Assessment of exercise capacity in pulmonary hypertension

Avaliação da capacidade de exercício na hipertensão pulmonar

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The pulmonary circulation, organized in series with the systemic circulation and receiving all of the cardiac output, is a vascular circuit of high compliance, characterized by high flow, low resistance and low relative pressures.[1]

Physical exercise, at low to moderate levels and under conditions of normality, has little effect on pulmonary artery pressure, which typically does not exceed the upper limits of normality during exercise. The elevation of cardiac output that occurs during exercise produces vasodilation (distention), as well as recruitment and redistribution of the pulmonary blood flow, making the pulmonary pressure gradients increase proportionally less, and, as a consequence, the estimated pulmonary vascular resistance is reduced.[1]

The structural and functional exchanges that constitute remodeling of the vascular walls, principally of the pulmonary artery segment in pulmonary hypertension, significantly reduce compliance in the pulmonary circulation. This remodeling, which characterizes pulmonary arterial hypertension (PAH) and reduces the capacity for vasodilation, leads to a reduction in the cross-sectional area of the pulmonary vascular bed. This creates the conditions for the elevation of pressure values and pulmonary vascular resistance in response to increased cardiac output, such as that occurring on exertion, during controlled exercise or even at rest, being proportional to the degree of remodeling and to the reduction in the functional reserve of the pulmonary circulation.[1,2]

Cardiopulmonary exercise testing,[3] which is an excellent resource for measuring physical capacity, has been employed in the evaluation of the functional reserve and as a prognostic marker in patients with heart disease or lung disease. It is known that such testing requires instrumentation that is more specialized, as well as requiring trained operators. In addition, the maximal effort level might not be attained by patients incapable of producing a significant increase in cardiac output, such as patients with PAH. In such patients, the testing is typically interrupted due to intolerable dyspnea.

Dyspnea on exertion is characteristic of patients with PAH up to New York Health Association functional class IV, and limitations in the performance of activities of daily living characterizes the most prevalent clinical presentations (functional class II and III), as well as, obviously, functional class IV, resulting in impaired quality of life for all such patients. The consequent operational difficulties in performing cardiopulmonary exercise testing in patients with PAH call for the use of tests of submaximal effort, which would more closely approximate activities of daily living, in the evaluation of these patients.

Based on the twelve-minute run test devised by Cooper,[4] which was designed to evaluate the physical aptitude of healthy young men, McGavin et al.[5] introduced the "twelve-minute walking test" in 1976. The authors applied their twelve-minute walking test as an exercise test in a group of 35 patients, between 40 and 70 years of age, with chronic bronchitis or obstructive lung disease. The results were compared with those of other indices of respiratory function, in order to evaluate their potential value in guiding the evaluation of impaired pulmonary function. The authors concluded that the twelve-minute walking test provided useful, objective data regarding exercise tolerance in patients with chronic bronchitis.

Butland et al.,[6] who hypothesized that shorter times might be more appropriate for patients with severe dysfunction, compared the distance covered in 12 min with that covered in 2 min and 6 min. The authors studied a group of 53 patients with obstructive lung disease. They determined that, on the twelve-minute walking test, after a peak of velocity, patients began to walk at a constant velocity, suggesting that shorter tests would be equally useful. The strong correlation found among the distances covered at the three times studied led to the conclusion

that these tests were of similar value as measures of exercise tolerance.

Guyatt et al.[7] applied the six-minute walk test (6MWT) as a new measure of exercise capacity in patients with chronic heart failure (CHF). The authors applied the test six times, over 12 weeks, in 18 patients with CHF. The patients were also submitted to the cycle ergometer test and to routine functional evaluation. The 6MWT proved to be quite well accepted by the patients, and the results were consistent and reproducible. In addition, the 6MWT results correlated with the standard measures, as well as proving to constitute a measure of functional status and exercise capacity. The authors concluded that the distance covered in 6 min is a useful measure of functional capacity, as well as an appropriate measure of the prognosis of clinical exercise for patients with CHF. Their study functioned as a validation of the 6MWT, which came to be widely used in the evaluation of patients, as well as in clinical trials in which functional evaluation is required. In patients with advanced disease and severe functional limitation, tests designed to evaluate submaximal effort can be considered tests of maximal effort.

Enright & Sherrill[8] established reference equations for healthy adults, and the technical norms of the American Thoracic Society[9] defined the guidelines for standardizing the test. The 6MWT was indicated for comparisons between pre- and post-treatment periods, as well as for the definition of functional status and for the prediction of outcomes (morbidity and mortality). The need for a 30-m corridor was stated, and factors of variability were recognized.

Miyamoto et al.[10] studied 43 patients with idiopathic PAH, determining that the 6MWT decreased in proportion to the severity of the functional class, as categorized using the New York Health Association system. The authors also determined that the distance covered was significantly correlated with the baseline values for cardiac output, pulmonary vascular resistance and mean pulmonary artery pressure, as well as correlating strongly with maximal oxygen uptake, SpO_2 and the ventilatory equivalent for CO_2, determined by tests of maximal effort. Therefore, the 6MWT reflects the capacity determined by maximal cardiopulmonary exercise testing in patients with PAH, and the distance covered presents a strong, independent association with mortality, with a cut-off value of 332 m.

Solway et al.,[11] in a qualitative systematic review regarding the walk tests employed in the field of heart and lung disease, recognized the advantage of the 6MWT over other walk tests, stating that, in comparison with other tests of submaximal effort, it is more easily administered, better tolerated and more closely reflects day-to-day activity.

In a systematic review regarding the 6MWT in patients with CHF, Olsson et al.[12] questioned the capacity of the test in distinguish between efficacious and inefficacious treatments tested in clinical trials, despite being useful to provide supporting evidence of symptomatic benefits.

Stevens et al.[13] introduced the treadmill 6MWT (tread6MWT), comparing the results with those of the original (corridor) 6MWT in a group of adult patients enrolled in a pulmonary rehabilitation program. The patients were given oxygen as needed; heart rate and SpO_2 were monitored. The initial velocity of the treadmill was 1 mile/h (1.6 km/h), and the minimum velocity was 0.6 miles/h (0.96 km/h). The patients were instructed in the use of the treadmill (how to increase or reduce the velocity, how to stop and how to restart), as necessary. Additional instructions given before and during the test were the same as those employed in the original 6MWT. The tread6MWT was administered to 21 patients. The test was quite well tolerated, and there were no complications. The mean distance covered on the tread6MWT was 1.060 ± 389 m, compared with $1,228 \pm 255$ m for the 6MWT, a statistically significant difference ($p = 0.01$). The intratest variability was similar, and the coefficient of variation did not presented a significant difference. When three tests were performed in the same session, there was intratest reproducibility. The authors concluded that the tread6MWT is practical and easily administered, as well as being a test that facilitates the monitoring of the patients. However, due to the difference between the tread6MWT and the 6MWT, the former could be considered a different walk test, not necessarily interchangeable with the original 6MWT.

In the current issue of the Brazilian Journal of Pulmonology, Camargo et al.[14] present an original study in which they designed and vali-

dated a protocol for using the tread6MWT in order to evaluate patients with PAH—the first study of its type. The study involved 73 patients in whom the diagnosis of PAH had been confirmed through right heart catheterization. Careful interpretation of their data leads to the conclusion that the results obtained using the tread6MWT protocol constitute another functional and prognostic marker for patients with PAH, with certain operational advantages over the 6MWT.

In summary, tests of submaximal effort, also known as clinical field tests—principally the 6MWT—are clinical-functional measures that are well accepted by patients, easily performed and reproducible, without risks or major complications. However, that does not dispense with the need to take methodological precautions to reduce the variability in the results obtained using such tests. The results of tests of submaximal effort correlate well with those of tests of maximal effort and with functional variables, as well as having prognostic value and being predictive of mortality. Their greatest importance, however, is that they allow subjective patient complaints to be quantified, providing a satisfactory evaluation of limitations in the performance of activities of daily living. Attempts to characterize these tests as efficacious measures of the effects of new pharmacological agents have been unsuccessful. The tread6MWT can be seen as an improved, enriched technique of evaluating submaximal effort during exercise.

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