EDITORIAL

6-minute walk testing in COPD: is it reproducible?

G. Criner

The 6-min walk test (6MWT) has historically been used to characterise the functional status of chronic obstructive pulmonary disease (COPD) patients. However, over the past few years, the 6MWT has assumed a more central role in the assessment and management of COPD. In COPD, the 6MWT is now routinely used as an outcome measure in clinical trials [1, 2], a prognostic indicator either by itself [3] or as part of a multidimensional index [4], and as a functional threshold that patients must achieve before being considered acceptable candidates for lung volume reduction surgery (LVRS) [2] or lung transplantation [5]. Much of the attraction of the 6MWT as an assessment tool in COPD is due to its simplicity of performance, inexpensiveness, responsiveness to standardisation and embodiment of an important functional task (*i.e.* ambulation). New insights that the manifestations of COPD go well beyond the lung, and include its cardiac and peripheral muscle wasting effects, are additional factors that make a test of functional performance like the 6MWT attractive as an assessment tool [6]. However, to be considered a reliable tool in the assessment of COPD patients, the performance of the 6MWT must be proven to be reproducible in clinical trials as well as in commonly encountered clinical settings.

Many variables may affect the performance of a 6MWT. These variables include course length, course layout (linear, oval or continuous circle), whether a practice walk is done before the final walk, and whether the better of two walks or the second of two walks should be taken as the final walk distance. The impact of a learning effect on the distance walked during a 6MWT in COPD has been the focus of multiple small studies over the past three decades. LEACH *et al.* [7] attributed a 14.9% improvement in subsequent 6MWT performances in 30 hypoxaemic patients with COPD and/or restrictive diseases to a learning effect. SWINBURN *et al.* [8] reported a 16% increase in 6MWTs conducted in 17 COPD subjects who performed four successive 12-min walks over a period of 1 week. STEVENS *et al.* [9] performed three 6-min walks in 21 COPD patients on separate days and found a mean increase of 10% on the second test and a further 3% increase in distance walked on the third test.

In a large, multicentre clinical trial that evaluated the use of LVRS *versus* medical treatment, the National Emphysema Treatment Trial studied the reproducibility of the 6MWT and the impact of course layout on 6MWT performance in 470 severe emphysema patients that had two 6MWTs on subsequent days [10]. The second 6MWT performed on the

subsequent day improved by a mean $\pm$ SD of $7.0 \pm 15.2\%$ or 66.1 ± 146 feet (intraclass correlation coefficient (ICC) 0.88; $p < 0.0001$). Additionally, 70% of the patient population improved on the second day. Course layout was also reported to significantly impact the distance walked. Patients who were tested on a continuous course (circular or oval) walked 92.2 feet (28.1 m) farther than those tested on a linear course layout.

In this issue of the *European Respiratory Journal* (ERJ), HERNANDES *et al.* [11] contribute to our understanding of the reproducibility of the 6MWT performed in the assessment of a large number of COPD patients with a wide range of disease severity, in a clinical setting. In a retrospective observational study, the authors studied the reproducibility of two 6MWTs performed on subsequent days in 1,514 COPD patients (forced expiratory volume in 1 s $45 \pm 18\%$ predicted; 41% female). Measurements of body composition, dyspnoea and comorbidity (Charlson Index) were also performed. Patients had a range of COPD severity (5% Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage I, 31% GOLD II, 44% GOLD III and 20% GOLD IV) and comorbidities (59% Charlson index < 1 , 23% Charlson index < 2 and 18% Charlson index > 2). Patients who used walking aids in normal daily life were allowed to use them during performance of the 6MWTs. 32% of the patient population used a rollator during the 6-min walk and 1.3% used a stick. 24% of patients used ambulatory oxygen. The 6MWT was reproducible (ICC 0.93; $p < 0.0001$), but patients walked further in the second test by an average of 27 m or 7% of the first test distance (391 m (95% CI 155–585 m) *versus* 418 m (95% CI 185–605 m); $p < 0.0001$). 82% of the patients improved in the second test. Factors that determined an improvement ≥ 42 m in the second walk test (upper limit of minimal clinically important difference) included initial 6-min walk distance < 350 m, Charlson index < 2 and body mass index < 30 kg·m⁻² (OR 2.49, 0.76 and 0.60, respectively). However, none of these factors determined a decrease in performance of the second walk tests. Notably, no differences were noted when comparing changes in the two walk distances based on disease severity by GOLD stage.

Reasons for the improved performance in the second 6MWTs are not entirely known but may include motivational factors, better pacing, or familiarity with the 6MWT process or course layout. It is reassuring that the two largest trials that have looked at reproducibility with the 6-min walk, one a large multicentre trial of severe emphysema patients [10] and the other an observational report conducted in COPD patients with a range of severity [11], report the same magnitude of improvement on the subsequent test: 7% in both studies.

CORRESPONDENCE: G. Criner, Temple University, 745 Parkinson Pavilion, 3401 North Broad Street, Philadelphia, PA 19140, USA. E-mail: Gerard.Criner@tuhs.temple.edu

Moreover, both studies demonstrated that the majority of patients (70% [10] and 82 % [11]) had an improved 6-min walk distance on the second test. HERNANDES *et al.* [11] extend our knowledge further by demonstrating that the presence of multiple comorbidities, obesity and poorer performance on the first 6-min walk may influence walking distance improvement on the second test.

So what are the implications of this study to the use of the 6MWT by the clinical researcher or clinician? Clearly, clinical trials that utilise 6MWT as an outcome variable must account for the learning effect when designing their study protocols. The use of an appropriate control group, spacing the 6-min walks several weeks apart to minimise the learning effect or the use of repeated tests, as outlined by HERNANDES *et al.* [11] and SCIURBA *et al.* [10], may be ways to minimise any impact of the learning effect clouding the interpretation of the 6-min walk as an outcome parameter in a clinical trial. In clinical scenarios where it is crucial for patients to achieve an established threshold to be considered a viable candidate for surgical intervention (*e.g.* lung transplantation or LVRS), a practice walk or 6-min walks on subsequent days should be considered to obtain data that reflects the patient's optimum walk performance and utilise the learning effect to maximise their performance.

Because the 6-min walk is a simple measure of integrated cardiopulmonary and musculoskeletal function, it is rightly becoming an essential tool in the assessment profile of the COPD patient. Studies like the one reported in this issue of the *ERJ* by HERNANDES *et al.* [11] are essential in demonstrating the reliability and applicability of the 6MWT as a COPD assessment tool in routinely encountered clinical scenarios.

STATEMENT OF INTEREST

None declared.

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