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Running title: Intermittent exercise in CHD patients

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ABSTRACT

Purpose: While the acute physiological responses to continuous exercise have been well documented in coronary patients, no previous study has examined the responses to high-intensity intermittent exercise in these patients. The purpose of this study was to compare the physiological responses to a high-intensity interval exercise protocol (HIIE) versus a moderate intensity continuous training (MICE) protocol of similar energy expenditure in coronary patients.

Methods: Twenty patients with stable coronary disease (19 males, 1 female, 62 ± 11 years) were assigned in random order to a single session of high-intensity interval exercise corresponding to 15s intervals at 100% of peak power output (PPO) and 15s passive recovery intervals and two weeks later to an isocaloric MICE corresponding to 70% of PPO.

Results: Both protocols were equivalent in term of energy expenditure. The HIIE protocol resulted in lower mean ventilation ($p < 0.001$) for a small difference in metabolic demand. All participants preferred the HIIE mainly because the perceived exertion measured by the Borg scale was lower ($p < 0.05$). No elevation of serum concentration of Troponin T were found in all participants at baseline, at 20 min and 24 h after the exercise sessions, thus excluding the presence of any exercise-induced myocardial injury in our patients.

Conclusion: When considering physiological responses, safety and perceived exertion, the HIIE protocol appeared to be well tolerated and more efficient in this group of stable coronary patients.

Key words: Physiological responses; Coronary heart disease; Comparative study; Cardiac troponin t

INTRODUCTION

Paragraph # 1

Physical activity is a recognized non-pharmacological intervention recommended for both primary and secondary prevention of coronary heart disease (CHD) (11). Current guidelines encourage the participation in moderate to vigorous-intensity aerobic exercise of 20 to 30 minutes duration on most, and preferably all, days of the week to promote or maintain health (4, 12, 14). As for secondary prevention, the health benefits of exercise-based cardiac rehabilitation are well-documented (21, 22, 29). However, the randomized controlled trials included in these meta-analyses exclusively used moderate intensity continuous exercise (MICE) protocols ranging from 40 to 80% of maximal oxygen consumption (VO_{2max}). These exercise protocols follow current recommendations of the American Heart Association (4). However, they do not consider recent advances in exercise physiology (9, 15) which may explain why cardiac rehabilitation exercise protocols have remained largely unchanged (2). High-intensity interval exercise (HIIE) represents another form of exercise training that is only occasionally used in cardiac rehabilitation (23, 33, 34). HIIE involves repeated 30 to 300-second phases of aerobic exercise at an intensity ranging from 95% to 100% of VO_{2max} , interspersed by recovery periods of equal, shorter or longer duration (8, 17). Interval training has been proven to be more effective than MICE in improving both in healthy (9, 15) and CHD patients (23, 33). Despite this fact, the acute cardiovascular responses of coronary patients to HIIE have not been studied in detail; this information is required for safety and efficacy reasons before considering the use of HIIE in cardiac rehabilitation programs (18). We recently compared the physiological responses of 20 coronary patients to four different single sessions of HIIE which varied in exercise phase duration (15 s or 60 s) and type of recovery (active or passive) (13). The optimal

mode with respect to safety, patient comfort and time spent at a high level of VO_2 involved an exercise session consisting of repeated 15-s phases of exercise at 100% of peak power output (PPO) (measured at the maximal graded exercise test) interspersed by recovery periods of equal duration. This initial study however did not address the issue of potential myocardial injury with HIIE. Furthermore, whether similar physiological responses occur with this mode of high-intensity interval training relative to a MICE session of equal energy expenditure is unknown. The objectives of the current study were therefore to 1) verify that myocardial injury (cardiac troponin T release) does not occur during HIIE 2) compare the acute cardiovascular physiological responses between the two exercise modes and 3) propose a method of isocaloric calculation for HIIE and MICE sessions.

MATERIAL AND METHODS

Paragraph # 2

Participants

Twenty patients with stable coronary heart disease providing written informed consent were recruited at the cardiovascular prevention centre of the Montreal Heart Institute. Inclusion criteria were: a history of $\geq 70\%$ arterial diameter narrowing of at least one major coronary artery and/or documented prior myocardial infarction and/or perfusion defect on Sesta MIBI exercise testing. Exclusion criteria were: recent acute coronary syndrome (≤ 3 months), significant resting ECG abnormality, severe arrhythmias, history of congestive heart failure, uncontrolled hypertension, recent bypass surgery intervention ≤ 3 months, recent percutaneous coronary intervention ≤ 6 months, left ventricular ejection fraction $\leq 45\%$, pacemaker, recent modification of medication < 2 weeks, and musculoskeletal conditions making exercise on ergocycle difficult or contra-

indicated. Demographic and baseline characteristics are presented in Table 1. The research protocol was approved by the Montreal Heart Institute Ethics Committee.

Paragraph # 3

Experimental design

On the first visit, patients underwent a complete medical evaluation which included measurement of height, weight, body composition, resting ECG and a maximal continuous graded exercise test. During two subsequent weeks, in random order, subjects performed the two exercise sessions (interval and continuous) under the supervision of an exercise physiologist, a nurse and a cardiologist. All tests were conducted on an electro-mechanically braked bicycle ergometer (Ergoline 800S, Bitz, Germany). Cycling position, which is known to affect energy expenditure, was standardized by adopting a top bar position. Saddle height was adjusted according to the participant's inseam leg length. Each participant used toe-clips and was instructed to stay seated down.

Paragraph # 4

Maximal continuous graded exercise test

A 3-min warm up at 20 W was performed before the test. Thereafter, initial power was set at 60W and increased by 15 W every minute. Verbal encouragements were given throughout the test. Criteria for exercise test cessation were volitional exhaustion, significant ECG abnormalities (ST-depression > 2 mm or ventricular arrhythmias), or abnormal blood pressure response. Oxygen uptake (VO_2) was determined continuously on a 30-s basis using an automated cardiopulmonary exercise system (Oxycon Alpha, Jaeger, Germany). Gas analyzers were calibrated before each test, using a gas mixture of known concentration (15% O_2 and 5% CO_2) and ambient air. Participants breathed through a facemask connected with the turbine. The turbine was calibrated before each test using a 3-liter syringe at several flow rates.

Electrocardiographic activity was monitored continuously using a 12-lead ECG (Marquette, Missouri) and blood pressure was measured manually every two minutes using a sphygmomanometer. The highest over a 30-s period and the highest heart rate over a 5-s period during the test were considered as peak oxygen consumption (VO_2peak , in $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) and peak heart rate (HR peak, in $\text{b}\cdot\text{min}^{-1}$). Power of the last completed stage was considered as the peak power output (PPO, in W).

Paragraph # 5

Exercise sessions

General setting.

Participants were asked to arrive fully hydrated to the laboratory, at least three hours after their last meal. No attempt was made to control meal size or content. Oxygen consumption (Oxycon Alpha, Jaegger, Germany) and electrocardiographic activity (Marquette, Missouri) were monitored continuously during both sessions according to the same modalities as for the maximal continuous graded exercise test. Blood pressure was measured manually every two minutes with a sphygmomanometer. Perceived exertion was measured every three minutes with the 20-point Borg scale (6). Feedback on elapsed time and verbal encouragement were given throughout the sessions, which were interrupted when ECG or blood pressure abnormalities were observed. Participants were monitored for 5 min after exercise cessation in a sitting position. A venous blood sample was taken 10 min before exercise for cardiac troponin T (cTnT) determination, and was repeated 20 min and 24 h after exercise cessation (20).

Paragraph # 6

MICE session.

This exercise session was based on recommendations of the American Heart Association on exercise prescription in CHD patients, suggesting that exercise intensity should lie between 50%

and 80% of PPO (4). We opted for an intensity of 70% of PPO. Duration was adjusted to match total energy expenditure of the HIIE, according to the method presented in the *Isocaloric calculation* section (see below). We chose to include the warm-up and the recovery in the exercise session and kept the intensity of exercise at 70% of PPO. A mean duration of 28.7 minutes was calculated.

Paragraph # 7

High-intensity interval exercise (HIIE) session.

This HIIE session was based on a previous study conducted in our laboratory that compared physiological, psychological and electrocardiological tolerance of four different single sessions of HIIE in coronary patients (13). The selected HIIE session represented the best compromise between safety, time spent at a high level of VO_2 peak and psychological adherence. This HIIE session consists of a 10-min warm-up at 50% of PPO, followed by two sets of 10 min composed of repeated phases of 15 s at 100% of PPO interspersed by 15 s of passive recovery. Four minutes of passive recovery were allowed between the two sets, as well as a 5-min cool-down after the last 15-s exercise phase.

Paragraph # 8

Isocaloric calculation

An important feature when comparing the physiological response to different exercise sessions is to ensure that energy expenditure is similar. The typical method consists of calculating cumulated work of the different exercise sessions, and thereafter to adjust their respective intensity or duration to obtain isocaloric sessions. The major drawback of this method is the assumption that there is no energy expenditure when the patient does not exercise during the recovery period, as is the case in our study, while VO_2 remains elevated. A pilot study on 18 CHD patients

performing two randomly ordered exercise sessions of 10 min composed of repeated phases of 15 s at 100% of PPO interspersed by 15 s of either active (50% of PPO) or passive recovery (0% of PPO), allowed us to estimate that mean VO_2 during passive recovery represented $77\pm 8\%$ of mean VO_2 during active recovery. We assumed that energy expenditure estimated from mechanical power and VO_2 was equivalent, and converted this percentage of VO_2 into a percentage of the power maintained during active recovery. An example is given in table 2. Once energy expenditure was calculated for the HIIE session, it was possible to adjust the duration of the MICE session to match this value.

Paragraph # 9

Cardiac troponin T determination.

For each blood sample, 10 ml of venous blood was drawn from the antecubital vein with patients in a sitting position. Blood samples were then centrifuged and separated serum was stored at -80°C for subsequent analysis. The measurements of Cardiac troponin T were performed in the hospital clinical laboratory using the only available commercial assay (Roche Diagnostics, Mannheim, Germany). The decision limit for myocardial injury was set at 0.04 mg.l^{-1} (3).

Paragraph # 10

Statistical analysis

Standard statistical methods were used for the calculation of means and standard deviations. Normal Gaussian distribution of the data was verified by the Shapiro-Wilk test, and homoscedasticity by a modified Levene Test. Since none of the variables met these underlying hypotheses, we opted for a non parametric procedure. A Wilcoxon test for matched pairs was performed to test the null hypothesis that there was no difference between each training sessions.

The magnitude of the difference was assessed by the Effect Size (ES), calculated according to the following equation:

$$\text{Eq. 1} \quad \text{ES} = \frac{M_1 - M_2}{\text{SD}_{\text{pooled}}}$$

where ES is the effect size, M_1 and M_2 are the mean of MICE and HIIE sessions, respectively, and $\text{SD}_{\text{pooled}}$ is the pooled standard deviation, calculated as follows:

$$\text{Eq. 2} \quad \text{SD}_{\text{pooled}} = \sqrt{\frac{(S_1^2 \times (n_1 - 1)) + (S_2^2 \times (n_2 - 1))}{(n_1 + n_2 - 2)}}$$

where S_1^2 and S_2^2 are the variance of MICE and HIIE protocols, respectively, and n is the number of participants in each group. The scale proposed by Cohen (1988) was used for interpretation (7). The magnitude of the difference was considered either trivial ($\text{ES} < 0.2$), small ($0.2 < \text{ES} \leq 0.5$), moderate ($0.5 < \text{ES} \leq 0.8$), or large ($\text{ES} > 0.8$). All calculations were made with Statistica 6.0 (Statsoft, Tulsa, USA).

Paragraph # 11

RESULTS

Results from the maximal continuous graded exercise test are presented in table 3. Peak oxygen consumption and other relevant variables suggest that exercise tolerance in our sample is comparable to age-based predicted values (25). Nineteen participants were able to complete both MICE and HIIE sessions, while one participant stopped the MICE session after 20 min of exercise. Data from this patient were excluded from the analyses.

Paragraph # 12

No significant ventricular arrhythmias or abnormal blood pressure response occurred during either exercise session. Although 35% of our sample had exercise-induced ischemia during the maximal exercise stress test, neither session induced prolonged ischemia. Only three subjects had

demonstrable myocardial ischemia during the HIIE session, with ST-segment depression never surpassing 2 mm and always normalizing during the 15-s passive recovery periods. Maximal ST segment depression was 1.2 ± 0.3 for HIIE. Serum concentration of cTnT was $<0.04 \text{ mg.l}^{-1}$ in all participants at baseline and did not exceed this value at 20 min and 24 h after the exercise sessions, thus excluding the presence of any exercise-induced myocardial injury in our patients.

Paragraph # 13

Typical VO_2 , heart rate and ventilation responses of one participant during the MICE and HIIE sessions are presented in Figure 1. This patient was a well-trained 78-year-old male without evidence of myocardial ischemia during the maximal graded exercise test. Peak oxygen consumption ($25.9 \text{ ml.min}^{-1}.\text{kg}^{-1}$ or 7.4 METs) and peak heart rate (125 b.min^{-1}) were reached at 150 W.

Paragraph # 14

When considering the entire sample, we found a large difference in mean ventilation between MICE and HIIE sessions (58.9 ± 14.2 and $49.8 \pm 8.2 \text{ l.min}^{-1}$, respectively; $p < 0.001$, $\text{ES} = -0.81$), and a small difference in mean VO_2 (1773 ± 589 and $1604 \pm 468 \text{ l.min}^{-1}$, respectively; $p < 0.01$, $\text{ES} = 0.31$). Therefore, relative to the MICE session, the HIIE session was associated with a lower ventilatory demand and a higher metabolic rate during the 15-s exercise phases (70 and 100% of PPO, respectively). This calculation was based on total training in MICE and both 10-min sets of the HIIE session. In HIIE and MICE sessions, the mean PO was 27% below and 10% above the first ventilatory threshold, respectively. We also calculated the total energy expenditure between both HIIE sets in order to verify if drift was present for a same power output. In the first and second sets, mean oxygen uptake and energy expenditure did not change, (16.2 ± 4.4 versus 16.1 ± 4.5 liters; 340 ± 94 versus $338 \pm 96 \text{ KJ}$, for the first and second sets respectively, $p = \text{ns}$).

Paragraph # 15

All participants rated the HIIE session as their preferred one, which was also considered as less difficult than the MICE session (Borg scale ratings of 14 ± 2 and 16 ± 2 , respectively; $p < 0.05$).

Paragraph # 16

Results from the isocaloric calculation are presented in table 4. We found a trivial but significant difference in energy expenditure between the MICE and HIIE sessions (988 ± 336 and 931 ± 286 KJ, respectively; $p < 0.01$, ES = -0.18) when using the original method. However, this difference disappeared when adding total VO_2 of the 4-min passive recovery period that separated the two sets of HIIE (988 ± 336 and 983 ± 296 KJ, respectively; NS, ES = -0.02). The two sessions could therefore be considered as isocaloric.

Paragraph # 17

Based upon oxygen uptake values obtained during a 10-min HIIE session, we found retrospectively that repeated 15-sec phases of exercise at 100% of PPO interspersed by 15-sec phases of passive recovery corresponds to approximately 60% of PPO during continuous aerobic training.

DISCUSSION

Paragraph # 18

The aim of this study was to compare the acute responses of coronary patients to a HIIE and a MICE training sessions of similar energy expenditure. Our main finding was that the high-intensity interval exercise session was safe and induced acute physiological adaptations that could potentially be used to improve adherence of stable coronary patients to a cardiac rehabilitation program while improving its efficiency. Current guidelines encourage the

accumulation of 20-30 minutes per day of moderate-intensity physical activity on most, and preferably all, days of the week to promote or maintain health (4, 12, 14). Notwithstanding the huge body of knowledge that supports this recommendation, it is important to note that contemporary exercise training studies have often employed a quantitative vision of exercise prescription, the increase in energy expenditure being generally obtained by an increase in exercise duration and frequency (2). Interval training is an alternative form of exercise that is occasionally used in cardiac rehabilitation, and that is known to affect positively both endothelial (30) and cardiac function (34). The uniqueness of the high-intensity interval exercise session used in the present study is the use of very short phases of maximal-intensity exercise. This inevitably raises questions regarding safety. We found no evidence of severe or prolonged ischemia, significant arrhythmias or abnormal blood pressure responses. Moreover, cardiac troponin T levels at 20 minutes and 24 hours after exercise remained well within normal limits thereby excluding any myocardial injury. This HIIE session therefore appears safe and very well tolerated for selected stable coronary patients. In accordance with our results, two recent studies showed that continuous training above the ischemic threshold is safe and well tolerated without evidence of myocardial damage, significant arrhythmias, or left ventricular dysfunction (16, 20). In theory, HIIE might be safer than continuous aerobic training above the ischemic threshold, resulting in intermittent rather than prolonged periods of ischemia. Furthermore, intermittent periods of ischemia might lead to ischemic preconditioning as is witnessed during warm-up angina (19, 31, 32). Brief, repetitive episodes of ischemia have also been shown to promote collateral formation in animals (10).

Paragraph # 19

Interestingly, all patients rated the HIIE session as their preferred one. A possible explanation for this result is the lower sensation of breathlessness associated with HIIE. In comparison with the

MICE session, mean and peak ventilation were lower during the HIIE session. Knowing that breathlessness is a major reason for stopping exercise or reducing its intensity, this feature of the HIIE session could be used in order to improve long-term adherence to a cardiac rehabilitation program. Furthermore, the very short (15-second) intervals with a 1:1 exercise – recovery ratio imposed a rhythm that was appreciated by the patients. If the recovery had been active at 40% of PPO in HIIE session, the mean power output would have been identical to MICE session. This response to the HIIE may be the attractive part of HIIE application in patients by inducing a high peripheral metabolic load and a lower central load reducing strain to the cardiorespiratory system albeit high muscular load, which may be the safe way to train patients although using high (and even PPO) work loads. The work phases are too short to reach a high cardiorespiratory strain although high metabolic load on the working muscles. This method of HIIE allows patients to train at a high percentage of VO_{2max} that may constitute the main target for training adaptation by inducing an increase of VO_{2max} and probably, a several number of peripheral adaptations as muscular, metabolic and endothelial.

From a practical standpoint, the prescription of exercise intensity using the high-intensity interval training session should be based on mechanical power output instead of heart rate. It is now accepted that monitoring exercise intensity with heart rate, as is often done in cardiac rehabilitation programs (33, 34), suffers from several limitations, in particular during high intensity exercises. Besides the difficulty in predicting maximal heart rate (27), the major drawback is the tendency for heart rate to level off before the attainment of VO_{2max} (1). Consequently, the estimation of heart rate at maximal intensity from the submaximal heart rate – VO_2 linear relationship is not possible.

Paragraph # 20

The minimum power output that allows eliciting VO_2max during a maximal graded exercise test has been shown to be a good alternative for the purpose of monitoring exercise intensity (5). This enables subjects to obtain maximum benefit for minimum work. Our finding showed that with respect to energy expenditure, repeated phases of 15 s at 100% of PPO interspersed by 15 s of passive recovery (0% of PPO) corresponds to approximately 60% of PPO in continuous mode. Therefore, this specific HIIE session appears to be more efficient.

Paragraph 3

In a recent study, Ades et al. (2) modeled a new approach to cardiac rehabilitation for overweight coronary patients. This study was based on high-calorie expenditure exercise (3000 to 3500 Kcal/wk). This new approach promotes greater weight loss and more favorable cardiometabolic risk profiles than standard cardiac rehabilitation. They showed significant weight loss, fat mass loss and waist reduction accompanied by an improvement of metabolic components using high-calorie expenditure exercise training combined with a hypocaloric diet. In this study, patients were told to walk often and walk far. This approach requires a significant time commitment and willpower on the part of patients, both limiting the application of this training program to most individuals with coronary disease. We believe that shorter periods of higher intensity aerobic interval training may be an alternative to achieve similar benefits.

It is well established that exercise intensity is the key factor for the improvement of VO_2 peak in cardiac patients by resulting from both peripheral and central adaptations (23, 33, 34). Even if training volume is important for cardiovascular health factors, aerobic interval training seems to have also a favorable effect for the improvement of VO_2peak , insulin sensitivity and endothelial function in metabolic syndrome patients (30). When comparing to moderate intensity, vigorous intensity seems to be superior for reducing risk of CHD (24, 28), and appears to convey greater

cardioprotective benefits (26). The studies that form the basis for modern rehabilitation programs were conducted several decades ago when metabolic syndrome was less common. For this reason, it is important to propose a cardiac rehabilitation training program based on a different type of exercise, which promotes both the improvement of fitness, the metabolic profile and possibly compliance.

Limitations of the current study include the small, predominantly male, sample. However, we have no reason to believe that our results would have differed in women. In addition, the sample was selected among a cohort of stable coronary patients who were followed closely and performed exercise on a regular basis.

CONCLUSION

The finding of the present study suggests that a high-intensity interval exercise session employing very short periods of exercise interspersed by short periods of passive recovery appears safe for selected stable coronary patients. Future studies will require comparing long-term HIIE training sessions to MICE training sessions for safety and efficacy purposes. Ultimately, HIIE could potentially be incorporated into phase III cardiac rehabilitation for selected, stable patients should it prove safe while providing similar cardiovascular benefits to conventional cardiac rehabilitation while improving patient comfort and compliance.

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ACCEPTED

Figure caption.

Typical VO_2 , heart rate and ventilation responses of a participant during moderate intensity continuous exercise (left) and high intensity intermittent exercise (right) protocols. Dashed lines represent $\text{VO}_{2\text{max}}$, maximal heart rate and maximal ventilation.

ACCEPTED

Figure 1

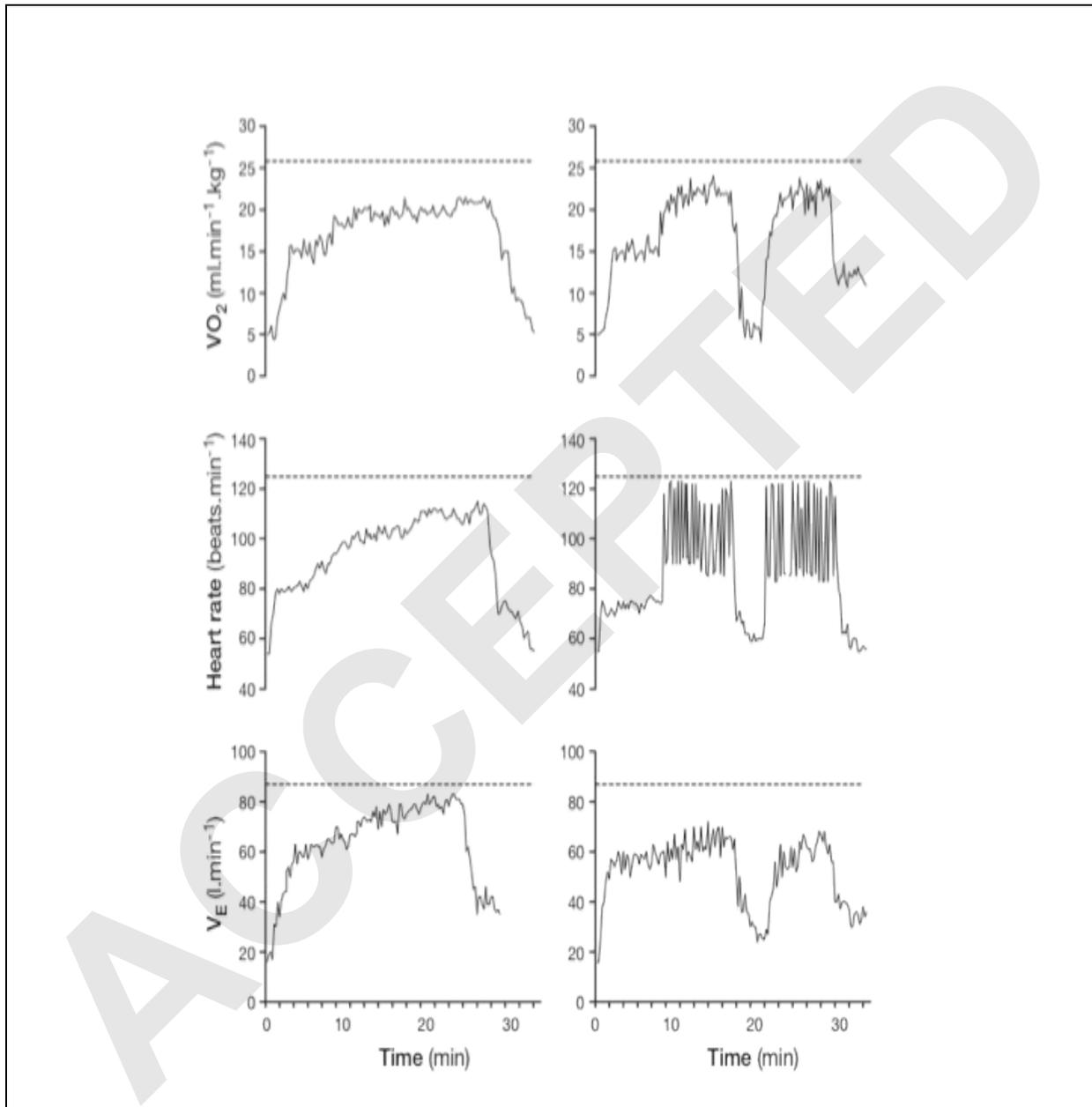


Table 1. Patients characteristics and medication use. Results are reported as mean \pm SD or row value (% of the sample).

Anthropometrics	
Age (years)	62 \pm 11
Men	19 (95%)
Body mass index (kg/m ²)	27 \pm 4
Waist circumference (cm)	97 \pm 10
Body fat (%)	27 \pm 4
Risk factors	
Diabetes Mellitus	2 (10%)
Hypertension	5 (25%)
Dyslipidemia	17 (85%)
Smoking	0 (0%)
Medical history	
Symptoms of angina pectoris	8 (40%)
Myocardial ischemia (ST-depression)	7 (35%)
Ejection fraction (%)	59 \pm 5
Previous myocardial infarction	10 (50%)
PCI	7 (35%)
CABG	7 (35%)
Medications	
Anti platelets agents	19 (95%)
Betablockers	10 (50%)
Calcium channel blockers	0 (0%)

ACE inhibitors	3 (15%)
Angiotensin receptor antagonist	6 (30%)
Statins	17 (85%)
Nitrates	0 (0%)

PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting surgery;

ACE = angiotensin-converting enzyme

ACCEPTED

Table 2. Example of an isocaloric calculation for an individual with a peak power output of 100 W

	Exercise duration (min)	Exercise intensity (% PPO)	Exercise intensity (W)	Oxygen uptake (l)	Energy expenditure (Kj)
MICE					
Total	28.7	70	70	31.88	669
HIIE					
Warm-up	10	50	50	7.9	166
Exercise	10	100	100	15.9	333
Recovery	10	38.5	38.5	6.1	128
Cool-down	5	25	25	2	41
Total				31.9	670

MICE: moderate intensity continuous exercise; HIIE: specific high-intensity interval exercise used in this study; PPO: peak power output.

Table 3. Results from the maximal continuous graded exercise test. Results are reported as mean \pm standard deviation

VO _{2peak} (ml. min. ⁻¹ kg. ⁻¹)	28.4 \pm 9.1
VO _{2peak} (ml. min. ⁻¹)	2301 \pm 831
Exercise tolerance (METs)	8.1 \pm 2
PPO (Watts)	177 \pm 63
VT 1 (Watts)	114 \pm 46
VT 1 (% PPO)	62 \pm 8
VT 2 (Watts)	156 \pm 54
VT 2 (% PPO)	85 \pm 6
Resting heart rate (bpm)	63 \pm 11
Peak heart rate (bpm)	145 \pm 19
Heart rate at 1 min recovery (bpm)	120 \pm 20
Delta heart rate at 1 min recovery (bpm)	24 \pm 10
Resting systolic blood pressure (mmHg)	129 \pm 13
Maximal systolic blood pressure (mmHg)	176 \pm 25

VO_{2peak}: peak oxygen consumption; MET: metabolic equivalent (multiple of 3.5 ml.min⁻¹.kg⁻¹);

PPO: Peak power output; VT 1: first ventilatory threshold; VT 2: second ventilatory threshold.

Table 4. Results of the isocaloric calculation for MICE and HIIE protocols.

	MICE	HIIE	Magnitude of the difference	
			ES	Interpretation
Method 1				
Oxygen uptake (L)	47.1 ± 16	44.4 ± 14 *	-0.18	Trivial
Energy expenditure (Kj)	988 ± 336	931 ± 286 *		
Method 2				
Oxygen uptake (L)	47.1 ± 16	46.8 ± 14	-0.02	Trivial
Energy expenditure (Kj)	988 ± 336	983 ± 296		

MICE: moderate intensity continuous exercise; HIIE: specific high-intensity interval exercise used in this study; ES: effect size. * Different from MICE ($p < 0.05$).

Total oxygen uptake and energy expenditure of HIIE protocol were calculated with (method 2) and without (method 1) oxygen uptake of the passive recovery period between the two sets of high intensity intermittent exercise.