

## Six-minute walk test: a valuable tool for assessing pulmonary impairment<sup>\*,\*\*</sup>

Teste de caminhada de seis minutos: uma ferramenta  
valiosa na avaliação do comprometimento pulmonar

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### Abstract

Over the last few years, the use of exercise tests has come to be recognized as a convenient method of evaluating respiratory function, because the reserves of the various systems in the human body should be known in order to provide a more complete portrayal of the functional capacities of the patient. Because walking is one of the main activities of daily living, walk tests have been proposed in order to measure the state or the functional capacity of patients. The six-minute walk test has proven to be reproducible and is well tolerated by patients. It evaluates the distance a person can walk on a flat, rigid surface in six minutes. Its main objective is to determine exercise tolerance and oxygen saturation during submaximal exercise. In this review, we present various clinical areas in which the test can provide useful data.

**Keywords:** Hypertension, pulmonary; Pulmonary circulation; Pulmonary heart disease; Exercise.

### Resumo

Nos últimos anos, o uso de testes de exercício é reconhecido como um método conveniente na avaliação da função respiratória em função da necessidade de se conhecer as reservas dos vários sistemas corporais a fim de que uma ideia mais completa sobre as capacidades funcionais do paciente seja obtida. Visto que o ato de andar é uma das principais atividades da vida diária, os testes de caminhada têm sido propostos para medir o estado ou a capacidade funcional do paciente. O teste de caminhada de seis minutos provou ser reproduzível e é bem tolerado pelos pacientes. Ele avalia a distância que uma pessoa pode percorrer sobre uma superfície plana e rígida em seis minutos e tem como principal objetivo a determinação da tolerância ao exercício e da saturação de oxigênio durante um exercício submáximo. Nesta revisão, apresentamos várias áreas clínicas nas quais o teste pode fornecer informações úteis.

**Descritores:** Hipertensão pulmonar; Circulação pulmonar; Doença cardiopulmonar; Exercício.

### Introduction

Physicians have long been fundamentally dependent on spirometry for the determination of FEV<sub>1</sub> in order to characterize the degree of impairment in patients with pulmonary diseases, especially COPD. The six-minute walk test (6MWT) is used in order to evaluate the response to exercise of an individual, providing a global analysis of the respiratory, cardiac, and metabolic systems.<sup>(1)</sup> The main advantages of the 6MWT are its simplicity and the minimal technological requirements, as well as the fact

that vital signs and symptoms can be measured during the test.<sup>(2,3)</sup> Therefore, it is inexpensive and has broad applications, given that walking is an activity of daily living that almost every patient is capable of, except for those that are most affected by illness.<sup>(2)</sup>

Walking, together with breathing, hearing, seeing, and talking, is considered one of the five major life activities.<sup>(4)</sup> Oxygen uptake (VO<sub>2</sub>) during the 6MWT corresponds to submaximal exercise, characterized by VO<sub>2</sub> reaching a plateau

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but not increasing to the maximal value. In addition, the 6MWT more accurately reflects limitations in the activities of daily living and has been demonstrated to be more sensitive than are treadmill tests because it objectively tests oxygen desaturation during exercise in patients with COPD. In the early 1970s, a simple test was developed in order to evaluate the functional capacity of a subject by measuring the distance walked during a given period of time.<sup>(2)</sup> According to the American Thoracic Society (ATS), the most precise indication for the performance of the 6MWT is mild or moderate lung or heart disease,<sup>(2)</sup> in which it is used in order to measure treatment response, as well as to predict morbidity and mortality. The presentation of the complete and detailed methodology for the test performance is beyond the scope of this review. However, we present the various clinical areas in which the test can provide useful data.

## Test performance

In 2002, the ATS published guidelines for the performance of the 6MWT. In order to avoid complications and unnecessary risks, it is important to mention that the 6MWT should be performed in a place with immediate access to emergency equipment, considering that patients who undergo the test might have cardiovascular pathologies that could limit exercise tolerance and, as a consequence, tissue oxygenation. Although it is not necessary for a physician to be present during the test, it is recommended that the technician who applies the test be certified in cardiopulmonary resuscitation or have immediate access to a telephone or other means of communication in order to get help if necessary.<sup>(2)</sup> Various studies have demonstrated that the six-minute walk distance (6MWD) tends to increase with the repeated administration of the test.<sup>(5)</sup> Some authors have asserted that subjects walked a longer distance while performing the 6MWT in an open area than did those who performed the 6MWT in an enclosed area.<sup>(6)</sup> Reference equations should be considered when the 6MWT is performed in healthy subjects.<sup>(7)</sup> As recommended by the ATS, the information provided by the 6MWT should be considered complementary to, rather than a substitute for, a cardiopulmonary study protocol. Worldwide, the 6MWT has been

used as a predictor of mortality in various pathologies, such as heart failure, COPD,<sup>(8)</sup> and, more recently, idiopathic pulmonary arterial hypertension. The results have varied widely. Researchers at the National Cardiovascular Centre in Osaka, Japan, demonstrated that the 6MWD is strongly associated with mortality in subjects with idiopathic pulmonary arterial hypertension.<sup>(9)</sup> The 6MWT has also been utilized in the evaluation of ambulatory oxygen therapy,<sup>(10)</sup> as well as of idiopathic pulmonary fibrosis.<sup>(11)</sup> In addition, the test has proven useful in the preoperative and postoperative evaluation of patients undergoing thoracic surgery (lung transplantation, lung resection, and lung volume reduction surgery)<sup>(12-14)</sup> or bariatric surgery for morbid obesity,<sup>(15)</sup> as well as in the evaluation of patients with COPD,<sup>(16)</sup> cystic fibrosis,<sup>(17,18)</sup> or fibromyalgia.<sup>(19)</sup>

## Sources of variability

### *Factors that reduce the 6MWD*

Various factors can reduce the 6MWD: short stature; advanced age; excess weight; female gender; impaired health status; performance of the test in a corridor that is shorter than the standard (more turns); lung disease (COPD, asthma, cystic fibrosis, and interstitial lung disease); cardiovascular disease (angina, heart failure, and acute myocardial infarction); and musculoskeletal disorders (arthritis and muscle wasting, as well as ankle, knee, or hip injuries). To give an example of how these factors come into play, we can state that a 70-year-old female with a history of COPD and acute coronary syndrome would be expected to walk a shorter distance than would a 30-year-old male with mild asthma.

### *Factors that increase the 6MWD*

Some of the factors that can increase the 6MWD are as follows: tall stature; male gender; high motivation; previous experience with the 6MWT; oxygen supplementation (in patients with exercise-induced hypoxemia); and the pre-test use of medications taken for a disabling disease.<sup>(2)</sup>

A study conducted in 2003 demonstrated that there is a learning effect when the 6MWT is administered repeatedly to the same individual;

this learning effect was shown to persist for a period of two months. The authors found that, when the 6MWT was administered repeatedly, the 6MWD increased significantly between the first and the third test ( $620.00 \pm 69.49$  m and  $668.73 \pm 81.07$  m, respectively).<sup>(5)</sup>

## Interpretation of the 6MWT

The most important part of performing the 6MWT is analyzing the 6MWD. Enright & Sherrill reported that the mean 6MWD was 576 m and 494 m for men and women, respectively.<sup>(7)</sup> The distance was considerably shorter for elderly men and women, as well as for people with greater body weight and for men of short stature. The authors developed equations that explained approximately 40% of the variance in the 6MWD for healthy adults. The results suggested that those reference equations can be used in order to predict the 6MWD for adult patients performing the 6MWT for the first time, as long as caution is exercised when applying the equations to patients whose characteristics fall outside the cohort studied, including non-Whites and those younger than 40 or older than 80 years of age.<sup>(7)</sup> However, it should be borne in mind that there are equations other than those proposed in that study. Various studies have been conducted in a variety of populations composed of diverse ethnicities.

In 2000, Padrón et al. proposed a standardization of the 6MWT in healthy Mexican subjects.<sup>(20)</sup> In their study, the 6MWD values, for men and women, were greater than those reported in the study conducted by Enright & Sherrill.<sup>(7)</sup> However, most of the patients that performed the test in the Padrón et al. study were younger than were those evaluated by Enright & Sherrill.<sup>(7)</sup> In the Padrón et al. study, 200 healthy Mexican subjects were recruited, and the 6MWT was performed in an open area. Each of the participants walked slowly or at a normal pace, and no verbal encouragement was given. The mean 6MWD was  $481 \pm 51$  m and  $463 \pm 55$  m for males and females, respectively. Subsequently, the participants were asked to walk as fast as they could without running; the mean 6MWD was, respectively,  $605 \pm 56$  m and  $563 \pm 57$  m for males and females. In 1997, another group of authors suggested that differences in the functional status could be statistically significant and yet be below

the threshold at which patients would notice a difference in their performance in relation to that of others; identifying the smallest difference in the 6MWD that is noticeable to patients might help clinicians interpret the effectiveness of symptomatic treatments for COPD.<sup>(21)</sup>

There are other important measurements to analyze, such as fatigue, dyspnea (using the Borg scale), and oxygen saturation during the performance of the 6MWT. A 4% fall in  $SpO_2$  from the baseline level or an  $SpO_2 \leq 86\%$  must be classified as oxygen desaturation.<sup>(3)</sup> In 2005, one group of authors stated that the 6MWT is an efficient method to detect oxygen desaturation during activities of daily living and to establish the oxygen flow for correcting exertional desaturation. The authors demonstrated a significant relationship between the  $SpO_2$  obtained by ambulatory pulse oximetry and that obtained by the 6MWT. The median  $SpO_2$  was  $84 \pm 7\%$  and  $89 \pm 4\%$  for the 6MWT and for the ambulatory pulse oximetry, respectively ( $p < 0.001$ ).<sup>(10)</sup>

## Pulmonary diseases

Walk distance has been employed as an indicator of functional capacity since the introduction of the 12MWT by McGavin et al. in 1976.<sup>(22)</sup> Those authors used the 12MWD to measure exercise tolerance in patients with chronic bronchitis and concluded that the test was a simple method of evaluating disabilities in such patients. Later, another group of authors demonstrated that results obtained with the 12MWT were equivalent to those of the 6MWT, which was also found to have the advantage of being efficient and less stressful for the patients, reflecting appropriately an activity performed daily by the patients.<sup>(23)</sup> Over the last decade, studies have concentrated on determining the clinical correlation of the 6MWT with various pathologies, such as pulmonary hypertension, COPD, and heart failure, as well as on identifying variations among specific age groups and among healthy subjects.<sup>(1,9,24,25)</sup>

In order to grade the severity of COPD, Celli et al. conducted a multicenter study involving 207 COPD patients.<sup>(26)</sup> The authors identified four main predictors of mortality: Body mass index, degree of airflow Obstruction, degree of Dyspnea, and Exercise capacity (as measured by the 6MWT). After the evaluation of a cohort

of 625 patients who died (from any cause), the authors employed these factors in devising what is now known as the BODE index. The BODE index proved to be better than the FEV<sub>1</sub> at predicting the risk of death from respiratory causes in patients with COPD. In that study, the cut-off point for the 6MWD was 350 m.

In 1997, one group of authors conducted a retrospective chart review of patients, including patients who were accepted or died waiting for acceptance for lung transplantation by the Toronto Lung Transplant Program between January of 1991 and June of 1995.<sup>(27)</sup> That study included 145 patients with various types of lung diseases, such as emphysema, alpha-1 antitrypsin deficiency, idiopathic pulmonary fibrosis, idiopathic pulmonary arterial hypertension, Eisenmenger syndrome, and cystic fibrosis. As a predictor of mortality, a 6MWD < 400 m showed the following characteristics: sensitivity, 0.80; specificity, 0.27; positive predictive value, 0.27; and negative predictive value, 0.91. Similar findings were found for a 6MWD < 300 m (0.52, 0.80, 0.38, and 0.88, respectively). Therefore, the 6MWT is considered useful in the determination of the point at which patients should be listed for transplantation, a 6MWD < 400 m appearing to be a reasonable marker.<sup>(27)</sup> Important data from a study including 460 COPD patients revealed that a change of 35 m in the 6MWD (10% of baseline 6MWD) represents a meaningful finding in patients with moderate or severe COPD. In addition, and it is of utmost importance that Latin-American patients were included in that study, the 6MWT proved to have significant correlations with FEV<sub>1</sub> and PaO<sub>2</sub>.<sup>(28)</sup> With the inclusion of patients with similar characteristics, another study revealed that the 6MWT should be recommended for COPD patients enrolled in rehabilitation programs.<sup>(29)</sup> The results obtained in that study did not differ from those reported by Enright & Sherrill.<sup>(7,29)</sup>

## Cardiovascular diseases

The first publications on the use of the 6MWT in patients with heart failure focused on measuring functional capacity. The data were collected during a prospective cohort study, designated the Studies Of Left Ventricular Dysfunction (SOLVD) Registry Substudy. A stratified random sample of 898 patients, from the SOLVD registry, who had either radiological

evidence of congestive heart failure or an ejection fraction  $\leq 0.45$  were enrolled in the substudy and underwent a detailed clinical evaluation, including the 6MWT. The patients were followed up for a mean period of 242 days. During the follow-up period, 52 participants (6.2%) died, and 252 (30.3%) were hospitalized. Hospitalization for congestive heart failure occurred in 78 participants (9.4%), and the combined endpoint of death or hospitalization for congestive heart failure occurred in 114 (13.7%). Compared with the patients with the highest performance level on the 6MWT, patients with the lowest performance level had a significantly greater chance of dying (10.23% vs. 2.99%;  $p = 0.01$ ), of being hospitalized for any cause (40.91% vs. 19.90%;  $p = 0.002$ ), and of being hospitalized for heart failure (22.16% vs. 1.99%;  $p < 0.0001$ ). The authors concluded that the 6MWT was able to predict morbidity and mortality in patients with left ventricular dysfunction.<sup>(30)</sup>

In 1996, one group of authors studied the utility of the 6MWT in patients with advanced heart failure who were evaluated for heart transplant and concluded that the 6MWD was able to predict peak VO<sub>2</sub> and survival.<sup>(31)</sup>

## Validation in pediatrics

In 2005, one group of authors published a study in which 74 patients (43 females and 31 males), with a mean age of  $14.2 \pm 1.2$  years, were recruited.<sup>(1)</sup> The authors concluded that, among all of the existing types of walk tests, the 6MWT is the best indicator of functional capacity, because it more appropriately reflects the activities in daily living, which are performed at submaximal levels of exertion similar to those required to perform the 6MWT. Validity was demonstrated by the correlation between the 6MWD and maximal VO<sub>2</sub> on an exercise treadmill. That study was the first to assess the reliability and validity of the 6MWT in healthy children. The authors reported that one of the factors determining the 6MWD was height, probably because taller children have a longer stride and, as a result, a greater distance is achieved.<sup>(1)</sup> Another group of authors supported the idea that the 6MWT contributes to the classical evaluation of pulmonary function, offering a more complete profile of the functional capacity among individuals. The authors suggested that

the 6MWT be performed in the evaluation and screening of pediatric patients with cardiopulmonary disease, especially in those with cystic fibrosis or bronchiolitis obliterans.<sup>(25)</sup>

## Validation in geriatrics

Elderly subjects constitute a group that frequently shows a great burden of cardiopulmonary and metabolic pathologies correlating with the normal aging process. Therefore, cardiopulmonary function tests play an important role in the appropriate evaluation of this age group. Studies have shown that the use of the 6MWT is of great value in the evaluation of functional capacity in the elderly. In 1999, one group of authors published a study in which 51 healthy subjects between the ages of 50 and 85 were evaluated.<sup>(32)</sup> The subjects performed the 6MWT in a quiet hospital corridor, 50 m in length. The mean 6MWD was 631.39 m, and it was 84 m greater in the male subjects than in the female subjects ( $p < 0.001$ ). The 6MWD showed significant correlations with age ( $r = -0.51$ ;  $p < 0.01$ ) and height ( $r = 0.54$ ;  $p < 0.01$ ). That study demonstrated that, for healthy subjects in the 50–85 age bracket, there is considerable variability in the 6MWD (range, 383–820 m). That variability was explained largely by differences in age, gender, height, and weight. The authors of that study stated that, in that population, the 6MWT could not be used as a replacement for an incremental maximal exercise test.

In 2004, another group of authors published a study in which 53 male and 103 female subjects were recruited. The results showed that, in elderly individuals, there are significant differences in the 6MWD according to the health status.<sup>(33)</sup> To distinguish between healthy and ill subjects, the authors used criteria derived from a protocol that was originally created to select participants for studies concerning age-related changes in the immune system. Therefore, the study was able to distinguish between age-related and disease-related changes. The authors developed a classification system, as well as stratifying health categories corresponding to an increasing risk for complications during physical exercise. The participants identified as being completely healthy were included in group A, those with stabilized noncardiovascular conditions were included in group B1, those taking cardiovascular

medications without any signs of active disease were included in group B2, those presenting with a history of signs of cardiovascular disease other than hypertension were included in group C, and acutely ill patients, together with those who were unable to participate in an exercise program, were included in group D. The study demonstrated that the proposed categorization was able to detect significant reductions in the physical capacity of the subjects due to individual parameters, such as medical history, medication use, and current health status, whereas age and gender explained only 18% of the variability. Conclusively, the authors proposed the incorporation of that health classification system as a predictor of the outcome, making the system a useful tool for medical screenings preceding the initiation of a physical exercise program in elderly subjects.<sup>(33)</sup>

## Perspectives

It has been demonstrated that, in patients with COPD, the 6MWD declines progressively over time, and that the 6MWT contributes to the complete evaluation of patients affected by the disease.<sup>(8,34–40)</sup> The 6MWT can be applied in advanced heart failure patients who are being evaluated for heart transplant. As previously mentioned, the 6MWD is predictive of peak  $\text{VO}_2$  and survival.<sup>(7)</sup> Various studies have shown that the 6MWT is valid and reproducible in patients with heart failure, providing evidence that it is a reliable means of evaluating functional capacity in such patients.<sup>(41–50)</sup>

As a predictor of mortality in patients who are candidates for lung transplantation, the 6MWT has shown high sensitivity; a 6MWD of less than 300 m was associated with much earlier mortality among patients on the waiting list for transplantation.<sup>(26)</sup> Recently, there have been a few studies demonstrating the utility of the 6MWT in the field of solid organ transplantation, and the results have varied across studies. Organ transplantation represents the ideal intervention for various terminal diseases affecting multiple organs, such as the heart, lung, kidney, pancreas, and liver. Although transplant recipients might survive the surgical procedure, they all present with reduced exercise capacity.<sup>(51)</sup> Cardiovascular disease is the leading cause of morbidity and mortality in patients with end-stage renal disease. Traditional risk factors, such as hypertension,

dislipidemia, diabetes, smoking, obesity, and renal failure, have long been linked to increased cardiovascular risk. Recently, there has been increasing interest in other types of risk factors, such as low aerobic capacity and peripheral vascular endothelial dysfunction, which are associated with the sedentary lifestyle.<sup>(52)</sup> The understanding of the mechanisms responsible for decreases in functional capacity is based on data obtained by maximal exercise tests. However, as previously stated, activities of daily living require submaximal effort. Patients with end-stage renal disease show a significant reduction in maximal  $\text{VO}_{2\text{T}}$ , which translates to lower exercise capacity.<sup>(53,54)</sup> One group of authors found that diminished exercise capacity was the best predictor of mortality in patients with end-stage renal disease.<sup>(55)</sup> Another group of authors found that, in patients with end-stage renal disease, 6MWD values were 28% lower than the values predicted for individuals in the same age bracket ( $495 \pm 92$  m vs.  $692 \pm 56$  m;  $p = 0.0001$ ). As expected, the 6MWD was significantly lower in older patients than in younger patients ( $446 \pm 76$  m vs.  $523 \pm 98$  m).<sup>(56)</sup> The 6MWT represents a promising tool for use in the field of medical research. Transplantation specialists should also be aware of the advantages of the 6MWT.

## Final considerations

The use of the 6MWT is recommended as a complement to the evaluation of patients with pulmonary and cardiovascular diseases. It is inexpensive and has great application, because it can be performed by almost any patient, except by those who are severely ill. The 6MWT is a useful test that is accessible to any physician, and it represents an accurate and efficient method of quantifying exercise tolerance. Standardization of and training in the use of the 6MWT are essential for health professionals, especially for those involved in the treatment of patients with cardiovascular impairment, respiratory impairment, or both.

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