Much Potential but Many Unanswered Questions for High-Intensity Intermittent Exercise Training for Patients with Heart Failure

Sherry O. Pinkstaff, PhD, PT

KEYWORDS

• Heart failure • Exercise • High intensity • Intermittent • Interval

KEY POINTS

- Moderate-intensity continuous exercise (MICE) has been the clinical standard for patients with heart failure (HF) but evidence is mounting for the effectiveness of high-intensity intermittent exercise (HIIE).
- HIIE is associated with clinically significant improvements in peak oxygen consumption (Vo_{2peak}) as well as many other variables associated with exercise capacity and cardiovascular function.
- The number of studies in which HIIE was used to treat patients with HF remains small, representing fewer than 200 patients.
- HIIE has not been associated with adverse events in the studies conducted to date.
- More research is needed before HIIE can become the clinical standard for patients with HF.

INTRODUCTION

There is a robust trove of scientific studies that support the positive physical and mental health benefits associated with aerobic exercise for apparently healthy individuals. This evidence underlies the government-backed physical activity guidelines, which suggest 30 minutes of moderate-intensity exercise on most if not all days of the week.[1,2] These recommendations also suggest that more vigorous exercise can be performed on fewer days for the same benefit, a recommendation that reflects the inverse dose-response relationship between physical activity and disease.[3–5] Those benefits include significant reductions in the risk factors associated with cardiovascular disease (CVD). There is also ample evidence for the use of aerobic exercise in CVD patient populations to improve numerous health-related outcomes.

Aerobic exercise was once contraindicated for patients with HF. In the early days of its use in this patient population, no greater than moderate-intensity training was recommended. Current guidelines recommend that patients with clinically stable HF perform aerobic MICE training (ie, 50%–80% of peak capacity) for up to 45 minutes on most days of the week.[6,7] Since the 1980s, many studies have demonstrated the safety and effectiveness of aerobic MICE in patients with HF.[8] Despite these positive results, a recent large, multicenter, randomized clinical trial, Heart Failure: A Controlled Trial Investigating Outcomes of

Disclosures: This author has no conflicts of interest to disclose.

Physical Therapy Program, Department of Clinical and Applied Movement Sciences, University of North Florida, 1 UNF Drive, Jacksonville, FL 32224, USA
E-mail address: s.pinkstaff@unf.edu

Heart Failure Clin 11 (2015) 133–148
http://dx.doi.org/10.1016/j.hfc.2014.08.008

Exercise Training (HF-ACTION), demonstrated no overall improvement in all-cause mortality and hospitalization.[9] Importantly, after adjusting for highly prognostic clinical values for the same endpoints, exercise training did result in a modest prognostic improvement. Nonetheless, to many investigators, this remains a disappointing result.

Recently clinicians and researchers have begun to investigate HIIE training as an intervention for this patient population. This type of training has been used extensively in healthy populations, in the context of athletic performance. A vast majority of the studies investigating the effect have been done in these populations. Although many fewer studies have been conducted in a patient population representing a much smaller number of patients, the results are promising. HIIE training seems safe and improves physiology, quality of life, and functional capacity.[10–14] Many unanswered questions, however, remain.

Therefore, the objective of this review is to define HIIE, discuss its physiologic benefit for patients with HF, outline the studies that have been conducted to date, and discuss the issues that need to be resolved before this exercise intervention is more widely embraced by the clinical community.

PRINCIPLES OF HIGH-INTENSITY INTERMITTENT EXERCISE

HIIE involves the use of short periods of exercise interspersed with rest periods. The duration and intensity of the exercise and rest can be varied in numerous ways. The American College of Sports Medicine defines intensity as a percentage of heart rate (HR) reserve or $\dot{V}O_2$ reserve ($\dot{V}O_2R$). These are relative values that must be individually prescribed. Hard or very hard intensity is 60% to less than 85% and 85% to less than 100%, respectively. Exercise training at greater than 100% HR reserve (HRR) or $\dot{V}O_2R$ has been used primarily for athletic training and is not considered for this review. For comparison, moderate intensity is defined as 40% to less than 60% HR reserve or $\dot{V}O_2R$. The rationale for HIIE is that the short periods of exercise followed by rest periods allow for greater time spent at a higher intensity of exercise (compared with continuous exercise).[15] This greater intensity requires different energy production pathways to be used as well as additional muscle fiber recruitment. Together, these provide an increased potential for both central and peripheral adaptation. In a study of more than 5000 apparently healthy men and women, relative exercise training intensity was more important than duration in reducing the risk of all-cause and coronary heart disease mortality.[15]

There seems to be a mechanistic basis for this exercise intensity dependence. HF is characterized on the cellular level by dysfunctional cardiomyocyte activity. Aerobic exercise can repair or reverse some of these pathologic changes, especially when that exercise is high intensity (>90% of $\dot{V}O_{2peak}$). In animal studies, the physiologic adaptations to chronic exercise training are explained by changes to cardiomyocyte function. In rats and mice, improvement in cardiac pump function, as a result of positive changes to the cardiomyocyte, is achieved by high-intensity exercise.[16] Furthermore, it has been suggested that for patient populations, high-intensity exercise training may be required for positive central adaptations, such as cardiac dilatation, ejection fraction, stroke volume, or other systolic parameters.[17]

EFFICACY/PHYSIOLOGIC BENEFITS OF HIIE TRAINING

Acute Effects

Recent studies have evaluated the acute effects of HIIE training in patients with HF (**Table 1**). In the most recent, a total of 13 patients with systolic HF were randomized to perform a single bout of high HIIE or MICE during which gas exchange and central hemodynamic factors were measured.[18] The HIIE bout resulted in similar cardiac output (CO), stroke volume, and oxygen extraction compared with MICE. Importantly, the hemodynamic response to HIIE was stable throughout the training session. This stability is consistent with the lack of adverse events in this cohort, a finding that is similar to other published accounts of this type of training. Participants also tended to rate the perceived exertion lower and were more likely to be able to complete the bout of HIIE. This study complements an earlier study that demonstrated that when compared with steady state exercise, HIIE resulted in comparable increases in left ventricular (LV) ejection fraction, stroke volume, CO, ratings of leg fatigue, and dyspnea.[19] The investigators also concluded that these results spoke to the safety of HIIE training.

Tomczak and colleagues[20] used MRI to assess the changes in biventricular function after a single bout of HIIE. The major finding was that biventricular function improved with a decrease in end-systolic volume and an increase in LV ejection fraction. The investigators suggested this improvement may be related to reduced systemic peripheral resistance or alternatively to improved cardiomyocyte contractility. Diastolic function was also improved as demonstrated by an