according to international recommendations.[8] Heart rate, blood pressure, oxygen saturation, dyspnea and fatigue perception according to the modified Borg scale (0–10)[20] were recorded before and immediately after finishing the test. The predicted values for the 6MWD were calculated according to five reference equations[14–17] developed specifically for the Brazilian population (Iwama; Britto1; Britto2; Dourado; Soares) and two non-Brazilian equations[12,13] which are the most frequently cited worldwide, according to Web of Science™ as of January 2017 (Troosters; Enright) (Table 1). The lower limit of normal (LLN) for each reference equation (one-tailed) was

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