

## Six-minute walk test in chronic respiratory disease: Easy to perform, not always easy to interpret

Teste da caminhada de seis minutos na doença respiratória crônica: Simples de realizar, nem sempre fácil de interpretar

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*“The art of simplicity is a puzzle of complexity. . .”*

– Douglas Horton, 1891-1968

Chronic respiratory diseases are habitually accompanied by a (variable) reduction in the ability to perform activities of daily living with a degree of discomfort considered “acceptable” by individuals. In fact, it has long been held that standardized measurement of physical performance during a simple test involving an activity with which patients are familiar can provide clinically useful information regarding the ability of patients to face the increased physical demands that characterize daily life.

In this context, it would be highly desirable to have a test with the following characteristics: a) involving the dislocation of the entire body mass (“dynamic exercise”) during an activity that is common to most individuals; b) being of sufficient duration for the physiological adjustments to the exercise to reach some degree of stability but not long enough to be limited by symptoms; and, last but not least, c) the intensity of the effort put forth being defined by the patients—although they are aware that their degree of exercise tolerance will be measured—meaning that patients will pace themselves on the basis of how much farther they have to go. Such premises seem to be addressed by a walk test (premise a) that lasts six minutes (premise b) and is performed at a pace defined by patients, with standardized encouragement (premise c).<sup>(1)</sup> The applications of this test in different settings and clinical populations constitute the subject of an extensive and timely review article published in this issue of the Brazilian Journal of Pulmonology.<sup>(2)</sup> In that review, Morales-Blanhir et al. emphasize that, although the six-minute walk test (6MWT) provides limited information regarding the underlying mechanisms of exercise intolerance, the test can, when performed in accordance with a standard protocol,<sup>(1)</sup> provide the following indicators: of functional capacity—based on the six-minute walk distance

(6MWD); of the integrity of intrapulmonary gas exchange—based on oxygen-hemoglobin saturation; of cardiovascular stress—based on the heart rate; and of the stress associated with submaximal exercise—based on dyspnea and fatigue scores. Contrary to what the title of the review article suggests,<sup>(2)</sup> the 6MWT cannot be characterized as a test to assess respiratory dysfunction exclusively, because any physical activity involves the integrated functioning of multiple organ systems. However, the procedure has undoubtedly passed “the test of time”, and, as appropriately reviewed by the authors, there is clear evidence that the 6MWT is useful in different populations.

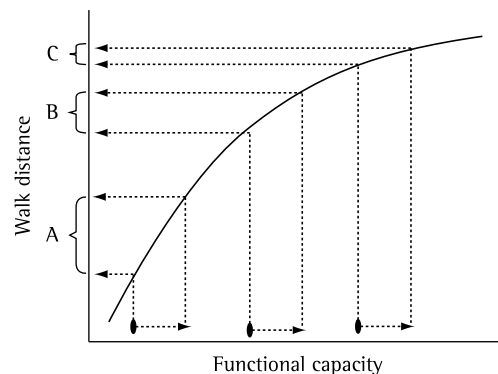
Paradoxically, the interpretation of the 6MWD (from an intraindividual or interindividual perspective), which is modulated by whether there is one or more previous test results for comparison, remains the most critical aspect of the 6MWT. In clinical practice, the most common challenge is to determine, in an adequate manner, the remaining functional capacity of patients without a previous 6MWT and in whom the 6MWD is not severely reduced (e.g., < 300-350 m in patients with COPD) or clearly normal (> 550-600 m). Because in this case patients cannot be their own “control” over time, two options remain: to compare the 6MWD to disease-specific severity intervals or to reference values. Currently, there are simply no disease-specific severity intervals for the most prevalent chronic lung diseases. The reference values also seem to be of little use, considering that, at best, predictive equations have coefficients of determination of 0.4 (i.e., 60% of the variability of the 6MWD in healthy individuals remains uncertain).<sup>(3-5)</sup> More importantly, there is a wide variation in the lower limits of normality in distinct populations. In fact, a recent study sponsored by the Latin-

American Thoracic Association<sup>(5)</sup> demonstrated that 6MWD values were higher in samples in Latin America (including a sample in the city of São Paulo, Brazil) than in those in countries in the northern hemisphere (Spain and the United States), a finding that might be related to the fact that Brazilian patients with COPD tend to walk more than do their counterparts (with the same degree of functional loss) in the United States. Therefore, except in extreme cases, there is still no definitive answer as to which 6MWD values clearly characterize and grade the functional incapacity of patients with chronic lung disease. Another alternative to maximize the information provided by the 6MWT involves the use of combined indices that take into consideration the metabolic cost of achieving a certain 6MWD (such as the 6MWD  $\times$  body weight product) or, as recently suggested in a study conducted in Brazil, for patients with interstitial lung disease, the intensity of exercise-induced hypoxemia (such as the 6MWD/desaturation ratio).<sup>(6)</sup>

The 6MWT can also be used over time to analyze, in an objective manner, the progression of functional loss or the potentially positive effect of therapeutic or rehabilitation interventions. The interpretation of variations in the 6MWD is even more complex, because the suggested values for the minimal important difference (MID)—“the smallest difference in score in the outcome of interest that informed patients or informed proxies perceive as important, either beneficial or harmful, and which would lead the patient or clinician to consider a change in the management”<sup>(7)</sup>—vary widely. In COPD, for instance, the MID for the 6MWD varies widely in terms of absolute values (from 25 m to 80 m) and relative values (from 10% to 40%).<sup>(7-11)</sup> Methodological considerations aside, most of this variability might be due to the fact that the relationship between the 6MWD and functional capacity is not linear. In fact, as can be seen in Figure 1, the relationship is curvilinear (hyperbolic), the slope of the curve decreasing progressively as both variables increase. This means that a patient in range A of Figure 1 (a patient who presents with a short 6MWD and low functional capacity) has greater room for improvement than does a patient in range C of Figure 1 (a patient who presents with a long 6MWD and near peak functional capacity). However, the same absolute improvement (in

meters) will constitute a much greater fraction of the baseline value for the patient in range A than for that in range C (Figure 1). In addition, it remains unclear whether this relationship remains hyperbolic and with the same curvature when there is functional loss. Can we assume that a given absolute and relative reduction in the 6MWD essentially represents the same decrease in functional capacity that would have been expected had both values increased? Future studies should address those issues. At present, perhaps the best alternative is to recognize that the MID for the 6MWD probably depends on the baseline (or pre-intervention) 6MWD: shorter for patients with more severe disease and longer (albeit more difficult to achieve) for those with less severe disease (Figure 1).

Review articles that are conceptually precise and adequately balanced by the best evidence available are always welcome. The article by Morales-Blanchir et al.<sup>(2)</sup> has those qualities and will certainly be useful for clinical pulmonologists



**Figure 1** - Hyperbolic relationship between functional capacity (FC) and the six-minute walk distance (6MWD). Note the progressive reduction in the sensitivity of the 6MWD in reflecting positive variations in FC as a result of interventions (circle-arrow interval on the x-axis). Therefore, a given improvement in FC will translate to a lower variation in the 6MWD if the pre-intervention 6MWD is longer (patient “C” vs. patient “A”). However, patient “A”, despite having greater theoretical potential for improvement in the 6MWD, commonly presents with worse baseline health status (i.e., lower biological potential for improvement). Another complicating factor is that improvement in FC is not linearly related to clinical outcomes that are relevant to the patient and attending physician. Therefore, the minimal important difference<sup>(7)</sup> for the 6MWD is expected to vary widely, as consistently demonstrated.<sup>(8-11)</sup>

and fellow physicians who specialize in different areas of medicine, as well as for paramedical professionals, who use the 6MWT to assess functional capacity. However, the definitive incorporation of the 6MWT into clinical practice seems to depend on the resolution of the complexities of the interpretation of specific values and their longitudinal variations in different populations of patients with chronic respiratory disease.

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