

Understanding the Basics of Cardiopulmonary Exercise Testing

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Cardiopulmonary exercise testing adds important additional information to that provided by the standard exercise test. In particular, cardiopulmonary exercise testing provides precise determination of aerobic capacity, the causes of dyspnea with exertion, and prognosis in patients with systolic heart failure. This review provides basic, practical information about cardiopulmonary exercise testing for the clinician.

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AT = anaerobic threshold; BR = breathing reserve; CaO_2 = arterial oxygen concentration; CO = cardiac output; CvO_2 = mixed venous oxygen content; HF = heart failure; HR = heart rate; MET = metabolic equivalent; MVV = maximum voluntary ventilation; $Pk\dot{V}O_2$ = peak oxygen consumption per unit time; RER = respiratory exchange ratio; SV = stroke volume; $\dot{V}CO_2$ = carbon dioxide output; \dot{V}_E = minute ventilation; $\dot{V}_E/\dot{V}CO_2$ = ventilatory equivalent for carbon dioxide; $\dot{V}O_2$ = oxygen consumption per unit time; $\dot{V}O_{2max}$ = maximum oxygen consumption per unit time

Exercise stress testing is commonly used to evaluate the presence and severity of coronary ischemia, as well as exertional symptoms, heart rate (HR) and blood pressure responses, and estimated aerobic capacity.^{1,2} Additional important clinical information may be obtained by direct measurement of exercise respiratory gas exchange, referred to as cardiopulmonary exercise testing.³ This review updates the clinician on the indications and interpretation of cardiopulmonary exercise testing in modern medicine.

WHY MEASURE GAS EXCHANGE?

An important prognostic component of exercise stress testing is the evaluation and quantification of work performed, also known as functional capacity.⁴ Because energy consumption, generally quantified as caloric expenditure, is difficult to measure during exercise, a more readily measurable metabolic equivalent (MET) was sought to quantify the work performed at various stages of exercise. In humans, total oxygen consumption approximates caloric expenditure, with both parameters increasing during exercise in a similar fashion. Thus, 1 MET of caloric expendi-

ture was set at the resting level of oxygen consumption of a healthy man weighing 70 kg or 3.5 mL/kg per minute. Therefore, any physical activity can be viewed as a multiple of this unit measure, with threshold requirements identified for individuals who want to perform unique activities. Typically, simple household activities and light work activities require an energy expenditure of approximately 1.5 to 4 METs, moderate work and typical sexual activities require an energy expenditure of approximately 3 to 6 METs, and heavy work or high-level sports activities require an energy expenditure of 5 to 15 METs.⁵ Direct assessment of METs has become an integral component in occupational development and disability determination, and cardiopulmonary exercise testing remains the sole modality for its determination.

HOW IS GAS EXCHANGE MEASURED?

Like the lungs, the primary function of the cardiovascular system is gas exchange, supplying oxygen and other fuels to working muscles and removing carbon dioxide and other metabolites. The heart, lungs, and pulmonary and systemic circulations form a single circuit for exchange of respiratory gases between the environment and the cells of the body.^{6,7} Under steady-state conditions, oxygen consumption per unit time ($\dot{V}O_2$) and carbon dioxide output ($\dot{V}CO_2$) measured at the mouth are equivalent to oxygen utilization and carbon dioxide production occurring in the cell; thus, external respiration equals internal respiration (Figure 1).⁷ Cardiopulmonary exercise testing measures fractions of oxygen and carbon dioxide in expired gas, expired air volume, or flow and calculates $\dot{V}O_2$, $\dot{V}CO_2$, and minute ventilation (\dot{V}_E) with a nonbreathing valve connected to a metabolic cart (Figure 2). Samples of expired air are typically assessed every 15 seconds (some systems use 30- to 45-second increments), and real-time data are expressed in both a tabular and a graphic format. Additionally, oxygen saturation using finger, ear lobe, or forehead oximetry is monitored and recorded. From these data, numerous clinically relevant metabolic parameters can be derived (Table 1).

To obtain reliable metabolic data that reflect steady-state conditions, it is imperative to avoid high increments in workload, which are often present when using a Bruce exercise protocol, and extremes of test duration. Many laboratories use ramping treadmill and/or bicycle exercise protocols, which are tailored to the patient's activity his-

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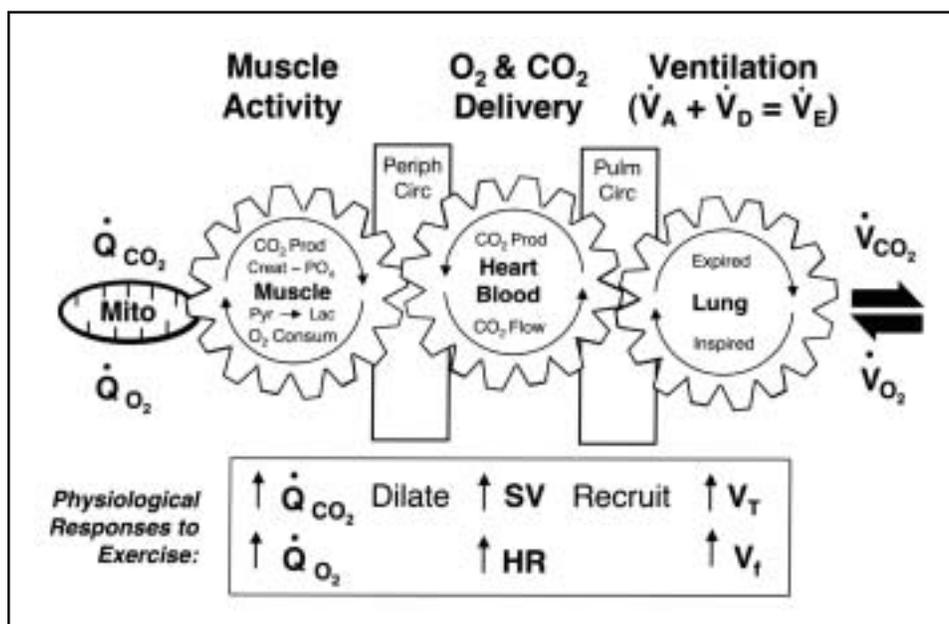


FIGURE 1. Gas transport mechanisms coupling cellular (internal) respiration to pulmonary (external) respiration. Circ = circulation; CO_2 = carbon dioxide; Consum = consumption; Creat = creatine; Lac = lactate; HR = heart rate; Mito = mitochondria; PO_4 = phosphate; O_2 = oxygen; Periph = peripheral; Prod = production; Pulm = pulmonary; Pyr = pyruvate; \dot{Q}_{CO_2} = carbon dioxide production; \dot{Q}_{O_2} = oxygen utilization; SV = stroke volume; \dot{V}_A = minute alveolar ventilation; \dot{V}_D = minute dead space ventilation; \dot{V}_E = minute ventilation; V_f = breathing frequency; V_T = tidal volume; \dot{V}_{CO_2} = carbon dioxide output; \dot{V}_{O_2} = oxygen uptake. From *Principles of Exercise Testing and Interpretation*, 3rd ed,⁷ with permission from Lippincott Williams & Wilkins.

tory, to achieve an exercise test time between 8 and 12 minutes. Shorter durations may produce a nonlinear relationship between \dot{V}_{O_2} and work rate, whereas durations longer than 12 minutes may cause patients to terminate

exercise because of muscle fatigue or orthopedic factors.⁸ A ramping protocol generates almost imperceptible increases in the treadmill speed and grade every 15 seconds and more consistently achieves steady-state conditions



FIGURE 2. A patient undergoing a cardiopulmonary stress test. The head harness worn by the patient holds the mouthpiece and nonbreathing valve that is connected to a metabolic cart to the immediate left of the patient.

when compared with other exercise protocols, including the Bruce protocol.⁸⁻¹⁰ The Balke and Naughton protocols can also be considered because they involve only modest increases in treadmill elevations at a constant speed.⁴

With standard exercise testing, METs can be estimated by regression formulas, standard accessories on most commercially available treadmills. Several studies have demonstrated that these formulas are often inaccurate and typically overestimate METs when using fixed work-rate exercise protocols such as the Bruce treadmill protocol, which uses large or unequal increments in work.⁸ Ramping exercise protocols permit increases in external work to occur in a constant or continuous fashion such that increases in workload can be individualized throughout a wide range of patient capabilities.¹¹

CARDIOPULMONARY RESPONSES TO INCREMENTAL EXERCISE

In healthy people, predictable physiologic changes occur during exercise. These changes include a reduction in systemic vascular resistance, increases in oxygen extraction, and augmentation of stroke volume (SV) and HR, resulting in an increase in cardiac output (CO). The coupling between oxygen transport and circulatory function is revealed in the Fick equation, which states $\dot{V}O_2 = CO \times (CaO_2 - CvO_2)$, in which CaO_2 is the arterial oxygen concentration and CvO_2 is the mixed venous oxygen content. This formula can be rewritten as $\dot{V}O_2 = (HR \times SV) \times (CaO_2 - CvO_2)$. The Fick equation can be modified to reflect the changes in each variable at peak exercise, which contribute to the maximum oxygen consumption per unit time ($\dot{V}O_{2max}$) as $\dot{V}O_{2max} = (HR_{max} \times SV_{max}) \times (CaO_{2max} - CvO_{2min})$, with max indicating maximum and min indicating minimum.

PHYSIOLOGIC RESERVE

Although the lungs and the heart are coupled in gas exchange, they differ with regard to physiologic reserve during maximal exercise. By definition, under maximal stress, the HR reserve is zero. Defining the maximal predicted HR as $220 - \text{age}$, stress tests are considered less than adequate (reduced sensitivity) when HR does not exceed 85% of predicted, thus leaving a reserve of greater than 15%. However, this formula is not accurate in predicting maximal HR for all patients (particularly those taking β -blockers and those with diabetes). A desirable HR reserve under maximal stress is less than 15% and is ideally close to zero. In contrast, the ventilatory reserve or breathing reserve (BR) in healthy controls cannot be less than 20% and is typically between 30% and 50%. Baseline spirometry, including maximum voluntary ventilation (MVV), is measured as part of the testing procedure before exercise. The BR is

TABLE 1. Metabolic Parameters Derived From Cardiopulmonary Stress Testing

Peak oxygen consumption per unit time
Breathing reserve*
Oxygen saturation
Anaerobic threshold
Respiratory exchange ratio
Oxygen pulse
Ventilatory equivalent for carbon dioxide
Peak oxygen consumption per unit time adjusted for lean body mass†
Oxygen pulse adjusted for lean body mass†

*Requires pretest spirometry with maximum minute ventilation.

†Requires body composition assessment.

calculated as follows: $BR = 1 - \dot{V}_{Emax}/MVV$. Thus, lung mechanics are not limiting in healthy individuals but can become compromised by obstruction of airflow, restriction of lung volumes, or ventilation-perfusion mismatch. These conditions may additionally result in arterial oxygen desaturation at peak exercise, a situation that does not occur in patients with coronary artery disease or cardiomyopathy but may occur in patients with congenital heart disease and/or pulmonary hypertension.¹²

ANAEROBIC THRESHOLD

When the metabolic demands of exercise begin to exceed oxygen delivery to working muscles, anaerobic metabolism ensues.^{3,7,12} However, even with low-intensity exercise, anaerobic energy production may make a small contribution that markedly increases at exercise intensities greater than the anaerobic threshold (AT). This is evidenced by rising blood lactate levels and lactate-pyruvate ratios. Lactic acid is then buffered by bicarbonate, producing excess nonmetabolic carbon dioxide via the carbonic anhydrase reaction: $H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons CO_2 + H_2O$. The resultant increase in carbon dioxide output is detected by chemoreceptors in the carotid bodies, which mediate an increase in \dot{V}_E . The AT, also known as the ventilatory threshold, is defined as the highest $\dot{V}O_2$ attained without a sustained increase in blood lactate concentration and lactate-pyruvate ratio. It is detected metabolically as the point of inflection at which $\dot{V}CO_2$ and \dot{V}_E increase relative to $\dot{V}O_2$. The most common means for identifying the AT is the \dot{V} -slope method, which uses regression analysis to present the inflection point on a plot of $\dot{V}CO_2$ vs $\dot{V}O_2$.¹³⁻¹⁵ The AT occurs typically between 47% and 64% of the $\dot{V}O_{2max}$ in healthy untrained individuals and generally at a higher percentage of $\dot{V}O_{2max}$ in endurance-trained individuals.^{3,7,12,14}

For the purposes of exercise prescription, knowledge of the AT can be useful. At workloads below the AT, blood lactate levels remain low, slow-twitch (type I) fibers with high oxidative capacity are used, and exercise can be sustained for prolonged periods, limited only by substrate

availability and musculoskeletal trauma. At workloads above the AT, blood lactate levels increase, fast-twitch (type II) fibers with low oxidative capacity are used, and exercise duration shortens progressively with increasing load.^{3,7,12} The AT affects activities of daily living and can be extended in health by exercise training and reduced through deconditioning. In addition, an AT below 11 mL/kg per minute and/or ischemia on the electrocardiographic portion of the cardiopulmonary exercise test has been used to identify a high risk of perioperative death in elderly patients undergoing major surgical procedures.¹⁶

RESPIRATORY EXCHANGE RATIO

The respiratory exchange ratio (RER) is related but not equivalent to its cellular counterpart the respiratory quotient and is defined as the ratio of \dot{V}_{CO_2} to \dot{V}_{O_2} : $RER = \dot{V}_{CO_2}/\dot{V}_{O_2}$. The RER represents the metabolic exchange of gases in the body's tissues and is dependent in part on the predominant fuel (carbohydrate vs fat) used for cellular metabolism.¹⁷ At rest and with early exercise, the \dot{V}_{CO_2} curve runs slightly below the \dot{V}_{O_2} curve. Once the AT is passed, additional nonmetabolic carbon dioxide is produced, resulting in a steep rise in \dot{V}_{CO_2} and an accompanying rise in RER to values ultimately exceeding 1.0. As lactate builds in exercising muscle, exercise becomes progressively uncomfortable. Because the level of RER is directly related to muscle lactate accumulation, it can be used as an objective means of quantifying effort. Respiratory exchange ratio values less than 1.0 generally indicate poor effort, 1.0 to 1.1 indicate fair effort, 1.1 to 1.2 indicate good effort, and values that exceed 1.2 indicate an excellent effort. Exceptions to this rule include neuromuscular limitations that prevent sustained exercise, low threshold peripheral or myocardial ischemia, severe ventilatory impairment, failure of testing personnel to encourage good patient effort, or test stoppage due to worrisome symptoms or signs.

PEAK \dot{V}_{O_2}

The peak \dot{V}_{O_2} ($Pk\dot{V}_{O_2}$) is the highest \dot{V}_{O_2} achieved during the cardiopulmonary exercise testing and generally occurs at or near peak exercise. Moreover, if the \dot{V}_{O_2} curve demonstrates a plateau, such that \dot{V}_{O_2} no longer increases despite progressive increments in workload, then the $Pk\dot{V}_{O_2}$ can be labeled the $\dot{V}_{O_2,max}$.¹⁸ The $\dot{V}_{O_2,max}$ is the best and most reproducible index of cardiopulmonary fitness or disability.^{3,7} The $Pk\dot{V}_{O_2}$, $\dot{V}_{O_2,max}$, and AT are reported as a weight-adjusted value in milliliters of \dot{V}_{O_2} per kilogram of body weight per minute to facilitate intersubject comparisons. To convert $Pk\dot{V}_{O_2}$ or $\dot{V}_{O_2,max}$ to METs, divide by 3.5 mL/kg per minute.

Normally, $\dot{V}_{O_2,max}$ decreases with age, declining 8% to 10% per decade in nonathletic individuals and approximately 5% per decade in trained individuals who continue

to exercise vigorously.⁴ At any age, $\dot{V}_{O_2,max}$ is 10% to 20% higher in men than women, in part because of a higher hemoglobin concentration, a larger muscle mass, and a greater SV in men.^{4,19,20} These age and sex differences in $\dot{V}_{O_2,max}$ must be considered when interpreting cardiopulmonary exercise testing. As a result, the measured $\dot{V}_{O_2,max}$ will be compared with a predicted value generated from empirically derived formulas based on age, sex, and height.^{7,12,21,22} The $\dot{V}_{O_2,max}$ would be considered decreased if the measured value is less than 85% of predicted.

OXYGEN PULSE

The amount of oxygen consumed from the volume of blood delivered to tissues by each heart beat is termed the oxygen pulse and depends on the size of the SV and the arteriovenous oxygen difference and may be more dependent than $Pk\dot{V}_{O_2}$ on cardiac pump function reserve (because it does not incorporate HR reserve). The oxygen pulse is calculated as \dot{V}_{O_2} divided by HR.

Thus, by altering the Fick equation as follows, the oxygen pulse can provide an index of the SV and arteriovenous oxygen difference:

$$\dot{V}_{O_2} = (HR \times SV) \times (CaO_2 - CvO_2)$$

$$\dot{V}_{O_2}/HR = SV \times (CaO_2 - CvO_2)$$

Since oxygen extraction is maximal and relatively constant at peak exercise, the oxygen pulse becomes a reasonable surrogate of SV and is diminished in patients with severe left ventricular dysfunction and/or valvular heart disease.

VENTILATION-CARBON DIOXIDE PRODUCTION RATIO

The major link between the circulatory and ventilatory responses to exercise is carbon dioxide production. Ventilatory efficiency is defined by linking ventilation relative to carbon dioxide production, resulting in the matching of ventilation and perfusion.^{23,24} The breathing requirements of exercise can be described from the equation $\dot{V}_E = \dot{V}_{CO_2} \times \dot{V}_E/\dot{V}_{CO_2}$, in which \dot{V}_E/\dot{V}_{CO_2} is the ventilation-carbon dioxide production ratio, also known as the ventilatory equivalent for carbon dioxide. \dot{V}_E/\dot{V}_{CO_2} is a respiratory control function that reflects chemoreceptor sensitivity, acid-base balance, and ventilatory efficiency at the alveolar-capillary interface.^{12,25,26} At the onset of exercise, \dot{V}_E/\dot{V}_{CO_2} typically decreases because of improved ventilation and perfusion matching. As exercise progresses, \dot{V}_E/\dot{V}_{CO_2} remains fairly constant because \dot{V}_E tracks \dot{V}_{CO_2} linearly. Finally, as exercise peaks, the development of metabolic acidosis results in an additional ventilatory stimulus, resulting in a small increase in \dot{V}_E/\dot{V}_{CO_2} . Increased \dot{V}_E/\dot{V}_{CO_2} is commonly observed in patients with pulmonary disease and heart failure (HF).

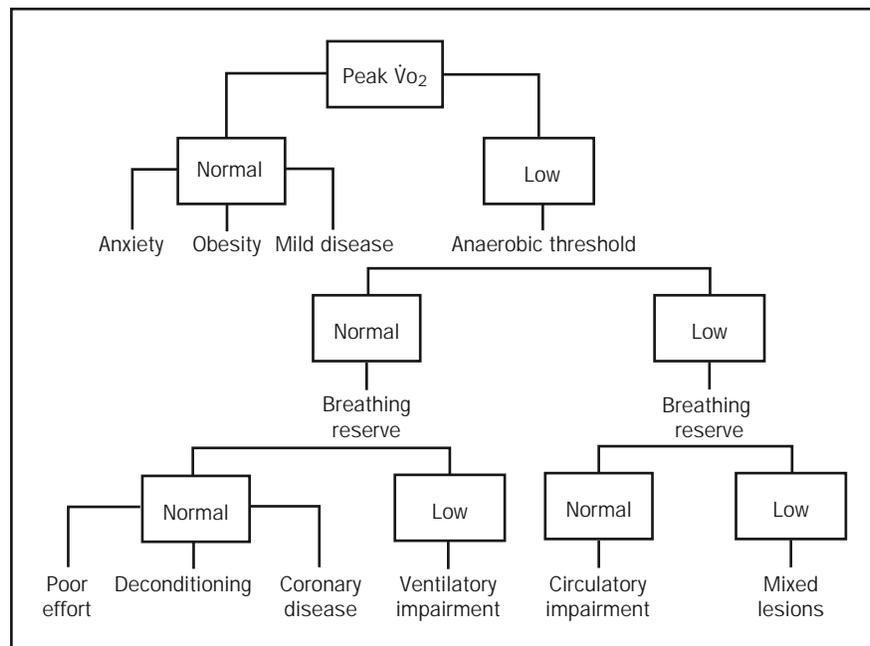


FIGURE 3. Flowchart for the differential diagnosis of exertional dyspnea and fatigue. $\dot{V}O_2$ = oxygen consumption per unit time. From *Arch Intern Med*¹² with permission. Copyright 1988 American Medical Association. All rights reserved.

WHAT WILL THE TEST RESULTS TELL ME?

Besides precise assessment of peak aerobic capacity (ie, measured METs as opposed to estimating METs), cardiopulmonary exercise testing is invaluable in determining the cause of dyspnea on exertion and determining normality of cardiac and pulmonary responses to exercise. The most common indications for cardiopulmonary exercise testing are outlined in Table 2.

Metabolic derangements can occur at multiple sites within the circuitry of gas exchange, including the consumers at the muscle mitochondria, the transporters within the circulatory system, and the exchangers at the site of ventilation (Figure 1). Knowledge of site and extent of metabolic dysfunction through cardiopulmonary exercise testing can have a wide application in clinical medicine.

Cardiopulmonary exercise testing provides an ideal modality for the evaluation of patients who present with exertional dyspnea and fatigue, when the clinician is faced with a breadth of differential diagnoses ranging from circulatory impairment to deconditioning.¹² Standard diagnostic studies may not identify the true cause because circulatory and ventilatory reserves cannot be fully assessed from indices of resting cardiac and pulmonary function. By virtue of obtaining gas exchange data under the provocation of exercise, cardiopulmonary exercise testing can identify potential deficiencies within these systems.

Using the algorithm provided in Figure 3, a $Pk\dot{V}O_2$ less than 85% of age- and sex-predicted values is considered low, and, as discussed previously, a normal AT is generally closer to 60% of the predicted $Pk\dot{V}O_2$. However, for purposes of classification an AT less than 40% of the predicted $Pk\dot{V}O_2$ is considered pathologically reduced and indicative of circulatory insufficiency. A BR less than 30% would indicate ventilatory impairment, especially when accompanied by oxygen desaturation with exercise, although a BR of 20% to 30% is deemed a borderline value. Cardiopulmonary exercise testing is useful in dyspneic patients with combined cardiac and pulmonary diseases who may have a reduction in AT and/or BR, the more dominant of which may indicate the primary cause of the patient's functional

TABLE 2. Potential Indications for Cardiopulmonary Stress Testing

Evaluation for exertional dyspnea
Development of an exercise prescription
Direct measurement of peak oxygen consumption per unit time (functional capacity)
Risk stratification and prognosis in heart failure
Optimization of rate-adaptive or biventricular pacemaker
Congenital heart disease: determination of need for surgical repair and response to treatment
Disability determination; work-site readiness
Assess functional significance of regurgitant valvular heart disease
Assess the results of medical and surgical therapies

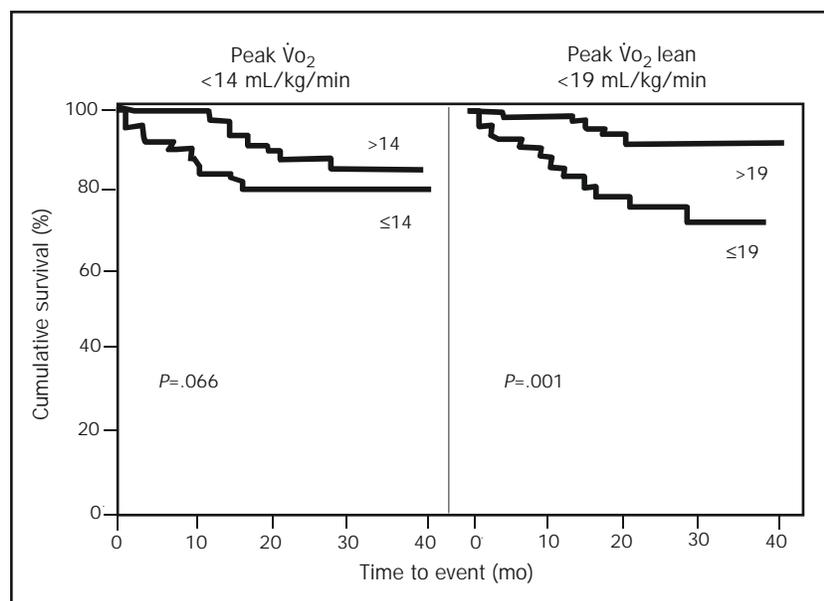


FIGURE 4. Kaplan-Meier survival curves using both peak oxygen uptake ($Pk\dot{V}O_2$) of 14 mL/kg per minute and $Pk\dot{V}O_2$ adjusted for lean body mass of 19 mL/kg per minute as cutoffs showing a stronger prognostic value to the fat-adjusted $Pk\dot{V}O_2$ by log-rank testing. From *J Am Coll Cardiol*,³³ with permission from The American College of Cardiology Foundation.

limitation.³ An RER of less than 1.1 (particularly <1.0) in the absence of other metabolic abnormalities suggests poor effort, anxiety, or mild disease.

CARDIOPULMONARY EXERCISE TESTING IN HF

From a clinical standpoint, cardiopulmonary exercise testing has gained widespread use in the evaluation of patients with advanced systolic HF.²⁷ Although left ventricular ejection fraction does not predict $Pk\dot{V}O_2$, numerous studies have confirmed the prognostic utility of measuring gas exchange in patients with systolic HF. In the Veterans Administration Heart Failure Trial, mortality of patients with a $\dot{V}O_{2max}$ of 14.5 mL/kg per minute or less was double that of patients whose $\dot{V}O_{2max}$ exceeded this value.²⁸ In a separate investigation of patients with HF referred for cardiac transplantation, Mancini et al²⁹ found that $Pk\dot{V}O_2$ was the single best predictor of survival. Moreover, transplantation could be safely deferred in patients whose $Pk\dot{V}O_2$ values were greater than 14 mL/kg per minute, in which their survival exceeded that of patients undergoing heart transplantation. As a result of these seminal studies, cardiopulmonary exercise testing remains a pivotal modality in the initial evaluation of patients with advanced HF, especially those who are considered for heart transplantation.

Although the $Pk\dot{V}O_2$ cutoff of 14 mL/kg per minute remains an important prognostic discriminator in patients with HF, disparities in its prognostic utility may occur

when evaluating special populations, including women and obese people.^{20,30,31} A fundamental understanding of oxygen consumption may explain these disparate observations. Although $Pk\dot{V}O_2$ is usually corrected for total body weight, body fat is metabolically inert, consuming essentially no oxygen, and can represent a significant portion of total weight. Moreover, considerable variability in body composition is present across populations, including those with HF. Correcting $Pk\dot{V}O_2$ for lean body mass provides a more refined discriminator of outcome than traditionally reported total weight-adjusted values.^{32,33} In patients with HF, a $Pk\dot{V}O_2$ corrected for lean body mass cutoff of 19 mL/kg per minute provides a more robust discriminator of major cardiac events (death and/or urgent heart transplantation) than the total weight-adjusted figure of 14 mL/kg per minute (Figure 4). As such, routine assessment of body fat using the 3-site skinfold method before each cardiopulmonary exercise study can be used to calculate lean body mass.³⁴ From a practical standpoint, this adds only 3 to 4 minutes to the time required to perform cardiopulmonary exercise testing. Using the lean body mass-adjusted $Pk\dot{V}O_2$ may eliminate previously observed disparities between the sexes, as well as in obese individuals, in predicting outcome in patients with HF.

Recently, oxygen pulse has been studied to assess prognosis in patients with HF.^{35,36} We recently reported that an uncorrected peak oxygen pulse of 10 mL/beat separated those with clinical events compared with event-free survivors, whereas a lean body mass-adjusted value of 14 mL/

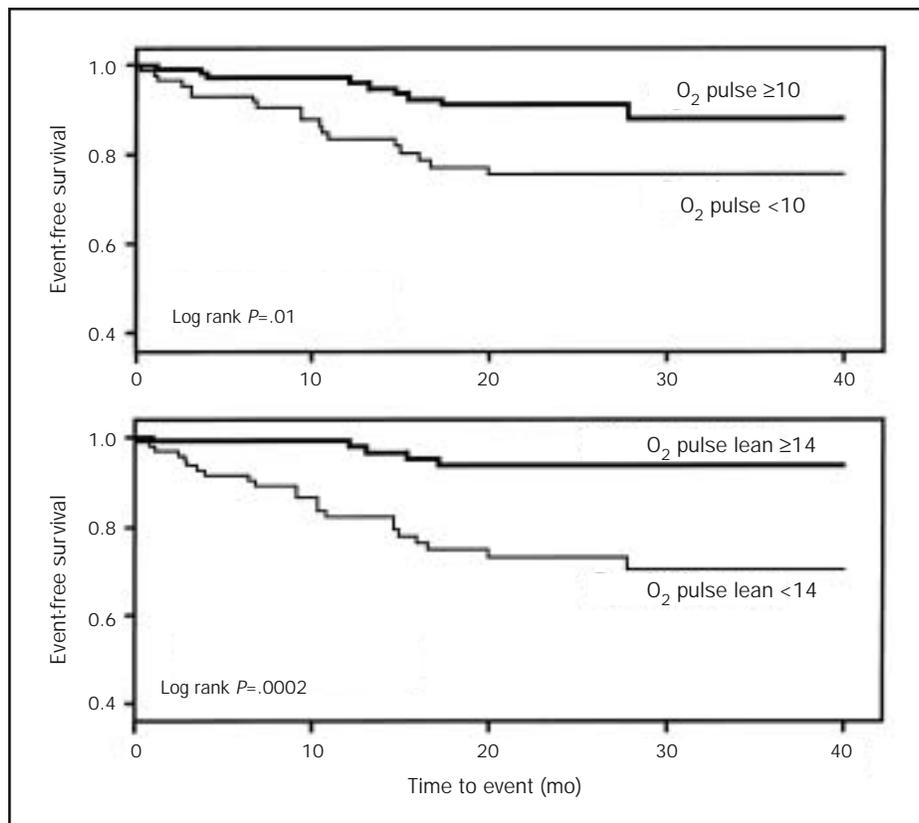


FIGURE 5. Kaplan-Meier survival curves using both peak oxygen pulse of 10 mL/beat and peak oxygen pulse adjusted for lean body mass of 14 mL/beat as cutoffs for predicting event-free survival. O_2 = oxygen. From *Am J Cardiol*,³² with permission from Elsevier.

beat for peak oxygen pulse provided an even better prognostic ability for HF event-free survival (Figure 5).³² In fact, in multivariate models that contained clinical and cardiopulmonary variables, a higher lean body mass-adjusted oxygen pulse was the strongest independent predictor of event-free survival, and this was particularly the case in patients with class III HF.

Several studies have suggested that additional cardiopulmonary variables, including indexed $Pk\dot{V}O_2$,^{37,38} percent predicted $Pk\dot{V}O_2$,³⁹ $\dot{V}_E/\dot{V}CO_2$ or the slope of $\dot{V}_E/\dot{V}CO_2$,^{25,38,40,41} $\dot{V}O_2$ recovery (defined as the time needed for $\dot{V}O_2$ to decrease by 50% from its peak value), and cardiac or peak circulatory power (defined as the product of $Pk\dot{V}O_2$ and systolic arterial pressure),³⁶ may contribute additional prognostic information in the evaluation of patients with HF. Recently, the applicability and prognostic role of cardiopulmonary exercise testing in patients with chronic HF who are maximally treated with an up-to-date pharmacological armamentarium, including β -blocking agents, which result in lower HRs during exercise, have been questioned, with several studies suggesting that $Pk\dot{V}O_2$ loses some prognostic ability.^{27,32,42-44} In patients taking β -

blockers, a $Pk\dot{V}O_2$ of less than 14 mL/kg per minute has shown reduced prognostic stratification, whereas variables less affected by HR reserve, such as peak oxygen pulse or peak lean body mass-adjusted oxygen pulse, may be superior. A lean body mass-adjusted peak oxygen pulse (cutoff < 14 mL/beat) was superior in risk stratification (7% vs 22% events) compared with $Pk\dot{V}O_2$ (cutoff < 14 mL/kg per minute) (10% vs 17% events).³²

Less commonly, patients with HF may have limited exercise tolerance because of low-threshold angina or severe ventricular arrhythmias, in which an early exercise surrogate of $Pk\dot{V}O_2$ would be needed for risk stratification. Our laboratory and others have successfully used the pattern of $\dot{V}_E/\dot{V}CO_2$ change during early exercise to predict $Pk\dot{V}O_2$ and subsequent outcome in such patients.^{25,45,46} A decrease in $\dot{V}_E/\dot{V}CO_2$ of less than 10% early in exercise predicts a $Pk\dot{V}O_2$ of less than 14 mL/kg per minute and poor outcome in patients with HF.²⁵

Currently, $Pk\dot{V}O_2$ is a commonly used end point in various clinical investigations, particularly HF trials.⁴⁷⁻⁴⁹ In addition to the prognostic importance of baseline $Pk\dot{V}O_2$, changes in $Pk\dot{V}O_2$ may have prognostic and therapeutic

consequences.^{50,51} An increase in $Pk\dot{V}O_2$ by as little as 1 mL/kg per minute can mean nearly a 70-second gain in treadmill exercise time, as well as improved cardiovascular outcomes.^{51,52} Therefore, it is important to recognize that several factors, including effort, can influence the $Pk\dot{V}O_2$ value. Consequently, $Pk\dot{V}O_2$ alone may not always be the appropriate metabolic end point to evaluate the effects of a given intervention. Therefore, both AT and RER should accompany $Pk\dot{V}O_2$ data when making important clinical decisions, especially regarding therapeutic interventions.⁵³ In the event that the AT is not obtained (which is uncommon but present in up to 30% of our HF studies),^{32,33} the pattern of $\dot{V}_E/\dot{V}CO_2$ change in early exercise can predict $Pk\dot{V}O_2$ and subsequent outcomes in patients with HF.^{3,25,45,46}

OTHER USES OF CARDIOPULMONARY EXERCISE TESTING

Cardiopulmonary exercise testing is frequently an integral component in the work-up of patients being evaluated for employment disability, in which direct measurement of RER and $Pk\dot{V}O_2$ can often discriminate between true disability and malingering. Assessment of $Pk\dot{V}O_2$ can be important for patients who wish to return to physically vigorous occupations. This technology is also useful in determining precise functional capacity in young and middle-aged, presumably asymptomatic, patients with moderate to severe valvular disease to help with decisions regarding necessity of earlier surgical intervention, especially if symptoms of early fatigue and/or dyspnea may be due to noncirculatory causes, particularly deconditioning.⁵⁴⁻⁵⁶ In patients with rate-adaptive or biventricular pacemakers, direct measurement $Pk\dot{V}O_2$, AT, and oxygen pulse have been used to optimize arteriovenous delay to maximize circulatory efficiency.⁵⁷⁻⁵⁹ Finally, as with the assessment of valvular heart disease, cardiopulmonary exercise testing is commonly used to determine functional capacity, prognosis, and the potential need for medical or surgical interventions in children and adults with congenital heart disease.⁶⁰⁻⁶²

TECHNICAL PERFORMANCE ISSUES

Although most data obtained from cardiopulmonary exercise testing are reliable and reproducible, as with most clinical modalities, there may be pitfalls in collecting and interpreting these metabolic data during exercise. The technician who performs the cardiopulmonary exercise test must be well trained in the calibration and maintenance of the metabolic cart and provide thorough instruction to patients before testing, including the use of preassigned hand signals to relay patient symptoms, as well as provide appropriate encouragement during the test. The technician

should be meticulous in monitoring data as they are acquired and be cognizant of system leaks (including breathing around mouthpiece, nasal breathing, and sampling line leaks) in data acquisition. Functional impairment in patients, whether volitional, musculoskeletal, cardiopulmonary, or rare inborn errors of metabolism (eg, glycogen storage disease), can profoundly affect both the technical aspects and the interpretation of the test.

CONCLUSION

Cardiopulmonary exercise testing remains a relevant modality in the clinician's diagnostic armamentarium for evaluation and treatment of many commonly encountered clinical problems. Measurement of exercise gas exchange provides objective and reproducible indices of functional capacity, generates invaluable information in determining the origin of dyspnea on exertion, and provides unique prognostic capabilities in the assessment of patients with systolic HF. Physicians should be comfortable with the basics of gas exchange presented herein and therefore better able to use cardiopulmonary exercise testing in the appropriate clinical settings.

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