Central hemodynamic responses during acute high-intensity interval exercise and moderate continuous exercise in patients with heart failure

Mathieu Gayda, Eve Normandin, Philippe Meyer, Martin Juneau, Mark Haykowsky, and Anil Nigam

Abstract: The aim of this study was to compare the acute hemodynamic responses during high-intensity intermittent exercise (HIIE) session compared with moderate-intensity continuous exercise (MICE) session in patients with heart failure and reduced ejection fraction (HFREF). Thirteen patients with HFREF (age, 59 ± 6 years; left ventricular ejection fraction, 27% ± 6%; New York Heart Association class I to III) were randomly assigned to a single session of HIIE (2 × 8 min) corresponding to 30 s at 100% of peak power output (PPO) and 30 s passive recovery intervals or to a MICE (22 min) at 60% of PPO. Gas exchange and central hemodynamic parameters (cardiac bioimpedance) were measured continuously during exercise. Oxygen uptake, stroke volume (SV), cardiac output (CO), and arterio-venous difference ($C(a\text{-}v)O_2$) were compared. Mean oxygen uptake and ventilation were lower during HIIE vs. MICE. CO, SV, and $C(a\text{-}v)O_2$) were not different between MICE and HIIE. Optimized HIIE was well tolerated (similar perceived exertion) and no significant ventricular arrhythmias and (or) abnormal blood pressure responses occurred during HIEE session. Compared with MICE, optimized HIIE elicited similar central hemodynamic and $C(a\text{-}v)O_2$ responses in HFREF patients with lower oxygen uptake and ventilation. HIIE may be an efficient exercise training modality in patients with HFREF.

Key words: intermittent exercise, continuous exercise, central hemodynamic, heart failure.

Résumé : Le but de cette étude était de comparer les réponses hémodynamiques aigües pendant un exercice intermittent de haute intensité (EIHI) par rapport à celles d'un exercice continu à intensité modérée (ECIM) chez des patients insuffisant cardiaque avec fraction d'éjection réduite (ICFER). Treize patients ICFER (59 ± 6 ans, fraction d'éjection ventriculaire gauche: 27 ± 6 %, Classe « New York Heart Association » de I à III) ont été assignés aléatoirement à une session d'EIHI (2 × 8 min) avec 30 s à 100 % de la puissance maximale aérobie (PMA) et 30 s de récupération passive et à une session d'ECIM (22 min à 60 % de la PMA). Les échanges gazeux et les paramètres hémodynamiques centraux (bioimpédance cardiaque) ont été mesurés en continu durant l'exercice. Le prélèvement d'oxygène ($\dot{V}O_2$), le volume d'éjection systolique (VES), le débit cardiaque (DC), et la différence artério-veineuse ($C(a\text{-}v)O_2$) ont été comparés. Le $\dot{V}O_2$ et la ventilation ($\dot{V}E$) étaient plus faible pendant l'EIHI vs. l'ECIM. Le DC, le VES et la $C(a\text{-}v)O_2$ étaient similaires pendant l'EIHI et l'ECIM. L'EIHI optimisé était bien toléré (perception de l'effort identique) et aucunes arythmies et (ou) réponses anormales de la pression artérielle n'ont été notées pendant les sessions d'EIHI. Par rapport à l'ECIM, l'EIHI optimisé a occasionné des réponses hémodynamiques centrales et de la $C(a\text{-}v)O_2$ similaires chez les patients ICFER, avec un $\dot{V}O_2$ et une $\dot{V}E$ plus faible. L'EIHI pourrait s'avérer être une modalité de réentrainement efficace chez les patients ICFER.

Mots-clés : exercice intermittent, exercice continu, hémodynamie centrale, insuffisance cardiaque.

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Introduction

Exercise training is a main component of cardiac rehabilitation for patients with heart failure and reduced ejection fraction (HFREF) (Balady et al. 2007; O'Connor et al. 2009; Piepoli et al. 2010). Exercise training improves heart failure (HF) symptoms, including breathlessness and fatigue through favorable effects on the cardiopulmonary, vascular, and musculoskeletal function, and decreases hospitalization and improves quality of life (Smart and Marwick 2004; van Tol et al. 2006; Davies et al. 2010). Among the available modes of aerobic exercise training, either continuous and (or) aerobic interval training are prescribed for individuals with cardiovascular risk factors and coronary heart disease (CHD) or HF patients (Balady et al. 2007; Wisløff et al. 2007; Tjønna et al. 2008). Compared with continuous aerobic training, high-intensity interval training results in a greater improvement in peak oxygen uptake ($\dot{V}O_{2peak}$), cardiac, peripheral vascular endothelial function, skeletal muscle function, and quality of life in healthy subjects, CHD and HFREF patients (Dubach et al. 1997; Rognmo et al. 2004; Warburton et al. 2005; Daussin et al. 2007; Helgerud et al. 2007; Wisløff et al. 2007; Tjønna et al. 2008; Cornish et al. 2011). We recently demonstrated in patients with CHD or HFREF that an optimal high-intensity intermittent exercise (HIIE) protocol consists of repeated short bouts (15 or 30 s) of exercise at 100% of peak power output (PPO) interspersed by passive recovery intervals of equal duration (Guiraud et al. 2010; Meyer et al. 2012). This protocol was associated with a longer total exercise time, a similar time spent near $\dot{V}O_{2peak}$, a lower perceived exertion, a better patient's comfort, and exercise adherence compared with moderate-intensity continuous exercise (MICE) (Guiraud et al. 2010; Meyer et al. 2012). We also found that compared with MICE, optimized HIIE was well tolerated and did not induce significant arrhythmias or myocardial injury in stable CHD or HFREF patients (Guiraud et al. 2010; Meyer et al. 2012). Two prior studies also demonstrated that central hemodynamic and left ventricular function were similar during intermittent and continuous exercise in healthy subjects and patients with HFREF (Meyer et al. 1998; Foster et al. 1999). Moreover, Tomczak et al. recently reported an increase in postexercise biventricular function in clinically stable HFREF patients (Tomczak et al. 2011). In the above studies, radionuclide ventriculography and cardiac magnetic resonance imaging (MRI) were used to assess ventricular function during and after exercise (Meyer et al. 1998; Tomczak et al. 2011). Both modalities represent a technical challenge, are expensive, and have a poor time resolution. For example, radionuclide ventriculography requires injection of radioactive tracer and MRI does not allow measurement of ventricular function during HIIE. Additionally, exercise intensity prescription (from maximal short exercise capacity test) and nature of recovery (1 min at 10 W) were different from our HIIE protocol (Meyer et al. 1998). In healthy subjects and patients with CHD or HFREF, impedance cardiography was found to be an accurate and reproducible method for central hemodynamic measurement during exercise with an excellent time resolution (beat to beat basis) (Charloux et al. 2000; Palmieri et al. 2006; Daussin et al. 2007). No previous study has been performed on hemodynamic responses during our optimized HIIE protocol compared with MICE sessions in patients with HFREF. The aim of this study was to compare central hemodynamic responses during our optimized HIIE protocol compared with that of a MICE session in patients with HFREF. We tested the hypothesis that central hemodynamic responses during HIEE would be similar to that measured during MICE.

Materials and methods

Study design

This study incorporated a crossover design whereby optimized HIIE or a MICE session were performed at the Cardiovascular Prevention and Rehabilitation Centre (ÉPIC) of the Montreal Heart Institute. On the first visit, anthropometric data, vital signs, and resting electrocardiogram (ECG) 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 HIIE and 1 MICE) under the supervision of an exercise physiologist and a cardiologist, each single session 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.

Participants

We enrolled 13 patients with stable chronic HFREF from the ambulatory HF and cardiac transplantation clinics of the Montreal Heart Institute. Inclusion criteria were age $\geq$ 18 years, left ventricular ejection fraction $<$ 40% (measured within 6 months of enrolment by echocardiography, radionuclide ventriculography, or MRI, stage C HF defined by American College of Cardiology/American Heart Associaton guidelines, New York Heart Association (NYHA) functional class I to III, stable optimal medical therapy, including a β-blocker and an ACE inhibitor or angiotensin II receptor blockers for at least 6 weeks, ability to perform a maximal cardiopulmonary exercise test, and capacity and willingness to sign the informed consent form. Exclusion criteria consisted of any relative or absolute contraindications to exercise training for HFREF patients according to current recommendations, fixed-rate pacemaker or ICD devices with heart rate limits set lower than exercise training target heart rate, major cardiovascular event or procedure within the 3 months preceding enrolment, chronic atrial fibrillation, HF secondary to significant uncorrected primary valvular disease (except for mitral regurgitation secondary to left ventricalar dysfunction), and HF secondary to congenital heart disease or obstructive cardiomyopathy. Demographic and baseline characteristics are presented in Table 1.

Maximal cardiopulmonary exercise test

Maximal cardiopulmonary exercise testing was performed according previous published methodology (Meyer et al. 2011, 2012). A continuous progressive exercise protocol was performed on a cycle ergometer (Ergoline 800S, Bitz, Germany). The pedalling speed was settled at 60 r·min^{-1} during the entire test. A 2-min warm-up at 20 W was performed before the test and the power was increased by 10 W every minute until exhaustion. PPO was defined as the power output reached at the last fully completed stage. Gas exchange variables were measured breath by breath during testing, and then averaged every 15 s for minute ventilation ($\dot{V}E$, L·min^{-1}, BTPS), oxygen uptake ($\dot{V}O_2$, L·min^{-1}, STPD),

Table 1. Baseline characteristics of the patients with heart failure and reduced ejection fraction.

Clinical variables	$n = 13$
Age (y)	59±7
Male	13 (100%)
BMI (kg·m^{-2})	29.5±4.5
LVEF (%)	27±6
Duration of heart failure (y)	6.9±5
NYHA functional class	
I	5 (38%)
II	6 (46%)
III	2 (15%)
Weber–Janicki class	
A	2 (31%)
B	8 (62%)
C	2 (31%)
D	1 (8%)
Etiology of heart failure	
Ischemic heart disease	7 (54%)
Idiopathic dilated cardiomyopathy	5 (38%)
Other cause	1 (7%)
Risk factors	
Diabetes mellitus	6 (46%)
Hypertension	9 (69%)
Smoking	0 (0%)
Dyslipidemia	11 (85%)
Obesity (BMI ≥30 kg·m^{-2})	6 (46%)
Medical history	
Previous myocardial infarction	6 (46%)
Previous CABG	1 (8%)
Previous PCI	4 (31%)
Medications	
ACE inhibitors	7 (54%)
ARBs	6 (46%)
β-Blockers	13 (100%)
Digoxin	7 (54%)
Furosemide	12 (92%)
Oral hypoglycemic agents	5 (38%)
Insulin	3 (23%)
Spironolactone	5 (38%)
Devices	
ICD	10 (77%)
CRT	2 (15%)

Note: Values are means ± SD or number of patients (%). ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; BMI, body mass index; CABG, coronary artery bypass grafting; CRT, cardiac resynchronization therapy; ICD, internal cardioverter–defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

CO_2 production (L·min^{-1}, STPD), and respiratory frequency by using an automated gas analyzer system (Oxycon Pro, Jaegger, Germany), of which the calibration procedure has been described previously (Guiraud et al. 2010, 2011; Meyer et al. 2011, 2012). All subjects were encouraged to provide a maximal effort. Heart rate, manual brachial blood pressure, and rating of perceived exertion using the Borg scale (level 6 to 20) were recorded before the test and at 2-min intervals during exercise and recovery. Electrocardiographic activity was monitored continuously using an 8-lead ECG (Marquette, Missouri, USA). Criteria for maximal $\dot{V}O_2$ were the attainment of the primary maximal criteria: a levelling off of $\dot{V}O_2$ (<150 mL·min^{-1}) despite increased workload, or 1 of the 3 secondary maximal criteria: (*i*) a respiratory exchange ratio >1.05, (*ii*) inability to maintain 60 r·min^{-1}, (*iii*) patient exhaustion because of fatigue or other clinical symptoms (dyspnea, ECG, and (or) blood pressure abnormalities). The average value of the $\dot{V}O_2$ recorded during the last 15 s of exercise was considered as the $\dot{V}O_{2peak}$. The ventilatory threshold was determined using a combination of the V-slope, ventilatory equivalents, and end-tidal oxygen pressure methods. Hemodynamic and gas exchange parameters were recorded during the 5-min passive recovery following the test.

Cardiac bioimpedance

Cardiac bioimpedance (PhysioFlow, Enduro model, Manatec, France) was used to measure central hemodynamic modifications during the maximal cardiopulmonary exercise test, the MICE session, and the HIIE session. This noninvasive technique was found to be valid, accurate, and reproducible at rest and during exercise in healthy subjects and coronary and HF patients (Charloux et al. 2000; Palmieri et al. 2006; Daussin et al. 2007). Stroke volume (SV) and cardiac output (CO) were measured with this device on a beat to beat basis and were then averaged every 15 s for data analysis. $C(a\text{-}v)O_2$ was calculated according to the Fick principle: $C(a\text{-}v)O_2 = \dot{V}O_2/CO$.

MICE session

This exercise session was based on recommendations of the American Heart Association on exercise prescription in patients with HFREF (i.e., between 50% to 80% PPO) (Balady et al. 2007). In accordance with our prior study, the intensity and duration incorporated in this study was 60% of PPO and 22 min, respectively (Meyer et al. 2011).

Optimized HIIE session

As previously described, the optimized HIIE session consisted of a 2-min warm-up at 50% of PPO, followed by 2 sets of 8-min intervals at 100% of PPO. Each interval block was composed of repeated bouts of 30 s at 100% of PPO interspersed by 30 s of passive recovery. Four minutes of passive recovery were allowed between the 2 sets, as well as a 1-min cool-down at 25% of PPO after the last 30-s exercise bout.

Statistical analyses

Descriptive statistics were reported for demographics, baseline clinical characteristics, as well as for the maximum graded exercise (Tables 1 and 2). They were also reported by exercise mode, i.e., 2 × 8 min of HIIE and MICE (Table 3). Mean and standard deviation were reported for continuous variables while frequencies and percent were reported for categorical values. For hemodynamic comparisons, p values were calculated from a 1-way repeated measure ANOVA with a factor for "group" (2× 8 min HIIE and MICE) (Table 4). $\dot{V}O_2$ and hemodynamic variable kinetics were compared during HIIE

Table 2. Results from the maximal cardiopulmonary exercise test.

Cardiopulmonary variables	Results (n = 13)
Variables at rest	
Resting HR (beats·min^{-1})	71±12
Resting SBP (mm Hg)	109±11
Resting DBP (mm Hg)	63±8
Ventilatory threshold	
Exercise time (s)	278±148
Power output (W)	57±16
$\dot{V}O_2$ (L·min^{-1})	1.01±0.25
% of $\dot{V}O_2$peak	71±9
$\dot{V}O_2$ (mL·min^{-1}·kg^{-1})	12±2
HR (beats·min^{-1})	100±12
Peak exercise level	
$\dot{V}O_{2peak}$ (L·min^{-1})	1.5±0.4
% of $\dot{V}O_{2peak}$ predicted (%)	61±14
$\dot{V}O_{2peak}$ (mL·min^{-1}·kg^{-1})	17.3±4.2
METs	4.87±1.27
Peak $\dot{V}$E (L·min^{-1})	62.9±16.9
$\dot{V}E/\dot{V}CO_2$	39.3±9.9
RER_{max}	1.13±0.11
Peak HR (beats·min^{-1})	124±19
% of maximum HR predicted (%)	77±11
Maximal SBP (mm Hg)	135±14
Maximal DBP (mm Hg)	72±9
Exercise time (s)	551±186
Peak power output (W)	97±30

Note: Values are means ± SD. DBP, diastolic blood pressure; HR, heart rate; RER, respiratory exchange ratio; SBP, systolic blood pressure; $\dot{V}O_2$, oxygen uptake; $\dot{V}O_{2peak}$, peak oxygen uptake; $\dot{V}$E, ventilation; $\dot{V}CO_2$, carbon dioxide output.

Table 3. Central hemodynamic results during maximal cardiopulmonary exercise test.

Central and peripheral hemodynamic parameters	Results (n = 13)
Ventilatory threshold level	
Cardiac output (L·min^{-1})	11.3±3.6
C(a-v)O_2 (mL/100 mL)	9.6±2.9
Heart rate (beats·min^{-1})	100±12
Stroke volume (mL)	111±30
Total vascular resistance (dyne·s^{-1}·cm^{-5})	607±141
Peak exercise level	
Cardiac output (L·min^{-1})	14.5±4
C(a-v)O_2 (mL/100 mL)	10.7±2.8
Peak heart rate (beats·min^{-1})	124±19
Stroke volume (mL)	120±23
Total vascular resistance (dyne·s^{-1}·cm^{-5})	497±103

and MICE using a repeated measure ANOVA with time and group factors (Fig. 1). For acute and kinetics responses, statistical differences were localized using a Bonferroni test with a p value <0.05 considered to be significant. Most statistical analyses were performed using Statview software version 5.0 (SAS Institute Inc., Cary, N.C., USA).

Table 4. Central and peripheral hemodynamic responses during moderate intensity continous exercise (MICE) and optimized high intensity intermittent exercise (HIIE).

Parameters	MICE (22 min)	HIIE (16 min)	ANOVA (p value)
Cardiac output (L·min^{-1})	10.06±3.14	9.26±1.93	0.2421
Cardiac index (L·min^{-1}·m^{-2})	4.99±1.65	4.58±096	0.2198
C(a-v)O_2 (mL/100 mL)	11.59±3.71	11.41±2.77	0.7169
Stroke volume (mL)	96±22	93±21	0.5324
Total vascular resistance (dyne·s^{-1}·cm^{-5})	735±229	764±191	0.3545

Results

Baseline characteristics

Participants were males aged between 48 to 71 years. The majority had a diagnosis of ischemic heart disease, NYHA class I and II, and were on optimal medical therapy (Table 1).

Cardiopulmonary exercise and hemodynamic variables at ventilatory threshold and maximal exercise

Cardiopulmonary and hemodynamic variables are presented in Tables 2 and 3 and in Fig. 1. Mean $\dot{V}O_{2peak}$ and power output were 17.3 ± 4.2 mL·min^{-1}·kg^{-1} (61% ± 14% of predicted value) and 97 ± 30 W, respectively.

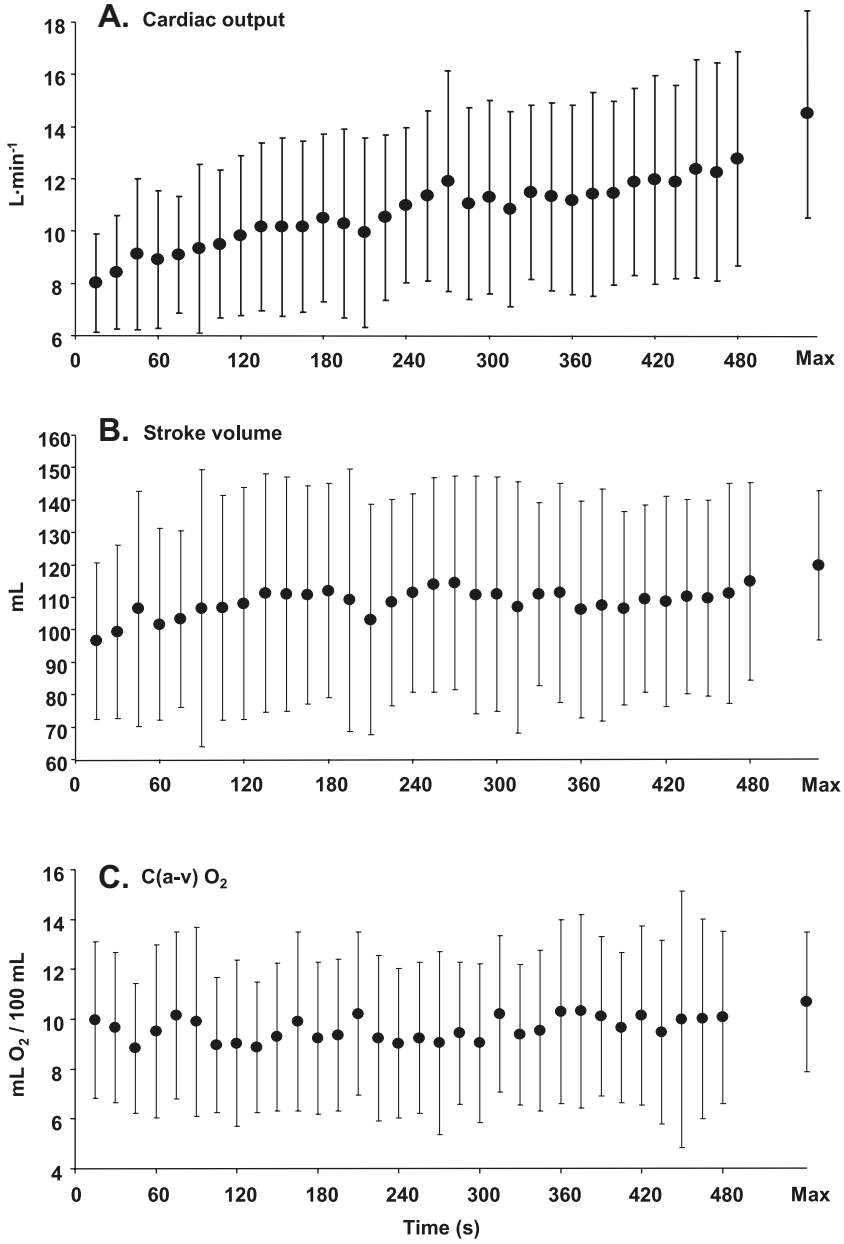
Cardiopulmonary exercise and hemodynamic variables during MICE and HIIE

Mean $\dot{V}O_2$ (1127 ± 260 vs. 998 ± 204 mL·min^{-1}, $p <$ 0.01), $\%\dot{V}O_{2peak}$ (76% ± 8% vs. 68% ± 8%, $p < 0.01$), and $\dot{V}$E (39 ± 5 vs. 34 ± 6 L·min^{-1}, $p < 0.01$) were higher during MICE vs. HIIE. There was a nonsignificant tendency for lower perceived exertion during HIIE vs. MICE (14 ± 1 vs. 12 ± 2, p = 0.07, respectively). Mean hemodynamic variables and their kinetics were not different during MICE and HIIE (Table 4 and Fig. 2). No significant ventricular arrhythmias and (or) abnormal blood pressure response (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 during MICE and HIEE session.

Discussion

The main findings of this study are that(*i*) a single bout of HIIE elicited a similar central SV, CO, and C(a-v)O_2 compared with MICE in HFREF patients; (*ii*) $\dot{V}O_2$ and ventilation were lower during HIIE vs. MICE and the perceived exertion tended to be lower; and (*iii*) HIIE elicited moderate central hemodynamic responses that were quite stable during exercise. When examining the time evolution of those variables (Fig. 2), our study demonstrated the relative stability of central hemodynamic (CO and SV) during HIIE and by consequence the safety of this mode of exercise in relation to cardiac stress. This relative hemodynamic stability is consistent with our clinical observation from our previous studies and lack of complications during HIIE in both patients with CHD and

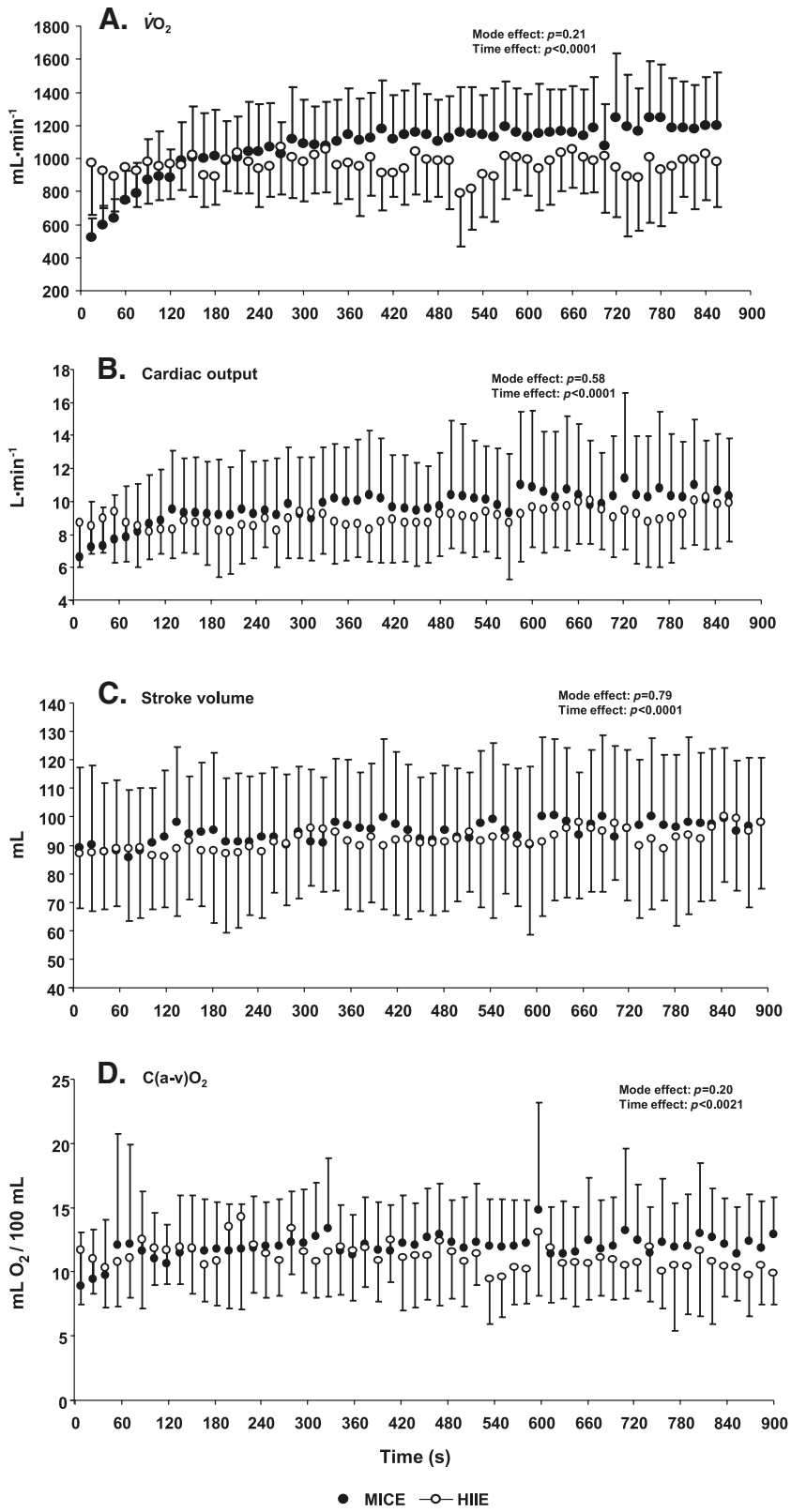
Fig. 1. Hemodynamic kinetics during maximal cardiopulmonary exercise testing in patients with heart failure and reduced ejection fraction. Values are means (point) ± SD (bar).



HFREF (Guiraud et al. 2010, 2011; Meyer et al. 2010, 2012); this point had been previously demonstrated by other groups (Meyer et al. 1998; Rognmo et al. 2004; Warburton et al. 2005; Wisløff et al. 2007; Tomczak et al. 2011).

Another interesting finding is that SV and CO increase slightly during both exercise bouts (Fig. 2) in patients with HFREF, a finding consistent with 2 previous studies in healthy subjects and patients with HFREF (Meyer et al. 1998; Foster et al. 1999). Central hemodynamic during exercise are dependent on the loading conditions, heart rate, and contractility (Meyer et al. 1998; Foster et al. 1999). During MICE bouts, CO tended to increase as a result of a higher heart rate compared with HIIE (data not shown). During HIIE and MICE, SV increased slightly secondary to an increase in end diastolic volume (data not shown). High intensity intermittent exercise allows for a higher power output to be generated for a short duration (15 to 30 s) that results in a greater physiological stimulus, particularly for muscular systems without overloading the cardiovascular system (Meyer et al. 1998; Rognmo et al. 2004; Warburton et al. 2005; Helgerud et al. 2007; Wisløff et al. 2007). The use of interval exercise as a component during cardiac rehabilitation programs has been recently advocated by the American Heart Association and the Canadian Association of Cardiac Rehabilitation (Balady et al. 2007; Stone 2009). However, to date, there may be still some hesitation to use HIIE for exercise training in patients with HFREF, probably because of fear of acute ventricular dysfunction and (or) worsening of symptoms following HIIE.

Fig. 2. Oxygen uptake ($\dot{V}O_2$) and hemodynamic kinetics during MICE and HIIE in patients with heart failure and reduced ejection fraction. MICE, moderate intensity continous exercise; HIIE, high intensity intermittent exercise. Values are means (point) ± SD (bar).



The interesting new finding is that both CO and C(a-v)O_2 were similarly increased during HIIE and MICE; whereas $\dot{V}O_2$ and ventilation were slightly lower during HIIE. This suggests that during HIIE, patients would have similar central and peripheral physiological responses but with significant less metabolic and ventilatory demand than compared with MICE. This result agrees with our previous work where our optimized HIIE was associated with a lower mean ventilation and reduced sensation of breathlessness in CHD patients (Guiraud et al. 2011). Breathlessness is a major reason for stopping exercise or reducing its intensity in cardiac patients, this particularity of the HIIE is important for patient's comfort and tolerance during exercise session and also to improve long-term adherence to a cardiac rehabilitation program (Guiraud et al. 2011). During MICE and HIIE, CO reached 69% and 63% of value measured during the maximal exercise test and slightly lower than the value measured at the ventilatory threshold (Table 3), indicating a moderate level of CO. In contrast, during MICE and HIIE, C(a-v)O_2 reached 108% and 106% of value measured during maximal exercise test, indicating greater O_2 extraction by muscles. We found similar temporal and mean central hemodynamic responses during MICE and HIIE (Table 4, Fig. 1) in agreement with prior studies that used different hemodynamic techniques (Meyer et al. 1998; Foster et al. 1999). Radionuclide ventriculography is a strong validated methodology for left ventricular function assessment during exercise (Meyer et al. 1998; Foster et al. 1999). However, this technique has limitations, including technical challenges, high cost, and, in particular, poor time resolution. Because of its important time resolution, the use of cardiac bioimpedance is particularly suitable when HIIE is studied on account of its relative short exercise and recovery phase (30 s.).

In patients with HFREF, a goal of HIIE is to exercise at a high power output without overloading the cardiopulmonary system, a finding consistent with our results. Intermittent exercise allows patients to work at a high intensity for limb muscle (100% PPO) for a short period of time, this being not possible with continuous exercise. In addition, HIIE was also associated with a trend towards lower perceived rating of exertion ($p = 0.07$), and a higher number of patients were able to complete the exercise, which indicated that HIIE is very well tolerated by patients with HFREF.

We demonstrated the stability of left ventricular function during our optimized HIIE protocol and thus its safety regarding central hemodynamic and function; this stability was associated with no significant arrhythmias and (or) abnormal blood pressure responses. Other groups have demonstrated similar results regarding hemodynamic safety during HIIE (Meyer et al. 1998, 2012; Wisløff et al. 2007) and even improved biventricular function after HIIE in patients with HFREF (Tomczak et al. 2011). We previously demonstrated that acute HIIE was not responsible for any significant arrhythmias, myocardial damage (elevation of cardiac troponin), or abnormal blood pressure responses in stable patients with CHD (Guiraud et al. 2010, 2011; Meyer et al. 2010) and in patients with HFREF (Meyer et al. 2011, 2012). Finally, recently, 1 acute session of our HIIE protocol was found to significantly improve ventricular arrhythmias and heart rate variability in patients with HFREF (Labrunee et al. 2011).

Study limitations

Several limitations of this study need to be outlined. First, our sample size was small and our results should be interpreted with caution and confirmed in a larger study population. Second, the participants were relatively young males with few co-morbidities and NYHA class I-II HF. Therefore, our results cannot be generalized to all patients with HFREF. Also, no age-matched control group was recruited in our study and potential effects of a patient's medication might have influenced our physiological measurements during exercise. Finally, the impact on chronic HIIE on aerobic capacity and other fitness and clinical outcomes should be assessed in a large randomized clinical exercise training study.

In conclusion, HIIE elicits similar SV, CO, and C(a-v)O_2 responses compared with MICE in clinically stable HFREF patients. With a lower metabolic and ventilatory demand, optimized HIIE was more efficient, was well tolerated, and allowed our patients high power outputs. Finally, optimized HIIE was safe, with moderate central hemodynamic response and no significant arrhythmias or abnormal blood pressure noted in this population of patients with HFREF. However, larger studies with long-term exercise training using optimized are needed to confirm the benefits and safety of HIIE in this population.

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