AHA Scientific Statement

Assessment of Functional Capacity in Clinical and Research Settings

A Scientific Statement From the American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology and the Council on Cardiovascular Nursing

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The assessment of functional capacity reflects the ability to perform activities of daily living that require sustained aerobic metabolism. The integrated efforts and health of the pulmonary, cardiovascular, and skeletal muscle systems dictate an individual's functional capacity. Numerous investigations have demonstrated that the assessment of functional capacity provides important diagnostic and prognostic information in a wide variety of clinical and research settings. This scientific statement, an update of the previously published American Heart Association (AHA) document,[1] highlights the major clinical and research applications of functional capacity assessment. For a comprehensive review of exercise testing, the reader is referred to the American College of Cardiology (ACC)/AHA Guidelines for Exercise Testing.[2,3]

Maximal Oxygen Uptake

Functional capacity is the ability of an individual to perform aerobic work as defined by the maximal oxygen uptake ($\dot{V}O_{2max}$), that is, the product of cardiac output and arteriovenous oxygen ($a-\dot{V}O_2$) difference at physical exhaustion, as shown in the following equation:

$$\dot{V}O_{2max} = (HR \times SV) \times a\text{–}\dot{V}O_2 diff,$$

Where HR indicates heart rate and SV indicates stroke volume.

Because $\dot{V}O_{2max}$ typically is achieved by exercise that involves only about half of the total body musculature, it is generally believed that $\dot{V}O_{2max}$ is limited by maximal cardiac output rather than peripheral factors.[4]

Although $\dot{V}O_{2max}$ is measured in liters of oxygen per minute, it usually is expressed in milliliters of oxygen per kilogram of body weight per minute to facilitate intersubject comparisons. In addition, functional capacity, particularly when estimated from the work rate achieved rather than directly measured $\dot{V}O$, is frequently expressed in metabolic equivalents (METs), with 1 MET representing the resting energy expenditure ($\approx$3.5 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$). In this instance, functional capacity is commonly expressed clinically as a multiple of the resting metabolic rate.

$\dot{V}O_{2max}$ is affected by age, gender, conditioning status, and the presence of disease or medications that influence its components. $\dot{V}O_{2max}$ in a young world-class male endurance athlete can exceed 80 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$, whereas a value of 15 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ falls within the 50th percentile for a sedentary but healthy 80-year-old woman. Aerobic capacity typically declines an average of 10% per decade in nonathletic subjects,[5,6] mediated by a decrease in stroke volume,[5] maximal heart rate,[7] blood flow to skeletal muscle,[8] and skeletal muscle function.[6] This rate of decline in fitness appears to accelerate with advancing age, increasing from 3% to 6% per decade in young individuals (20s and 30s) to >20% per decade in the elderly (70s and older).[5] At any age, $\dot{V}O_{2max}$ in men is 10% to 20% greater than that in women, in part because of a higher hemoglobin concentration, a larger proportion of muscle mass, and a greater stroke volume in men. Consideration of these age and gender differences in $\dot{V}O_{2max}$ is important when functional capacity in a given individual is interpreted. Numerous equations for age-

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predicted standards have been published for $\dot{V}O_{2max}$,[9] and population specificity must be considered when ascribing a percentage of an age-predicted $\dot{V}O_{2max}$ achieved for an individual. Endurance training augments $\dot{V}O_{2max}$ by 10% to 30% primarily by increasing maximal stroke volume and $a-\dot{V}O_2$ difference.[10]

Functional capacity, exercise capacity, and exercise tolerance are generally considered synonymous and imply that a maximal exercise test has been performed and maximal effort has been given by the individual. However, these terms also are used occasionally to express an individual's capacity to perform submaximal activities using one of a variety of tests; therefore, to avoid confusion, the type of exercise evaluation should be specifically described. A distinction also should be made between estimated and directly measured $\dot{V}O_2$. This issue becomes particularly important in patients with cardiovascular disease; slower oxygen uptake on-kinetics can create a large discrepancy between estimated and measured $\dot{V}O_2$ in which the former dramatically overestimates the latter, especially when aggressive exercise testing protocols are used.[11] Directly measured $\dot{V}O_2$ is more precise and is the preferred measure clinically, but it is less often available, requires secondary expertise to operate, and includes costs to purchase/maintain the required equipment. Reference equations for normal standards should be specific as to whether $\dot{V}O_2$ was measured or estimated because estimated values require several assumptions and tend to overpredict $\dot{V}O_2$. Reference equations also should be specific as to whether the test was performed on a treadmill or cycle ergometer because exercise capacity is typically higher on a treadmill.[11,12]

The measurement of $\dot{V}O_{2max}$ implies that an individual's physiological limit has been reached. True attainment of $\dot{V}O_{2max}$ (physiological $\dot{V}O_{2max}$) has historically been defined by a plateau in $\dot{V}O_2$ between the final 2 exercise work rates, indicating that maximal effort is achieved and sustained for a specified period. Because this determination is subjective, can be difficult to define, and is rarely observed in tests of patients with cardiovascular or pulmonary disease, the term peak $\dot{V}O$ is more commonly used clinically to express exercise capacity. Conversely, the term $\dot{V}O_{2max}$ typically is used to describe aerobic capacity in apparently healthy individuals in whom achievement of a plateau in $\dot{V}O_2$ is more likely. It should be noted, however, that a large proportion of apparently healthy individuals may not reach a plateau in $\dot{V}O_2$ and that the absence of this response does not necessarily imply submaximal effort.[13]

Because most daily activities do not require maximal effort, a widely used submaximal index of aerobic capacity is the anaerobic or ventilatory threshold (VT), defined by the exercise level at which ventilation begins to increase exponentially relative to the increase in $\dot{V}O_2$. The term anaerobic threshold is based on the concept that at a given work rate, oxygen supply to the muscle does not meet the oxygen requirements. This imbalance increases anaerobic glycolysis for energy generation, yielding lactate as a metabolic byproduct (lactate threshold).[14] An increase in ventilation is needed to eliminate the excess CO_2 produced in response to a sustained rise in blood lactate. However, whether muscle hypoxia is the major stimulus for increased lactate production remains controversial, and methodologies used to detect anaerobic threshold are not universally accepted.[15] Thus, although the terms anaerobic threshold, VT, and lactate threshold are commonly used interchangeably, they should be considered different but related events.

Although the VT usually occurs at 47% to 64% of measured $\dot{V}O_{2max}$ in healthy untrained subjects,[16] it generally occurs at a higher percentage of $\dot{V}O_{2max}$ in endurance-trained individuals.[17] Exercise training has been shown to increase $\dot{V}O_2$ at the VT to a degree that is similar to that for $\dot{V}O_{2max}$ (typically 10% to 25% for previously sedentary individuals); thus, it is an important response to document clinically. Several methods have been proposed for determining the VT, but no universal agreement exists regarding which is best. The 3 most common definitions of the VT are the following: (1) the point at which a systematic increase in the ventilatory equivalent for oxygen ($\dot{V}E/\dot{V}O_2$) occurs without an increase in the ventilatory equivalent for carbon dioxide ($\dot{V}E/\dot{V}CO_2$), (2) the point at which a systematic rise in end-tidal oxygen pressure ($P_{ET}O_2$) occurs without a decrease in the end-tidal carbon dioxide pressure ($P_{ET}CO_2$), and (3) the departure of $\dot{V}CO_2$ from a line of identity drawn through a plot of $\dot{V}CO_2$ versus $\dot{V}O$, often called the V-slope method.[18] When determined visually, these methods on average result in VT values at a similar percentage of $\dot{V}O_{2max}$.[19] Although modern equipment that measures metabolic parameters usually quantifies this point automatically using one of several published or empirical algorithms, it should be validated visually by an experienced reviewer. The confidence in determining the VT may be increased by having 2 or 3 experienced observers independently calculate this point.[19,20]

Exercise Mode and Protocol Selection

Assessment of functional capacity typically is performed on a motorized treadmill or a stationary cycle ergometer. In the United States, however, treadmill exercise is generally the preferred modality. Furthermore, untrained subjects will usually terminate cycle exercise because of quadriceps fatigue at a work rate 10% to 20% below their treadmill peak $\dot{V}O_2$.[21] Cycle ergometry also requires subject cooperation in maintaining pedal speed at the desired level, usually about 60 rpm, although modern ergometers that are electronically braked maintain a steady workload at variable speeds. Several studies have demonstrated a consistent relationship between aerobic capacity determined with a treadmill and a cycle ergometer, although the latter mode of exercise tends to produce a lower peak $\dot{V}O_2$.[22,23] To rectify the discrepancy between treadmill and cycle ergometry peak $\dot{V}O_2$, the following formula has been suggested: treadmill METs=0.98(cycle ergometer METs)+1.85.[24] Multiplication of the value obtained from this equation by 3.5 produces a treadmill peak $\dot{V}O_2$ value in milliliters of O_2 per kilogram per minute. In addition, cycle ergometry may be preferred in subjects with gait or balance instability, severe obesity, or orthopedic limitations or when simultaneous cardiac imaging is planned. Although arm ergometry may be used to assess the aerobic capacity of wheelchair athletes or other individuals with lower-limb disabilities, most persons cannot achieve work

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rates comparable to those obtained with leg exercise because of the smaller, often deconditioned muscle mass.[25]

The selection of an appropriate exercise test protocol for assessing functional capacity is of critical importance, especially when aerobic capacity is to be estimated from exercise time or peak work rate. Exercise test protocols with large stage-to-stage increments in energy requirements generally have a weaker relationship between measured $\dot{V}O_2$ and work rate.[11] The Balke and Ware[26] and Naughton et al[27] protocols, which involve only modest increases in treadmill elevation at a constant speed, are recommended for this reason. Functional capacity also can be accurately determined with the use of a "ramp" protocol in which small increments in work rate occur at intervals of <10 to 60 seconds.[11] Regardless of the specific protocol chosen, the protocol should be tailored to the individual to yield a fatigue-limited exercise duration of ≈8 to 12 minutes. Even with exercise test protocols using modest increases in workload, results may still indicate a nonlinear relationship between $\dot{V}O_2$ and work rate when test duration is <6 minutes. Conversely, when such protocols result in exercise durations >12 minutes, subjects may terminate exercise because of specific muscle fatigue or orthopedic factors rather than cardiopulmonary end points. In instances in which there is an expectation of >12 minutes of exercise, a test protocol using a more aggressive approach to increasing workload, for example, the Bruce protocol,[28] should be considered. Finally, minimal or no handrail support should be encouraged during treadmill exercise testing secondary to the discrepancy created between estimated (from treadmill speed and grade) and actual $\dot{V}O_2$ when it is used. Given the challenges of precisely estimating $\dot{V}O_2$ from the exercise workload, the measurement of aerobic capacity through ventilatory expired gas analysis is highly recommended when accuracy is critical such as in the heart failure population.

A frequent consideration in the assessment of functional capacity, especially in nonclinical settings, is whether to perform maximal or submaximal testing. Although maximal testing provides the only accurate determination of aerobic capacity, submaximal testing may be desirable in several situations. These include fitness assessments in facilities in which maximal testing increases subject risk and exposure to potential facility liability, especially in individuals who may be at greater risk for cardiovascular events and particularly when a physician is not on site, and when field testing large numbers of subjects. Submaximal testing typically relies on an extrapolation from the work rate achieved at a given submaximal heart rate relative to an age-predicted maximal heart rate to estimate maximal aerobic capacity. Achievement of 70% of heart rate reserve {0.70×[(220−age)−resting heart rate]+resting heart rate} and 85% of age-predicted maximal heart rate [0.85×(220−age)] have been proposed as termination criteria for submaximal testing.[29] Percent heart rate reserve tends to more accurately reflect percentage of $\dot{V}O_{2max}$, whereas age-predicted maximal heart rate overestimates volitional effort, leading to the difference in heart rate termination criteria, depending on the equation used.[30] It should be noted that submaximal exercise testing typically is terminated before the heart rate criteria are achieved, particularly in individuals with a high aerobic capacity in whom the increase in heart rate is lower for each adjustment in work rate. Regardless of the equation used, a significant potential for error exists because of the 10- to 12-bpm SD in the estimate of maximal heart rate in normal subjects. Even greater heart rate variation is encountered in patients with cardiac disease.[31,32] Additionally, individuals taking cardioactive medications may have an altered heart rate response to exercise, further reducing the ability to accurately predict maximal aerobic capacity.[33] Lastly, the potential error in estimating maximal heart rate will be compounded by the errors inherent in estimating aerobic capacity from the highest work rate achieved. For these reasons, maximal exercise testing in a clinical laboratory setting is recommended when an accurate assessment of maximal aerobic capacity is imperative. In addition, given the inherent intersubject variability in the heart rate response to exercise, maximal exercise tests should be terminated according to signs/symptoms as opposed to the achievement of a predefined percentage of predicted maximal heart rate.

Another form of submaximal exercise evaluation is the 6- or 12-minute walk test, which has become widely applied to assess the responses to various treatment interventions, particularly pharmacological therapies or exercise training, in patients with pulmonary disease or heart failure. The distance covered during the time period also can be a powerful prognostic indicator.[34] Additional advantages of such testing protocols are their simplicity, safety, negligible cost, and applicability to everyday activities. In patients with pulmonary disease, the distance covered in these timed-walk tests is highly reproducible (r=0.86 to 0.95) and correlates moderately well with peak $\dot{V}O_2$ (r=0.52 to 0.71).[35] A similar correlation with peak exercise duration also has been found in patients with heart failure.[36] In patients who have pacemakers, a correlation of 0.74 with cycle ergometry performance has been reported.[37] The reproducibility of timed-walk tests is generally good, with intrasubject coefficients of variation averaging <10%.[35] Nevertheless, modest improvements (usually <10%) on repeat testing may necessitate 2 to 3 tests to produce reliable results; most investigators use the best of these efforts as the true measurement.[38] Specific situations in which these timed-walk tests can be appropriately substituted for the traditional, but more demanding, tests of functional capacity in assessing prognosis and responses to therapy are unclear. Studies comparing the prognostic value and the ability to detect meaningful change after an intervention between traditional exercise testing procedures and timed-walk tests are required before a more definitive recommendation is made. Some studies, however, have suggested that a threshold value of ≥300 m during the 6-minute walk test may be prognostically optimal in patients with heart failure.[39–41] At this time, timed-walk tests should not be considered an equivalent substitute for treadmill/ergometry exercise testing.

Level of Supervision, Monitoring Issues, and Risk of Adverse Events

Major complications of exercise testing include death, myocardial infarction, arrhythmia, hemodynamic instability, and orthopedic injury. Fortunately, adverse events are rare during

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properly supervised tests. Among large series of subjects with and without known disease, serious complications (including myocardial infarction and other events requiring hospitalization) have been reported to occur in <1 to as many as 5 per 10 000 tests, and death has occurred in ≈0.5 per 10 000 tests,[42–44] although the incidence of adverse events varies depending on the study population. Among asymptomatic low-risk subjects tested at a single institution, Gibbons et al[45] reported only 5 major complications and 1 death among >70 000 subjects (overall event rate, 0.8 per 10 000 tests), with no complications or deaths in the most recent 45 000 subjects. Finally, in a survey of 570 institutions including 151 949 exercise tests conducted ≤4 weeks after myocardial infarction, Hamm et al[46] reported fatal, major nonfatal, and other cardiac complication event rates of 0.03%, 0.09%, and 1.4%, respectively.

Although the event rate is relatively low regardless of the patient population studied, complications resulting from exercise testing do occur. Consequently, it is essential that exercise test supervisory personnel are familiar with the clinical indications for the use of such testing, as well as the signs and symptoms of and clinical responses to adverse events to minimize patient risk. The ACC/AHA Clinical Competence statement on stress testing outlines a series of cognitive skills necessary for performance and interpretation of exercise tests.[42] The level of supervision necessary for the individual patient is ultimately determined by the physician overseeing the exercise laboratory who is appropriately trained in testing procedures. In relatively low-risk patients (younger, apparently healthy individuals with no more than 1 cardiovascular risk factor), tests may be directly supervised by specially trained personnel, for example, nurses, nurse practitioners, physician assistants, and exercise physiologists, working under the supervision of a physician who is on site and immediately available. The level of supervision required for moderate-risk patients (individuals with ≥2 cardiovascular risk factors) varies and is left to the discretion of the physician overseeing the exercise laboratory. In higher-risk patients (signs and symptoms of or known cardiovascular/pulmonary disease), direct physician supervision of the exercise test may be warranted.[47] A detailed description of risk stratification procedures before exercise testing is provided elsewhere.[48]

General methodological guidelines for exercise testing laboratories are available.[49] ECG monitoring of heart rate with multiple-lead ECG waveforms should be continuous throughout exercise and for at least 6 minutes into recovery for diagnostic testing in patients with suspected disease. It must be recognized that activity-compatible torso electrodes may produce significant changes in ECG morphology compared with the standard limb leads. Consequently, the former cannot be used as a substitute for, or for comparison with, the standard resting 12-lead ECG.[50] Blood pressure should be measured periodically throughout the test, at least at every stage and more frequently in some high-risk patients, as well as in recovery during ECG monitoring. Patients should be questioned about symptoms periodically during and after exercise, and for research and comparison purposes, an angina scale, dyspnea scale, and/or rating of perceived exertion should be used.

Ventilatory Expired Gas Analysis

Ventilatory expired gas techniques during exercise testing, commonly called cardiopulmonary exercise testing (CPX), have become more widely applied because they significantly increase the precision and yield of information from the exercise test. A shortcoming of standard exercise testing is the inherent inaccuracy in the estimation of exercise capacity from the work rate achieved on a treadmill or cycle ergometer.[51] Oxygen uptake estimated from the work rate, that is, estimated METs, is commonly used clinically, but the limitations associated with estimating the MET level have been widely described. The accuracy of these estimations is affected by the presence and extent of disease (the estimate is less accurate when patients with cardiovascular or pulmonary disease are tested), the exercise protocol used (exercise capacity is more accurately estimated when more gradual, evenly incremented protocols are used), serial testing (estimations are more accurate with testing experience), and whether the subject is allowed to hold onto the handrails (holding the handrails significantly decreases the oxygen demands of the work rate, resulting in overestimation of METs). There is also uncertainty related to defining maximal work capacity because the test usually ends during an incomplete stage. It is recommended that the estimated MET level for a given stage be ascribed for a patient only when more than half the stage has been completed, but the accuracy of this practice depends on the size of the increment in work rate and the relative exercise intensity for a given patient and is inconsistently applied.

The direct measurement of $\dot{V}O_2$ obviates these problems because it is more accurate and reproducible than estimated values from the peak work rate achieved. Information obtained from CPX also has applications for helping to establish the cause of exercise intolerance, estimating prognosis, determining disability, and making judgments concerning therapeutic interventions. Peak $\dot{V}O_2$ is now widely recognized as an important factor in risk stratifying patients with cardiovascular disease. In particular, numerous studies have been published over the past 15 years demonstrating that ventilatory gas exchange responses to exercise predict outcomes in patients with chronic heart failure,[51–53] and these measurements have become a standard tool in the clinical evaluation of these patients.

A large body of research also has evolved regarding CPX variables other than peak $\dot{V}O_2$ in the context of prognosis. Responses such as the VT, $\dot{V}E/\dot{V}CO_2$ slope, $\dot{V}E/\dot{V}CO_2$ at peak exercise, oscillatory ventilation, oxygen uptake on-kinetics, rate of recovery of $\dot{V}O_2$, and oxygen uptake efficiency slope have been used with greater frequency to classify functional limitations and to stratify risk in patients with heart disease. Many of these are expressions of ventilatory efficiency and reflect the various underlying pathophysiological factors that lead to inefficient breathing associated with heart failure or pulmonary disease. There has been a particular focus on the clinical significance of the $\dot{V}E/\dot{V}CO_2$ slope in patients with

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heart failure. This response usually is expressed as the slope of the best-fit linear regression line relating $\dot{V}_E$ and $\dot{V}_{CO_2}$. Among patients with heart failure, the $\dot{V}_E/\dot{V}_{CO_2}$ slope has been demonstrated to predict mortality, hospitalization, and other outcomes at least as well as, and independently from, peak $\dot{V}_{O_2}$.[51,52,54–58] A more thorough review of CPX variables can be found elsewhere.[59]

Lastly, it should be noted that the accuracy of data collected by ventilatory expired gas equipment depends heavily on proper maintenance and precise calibration procedures conducted by appropriately trained personnel. Exercise laboratories performing ventilatory expired gas analysis should have quality assurance procedures in place and strictly follow them. A detailed description of the appropriate use and maintenance of ventilatory expired gas equipment and quality assurance measures can be found elsewhere.[60,61]

Application to Specific Populations

Coronary Artery Disease

The longstanding use of exercise testing in the diagnostic and prognostic evaluation of patients with suspected or known coronary artery disease (CAD) has provided a large body of data on the utility of functional capacity assessment in such populations. Using the Duke University database of patients undergoing diagnostic exercise testing, McNeer et al[62] observed that patients who exercised into stage 4 and beyond on a standard Bruce protocol (4.2 mph, 16% grade) with a negative or indeterminate ST-segment response had <15% prevalence of 3-vessel CAD and <1% prevalence of left main disease. Such patients had a 48-month survival rate of 95%. Conversely, the survival rate in patients who failed to complete stage 1 (1.7 mph, 10% grade) was only 78% at 36 months.[62] Even more marked survival differences as a function of exercise duration were noted in patients with known CAD. Numerous additional studies have verified the strong prognostic effect of exercise duration and functional capacity in patients with suspected or documented CAD.[63–66] Among patients with CAD, those with prior myocardial infarction underlying reduced functional capacity appear to have reduced survival compared with similarly reduced capacity in the absence of infarction.[67] It should be noted that other variables obtained from exercise testing such as heart rate recovery and chronotropic incompetence also have demonstrated prognostic value in patients with CAD independent of functional capacity.[68,69] Consideration of these variables in addition to functional capacity may therefore improve prognostic accuracy.

The updated ACC/AHA guidelines of 2002 recommend exercise testing after acute myocardial infarction for prognostic assessment, activity prescription, evaluation of medical therapy, and cardiac rehabilitation.[2,3] After infarction, the MET level or exercise duration achieved has been a powerful predictor of future adverse cardiac events; a commonly used marker for increased risk has been the failure to achieve 5 METs during treadmill exercise. In a meta-analysis of 28 studies from 1980 to 1995, Shaw et al[70] found the absolute rate of death in the year after infarction to be increased from 1.5% to 3.4% in patients with limited effort tolerance. Strikingly, the highest mortality rate in postinfarction studies occurs in the subset of patients who are unable to undergo exercise testing at all.[71,72] Villella et al[72] found 6-month mortality to be only 1.3% among Gruppo Italiano per lo Studio della Sopravvivenza Nell'Infarto (GISSI-2) patients with ST-elevation infarction who were able to exercise, including those with positive and negative tests, but it was 7.1% in the 38% of patients who were unable to exercise for any reason. Proportionally similar findings were reported by Krone et al[73] in patients with non–Q-wave infarction. In the Research on Instability in Coronary Artery Disease study, the major predictors of 1-year infarction-free survival in 740 men with unstable angina or non–Q-wave myocardial infarction who underwent predischarge cycle ergometer exercise testing were the number of leads with ischemic ST-segment depression and peak workload attained.[74]

The use of predischarge exercise testing to assess persistent ischemia after myocardial infarction has decreased substantially over the past 20 years for a number of reasons. A major factor is the widespread use of early angiography for risk assessment after thrombolysis or primary coronary intervention after infarction. This has led to early revascularization in those patients at highest risk who would previously have been identified by the predischarge exercise test. Other factors include lower subsequent event rates after infarction as a result of pharmacological interventions, lifestyle changes, smoking cessation, management of diabetes and hypertension, and cardiac rehabilitation. Another factor has been the decreasing length of patient hospitalization after acute intervention for infarction. The ACC/AHA guidelines, however, continue to recommend predischarge submaximal exercise testing at 4 to 6 days after myocardial infarction for previously stated purposes (prognostic assessment, activity prescription, and evaluation of medical therapy).[2]

Exercise testing in CAD patients referred for cardiac rehabilitation is essential for a baseline assessment of functional capacity, development of an appropriate exercise prescription, and evaluation of the results of training. In a large cohort of patients (n=2896) entering cardiac rehabilitation, Ades et al[75] recently established normative values for exercise capacity and subsequently created nomograms allowing percent-predicted calculations according to age, gender, and diagnosis. Serial testing may be useful in revising the exercise prescription, evaluating improvement in aerobic capacity, and providing patient feedback. Meta-analyses of randomized cardiac rehabilitation trials have calculated a 20% to 25% reduction in cardiovascular deaths in patients enrolled in these exercise programs.[76] Improvement in exercise capacity after coronary bypass surgery generally parallels the completeness of revascularization.[77]

The use of preoperative exercise testing to predict the risk of perioperative events in patients undergoing noncardiac surgery has not been well studied. From the data available, it appears that the ability to achieve a high exercise workload is a consistent predictor of low postoperative cardiac risk, regardless of associated symptoms or ST-segment changes. Conversely, patients with an exercise capacity below ≈5 METs experience a significant risk of postoperative cardiac events, even in the absence of symptoms or ischemic ECG

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TABLE 1. Functional Impairment During Incremental Treadmill Testing in Heart Failure: The Weber Classification

Class	Severity	Peak $\dot{V}o_2$, mL O_2 · kg^{-1} · min^{-1}	VT	CI max, L · min^{-1} · m^{-2}
A	Mild to none	>20	>14	>8
B	Mild to moderate	16–20	11–14	6–8
C	Moderate to severe	10–16	8–11	4–6
D	Severe	6–10	5–8	2–4
E	Very severe	<6	<4	<2

CI max indicates maximum cardiac index. Adapted with permission from Weber et al.[141] Copyright 1982, American Heart Association.

changes. Patients most likely to benefit from preoperative exercise testing are those with 1 or 2 of the following conditions: diabetes mellitus, angina pectoris, pathological Q waves on ECG, or compensated heart failure.[78]

Heart Failure

By definition, heart failure is the inability of the heart to maintain or increase cardiac output at a rate commensurate with systemic aerobic requirements. Heart failure may be caused by either systolic or diastolic dysfunction. It is difficult to estimate the true prevalence of systolic and diastolic heart failure; estimates range from 50% to 80% and 20% to 50%, respectively.[79] There does, however, appear to be general agreement that the prevalence of diastolic heart failure increases with age. In patients with diastolic heart failure, systolic function and ejection fraction can be normal, but filling pressure is usually elevated as a result of a stiff, noncompliant ventricle, with reduced end-systolic and end-diastolic volumes.[80] Nearly all patients with systolic dysfunction also have some degree of diastolic dysfunction. Both conditions result in a reduction in the cardiac output response to exercise and thus reduced exercise tolerance.[81–83]

Symptoms of both systolic and diastolic heart failure may first manifest as dyspnea or fatigue during physical activity. Therefore, it is appropriate to assess the functional capacity of patients with confirmed or suspected heart failure to determine whether, in fact, such impairment exists. It is well documented that resting indexes of ventricular function correlate poorly with exercise capacity.[84] Moreover, as discussed earlier, estimates of functional capacity such as exercise duration or peak work rate achieved are particularly less reliable in patients with heart failure than direct measurements of gas exchange.[85] Measurement of cardiopulmonary indexes during exercise has therefore become the standard for assessing functional capacity in patients with heart failure, for functionally classifying patients (Table 1), for evaluating therapy, for estimating risk, and for helping to stratify patients appropriately for transplantation[86] (Table 2). In patients with stable chronic heart failure, peak $\dot{V}O_2$ and the VT are highly reproducible and thus recommended for routine evaluation in this unique population.[20,87] It is worth mentioning, however, that the reproducibility of peak $\dot{V}O_2$ may be slightly higher than the VT.[87] Tables 1 and 2 list common classification procedures based on peak $\dot{V}O_2$ and the VT in patients with heart failure.

TABLE 2. Guidelines for Peak Exercise Oxygen Uptake as a Criterion for Cardiac Transplantation

Category for Transplantation	Peak $\dot{V}o_2$, mL O_2 · kg^{-1} · min^{-1}
Accepted indication	<10
Probable indication	<14
Inadequate indication	>15

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Many nonexercise functional tools such as symptom questionnaires and health status measures have been developed for patients with heart failure.[88–90] These tools can be useful for assessing functional or clinical status and evaluating interventions.

These instruments have the advantage of being quick, inexpensive, and safe. Although some studies have shown that functional questionnaires are sensitive to changes in clinical status,[89,91,92] others have reported that they can be unreliable or may provide incomplete information.[88,91,93,94] The relationships between measured exercise capacity and nonexercise estimates of functional status have generally been shown to be only modest[95–99]; therefore, none of these instruments is considered an appropriate surrogate for directly measured peak $\dot{V}O_2$. Table 3 lists common functional and health status tools used in heart failure.

Because determining maximal effort can be particularly subjective in patients with heart failure, CPX responses other than peak $\dot{V}O_2$ should be recorded. The VT is independent of effort and protocol and usually is a minimal target for testing. If properly measured, the VT also is reproducible with repeat testing and can be used as a clinical and prognostic tool.[99,100] The VT can be adequately measured by the V-slope method in most heart failure patients. However, in patients with markedly impaired functional capacity, arterial lactate accumulation may occur very early during exercise, and identifying the VT may be difficult. Recent studies have documented the clinical utility of the $\dot{V}E/\dot{V}CO_2$ slope in patients with heart failure in whom a value ≥34 indicates an abnormal response.[54,101] A heightened $\dot{V}E/\dot{V}CO_2$ slope reflects the combination of factors that underlie ventilatory inefficiency in heart failure, is independent of patient effort, and powerfully predicts health outcomes.[51,52,54–58] Although peak $\dot{V}O_2$ and the $\dot{V}E/\dot{V}CO_2$ slope provide prognostic information independent of clinical data and other exercise test responses, recent studies have underscored the importance of applying clinical and CPX responses in combination to optimally stratify risk.[56,102,103]

Valvular Heart Disease

Assessment of functional capacity is an integral part of the clinical management of patients with valvular heart disease because interventions often are based on the deterioration of aerobic capacity that results from the progressive hemodynamic consequences of valvular stenosis or insufficiency. In many instances, the reduction in aerobic capacity is readily apparent to the patient, but in some circumstances, it can be masked by insidious onset or a generally low level of daily

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TABLE 3. Description and Metrics Used for Functional and Health Status Tools in Heart Failure

Measurement	Description	Metric
Peak $\dot{V}O_2$	Measured oxygen uptake	Continuous variable
Estimated METs	Multiple of RMR estimated from work rate achieved	Continuous variable
Weber scale[142]	Functional classification	5-Category scale based on peak $\dot{V}o_2$(A–E)
6-Minute walk[36]	Distance walked in 6 min	Meters
NYHA[143]	Functional classification	4-Category scale (1–4)
DASI[144]	Estimate of exercise tolerance	Transformed continuous variable in METs
VSAQ[145]	Pretest estimation of exercise capacity based on symptoms	13-Category scale using METs
KCCQ[89]	HF-specific health status measure with 8 domains	Transformed 0–100 scale
MLHFQ[146]	HF-specific QOL questionnaire	Continuous variable

RMR indicates resting metabolic rate; NYHA, New York Heart Association functional class; DASI, Duke Activity Status Index; VSAQ, Veterans Specific Activity Questionnaire; KCCQ, Kansas City Cardiomyopathy Questionnaire; MLHFQ, Minnesota Living with Heart Failure Questionnaire; HF, heart failure; and QOL, quality of life. Modified with permission from Myers et al.[95] Copyright © 2006, Elsevier.

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physical activity, particularly among the elderly. A reduction in aerobic capacity in these situations can be determined and quantified by exercise testing, which also can be useful in assessing the hemodynamic significance of some valvular disorders. Additional studies are needed to evaluate the independent prognostic value of measures obtained from exercise testing in patients with asymptomatic valvular heart disease.

The ACC/AHA guidelines address the role of exercise testing in the evaluation and management of valvular heart disease in adult and pediatric populations.[104] In aortic stenosis, exercise testing should not be used in symptomatic patients, but it can be useful in asymptomatic patients to define the degree of functional limitation and to elicit symptoms and abnormal blood pressure responses.[105,106] To avoid complications induced by exercise in these patients, particular attention must be paid to the rhythm and hemodynamic response throughout the test. In asymptomatic chronic aortic regurgitation, exercise testing may be useful for assessment of functional capacity and symptomatology, evaluation of individuals before the initiation of athletic activity or an exercise program, and prognostic assessment before valve surgery.[3,104,107] In asymptomatic chronic mitral regurgitation and mitral stenosis, exercise testing may be useful for the reasons mentioned previously. Furthermore, measurement of pulmonary artery pressure during exercise testing can assist in the evaluation of the functional severity of the disorder.[104] In patients with mitral valve prolapse and no valvular regurgitation at rest, the one third of patients who developed mitral regurgitation during supine cycle ergometry (evaluated using Doppler echocardiography) experienced a higher rate of subsequent syncope, heart failure, and progressive valvular regurgitation than those who did not.[108] In this instance, exercise testing may assist in identifying individuals at higher risk for future adverse events. Finally, the Center for Medicare and Medicaid Services recently added valvular heart disease to the list of approved indications for cardiac rehabilitation. This fact should result in an increase in exercise testing of patients with valvular repair/replacement.

Peripheral Arterial Disease

In patients with peripheral arterial occlusive disease, exercise testing offers an objective assessment of functional limitation and ensures safe and accurate exercise recommendations.[1] Because many patients with peripheral arterial disease stop exercising because of claudication pain and not cardiopulmonary limitations, quantification of total exercise time and time to the onset of claudication can be used to develop an exercise prescription and to monitor the response to training. Measurement of foot transcutaneous oxygen tension and the ratio of ankle to brachial systolic pressure before and after exercise also may help to determine the functional deficit and response to training. Increases in aerobic capacity, daily physical activity, 6-minute walk distance, and 6-minute pain-free walk distance have been demonstrated with exercise rehabilitation.[109] Large increases in maximal calf blood flow also have been documented after such exercise programs.[109,110]

Pacemakers

The development of rate-responsive and dual-chamber pacemakers has provided important alternatives to fixed-rate ventricular pacing. Several studies have documented that exercise cardiac output and aerobic capacity are improved by these newer pacing modalities. However, it appears that the enhancement of chronotropic response contributes to this improvement more than atrioventricular synchrony.[111] Exercise testing may therefore be useful in deciding on the optimal pacing mode and response factor for accelerometer or minute ventilation sensors in a given patient. In addition, assessment of chronotropic incompetence with exercise stress testing in patients with pacemakers is useful, with a lower exercise duration and peak $\dot{V}O_2$ noted in chronotropically incompetent patients.[112]

Cardiac resynchronization therapy in patients with heart failure may benefit from evaluation and follow-up with exercise testing. Successful cardiac resynchronization therapy results in improvement in distance walked in 6 minutes and peak $\dot{V}O$,[113,114] likely because of improved autonomic nervous system modulation.[114] Other factors that may positively affect aerobic capacity as a result of cardiac resynchronization therapy include decreased mitral regurgitation[115] and increased left ventricular efficiency.[116]

Congenital Heart Disease

Assessment of functional capacity has proved useful in a wide variety of congenital cardiac abnormalities in determin-

TABLE 4. Cardiopulmonary Exercise Test Parameters Used to Differentiate Cardiac and Pulmonary Causes of Exertional Dyspnea

	Cardiac	Pulmonary
Peak $\dot{V}O_2$	Reduced	Reduced
VT	May be reduced	May be reduced
$V_{E\ MAX}$	≤80% of MVV	>80% of MVV*
Spo_2	>90% throughout exercise	May drop to <90%*
CO	May be reduced	Normal
Pre-exercise PFT	Normal	May have obstructive or restrictive pattern*
FEV_1 postexercise	No change from pre-exercise	≥15% decrease from pre-exercise†
PEF postexercise	No change from pre-exercise	≥15% decrease from pre-exercise†

MVV indicates maximal voluntary ventilation; PFT, pulmonary function test; and PEF, peak expiratory flow.

*These responses should not be considered the gold standard for defining a pulmonary limitation to exercise. Rather a $V_E$max >80% of MVV, a drop in Spo_2, and/or abnormal resting PFT values indicate a pulmonary limitation that must be supported by additional testing (rule out cardiac shunts, coexisting cardiac and pulmonary disease, etc).

†Compatible with exercise-induced bronchospasm.

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ing both the need for surgical repair and the response to treatment. In addition, exercise testing may be of value in confirming exertion-induced supraventricular or ventricular tachycardia in individuals with a suggestive history. Specific conditions in which exercise testing has proved useful include unoperated or palliated cyanotic defects, dilated cardiomyopathy, congenital complete atrioventricular block, chest discomfort, syncope, suspected tachyarrhythmia, aortic stenosis, and pulmonic stenosis; after repair of aortic coarctation, tetralogy of Fallot, and Ebstein's anomaly; and after the Fontan operation.[117] Recently, CPX has been shown to be useful for stratifying risk in those with adult congenital heart disease. In particular, an abnormal ventilatory response to exercise ($\dot{V}E/\dot{V}CO_2$ slope) was the strongest predictor of mortality in those adults with noncyanotic congenital heart disease.[118]

Patients With Unexplained Dyspnea

Cardiopulmonary exercise testing is an important evaluation component of unexplained exertional dyspnea.[3] Pulse oximetry and pulmonary function testing should be added to the exercise evaluation in individuals with a suspected pulmonary limitation. An estimated arterial oxygen saturation (Spo_2) dropping below 90% during exercise indicates a pulmonary limitation. Abnormal pulmonary function testing values at baseline (obstructive or restrictive pattern) are also an indication that a pulmonary limitation to exercise may be present. The ratio between the minute ventilation ($\dot{V}E$) at peak exercise and maximal voluntary ventilation (MVV) is typically between 0.50 and 0.80 in individuals without a pulmonary limitation.[119] A breathing reserve <20% ($\dot{V}E$/MVV >0.80) is consistent with a pulmonary limitation to exercise. Maximal voluntary ventilation can be directly measured before exercise by maximally ventilating for 12 to 15 seconds. The assessment of MVV is heavily influenced by effort and can be uncomfortable for the subject. Multiplying forced expiratory volume in 1 second (FEV_1) by 40 provides an accurate estimation of MVV.[120,121] Exercise-induced bronchospasm is believed to be present in 50% to 90% of individuals with[122] and 10% of individuals without[123] a history of asthma. Cough, dyspnea, chest discomfort, and wheezing during exercise are possible symptoms of exercise-induced bronchospasm.[124] Subjects with exercise-induced bronchospasm may also have a diminished aerobic capacity limited by shortness of breath. A ≥15% reduction in FEV_1 and/or peak expiratory flow after the cessation of exercise (0 to 10 minutes into recovery) indicate exercise-induced bronchospasm.[124] It should be noted that the reduction in pulmonary function may become apparent only several minutes after termination of the exercise test. Pulmonary function should therefore be monitored for at least 10 minutes into the recovery phase. Table 4 lists CPX variables used to differentiate between cardiac and pulmonary limitations to exercise.

Pediatric Populations

The role of exercise testing in the pediatric population has been well described. Exercise testing is commonly used in children to evaluate signs or symptoms that are induced or aggravated by exercise, to identify arrhythmias induced by exercise, and to assess medical and surgical therapies. Exer-

TABLE 5. Methodological Considerations to Improve Reproducibility Before and During Serial Exercise

Serial testing should be performed
At the same time of day because of diurnal variability in exercise capacity and ischemic threshold.
At ≥3 h after eating or intake of caffeine or tobacco products to avoid their effects on cardiovascular hemodynamics, including rest and exercise heart rate and blood pressure, cardiac output, and myocardial oxygen demand.
In a temperature-controlled room with good ventilation.
With background medications taken in the same doses and time intervals before each test.
With consistent handrail support between tests, which should be minimized, especially when respiratory gases are not monitored.
With protocols that use small, graded increments of work rate that will generally provide the most accurate estimate of aerobic capacity when oxygen uptake is not measured directly.[11,134]

TABLE 6. Uses and Limitations of Some Common Methods for Assessing Functional Capacity

	Type of Exercise			
	Maximal, No Respiratory Gas Analysis	Maximal, Respiratory Gas Analysis	Submaximal, No Respiratory Gas Analysis	Walk Tests
Variables of interest	Duration	Peak/max $\dot{V}O_2$	Estimated METs	Distance walked
	Estimated METs	VT	ECG	
	ECG	$\dot{V}E/\dot{V}CO_2$ slope	HR	
	Peak HR	Peak RER ($\dot{V}O_2/\dot{V}CO_2$)	SBP and DBP	
	Peak SBP and DBP	PFT	Perceived exertion and dyspnea	
	HRR	Oxygen uptake/recovery kinetics		
	Pulse oximetry	Variables included in column 1		
	Perceived exertion and dyspnea			
Utility	General fitness assessment	Gold standard for assessing aerobic fitness	Estimation of aerobic testing when maximal testing not indicated (predischarge after acute MI)	Estimation of aerobic fitness
	Prognostic assessment	Prognostic assessment	Can be used to formulate exercise prescription	Measures response to medical or surgical intervention
	Exercise prescription	Classifies CHF severity		
		Decision tool for heart transplantation		
		Quantifies response to medical or surgical intervention		
		Differentiates cardiac vs pulmonary limitation		
Advantages	Modest cost	Best method for assessing aerobic fitness	Risk reduction vs maximal testing	Negligible cost
	Good reproducibility	Demonstrated prognostic value	Modest cost	Good reproducibility
	Demonstrated prognostic value	High reproducibility	Well tolerated	Well tolerated
		Assessment of ventilatory response to exercise		
Limitations	Influenced by familiarity with testing and handrail use	Higher cost and higher level of expertise	Indirect assessment of aerobic capacity	Influenced by familiarity with testing
	Less reliable than testing with respiratory gas analysis	Possible patient apprehension/discomfort	Shares weaknesses of maximal testing without respiratory gas analysis	
	Can overestimate aerobic capacity			

HR indicates heart rate; RER, respiratory exchange ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HRR, heart rate recovery; CHF, congestive heart failure; and MI, myocardial infarction.

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cise testing also is performed before certain athletic, recreational, or vocational activities or to establish baseline data before rehabilitation, including cardiac, pulmonary, or musculoskeletal information. In those with congenital heart disease, exercise testing can be used to evaluate prognosis (see Congenital Heart Disease). For further information, see the AHA scientific statement on clinical stress testing in the pediatric age group.[125]

Asymptomatic Adults

Physical fitness testing, by providing an objective assessment of functional capacity, is a more powerful predictor of cardiovascular disease mortality than is self-reported physical activity, with risk ratios of 4 to 9 for the least-fit and most-fit categories, respectively. Numerous prospective studies have verified this relationship between fitness and cardiovascular risk in asymptomatic populations, even when submaximal exercise testing is used.[126–129] In >13 000 men and women who underwent maximal treadmill exercise testing at the Cooper Clinic in Dallas, Tex, subjects in the lowest quintile of age- and sex-adjusted fitness suffered an 8- to 9-fold increased risk of cardiovascular death over a follow-up period of 8.2 years.[10]

Even so, conventional guidelines recommend against the routine use of exercise testing for risk assessment in asymptomatic subjects with a low (<10%) pretest likelihood of underlying significant CAD.[3] Although a 10% level of pretest risk is low, it includes most of the asymptomatic population

<50 years of age who do not have ≥1 standard coronary risk factors. There are several related reasons for this recommendation. The absolute posttest increase in the already-low likelihood of disease is small when a positive exercise test with imperfect specificity is found in subjects with a low pretest likelihood of disease. The resulting low positive predictive value of the test means that a large number of "false-positive" test responses will occur, and these may considerably exceed the number of "true-positive" findings. Moreover, few substantive data have been accumulated to suggest that intervention alters coronary risk in asymptomatic subjects who might be determined to be at increased risk in this way.[130]

Conversely, exercise testing has been shown to have useful predictive value in the large proportion of the general population who are at intermediate levels of risk.[131] The potential role of exercise testing as a routine screening tool to assess risk in asymptomatic adults has been evaluated by a recent AHA scientific statement.[132] This document emphasizes the prognostic value of non-ECG findings during exercise testing, including functional capacity, chronotropic response, and heart rate recovery, in combination with advanced standard risk factor assessment.[133] It calls for a definitive randomized trial to test the hypothesis that intervention after exercise screening can favorably affect cardiac morbidity and mortality in asymptomatic subjects.

Research Applications of Aerobic/Functional Capacity Assessment

In addition to its value in the management of patients with cardiovascular disease, the assessment of aerobic/functional capacity is an important research tool. Much of the information regarding the utility of this measurement has been derived from cross-sectional studies, typically involving a single measurement of exercise capacity to determine the degree of exercise limitation and its prognostic significance. However, increasing attention has been directed toward using exercise testing to measure the therapeutic response to medical, surgical, and/or lifestyle interventions, often through serial assessments.

Serial assessment of exercise capacity, that is, several tests in close proximity to characterize baseline function and changes in function over time, presents several challenges. A primary challenge is the reproducibility of data collected, which is influenced by the choice of the exercise testing protocol, as mentioned above. Other considerations include frequent calibration of the treadmill/cycle ergometer and ventilatory expired gas unit, appropriate training of laboratory personnel, the time of day of testing, alterations to the pharmacological regimen, exercise testing experience by the subject, a training effect (particularly when repeat tests are over several days and/or sedentary individuals are tested), pretest directions and compliance to those directions, and the subject's ability/willingness to provide maximal effort (Table 5). With respect to the last concern, attainment of a peak respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O$) ≥1.10 during serial testing is an objective indication that a subject consistently put forth a maximal effort and is an advantage of ventilatory expired gas analysis.

These effects may be magnified if testing is performed by different personnel or in multi-institutional laboratories. If not adequately controlled, such variables can be expected to affect peak $\dot{V}O_2$ and to limit the reproducibility of measurements. Defining an acceptable magnitude of difference in functional capacity between serial tests, particularly at baseline, is valuable.

Although no universal criteria exist for test reproducibility, peak/maximal $\dot{V}O_2$ is generally considered reproducible if values vary by <10% on separate days.[134] Thus, if values vary by ≥10%, one must consider the extent to which potential confounders may have contributed to the differences between test results. When respiratory gases are not monitored, exercise duration should not vary by ≥10% of the total exercise test time in seconds on repeat testing; for example, for a test lasting 10 minutes (600 seconds), this would translate to an acceptable difference of <60 seconds compared with another test. If 2 exercise tests do not meet these criteria, additional testing should be performed until these criteria are fulfilled. Because peak/maximal $\dot{V}O_2$ is generally more reproducible than treadmill time, gas exchange should be monitored in intervention studies whenever possible to minimize the standard deviation of the measurement, thereby reducing the sample size required. In addition, test end points should be consistent; eg, in a given patient with angina pectoris or claudication, exercise may be consistently terminated at the same level of chest or leg pain on repeat tests. Variables of interest, utility, advantages, and limitations of common methods for assessing functional capacity are summarized in Table 6.

Research Applications in Asymptomatic Populations

Low levels of habitual physical activity are associated with increased risk of future cardiovascular disease, particularly CAD, with the risk in sedentary subjects approximately double that of active persons.[135] To this end, an objective assessment of functional capacity is a more powerful predictor of cardiovascular disease mortality than self-reported physical activity.[1] Despite the potential discrepancies between estimated and direct measurement of peak/maximal $\dot{V}O$, either method aids in the prediction of mortality and cardiovascular risk in asymptomatic subjects.[129,132,136–140] Furthermore, impaired functional capacity predicts increased risk to a greater degree than demographics and presence of standard risk factors in both women and men.[1] In addition, numerous prospective studies have verified the relationship between fitness and cardiovascular risk in asymptomatic populations, even when submaximal exercise testing is used.[126–129] Although it is certainty not cost-effective to perform exercise testing on the entire adult population to assess aerobic fitness, such testing might be judiciously applied to sedentary individuals with high coronary risk profiles to further stratify their cardiac risk and to motivate them to begin an exercise program.

Summary

In summary, the measurement of functional capacity provides a valuable tool for diagnosis, treatment, and prognostic

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*Modest.

†Significant.

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assessment in a wide variety of settings. The specific aspects of testing such as the mode of exercise, protocol, end point, and analysis of respiratory gases are highly dependent on the population being tested and the questions being addressed.

Regardless of these specifics and despite the many recent advances in cardiac imaging, functional capacity assessment remains an important procedure.

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Assessment of Functional Capacity in Clinical and Research Settings: A Scientific Statement From the American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology and the Council on Cardiovascular Nursing

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