Abstract

There are different modalities of exercise testing that can provide valuable information to physicians about patient and athlete fitness and cardiopulmonary status. Cardiopulmonary exercise testing (CPX) is a form of exercise testing that measures ventilatory and gas exchange, heart rate, electrocardiogram, and blood pressures to provide detailed information on the cardiovascular, pulmonary, and muscular systems. This testing allows an accurate quantification of functional capacity/measure of exercise tolerance, diagnosis of cardiopulmonary disease, disease-progression monitoring or response to intervention, and the prescription of exercise and training. CPX directly measures inhaled and exhaled ventilator gases to determine the maximal oxygen uptake, which reflects the body’s maximal use of oxygen and defines the limits of the cardiopulmonary system.

CPX is the ideal modality to evaluate causes of exertional fatigue and dyspnea, especially in complex cases in which the etiology could be cardiac, pulmonary, or deconditioning. Exercise tolerance has become an important outcome measure in patients with chronic obstructive pulmonary disease and congestive heart failure, as well as other chronic diseases, and is a well-recognized predictor of mortality. Older athletes or those with underlying medical conditions could benefit from exercise testing for risk stratification and clearance to participate, as well as to help set their training zones and determine their functional limitations.

Introduction

Exercise testing (ET) can be a valuable tool in the assessment of patient functional capacity, diagnosis of cardiopulmonary disease, and the prescription of exercise and training. There are several different modes and modalities available for ET that can provide different types of information to the clinician to help patients/athletes improve their fitness or cardiopulmonary status. Through cardiopulmonary exercise testing (CPX), ventilatory and gas exchange, as well as heart rate, electrocardiogram, and blood pressures, are measured to provide detailed information on the cardiovascular, pulmonary, and muscular systems. The purpose of this article is to review who needs ET, when the testing should occur, which test to perform and why, and how to apply this information in a practical manner.

What Is CPX?

Simply put, ET is used to evaluate the body’s reaction to a measured exercise stress. Exercise can elicit cardiovascular responses that may not be present at rest and can be used to assess the function of the cardiovascular system. The most important measure provided by ET is functional capacity. ET can help determine functional capacity by calculating the amount of metabolic equivalents (METs) an individual can perform, with 1 MET defined as an oxygen use of 3.5 mL O₂/ks-min—the energy an average person expends seated at rest.

The reliance on METs, however, significantly overestimates actual oxygen use [1,2]. This measure of exercise quantification is relatively simplistic and does not provide much clinical utility. CPX allows a more dependable assessment of function, as well as an ability to provide prognostic or clinical information by the use of ET with the addition of ventilator gas exchange. CPX directly measures inhaled and exhaled ventilator gases to determine the maximal oxygen uptake (VO₂max), which is a more accurate quantification of functional capacity. This information can then be used for a better functional evaluation in the clinical setting. Furthermore, CPX should be considered the gold standard in evaluating the causes of exercise intolerance in patients with pulmonary and cardiac disease [3].
The lungs, heart, pulmonary, and systemic circulations form a single circuit for the exchange of respiratory gases between the cells of the body and the environment. Under steady-state conditions, oxygen consumption and carbon dioxide output measured at the mouth are equivalent to oxygen use and carbon dioxide production at the cell. Therefore, external respiration equals internal respiration [4]. CPX capitalizes on this principle and measures the fraction of oxygen and carbon dioxide in expired gas and expired air volume, which can then be used to determine oxygen consumption (VO₂) per unit time, carbon dioxide output (VCO₂), and minute ventilation (VE). From these measures, many clinically relevant parameters can be determined.

ET should be conducted by trained personnel with baseline knowledge of exercise physiology. The American Heart Association states, "Exercise testing of patients should be performed under the supervision of a physician who is trained to conduct exercise tests..." [5]. The degree of supervision needed will be determined by the testing facility and the risk level of the patients. The American College of Sports Medicine (ACSM) recommends that a physician does not need to be present for a person of low risk (1 or fewer risk factors) during ET [6]. In the case of moderate risk, a physician should be present during maximal testing but does not need to be present for submaximal testing. A high-risk individual should have a physician present during any ET [6]. It is recommended that persons trained in Advanced Cardiac Life Support be available during ET as up to 10 myocardial infarctions (MIs) can be expected to occur per 10,000 tests—this risk is greater in those with previous history of coronary artery disease or MI [7]. Although this number does not seem to be very high, preparation will prevent an unnecessary death during testing.

**Equipment and Protocols**

Performance of CPX requires the ability to measure 3 responses during inspiration and expiration: (1) the concentration of O₂; (2) the concentration of CO₂; and (3) a quantification of ventilation (usually VE, which refers to both tidal volume and respiratory rate). This measurement requires the patient to wear a facemask that covers the mouth and nose or a mouthpiece and a nose clip. CPX software systems can rapidly analyze the inhaled and exhaled gases.

Although a wide variety of tests are available, the best test is a symptom-limited, incremental test, which typically occurs by a progressive increase in work rate at a small fixed interval; however, newer, high-intensity constant load tests also are being used increasingly. The treadmill and the cycle ergometer are the most commonly used devices for this ET, but other devices also could be used. The treadmill is more commonly used in the United States, whereas the cycle ergometer is more used in Europe [8]. It is important to realize that ergometer-based tests generally produce a lower peak VO₂, usually 15%-20% less than the treadmill, because of the use of a smaller total muscle mass [9].

Protocols generally involve a "warm-up" period with an initial low load followed by a progressive increase in effort required, typically with a stepwise progression until maximal effort is reached, followed by a "cool-down" or recovery period.

The most widely used treadmill protocol is the Bruce protocol, first described by Robert Bruce in 1973 [10]. The Bruce protocol was developed as a clinical test to evaluate patients with suspected coronary heart disease, although it can also be used to estimate cardiovascular fitness. The Bruce protocol is a standard test in cardiology and is composed of multiple exercise stages of 3 minutes each. At each stage, the gradient and speed of the treadmill are elevated to increase work output, called METs. Stage 1 of the Bruce protocol is performed at 1.7 miles per hour (mph) and a 10% gradient. Stage 2 is 2.5 mph and 12%, whereas Stage 3 goes to 3.4 mph and 14% [11,12]. The Bruce treadmill test can be used indirectly to estimate VO₂ max by the use of a formula when direct ventilator gas exchange measurements are not available, thus making the test very versatile.

Although the Bruce protocol is one of the protocols most commonly used for ET, there are many other exercise protocols, one of which is the Balke protocol. In contrast to the Bruce protocol, where the gradient and the speed of the treadmill are increased each 3 minutes, in the Balke protocol, the speed remains constant at 3.3 mph whereas the slope is increased by 1% at each minute [13]. This gradual approach may be more accurate because of the more steady increase in workload; however, the test may take twice as much time to reach maximal state. Finally, when VO₂ max is calculated by the use of a formula rather than with direct measurements of oxygen consumption during the Bruce protocol, it has been found that VO₂ max in undertrained athletes is overestimated, whereas in well-trained athletes it is underestimated [14].

Despite the popularity and widespread use of the stepwise Bruce and Balke protocols, a ramp protocol will more consistently achieve steady-state conditions compared with other protocols [15]. Ramping protocols generate almost-imperceptible increases in treadmill speed every 15 seconds and permit increases in external work to occur in a constant or continuous fashion. Thus, increases in workload can be individualized through a wide range of patient capabilities [16].

Regardless of what protocol is used for testing, the protocol should be tailored to the individual to achieve a level of fatigue that limits exercise within 8-12 minutes [8]. When the duration of the test is less than 6 minutes, a nonlinear relationship between VO₂ and work
rate may exist. When the test goes longer than 12 minutes, orthopedic factors, such as joint pain and fatigue, may limit the ability to achieve a maximal heart rate with prolonged exercise protocols [1]. The key is that the exercise intensity should be individualized for the fitness level and be task-specific for the clinical concerns of the patients.

The exercise protocol should be terminated when maximal heart rate is achieved; however, there are other indications for terminating the protocol early for the safety of the patient, such as moderate-to-severe anginal symptoms, a decrease in systolic blood pressure of >10 mm Hg from baseline despite an increase in workload, ataxia, dizziness, near-syncope, signs of poor perfusion, sustained arrhythmia such as ventricular tachycardia, and/or ST-segment elevation on electrocardiogram [17]. Another indication to stop the test early is the patient’s desire to stop. The Borg Rating of Perceived Exertion Scale is a rating scale of perceived exertion and may be useful to assess patient’s fatigue and assist in assessing the patient’s functional capacity [17].

### Anaerobic Testing

Evaluation of the anaerobic energy systems is important to the power athlete in events lasting 10-120 seconds. Although laboratory procedures would be the best method of evaluation, it is often impractical for testing athletic teams or large groups because of the expense as well as the invasive (ie, blood draw, muscle biopsies) nature of the activity. Therefore, tests of performance have been developed that determine the athletes’ power capacity or anaerobic capacity quickly and easily. The Wingate Anaerobic Test is the most popular laboratory performance test that evaluates anaerobic energy system power and provides a fatigue index based on the ability of the individual to sustain peak power [18].

The Wingate Anaerobic Test requires the subject to pedal a mechanically braked bicycle ergometer (an arm ergometer also can be used), for 30 seconds, at an “all-out” pace [9]. The Wingate Anaerobic Test will provide values for peak power, relative peak power, anaerobic fatigue, and anaerobic capacity. These results can then be compared with previous testing to assess progress of a specific anaerobic or power training plan.

### Submaximal ET

Although maximal ET is considered the gold standard for the assessment of maximal aerobic capacity, this testing may be limited in those with medical conditions that lead to pain and fatigue, such as neurologic or orthopedic conditions, which can limit a maximal effort and therefore a maximal test. A maximal test has been defined classically as achieving a heart rate of at least 85% the age-predicted maximal heart rate. Another way to assess maximal ET is to monitor the respiratory exchange ratio (RER), which is the ratio of VCO2 to VO2. As maximal aerobic capacity is achieved, the VO2 peaks while the VCO2 increases. Although it is unclear why the CO2 production accelerates at this point, it is thought to be the result of CO2 being produced from bicarbonate buffering of lactic acid production to maintain internal homeostasis [19]. A high RER (≥1.10) is consistent with high patient exercise effort and maximal aerobic capacity [1]. Submaximal testing in CPX can be useful to predict maximal heart rate or estimate VO2max in those patients with functional limitations or inability to perform a maximal effort test.

The ventilatory threshold (VT), also known as the anaerobic threshold or lactate threshold, has utility as a submaximal index of exercise capacity. Often, VT is a more practical performance index for patients who may be debilitated or unable to reach maximal limits. The VT is considered to be fairly consistent with the person's ability to sustain daily activities, because exercising beyond the VT for sustained periods eventually leads to fatigue. Activities of daily living should not require maximal effort, and the VT is useful in gauging the functional benefits of therapy and ability to perform activities of daily living. Exercise training can increase the VT, whereas deconditioning decreases the VT. A VT less than 11 mL/kg/min has been used to identify high risk of perioperative death in elderly patients undergoing major surgery [2].

VT as the termination point for ET can be used to extrapolate exercise ability and deconditioning and can be a useful parameter in which to base an exercise prescription [6]. The point at which the test was terminated is used as the upper limit to the exercise prescription. Heart rate reserve can increase over time with an individualized exercise plan based on the VT [20].

### Key CPX Variables

**Metabolic Equivalent**

1 MET is equivalent to an oxygen use of 3.5 mL O2/kg-min. Simple household activities, or light work, require 1.5-4 METs of energy to perform. Moderate work, such as sexual activities, usually requires 3-6 METs, whereas heavy work and high-energy sports require 5-15 METs [2].

**Peak VO2 (VO2max)**

VO2max is a well-established measure of exercise performance that reflects the body’s maximal use of oxygen. It is based on the Fick equation \( VO_2 = CO \times [CO_2 - CVO_2] \) and is a reliable and reproducible index that can be modified with training or altered with
cardiovascular or pulmonary conditions. During exercise, VO2 increases linearly and when this rate of increase plateaus, the peak VO2 has been obtained. VO2max is commonly expressed in L/min; however, this value increases as body mass increases, and therefore is often normalized for body mass and expressed as mL O2/ kg-min. Peak VO2 is an important clinical measurement because in healthy people it defines the limits of the cardiopulmonary system. VO2max decreases with age, and it decreases 8%-10% per decade in trained individuals who continue to train vigorously [21]. Furthermore, VO2max is approximately 10%-20% greater in men than in women in part because of a greater hemoglobin concentration, larger muscle mass, and a greater cardiac stroke volume [10].

VT (Anaerobic/Lactate Threshold)

When metabolic demands exceed oxygen delivery to working muscles, anaerobic metabolism ensues. As anaerobic metabolism begins, the respiratory rate and in turn the VE increases to help remove CO2 from the blood stream. This can be detected by the individual as breathlessness. In the laboratory, it is the point where the lactate levels increase, VO2 peaks, and CO2 production accelerates because of a faster rate of lactate production and a shift from aerobic metabolism to anaerobic metabolism [22]. The most common method for determining the VT is the V-slope method, which uses computer-based regression analysis—this typically occurs between 47% and 64% of VO2max in healthy untrained individuals and at greater percentage of VO2max in trained athletes [23].

Respiratory Exchange Ratio

RER is defined as the ratio of carbon dioxide output and oxygen uptake (VCO2/VO2). The RER represents the metabolic exchange of gases in the body’s tissues. During CPX, the RER provides a physiological context to substantiate that a high exercise effort has been achieved. RER increases with exercise as exhaled CO2 increases; an RER > 1.10 is a criterion that can be used to determine that the peak VO2 reflects a peak physiological workload. A VO2 in the context of a low RER may be a significant underestimate of exercise capacity [24,25].

Oxygen Pulse

The amount of oxygen consumed from the volume of blood delivered to the tissues per heart beat is the oxygen pulse. It is calculated by dividing the VO2max by the peak heart rate and is expressed as mL O2 per heartbeat. It is essentially an index of O2 extraction in association with stroke volume and can function as a reasonable surrogate for stroke volume. The oxygen pulse tends to be reduced in conditions that impair stroke volume during peak exercise, such as left ventricular dysfunction, congestive heart failure, severe valvular disease, coronary heart disease, or chronic obstructive pulmonary disease [26].

Physiological Reserve

Physiological reserve is composed of heart rate reserve and ventilatory reserve. Heart rate reserve is

Table 1  Recommendations for exercise testing before beginning an exercise program

<table>
<thead>
<tr>
<th>Classification†</th>
<th>Indication</th>
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<tbody>
<tr>
<td>Class I</td>
<td>Evaluation of exercise capacity and response to therapy in candidates for heart transplant</td>
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<td>Evaluation of exertional dyspnea</td>
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<tr>
<td>Class Ila</td>
<td>Evaluation of exercise capacity when indicated medically</td>
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<tr>
<td></td>
<td>Functional significance of valvular disease</td>
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<td></td>
<td>Congenital heart disease, need for treatment/repair</td>
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<tr>
<td>Class Iib</td>
<td>Evaluation of response to medical and surgical interventions</td>
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<td></td>
<td>Determine intensity for exercise training as part of cardiac rehab</td>
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<tr>
<td>Class III</td>
<td>Routine evaluation of exercise capacity</td>
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</tbody>
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‡ Per ACC/AHA classification system, with class I indicating evidence of usefulness, class II having conflicting evidence with IIA weighing in favor of usefulness, IIB less well established, and class III indicating the test is not useful and may be harmful.

† ACC = American College of Cardiology; AHA = American Heart Association; VO2 = oxygen consumption.
the difference between maximal heart rate and resting heart rate. Maximal heart rate is calculated using 220 minus age. The patient should ideally achieve 85% of this predicted heart rate reserve during stress testing [2]. In contrast, the ventilatory reserve in healthy subjects cannot be less than 20% and is typically 30%-50%. This can be determined before the ET by performing baseline spirometry to include maximum minute ventilation [27].

Who Needs ET?

Metabolic derangements can occur at multiple sites within the body to include muscles, circulatory system, and pulmonary system. CPX can help differentiate causes of low fitness from cardiac or pulmonary processes and may be used to provide prognostic information to those with chronic diseases. The ACSM provides indications for ET for individuals with risk factors before they begin an exercise program, which are listed in Table 1 [28]. The American College of Cardiology/American Heart Association Update of Practice Guidelines for Exercise Testing list the indications for ordering a functional VO2 exercise test, or CPX, for those with cardiac disease (Table 2) [17]. CPX should be considered the gold standard for evaluating maximal/symptom-limited exercise in patients with pulmonary or cardiac disease [3]. CPX can provide an objective measure of exercise tolerance, establish a baseline for patient’s prognosis, and monitor disease progression or the response to intervention. Exercise tolerance is a well-recognized predictor of mortality in subjects of all ages [29]. Finally, exercise tolerance has become an important outcome measure in patients with chronic obstructive pulmonary disease, congestive heart failure, and other chronic diseases.

From a clinical standpoint, CPX provides the ideal modality to evaluate causes of exertional dyspnea and fatigue, especially in complex cases in which the etiology could be cardiac, pulmonary, or simple deconditioning (Figure 1). The addition of gas analysis from CPX over standard ET provides valuable information and allows for identification of possible deficiencies in the system responsible for the symptomology.

Exercise intolerance is a primary symptom in heart failure, which varies with the severity of disease. Decreased exercise capacity is associated with a greater New York Heart Association functional class, worse symptoms, poorer quality of life, and decreased life expectancy [30]. Exercise training, at the appropriate

Table 3
Other potential indications for exercise testing*  
<table>
<thead>
<tr>
<th>Indication</th>
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<tbody>
<tr>
<td>Evaluation for exertional dyspnea</td>
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<tr>
<td>Direct measure of functional capacity</td>
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<tr>
<td>Risk stratification and prognosis for congestive heart failure</td>
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<tr>
<td>Disability determination/readiness for work</td>
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<tr>
<td>Assess response to medical or surgical treatments</td>
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<td>Development of an exercise prescription</td>
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intensity, will increase functional capacity and quality of life and may prolong survival [31]. Many studies in heart failure have demonstrated the ability of ET to provide valuable prognostic information for patients. Patients with heart failure with a VO_{2,max} of less than 14.5 mL/kg had double the mortality rate as those with a VO_{2,max} greater than 14.5 mL/kg [32]. Further, transplantation can be deferred in those patients with a VO_{2,max} greater than 14 mL/kg, as the survival of those with greater than 14 mL/kg was higher than those who underwent transplantation [33].

Older athletes or those with underlying medical disease could benefit from ET for risk stratification and clearance to participate, as well as to allow them to set their training zones, and to determine what their functional limitations are [34,35]. In addition, CPX may help different causes of low fitness from cardiac or pulmonary causes.

CPX also has become an important part of the work-up for patients being processed for disability claims. With standard ET, the patient may claim fatigue or disability, but the addition of CPX will help to determine whether an appropriate RER was achieved and therefore if the patient gave an appropriate effort. If a high RER was not achieved, it may indicate malingering or inadequate effort [15]. Table 3 lists these other potential indications for ET.

### What are the Contradictions to ET?

There are some absolute contraindications to ET. Uncontrolled arrhythmia, unstable angina, and severe aortic stenosis would preclude ET until the patient is medically stable [17,36]. Relative contraindications included hypertrophic cardiomyopathy, moderate valvular stenosis, previous history of MI or coronary artery disease, and/or history of sudden cardiac death in a first-degree relative (Table 4). When assessing someone with a relative contraindication, it is important to weigh the risk of the procedure versus the benefit of the information gained; patients with these relative contraindications can still undergo testing with proper preparation and with appropriately trained staff [17]. A trained physician in ET should be present for the entirety of the test, and persons trained in Advanced Cardiac Life Support should be available during testing time. CPX may be particularly beneficial to these patients, because it can help distinguish the extent of exercise limitation as the result of cardiac, pulmonary, or other etiology [17,34].

### Using CPX to Prescribe Exercise or Training

The exercise prescription is an individualized program for exercise which is given to the patient much like a prescription for medication. Each exercise prescription has 4 essential components: frequency, intensity, time (duration), and type of exercise (F.I.T.T); The ACSM recommends these F.I.T.T. guidelines for cardiovascular exercise [6]. For cardiovascular benefits, they recommend a frequency of 3-5 times per week, an intensity of 65%-85% of maximal heart rate, and a duration of 20-60 minutes per session. Use of the F.I.T.T. guidelines is an easy way to prescribe exercise to most people.

With the addition of ET, it is possible to provide a more individualized exercise prescription based on the
current fitness level and desired fitness goal. There are several ways to choose target heart rate to guide exercise intensity: percent of maximal heart rate (MHR), heart rate reserve (HRR), or a direct determination. The 2 methods most commonly used are percent of MHR or percentage HRR. To set the target heart rate using the percent of MHR, the formula is target heart rate (HR) = MHR \times \% intensity. To use heart rate reserve, the formula is target HR = (MHR - resting HR) \times \% intensity + resting HR. Heart rate reserve is a more accurate estimate of energy expenditure as it takes into account the range of working heart rate. This is because the MHR method does not account for resting heart rate and assumes that the lower range of heart rate is zero. This discrepancy can result in a large difference when used for lower intensities; however, it becomes less apparent at near maximal intensity [1].

For high-level fitness, many athletes choose to use percentage of VO\(_{2}\)max or percentage of ventilatory (lactate) threshold to set their training zones (Table 5). Each zone carries its own benefits and purpose for the defined workout and can be used by an athlete or a coach to produce specific fitness gains [35].

### Sports Medicine Applications

CPX can be used to assess components of exercise performance with respect to aerobic versus anaerobic metabolism, such that performance or training can be evaluated. At workloads below VT, blood lactate levels should remain low and the aerobic metabolism is predominately used. In contrast, competitive athletes improve performance by adding several weekly workouts at levels above VT to improve their oxidative capacity.

### Conclusion

CPX is a valuable tool in the assessment of patient functional capacity, diagnosis of cardiopulmonary disease, and in the prescription of exercise and training regimens. Through CPX, ventilatory and gas exchange as well as the conventional measurements of heart rate, electrocardiogram, and blood pressure are measured during exercise stress testing, thus providing detailed information on the cardiovascular, pulmonary, and muscular systems. This allows for more precise diagnostic capabilities, which in turn can be used to determine an exercise prescription for the patient and/or athlete. Exercise prescriptions can be used in a variety of situations, from the professional athlete to reach specific fitness goals to the patient with heart failure to perform activities of daily living. CPX has a variety of applications and is an invaluable tool to understanding lung, cardiac, and muscular contribution to exercise and exercise tolerance.

### References


Disclosure

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