Impact of training intensity on cardiovascular responses in patients with coronary artery disease: extended systematic review and meta-analysis

Impacto de la intensidad del entrenamiento en las respuestas cardiovasculares en pacientes con enfermedad arterial coronaria: revisión sistemática extendida y metaanálisis

Authors

Noor Fatihah Ilias [1]
Mazlifah Omar [1]
Sazzli Shahlan Kasim [1,2]
Hashbullah Ismail [1]

[1] MARA University of Technology (Malaysia)
[2] Cardiovascular Advancement and Research Excellence Institute (CARE Institute) MARA University of Technology (Malaysia)

Corresponding author:
Hashbullah Ismail
hashbullah@uitm.edu.my

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Abstract

Introduction: Intensity plays a major role for optimal benefits from exercise for coronary artery disease (CAD) patients. The superior effect between high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) is still uncertain.
Objective: To investigate the effect of different aerobic exercise intensities on exercise capacity, hs-CRP, and lipid profile among CAD patients.
Methodology: An extensive search was carried out in databases such as PubMed, Scopus, ClinicalKey and ScienceDirect (from the earliest data available to May 2024) for randomised controlled trials comparing HIIT and MICT among CAD patients. Mean differences and 95% confidence interval (CI) were calculated using random effect model in Revman version 5.4, a funnel plot was used for publication bias and heterogeneity was reported using I_2 statistics.
Results: Thirty-five studies were identified, which included 1879 CAD patients. HIIT resulted in a significant improvement in peak VO_2 weighted mean difference (1.39 ml/kg/min, p <0.00001, 95% CI: 0.87 – 1.90, n = 1461, I_2=0%) compared with MICT. Moreover, HIIT resulted in a significant improvement in total cholesterol (TC) weighted mean difference (-0.08, p = 0.03, 95% CI: -0.15 – -0.01, n = 738, I_2=26%) compared with MICT. Both intensities improved in hs-CRP, LDL-C, HDL-C, and TG but there were no statistically significant differences.
Conclusions: This study confirmed that HIIT provides greater improvement in peak VO_2 and may be an important part of an effective exercise program for CAD patients. More well-designed, randomised controlled trials are needed to establish the safety of HIIT via inflammatory markers.

Keywords

Exercise capacity; high intensity interval training; hs-CRP; lipid profiles; moderate intensity continuous training.

Resumen

Introducción: La intensidad juega un papel importante para obtener el máximo beneficio del ejercicio en pacientes con enfermedad coronaria (CAD). El efecto superior entre el entrenamiento de intervalos de alta intensidad (HIIT) y el entrenamiento continuo de intensidad moderada (MICT) aún es incierto.
Objetivo: Investigar el efecto de diferentes intensidades de ejercicio aeróbico en la capacidad de ejercicio, hs-CRP y el perfil lipídico entre pacientes con CAD.
Metodología: Se realizó una búsqueda exhaustiva en bases de datos como Pebmed, Scopus, ClinicalKey y ScienceDirect (desde los datos más antiguos disponibles hasta mayo de 2024) para ensayos controlados aleatorios que comparan HIIT y MICT entre pacientes con CAD. Las diferencias medias y el intervalo de confianza (IC) del 95% se calcularon utilizando el modelo de efectos aleatorios en Revman versión 5. 4, se utilizó un gráfico de embudo para el sesgo de publicación y la heterogeneidad se informó utilizando estadísticas I_2.
Resultados: Se identificaron treinta y cinco estudios, que incluyeron a 1879 pacientes con CAD. El HIIT resultó en una mejora significativa en la diferencia media ponderada del VO_2 pico (1.39 ml/kg/min, p <0.00001, IC del 95%: 0.87 – 1.90, n = 1461, I_2=0%) en comparación con el MICT. Además, el HIIT resultó en una mejora significativa en el colesterol total (CT) con una diferencia media ponderada (-0.08, p = 0.03, IC del 95%: -0.15 – -0.01, n = 738, I_2=26%) en comparación con el MICT. Ambas intensidades mejoraron en hs-CRP, LDL-C, HDL-C y TG, pero no hubo diferencias estadísticamente significativas.
Conclusiones: Este estudio confirmó que el HIIT proporciona una mayor mejora en el VO_2 pico y puede ser una parte importante de un programa de ejercicio efectivo para pacientes con CAD. Se necesitan ensayos controlados aleatorizados mejor diseñados para establecer la seguridad del HIIT a través de marcadores inflamatorios.

Palabras clave

Capacidad de ejercicio; entrenamiento de intervalos de alta intensidad; hs-CRP; perfiles lipídicos; entrenamiento continuo de intensidad moderada.

Introduction

Coronary artery disease (CAD) also called ischemic heart disease (IHD), constitutes a significant health burden worldwide. According to data from the Global Burden of Disease Study (GBDS) in 2022, the biggest worldwide burden of cardiovascular disease (CVD) was CAD, with 315,390,626 prevalence cases and 9,239,181 deaths (Mensah et al., 2023). Due to the alarming prevalence of CAD worldwide, effective exercise intervention strategies are urgently needed. As an important part in the management of CAD patients, exercise has been a secondary approach for the treatment and prevention a variety of chronic conditions (Thompson et al., 2020). Current exercise interventions for CAD require a mechanistic approach and should be individualized treatment recommendations. Exercise prescription that optimises improvement in exercise capacity is a critical consideration in determining the efficacy of an exercise programme (Taylor et al., 2021). Generally, designing effective exercise interventions should be directed towards optimising exercise capacity as assessed by maximum oxygen uptake (peak VO_2) to improve the overall health of people with CAD.

A recent systematic review and network meta-analysis highlighted greater peak VO_2 improvement after high intensity interval training (HIIT) as compared to any type of exercise among CAD patients (Gomes-Neto et al., 2024). Another systematic review and meta-analysis also suggested that HIIT is more beneficial compared to moderate intensity continuous training (MICT) in increasing peak VO_2 in patients with CAD (Pattyn et al., 2018). Moreover, another systematic review and meta-analysis confirmed higher intensity of exercise does not appear to lower exercise adherence or increase mortality rates compared with other exercise intensities (Ismail et al., 2013). HIIT frequently recommended for patients with CAD, typically achieves around 80 - 95% heart rate reserve (HRR) or 15 - 18 a rating perceived exertion (RPE) or 80 - 90% of their peak VO_2 (Taylor et al., 2021). The data indicate that higher exercise intensities provide substantial advantages without jeopardising exercise adherence or worsening mortality risks.

However, with several published systematic reviews and meta-analyses that agreed with the effectiveness of HIIT, the American Heart Association (AHA) declared that HIIT is one of the activities that is potentially maladaptive, especially prescribing the exercise for frail individuals (Franklin et al., 2022). Intense exercise leads to higher pro-inflammatory levels and thus might increase the risk of CV events, and it was suggested that moderate to vigorous exercise is more appropriate to achieve maximum benefit (Cerqueira et al., 2020). Moreover, moderate intensity exercise with durations longer than 30 minutes may be beneficial to prevent/ reduce the pro-inflammatory response (Baygutalp et al., 2021). MICT commonly prescribed for CAD patients was reaching approximately 60 - 85% HRR or 11 - 14 RPE or 60 - 75% of their peak VO_2 (Taylor et al., 2021). Increased pro-inflammatory markers such as hs-CRP facilitate systemic inflammation, compromising cardiac and vascular function and increasing the risk of myocardial infarction (Denegri & Boriani, 2021).

This argument requires consideration due to its critical relevance to the safety of CAD patients. Exercise may not provide the desired results if there is a greater improvement in peak VO_2 but also an increase in inflammatory markers. Inflammation serves as a mechanism that connects changes in traditional risk factors with alterations in the biological processes of the arterial wall, ultimately leading to atherosclerosis (Libby, 2012). Hence, reporting on the safety of exercise interventions should be based on clinical evidence, such as high sensitivity C-reactive protein (hs-CRP). The rational, by understanding inflammatory markers, enables fast and precise non-invasive identification of mortality risk in CAD patients, allowing the tailoring of primary and secondary CAD prevention (Netto et al., 2022). Even though the interest among researchers grows, knowledge about cardiac and inflammation is still limited (Alfaddagh et al., 2020; Netto et al., 2022). Until recently, there was no direct evidence available in controlling inflammation that could improve outcomes in patients with atherosclerosis (Libby, 2021). Generally, the optimal exercise intensity for CAD patients remains elusive. Therefore, the objective of this study is to expand on previous publications by conducting another systematic review and meta-analysis comparing the efficacy of HIIT and MICT on peak VO_2, hs-CRP and lipid profile among CAD patients.

Method

Study protocol

The systematic review and meta-analysis was conducted in accordance with the guidelines from Preferred Reporting for Systematic Review and Meta-Analysis Protocols (Moher et al., 2009). The international prospective register of systematic reviews (PROSPERO) was preliminarily searched for similar literature review protocols. No similar review was identified.

Search strategy

A literature search in the electronic PubMed, Scopus, ClinicalKey, and ScienceDirect, using the following keywords: #1 “High intensity interval training” [Mesh] OR “Aerobic interval training” OR “high intensity exercise” [All fields] AND #2 “Moderate intensity continuous training” [Mesh] OR “continuous training” [All fields] AND #3 “aerobic exercise” OR “cardiovascular exercise” OR “cardiovascular training” [All fields] AND #4 “coronary artery disease” [Mesh] OR “ischemic heart disease” OR “coronary heart disease” AND “post myocardial infarction” AND “post percutaneous coronary intervention” AND “post coronary artery bypass graft”, #5 search #1 AND #4, #6 search #2 AND #4, #7 search #3 AND #4, and #8 search #1 AND #2 AND #3 AND #4. Articles were systematically searched simultaneously by two different independent investigators from the earliest available date up to May 2024, without language restrictions.

Furthermore, the reference list of the prior systematic review and meta-analysis was examined for additional qualifying trials. Grey literature was searched via the Proquest database. Hand searching on peer-reviewed studies was also conducted. For inaccessible full-text papers, we requested assistance via the Interlibrary Loan (UiTM library) and directly emailed the corresponding author.

Selection criteria

Randomized control trials with an English full text comparing the effects of HIIT and MICT in patients with CAD. CAD is defined as patients who have experienced myocardial infarction (MI) or have undergone a percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) (Wewege et al., 2018). HIIT training was limited to interval durations, with the intensity classified as being 70 – 85% VO_2 max or 75 - 90% HR max or > 70 - 85% of HRR or >14-16 RPE, 20 Borg scale (Hansen et al., 2022) or report intensity as high intensity. Meanwhile, MICT program includes continuous aerobic exercise is classified as 40 – 69% VO_2 max or 55 - 74% HR max or > 40 - 69% of HRR or >12-13 RPE, 20 Borg scale (Hansen et al., 2022) or report intensity as moderate intensity. Any form of aerobic exercise conducted, such as walking, running, cycling, stair climbing, rowing, elliptical, and swimming will be included with a minimum training duration of 4 weeks and sessions need to be either supervised or non-supervised with follow-up. Studies that include supplemental resistance training such as abdominal crunch, russian twist, bird dog, cat and camel will generally be included in this study, with both groups needing to undergo the same training regime.

These criteria provide a consistent comparison of the effects of HIIT and MICT in CAD patients, integrating diverse aerobic exercises and allowing interventions complemented with weight training to encompass a wider array of real-world programs while preserving group uniformity. For instance, where multiple publications present different data from the same overall study based on the clinical trial registration number or the same methodology and the same participants, only the study that represents the necessary data will be included. If both studies report the same variables with slightly different values, further clarification with the third author is required and the result is based on group consensus. Any study that did not fit any of the aforementioned criteria was excluded.

Data extraction and synthesis

The primary outcome for this meta-analysis was a change in peak VO_2 in ml/kg/min. Secondary outcomes included hs-CRP and lipid profiles which are low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), triglyceride (TG) and total cholesterol (TC). The two main authors (NFI and HI) independently extracted the characteristics of patients, exercise intervention, primary and secondary outcomes. Results were compared and discrepancies were resolved with the third and fourth authors (MO and SSK) after manual agreement.

All the information related to the research objective, including the exercise intervention protocol which is frequency, intensity, time and type was extracted from each of the reviewed articles. Moreover, data extracted from the selected study were the number of participants, mean age, medications, gender, severity of CAD and culprit lesion. Texts and tables have been used to provide a descriptive summary and explanation of study characteristics and findings. Subgroup analysis was performed to differentiate between short and long HIIT. Moreover, the result with a high I_2 was reassessed following the exclusion of the outliers.

Study quality

Selected articles were assessed using a Tool for the Assessment of Study Quality and Reporting in Exercise (TESTEX) (Smart et al., 2015). This tool consists of a 15-point scale, which is 5 points for study quality and 10 points for reporting. TESTEX is a comprehensive tool to assess the quality of the study, thus qualifying inferences and conclusions in the exercise science studies. The higher score reflects the high quality of the study. No trials were excluded based on quality.

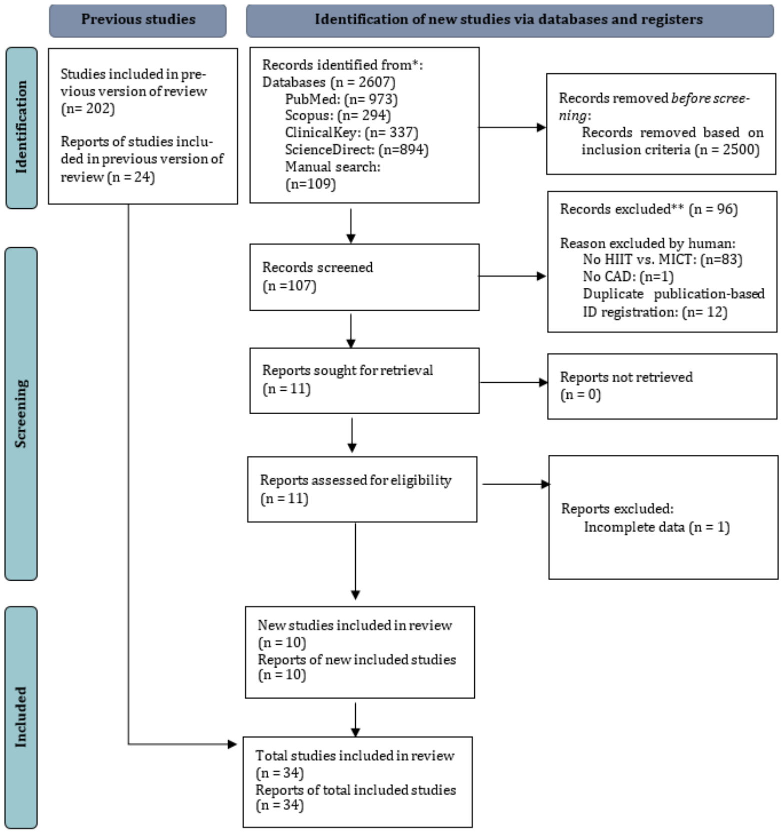
Statistical analysis

Statistical analyses were performed using random effect-model Review Manager Software (RevMan 5.4; Cochrane Collaboration, Oxford, UK). To assess the improvement across all outcome measures, we analysed the differences between pre- and post-intervention results. Descriptive data were reported as mean difference (MD) ± standard deviation (SD) and 95% confidence interval (CI) with the threshold for significance set to $p < 0.05$. Additionally, weighted mean differences (WMD) are used to further substantiate the findings. Publication bias was assessed using a funnel plot and the standard error (SE). A high SE indicates less reliability and less precision in the study, which likely results are considered premature. Once there is a presence of publication bias, the magnitude of bias or degree of heterogeneity is determined using I_2 statistics. Heterogeneity of 25% is considered low, 50% is considered moderate and 75% is considered high (Du et al., 2021). In instances of significant heterogeneity, the source of elevated I_2 should be examined, and a subgroup analysis excluding outliers should be performed (Pathak et al., 2020). If heterogeneity is small, the results can be interpreted as the objective of the study. If the data is unavailable, we will reach out to the author and exclude it from the study if they do not provide the information.

Results

A Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram for our literature search and selection is presented in Figure 1. The initial search has identified 2607 potentially relevant studies of which 107 were retrieved for full-text review. From this, 83 studies were excluded as did not compare HIIT and MICT, 1 study on heart failure and 12 studies produce more than one publication totaling 11. Another study was removed due to incomplete data after contacting the author. In total, 24 studies from previous systematic review and meta-analysis were included. We conducted our own search, resulting in the inclusion of an additional 10 publications for quantitative analysis, bringing the total to 34.

Figure 1. PRISMA flow diagram



Characteristics of the participant and study design

All 24 studies from the latest systematic review and meta-analysis by Gomes-Neto et al. (2024) were included, an additional 11 studies were analyzed in this work, totaling 35 studies. A summary of the 35 studies is presented in Table 1. A total of 1879 CAD patients were randomized to either HIIT or MICT. The mean age ranges from 47.83 to 69.6 years. Most studies included both sexes, but there was an overall predominance of men at 84.6% (n = 1454) and women at 15.4% (n = 263) at baseline. Four studies included only men (Benetti et al., 2010; Garneau et al., 2023; Ghardashi-Afousi et al., 2018; Warburton et al., 2005) and one study included only women (Lee et al., 2019). The number of participants in the included studies ranges from 6 to 154 per group.

Table 1. Characteristics of the Participants and Study Design

No.	Author, Year	Participants	Exercise Intervention (Report)			
			Frequency	Intensity	Duration	Type
1	Goncalves et al, 2024	CAD patients 8 weeks post angioplasty with LVEF > 45%	3x/week (6 weeks)	HIIT: 85 – 95% HR max MICT: 70 – 75% HR max	HIIT: 4 min x 4: 1 min RI_TD: 28 - 35 min MICT: 27.5 min TD: 35.5 – 42.5 min	Treadmill
2	McGregor et al, 2023	AMI, CABG, angiographically documented CAD and/or elective PCI with LVEF>35%	2x/week (48 weeks)	HIIT: > 85% HR max MICT: 40 – 70% HRR	HIIT: 1 min x 10: 1 min RI_TD: 29 – 34 min MICT: 20 – 40 min TD: 30 – 55 min	Bicycle ergometer
3	Garneau et al, 2023	CAD: post PCI or CABG in the previous 4 – 18 weeks	2x/week (12 weeks)	HIIT: 85 – 95% HR max MICT: HR 20 – 40 bpm above RHR	HIIT: 4 min x 4: 3 min RI_TD: 45 - 50 min MICT: 30 min TD: 55 – 60 min	Treadmill, cycle ergometer, elliptical etc or aerobic dance/movement sequences
4	Reed et al, 2022	Post PCI or CABG within the previous 18 weeks	2x/week (12 weeks)	HIIT: 85 – 95% HR max MICT: HR 20 – 40 bpm above RHR, RPE: 12-16	HIIT: 4 min x 4: 3 min RI_TD: 40 - 45 min MICT: 15 - 30 min TD: 45 – 60 min	HIIT: treadmill, cycle ergometer, elliptical & etc MICT: Nordic Walking continuously or intermittent walking

5	Eser et al, 2022	Post STEMI treated with PCI within 4 weeks.	3x/week (12 weeks)	HIIT: 90 – 95% HR max, RPE:>15 MICT: RPE 13-14	HIIT: 4 min x 4: 3 min RI_TD: 38 min combined 2xHIIT & 1xMICT MICT: 30 min, TD: 38 min	Cycle ergometer
6	Valentino et al, 2022	History of MI, post CABG and/or PCI	6 sessions within 4 weeks supervised & 3x/ week (8 weeks unsupervised)	HIIT: RPE 14 – 15 (vigorous pace) MICT: RPE 11 - 13	HIIT: 72 stairs climbing x 3: 90 sec RI_TD: NR MICT: 30 min, TD: 40 min	HIIT: stair climbing. MICT: pace walking, stationary cycle ergometer & treadmill
7	Okur et al, 2022	Post PCI or CABG with LVEF >50%	5x/week (24 sessions)	HIIT: 85 – 100% max workload MICT: 50 – 70% max workload	HIIT: short, 1 min x 10: 1 min RI_TD: NR HIIT: long, 4 min x 4: 3 min RI_TD: NR MICT: 20 - 30 min, TD: 40 - 50 min	Cycle
8	Yakut et al, 2022	3 months & 1 year after MI, LVEF>50%	2x/week (12 weeks)	HIIT: 85 – 95% HRR, RPE: 15- 18 MICT: 70 – 75% HRR, RPE: 12- 14	HIIT: 4 min x 4: 3 min RI_TD: NR MICT: 20 - 45 min, TD: 40 - 65 min	Home-based exercise: walking uphill, brisk walking, jogging, crouching, going up and down the front-side step.
9	Taylor et al, 2021	Angiographically proven CAD, at least 4 weeks post AMI, >3 weeks PCI and >4 weeks CABG.	Stage 1: 3x/week (4 weeks); 2 supervised & 1 home-based. Stage 2: 3x/week (8 weeks); home-based (weekly support). Stage 3: 3x/week (8 weeks); home-based (no routine support).	HIIT: 85 – 95% HR max, RPE: 15 – 18 MICT: 65 – 75% HR max, RPE: 11 – 13	HIIT: 4 min x 4: 3 min RI_TD: NR MICT: NR, TD: 40 min	Variety of aerobic exercise machines. Home-based: outdoor walking, bike, treadmill, elliptical
10	Lee et al, 2021	Postmenopausal women with documented CAD, LVEF >35%, >weeks post MI and PCI, >8 weeks CABG.	5x/week (24 weeks) HIIT:3 supervised, 2 unsupervised.	6 weeks MICT, continue with HIIT: 90 – 95% HR max, RPE>17. MICT: 60 – 80% VO_2 max	HIIT: 4 min x 4: 3 min RI_TD: 35 – 45 min MICT: NR, TD: 30 - 40 min	Walking or jogging on treadmill
11	Taraldsen et al, 2020	Angina pectoris or non-ST elevation ACS requiring revascularization with stent implantation.	3x/week (12 weeks)	HIIT: 85 – 95% HR max MICT: 70% HR max	HIIT: 4 min x 4: 3 min RI_TD: 38 min MICT: NR, TD: 46 min	Walk or run on treadmill
12	Tagashira et al, 2020	Post AMI	3x/week (16 weeks) 1 supervised, 2 unsupervised	HIIT: Over anaerobic threshold (1/3 HR between anerobic threshold (AT) and respiratory compensation MICT: AT	HIIT: NR TD:30 min MICT:TD: 30 min	Exercise bike with supplemented half squats from the chair while sitting, standing calf raise and hip abduction for 10 times.
13	Jaureguizar et al, 2019	CAD with 6 to 12 weeks following angina pectoris or MI, post PCI, post CABG.	3x/week (over 8 weeks) 24 sessions	HIIT: 50% of maximum load of steep step test MICT: 1st ventilatory threshold to +10%	HIIT: 20 sec x 15 to 30 rep; 40 sec R1_TD: 40 min MICT: 15 – 30 min, TD: 40 min	Cycle ergometer
14	Heber et al, 2019	Post ACS followed by PCI	4x/week (12 weeks) *HIIT + MICT 2 + 2	HIIT + MICT: 100% peak power output (PPO) MICT: 60% PPO	HIIT + MICT: 1 min X 15, 1 min RI + 35 min continuous. TD: 45 min MICT: 35 min, TD: 45 min	Bicycle ergometer
15	Biodin et al, 2019	ACS within 6 weeks, complete revascularization with residual stenosis >50%, no residual left main stenosis>40%, LVEF >40%.	2-3x/week (12 weeks) 36 sessions	HIIT: 100% PPO MICT: 60% PPO	HIIT: 10 min X 3 (15: 15 sec work rest ratio), 4 min rest in between, TD: 48 min MICT: 38 min, TD: 48 min	Bicycle ergometer
16	Ghardashi-Afousi et al 2018	Post CABG past 6 weeks, LVEF>40% after surgery	3x/week (6 weeks)	HIIT: 85 – 96% HR max MICT: 70% HR max	HIIT: 2 min X 10, 2 min RI, TD: 50 min MICT: 40 min, TD, 50 min	Walking or running on treadmill & stretching
17	Abdelhalem et al, 2018	LVEF > 35% - 50%, fully revascularized by PCI	2x/week (12 weeks)	HIIT: 85 – 96% HRR MICT: 40 - 60% HRR	HIIT: 2-5 min high, NR number of interval, RI, TD; 40 – 45 min MICT: 30 – 35 min, TD: 40 – 45 min	Treadmill
18	Choi et al, 2018	First time STEMI treated with PCI	1-2/week (18 sessions)	HIIT: 85 – 100% HR max	HIIT: 4 min X 4, 3 min R1, TD: 38 min MICT: 28 min, TD: 38 min	NR

				MICT: 60 – 70% HR max		
19	Pattyn et al, 2017	Angiographically documented CAD or 4- 12 weeks following AMI, PCI & CABG & LVEF >40% SAINTEX-CAD	3x/week (12 weeks)	HIIT: 85 – 95% HR max MICT: 70 – 75% HR max	HIIT: 4 min X 4, 3 min R1, TD: 38 min MICT: 38 min, TD, 47 min	Bicycle
20	Pernick et al, 2017	Post MI treated with PCI or CABG during the previous 10 months	2x/week (12 weeks)	HIIT: 60 – 85% VO_2 max; RPE, 14 - 16 MICT: 50 – 60% VO_2 max, RPE; 12-14	HIIT: 2 min x 8, 2 min RI for 30 min. MICT: 41 min	Treadmill, stationary bicycle & rowing
21	Santi et al, 2017	Anterior wall MI with exclusive involvement of anterior descending artery proximal third and asymptomatic ventricular dysfunction with LVEF<50%.	3x/week (12 weeks)	HIIT: 85 – 95% HR max MICT: 60 – 70% HR max	HIIT: 4 min X 4, 3 min R1, TD: 38 min MICT: 30 min, TD, 40 min	Treadmill
22	Moblus Winkler et al, 2016	Stable CAD for at least 8 weeks	5x/week (4 weeks) HIIT: 4x daily for 30 min MICT: 6- 8 exercise/ day for 20 min each.	HIIT: 95% ischemia/angina-free exercise capacity MICT: 60% ischemia/angina-free exercise capacity	HIIT: NR MICT: NR	NR
23	Kim C et al, 2015	Post AMI treated PCI (3 weeks) with drug- eluting stenting	3x/week (6 weeks)	HIIT: 85 – 95% HRR MICT: 70 – 85% HRR	HIIT: 4 min X 4, 3 min R1, TD; 45 min MICT: 25 min, TD: 45 min	Walking on treadmill
24	Prado et al, 2015	Stable CAD diagnose with angiography	3x/week (12 weeks)	HIIT: respiratory compensation point (RCP) MICT: ventilatory anaerobic threshold (VAT)	HIIT: 3 min X 7,3 min RI, TD; 42 min MICT: 50 min, TD; 60 min	Treadmill
25	Cardozo et al, 2015	History of CAD diagnosed by AHA, LVEF>50%	3x/week (16 weeks)	HIIT: 90% HR max MICT: 70 – 75 %HR max	HIIT: 2:2 min work rest ratio for 30 min, TD; 40 min MICT: 30 min, TD; 40 min	Treadmill
26	Keteyian et al, 2014	LVEF>40%, >3 weeks following M1 or PCI, >4-week post CABG	3x/week (10 weeks)	HIIT: 80 – 90% HRR MICT: 60 – 70% HRR	HIIT: 4 min X 4, 3 min R1, TD; NR MICT: 30 min, TD: 40 min	Treadmill
27	Tschentscher et al, 2014	Stable CAD with or without MI, PCI, or CABG.	3x/week (6 weeks)	HIIT: 85 – 95% HR max PRY: 65 – 95% HR max MICT: 65 – 85% HR max	HIIT: 4 min X 4, 3 min R1, TD; 25 PYR: 8 min x 3, 2 min RI, TD; 28 min MICT: 33 min, TD; 43 min	Cycle ergometer
28	Currie et al, 2013	Angiographically documented stenosis >50% in at least 1 major artery, MI, PCI, or CABG	2x/week (12 weeks)	HIIT: 80 – 110% (PPO) MICT: 51 – 65% (PPO)	HIIT: 1 min X 10, 1 min RI, TD; NR MICT: 30 – 50 min, TD; NR	Cycling
29	Mohaldt et al, 2011	Suffered a MI 2 - 12 weeks.	3x/week (12 weeks) 2 supervised, 1 home exercise	HIIT: 85 – 95% HR max MICT: vigorous	HIIT: 4 min X 4, 3 min R1, TD; 38 min MICT: 35 min, TD; 60 min	HIIT: Treadmill MICT: walking, jogging, lunges, and squats *Encourage exercise vigorously
30	Bouri et al, 2011	Post CABG in the previous 4 months	3x/week (8 weeks)	HIIT: 80 – 90% VO_2 max MICT: 50 - 70% HR max	HIIT: 4 min X 4, 3 min R1, TD; 33 min MICT: 41 min, TD: 49 min	Walking on treadmill
31	Benetti et al, 2010	Post AMI in the previous 12 months	5x/week (12 weeks)	HIIT: 85% HR max MICT: 75% HR max	HIIT: NR, TD; 45 min MICT: NR, TD; 45 min	Treadmill supplemented with stretching and muscular strength exercises
32	Mohaldt et al, 2009	4 – 16 weeks post CABG	5x/week (4 weeks)	HIIT: 90% HR max MICT: 70% HR max	HIIT: 4 min X 4, 3 min R1, TD; 38 min MICT: 46 min, TD; NR **Additional exercise variety exercise and intensities 45 – 60 minutes	Walking on treadmill
33	Amudsen et al, 2008	CAD had been documented at least 1 major artery	(10 weeks)	HIIT: 85 – 95% HR max	HIIT: 4 min X 4, 3 min R1, TD; 38 min MICT: 41 min, TD; 51 min	Uphill treadmill walking

				MICT: 50 – 60% VO_2 max		
34	Warburton et al, 2005	>6 months post CABG	2x/week (16 weeks)	HIIT: 85 - 95% HRR MICT: 65% HRR	HIIT: 2: 2 min work rest ratio for 30 min, TD; 50 min MICT: 30 min, TD; 50 min	Treadmill, stair climbing, arm and leg ergometer
35	Rognmo et al, 2004	Angiographically documented CAD at least 1 major artery, post MI, post CABG or PCI or ischemia during exercise ECG.	3x/week (10 weeks)	HIIT: 85 – 95% HR max MICT: 50 – 60% VO_2 max	HIIT: 4 min X 4, 3 min R1, TD; 33 min MICT: MICT: 41 min, TD; 49 min	Uphill treadmill walking

Abbreviations: Peak VO_2, peak volume of oxygen; HIIT, high intensity interval training; MICT, moderate intensity continuous training; PYR, pyramid; RI, rest interval; TD, total duration; CAD, coronary artery disease; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; MI, myocardial infarction; AMI, acute myocardial infarction; LVEF, left ventricular ejection fraction; STEMI, ST elevation myocardial infarction; AHA, American Heart Association; NR, not reported

Most of the CAD patients in this study underwent percutaneous coronary intervention (PCI). Data showed that in HIIT, 58.6% post PCI, 23.6% of participants undergo coronary artery bypass grafting (CABG) and 17.8% of participants undergo conservative treatment. For the MICT group, 68% post PCI, 25.5% post CABG and 6.5% conservative treatment. Most of the CAD patients underwent PCI as a main intervention. All studies continue the medication as prescribed. Focusing on statin, more than 90% of participants from HIIT and MICT take lipid-lowering drugs to manage blood lipid. Nine of these included studies were all patients on statins (Eser et al., 2022; Keteyian et al., 2014; Kim et al., 2015; Lee et al., 2019; Möbius-Winkler et al., 2016; Moholdt et al., 2012; Taraldsen et al., 2021; Valentino et al., 2022; Villelabeitia-Jaureguizar et al., 2019). Statin is highly prescribed to control lipids in CAD patients.

Out of 35 studies, only 4 reported culprit lesions (Abdelhalem et al., 2018; Eser et al., 2022; Tagashira et al., 2021; Taraldsen et al., 2021). Left anterior descending (LAD) is mostly affected followed by right coronary artery (RCA) and left circumflex artery (LCX) in both HIIT and MICT. Most of the studies stated that participants had a positive risk factor for cardiovascular disease (CVD) such as hypertension (65.7%), dyslipidemia (50%), type II diabetes (65.7%), smoking (55.6%), obesity (45.7%), family history (11.1%) and excess alcohol (2.8%).

Exercise intervention characteristics

The parameters used in designing the exercise intervention were consistent in most of the studies. Aerobic exercise is prescribed using a variety of modalities such as treadmills, bicycle ergometers, ellipticals, dance movements, walking outdoors and stair climbing with a frequency range of 1 to 5 times a week up to a 1-year follow-up. Methods for prescribing exercise intensity to CAD patients vary, probably depending on the available resources. In this work, the intensity is determined using heart rate reserved (HRR), heart rate maximum (HR max), anaerobic threshold (AT), rating perceived exertion (RPE), max workload, maximum volume of oxygen (VO_2 max), peak power output (PPO), respiratory compensation point (RCP), and ischemia free exercise capacity. A standard range of intensity prescribed for HIIT and MICT among CAD patients is presented in Table 2. HIIT training mostly prescribes more than 80% of intensity, except Villelabeitia-Jaureguizar et al. (2019) suggested that at 50% of peak workload from a steep ramp test. For MICT, intensity is prescribed in the range of 40 to 75%, except for studies by Kim et al. (2015), Taylor et al. (2020) and Tschentscher et al. (2014) prescribe up to 80% of intensity.

Table 2. Range of Intensity Prescribed for HIIT and MICT among CAD Patients

Method of intensity prescribed	HIIT	MICT
Heart rate maximum (HR max)	85 – 100 %	50 – 85%
Heart rate reserve (HRR)	80 – 95%	40 – 85%
Rating perceived exertion (RPE)	14 - 18	12 - 16
Maximum workload	50 – 100%	50 – 70%
Peak power output	80 – 110%	51 – 65%
Maximum volume of oxygen (VO_2 max)	60 – 85%	50 – 80%
Ischemia free	95%	60%

There are several ways to design HIIT interventions. Most of the studies use a 4-minute interval repeated four times with a 3-minute rest in between intervals which is called long HIIT. There are also studies that use a 1-minute interval repeated 10 times with a 1-minute rest in between intervals which is called short HIIT. There is also a 20 seconds interval repeated 15 to 30 times with a 40 seconds rest interval between intervals. Moreover, a 2-minute interval was repeated 10 times with a 2-minute rest interval between intervals.

Primary outcome

The primary outcome of this systematic review and meta-analysis was a change in peak VO_2. This work is an extension of the previous meta-analysis from Pattyn et al. (2018) which analysed 11 studies among CAD patients. 26 studies are available for analyzing changes in peak VO_2 among CAD patients in this work totaling 1461 participants (n=710) for HIIT and (n=751) for MICT after removing 1 study due to incomplete data from Heber et al. (2020). This author was contacted via email, yet no feedback was given. As shown in Figure 2, a significant improvement was observed after HIIT compared to MICT in the total group 1.39 ml/kg/min; 95% CI 0.87 – 1.90; $p < 0.00001$; $I_2 = 0\%$ with weighted mean changes of 18.16% in HIIT and 10.9% in MICT. Subgroup analysis on the HIIT protocols (Figure 3), either short HIIT, long HIIT or not reporting the protocol revealed no differences between protocols ($p = 0.70$, $I_2 = 0\%$).

Figure 2. Forest plot of peak VO_2 improvement following HIIT and MICT

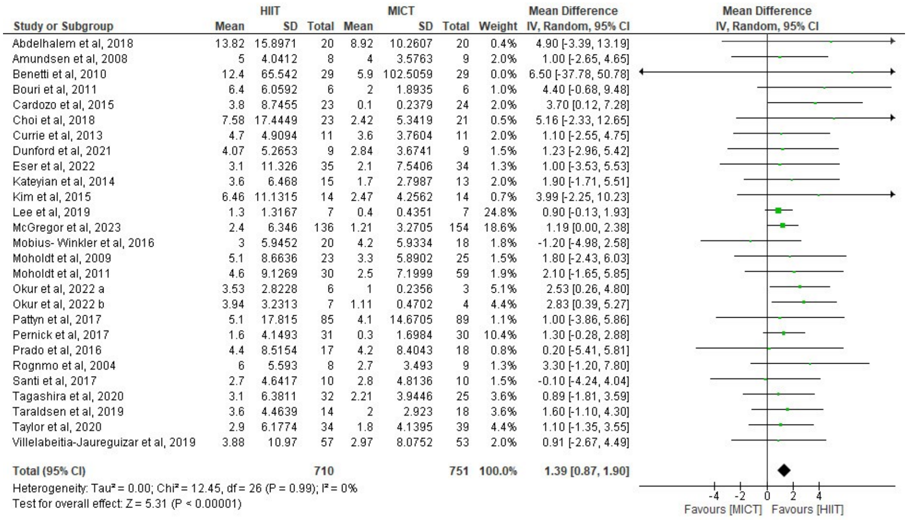
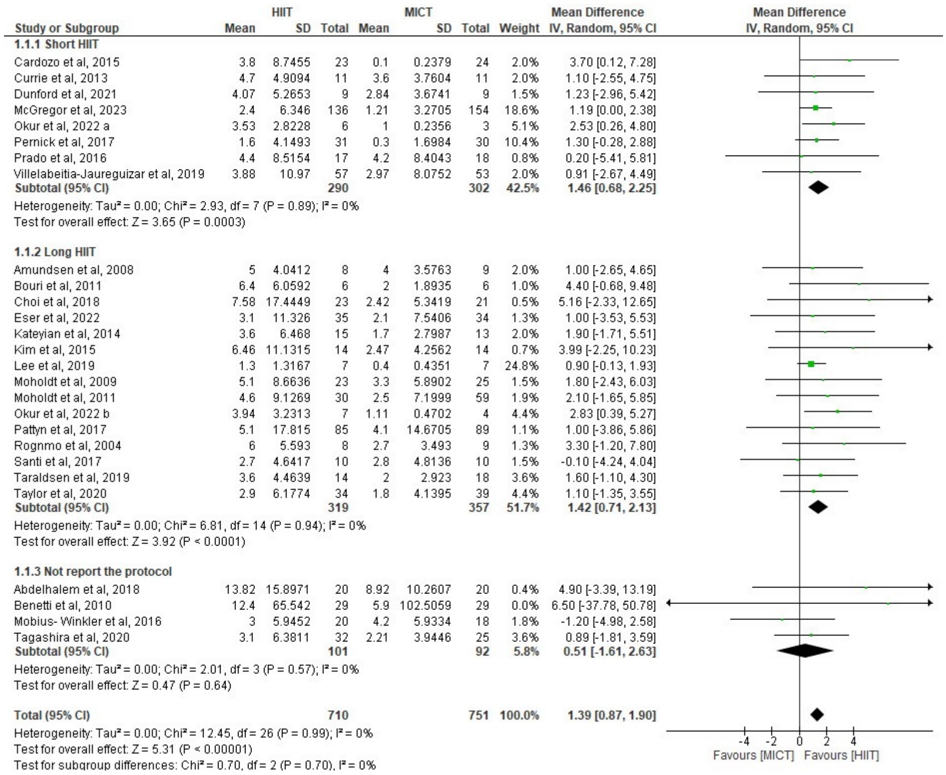


Figure 3. Forest plot of peak VO_2 improvement following short-HIIT and long-HIIT; sub-analysis



Secondary outcomes

Secondary outcomes for this work were hs-CRP, LDL-C, HDL-C, TG and TC. 7 studies reported on hs-CRP comparing HIIT and MICT among CAD patients, totaling 606 participants (n= 286) for HIIT and (n=320) for MICT. As shown in Figure 4, no significant differences were observed after HIIT compared to MICT in the total group -0.06 mg/L; 95% CI -0.56 – 0.43; p = 0.80; I_2 = 47% with a weighted mean reduction of 37.9% in HIIT and 39.3% in MICT. Since high I_2 was found, sensitivity analysis was conducted, excluding one study from a grey literature article by Pernick (2017) the result was 0.09 mg/L; 95% CI -0.09 – 0.27; p = 0.31; I_2 = 0% (Figure 5).

Figure 4. Forest plot of hs-CRP improvement following HIIT and MICT

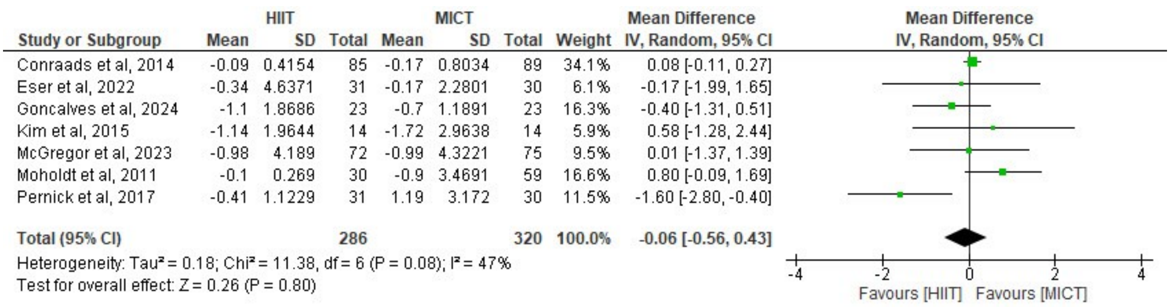
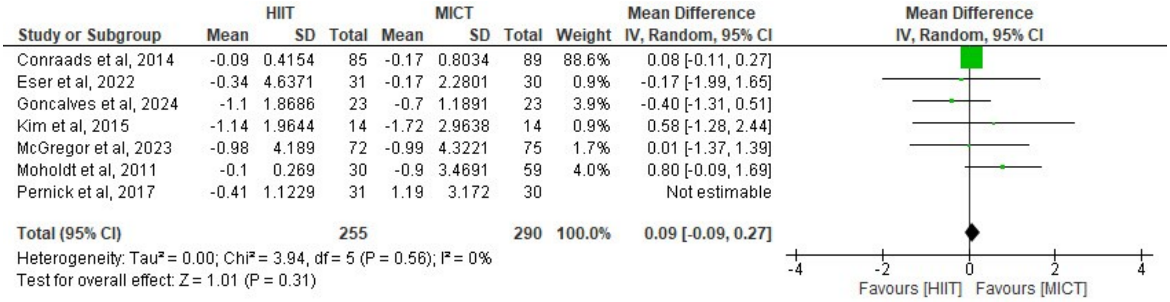
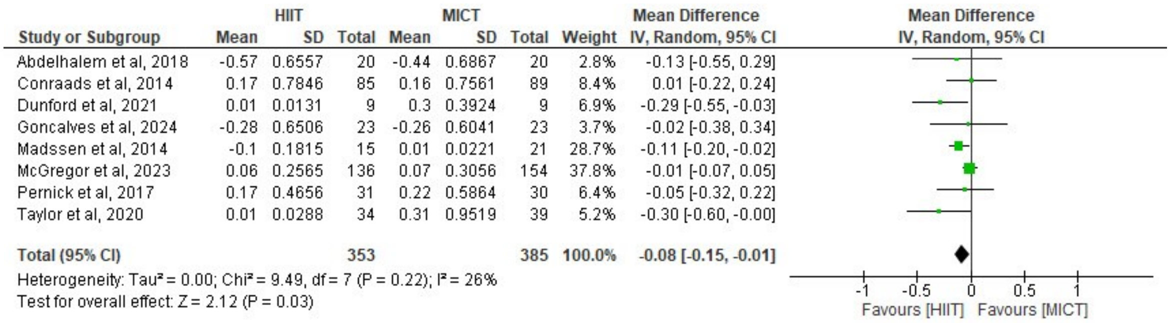


Figure 5. Forest plot of hs-CRP improvement following HIIT and MICT; sensitivity analysis



Eleven studies reported on LDC-C, twelve studies reported on HDL-C, and TG and eight studies reported on TC. For LDL-C, involving 828 participants (n= 397) for HIIT and (n=431) for MICT. For HDL-C and TG, involving 917 participants (n= 427) for HIIT and (n=490) for MICT. For TC, 738 participants (n= 353) for HIIT and (n=385) for MICT. Results showed no significant differences in LDL-C, HDL-C and TG comparing HIIT and MICT. For LDL-C, the mean difference was -0.07 mmol/L, p = 0.11, 95% CI: -0.15 – 0.02; I_2 = 63% with a weighted mean reduction of 4.12% in HIIT and 1.93% in MICT (Supplementary file 1, supplementary figure I: Funnel plot HIIT vs. MICT on LDL-C). For HDL-C, the mean difference was -0.00 mmol/L, p = 0.84, 95% CI: -0.03 – 0.02; I_2 = 39% with a weighted mean reduction of 7.29% in HIIT and 7.19% in MICT (Supplementary file 1, supplementary figure II: Funnel plot HIIT vs. MICT on HDL-C). For TG, the mean difference was -0.01 mmol/L, p = 0.69, 95% CI: -0.06 – 0.04; I_2 = 70% with a weighted mean reduction of 4.18% in HIIT and 4.14% in MICT (Supplementary file 1, supplementary figure III: Funnel plot HIIT vs. MICT on TG). Figure 6 showed a significant difference was observed after HIIT compared to MICT on TC -0.08 mmol/L; 95% CI -0.15 – -0.01; p = 0.03; I_2 = 26%.

Figure 6. Forest plot of TC improvement following HIIT and MICT



Publication bias

Overall, study quality was good, with a median TESTEX score of 11 (range, 9-14) presented in Table 3. Poor reporting mostly on exercise attendance and unblinding both participants and assessors. Overall compliance with the prescribed intensity was good, of which 26 studies had more than 85% adherence. Nine studies with poor adherence were mostly excluded from the final analysis and counted as dropouts. The funnel plot for our primary outcome, peak VO_2 showed a likelihood of small publication bias with a low standard error because of slightly different numbers of studies on the left and right sides of the funnel plot (Supplementary file 2, supplementary figure IV to IX: All the forest plot).

Table 3. Study Quality Analysis using TESTEX Scoring Tools

No	Author, year	Study quality					Study reporting										Total score
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
1	Goncalves et al, 2024	/	/	/	/	/	/	/	x	/	/	/	/	/	/	/	14
2	McGregor et al, 2023	/	/	/	/	/	x	/	/	/	/	/	/	/	/	x	13
3	Garneau et al, 2023	/	/	x	/	x	x	x	x	/	/	/	/	/	/	x	9
4	Reed et al, 2022	/	/	/	/	/	/	/	/	/	/	/	/	/	/	x	14
5	Eser et al, 2022	/	/	x	/	/	/	/	x	/	/	/	/	/	/	/	13
6	Valentino et al, 2022	/	/	x	x	/	/	/	/	/	/	/	/	/	/	/	13
7	Okur et al, 2022	/	/	x	/	x	/	/	/	/	/	/	/	/	/	/	13

8	Yakut et al, 2022	/	/	/	/	x	/	/	x	/	/	/	/	/	/	x	12
9	Taylor et al, 2021	/	/	x	/	x	x	/	/	/	/	/	/	/	x	/	11
10	Lee et al, 2021	/	/	/	x	/	x	/	/	/	/	/	/	/	x	/	12
11	Taraldsen et al, 2020	/	/	x	/	x	/	/	/	/	/	/	/	/	x	x	11
12	Tagashira et al, 2020	/	/	x	/	x	/	/	x	/	/	/	/	/	x	x	10
13	Jaureguizar et al, 2019	/	/	x	/	x	/	/	x	/	/	/	/	/	/	x	11
14	Heber et al, 2019	/	/	/	/	x	x	/	x	/	/	/	/	/	/	x	11
15	Biodin et al, 2019	/	/	x	/	/	/	/	/	/	/	/	/	/	x	x	12
16	Ghardashi-Afousi et al 2018	/	/	x	/	/	/	/	x	/	/	/	/	/	/	x	12
17	Abdelhalem et al, 2018	/	/	x	/	x	/	/	x	/	/	/	/	/	x	/	11
18	Choi et al, 2018	/	/	x	/	x	/	/	x	/	/	/	/	/	x	x	10
19	Pattyn et al, 2017	/	/	x	/	/	/	/	x	/	/	/	/	/	/	/	13
20	Pernick et al, 2017	/	/	x	/	x	/	/	x	/	/	/	/	/	/	/	12
21	Santi et al, 2017	/	/	x	/	x	/	/	x	/	/	/	/	/	x	x	10
22	Moblus Winkler et al, 2016	/	/	x	/	x	/	/	x	/	/	/	/	/	x	/	11
23	Kim C et al, 2015	/	/	x	/	x	/	/	x	/	/	/	/	/	/	x	11
24	Prado et al, 2015	/	/	x	/	x	/	x	x	/	/	/	/	/	/	/	11
25	Cardozo et al, 2015	/	/	x	/	x	/	/	x	/	/	/	/	/	x	/	11
26	Keteyian et al, 2014	/	/	/	x	/	x	/	x	/	/	/	/	/	/	x	11
27	Tschentscher et al, 2014	/	/	x	/	x	/	/	/	/	/	/	/	/	x	x	11
28	Currie et al, 2013	/	/	x	/	x	/	/	x	/	/	/	/	/	/	/	12
29	Mohaldt et al, 2011	/	/	/	/	/	x	/	x	/	/	/	/	/	/	/	13
30	Bouri et al, 2011	/	/	x	/	x	/	/	x	/	/	/	/	/	x	/	11
31	Benetti et al, 2010	/	/	x	/	x	/	/	x	/	/	/	/	/	x	x	10
32	Mohaldt et al, 2009	/	/	/	/	/	/	/	x	/	/	/	/	/	/	x	13
33	Amudsen et al, 2008	/	/	x	/	x	x	/	x	/	/	/	/	/	/	/	11
34	Warburton et al, 2005	/	/	x	/	x	/	/	x	/	/	/	x	/	/	x	10
35	Rognmo et al, 2004	/	/	x	/	/	x	/	x	/	/	/	/	/	/	/	12

Abbreviations: 1, eligibility criteria clearly stated; 2, method of randomization; 3, group allocation concealed from patients; 4, no differences at baseline between groups; 5, blind assessor for at least 1 primary outcome; 6, adherence more than 85%; 7, reported adverse events; 8, exercise attendance; 9, intention to treat analysis; 10, between group statistical comparison; 11, between group statistical comparison for at least one secondary outcome; 12, report point estimates; 13, activity monitoring in control group patients; 14, relative intensity constant (14) and exercise volume; 15, energy expenditure can be calculated.

Discussion

This systematic review and meta-analysis were an extension of the work from Gomes-Neto et al. (2024) and Pattyn et al. (2018) comparing the effects of HIIT and MICT in patients with CAD. In this updated analysis, the number of participants allowing us to make a more precise estimate of the effect on peak VO_2.

Primary outcome

The pooling of the results of 26 studies showed a higher increase in peak VO_2 in favors of HIIT 1.39 ml/kg/min; $p < 0.00001$ confirming the results of previous meta-analysis Pattyn et al. (2018) and network meta-analysis Gomes-Neto et al. (2024) that HIIT is superior to MICT in improving peak VO_2. The findings with respect to improving peak VO_2 are significantly important, as this is the gold standard in determining survival, CV events and mortality. An increment of every 1.0 ml/kg/min of peak VO_2 was associated with a 9% increase in survival (Kavanagh et al., 2002). Moreover, another study found that an increment of 1.0 ml/kg/min of peak VO_2 was associated with a 15% increase in survival (Keteyian et al., 2008). For every 1.0 ml/kg/min improvement in peak VO_2, reduce 21% of CV events and 13% of all-cause mortality (Mikkelsen et al., 2020). Furthermore, peak VO_2 is a powerful and useful prognostic indicator for mortality in patients with CVD (de Souza e Silva et al., 2022; Ezzatvar et al., 2021; Harb et al., 2020) and hospitalization (Novaković et al., 2022). Possibly, due to this clinically significant improvement of peak VO_2, the main objective to be achieved during cardiac rehabilitation (CR) is to improve peak VO_2. Exercise prescription that optimized improvement in exercise capacity is a critical consideration for the efficacy of exercise programme (Taylor et al., 2021). Hence, designing effective exercise interventions should be directed towards optimising exercise capacity as assessed by maximum oxygen uptake (peak VO_2) to improve the overall health of people with CAD. This is because peak VO_2 is a strong predictor of mortality in patients with CAD.

Although meta-analysis shows a greater benefit from HIIT over MICT for peak VO_2, a varying HIIT protocol was designed. Regarding the protocol of HIIT, it was either short HIIT as less than 4 minutes for each interval and long HIIT as 4 minutes for each interval, the protocol of interval did not influence the magnitude of the change in peak VO_2 (Pattyn et al., 2018). Results from this review aligned with previous findings where no significant difference between protocols for both short and long HIIT significantly greater improved peak VO_2 as compared to MICT. Therefore, it is confirmed that intensity is a major importance for determining the effectiveness of the CR programme. Hence, health practitioner could consider designing HIIT for CAD Patients regardless of any type of modalities used.

Practically, HIIT can be applied to CAD patients using a few approaches. This is important for adaptation purposes and indirectly reduces the potential risk of musculoskeletal injury, especially for those patients who are completely sedentary. Besides, this is important to maintain participants' compliance and ensure CAD patients gain optimal benefit from the intervention. HIIT can be applied after a few weeks of MICT as studied by Lee et al. (2019) conducted the familiarization of exercise was about six weeks of MICT before initiating HIIT. Next, HIIT can be combined with MICT as studied by Eser et al. (2022) two HIIT sessions interspersed with one MICT per week. Also, HIIT training begins with vigorous intensity and gradually increases to high intensity throughout the intervention. From this study, a new protocol may be applied by initially introducing short HIIT and gradually progressing to long HIIT for a variety of interventions to create joyfulness during the training session. Ideally, high intensity plays a major role in determining the effectiveness of the exercise intervention.

However, this conclusion contradicts a statement by the AHA which raised the issue that HIIT is one of the activities that may result in a CV event is highly concerned (Franklin et al., 2022). Exploring the American College of Sports Medicine (ACSM) guidelines in the classification of aerobic exercise intensity, high intensity is prescribed at > 90% VO_2 max, > 95% HR max, >89% HRR and >17 RPE. Our systematic review showed the intensity prescribed for CAD patients is slightly lower than the intensity typically stated by ACSM's guidelines. Refer Table 2 for the summary of the intensity prescribed among CAD patients. Most likely, in average, the intensity prescribed previously among CAD patients was vigorous to nearly high intensity only. Although HIIT involves in near-maximal intensities, the effort is still submaximal (Taylor et al., 2021). Ideally, HIIT that is commonly prescribed among CAD is not genuinely high but most likely a combination of vigorous high intensity. Therefore, "HIIT" can be considered safe to prescribe for CAD patients.

Secondary outcomes

This variable is hardly ever highlighted by the researchers, as only 7 studies are available measuring hs-CRP on HIIT and MICT as compared to other variables. This is probably due to the high cost of measuring this biomarker as the importance of understanding the atherosclerosis process on inflammatory markers was highlighted since 2002. Inflammation plays a major role in all stages of atherogenesis (Libby et al., 2002). In 2012, it was confirmed that inflammation provides a pathway that mechanistically links alterations in traditional risk factors and modifications in the biology of the artery wall that cause atherosclerosis (Libby, 2012). Out of 7 studies, there are five studies (Conraads et al., 2015; Eser et al., 2022; Kim et al., 2015; McGregor et al., 2023; Moholdt et al., 2012) that only highlight a reduction of hs-CRP after exercise intervention without discussing in detail. Only two studies (Gonçalves et al., 2024; Pernick, 2017) genuinely discussed in-depth of hs-CRP as an important outcome. A limited study was done to explore the effect of exercise on hs-CRP especially in HIIT as the most effective intervention compared to the other modes of exercise.

hs-CRP is an indicator of metabolic dysfunction associated with an elevated risk of CVD (Nathan & Ding, 2010) and it's linked to the progression of atherosclerosis, which is characterised by the deposition of cholesterol on the inner linings of blood vessels and inflammation within the vessel wall (Schaefer et al., 2016). Generally, a healthy hs-CRP level below 0.9 mg/dL (Libby, 2012) and a range between 1.0 – 10.0 mg/ dL are categorised as moderately elevated (Pearson et al., 2003). Data at the baseline showed that CAD patients who had undergone either PCI or CABG had a moderate elevation of hs-CRP, except for 2 studies (Conraads et al., 2015; Eser et al., 2022) had healthy values. It is shown that even after PCI or CABG, CAD patients have the potential to have a CV event as hs-CRP is slightly higher. Moreover, interpretation should be done carefully with other considerations. Generally, exercise acts as a stressor during and after exercise and it is caused by inflammation (Silveira et al., 2016). Interestingly, both exercise interventions lowered the hs-CRP, but one study by Pernick (2017) showed an increase in hs-CRP after MICT intervention. It can be concluded that exercise is a positive stressor which post-exercise hs-CRP is lower. Both exercise interventions, either HIIT or MICT, are effective in lowering the hs-CRP. Additionally, results showed there was no significant difference in hs-CRP between HIIT and MICT. Perhaps, due to a small study available that compares HIIT and MICT on hs-CRP, future research regarding the effect of exercise intervention, especially on HIIT among CAD patients is urgently needed. If exercise improves peak VO_2 but increases inflammatory markers, it may not produce the expected results.

However, this finding was contradicted with Cerqueira et al. (2020) who underlined that intense exercise led to higher hs-CRP and thus might increase the risk of CV events and suggested moderate to vigorous exercise is more appropriate to achieve maximum benefit and is favourably concern. The inclusion criteria for this systematic review were active, healthy adults aged between 18 - 65 years old with extremely intensive exercise that suits the population studied such as half and full marathons, 1 hour of cycling, 3 sets of intense resistance training, 8 hours of cycling competition, 1.75-hour cycling followed by 10 km of running, ultra-endurance foot races over 246 km, etc. This probably caused a higher increase in hs-CRP and required a longer recovery time. Probably, after 24 hours of rest, hs-CRP remains high as not enough recovery yet. This review seems not relevant to CAD patients as the exercise prescribed is not extremely high. In summary, understanding the effect of HIIT on hs-CRP among CAD patients is genuinely needed as it may provide insight into designing more effective exercise interventions for CAD patients specifically.

Considering the analysis of the CAD patient's lipid profiles, our findings showed no significant difference between HIIT and MICT on LDL-C, HDL-C and TG. With double the additional numbers of participants analyse by Pattyn et al. (2018), this finding found similar results where no significant improvement in lipid profile was found for either HIIT or MICT. Significantly, both exercise interventions demonstrated a trend of improvement in these parameters. Therefore, it is confirmed that whichever intensity improves lipid profile among CAD patients.

Based on a systematic review, greater improvement in LDL-C, TG, and TC in favor of HIIT than MICT. While HDL-C is in favor of MICT. Practically, it is hard to design an exercise training program to observe the effect of exercise on lipid profile because four lipid profile biomarkers favor in both interventions. For example, LDL-C and TG are favored in HIIT, while HDL-C is favored in MICT. Hence, which training intensities should be prescribed for optimal benefit? Perhaps, health practitioners need to identify the most important biomarkers to be improved at certain stages of rehabilitation and should be monitored frequently.

The result should be interpreted with caution considering the significant variability in LDL-C, HDL-C, and TG levels. This variability may arise from subtle alterations in the lipid profile following both interventions. This is because, the results from this systematic analysis indicated that CAD patients ideally exhibited normal to near-optimal levels of LDL-C, HDL-C, TG, and TC at baseline for both exercise regimens. This is probably because more than 90% of participants in HIIT and MICT were prescribed a lipid-lowering drug (statin). Therefore, small changes were observed in both HIIT and MICT which range from -0.15 to 0.01 in LDL-C, -0.04 to 0.03 in HDL-C, -0.08 to 0.02 in TG, and -0.15 to -0.01 in TC. In one study by Gonçalves et al. (2024) both groups' baseline TG was found to be borderline high, and the results indicated a greater reduction than in the other studies with normal baseline TG. Probably, if research is conducted among CAD patients with an abnormal lipid profile, greater changes may be seen.

Many patients are unable to tolerate with intensive statins because of side effects or do not achieve adequate LDL-C lowering with maximally tolerated statins (Arnold et al., 2020). Therefore, exercise is considered as an effective alternative lipid-lowering therapy for secondary prevention. Perhaps, since intensive statin may have side effects in the long-term, health practitioners should consider prescribing a lower dose of statin for patients, especially patients who are physically active as exercise is able to improve lipid profiles.

Clinical implications and practical recommendations

Health practitioners should implement a more intensive aerobic exercise regimen for CAD patients, as it provides greater health benefits. Health practitioners should incorporate HIIT into a comprehensive cardiac rehabilitation program by implementing two sessions of MICT and one session of HIIT each week. Patients with CAD should be advised to progressively increase the speed or gradient over time, transitioning from moderate intensity (40 – 60% HRR or 11-14 on the Borg RPE scale) to high intensity (80 – 95% HRR or 15-18 on the Borg RPE scale). To sustain patients' motivation, health practitioners should create a range of modes of training employing variations of modalities such treadmills, bicycles, swimming, and outdoor walking. Furthermore, HIIT should be recommended to CAD patients for daily practice, as it can mitigate the risk of falls. HIIT seems to be a safe and well-accepted adjunct to established fall prevention methods, owing to its impact on lower limb strength (Elboim-Gabyzon et al., 2021).

To apply HIIT among CAD patients, the benefit should outweigh the risk ratio. We recommend that health practitioners to perform exercise stress testing (EST), and a negative electrocardiographic (ECG) result is required for safety purposes. Ideally, the HIIT sessions should be implemented in intervals designed begin with short HIIT and gradually increase to long HIIT to minimize the risk of musculoskeletal overload. HIIT should be administered in a hospital setting, one-to-one supervised with regular monitoring on physiological responses such as blood pressure, rating perceived exertion (RPE), and oxygen saturation level during and immediately after a HIIT session is appropriate. Moreover, patients with CAD should be instructed to incorporate a warm-up and cool-down phase in their exercise regimen to reduce the risk of cardiac ischemia from abrupt, intense exercise and to prevent a reduction in central blood flow volume that may result from a sudden stop of exercise (Franklin et al., 2020).

Strength and limitations

This is an extension of a systematic review and meta-analysis with a larger sample size among CAD patients, focusing on peak VO_2, inflammatory markers and lipid profiles in depth. Moreover, these findings are important because they may help health practitioners to make decisions about designing the most effective aerobic exercise intervention. The limitation of this study was that only three studies were identified with a large sample size (McGregor et al., 2023; Pattyn et al., 2017; Villelabeitia-Jaureguizar et al., 2019) while the other studies had a quite small sample size in the range of 6 – 154 per group. The analysis incorporated data from both peer-reviewed and non-peer-reviewed publications. Non-peer-reviewed material may contribute to unresolved issues related to the risk of publishing bias. Therefore, sub-analysis was performed excluding outliers to mitigate bias. This study focuses on short-term effects rather than long-term adherence, and while the findings are valuable, further research is needed to confirm the results and explore the intervention's long-term impact and sustainability.

Conclusions

This meta-analysis further strengthens the larger peak VO_2 increment after HIIT regardless of any protocols than MICT among CAD patients. Both intensities are equally beneficial in reducing hs-CRP levels and improving lipid profiles among CAD patients. Future research is required to investigate the effect of intensities on inflammation and lipid profiles to assist healthcare professionals in developing optimal exercise interventions for the management of CAD patients.

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Authors' and translators' details:

Noor Fatihah Ilias	noorfatihah@uitm.edu.my	Main Author
Mazlifah Omar	mazlifahomar@uitm.edu.my	Author
Sazzli Shahlan Kasim	sazzlishahlan@uitm.edu.my	Author
Hashbullah Ismail	hashbullah@uitm.edu.my	Coresponding Author