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Study protocol for the FITR Heart Study: Feasibility, safety, adherence, and efficacy of high intensity interval training in a hospital-initiated rehabilitation program for coronary heart disease

Jenna Taylor[a,b], Shelley E. Keating, PhD[a], Michael D. Leveritt, PhD[a], David J. Holland, MBBS, PhD[a], Sjaan R. Gomersall, PhD[a,c], Jeff S. Coombes, PhD[a,*]

[a] School of Human Movement and Nutrition Sciences, The University of Queensland, St Lucia, Brisbane, QLD, 4072, Australia
[b] Cardiac Rehabilitation Department, The Wesley Hospital, Chasely St, Auchenflower, QLD, 4066, Australia
[c] School of Health and Rehabilitation Sciences, The University of Queensland, St Lucia, Brisbane, QLD, 4072, Australia

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ABSTRACT

Background: For decades, moderate intensity continuous training (MICT) has been the cornerstone of exercise prescription for cardiac rehabilitation (CR). High intensity interval training (HIIT) is now recognized in CR exercise guidelines as an appropriate and efficient modality for improving cardiorespiratory fitness, a strong predictor of mortality. However, the clinical application of HIIT in a real world CR setting, in terms of feasibility, safety, and long-term adherence, needs further investigation to address ongoing reservations. Furthermore, studies using objective measures of exercise intensity (such as heart rate; HR) have produced variable outcomes. Therefore we propose investigating the use of subjective measures (such as rating of perceived exertion (RPE)) for prescribing exercise intensity.

Methods: One hundred adults with coronary artery disease (CAD) attending a hospital-initiated CR program will be randomized to 1) HIIT: 4 × 4 min high intensity intervals at 15–18 RPE interspersed with 3-min active recovery periods or 2) MICT: usual care exercise including 40 min continuous exercise at a moderate intensity corresponding to 11–13 RPE. Primary outcome is change in exercise capacity (peak VO_2) following 4 weeks of exercise training. Secondary outcome measures are: feasibility, safety, exercise adherence, body composition, vascular function, inflammatory markers, intrahepatic lipid, energy intake, and dietary behavior over 12-months; and visceral adipose tissue (VAT) following 12 weeks of exercise training.

Conclusions: This study aims to address the ongoing concerns regarding the practicality and safety of HIIT in CR programs. We anticipate study findings will lead to the development of a standardized protocol to facilitate CR programs to incorporate HIIT as a standard exercise option for appropriate patients.

1. Introduction

Cardiac rehabilitation (CR) is a well established health service for the secondary prevention of heart disease, particularly following an acute event and/or hospitalization. Exercise training forms an integral part of lifestyle modification to improve health outcomes, and moderate intensity continuous training (MICT) has been the cornerstone of exercise prescription for CR. There is substantial evidence from several meta-analyses [1–4] that CR services involving exercise can significantly reduce cardiovascular disease and all-cause mortality by 20–35% and 20–40% respectively. Exercise capacity, measured directly as peak oxygen uptake (peak VO_2), has been shown to exert the largest influence on cardiovascular disease prognosis in this population [5]. High intensity interval training (HIIT), which involves alternating periods of high intensity exercise with light recovery exercise, has been shown to elicit greater improvements in peak VO_2 than moderate intensity continuous training (MICT) in people with coronary artery disease (CAD) [6–11] and remarkably in those with heart failure [12]. While HIIT is now recognized internationally in CR exercise guidelines as an appropriate and efficient modality for improving cardiovascular

Abbreviations: API, Application Programming Interface; CAD, Coronary artery disease; CR, Cardiac rehabilitation; DEXA, Dual energy x-ray absorptiometry; FMD, Flow-mediated dilation; FIT-TRACK, Fitness Tracking; HIIT, High intensity interval training; ^{1}H-MRS, Proton magnetic resonance spectroscopy; HR, Heart rate; HRpeak, Peak heart rate; MET, Metabolic equivalent; MICT, Moderate intensity continuous training; MRI, Magnetic resonance imaging; RPE, Rating of perceived exertion; TFEQ, Three factor eating questionnaire; VAT, Visceral adipose tissue; VO_2, Oxygen uptake

* Corresponding author.
E-mail address: jcoombes@uq.edu.au (J.S. Coombes).

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health in patients with CAD [13], a recent survey of CR centres by our team found safety concerns to be the leading barrier for implementing HIIT as standard care [14]. Although it has been demonstrated that higher exercise intensities elicit greater cardioprotective effects than MICT [15], there are still concerns that high intensity exercise may increase the risk of sudden cardiac death and myocardial infarction in susceptible persons [16].

The interest in use of HIIT for CR has resulted in large randomized controlled trials, such as the Saintex CAD study (n = 200) [17], the Smartex HF study (n = 220) [18] and studies by Aamot and colleagues (n = 83) [19], and Moholdt et al. (n = 59) [20]. These studies showed variable results, likely due to differing levels of adherence to prescribed exercise intensities of the HIIT and MICT protocols. To date, most studies utilize objective measures of exercise intensity (such as heart rate (HR)) rather than subjective measures (such as rating of perceived exertion (RPE)). RPE is more commonly used in Australian CR as few patients undertake a maximal exercise test to determine their true maximal HR [21]. Additionally, using a % of a measured 'maximal' HR may not be an accurate measure of intensity if maximal HR is not achieved during the graded exercise test, or beta blockade dose/timing is different between testing and training. Major limitations reported by the Saintex CAD study [17] was the lower average training HR of HIIT (88%HR_{peak}) and higher average training HR of MICT (80%HR_{peak}). Although training intensity was not determined by RPE in this study, the average reported RPE was 13.5 for HIIT and 12.5 for MICT. Additionally, while the Smartex HF study reported an average training HR of 90%HR_{peak} for HIIT, 51% of HIIT participants were training below their target HR. Both the Saintex CAD study [17] and Smartex HF study [18] highlighted the necessity in clinical practice to adjust objectively defined HR targets and workloads according to a patient's subjective feelings. Another limitation of the current literature is many studies also use only one exercise modality [17,20,22], which is not reflective of a real world setting where various exercise modalities are used.

Visceral adipose tissue (VAT) is also considered an important contributor to a lifetime risk of cardiovascular morbidity and mortality (cardiometabolic risk), in conjunction with traditional cardiovascular risk factors [23]. We have recently shown that exercise training can reduce both VAT and intra-hepatic lipid [24], and interval training protocols, of varying nature, have shown significant reductions in VAT of up to 48% in 8 weeks [25–28]. To our knowledge, no studies have investigated the effect of HIIT versus MICT on VAT in people with CAD.

The current study has been designed to assess feasibility, safety, adherence, and efficacy of HIIT compared with MICT, in a real-world CR setting. Specifically, it will assess whether HIIT is superior to MICT when subjective measures of exercise intensity (RPE) and various exercise modalities are utilized.

The primary aim of this study is to determine the effect of HIIT compared with MICT on cardiorespiratory fitness (VO_{2peak}) in patients with CAD undertaking a 4-week cardiac rehabilitation program.

The secondary aims of this trial are to investigate:

- If HIIT is equally feasible and safe, compared to MICT
- The effect of HIIT compared with MICT on cardiorespiratory fitness (VO_{2peak}) in patients with CAD following 3 months, 6 months, and 12 months of exercise training.
- The effect of HIIT compared with MICT in patients with CAD on exercise adherence, body composition, vascular function, inflammatory markers, intrahepatic lipid, energy intake, and dietary behavior following 4 weeks, 3 months, 6 months, and 12 months of exercise training.
- The effect of HIIT compared with MICT in patients with CAD on VAT following 3 months of exercise training.
- The effectiveness of HIIT and MICT coupled with technology (wrist worn monitors) on exercise adherence during an 8-week home-based program following a 4-week supervised cardiac rehabilitation program.

The feasibility and safety of prescribing HIIT within a real world environment is important as group settings can involve patients with varying levels of disease, functional limitation, and ability to exercise independently. We hypothesize that HIIT will be equally feasible and safe for a CAD population and HIIT will achieve superior outcomes for peak VO_2, VAT, and other cardiometabolic parameters. Additionally, we hypothesize the use of technology will improve exercise adherence during home-based training.

2. Methodology

2.1. Ethics and trial registration

The study protocol has been granted approval by UnitingCare Health Human Research Ethics Committee (#1522) and The University of Queensland Institutional Human Research Ethics Committee (#2015001938). The study adheres to the Helsinki Declaration and is prospectively registered with Australian New Zealand Clinical Trial Registry (anzctr.org.au) identifier: ACTRN12615001292561p (26 November 2015).

2.2. Study design and setting

The FITR Heart Study is a single centre prospective randomized controlled trial conducted within a tertiary hospital, which will facilitate voluntary participant recruitment and the supervised CR program component. All CR staff will receive training on how to integrate the intervention training into the current CR class timetable. All other aspects of the CR program will be unaffected. As this study runs parallel to clinical practice, all medical management, including medication prescription, will be at the discretion of the treating physician. Therefore these factors cannot be controlled but all changes will be documented and considered during analysis.

The study will consist of three stages (See Table 1)

Stage 1 will involve a 4-week supervised CR program, consisting of 2 supervised sessions and 1 home-based session per week. Four weeks was chosen as the current practice in this facility is 8–10 supervised exercise sessions throughout the cardiac rehabilitation program. Participants will receive education on how to monitor and progress their exercise training appropriately. RPE will be the primary method for prescribing exercise intensity for both groups.

Stage 2 will involve an eight-week home-based program with weekly support, consisting of at least 3 home-based sessions per week of their randomized training. Participants will be asked to submit exercise training records via email on a weekly basis and will be provided with support and motivation if they do not adhere with the exercise protocol. During this stage, participants will be further randomized to FIT-TRACK or non-FIT-TRACK groups for the duration of Stage 2. FIT-TRACK participants will be provided with a wrist worn **FIT**ness **TRACK**ing HR monitor (Fitbit Charge HR™, Fitbit Inc., San Francisco, United States), and instructions for use and integration with their smart phone or computer. Participants are instructed to use the device as they desire to monitor and track their exercise program and overall physical activity levels. Data will be automatically extracted from the Fitbit Application Programming Interface (API) using software developed by our team. The goal of FIT-TRACK is to use technology to increase exercise adherence following a CR program.

Stage 3 will involve maintenance of the Stage 2 program, whereby participants will be encouraged to continue their home-based exercise program but without weekly support.