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**Clinical Research****Acute Responses to Intermittent and Continuous Exercise in Heart Failure Patients**

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**ABSTRACT**

**Background:** The purpose of this study was to compare cardiopulmonary responses, exercise adherence, tolerance, and safety of optimized high-intensity interval exercise (HIE) compared with moderate-intensity continuous exercise (MICE) in patients with heart failure and reduced ejection fraction (HFREF).

**Methods:** Twenty patients with HFREF (aged  $61 \pm 9.9$  years) were randomly assigned to HIE corresponding to  $2 \times 8$  minutes of 30-second intervals at 100% of peak power output and 30-second passive recovery intervals and to a 22-minute MICE corresponding to 60% of peak power output. Gas exchange, electrocardiogram, and blood pressure were measured continuously. Cardiac troponin T (cTnT), C-reactive protein (CRP), and brain natriuretic peptide (BNP) were measured before, 20 minutes after, and 24 hours after HIE and MICE.

**Results:** Cardiopulmonary responses did not differ between MICE and HIE. Higher exercise adherence and efficiency were observed on HIE with a similar perceived exertion and time spent above 90% of peak oxygen consumption compared with MICE. Neither HIE nor MICE caused any significant arrhythmias or increased CRP, BNP, or cTnT.

**RÉSUMÉ**

**Introduction :** Le but de cette étude était de comparer les réponses cardiopulmonaires, l'observance à l'exercice, la tolérance et la sécurité de l'exercice par intervalles de haute intensité (EIHI) optimisé à l'exercice continu d'intensité modérée (ECIM) chez les patients ayant une insuffisance cardiaque avec fraction d'éjection diminuée (IC-FÉD).

**Méthodes :** Vingt (20) patients ayant une IC-FÉD (âgés de  $61 \pm 9,9$  ans) ont réalisé de manière aléatoire un EIHI correspondant à  $2 \times 8$  minutes avec des intervalles de 30 secondes à 100 % de la puissance maximale et des intervalles de récupération passive de 30 secondes, et un ECIM de 22 minutes correspondant à 60 % de la puissance maximale. Les échanges gazeux, l'électrocardiogramme et la pression artérielle ont été mesurés de manière continue. La troponine T cardiaque (TnTc), la protéine C réactive (CRP) et le peptide cérébral natriurétique (BNP) ont été mesurés avant, 20 minutes après et 24 heures après l'EIHI et l'ECIM.

**Résultats :** Les réponses cardiopulmonaires ne diffèrent pas entre l'ECIM et l'EIHI. Une plus grande observance et efficience de l'exercice a été observée lors de l'EIHI avec une perception de l'effort et un temps passé au dessus de 90% du VO<sub>2</sub> pic similaires à ceux de l'ECIM.

Exercise training is now accepted as a fundamental part of the clinical management of patients with heart failure and reduced ejection fraction (HFREF).<sup>1,2</sup> Exercise training improves sev-

eral manifestations of heart failure (HF) through effects on the cardiopulmonary, vascular, and musculoskeletal systems and has a favourable impact on risk of hospitalization and death, functional capacity, and quality of life.<sup>1-6</sup> Continuous exercise training and/or high-intensity interval training (HIIT) can be used in patients with elevated cardiovascular risk, coronary heart disease (CHD), or HFREF.<sup>1,7</sup> Relative to continuous aerobic training, HIIT is generally associated with greater improvements in peak oxygen consumption (VO<sub>2</sub>peak), cardiovascular and muscular function, and quality of life in cardiac

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See page XXX for disclosure information.

**Conclusions:** Compared with MICE, HIIIE demonstrated a higher exercise adherence and was well tolerated in patients with HFREF, while still providing a high-level physiological stimulus and leaving indices of inflammation (CRP), myocardial dysfunction (BNP), and myocardial necrosis (cTnT) unaffected.

Ni l'EIHI ni l'ECIM n'ont causé d'arythmies significatives ou d'augmentation de la CRP, du BNP ou de la TnTc.

**Conclusions :** Comparativement à l'ECIM, l'EIHI a démontré une plus grande observance à l'exercice et a été bien toléré chez les patients ayant une IC-FÉD, tout en fournissant un stimulus physiologique de haut niveau et en laissant les indices d'inflammation (CRP), de dysfonctionnement myocardique (BNP) et de nécrose myocardique (TnTc) inchangés.

and noncardiac subjects alike.<sup>8-14</sup> Among cardiac patients, high-intensity interval exercise (HIIIE) also appears to be safe and well tolerated,<sup>8,9,15,16</sup> although larger studies are required to confirm its safety aspects.

Previous HIIT studies in cardiac patients have used various HIIIE protocols (with different exercise and recovery intensity and interval duration), including long-stage exercise duration (2-4 minutes) prescribed at a high percentage of maximum heart rate (HR) and employing active recovery intervals.<sup>11,12,14</sup> In particular, a protocol employing 4-minute exercise and active recovery intervals at 90% of maximal HR has recently gained in popularity.<sup>11,14</sup> However, the acute physiological responses to this protocol have never been studied, nor has its rationale been detailed in the scientific literature. Among HFREF patients, only 2 studies evaluated the influence of different HIIIE protocols on acute physiological cardiovascular responses and patient tolerance and comfort.<sup>16,17</sup> We recently demonstrated in stable CHD and HFREF patients that an “optimized” HIIIE protocol consists of repeated short bouts (15 or 30 seconds) of exercise at 100% of peak power output (PPO) interspersed with passive recovery intervals of equal duration.<sup>9,16</sup> Relative to longer intervals (60-90 seconds) with active recovery, short (15- to 30-second) exercise and recovery intervals with passive recovery were associated with a longer total exercise time, a similar time spent near  $\dot{V}O_2$ peak, a lower rating of perceived exertion (RPE), greater patient comfort, and a greater likelihood of the patient's completing the prescribed exercise sessions.<sup>9,16</sup> We also showed that compared with moderate-intensity continuous exercise (MICE), an optimized HIIIE session is safe and does not induce significant arrhythmias or myocardial injury in stable coronary patients.<sup>18</sup> The acute physiological responses and safety of an optimized HIIIE session compared with an isocaloric MICE session have not been studied in patients with HFREF. Therefore, the first objective of this study was to compare the completion rate (percentage of individuals completing the prescribed exercise sessions) and acute cardiopulmonary responses of an optimized HIIIE session with those of an isocaloric MICE session in patients with HFREF. Our secondary objectives were to compare RPE, HIIIE efficiency, safety (cardiac arrhythmias, myocardial injury), inflammatory parameters, and ventricular mechanical stress (brain natriuretic peptide [BNP]) in response to the same 2 exercise sessions.

## Methods

### Study design

After an initial screening of 100 patients, we enrolled 20 patients with stable HFREF at the ambulatory HF and cardiac

transplantation clinics of the Montreal Heart Institute. On the first visit, anthropometric data, vital signs, and resting electrocardiogram were collected, and all participants underwent a maximal cardiopulmonary exercise test on ergocycle. In a random order, patients performed the 2 single exercise sessions (1 optimized HIIIE and 1 MICE) at the Cardiovascular Prevention and Rehabilitation Centre (EPIC) of the Montreal Heart Institute, under the supervision of an exercise physiologist and a cardiologist, the single sessions being separated by 1 week. The protocol was accepted by the ethics committee of the Montreal Heart Institute, and written informed consent was obtained from all patients. For details concerning inclusion and exclusion criteria, see Supplementary Material (section A). Demographic and baseline characteristics are presented in Table 1.<sup>19,20</sup>

### Maximal cardiopulmonary exercise test

Maximal cardiopulmonary exercise testing was performed according to the current guidelines.<sup>21</sup> A continuous progressive exercise protocol was performed on a cycle ergometer (Ergoline 800S, Bitz, Germany). Pedaling speed was set at 60 revolutions per minute during the entire test. A 2-minute warm-up at 20 W was performed before the test, and the power was increased by 10 W every minute until exhaustion.<sup>21</sup> PPO was defined as the power output reached at the last fully completed stage.<sup>9,16,18</sup> For details on gas exchange and exercise parameters measurement, see Supplementary Material (section B).

### MICE isocaloric session

This exercise session was performed on the ergocycle (Ergoline 800S) at an intensity of 60% PPO and consistent with current exercise training recommendations in patients with HFREF.<sup>1</sup> Exercise duration was 22 minutes and matched total energy expenditure of the HIIIE session according to our previous published methodology in coronary patients.<sup>18</sup> Exercise efficiency defined by gross efficiency of the external work (as a percentage) was calculated by the following formula:<sup>25</sup>

$$[\text{external work (J/s)}/\text{metabolic work (J/s)}] \times 100.$$

Brachial blood pressure was measured manually each 2 minutes.

### Optimized HIIIE session

The optimized HIIIE protocol was also performed on ergocycle and was based on our previous studies in CHD and HFREF patients.<sup>9,16,18</sup> This session consisted of a warm-up for 2 minutes at 50% of PPO, followed by two 8-minute interval training blocks. Each block consisted of repeated bouts of 30 seconds at 100% of PPO, interspersed with 30 seconds of passive recovery. Four minutes of passive recovery was allowed

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**Table 1.** Baseline characteristics of the patients with chronic heart failure

Clinical variables	n = 20
Age (years)	61 ± 9.9
Men	18 (90%)
BMI ( $\text{kg}/\text{m}^2$ )	29.9 ± 6.2
LVEF (%)	26 ± 7
Duration of heart failure (years)	6.1 ± 5
NYHA functional class	
I	5 (25%)
II	12 (60%)
III	3 (15%)
Etiology of heart failure	
Ischemic heart disease	9 (45%)
Idiopathic dilated cardiomyopathy	9 (45%)
LV noncompaction	2 (10%)
Risk factors	
Diabetes mellitus	7 (35%)
Hypertension	13 (65%)
Smoking	1 (5%)
Dyslipidemia	16 (80%)
Obesity (BMI $\geq 30 \text{ kg}/\text{m}^2$ )	8 (40%)
Medical history	
Previous myocardial infarction	10 (50%)
Previous CABG	1 (5%)
Previous PCI	7 (35%)
Medications	
ACE inhibitors	11 (55%)
ARBs	8 (40%)
$\beta$ -blockers	20 (100%)
Digoxin	13 (65%)
Furosemide	17 (85%)
Oral hypoglycemic agents	5 (25%)
Insulin	3 (15%)
Spironolactone	10 (50%)
Devices	
ICD	14 (70%)
CRT	3 (15%)

Values are means ± SD or numbers of patients (%).

ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; BMI, body mass index; CABG, coronary artery bypass graft; CRT, cardiac resynchronization therapy; ICD, internal cardioverter-defibrillator; LV, left ventricular; LVEF, LV ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

between the blocks, with 1-minute cooldown at 25% of PPO after the last 30-second exercise bout. The warm-up period and two 8-minute blocks were included in the isocaloric calculation. Exercise efficiency (as a percentage) was also calculated.<sup>25</sup> Brachial blood pressure was measured manually each 2 minutes during the passive recovery period bouts.

**Table 2.** Cardiopulmonary variables measured during MICE and optimized HIE

Parameters	MICE 22 minutes	HIE first 8 minutes	HIE second 8 minutes	ANOVA P value
$\dot{\text{V}}\text{O}_2$ ( $\text{mL}/\text{min}$ )	1092 ± 329	989 ± 253	992 ± 254	0.48
Ventilation ( $\text{L}/\text{min}$ )	37 ± 9	34 ± 8	33 ± 8	0.37
Heart rate (beats/min)	99 ± 18	87 ± 13	90 ± 11	0.16
$\text{O}_2$ pulse ( $\text{mL O}_2/\text{beat}$ )	11.2 ± 3.2	11.4 ± 2.4	11.2 ± 2.6	0.95
Mean power (W)	46 ± 20		51 ± 21	0.0188
% $\dot{\text{V}}\text{O}_2$ peak	76 ± 7	71 ± 10*	67 ± 8†	0.0039
Gross efficiency of the external work (%)	12.37 ± 2.85		15.05 ± 3.60	< 0.0001
Cycling exercise time (min)	17 ± 5		7.5 ± 1.5	< 0.0001
Perceived exertion at the end of sessions (Borg scale)	14.4 ± 1.4		13.4 ± 2.7	0.09
n (%) of exercise session completed	8 (40%)		17 (85%)	0.0075

ANOVA, analysis of variance; HIE, high-intensity intermittent exercise; MICE, moderate-intensity continuous exercise;  $\text{O}_2$  pulse,  $\dot{\text{V}}\text{O}_2$ /heart rate;  $\dot{\text{V}}\text{O}_2$ , oxygen consumption.

\*P < 0.05; †P < 0.01 vs MICE.

## Biomarker measurement

Venous blood samples were taken 10 minutes before exercise and 20 minutes and 24 hours after an exercise session. C-reactive protein (CRP), cardiac troponin T (cTnT), and BNP were measured. For more details, see Supplementary Material (section C).<sup>26</sup>

## Study end points

Our main end points were (1) percentage of individuals completing the exercise sessions and (2) time spent at high levels of  $\dot{\text{V}}\text{O}_2$  peak in each exercise mode (HIE and MICE). For more details, see Supplementary Material (section D).<sup>9,16,18</sup>

## Statistical analysis

Mean and standard deviation were reported for continuous variables. Frequencies and percentages were reported for categorical ones. For more details, see Supplementary Material (section E).

## Results

### Baseline characteristics

Participants were principally men (90%), aged 45 to 80 years. The majority had a diagnosis of ischemic heart disease, were in New York Heart Association class I and II, and were receiving optimal medical therapy (Table 1).

### Maximal cardiopulmonary exercise test

Peak cardiopulmonary variables are presented in Supplemental Table S1. Mean  $\dot{\text{V}}\text{O}_2$  peak was 16.9 ± 5.6 mL/min/kg (65% ± 19% of predicted value) corresponding to a mean PPO of 89 ± 37 W.

### Effects on primary end points

The proportion of patients completing the exercise session (HIE, 2 × 8 minutes; MICE, 22 minutes) was significantly higher during HIE (n = 17, or 85%) compared with MICE (n = 8, or 40%, P < 0.0075; Table 2). There was no significant difference in time > 90%, > 95%, or > 100% of  $\dot{\text{V}}\text{O}_2$  peak between exercise protocols. Time spent above > 80% and > 85% of  $\dot{\text{V}}\text{O}_2$  peak was significantly higher during MICE than during HIE (P < 0.05 and 0.01; Supplemental Table S2).

## Effects on secondary end points

Mean cardiopulmonary variables ( $\dot{V}O_2$ , ventilation [ $V_E$ ], HR, and  $O_2$ pulse [ie,  $\dot{V}O_2$ /heart rate]) did not differ during MICE and HIIIE (Table 2). Mean percentage of  $\dot{V}O_2$ peak attained during the 2 blocks of HIIIE was lower than during MICE (first block,  $P < 0.05$ ; second block,  $P < 0.01$ ; Table 2). Cycling exercise time was significantly longer during the MICE session ( $P < 0.0001$ ) compared with HIIIE (Table 2). RPE measured during HIIIE and MICE did not differ (HIIIE, 13 ± 3; MICE, 14 ± 1;  $P = 0.09$ ). Gross efficiency of the external work (as a percentage) and mean power output were higher for HIIIE vs MICE ( $P < 0.0001$  and  $P = 0.0188$ ; Table 2). Time spent > 95% and > 100% of  $V_E$ peak was similar during HIIIE and MICE but was significantly higher during MICE for time spent > 80%, > 85%, and > 90% of  $V_E$ peak. Time spent > 100% and > 95% of HRpeak and  $O_2$ pulse peak were similar during HIIIE and MICE sessions, but time > 80%, > 85%, and > 90% was significantly higher during MICE (Supplemental Table S2).

No significant ventricular arrhythmias or abnormal blood pressure responses (systolic blood pressure > 250 mm Hg or diastolic blood pressure > 110 mm Hg and/or systolic blood pressure drop > 10 mm Hg during exercise or no return to baseline values during recovery) occurred. Serum concentration of cTnT was < 40  $\mu\text{g/L}^{-1}$  in all participants at baseline and did not exceed this value at 20 minutes or at 24 hours after the exercise sessions, thus excluding the presence of any exercise-induced myocardial injury (Supplemental Table S3). There was no significant increase in CRP or BNP (measured after 20 minutes and 24 hours) with either exercise protocol, excluding the presence of an exercise-induced increase of inflammation and ventricular mechanical stress (Supplemental Table S3). One adverse event occurred. The patient was a woman, aged 77 years, with a documented ischemic cardiomyopathy. She underwent the HIIIE session on a Wednesday afternoon. The next day (Thursday), she developed signs of aphasia and dyspraxia (duration: 3 hours). A transitory cerebral ischemia was diagnosed, clopidogrel was given to the patient, and she recovered very well. We are uncertain whether the episode was related to the exercise session.

## Discussion

This study is the first to compare acute physiological responses and the rate of completion of exercise sessions during an optimized HIIIE and an isocaloric MICE in HFREF patients. The optimized HIIIE elicited a strong physiological stimulus associated with a greater proportion of subjects completing the prescribed exercise session, and a similar time spent over 90% of  $\dot{V}O_2$ peak and 95% of  $V_E$ peak, HRpeak, and  $O_2$ pulse peak. Mean cardiopulmonary responses were similar for both exercise sessions. Despite this fact, total active pedalling time was significantly greater during MICE, while both mean power and external work efficiency were lower, illustrating the optimized HIIIE efficiency. Additionally, the optimized HIIIE was well tolerated, with similar RPE, compared with MICE. Finally, the optimized HIIIE did not induce any significant arrhythmias, abnormal blood pressure responses, or increase in cTnT, BNP, or CRP, even though an adverse event occurred in 1 patient (a transitory cerebral ischemia) the day after the HIIIE session. These results add important physiological information

relating to the prescription of this aerobic exercise training modality in HFREF patients. Moreover, our results suggest that optimized HIIIE could potentially be used to improve exercise training adherence for stable HFREF patients.

We demonstrated that mean cardiopulmonary responses ( $\dot{V}O_2$ ,  $V_E$ , HR, and  $O_2$ pulse) were equivalent during HIIIE and MICE, indicating similar cardiopulmonary stimulus between the 2 exercise modes. However, during HIIIE, patients exercised for a shorter cycling exercise time, at a higher power output, and with higher external work efficiency. This illustrates the superior efficiency of optimized HIIIE compared with MICE, in accordance with previous published studies of CHD and HFREF patients.<sup>17,18,27,28</sup> In HFREF patients, one principle of HIIIE is to improve peripheral muscle power while providing a similar stimulus to the cardiac system.<sup>17,28</sup> This concept was demonstrated in our study by noting that HR and  $O_2$ pulse values were similar during MICE and HIIIE. Meyer et al.<sup>28</sup> showed that HIIIE (30 seconds at 71 W, 60 seconds at 15 W), compared with a MICE session (36 W), was associated with a similar exercise cardiac output, stroke volume, and ejection fraction. Despite a higher exercise power output, patients' RPE was similar for HIIIE in association with a significantly higher likelihood of completing the exercise session, indicating that optimized HIIIE was very efficient and well tolerated. Several mechanistic explanations can be put forth to explain these findings. First, passive recovery is associated with a slower decline of the muscle oxyhemoglobin signal compared with an active recovery, allowing for a higher rate of myoglobin reoxygenation and a better oxygen-dependent resynthesis of phosphocreatine in healthy people.<sup>29,30</sup> Second, during HIIIE, patients exercised at a significantly lower percentage of  $\dot{V}O_2$ peak associated with nonsignificant lower mean ventilation and HR. Time over 80% to 90% of  $V_E$ peak was also significantly lower during HIIIE relative to MICE, illustrating a lower solicitation of the ventilatory system. These findings indicate that ventilation and central hemodynamic function were not overloaded by HIIIE.<sup>17,28</sup> This is consistent with the lower sensation of breathlessness reported by HFREF patients during HIIIE and in accordance with our previous data in coronary patients demonstrating a significant lower RPE, lower mean ventilation, and reduced subjective sensation of breathlessness during HIIIE.<sup>18</sup>

Our results on mean cardiopulmonary responses during HIIIE are slightly higher than those found previously in patients with HFREF.<sup>17,28</sup> In those studies, patients'  $\dot{V}O_2$  uptake was approximately 65% of  $\dot{V}O_2$ peak, with mean HR between 73% and 84% of HRpeak and ventilation of approximately 26 L/minute. The RPE was similar during MICE and HIIIE (14.4 and 13.4), in agreement with previous studies,<sup>17,28</sup> and were slightly higher. The lower RPEs observed by Meyer et al.<sup>17,28</sup> are probably due to the longer recovery phase used in their protocol (60 seconds) compared with ours (30 seconds).

We found no evidence of severe or prolonged ischemia, significant arrhythmias, or abnormal blood pressure responses. In addition, cTnT levels did not increase after exercise, excluding any myocardial injury. Furthermore, BNP, an important biomarker of ventricular mechanical stress and prognosis in relation to the severity of ventricular dysfunction,<sup>31</sup> did not increase after HIIIE or MICE. These results are consistent with previous data showing the lack of effect of a single maximal exercise on BNP.<sup>32-34</sup> Finally, with respect to CRP, conflicting

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data exist on the impact of exercise on this biomarker. Two previous studies in healthy people<sup>35,36</sup> showed no increase in CRP after acute exercise (30%-70% of  $\dot{V}O_{2\text{peak}}$ ). In contrast, in stable coronary patients, Fernandes et al.<sup>37</sup> demonstrated a significant increase in CRP after acute exercise (at 65% of  $\dot{V}O_{2\text{peak}}$ ). No previous studies have evaluated the impact of exercise on CRP in HFREF patients.

A novel finding of our study is that HIE was associated with a similar time above 90% of  $\dot{V}O_{2\text{peak}}$  and above 95% of  $\dot{V}E_{\text{peak}}$ , HRpeak, and  $O_2\text{pulse}$  peak compared with MICE. These results illustrate that our optimized HIE protocol does not compromise time spent near maximal cardiopulmonary function. However, MICE was associated with a significantly higher time above 80% and 85% of  $\dot{V}O_{2\text{peak}}$  and above 80% and 90% of  $\dot{V}E_{\text{peak}}$  and HRpeak. It is important that absolute differences were less than 3 minutes for time above 80% of  $\dot{V}O_{2\text{peak}}$  and  $\dot{V}E_{\text{peak}}$  and less than 6 minutes for time above HRpeak and  $O_2\text{pulse}$  peak. These differences in our opinion have little clinical significance. In our study, during passive recovery intervals, optimized HIE allowed patients to stress their cardiopulmonary system without compromising time spent above 90% of  $\dot{V}O_{2\text{peak}}$  while they were not exercising (not pedaling). This particularity of HIE is very interesting in less fit HFREF patients, who can have considerable exercise intolerance, particularly during continuous long exercise periods. Although patients were pedaling at higher intensities during the HIE work phases (100% PPO), they did not perceive the total exercise time as more strenuous (similar RPEs).

This study contributes important clinical information for the cardiac rehabilitation of HFREF patients. **Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION)** failed to show significant reduction in mortality with MICE training in HFREF patients.<sup>3,4</sup> Some possible explanations include poor exercise training adherence and the relatively low intensity of the MICE training protocol.<sup>4</sup> In contrast, HIE training may provide a stronger training stimulus, may be more efficient and motivating, and may help to improve adherence to exercise training in HFREF patients.<sup>38</sup>

This study has several limitations, including a small number of patients and results reported during only 1 HIE session, which may differ from a prolonged HIE training program. Additionally, patients were mainly young men with few comorbidities, in class II HF with a mean left ventricular ejection fraction of 26% and a  $\dot{V}O_{2\text{peak}}$  at 65% of predicted. They were, however, representative of many HFREF patients seen in clinic.

In conclusion, optimized HIE strongly stimulates cardiopulmonary function in HFREF patients and is associated with a significantly higher exercise session completion rate (thus potentially increasing training adherence), without compromising time spent near peak cardiopulmonary variables. Additionally, optimized HIE was more efficient, allowing our HFREF patients to exercise at higher power output and similar tolerance, compared with MICE. Finally, a single optimized HIE session was completed without the occurrence of arrhythmias, myocardial injury, or cardiac decompensation. Larger randomized training studies using our optimized HIE protocol are needed to confirm the benefits and safety of HIE in this population.

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## Disclosures

The authors have no conflicts of interest to disclose.

## References

1. Balady GJ, Williams MA, Ades PA, et al. Core components of cardiac rehabilitation/secondary prevention programs: 2007 update: a scientific statement from the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee, the Council on Clinical Cardiology; the Councils on Cardiovascular Nursing, Epidemiology and Prevention, and Nutrition, Physical Activity, and Metabolism; and the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2007;115:2675-82.
2. Piepoli MF, Corra U, Benzer W, et al. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2010;17:1-17.
3. Flynn KE, Pina IL, Whellan DJ, et al. Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;301:1451-9.
4. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;301:1439-50.
5. Smart N, Marwick TH. Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *Am J Med* 2004;116:693-706.
6. van Tol BA, Huijsmans RJ, Kroon DW, Schothorst M, Kwakkel G. Effects of exercise training on cardiac performance, exercise capacity and quality of life in patients with heart failure: a meta-analysis. *Eur J Heart Fail* 2006;8:841-50.
7. Tjonna AE, Lee SJ, Rognmo O, et al. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: a pilot study. *Circulation* 2008;118:346-54.
8. Cornish AK, Broadbent S, Cheema BS. Interval training for patients with coronary artery disease: a systematic review. *Eur J Appl Physiol* 2011;111:579-89.
9. Guiraud T, Juneau M, Nigam A, et al. Optimization of high intensity interval exercise in coronary heart disease. *Eur J Appl Physiol* 2010;108:733-40.
10. Helgerud J, Hoydal K, Wang E, et al. Aerobic high-intensity intervals improve  $\dot{V}O_{2\text{max}}$  more than moderate training. *Med Sci Sports Exerc* 2007;39:665-71.
11. Rognmo O, Hetland E, Helgerud J, Hoff J, Slordahl SA. High intensity aerobic interval exercise is superior to moderate intensity exercise for increasing aerobic capacity in patients with coronary artery disease. *Eur J Cardiovasc Prev Rehabil* 2004;11:216-22.
12. Warburton DE, McKenzie DC, Haykowsky MJ, et al. Effectiveness of high-intensity interval training for the rehabilitation of patients with coronary artery disease. *Am J Cardiol* 2005;95:1080-4.
13. Wisloff U, Ellingsen O, Kemi OJ. High-intensity interval training to maximize cardiac benefits of exercise training? *Exerc Sport Sci Rev* 2009;37:139-46.

14. Wisloff U, Stoylen A, Loennechen JP, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation* 2007;115:3086-94.
15. Meyer K, Samek L, Schwaibold M, et al. Interval training in patients with severe chronic heart failure: analysis and recommendations for exercise procedures. *Med Sci Sports Exerc* 1997;29:306-12.
16. Meyer P, Normandin E, Gayda M, et al. High intensity interval training in patients with chronic heart failure: acute cardiorespiratory responses and protocol optimization. *J Cardiac Fail* 2012;18:126-33.
17. Meyer K, Samek L, Schwaibold M, et al. Physical responses to different modes of interval exercise in patients with chronic heart failure—application to exercise training. *Eur Heart J* 1996;17:1040-7.
18. Guiraud T, Nigam A, Juneau M, Meyer P, Gayda M, Bosquet L. Acute responses to high-intensity intermittent exercise in CHD patients. *Med Sci Sports Exerc* 2011;43:211-7.
19. Meyer K. Exercise training in heart failure: recommendations based on current research. *Med Sci Sports Exerc* 2001;33:525-31.
20. Piepoli MF, Conraads V, Corra U, et al. Exercise training in heart failure: from theory to practice: a consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. *Eur J Heart Fail* 2011;13:347-57.
21. Piepoli MF, Corra U, Agostoni PG, et al. Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation Part II: how to perform cardiopulmonary exercise testing in chronic heart failure. *Eur J Cardiovasc Prev Rehabil* 2006;13:300-11.
22. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377-81.
23. Duncan GE, Howley ET, Johnson BN. Applicability of V02max criteria: discontinuous versus continuous protocols. *Med Sci Sports Exerc* 1997;29:273-8.
24. Gaskell SE, Ruby BC, Walker AJ, Sanchez OA, Serfass RC, Leon AS. Validity and reliability of combining three methods to determine ventilatory threshold. *Med Sci Sports Exerc* 2001;33:1841-8.
25. Winter DA. A new definition of mechanical work done in human movement. *J Appl Physiol* 1979;46:79-83.
26. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959-69.
27. Meyer K, Lehmann M, Sunder G, Keul J, Weidemann H. Interval versus continuous exercise training after coronary bypass surgery: a comparison of training-induced acute reactions with respect to the effectiveness of the exercise methods. *Clin Cardiol* 1990;13:851-61.
28. Meyer K, Foster C, Georgakopoulos N, et al. Comparison of left ventricular function during interval versus steady-state exercise training in patients with chronic congestive heart failure. *Am J Cardiol* 1998;82:1382-7.
29. Astrand I, Astrand PO, Christensen EH, Hedman R. Intermittent muscular work. *Acta Physiol Scand* 1960;48:448-53.
30. Dupont G, Moalla W, Guinhouya C, Ahmadi S, Berthoin S. Passive versus active recovery during high-intensity intermittent exercises. *Med Sci Sports Exerc* 2004;36:302-8.
31. Yoshimura M, Yasue H, Okumura K, et al. Different secretion patterns of atrial natriuretic peptide and brain natriuretic peptide in patients with congestive heart failure. *Circulation* 1993;87:464-9.
32. Kruger S, Graf J, Merx MW, et al. Brain natriuretic peptide kinetics during dynamic exercise in patients with chronic heart failure. *Int J Cardiol* 2004;95:49-54.
33. McNairy M, Gardetto N, Clopton P, et al. Stability of B-type natriuretic peptide levels during exercise in patients with congestive heart failure: implications for outpatient monitoring with B-type natriuretic peptide. *Am Heart J* 2002;143:406-11.
34. Steele IC, McDowell G, Moore A, et al. Responses of atrial natriuretic peptide and brain natriuretic peptide to exercise in patients with chronic heart failure and normal control subjects. *Eur J Clin Invest* 1997;27:270-6.
35. Mendham AE, Donges CE, Liberts EA, Duffield R. Effects of mode and intensity on the acute exercise-induced IL-6 and CRP responses in a sedentary, overweight population. *Eur J Appl Physiol* 2011;111:1035-45.
36. Plaisance EP, Taylor JK, Alhassan S, Abebe A, Mestek ML, Grandjean PW. Cardiovascular fitness and vascular inflammatory markers after acute aerobic exercise. *Int J Sport Nutr Exerc Metab* 2007;17:152-62.
37. Lara Fernandes J, Serrano CV Jr, Toledo F, et al. Acute and chronic effects of exercise on inflammatory markers and B-type natriuretic peptide in patients with coronary artery disease. *Clin Res Cardiol* 2011;100:77-84.
38. Moholdt T, Aamot IL, Granoen I, et al. Long-term follow-up after cardiac rehabilitation: a randomized study of usual care exercise training versus aerobic interval training after myocardial infarction. *Int J Cardiol* 2011;152:388-90.

### Supplementary Material

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