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HIGHER INTENSITY INTERVAL TRAINING IMPROVES AEROBIC CAPACITY AND METABOLIC PROFILE IN MEN WITH CARDIAC DISEASE: A PILOT STUDY.

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ABSTRACT

Purpose: *We examined whether 12 weeks of higher intensity aerobic interval training plus progressive resistance training (HIIT+PRT) improved aerobic capacity, muscle strength, blood glucose and lipid profile in Phase 2 cardiac rehabilitation patients compared to standard care.*

Methods: *Twenty-five men (65 ± 11 yr SD) participated in either HIIT+PRT (N=17, 3 x 5 min intervals at 65% predicted peak heart rate (HRpeak) alternated with 2 x 5 min intervals at 85%, plus 30 min PRT) or remained in standard care (CON N=8). The following measures were assessed at baseline and post-12 weeks: resting HR, blood pressure (BP), muscle strength, aerobic power, fasting blood glucose and cholesterol.*

Results: *HIIT+PRT significantly increased aerobic power (+24%), elapsed test time (+29%), abdominal muscular strength (+13%) and decreased systolic and diastolic BP (-7.7%, -5%), rate-pressure product (-14%), body mass (-2%), resting HR (-8%), fasting glucose (-7%), LDL (-36%) and triglycerides (-27%) compared to CON (P < 0.05). CON showed significantly increased triglycerides after 12 weeks. There were no adverse cardiac events in either group during or after the study.* **Conclusions:** *HIIT+PRT significantly improved aerobic capacity and clinical measures in stable Phase 2 CAD patients to a greater extent than standard rehabilitation exercise, and without adverse cardiac events.*

Keywords: Cardiac rehabilitation; interval training; high intensity

Introduction

Low to moderate intensity rehabilitation exercise is normally recommended for Phase 2 cardiac patients, and has been shown to improve quality of life, functional capacity and all-cause and cardiac mortality rates (Jolliffe et al., 2001; Leon et al., 2005). However, low-moderate intensity steady state/ continuous exercise may not provide enough stimuli for cardiovascular and metabolic profile improvements in hemodynamically stable patients. Daily life consists of intermittent physical activities of varying intensities incorporating aerobic and muscular strength/endurance components (Meyer et al., 1996). Higher intensity exercise intervals may benefit cardiac patients wishing to return to recreational sport, physically demanding employment or vigorous activities for daily living (ADL). High intensity interval aerobic exercise (>90% maximal effort) has been shown to increase aerobic power, left ventricular function and endothelial function in heart failure and coronary artery disease (CAD) patients (Meyer et al., 1996; Rognmo et al., 2004; Wisløff et al., 2007) and to reduce in-stent restenosis following percutaneous coronary intervention (Munk et al., 2009). However, very high intensity interval aerobic exercise may not be a realistically sustainable or functional form of training for cardiac patients, given that there is mounting evidence that a mixed-model (aerobic and strength training) approach to chronic disease management may reduce metabolic risk factors as well as improving clinical cardiac symptoms (Bateman et al., 2011). No study has looked at the effects of combined aerobic and resistance higher intensity interval training on Phase 2 cardiac patients. As both aerobic capacity and strength are important for risk reduction of further cardiac events, and for improving ADL with CAD patients, we hypothesized that 12 weeks of higher intensity interval training plus progressive resistance training (HIIT+PRT) would improve aerobic capacity, muscle strength, flexibility, lipid profiles and fasting glucose compared to standard care in Phase 2 cardiac patients.

Methods

Ethical approval

The study was approved by the New Zealand Central Regional Health and Disability Ethics Committee, and written consent was obtained from all participants and their referring medical practitioners.

Participants

This pilot study was a non-randomised controlled intervention. Twenty-five men, (age = 64 ± 10 yr SD, BMI = 30 ± 6) with stable cardiac disease were recruited from the Massey University Cardiac Rehabilitation Exercise Programme. Participants chose to join the HIIT+PRT group (*N*=17) or to continue with standard care Phase 2 exercise (Control group, CON, *N*=8). Participants had a range of cardiac diseases and were on a variety of medications (Table 1). Participants were instructed to maintain their diet and medication doses throughout the study. The participants had already completed 12 weeks of typical Phase 2 exercise rehabilitation, consisting of 30 min aerobic exercise at 60% peak heart rate (HR_{peak}) plus 15 min light non-progressive resistance training, 3 times per week. Patients with angina, cardiac arrhythmias, symptomatic ventricular tachycardia, pulmonary disease or those who had a myocardial infarction in the previous 6 months were excluded from the study.

Table 1: Patient medications and medical conditions

	HIIT+PRT N=17	CON N=8
Mean Age (yr)*	65 ± 11	64 ± 9
Medication[a]		
Beta blockers	53	100
Antiplatelets	88	100
Statins	100	88
ACE inhibitors	35	25
Calcium antagonists	12	25
Diuretics	12	38
Sulphonylureas	6	13
Medical Condition[b]		
Myocardial infarction	53	25
Hypertension	59	63
CABG	41	88
Stents	59	50
Pacemaker	6	0
Implanted de-fibrillator	0	13

*Mean age ± SD
[a] Percentage (%) of each group taking the following medications
[b] Percentage (%) of each group with the following conditions and/or surgeries

Study protocol

Befor e and after the 12 week intervention, participants completed the following assessments, on the same day and in the following order: anthropometric measurements, fasting blood test, submaximal aerobic cycle test, hand grip strength, abdominal strength/endurance, upper body muscular strength/endurance and lumbar flexibility. Participants were given appropriate rest in between all tests. Pre- and post-study testing was conducted at the same time of day for each participant and post-training assessments were completed within a week of the final training session. To maintain inter-test reliability, the same researcher tested the same participants pre- and post-training.

Anthropometric measurements: Height was recorded by stadiometer (Hunan Changiiang Industry Co, Hunan, China) to the nearest 1cm. Body mass and percent body fat was measured with a body composition monitor (Tanita BC-532, Tokyo, Japan). Waist circumference and BMI were recorded as per American College of Sports Medicine guidelines (American College of Sports Medicine 2005).

Resting heart rate and blood pressure: Resting heart rate (HR) and resting blood pressure (BP) were measured after 5 min of rest in a seated position. BP was measured using a standard adult-sized cuff (Baume, Germany) to the nearest 2 mmHg.

Aerobic capacity: Aerobic power was measured with a submaximal graded exercise cycle test (Monark 875E, Vansbro, Sweden) to 85% of predicted maximum HR or a score of 16 on the 6-20 Borg Rate of Perceived Exertion scale (RPE) if the participant was taking beta blockers. Participants warmed up with 3 min of cycling at 10 W, and were instructed to keep a cadence of 60 rpm throughout the exercise test. The workload then increased by 10 W each minute until 85% of predicted HR_{max} or an RPE of 16 was reached. VO_2 was measured using a Sensormedics metabolic cart, (Yorba Linda, CA). Heart rate and blood pressure were continually monitored during exercise with a 12 lead ECG (Schiller, Switzerland) and standard auscultation (Baume, Germany) respectively. Predicted VO_{2peak} was calculated from standard equations determining the slope and ratio of difference between 2 sub-maximal (SM) workloads and corresponding change in sub-maximal HR (American College of Sports Medicine, ACSM 2005).

Muscular strength and endurance: Pre- and post-study forearm and hand strength, abdominal strength/endurance and upper body strength/endurance were respectively assessed using a hand grip strength dynamometer (Smedlays TTM Tokyo, Japan), the YMCA Curl Up test, and the YMCA Modified Push Up Test (ACSM 2005). Lower back flexibility was measured with the Sit and Reach Test (ACSM 2005).

Fasting blood test: Participants were asked to fast overnight and the morning prior to the blood tests, but were allowed to drink water *ad libitum*. All blood tests were conducted between the hours of 0070 and 0090, and were prior to exercise testing. Fasting serum triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (CHOL) and the cholesterol/HDL ratio were measured using a lipid analyser (CardioCheck PA Analyzer, Indianapolis, US). Glucose was measured with a glucometer (Medisense Optimum Xceed, Victoria, Australia).

HIIT+PRT protocol

The 12 week training intervention consisted of 3 weekly sessions of 35 min of cycling (alternating 3 x 5 min intervals of moderate and 2 x 5 min intervals of higher intensity) followed by 25 min of PRT plus 5 min stretching. Moderate intensity cycling intervals were 65% of predicted maximum HR or a Borg scale of 12; higher intensity 5 min intervals were 85% of predicted maximum HR, or a Borg scale of 16. HR and BP were recorded at rest (pre-exercise) and at the end of every 5 min training interval. Increases in cycling workload during the study maintained training intensities, as measured by training heart rates and RPE.

The PRT session consisted of upper and lower body, and abdominal exercises of moderate intensity (Borg scale 13) using either free weights or body weight as resistance, beginning with 1 set (12 repetitions) of each exercise followed by a second set

(12 repetitions) at a higher resistance (Borg scale 15-16). Lower body exercises included squats, lunges, leg abduction and adduction, calf raises, hip flexion and extension and sit-to-stands, where extra resistance for the second set was added with hand-held free weights, Therabands™ or ankle weights. Upper body exercises consisted of bicep curls, tricep kickbacks, lateral raises, shoulder press and seated rows, where the extra resistance was added with either increased free weights or more resistant Therabands™. Abdominal exercises consisted of crunches (trunk flexion), oblique crunches (trunk flexion plus trunk rotation), and four-point kneeling (with added difficulty of arm and leg extension). The resistance and number of repetitions were gradually increased during the training programme to maintain higher intensities. Five minutes of static stretching of the main muscle groups (hamstrings, quadriceps, calf, adductors, abductors, lower back, triceps, shoulder, chest and biceps) completed the exercise sessions.

The CON group continued with 12 weeks of the same Phase 2 moderate intensity programme (30 min steady state cycling at 60% HR_{peak} plus 15 min light, non-progressive resistance training) they had previously completed. Participants in both groups were instructed to notify supervising staff of any adverse cardiac symptoms such as chest pain, palpitations, breathlessness, dizziness and unusual fatigue, and to cease exercise under such circumstances. Abnormal changes in BP and HR were to be recorded and participants would be advised to inform their referring medical practitioner. All participants were advised to continue with ADL on non-training days, but not to undertake any extra exercise sessions.

Statistical Analysis

Changes in outcome measures over time, and between-group comparisons, were analysed with repeated measures ANOVA using SPSS for Windows (Version 16, SPSS, Chicago, IL). The significance level was set at $P < 0.05$. All values are expressed as mean ± standard deviation (SD).

Results

Participants in the HIIT+PRT completed 97% of

Table 2. Effects of 12 weeks of HIIT+PRT on physiological parameters

Variable	HIIT+PRT Pre N=17	HIIT+PRT Post N=17	%Δ pre-to post	P	CON Pre N=8	CON Post N=8	%Δ pre-to post	P
Resting HR (bpm)	64 ± 8	60 ± 3*	-8.0	0.023	67 ± 13	69 ± 13[b]	+3.0	0.956
Resting SBP (mmHg)	130 ± 15	120 ± 8*	-7.7	0.001	124 ± 8[a]	125 ± 10	+0.8	0.212
Resting DBP (mmHg)	80 ± 12	76 ± 8*	-5.0	0.007	72 ± 5	72 ± 7	0.0	0.926
Height (cm)	177 ± 5	177 ± 5	0.0	1.00	177 ± 6	176 ± 5	-1.1	0.807
Body Mass (kg)	93 ± 17	90 ± 15*	-3.3	0.036	94 ± 16	94 ± 15	0.0	0.485
BMI	30.1 ± 5	29.4 ± 5	-2.3	0.526	29.9 ± 6	30.0 ± 6	+0.3	0.688
Body Fat (%)	32 ± 4	31 ± 3	-3.1	0.412	32 ± 4	33 ±4	+3.1	0.910
Waist-hip ratio	0.96 ± 0.1	0.95 ± 0.1	-1.0	0.602	0.97 ± 0.1	0.98 ± 0.1	+1.0	0.624
Waist circumference (cm)	105 ± 14	103 ± 13	-2.0	0.213	103 ± 8	105 ± 10	+2.0	0.198

* HIIT+PRT Post significantly different to HIIT+PRT Pre; [a] HIIT+PRT Pre significantly different to CON Pre; [b] HIIT+PRT Post significantly different to CON Post, P < 0.05; %Δ = % pre- to post change, group x time interaction. Data presented as mean ± SD

Table 3. Effects of 12 weeks of HIIT+PRT on aerobic, strength and flexibility parameters

Variable	HIIT+PRT Pre N=17	HIIT+PRT Post N=17	%Δ pre- to post	P	CON Pre N=8	CON Post N=8	%Δ pre- to post	P
VO2 @ 85% HR_{peak} (mL/kg-1/min-1)	20.8 ± 3	26.6 ± 4*	+27.9	<0.001	20.3 ± 3	20.2 ± 3[b]	-0.5	0.912
Predicted $VO2_{peak}$ (mL/kg-1/min-1)	24.0 ± 3	31.2 ± 4*	-7.7	0.001	124 ± 8[a]	125 ± 10	+0.8	0.212
Peak power (W)	120 ± 16	149 ± 20*	+24.2	<0.001	130 ± 18[a]	132 ± 16[b]	+1.5	0.877
Elapsed test time (min)	9.7 ± 2	12.5 ± 2*	+28.9	<0.001	9.3 ± 2	8.7 ± 2[b]	-6.5	0.312
Push up test (reps/min)	24 ± 15	25 ± 15	4.2	0.652	23 ± 10	24 ±11	4.4	0.87
Sit-reach test (cm)	17 ± 11	18 ± 11	5.9	0.462	18 ± 10	17 ± 11	-5.6	0.478
Curl Up Test (reps/min)	38 ± 9	43 ± 12*	13.2	0.002	49 ± 13	50 ± 13	2	0.612
Hand grip strength (kg)	38 ± 9	43 ± 12*	13.2	0.002	49 ± 13	50 ± 13	2	0.612

* HIIT+PRT Post significantly different to Pre; [a] HIIT+PRT Pre significantly different to CON Pre; [b] HIIT+PRT Post significantly different to CON Post, P < 0.05; %Δ = % change pre- to post, group x time interaction. Data presented as mean ± SD

the training sessions. Three participants from the CON group withdrew from the study (personal reasons, relocation) before the start of actual training. There were no changes in medication for any participant, and there were no adverse cardiac events in either group during the study.

The effects of the training programme on body mass, physiological parameters, aerobic capacity, muscular strength, muscular endurance and flexibility are presented in Tables 2 and 3. There were significant pre- to post-study increases in predicted VO_{2peak} (+30%), VO_{2peak} @ 85% predicted HR_{peak} (+27.9%), elapsed test time (ETT) (+28.9%), peak power (+24.2%) and decreases in systolic and diastolic blood pressure (-7.7%, -5% respectively), in the HIIT+PRT group ($P < 0.05$).

HIIT+PRT significantly decreased resting HR (-8%, $P = 0.02$), total cholesterol (-14%, $P = 0.04$), LDL (-36%, $P = 0.001$), TG (-27%, $P = 0.004$), fasting glucose (-7%, $P = 0.02$) (Figure 1), and body mass (-2%, $P = 0.04$), and increased Curl Up test average score (13%, $P = 0.04$), compared to baseline. There were no training effects on other parameters. The HIIT+PRT group had significantly lower LDL (P = 0.007), TG ($P = 0.01$) and glucose ($P = 0.04$), than the CON group at week 12 of the study ($P < 0.05$, Figure 1). The CON group showed a significant increase in TG after 12 weeks ($P = 0.04$) but no other significant changes occurred. Resting Rate-Pressure Product (RPP), the product of HR and SBP and an index of myocardial work, was also calculated for all groups pre- and post-study. The HIIT+PRT had a post-study mean resting value of 7230±1998 which was significantly lower (-14%) than the pre-study value of 8384±2008 ($P = 0.03$), but there was no difference between the Con group pre- and post-study values (8348±2004 and 8625±2112 respectively).

Discussion

Our principal findings were that 12 weeks of HIIT+PRT improved aerobic capacity, abdominal muscular strength, body composition, fasting cholesterol and glucose in male Phase 2 cardiac rehabilitation patients, compared to a standard exercise rehabilitation protocol. Few studies have investigated higher intensity exercise training during Phase 2 cardiac rehabilitation, as well as the combination of HIIT+PRT in this population. Meyer et al (1996), Rognmo et al (2004) and Wisløff et al (2007) found significantly increased aerobic capacity

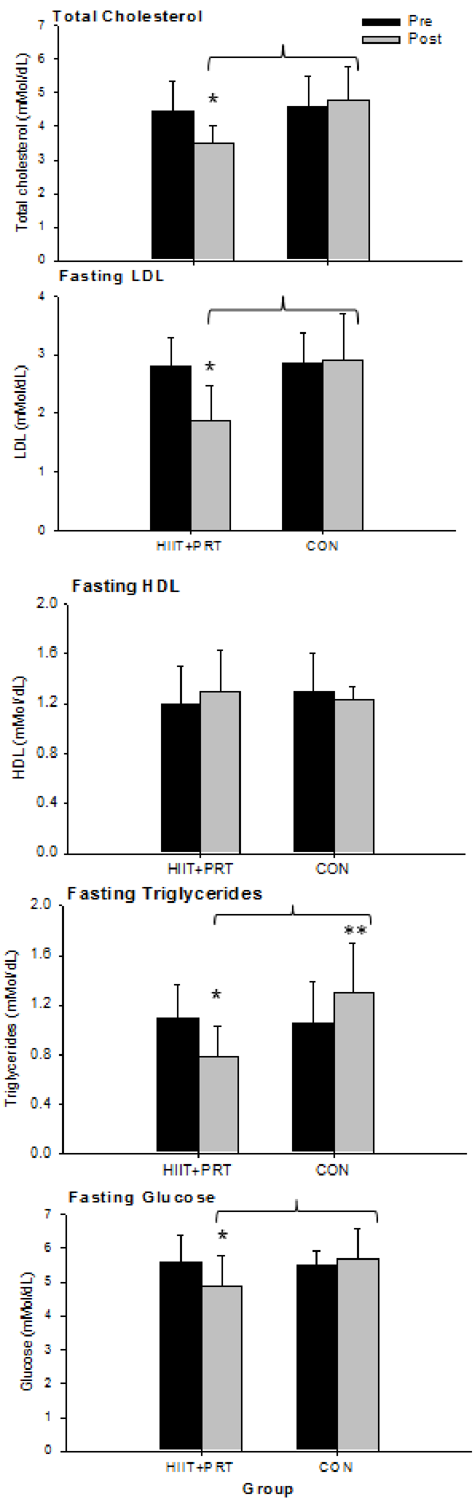

Figure 1. Changes in fasting lipids and glucose during 12 weeks of HIIT+PRT
*Significant decrease between week 0 and 12, HIIT+PRT group;
**Significant increase between week 0 and 12, CON group, $P < 0.05$
Significant group x time interaction at Week 12, $P < 0.05$. Data presented as mean ± SD

with HIIT >90% VO_{2peak} in CAD and heart failure patients, but very high intensity exercise may be a risk factor for further cardiac events and may not be sustainable for cardiac patients. The current pilot study aimed to find a sustainable exercise intensity high enough to significantly increase aerobic capacity, reduce cholesterol and blood glucose, and to improve muscular strength. Our findings support the use of HIIT to safely improve exercise capacity and some metabolic risk factors in CAD patients.

Compared to standard care, HIIT+PRT produced significant increases in VO_2 at 85% HR_{peak}, predicted VO_{2peak}, ETT and peak power output, demonstrating improvements in aerobic capacity. Adaptations to HIIT+PRT with no adverse cardiac symptoms suggest a greater tolerance to strenuous exercise, which is of particular benefit for patients wanting to participate safely in sporting activities, employment and/or ADL requiring intermittent vigorous activity (Meyer et al., 1996; Warburton et al., 2005). Increased VO_{2peak} is the strongest independent predictor of all-cause and cardiovascular mortality (Myers et al., 2002; Keteyian et al., 2008) and the current study reported a significant improvement in aerobic power. This finding is in agreement with other studies that reported an increase VO_{2peak} (by 37-42%) and exercise tolerance in several groups of cardiac patients with exercise intensities of 90-95% of VO_{2peak}, compared to standard care or moderate intensity exercise (Ehsani et al., 1981, 1982; Meyer et al., 1996; Rognmo et al., 2004; Wisløff et al., 2007). In the current study HIIT+PRT achieved significant improvements in 12 weeks, comparable to longer studies, (Ehsani et al., 1981, 1982; Warburton et al., 2005; Munk et al., 2009), suggesting that the improvements in cardiac function are dependent on training intensity rather than time course (Tanasecu et al., 2002). Such improvements in aerobic capacity may be attributed to adaptations in peripheral vasculature, skeletal and cardiac muscle (Wisløff et al., 2009), and may contribute to reduced myocardial oxygen demands, increased oxidative capacity and muscle metabolism in cardiac patients (Gibala et al., 2006; Wisløff et al., 2007). High intensity interval exercise also induces hypertrophy of cardiomyocytes (Kemi et al., 2005; Wisløff et al., 2009) which contributes to improved cardiac contractility.

HIIT+PRT significantly increased abdominal muscular strength but not other muscular strength/ endurance measurements. Our PRT regimen maintained the participants' overall strength but may not have incorporated enough training stimulus for cardiac patients who had already undertaken light resistance training for 12 weeks (Marzolini et al., 2008). Three sets of exercises, greater increases in resistance and/or more frequent PRT sessions may be needed to increase strength and endurance in CAD patients (Adams et al., 1999; Beniamini et al., 1999). There were no improvements in lower back and hamstring flexibility, perhaps because more frequent stretching (i.e. daily) was needed to improve flexibility in these areas. However, we did find significant but modest changes in body mass. It is possible that more frequent, longer duration or more intense, exercise sessions per week are required to significantly reduce adiposity, which is itself a cardiovascular disease risk factor (Slentz et al., 2007).

HIIT+PRT also reduced resting systolic and diastolic blood pressure. This finding has important clinical implications for "exercise as medicine" especially to those who suffer from hypertension. HIIT+PRT may produce greater peripheral capillary density and vasodilation, thus reducing peripheral vascular resistance and BP (Katz et al., 1997; Wislǿff et al., 2009). Moreover, the combination of significant reductions in resting SBP and HR, and RPP, indicates that the myocardial oxygen demand was significantly reduced by HIIT+PRT, which may in turn decrease the risk of myocardial ischemia (Meyer et al., 1996).

Ninety percent of our participants were using statins for control of blood lipids prior to and during the study but HIIT+PRT still produced significant improvements in LDL and TG. The reason for the non-increase in HDL is unclear, but it is a similar finding to Seki et al., (2008) who reported that 6 months of moderate intensity aerobic training in cardiac patients did not alter HDL levels. The STRRIDE study (Slentz et al., 2007) found that large volumes of vigorous intensity steady state exercise (23 kcal..kg^{-1}.wk^{-1}) produced the greatest increases in HDL compared to moderate intensity steady state exercise (14 kcal.kg^{-1}.wk^{-}1), possibly explained by tissue- and enzyme-specific effects of exercise at different intensities, for example on lipoprotein lipase. The current study HIIT may not have provided enough training volume to improve HDL but it did significantly reduce LDL and TG in the HIIT+PRT group, which is important, given that high LDL and TG are risk factors for cardiac events. HIIT+PRT may increase LDL and TG mobilisation from fat stores in response to higher catecholamine concentrations. In addition, others found non-significant decreases in LDL and TG after HIIT alone (no PRT) (Ehsani et al., 1982), and decreases in LDL but no changes in TG after moderate intensity aerobic training (Slentz et al., 2007; Perry et al., 2008; Seki et al., 2008). Our results indicate the combination of HIIT+PRT may be important for improvements in LDL and TG, and as such should be combined in Phase 2 cardiac rehabilitation. The CON group mean TG actually increased during the study. Although we asked participants not to change their diet during the study, some CON individuals may have done so, affecting their TG levels. It is also possible that after initial adaptations in the 12 weeks of Phase 2 cardiac rehabilitation prior to the study, the ongoing low/ moderate exercise regime of the CON group did not provide enough stimuli for maintaining TG levels.

Fasting blood glucose also improved following HIIT+PRT. This finding is important as it may contribute towards a reduction in global risk in insulin resistance and type 2 diabetes in this clinical population. HIIT+PRT may reduce blood glucose more than low-moderate intensity exercise due to the greater recruitment of type 2 glycolytic muscle fibres, increased mitochondrial capacity (Bajpeyi et al., 2009; Little et al., 2011), enhanced activity of GLUT-4 transporters, increased GLUT-4 protein content of skeletal muscle (Little et al., 2011) and an increased capacity for carbohydrate oxidation (Perry et al., 2008; Little et al., 2011). Increased GLUT-4 protein content is directly related to the increase in muscle glucose uptake at any given insulin concentration, thus improving glycaemic regulation (Little et al., 2011). HIIT+PRT may be of more benefit to cardiac patients with glucose intolerance or type 2 diabetes, than low/ moderate intensity aerobic exercise alone (Tjǿnna et al., 2008).

The current pilot study may have some potential limitations including the relatively small sample size and the group allocation. However, our results are comparable with studies of similar numbers, (Warburton et al., 2005; Wisløff et al., 2007). Further randomised controlled studies with a larger number of participants should be conducted to fully translate the results obtained in the current pilot study to the general CAD population.

In conclusion, twelve weeks of HIIT+PRT significantly reduced resting and exercise HR and BP, increased aerobic capacity, exercise tolerance, reduced blood lipids and glucose, and improved body composition in CAD men undertaking rehabilitation exercise. HIIT+PRT was well tolerated and would be of benefit for preparing participants for a return to employment and ADL requiring vigorous physical activity. This study provides further evidence of the efficacy and safety of mixed-model exercise regimens incorporating HIIT+PRT for cardiac and other clinical populations.

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Declaration of Conflicting Interest

The authors declare no conflicting interests.

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