Exercise Capacity and Prognosis in Chronic Heart Failure

Jonathan Myers, PhD

The association among fitness, health, and longevity is probably as old as there are historical records. The writings of the classic Greek physicians Herodicus, Hippocrates, and Galen are replete with references to fitness, and each believed that a healthy body was a prerequisite for mental well-being.1 The US founding fathers were also conscious of the importance of fitness. Benjamin Franklin advocated 15 minutes of brisk stair climbing at intervals throughout the day, along with swimming and the use of dumbbells for health purposes.2 Thomas Jefferson recognized the need for fitness, although perhaps to an extreme, when he wrote, “Not less than 2 hours a day should be devoted to exercise and the weather shall be little regarded. If the body is feeble, the mind will not be strong.”3 Of course, none of these historical icons was cognizant that we would one day routinely measure an individual’s maximal physiological response to maximal exertion under controlled circumstances. Nor could they have imagined that the exercise test would be a valuable tool to predict the consequences of diseases related to 21st-century lifestyles.

The use of the exercise test to stratify risk and optimize clinical management for patients with cardiovascular disease (CVD) spans several decades. However, evidence of the importance of exercise capacity as a risk marker in patients with CVD is relatively recent, and clinical practice has yet to embrace this evidence. In a growing number of studies, exercise capacity has been shown to outperform traditional markers of risk (including clinical history, hypertension, obesity, hyperlipidemia, and other exercise test responses) in persons with and without CVD. In patients with chronic heart failure (CHF), exercise capacity has even been demonstrated to outperform invasive hemodynamic data (cardiac output, pulmonary wedge pressure, and ejection fraction) in stratifying risk. Because exercise capacity measured directly (using cardiopulmonary exercise testing techniques [CPX]) represents a precise, direct, and physiological measure of exercise capacity (expressed as peak \( \text{V} \dot{O}_2 \)), it has become established as the standard index to estimate risk in patients with CHF.4 During the last 2 decades, numerous studies have demonstrated peak \( \text{V} \dot{O}_2 \) to be a noninvasive index that powerfully predicts outcomes in CHF,4 and it has evolved to become a particularly important measurement for assessing the timing of cardiac transplantation.4,5

Because CPX equipment is not always available and requires some technical expertise, it is not routinely performed in many centers. The question of when CPX techniques are most useful (and among which patients) has been asked for many years. In this issue of Circulation, Hsich et al6 studied 2231 patients with reduced systolic function who underwent CPX and followed the subjects for a mean of 5 years. The major objectives were to determine whether exercise capacity (as estimated from exercise time achieved using a Naughton protocol) predicts survival and whether exercise time adds prognostic information beyond that provided by peak \( \text{V} \dot{O}_2 \) and other risk factors, which have long been established. End points included death and a composite outcome of death and United Organ Sharing Network status-1 heart transplantation. They observed that exercise time on the treadmill predicted death and the composite outcome in both women and men, even after accounting for peak \( \text{V} \dot{O}_2 \) and other clinical factors, including cardiac history, body mass index, diabetes mellitus, medication use, and ejection fraction. Treadmill exercise time provided similar prognostic value to peak \( \text{V} \dot{O}_2 \) in both high- and low-risk patients (peak \( \text{V} \dot{O}_2 \leq 14 \text{ and } >14 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \)). They suggested that exercise capacity expressed as treadmill time is a valuable initial prognostic screening tool in patients with reduced systolic function.

Three salient issues are raised by this provocative study. The first issue is that exercise capacity, regardless of how it is measured, is a powerful and greatly underappreciated predictor of risk. The second issue involves a question that has long been debated, that is, should exercise capacity be measured directly (ie, with peak \( \text{V} \dot{O}_2 \)), or is exercise capacity estimated from treadmill time or work rate achieved an adequate surrogate? If exercise time is an adequate surrogate for peak \( \text{V} \dot{O}_2 \) in the particular patients studied by Hsich et al,6 in what circumstances and in what populations should we advocate that exercise capacity be measured directly? The third issue is consideration of the maxim in the American Heart Association and other exercise testing guidelines to use “metabolic equivalents [METs] not minutes,” so that exercise capacity can be expressed interchangeably between different cycle ergometer or treadmill protocols.

The first issue, the fact that exercise capacity powerfully predicts outcomes, is not particularly new, but in my experience, it comes as a surprise to most clinicians when this is pointed out in lectures and meetings. In recent years, many groups have reported that exercise capacity outperforms traditional risk factors and other exercise test responses (including markers of ischemia) in terms of estimating risk.7–10 The prognostic power of exercise capacity has been
demonstrated in many different populations during the last decade, including asymptomatic subjects, patients with known coronary disease, those at high risk for CVD, patients with CHF, and those who are hypertensive, obese, or diabetic. Exercise capacity is often overlooked because clinicians tend to focus on fixing the coronary circulation and the potential need for revascularization. A related concept that remains largely unappreciated by the medical community is that relatively small increments in exercise capacity result in large health outcome benefits. The observation that each 1-minute reduction in exercise time (approximately 0.5 METs on the Naughton protocol) in the Hsich et al study provided a 7% increase in risk of death parallels many recent studies indicating that each 1-MET increment in exercise capacity is associated with roughly 10% to 25% reductions in mortality. Getting patients out of the lowest fitness category (typically a quintile <5 or <6 METs) is particularly important because this shift alone is associated with >40% to 50% reductions in risk.

Low exercise capacity as a therapeutic target appears to be an investment that yields significant returns, but clinicians rarely discuss exercise with their patients. Targeting an improvement in exercise capacity to improve outcomes would entail encouraging patients to increase their activity level. Motivating habitually sedentary patients to make the changes necessary to increase their exercise capacity has unique challenges, but a few minutes spent discussing activity has been shown to result in significant increases in physical activity patterns. Meeting the minimal guidelines for activity (30 minutes of moderate activity most days of the week) has been associated with 20% to 40% reductions in all-cause and cardiovascular mortality.

Exercise is a nonpharmaceutical, nonsurgical, and nondevice management intervention that has well-documented benefits. Although the treatment of CHF is certainly complex and few clinicians are versed in the nuances of exercise prescription, nearly all stable CHF patients can safely increase their daily activity level. Increasing physical activity is the common denominator for the clinical treatment of low exercise capacity and reduction in risk for numerous comorbid conditions, including hypertension, diabetes mellitus, and obesity.

The foundation of the second issue involves whether exercise capacity should be measured directly using ventilatory gas exchange techniques or whether exercise time can be considered an adequate marker of risk in most patients with heart failure. This question is not simple, and it cannot be answered in a single study. The implications of the Hsich et al study are that, because CPX is not available in many hospitals, exercise time is a valuable initial prognostic screening tool; the authors observed that exercise time had prognostic power similar to peak VO2. This finding is similar to that of Kavanagh et al in their large cardiac rehabilitation experience. However, using more sophisticated statistical methods than previous approaches (bootstrap sampling, c-index, net reclassification improvement, and integrated discrimination improvement), Hsich et al observed that peak VO2 was a somewhat more powerful predictor of mortality than exercise time. Although peak VO2 has gained widespread acceptance as a prognostic tool in patients with CHF, surprisingly few studies have addressed its added value over treadmill time. Intuitively, peak VO2 should be a better index of risk because it is a more precise, reproducible, and physiological measure than exercise time. In the few studies that addressed this issue, peak VO2 more powerfully predicted all-cause mortality than peak METs estimated from work rate in patients with CHF.

Although the focus of studies using CPX to risk stratify patients with CHF has been on peak VO2, it is important to consider that studies during the last decade have consistently demonstrated that indices of ventilatory inefficiency are stronger markers of risk than peak VO2, and these indices are only obtained using CPX. Most notably, the slope of the relation between minute ventilation and CO2 production (the VE/VC02 slope) is a particularly powerful risk marker in CHF. In some of these studies, peak VO2 complements ventilatory inefficiency in the estimation of risk whereas in others peak VO2 falls out of the multivariable model when the VE/VC02 slope, oscillatory breathing pattern, the lowest VE/VC02 ratio, or other indices of ventilatory inefficiency are measured. As is often the case, these studies tend to focus on a single variable or a favorite “new” marker, but no doubt the highest predictive accuracy comes from multivariable approaches. The VE/VC02 slope and peak VO2, in particular, measure 2 different pathophysiological responses in CHF, and predictive accuracy is higher when they are combined. Indices of ventilatory inefficiency appear to be responsive to interventions such as exercise training, cardiac resynchronization, and other therapies in CHF. It has become increasingly apparent that an additional asset of CPX is the ability to quantify ventilatory inefficiency and that this should be routinely quantified when assessing patients with CHF.

A final provocative issue that the Hsich et al study raises is the possibility that treadmill time on the Naughton protocol could routinely represent a simple and inexpensive screening tool for patients with CHF, such that an approximate risk estimation could be part of an initial evaluation. Those determined to be at elevated risk could be referred for CPX testing or other evaluations as deemed appropriate. In the Hsich et al study, high-risk subjects (those in the lowest quartile for exercise time) were those achieving <5 minutes for women and <6 minutes for men. Again, this value should be expressed as METs rather than minutes so that the results are applicable using different protocols; these cut points represent roughly 3 METs for women and 4 METs for men. This screening test would also provide an opportunity to assess the presence and severity of symptoms (CHF patients limited by dyspnea have roughly double the risk compared with those limited by fatigue), in addition to electrocardiographic changes and rhythm abnormalities, and to determine an appropriate exercise prescription.

A clear message from the Hsich et al study is that exercise capacity is a potent risk predictor in patients with CHF, as it is in other populations with and without CVD. Whether the test is performed to screen apparently healthy individuals, evaluate the severity of CHF, or to assess coronary disease, exercise capacity needs to be considered at least as important as the traditional risk markers and other exercise test responses, including ischemia. The study by Hsich et al
provides more support for health professionals to counsel patients on a health behavior that is vitally related not just to prognosis but overall health. Although the context has obviously changed, perhaps we can learn from the classic Greek physicians of more than 2000 years ago who held fitness in such high regard.1

**Disclosures**

None.

**References**


**Key Words:** Editorials ■ epidemiology ■ exercise ■ heart failure
Exercise Capacity and Prognosis in Chronic Heart Failure
Jonathan Myers

Circulation. 2009;119:3165-3167; originally published online June 15, 2009;
doi: 10.1161/CIRCULATIONAHA.109.873430
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/119/25/3165

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/