Cardiopulmonary exercise testing in COPD patients: beyond maximal oxygen uptake

Teste cardiopulmonar de exercício na DPOC: indo além do consumo máximo de oxigênio

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Worldwide, COPD is one of the leading causes of morbidity and mortality, causing significant impairment in quality of life and an enormous resource burden due to increased outpatient and inpatient costs. One of the main characteristics of the disease is the presence of dyspnea on exertion, which becomes increasingly limiting as the disease progresses. In COPD, exercise intolerance is multifactorial and integrally involves the respiratory, cardiovascular, and musculoskeletal systems, with the presence of airflow limitation (due to reduced ventilatory capacity), respiratory muscle dysfunction, lung hyperinflation, metabolic abnormalities, gas exchange abnormalities, peripheral muscle dysfunction, and cardiovascular abnormalities.[1] All of these factors contribute to dyspnea and fatigability at low exercise intensities, therefore limiting activities of daily living.

A variety of tests of proven prognostic importance are available to assess COPD patients during exercise, including the six-minute walk test combined with the Body mass index, airway Obstruction, Dyspnea, and Exercise capacity (BODE) index. However, the six-minute walk distance is only a marker of functional capacity, given that it does not evaluate the mechanisms of exercise limitation. In contrast, cardiopulmonary exercise testing (CPET) can provide more useful information regarding multiple limiting factors.[1] Traditionally, oxygen uptake at peak incremental CPET has been the variable to which the most weight has been given. However, because this variable is highly effort-dependent and because the determinants of exercise intolerance are nonspecific, other variables, particularly those measured during testing (i.e., submaximal variables), have been progressively incorporated into clinical assessment by CPET.

In 1996, Baba et al.[2] proposed that the slope of the linear relationship between oxygen uptake (y) and the logarithm of minute ventilation (x) be used as a marker—the oxygen uptake efficiency slope (OUES)—a steeper slope translating to greater oxygen uptake efficiency. At least theoretically, the OUES involves the integration of multiple systems during exercise and is influenced by oxygen supply and use, as well as by the muscle mass involved and the ventilatory response to exercise. It is known that the ventilatory response to exercise depends on the metabolic demand (carbon dioxide production and lactic acidosis), as well as on ventilatory efficiency (dead space to tidal volume ratio) and on factors affecting the respiratory drive (hypoxemia and the carbon dioxide set point). Therefore, the OUES is influenced by various systems, constituting an indirect marker of cardiopulmonary reserve.[2,3] The OUES has been studied especially in patients with cardiovascular dysfunction, its importance as a prognostic factor in chronic heart failure having been demonstrated.[4] However, it is of note that, despite being considered a submaximal variable, the OUES is influenced by exercise intensity, and it should be given weight especially when patients with chronic heart failure have exercised enough, as indicated by a ratio of carbon dioxide production to oxygen uptake > 1.0.[3]

In the current issue of the Brazilian Journal of Pulmonology, Müller et al.[5] investigated cardiovascular impairment and the role of peripheral and respiratory muscle strength in reducing the OUES in patients with mild-to-moderate COPD. This approach makes sense within the current concept that such patients have various comorbidities, including cardiovascular dysfunction.[6,7] Nutritional changes, weight loss, and skeletal muscle dysfunction can also occur, especially in the later stages of the disease.[8] However, in the study in question, the authors found that the OUES was within the predicted range for normal individuals. This finding suggests that cardiopulmonary reserve was adequate in the study population. In fact, the patients evaluated had relatively preserved aerobic capacity, their anaerobic threshold was within the expected

range, they had no cardiovascular impairment, and most had no signs of airflow limitation, meaning that the factors that could have affected oxygen uptake efficiency were absent or only slightly altered. In addition, peripheral muscle strength and respiratory muscle strength were found to be relatively preserved. These findings are in contrast with those reported by Terziyski et al.[9] and, in particular, with those reported by Tzani et al.[10] in patients with more advanced disease, in whom the OUES was actually reduced.

A joint analysis of the results of the study by Müller et al.[5] and those reported in the abovementioned studies[9,10] allows us to conclude that evaluating the OUES seems to be more relevant in patients with COPD that is more severe, in whom airflow limitation and cardiovascular limitation are more common, and in those with mild COPD and underlying cardiovascular disease. In that same line of thought, it is expected that reduced OUES, together with other CPET variables, can assist in the prognostic evaluation of this population, especially if we take into consideration the central role that cardiovascular comorbidities play in COPD mortality. These questions remain unanswered, and more studies like the study by Müller et al.[5] will certainly contribute to incorporating CPET into the clinical assessment of COPD patients.

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References

1. ERS Task Force, Palange P, Ward SA, Carlsen KH, Casaburi R, Gallagher CG, et al. Recommendations on the use of exercise testing in clinical practice. Eur Respir J. 2007;29(1):185-209. PMid:17197484.
2. Baba R, Nagashima M, Goto M, Nagano Y, Yokota M, Tauchi N, et al. Oxygen uptake efficiency slope: a new index of cardiorespiratory functional reserve derived from the relation between oxygen uptake and minute ventilation during incremental exercise. J Am Coll Cardiol. 1996;28(6):1567-72. http://dx.doi.org/10.1016/S0735-1097(96)00412-3
3. Hollenberg M, Tager IB. Oxygen uptake efficiency slope: an index of exercise performance and cardiopulmonary reserve requiring only submaximal exercise. J Am Coll Cardiol. 2000;36(1):194-201. http://dx.doi.org/10.1016/S0735-1097(00)00691-4
4. Davies LC, Wensel R, Georgiadou P, Cicoira M, Coats AJ, Piepoli MF, et al. Enhanced prognostic value from cardiopulmonary testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope. Eur Heart J. 2006;27(6):684-90. PMid:16338939. http://dx.doi.org/10.1093/eurheartj/ehi672
5. Mueller PT, Viegas CA, Patusco LA. Muscle strength as a determinant of oxygen uptake efficiency and maximal metabolic response in patients with mild-to-moderate COPD. J Bras Pneumol. 2012;38(5):540-548.
6. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. Eur Respir J. 2009;33(5):1165-85. PMid:19407051. http://dx.doi.org/10.1183/09031936.00128008
7. Miranda EF, Malaguti C, Corso SD. Peripheral muscle dysfunction in COPD: lower limbs versus upper limbs. J Bras Pneumol. 2011;37(3):380-8. PMid:21755195. http://dx.doi.org/10.1590/S1806-37132011000300016
8. Borghi-Silva A, Oliveira CC, Carrascosa C, Maia J, Berton DC, Queiroga F Jr, et al. Respiratory muscle unloading improves leg muscle oxygenation during exercise in patients with COPD. Thorax. 2008;63(10):910-5. PMid:18492743. http://dx.doi.org/10.1136/thx.2007.090167
9. Terziyski KV, Marinov BI, Aliman OI, St Kostianev S. Oxygen uptake efficiency slope and chronotropic incompetence in chronic heart failure and chronic obstructive pulmonary disease [abstract]. Folia Med (Plovdiv). 2009;51(4):18-24.
10. Tzani P, Aiello M, Elia D, Boracchia L, Marangio E, Olivieri D, et al. Dynamic hyperinflation is associated with a poor cardiovascular response to exercise in COPD patients. Respir Res. 2011;12:150. PMid:22074289 PMCid:3225311. http://dx.doi.org/10.1186/1465-9921-12-150