

CLINICAL APPLICATIONS:

Cardiopulmonary Exercise Testing

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The exercise test plays an important role clinically in the diagnostic, prognostic, and functional assessment of patients with cardiovascular and pulmonary disease.¹ Exercise capacity is widely recognized as an important factor in the risk paradigm among patients with coronary artery disease and chronic heart failure (CHF).

In the 1990s, there has been increased interest in the use of direct measurement of exercise capacity using ventilatory gas exchange techniques. Studies have demonstrated that measured peak oxygen uptake (VO_2) provides a more reliable and reproducible measure of exercise tolerance.^{2,3} Recent follow-up studies suggest that peak VO_2 is a more powerful prognostic marker relative to indirect indices of exercise capacity, such as watts achieved,

exercise time, or the metabolic equivalent value predicted from the exercise workload.^{4,5}

Moreover, interest in this technology has become more widely applied because it substantially increases the yield of information related to cardiopulmonary function. This information has applications not only for helping to establish the cause of exercise intolerance, but for diagnosis, prognosis, determination of disability, and making judgments concerning therapeutic interventions. The purpose of this article is to briefly describe the clinical applications of ventilatory gas exchange responses obtained during exercise testing.

Problems with estimating VO_2

Predicting oxygen uptake from the treadmill or cycle

ergometer workload is common clinically, but it can be very misleading. There are both physiologic and methodological reasons to explain why estimating VO_2 is inaccurate.

Although measured VO_2 and treadmill or cycle ergometer workload are directly related, with correlation coefficients ranging between 0.8 and 0.9, there is a wide scatter around the regression line. This inaccuracy has been attributed to such factors as:

- Subject habituation (less variation occurs with treadmill experience);
- Fitness (less variation occurs with increased fitness);
- Heart disease (oxygen uptake is overpredicted for diseased individuals);
- Handrail holding (the oxygen cost of the work is markedly

reduced if the subject is allowed to hold on to the handrails); and

- The exercise protocol (less variation occurs when more gradual, individualized protocols are used).

Thus, if quantifying work with precision is an important objective, such as in research studies, a direct measurement is essential.

Numerous studies have described the factors affecting the relationship between measured and predicted oxygen uptake. The variability between oxygen uptake and exercise time or workload is well documented yet poorly appreciated. Most pharmaceutical trials, for example, continue to report work in terms of the relatively unreliable measure: exercise time. This is particularly a concern since many studies have shown that the presence of heart disease can greatly increase the error associated with predicting oxygen uptake. This is because the rate of increase in VO_2 with progressive exercise is slower in patients with heart disease, particularly those with reduced left ventricular function.^{6,7}

In addition, it has been demonstrated that protocols that contain large or unequal

increments in workrate tend to accentuate the overestimation of exercise capacity commonly observed in patients with heart disease.^{3,6}

Recommendations of major organizations

The most recent edition of the exercise testing guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) lists specific indications for the use of ventilatory gas exchange (see Table 1).⁸ The foremost application (a Class I indication, or one for which there is evidence or general agreement that the technol-

The American Thoracic Society "Statement on Evaluation of Impairment/Disability Secondary to Respiratory Disorders,"⁹ stratifies impairment based on achieved VO_{2max} and employs a criteria for respiratory impairment based on low breathing reserve (defined below), presence of submaximal hyperventilation, and ability to achieve the ventilatory threshold.

Abnormalities in ventilation

Patients with cardiovascular and pulmonary limitations during exercise often manifest their

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ogy is useful or effective) is for the evaluation of patients with CHF who are being considered for transplantation. This is largely due to the many studies performed in recent years demonstrating that VO_2 , when measured directly, has a very important place in the risk paradigm in these patients.^{4,5} This is addressed in the AHA "Position Statement on Selection and Treatment of Candidates for Heart Transplantation," discussed below.

An additional Class I indication, the differentiation of cardiac versus pulmonary exercise limitations, has important implications for optimizing treatment options for these conditions.

impairments as abnormalities in minute ventilation (V_E) or carbon dioxide production (VCO_2). Unlike normal individuals and most patients with coronary artery disease, patients with CHF and pulmonary disease often exhibit dyspnea as their limiting symptom. Ventilation is typically heightened at any matched submaximal work rate.¹⁰⁻¹² In CHF, this occurs due to a combination of several factors, the most important of which are early lactate accumulation and a mismatching of ventilation to perfusion in the lung.^{12,13} In many types of pulmonary disease, heightened ventilation or dyspnea during exercise can also be caused by abnormal diffusion capacity.



Table 1. American Heart Association/American College of Cardiology Indications for Use of Exercise Testing Using Ventilatory Gas Analysis.

Class I	Class IIa	Class IIb	Class III
1. Evaluation of exercise capacity and response to therapy in patients with heart failure who are being considered for heart transplantation.	1. Evaluation of exercise capacity when indicated for medical reasons in patients in whom subjective assessment of maximal exercise is unreasonable.	1. Evaluation of the patient's response to specific therapeutic interventions in which improvement of exercise tolerance is an important goal or endpoint.	1. Routine use to evaluate exercise capacity.
2. Assistance in the differentiation of cardiac vs. pulmonary limitations as a cause of exercise-induced dyspnea or impaired exercise capacity when the cause is uncertain.		2. Determination of the intensity for exercise training as part of comprehensive cardiac rehabilitation.	

SOURCE

ACC/AHA Guidelines for Exercise Testing: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). *Journal of the American College of Cardiology*, 1997, Vol. 30.

An index frequently used to help distinguish pulmonary and cardiovascular disease is known as the "breathing reserve" or "dyspnea index." This is the ratio of maximal minute ventilation during exercise to maximal voluntary ventilation at rest (V_E/MVV). Most healthy subjects achieve a maximal ventilation of only 60 to 70 percent of MVV at peak exercise. One characteristic of chronic pulmonary disease is a maximal ventilation that approaches or equals an individual's MVV. These patients reach a "ventilatory" limit during exercise, while normal subjects, and those with cardiovascular disease, generally have a substantial ventilatory reserve (20 to 40 percent) at peak exercise and are limited by other factors.

An abnormally heightened VCO_2 is also a characteristic of CHF; the slope of the relation-

ship between V_E and VCO_2 increases in accordance with the severity of this condition,¹⁰ and recently this index has been shown to be an important prognostic marker.¹⁴ The ratio of V_E to VCO_2 at maximal exercise is inversely related to cardiac output and dead space ventilation.^{12,13} This suggests that reduced pulmonary perfusion underlies the excess ventilatory response to exercise, in part, through a mismatching of ventilation and perfusion in the lung.

Prognosis

An important application of cardiopulmonary exercise testing that has emerged during the 1990s is its role in prognosis, particularly in the context of CHF. Recent AHA/ACC consensus reports have recommended that peak VO_2 be used to help determine the timing of heart transplantation in ambulatory

patients with CHF.^{8,15} Several reports suggest that a cutpoint less than or equal to 14 mL/kg/min. for peak VO_2 be used as a criterion for listing patients for transplantation,⁵ because it appears that for patients who achieve values greater than 14 mL/kg/min., one-year survival is similar to those who receive a transplant. Although the optimal cutpoint for peak VO_2 has been debated,¹⁶ such observations are extremely valuable in the current health care climate because they help to direct scarce resources toward patients who are most likely to benefit.

Technique proves its worth

The value of using ventilatory gas exchange techniques during exercise testing, including improved precision and a greater yield of clinically useful information, is underscored by a growing

body of literature. With technological advances available in the current metabolic systems, the test can be performed with minimal inconvenience to the patient and minimal time commitment on the part of the operator. Gas exchange techniques have many applications among patients with cardiovascular and pulmonary disease, including the assessment of therapeutic interventions, a better understanding of the

pathophysiology of exercise intolerance, and disability.

Recent studies suggest that the added precision provided by this technology has important prognostic utility. A cardiopulmonary exercise test can supplement other clinical and exercise test information when precision is important, the patient's symptoms are mixed, or when it is unclear why the patient was referred for testing. 🦋

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See the “Tools of the Trade” column on the “Table of Contents” in this issue for additional resources on this topic.

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