REVIEW ARTICLE

Evaluation Exercise Tolerance in COPD Patients: the 6-Minute Walking Test

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Introduction

Dyspnea brought on by exercise is one of the basic symptoms of patients with chronic obstructive pulmonary disease (COPD). It appears in the initial phases of the disease, affects activities of daily living,[1] and determines, to a large extent, the perception of the degree of illness and extent of deterioration in quality of life. Tolerance to exercise in these patients is an indicator of severity, regardless of forced expiratory volume in the first second.[2-4] In fact, the evaluation of both factors—severity of obstructive ventilation (forced expiratory volume in 1 second) and the limitation of tolerance to exercise—are vital in controlling the progression of COPD.

Among the simple tests used to evaluate tolerance to exercise, the 6-minute walking (6MW) distance has proved to be a predictor of survival independent of other variables[5] and, at the same time, indicates frequency of hospitalizations from exacerbations.[6] This is important considering that the progression of the disease is influenced by the frequency of these episodes which signify an associated mortality of from 3% to 10%, or more if the patient is admitted to intensive care.[7] The 6MW distance has also been shown to predict postoperative outcome in candidates for volume reduction surgery by identifying patients with a potentially unfavorable outcome.[8] Among patients that present postoperative functional improvement, an improvement in tolerance to exercise has a longer duration than changes in forced expiratory volume in 1 second.[9] This discrepancy can be explained by the fact that exercise tests reflect not only lung changes but also interactions with other systems that respond to exercise such as the cardiovascular and muscular systems. Thus, the high predictive value of exercise tolerance lies in its multifaceted nature, being affected by: *a)* airflow limitation from mechanical dysfunction; *b)* impaired gas exchange; *c)* insufficient increase in heart rate during exercise, and *d)* peripheral muscle dysfunction. This multifaceted nature together with lung function limitations measured at rest makes exercise tolerance valuable in characterizing COPD patients.[10] However, exercise protocols that can be clinically applied outside lung function laboratories are a practical consideration.

Exercise Tests

There are two main groups of clinically applicable exercise tolerance tests: *a)* exercise protocols that require lung function laboratory installations, and *b)* simple exercise tests that can be regularly performed in the field. Conventional incremental exercises tests belong to the first category with the cycle ergometer as the gold standard[11] as it provides information on several systems of the organism (cardiovascular, respiratory, skeletal muscles) involved in the response. Incremental exercise with a cycle ergometer determines: a) the relation between the work load of the cycle ergometer (W) and the patient's oxygen consumption ($\dot{V}O_2$) during the test; *b)* the transition zone between moderate and intense exercise (lactate threshold) by noninvasive

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means; *c)* W and $\dot{V}O_2$ tolerated comfortably by the patient and, on occasion, maximal W and $\dot{V}O_2$, and *d)* the causes of intolerance to exercise and the degree of overload of the various systems that contribute to it. The relation between $\dot{V}O_2$ and W of the cycle ergometer in incremental exercise is normally found to be between 9 and 11 mLO_2/W and indicates the degree of efficiency of the muscles used in the exercise.

Constant work load protocols are another kind of exercise test in which the same intensity of work load is maintained throughout the test. Three aspects of interest can be measured with this kind of test: *a)* the time the patient is capable of maintaining a particular exercise work load (endurance); *b)* the behavior of physiological variables at a given moment (airflow, heart rate, $\dot{V}O_2$) before and after the administration of drugs or undergoing a physical training program, and *c)* the time constant of $\dot{V}O_2$ kinetics, a parameter that reflects the oxidative capacity of the muscle. However, although laboratory exercise tests (incremental or constant-load) are useful, indeed essential for analyzing certain problems,[11] the fact that they require a laboratory with relatively complex equipment and specialized technicians limits their availability in the day to day characterization of clinical patients.

Simple exercise tests require less technical equipment, making makes them more practical for the assessment of tolerance to exercise in the field. These tests should not be regarded as alternatives to laboratory tests but rather as complementary, for use in conventional clinical settings. The more common simple exercise protocols are *a)* the walking test with a fixed time limit (6 or 12 minutes); *b)* shuttle test, and *c)* stair climbing test. Currently, the 6MW test is the most used simple exercise test. The profiles of the metabolic requirements ($\dot{V}O_2$) of the different modes of exercise tolerance tests are compared in Figure 1, followed by a description of the characteristics of simple exercise tests.

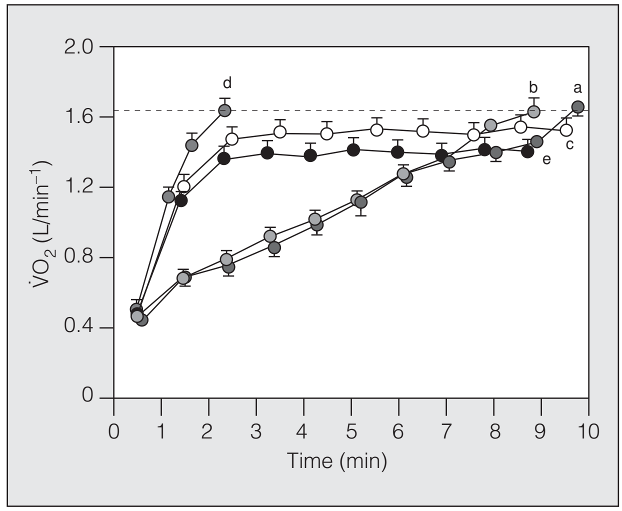

Figure 1. Profile of oxygen consumption ($\dot{V}O_2$) in 5 exercise tests performed by the same patients with chronic obstructive pulmonary disease: *a)* incremental protocol with a cycle ergometer; *b)* shuttle test; *c)* 6-minute walking (6MW) test; *d)* stair climbing with patient encouragement, and *e)* time-regulated stair climbing. Only the 6MW test and the time-regulated stair climbing present characteristics of being submaximal (plateau in the $\dot{V}O_2$ curve). Although the shuttle test and cycle ergometer test involve a different type of exercise and a different amount of active muscle mass, both are incremental protocols that reach similar peak $\dot{V}O_2$ values. In the test of stair climbing with encouragement, the patient is instructed to climb the stairs as fast as possible. This imposes an extremely high metabolic load which forces the patient to terminate the test once the maximal predicted $\dot{V}O_2$ is reached (dotted line).

The Stair Climbing Test

Stair climbing was one of the first simple tests to assess exercise tolerance in patients with diverse diseases. In 1948, Baldwing et al[12] described its utility in classifying the degree of respiratory insufficiency *(sic)*. In the 1960s, the stair climbing test was used in preoperative evaluation before lung parenchyma resection.[13] The degree of intraindividual reproducibility is acceptable[14] when the test is given under controlled conditions and it is easily applied (there are stairs in all hospitals). However it lacks sufficient standardization as several studies have shown that the metabolic requirements can vary considerably depending on the characteristics of the performance of the test[14,15] (Figure 1). Metabolic requirements during the test depend on factors such as the patient's weight, the height of the steps, how fast they are climbed or the amount of support placed on the hand rail. The logistics of implementing recommendations to standardize the test between different hospitals are thus made difficult. The consequent lack of reference scores is an additional inconvenience to the clinical use of this test.

The Shuttle Test

The shuttle test was introduced by Singh[16] in 1992 as an incremental test (Figure 1) to assess exercise tolerance in COPD patients. A recorded sound signal indicates the walking pace of the patient along a 10 meter corridor which is marked by 2 cones 0.5 meter in from either end. The patient has a predetermined time to complete the distance from one cone to the other. Walking pace increases every minute to a maximum of 12 increments. The total number of meters walked is calculated at the end of the test which happens either on the appearance of symptomatic limitations (dyspnea, leg fatigue, chest pain, etc) or when the patient fails, twice in a row, to reach the cone within the time limit. The shuttle test clearly demonstrates the correlation between the peak $\dot{V}O_2$ obtained during a conventional, incremental exercise test with the distance walked in the 6MW test and with health related quality of life.[17] A high degree of standardization and reproducibility[18] allows results from different hospitals to be compared. The shuttle test is highly sensitive in detecting physiological changes resulting from physical training programs.[19] However, the lack of reference scores limits its clinical use. In summary, the shuttle test is a potentially useful, simple, incremental exercise test, but not as used as the 6MW test and therefore with fewer available data for clinical validation. Compared with the 6MW test, it entails greater potential cardiovascular risk, particularly among patients with pulmonary vascular disease.

The 6MW Test

The first attempts to assess functional capacity by measuring distance walked in a controlled length of time were carried out by Balke[20] in the 1960s. In 1968, Cooper[21] developed the 12-minute walk protocol to assess the functional capacity of a group of 100 airmen in the US air force. But it was not until 1976 that McGavin et al[22] introduced the 12-minute walk test to evaluate COPD patients. In 1982, Buttland et al[23] compared the 12-minute walk test with other shorter variations (2, 6, and 12 minutes). That study showed how the variability of the results increased but the power of discrimination decreased with the duration of the test. The authors[23] proposed the 6MW test as a just balance between reproducibility and power of discrimination. Since this study, use of the 6MW test has become generalized. A recent review[24] concludes that "the 6-minute walk test is easy to administer, better tolerated, and more reflective of activities of daily living." The test is a very simple one: it evaluates an activity carried out daily by the patients (walking) and has few technical requirements. The 6MW distance correlates well with peak $\dot{V}O_2$[25] and with health related quality of life,[26] and is highly sensitive in detecting changes following therapy such as physical training.[27] Changes in 6MW distance also correlate well with changes in perception of dyspnea.[28] Approximately 80% of COPD respiratory rehabilitation programs use the test[29] for which predictive equations have been published.[30-32] Fifty-four meters has been found to be the minimum difference at which a COPD patient perceives a clinically significant improvement between one test and another.[33]

Standardization of the 6MW test is very important in order to optimize the utilization of the test by sharply reducing the intraindividual and inter-center variability. The test is highly reproducible, with a variation coefficient near 8% for COPD patients.[34] The instructions for its application are extremely important. An example of how patients should be instructed before performing the test is as follows[34]: "This is a walking test that lasts 6 minutes. You are not permitted to run. The object is to walk as far as possible in 6 minutes. You will walk as fast as possible back and forth along this corridor, trying not to slow down when you turn at the end. The test lasts 6 minutes. If you have to rest you may but must resume walking as soon as you are able. Every 60 seconds we will tell you how much time has passed and how much is left to complete the test." Aspects relevant to acceptable standardization, such as the degree of incentive during the test, the length of the corridor, the number of tests a particular patient needs for assessment, and criteria for the administration of oxygen are discussed below.

Encouragement. The use of phrases of encouragement at regular intervals increases the distance walked.[35] Although the reproducibility of the test is the same with or without encouragement, using it guarantees the test's high predictive value. In this way the reliability of comparison with previous tests performed by the same patient and the results obtained in other centers is assured, and equations of normality that have been obtained through tests performed with encouragement can be utilized.[31] Standard phrases at regular intervals—every 60 seconds—should be used, like: "you are doing well," "keep up the good work"; at the same time as the patient is informed of how much time has passed and how much is left before the test is completed.[34]

Length of the corridor. The corridor should be at least 30 meters long, flat, and transit-free. Shorter corridors should be avoided as patients have to turn more often which slows their pace.[34,36] The temperature should be agreeable which means the walk is normally performed indoors but it can be performed outside if the weather is appropriate.

Practice tests. Training effects make it advisable to perform at least 2 tests, taking the longest distance walked as valid.[35] Patients must be allowed to rest for at least 30 to 60 minutes between tests.[34] In agreement with data given in the references, we have found that a third test did not change the results of two.

The effect of supplemental oxygen. Supplemental oxygen administered during the test increases the distance walked,[37] and low flow oxygen is the most beneficial.[38] All patients needing continuous oxygen therapy[39] must perform the test with supplemental oxygen; and if, when performing the test without supplemental oxygen, a patient's oxygen saturation falls below 90%, the test should be repeated with the administration of oxygen, and the greater distance of the 2 tests be taken as valid. If, under any circumstances, the saturation should fall below 80%,[40] the test should be suspended. Liquid oxygen should be used as it is easy to carry. The oxygen delivery device should be carried by a technician walking 2 paces behind the patient. Administration of oxygen, the system used, and the flow must be recorded on the worksheet so the same conditions can be repeated in subsequent tests.

Monitoring. The conditions of the test are recorded on a worksheet (whether oxygen has been administered and if so, the system used and the flow) and the vital signs measured during the test (heart rate and oxyhemoglobin saturation). Before the test starts, and with the patient stationary at one end of the corridor, heart rate, oxyhemoglobin saturation (by pulse oximetry), perception of dyspnea (Borg scale), and the degree of leg discomfort (Borg scale) are recorded. The same variables are taken at the end of the test. During the test, heart rate and oxygen saturation are measured every 60 seconds. The number of times the patient stops is also recorded. Finally, the distance walked in 6 minutes is recorded in meters.

Reference values. There are at least 3 predictive equations of reference values.[30-32] Among the Spanish population, Enright and Sherril's[30] equation underestimates the distance walked. This implies that COPD patients would present falsely normal 6MW test values. A possible explication for this is that in Enright and Sherril's[30] study only 1 test was performed whereas in the studies of Troosters et al[31] and Gibbon et al,[32] a practice test was performed and the best result taken as valid. At present the references values of Troosters et al[31] and Gibbon et al[32] are used when the 6MW test is used in Spain although it would surely be useful to develop equations specifically for the local population.

Some tests that assess patients' functional state are difficult to interpret. Differences are often statistically significant but lack relevant clinical value. Redelmeier et al[33] has established 54 meters to be the minimum difference in distance at which a patient perceives a clinically significant improvement.

Oxygen Consumption During the 6MW Test

We have shown recently that $\dot{V}O_2$ during the 6MW test is comparable to the peak $\dot{V}O_2$ reached by a group of COPD patients during incremental exercise on a cycle ergometer[41] (Figure 2). In that study, all patients reached a plateau in the $\dot{V}O_2$ curve after the third minute, indicating that a high intensity constant-load exercise was being performed.

The fact that patients adopted a fast but sustainable walking rate of their own accord gave rise to the hypothesis that the load self-imposed by patients in the 6MW test is of a comparable intensity to the patient's critical load, taken to be the maximal load (or $\dot{V}O_2$) that can be maintained over time. Another recent study carried out in our laboratory[42] has shown that the walking rate during the 6MW test does not differ from the mean critical rate measured for the same patients. This could explain the high prognostic value the test has in predicting survival of COPD patients, frequency of hospitalizations due to exacerbations of the disease, and postoperative evolution after lung parenchyma resection.

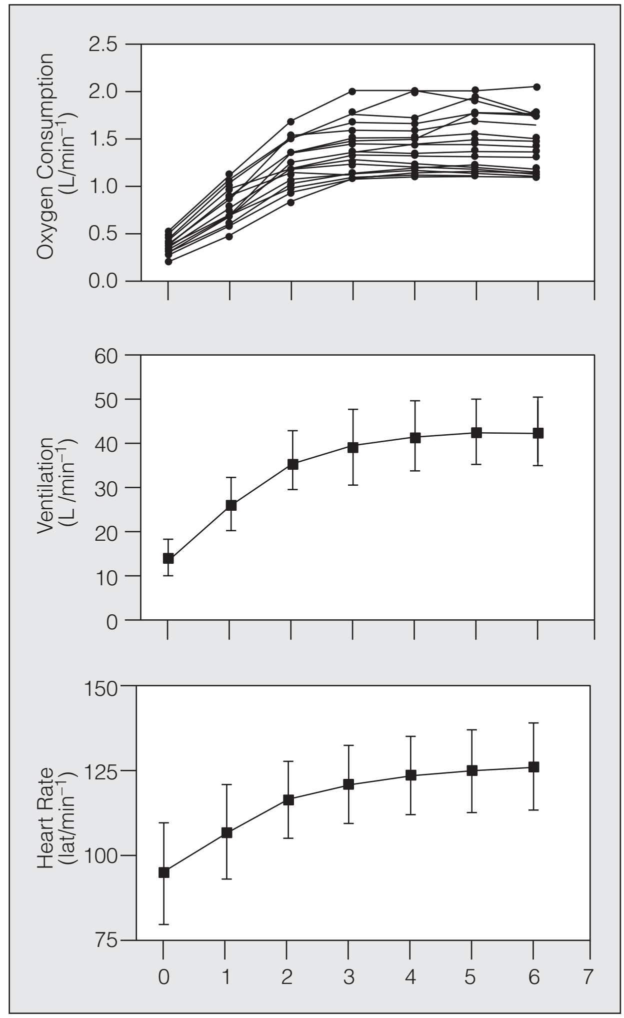

Figure 2. Cardiopulmonary response during the 6-minute walking test: individual scores of oxygen consumption (upper panel); mean (SD) values of ventilation (middle panel), and mean values of heart rate (lower panel).

Conclusion

Given that exercise tolerance has a high predictive value for COPD progression, survival, and frequency of hospital admissions due to exacerbations (probably because it reflects an integrated response of the whole organism), it should be systematically included in the assessment of COPD patients. Simple exercise tests are useful in the conventional clinical characterization of COPD patients with respect to limitations of exercise tolerance and should be considered as complementary to conventional incremental exercise, which provides essential information. The type of test used should be determined according to specific clinical questions in each case. It should be mentioned that the 6MW test probably fulfills the necessary criteria to be recommended as the reference test in characterizing COPD patients, the test being simple, requiring little technology, with good reproducibility, and reduced cardiopulmonary risk. The high discriminatory potential and the predictive power of the test could be due to the fact that it identifies the critical load of the patient. To summarize, we recommend the regular inclusion of exercise tolerance, through the 6MW test, in the assessment of COPD patients, together with lung function tests measured at rest.

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