Swing and a Miss or Inside the Park Home Run: Which Fate Awaits High Intensity Exercise Training?

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As we bask in the fading glow of the 2012 Summer Olympics games, it seems apropos to discuss the clinical application of an exercise training regimen that was systematically applied to elite athletes nearly 80 years ago. Then Drs. Woldemar Gerschler and Herbert Reindel, a professor of physical education and a physician, used the scientific method to develop the basic principles of what is referred to today as high intensity interval training (HIIT). The use of HIIT, which consists of a series of repeated bouts of high intensity exercise intervals alternated with periods of low to moderate intensity recovery, remains a mainstay in the training regimen of many of today’s athletes, regardless of whether they are our youth participating in middle school track or seasoned veterans competing for Olympic Gold.

However, given the many recent published small-sample studies that incorporated HIIT in patients with stable metabolic or cardiovascular disease, one can’t help but think that this exercise regimen might also represent a potentially new approach to patient care. Truth be told, HIIT was evaluated in the clinical setting in patients with chronic heart failure more than 25 years ago. Although the duration of the work and recovery periods can vary from one study to another, one common model for HIIT prescribes 4 to 5 work bouts of 3 to 4 minutes each, during which exercise intensity is set as high as 85% to 90% of heart rate reserve \( [i.e., \text{peak heart rate} - \text{resting heart rate}] \times 0.9 + \text{resting heart rate} \) (Figure 1). Interspersed among these higher intensity bouts are recovery bouts of similar duration, prescribed at 60-70% of heart rate reserve. This approach to exercise training stands in stark contrast to today’s guideline-based method of moderate continuous training (MCT), which maintains exercise intensity between 60% and 80% of heart rate reserve throughout the full session of exercise. Among both athletes and several patient groups, HIIT allows for more total work to be completed in a given period of time. Among patients with stable cardiovascular disease (CVD), HIIT (compared to MCT) can also
result in a two-fold greater improvement in exercise capacity, as measured by peak oxygen uptake\textsuperscript{5}.

In this issue of Circulation, Rognmo and colleagues\textsuperscript{6} are the first to address the important issue pertaining to the safety of HIIT. Using a retrospective analysis involving 4,846 patients with CVD (mean age: 58 yr), they report on more than 175,000 exercise training hours gathered from three different rehabilitation units in Norway. On average, each patient completed 37 cardiac rehabilitation sessions, of which the majority were MCT and the balance HIIT. An event was defined as a cardiac arrest or myocardial infarction during exercise or within one hour afterwards. They observed one fatal cardiac arrest per 129,456 exercise hours of MCT and two non-fatal cardiac arrests per 46,364 HIIT sessions (1 per 23,182 exercise hours). Based on the “low events rates” observed in both group, the authors recommended that HIIT be considered in the rehabilitation of patients with CVD.

Although the strength of the study by Rognmo et al.\textsuperscript{6} lies in its novelty, I would be remiss if I did not point out that there are shortcomings that deserve our attention as well. First, as the authors correctly allude to in their discussion, with a calculated power of only 23\% one is compelled to view their safety data as exploratory at best. Using their own data they properly estimate that an adequately powered randomized trial would require more than 20,500 patients (and generate more than 750,000 exercise hours) to determine the safety of HIIT. Obviously, an exercise intervention trial of such magnitude would be a challenge to both operationalize and secure funding for.

The above notwithstanding, a close look at the author’s safety data suggests that we simply cannot ignore this issue. Specifically, one exploratory interpretation of their data might be that MCT is safer than HIIT (MCT: 1 event per 129,456 hours of exercise versus HIIT: 1
event per 23,182 hours of exercise). Supporting this potential concern is the 2005 paper by Leon et al., who estimated the rate for major cardiovascular events in cardiac rehabilitation programs, which traditionally use MCT, to be between approximately 1 per 50,000 and 1 per 120,000 patient-hours. We can indirectly get at this question of safety by first conducting more adequately powered randomized trials that assess the effect of HIIT on other end points of interest (e.g., cardiovascular characteristics, the pathophysiology of the disease, and clinical outcomes). From these other studies safety data can also be collected and subsequently combined for a better determination of safety using a meta-analytic approach. One such trial that is presently underway at seven centers in Europe, but is itself underpowered to determine safety (n=200), is SMART-HF (Controlled Study of Myocardial Recovery after Interval Training in Heart Failure). The primary aim of SMART-HF is to evaluate the effects of HIIT on left ventricular end-diastolic diameter.

A second shortcoming of the present study pertains to the fact that patients were not prospectively randomized to MCT or HIIT, so we can not truly determine the isolated effect of HIIT on safety. Instead of testing the cumulative or repetitive effect of HIIT alone, what their study did do was help us better understand the safety associated with a combined approach to training … one that involves both HIIT and MCT. Viewed as such, the over-all event rate for a program that combined HIIT and MCT becomes 3 per 175,820 exercise hours (1 event per 58,600 exercise hours). Practically speaking, should HIIT someday become part of evidence-based care for patients with CVD, most cardiac rehabilitation programs will likely incorporate it in a manner that mixes both types of training (HIIT and MCT) into the exercise plan for their patients. So viewing safety data pertaining to HIIT in this manner may, in fact, be more generalizable.
The effect of HIIT on subsequent clinical end points has not been investigated to date. Using surrogate logic one might hypothesize that since peak oxygen uptake is related to mortality in patients with CVD and given that HIIT has been shown to provide greater improvements in this measure of exercise capacity than MCT, then HIIT should lead to a greater reduction in risk for mortality or other clinical end points. Tempting as it might be, we are all aware that such logic does not always pan out. The clinical benefit of MCT in patients with CVD is well appreciated and similar clinical end point information can (and should) be gathered for HIIT through a randomized trial an endeavor that is feasible from both an operational and funding perspective. For those among you who are of the mindset that large, multi-center clinical-end point driven trials that rely on the adherence of humans to prescribed healthy behaviors may represent a poor utilization of limited resources or are operationally unfeasible, I point out that two such trials were recently completed (Claudication: Exercise versus Endoluminal Revascularization, CLEVER; Heart Failure and a Controlled Trial Investigating Outcomes of Exercise Training, HF-ACTION) and a third remains underway (Look AHEAD: Action for Health in Diabetes). Beyond any effect an exercise regimen (e.g., HIIT) might have on exercise capacity, for the regimen to be included in the evidence-based care of patients with CVD it too should be held to the same effectiveness standards that are imposed on drug and device therapies.

Slightly tangential to the above discussion about the safety and benefits of HIIT, the trial by Rognmo et al. also helps us re-engage the discussion about two issues that continue to challenge the use of exercise of any type (HIIT or MCT) in the care of patients with CVD. Specifically, the two 800-pound gorillas in the room that we must address better are (a) ensuring that patients that are eligible for cardiac rehabilitation are both referred and participate and (b)
improving the long-term compliance of these patients to program recommendations. Those of us working in preventive cardiology are well aware of the challenges that impact program referral and participation, ranging from operational barriers and physician training to insurance coverage and patient-specific issues\textsuperscript{10-12}. Due to a variety of forces, the over-all participation rate for cardiac rehabilitation is $<40\%$ in the U.S., a rate that requires improved performance from all involved partners, including providers, professional organizations, public policy makers, insurance carriers, and hospital administrators.

Equally important is the need for demonstrated improvement in long-term patient adherence. Presently, patient adherence to a prescribed exercise training regimen can be modest, ranging from 40-70\% at 12 months\textsuperscript{13-16}. Therefore, as we move to conduct future trials aimed at assessing the efficacy or effectiveness of new exercise methods, it seems only right that we first, or at least in parallel, engage in the study of behavioral and exercise programming strategies that target improved adherence in both clinical trials and routine clinical care. It is difficult for even large trials to prove effectiveness if too many of the subjects assigned to the exercise intervention of interest don’t adhere. One current trial that has as its primary aim the study of the effects of several behavioral and exercise programming strategies (e.g., moderate intensity interval training or MIIT) that target improved adherence is HEART Camp (Heart failure Exercise And Resistance Training Camp). Recently, the National Heart, Lung, and Blood Institute stated its interest to fund studies that “minimize special infrastructure” and test “novel methods that enable low-cost conduct”\textsuperscript{17}. A policy direction that seems consistent with a potentially low-cost and accessible intervention such as exercise … a therapy that can be studied in various settings (facility-based versus home-based) and using different types of programs (e.g., HIIT, MIIT, MCT, resistance training) or methods of delivery (e.g., internet or computer-based).
In closing, Rognmo and colleagues are to be commended for both recognizing the
critical importance of assessing the safety of HIIT and providing us with our first glimpse of such data.
Their trial, however, does much more. It highlights that more work remains relative to better understanding the nature and scope of exercise training in the care of patients with CVD. As clinical investigators interested in the study of exercise, now is a good time to increase the “intensity” of our scientific efforts.

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**Figure Legend:**

**Figure 1.** Heart rate (HR) response during a cardiac rehabilitation session involving high intensity interval training in a 41-old male seven weeks after a percutaneous coronary intervention.
Prescribed HR range for higher intensity interval = 130-139/min
Prescribed HR range for recovery interval = 114-124/min
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