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Cardiopulmonary Exercise Testing

Current Applications and Future Clinical Potential

Exercise testing remains a valuable tool in the diagnosis and prognosis of cardiovascular and pulmonary disorders. When combined with additional imaging techniques, including nuclear medicine or echocardiography, additional information regarding the function and structure of the heart are made available. Cardiopulmonary exercise (CPX) testing traditionally has been used as a research tool or in the evaluation of athletic performance, yet has been underused in the clinical setting for various reasons (see Table). Despite this, however, CPX testing has been found to provide unique clinical information that can provide adjunctive diagnostic or prognostic information in many patient populations.

GAS EXCHANGE PHYSIOLOGY: A REVIEW

The ability to perform physical exercise is related to the cardiovascular system's capacity to supply oxygen to the muscles and the pulmonary system's ability to clear carbon dioxide from the blood *via* the lungs (3). This usually occurs in four distinct steps (see Figure) and by taxing the mechanisms responsible for the gas exchange *via* exercise, abnormalities often can be determined that often are not apparent at rest or by exercise testing alone (3).

Increased oxygen uptake during physical activity primarily is determined by an increase in cardiac output. To facilitate oxygen delivery to muscles during exercise, minute ventilation (V_E) increases in proportion to the work rate, and blood volume is redistributed away from inactive tissues to the active skeletal muscles. In addition, blood flow to the lungs is increased, resulting in improved blood oxygen availability. The combination of improved oxygen availability and enhanced oxygen extraction results in a widening of the arteriovenous (a-$\dot{V}O_2$) oxygen difference (3). Failure of one of these mechanisms to perform could indicate an underlying issue related to a cardiovascular or pulmonary disorder.

CPX VARIABLES AND CLINICAL INDICATIONS

CPX testing can be used in the clinical setting to provide important information beyond that found with traditional exercise testing. Variables obtained from CPX testing have been identified that play a key role in the prognosis or diagnosis of various cardiovascular and pulmonary diseases. Maximal aerobic capacity ($\dot{V}O_{2max}$) is considered one of the most important variables measured during CPX testing because it defines the limits of the cardiopulmonary system (3). $\dot{V}O_{2max}$ typically is measured in liters of oxygen per minute (absolute measure) but usually is expressed relative to body weight (milliliters of oxygen per kilogram body weight per minute). This relative measure of oxygen consumption allows for comparison of fitness levels independent of body weight, while allowing for conversion of aerobic capacity to energy expenditure (metabolic equivalents (METs)) to simplify exercise prescription.

Ventilatory threshold (VT) is a submaximal measure of exercise capacity that is identified as the point during which ventilation exponentially increases relative to the increase in oxygen consumption. The VT is related to the sudden increase in the blood lactate concentration, the lactate threshold, that occurs during a CPX test. The increased lactic acid production results in increased carbon dioxide production and an increased ventilatory response to the exercise (24). The VT usually occurs between 45% and 65% of $\dot{V}O_{2max}$ in most healthy individuals but can occur at a higher percentage of $\dot{V}O_{2max}$ in trained endurance athletes (5,14).

Photo courtesy of Elizabeth DeBeliso, Beaumont Hospitals.

Respiratory exchange ratio (RER) often is considered the lie detector of CPX testing and is defined as the ratio between carbon dioxide output ($\dot{V}CO_2$) and oxygen uptake ($\dot{V}O_2$). It is used to identify subject effort during CPX testing, with a peak RER of greater than or equal to 1.10, often considered an indication of excellent subject

TABLE: Reasons for the Underuse of CPX Testing

Requires additional equipment
Specialized personnel and training
Limited or absence of trained cardiovascular or pulmonary specialists
Lack of understanding of CPX value

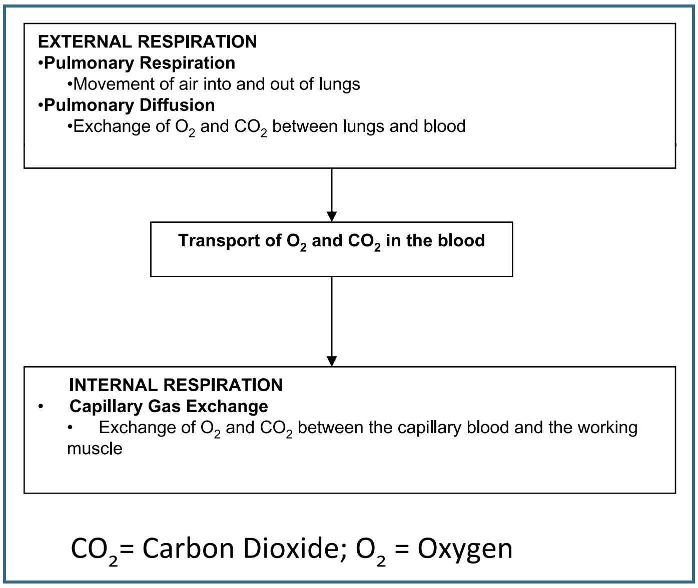

Figure. External and internal respiration associated with cardiopulmonary gas exchange.

effort (3). The prognostic or diagnostic capability of CPX testing is reduced, however, when RER values fall below 1.0, as this value is considered to indicate suboptimal subject effort (3).

Newer variables also have been identified that may provide clinically significant information for various patient populations. Oxygen uptake efficiency slope is a submaximal variable that evaluates the integrated function of the pulmonary, cardiovascular, and skeletal muscle systems (12). This variable has shown strong correlation with $\dot{V}O_{2max}$ (12) and has been tied to various degrees of cardiovascular health and disease (22). In addition, the oxygen pulse (O_2 pulse), or the ratio of $\dot{V}O_2$ to heart rate, reflects the amount of oxygen extracted per heart beat. This variable provides an estimate of left ventricular stroke volume during exercise (3). A flattening or downward displacement of the O_2 pulse during progressive exercise is felt to represent cardiogenic limitation to exercise performance (3).

CURRENT AND EMERGING CLINICAL APPLICATIONS

Although CPX testing primarily has focused on athletic performance, the use of this specialized testing procedure in the clinical setting has become more commonplace as computerized systems have allowed easier use and greater data storage capabilities (3). This has led to an ability to better evaluate the effect of various disease states on functional performance. In fact, CPX testing has gained widespread application in the functional evaluation of heart failure patients, who often demonstrate impaired aerobic capacity (4,8). Not only is CPX testing useful in determining the severity of the disease, it also can identify heart failure as the underlying cause of functional limitation while providing important prognostic information relative to disease status. In addition, CPX testing is the primary source to identify candidates for heart transplantation (13). Lastly, use of CPX testing helps facilitate appropriate exercise prescription during the rehabilitation of the heart failure patient and also can assess the efficacy of new drugs and devices in this specialized patient population (13). This has been found to be true both in heart failure patients demonstrating compromised ejection fractions, as well as those patients with normal ejection fractions (diastolic heart failure) (10,11).

CPX testing also commonly is used to evaluate unexplained dyspnea. This complaint is associated with a variety of potential underlying causes, many of which can be determined by history, physical examination, or basic screening tests (1,23). In instances where additional information is required, CPX testing can be used to determine the underlying cause of the unexplained dyspnea. Although most causes of unexplained dyspnea are related to pulmonary or cardiovascular causes, CPX testing can identify a wide range of disorders that may cause dyspnea, including neuromuscular, hormonal, myopathic, metabolic, and psychogenic conditions (6,17,20). Cardiovascular disorders, when identified using CPX testing, will typically include an impaired ability to deliver oxygen at a rate necessary to maintain the desired work rate (3). This usually is manifested in a reduced $\dot{V}O_{2peak}$ and tidal volume during maximal exercise testing. A reduced cardiac stroke volume, resulting in a steep increase in heart rate relative to measured $\dot{V}O_2$, also may be noted in this population (3).

Like those with heart failure, patients with skeletal muscle abnormalities also can benefit from CPX testing. In particular, patients with primary mitochondrial myopathies are unable to adequately use oxygen, resulting in early lactic acid accumulation and early fatigue with exercise (21). In these situations, CPX testing demonstrates low $\dot{V}O_{2peak}$ with an associated elevation in minute ventilation-consumed oxygen ($V_E/\dot{V}O_2$) ratio (21).

CPX testing also shows promise in the evaluation of additional clinical populations, including those with congenital heart defects (9,7), pulmonary resection surgery (16), pulmonary hypertension (1,2), ischemic heart disease (3), those with cardiac pacemakers (15,18), and in the morbidly obese (19). In each circumstance, CPX testing demonstrates diagnostic or prognostic information relative to disease severity. However, despite these encouraging early returns, additional research is needed before CPX use can be recommended fully.

OPPORTUNITIES FOR THE CLINICAL EXERCISE PROFESSIONAL

CPX testing remains an underused clinical option. Increasingly, however, data supports CPX testing in the clinical environment, setting the stage for increased use

of this important testing option. Exercise professionals, particularly those with significant clinical experience, are uniquely qualified to participate in this form of testing and can play a significant role in the coordination of testing, protocol use, and the presentation of data. Although CPX testing appears to be most useful in patients with cardiovascular and pulmonary diseases, particularly in those with heart failure and unexplained dyspnea, future clinical uses are sure to be validated to expand the scope of CPX testing use. Thus, the clinical exercise physiologist who becomes adept at the standardized performance of CPX testing, and who can assist in the use and interpretation of these important clinical data, can become a highly valuable member of a multidisciplinary clinical evaluation team.

References

1. American Thoracic Society; American College of Chest Physicians. ATS/ACCP statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med.* 2003;167:211–77.
2. Arena R, Lavie CJ, Milanie RV, Myers J, Guazzi M. Cardiopulmonary exercise testing in patients with pulmonary hypertension: an evidence-based review. *J Heart Lung Transplant.* 2010;29:159–73.
3. Balady GJ, Arena R, Sietsema K, *et al.* Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. *Circulation*. 2010;122:191–225.
4. Brubaker PH, Marburger CT, Morgan TM, Fray B, Kitzman DW. Exercise responses of elderly patients with diastolic versus systolic heart failure. *Med Sci Sports Exerc.* 2003;35:1477–85.
5. Davis JA, Vodak P, Wilmore JH, Vodak J, Kurtz P. Anaerobic threshold and maximal aerobic power for three modes of exercise. *J Appl Physiol*. 1976;41:544–50.
6. DePaso WJ, Winterbauer RH, Lusk JA, Dreis DF, Springmeyer SC. Chronic dyspnea unexplained by history, physical examination, chest roentgenogram, and spirometry: analysis of a seven-year experience. *Chest.* 1991;100:1293–9.
7. Diller GP, Dimopoulos K, Okonko D, *et al.* Exercise intolerance in adult congenital heart disease: comparative severity, correlates, and prognostic implication. *Circulation*. 2005;112:828–35.
8. Farr MJ, Lang CC, Lamanca JJ, *et al.* Cardiopulmonary exercise variables in diastolic versus systolic heart failure. *Am J Cardiol*. 2008;102:203–6.
9. Fredriksen PM, Veldtman G, Hechter S, *et al.* Aerobic capacity in adults with various congenital heart diseases. *Am J Cardiol*. 2001;87:310–4.
10. Guazzi M, Myers J, Arena R. Cardiopulmonary exercise testing in the clinical and prognostic assessment of diastolic heart failure. *J Am Coll Cardiol*. 2005;46:1883–90.
11. Guazzi M, Myers J, Peberdy MA, *et al.* Exercise oscillatory breathing in diastolic heart failure: prevalence and prognostic insights. *Eur Heart J*. 2008;29:2751–9.
12. 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;36:194–201.
13. Hunt SA. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol.* 2006;46:e1–e82.
14. Jones AM, Carter H. The effect of endurance training on parameters of aerobic fitness. *Sports Med*. 2000;29:373–86.
15. Lewalter T, Rickli H, MacCarter D, *et al.* Oxygen uptake to work rate relation throughout peak exercise in normal subjects: relevance for rate adaptive pacemaker programming. *Pacing Clin Electrophysiol.* 1999;22:769–75.
16. Loewen GM, Watson D, Kohman L, *et al.* Preoperative exercise VO_2 measurement for lung resection candidates: results of Cancer and Leukemia Group B Protocol 9238. *J Thorac Oncol*. 2007;2:619–25.
17. Martinez FJ, Stanopoulos I, Acero R, *et al.* Graded comprehensive cardiopulmonary exercise testing in the evaluation of dyspnea unexplained by routine evaluation. *Chest*. 1994;105:168–74.
18. Mathony U, Schmidt H, Groger C, *et al.* Optimal maximum tracking rate of dual-chambered pacemakers required by children and young adults for maximal cardiorespiratory performance. *Pacing Clin Electrophysiol*. 2005;28:378–83.
19. McCullough PA, Gallagher MJ, deJong AT, *et al.* Cardiorespiratory fitness and short-term complications after bariatric surgery. *Chest.* 2006;130:517–25.
20. Pratter MR, Curley FJ, Dubois J, Irwin RS. Cause and evaluation of chronic dyspnea in a pulmonary disease clinic. *Arch Intern Med*. 1989;149:2277–82.
21. Taivassalo T, Jensen TD, Kennaway N, *et al.* The spectrum of exercise tolerance in mitochondrial myopathies: a study of 40 patients. *Brain*. 2003;126:413–23.
22. Van Laethem C, Bartunek J, Goethals, *et al.* Oxygen uptake efficiency slope, a new submaximal parameter in evaluating exercise capacity in chronic heart failure patients. *Am Heart J*. 2005;149: 175–80.
23. Waraich S, Sietsema KE. Clinical cardiopulmonary exercise testing: patient and referral characteristics. *J Cardiopulm Rehabil Prev*. 2007;27:400–6.
24. Wasserman K, Beaver WL, Whipp BJ. Gas exchange theory and the lactic acidosis (anaerobic) threshold. *Circulation*. 1990;81(Suppl):II-14–II-30.

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