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Review Article

The effects of high-intensity interval training and moderate-intensity continuous training on patients underwent Coronary Artery Bypass Graft surgery; a systematic review

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Abstract: Objectives: To our knowledge, there is no clear consensus on a definitive cardiac rehabilitation method for patients undergoing Coronary Artery Bypass Graft (CABG). We conducted this systematic review to compare and evaluate the effects of two of the most frequent cardiac rehabilitation modalities, high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT), on cardiopulmonary variables. Methods: We carried out a systematic search of the databases PubMed, Web of Science, Embase, Scopus, and Google Scholar. Following the removal of duplicate results, the original search yielded 385 citations. We identified four randomized clinical trials after reviewing titles, abstracts, and potential full-text studies. We utilized the Cochrane Risk of Bias Tool (RoB2) to assess the risk of bias. Results: We included four randomized clinical trials involving 143 people. All trials included individuals who had CABG and completed HIIT or MICT sessions for at least four weeks. The findings indicated that HIIT programs may improve functional capacity, heart rate variability indices, and blood pressure management while lowering brain natriuretic peptide (BNP_{1-32}) and N-terminal pro-b-type natriuretic peptide ($NT\text{-}proBNP_{1-76}$) levels. Conclusion: Given the findings, it appeared that supervised high-intensity exercise regimens could be more useful to patients. Following the surgery, HIIT therapy improves exercise capacity, the autonomic nervous system, volume overload, and blood pressure regulation.

Keywords: Coronary Artery Bypass Graft (CABG), high-intensity interval training (HIIT), moderate intensity continuous training (MICT)

Introduction

Since 1975, cardiovascular disease (CVD) has consistently been one of the leading causes of death in the United States [1]. Coronary artery disease (CAD), primarily affecting the coronary arteries, causes about 85% of all cardiovascular-related deaths [2]. The Coronary Artery Bypass Grafting (CABG) procedure reroutes blood flow around severely blocked coronary arteries caused by atherosclerosis [3]. Several difficulties may result from this procedure, including diminished cardiopulmonary function, reduced exercise capacity, poor psychological well-being resulting from anesthesia effects, dysregulation of autonomic nervous systems following myocardial damage during surgery, and decreased pulmonary muscle function following mechanical ventilation. These complications may lead to intensive care unit admission and extended periods of inactivity, which, in turn, worsen cardiopulmonary fitness [4].

The American Association of Cardiovascular and Pulmonary Rehabilitation [5] recommends cardiac rehabilitation (CR) to address cardiopul-

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monary weakness after cardiac surgery. Cardiac rehabilitation programs encompass a variety of therapeutic interventions, including regular physical activity, dietary changes, medical therapy, risk factor (i.e., blood pressure, obesity, and blood glucose) management through education, and stress reduction measures [6, 7]. Previous studies have shown that CR can reduce the risk of sudden cardiac death and arrhythmias by modulating the autonomous nervous system (ANS). Also, CR can contribute to pulmonary muscle strength and improve cardiopulmonary capacity following surgery [8]. Exercise-based training mitigates common cardiovascular risk factors like hypertension, hyperlipidemia, diabetes, and obesity [9], while also reducing chronic systemic inflammation, a known contributor to cardiovascular system dysfunction [9, 10].

The American Heart Association established two forms of aerobic exercise-based CR programs for CVD patients: moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) [7, 11]. HIIT is defined as short bursts of strenuous activity at 85-100% of the maximum volume of oxygen uptake during exercise (VO_2peak), followed by rest or low-intensity activity to allow for recovery. MICT entails prolonged periods of aerobic activity at a moderate intensity, usually between 60% and 80% of VO_2peak or reserve heart rate [12, 13]. Prior studies have demonstrated varying results after various forms of exercise training regimens. Early research generally advised CAD patients to participate in MICT programs. Patients with CAD are especially vulnerable to these forms of physical activity since HIIT programs often put more strain on the cardiovascular system. Recent research has shown that HIIT programs are safe for people with CAD, and medical practitioners are paying more attention to HIIT strategies. Numerous studies have demonstrated that HIIT programs can enhance the cardiopulmonary fitness metrics of patients [14-16]. Some studies have also compared the effects of HIIT and MICT programs on patients' outcomes [17]. However, little is known about how these CR regimens affect patients who have had CABG.

There is no universal agreement on the optimum CR treatment after CABG surgery. The purpose of this systematic review is to examine research that evaluates the effectiveness of HIIT against standard MICT regimens in patients recovering from CABG.

Materials and methodology

The present study is a systematic review conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) recommendation [18] (see Supplementary Table 1). Additionally, we have prospectively registered the study protocol on the International Prospective Registry of Systematic Reviews (PROSPERO) under the registration number CRD42023403432.

Search strategy

This systematic review is based on a thorough search of electronic literature across several databases, including PubMed, Scopus, Web of Science, Google Scholar, and Embase. Each database has distinct characteristics and guidelines, necessitating the use of several search syntaxes to construct an effective search strategy. We used various keywords and search algorithms relevant to each database, as shown in Supplementary Table 2. There were no limitations to the search strategies.

Eligibility criteria and study selection

In this systematic review study, the researchers concentrated on a specific cohort that had undergone CABG and participated in fitness training programs as part of their CR programs. The study compared two types of training strategies: high-intensity interval training and moderate-intensity continuous training. Only randomized clinical trials (RCTs) were included if individuals were ≥ 18 years old and at least 70% of participants had undergone CABG surgery. We also deemed it necessary to compare HIIT and MICT as postoperative rehabilitation treatments. Only English-written studies were included. We also evaluated all relevant references provided by systematic reviews and meta-analyses. Exclusion criteria consisted of the following items: a) Any study design other than RCTs; b) Studies with participants under the age of 18; c) Studies with irrelevant cardiovascular therapies; and d) Studies that report just one rehabilitation program outcome (HIIT or MICT). We also omitted research conducted in languages other than English or published before 2003. **Table 1** contains information about all the study populations and reported results. **Table 2** includes details of the training programs of the included studies.

Data extraction

Five members of the panel screened titles and abstracts individually, utilizing inclusion and exclusion criteria and taking into account the topic's relevance. All studies were reviewed by at least two independent researchers. After reviewing all full-text publications, all team members discussed and reached consensus on which studies to include. After the studies had included, they were investigated and evaluated for methodological quality. Despite an extensive literature search, we identified fewer than the minimum of three studies reporting a consistent outcome measure required to conduct a meta-analysis. Therefore, the quantitative synthesis was not feasible due to insufficient data with comparable outcomes across the included studies.

Evaluation of bias

We assessed the methodological quality of the included RCTs using the Revised Cochrane risk-of-bias tool (RoB2). This instrument evaluates prejudice in five domains: selection, performance, detection, attrition, reporting, and additional biases [19]. The figures (**Figures 2** and **3**) were generated using RStudio software 4.3.3 version (robvis package).

Results

Results of the literature search

The initial search resulted in 588 citations; after removing duplicated ones, 385 citations underwent title and abstract review. After the removal of irrelevant citations, 19 studies were considered for full-text review (**Figure 1**).

Included and excluded studies

After analyzing the entire texts, 15 studies were removed for the following reasons: One conference abstract, one preprint study, three studies did not focus on CABG patients (< 70%), one study with insufficient information, four papers missing one of the rehabilitation strategies (HIIT or MICT), and five studies written in non-English languages or rated as high risk of bias. This systematic review included only four studies, involving 143 participants (**Figure 1**).

Risk of bias assessment

We used the Cochrane Risk of Bias Tool (RoB2) for an evaluation of the risk of bias in randomized controlled trials, as shown in **Figures 2** and **3**. Only 4 studies were appraised and all were judged as "some concern" (**Figures 2** and **3**). Inter-examiner reliability had a high level of agreement (k = 0.880).

1. Randomization process: Three studies received a "some concern" rating because the randomization process lacked sufficient information. We categorized one study [20] "low risk of bias", sharing appropriate information on the randomization method (**Figure 2**).

2. Deviations from the intended interventions: The study by Dini Fitriani et al. [21] was considered to have some concerns in this domain because of a high rate of participants' non-adherence (50% of the HIIT and 40% of MICT program participants). We classified other studies as having a low risk of bias (**Figure 2**).

3. Missing data: With providing enough information about missing data, all studies were considered "low risk of bias" (**Figure 2**).

4. Outcome measurement: All studies used the same measurement tools for outcome assessment in all comparing groups and were considered "low risk of bias" (**Figure 2**).

5. Selection of the reported result: Two studies [22, 23] mentioned their prior research protocols in the methods sections and were considered "low risk". Others had some concerns in this domain (**Figure 2**).

Effects of HIIT versus MICT on cardio-metabolic indices and quality of life

Generally, the included studies examined functional capacity, echocardiography and electrocardiography parameters, cardio-metabolic blood tests, blood pressure, and quality of life in patients who participated in HIIT and MICT programs. Only one or two papers provided each outcome, making a meta-analysis impossible due to insufficient data.

Table 1. Summary of the included studies

Author, Year	*Study Design*	*Subjects (number, gender, age)*	*Groups size*	*Reported Results*
Ghardashi-Afousi et al., 2018	Randomized clinical trial (RCT)	42, 0 female, 55.12 ± 3.97 years	HIIT, 14 MICT, 14 Control, 14	-Following the rehabilitation programs, the left ventricular ejection fraction (LVEF) markedly improved in the high-intensity interval training (HIIT) group (58.53 ± 7.26%) compared to the moderate-intensity continuous training (MICT) group (52.26 ± 7.91%, $P < 0.001$). The HIIT training significantly enhanced the end-diastolic volume (EDV) and reduced end-systolic volume (ESV) ($P < 0.010$, $P < 0.050$). The average R-R interval and SDRR in the HIIT group significantly enhanced in comparison to the MICT group ($P < 0.001$). High-frequency power (HF) increased, while low-frequency power (LF) and LF/HF ratio significantly decreased in the HIIT group compared to the MICT group ($P < 0.010$). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) exhibited a substantial reduction in participants engaged in the HIIT and MICT programs, with a more pronounced decline observed in the HIIT group. The increase in maximum heart rate (HR max) and the decrease in resting heart rate (HR rest) in the HIIT group were significantly greater than those in the MICT group ($P < 0.050$).
Fitriani et al., 2020	RCT	6, 0 female, 55.67 ± 6.43 years	HIIT, 3 MICT, 3	-Following rehabilitation, the metabolic equivalent of tasks (METs) improved in both groups; HIIT: 0.98, $P = 0.03$, MICT: 0.79, $P = 0.04$, with no statistically significant distinction between the groups ($P = 0.792$).
Zare-Karizak et al., 2023	RCT	36, 9 females 60.3 ± 5.81 years	HIIT, 12 MICT, 12 Control, 12	-The plasma corin concentration increased, whereas the ratios of pro b-type natriuretic peptide/b-type natriuretic peptide ($proBNP_{1-108}/BNP_{1-32}$) and N-terminal pro b-type natriuretic peptide/b-type natriuretic peptide ($NT\text{-}pro\text{-}BNP_{1-76}/BNP_{1-32}$) diminished in both training cohorts. The specified items exhibited no notable difference among the training groups. Nonetheless, reductions in subcutaneous fat, systolic blood pressure (SBP), diastolic blood pressure (DBP), BNP_{1-32} (pg/mL), and $NT\text{-}proBNP_{1-76}$ (pg/mL) levels were more pronounced in the HIIT group.
T. Moholdt et al., 2009	RCT	59, 11 females, 60.2 ± 6.9 years	HIIT, 28 MICT, 31	-Maximum oxygen consumption (VO_2peak) rose after 4 weeks in both HIIT (27.1 ± 4.5 vs. 30.4 ± 5.5 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, $P < 0.001$) and MICT groups (26.2 ± 5.2 vs. 28.5 ± 5.6 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, $P < 0.001$; no significant group difference). Aerobic high-intensity interval training elevated VO_2peak after 6 months (30.4 ± 5.5 vs. 32.2 ± 7.0 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, $P < 0.001$), but no significant change alteration was observed in the MICT patients (28.5 ± 5.6 vs. 29.5 ± 5.7 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$). Quality of life, hemoglobin, and adiponectin levels enhanced in both groups.

NT-pro-BNP: N-Terminal Pro-Brain Natriuretic Peptide; BNP: Brain Natriuretic Peptide; HIIT: High-Intensity Interval Training; MICT: Moderate-Intensity Continuous Training; LF: Low-Frequency Power; HF: High-Frequency Power; min: minutes; LVEF: Left Ventricle Rejection Fraction; EDV: End Diastolic Volume; ESV: End Systolic Volume; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; METs: metabolic equivalent of tasks; VO_2peak: maximum oxygen consumption; RCT: Randomized clinical trial.

Table 2. Details of training programs of included studies

Author, year	Modality, intensity (%)	Intervention duration (weeks)/frequency (weekly)	Bouts time, Recovery time, Total time (min)
Ghardashi-Afousi et al., 2018	HIIT: continuous cycle ergometer exercise, 85-95% of HR peak. MICT: continuous cycle ergometer exercise, 70% of HR peak.	6 weeks, 3 times/week	HIIT: 2 min, 5 min, 30 min MICT: 40 minutes consciously
Fitriani et al., 2020	HIIT: training on treadmill or leg ergocycle, 80-90% HR peak. MICT: training on treadmill or leg ergocycle, 70-80% HR peak.	4 weeks, 3 times/week	HIIT: 4 min, 3 min, 40 min MICT: 40 min totally, 5 min cool down
Zare-Karizak et al., 2023	HIIT: running on a treadmill, 80-95% HR peak. MICT: running on a treadmill, 65-80% HR peak.	8 weeks, 3 times/week	HIIT: 2.30 min, 2.30 min, 30 min MICT: 33 min totally, 3 min cool down
T. Moholdt et al., 2009	HIIT: treadmill walking, 90% HR peak. MICT: treadmill walking, 70% HR peak.	24 weeks, 5 times/week	HIIT: 4 min, 3 min, 41 min MICT: 46 min continuously

HIIT: high-intensity interval training; MICT: moderate-intensity continuous training; min: minutes; HR: heart rate.

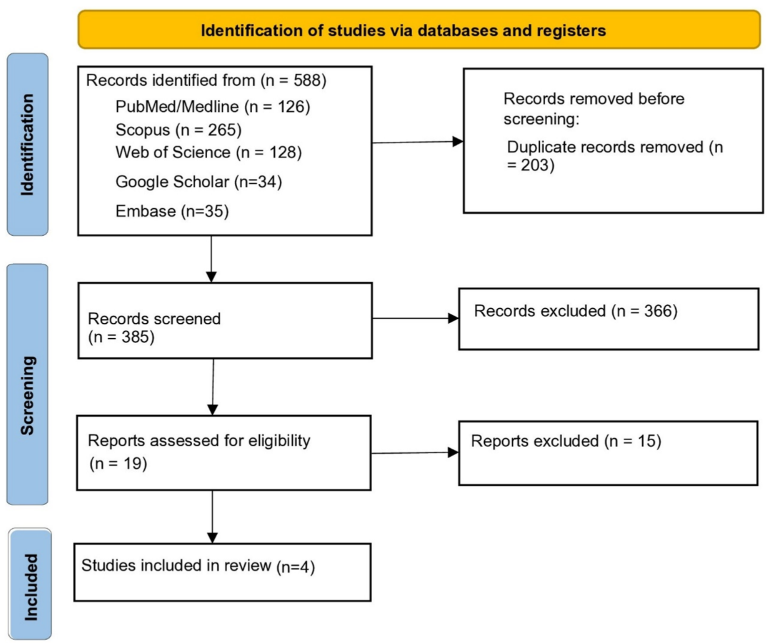

Figure 1. PRISMA Flow chart 2020 for new systematic reviews, including searches of databases and registers.

Two studies looked at functional capacity (FC) markers, such as the maximum oxygen consumption (VO_2peak) or metabolic equivalent of tasks (METs) during exercise. Fitriani et al. found a considerable increase in patients' METs after four weeks of rehabilitation in both the MICT and HIIT groups, with no significant difference between the two regimens (HIIT program: 0.98 ± 0.48 increase in METs (P = 0.03), MICT program: 0.79 ± 1.03 increase in METs (P = 0.04), between groups difference: P = 0.79). Similarly, the study by T. Moholdt et al. demonstrated similar outcomes after four weeks, whereas the HIIT program caused higher changes in VO_2peak measures than the MICT program after six months of training (27.1 ± 4.5 to 32.2 ± 7.0 $mL \cdot kg^{-1} \cdot min^{-1}$ in the HIIT group, 26.2 ± 5.2 to 29.5 ± 6.7 $mL \cdot kg^{-1} \cdot min^{-1}$ in the MICT group, between groups difference: P < 0.05) [20, 21].

Two investigations were conducted to examine echocardiography and electrocardiography parameters. According to Ghardashi-Afousi et al., increase in heart rate variability indices such as heart rate maximum (HR_{max}, HIIT vs. MICT: 7.50 ± 4.46 vs. 2.50 ± 4.26, P < 0.05), mean R-R interval (HIIT vs. MICT: 133 ± 55.14 vs. 74.60 ± 29.11, P < 0.005), high-frequency power (HF, HIIT vs. MICT: 13.30 ± 5.29 vs. 4.70 ± 1.33, P < 0.005), and standard deviation of all the R-R intervals (SDRR, HIIT vs. MICT: 8.00 ± 3.43 vs. 3.70 ± 2.40, P < 0.05) were more prominent in the HIIT group than in the MICT group [22]. Furthermore, the heart rate at rest (HR_{rest}, HIIT vs. MICT: -8.00 ± 2.62 vs. -4.60 ± 1.50, P < 0.05), and low-frequency power (LF, HIIT vs. MICT: -22.10 ± 7.72 vs. -14.90 ± 6.83, P < 0.05) decreased considerably in the HIIT group compared to the MICT group.

Regarding echocardiography parameters, we found inconsistent results between the studies. The study by Ghardashi-Afousi et al. found that HIIT program had a stronger effect on left ventricular ejection fraction (LVEF) increase (HIIT vs. MICT: 6.46% ± 3.76 vs. 3.59% ± 3.73, P < 0.05) and end-systolic volume (ESV) de-

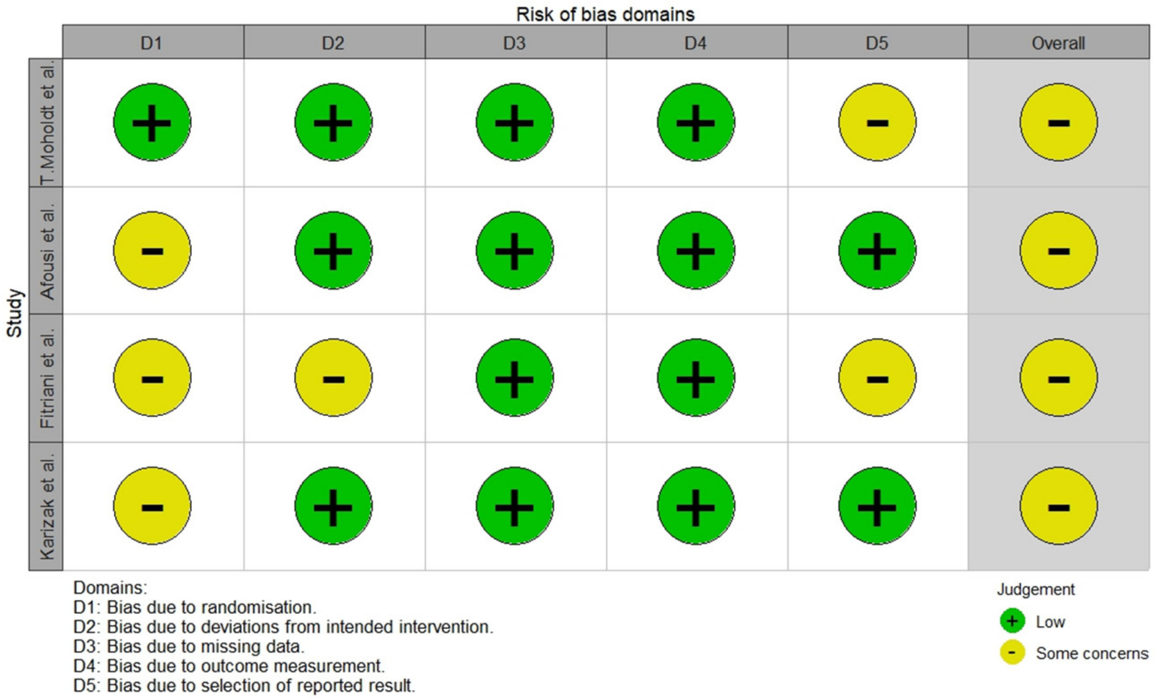

Figure 2. Evaluating the risk of bias of the included studies according to the Cochrane Risk of Bias Tool (RoB2).

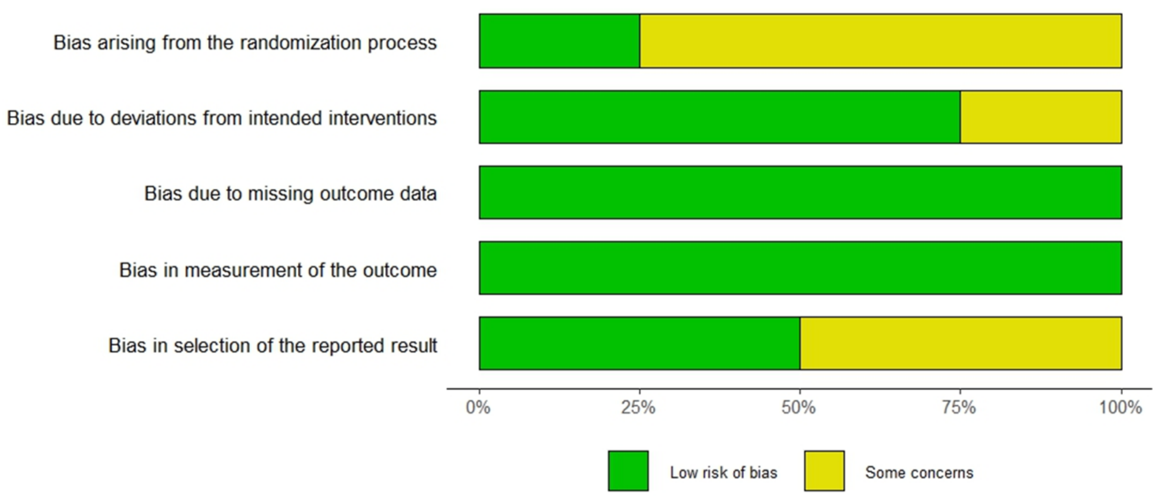

Figure 3. Risk of Bias 2 (RoB2) assessment by domains.

crease (HIIT vs. MICT: -5.20 ± 4.13 vs. -1.60 ± 4.03 mL, $P < 0.05$) [22]. T. Moholdt et al. showed no difference between the two CR programs in influencing EF and ESV after four weeks ($P > 0.05$) [20]. Other echocardiography markers, including end diastolic volume (mL), mitral annular excursion (mm), systolic mitral annular velocity (cm/s), and late and early diastolic mitral velocity (cm/s), remained steady.

Two of the included studies examined the effects of CR programs on cardio-metabolic blood tests [20, 23]. Zare Karizak et al. found no difference between HIIT and MICT programs on pro b-type natriuretic peptide/b-type natriuretic peptide ($ProBNP_{1-108}/BNP_{1-32}$, HIIT-MICT difference P = 450) and N-terminal pro b-type natriuretic peptide/b-type natriuretic peptide ($NT\text{-}pro\text{-}BNP_{1-76}/BNP_{1-32}$, HIIT-MICT difference P = 0.295) ratios. However, the HIIT program was more successful at lowering BNP_{1-32} (HIIT-MICT difference P = 0.010) and NT-proBNP_{1-76} (HIIT-MICT difference P = 0.013) levels [23]. Furthermore, T. Moholdt and coworkers found an increase in serum adiponectin and hemoglobin, as well as a drop in ferritin levels in both groups after rehabilitation programs compared to baseline, with no statistical significant difference between the groups [20].

Ghardashi-Afousi et al. and Zare Karizak et al. assessed blood pressure (BP) [22, 23]; the study by Ghardashi-Afousi et al. showed HIIT program superiority with greater systolic blood pressure (SBP) reduction (HIIT vs. MICT: -15.70 ± 7.54 mmHg vs. -6.10 ± 5.44 mmHg, P < 0.05). Similar results were also reported by Zare Karizak et al. (HIIT vs. MICT: P = 0.00). Both studies found that cardiac rehabilitation affected SBP, with HIIT sessions significantly lowering SBP levels. Both HIIT and MICT workouts reduced diastolic blood pressure (DBP) without between-group difference.

The study by Zare Karizak et al. found that subcutaneous fat decreased more dramatically in the HIIT group than in the MICT group after 8 months (HIIT-MICT difference P = 0.040) [23].

T. Moholdt et al.'s findings show that both CR programs consistently improved patients' quality of life after 4 weeks and 6 months, with no significant difference between groups [20].

Discussion

We performed a comprehensive review on the impact of HIIT compared to MICT programs on post-CABG patients. Our findings indicate that both exercise modalities enhanced aerobic exercise capacity, with the HIIT program seemingly to be more successful in augmenting aerobic exercise capacity, heart rate variability metrics, heart failure biomarkers, blood pressure, and subcutaneous fat percentage. However, the findings of this study showed that the HIIT program was not superior to the MICT regarding quality of life improvement.

The reported studies indicated that both HIIT and MICT modalities resulted in considerable enhancement in cardiopulmonary functional capacity; however, the HIIT rehabilitation program was more successful. A growing body of research supports the superiority of HIIT over MICT programs in improving participants' VO_2peak [24-26]. Fitriani et al. conducted a study with six individuals, with three patients in each group, who received high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) for four weeks. The results indicated that both groups exhibited enhancement in functional capacity following supervised training exercise-based sessions with insignificant difference between the modalities. The other study by T. Moholdt et al. involved 59 post-CABG patients. The results demonstrated that peak VO_2 improved in both groups after 4 weeks, with no statistically significant distinction between groups (HIIT program: 27.1 ± 4.5 vs. 30.4 ± 5.5 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, P < 0.001, MICT program: 26.2 ± 5.2 vs. 28.5 ± 5.6 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, P < 0.001). Continuing the training programs revealed that the patients in the HIIT program had a more significant increase in VO_2peak measures after 6 months compared to the MICT group (P < 0.05) [20]. Similar to our findings, Cuihua Wang et al. found that employing HIIT for under 8 weeks improved peak VO_2 more than MICT, and there was no significant difference in cardiovascular risk factor modification between 8 and 12 weeks of training results [27]. Similarly, Tian Yue et al. suggested that intervention duration exceeding 12 weeks yielded more significant improvement in VO_2peak in the HIIT group compared to moderate-intensity continuous exercise (MICE) [28]. Furthermore, Lee et al. indicated that the HIIT program yielded greater improvement in VO_2peak compared to the MICT program over 6 months; however, because of the limited sample size and significant dropout rates in both groups, this conclusion should be approached with caution [29]. Considering the cited studies, 4 weeks of exercise-based training can be advantageous to all patients with a history of CABG; however, extended training durations, up to 6 months, indicated that the HIIT program can yield greater benefits for enhancing functional capacity [19]. It has been demonstrated that elevating exercise intensity markedly enhances cardiac output and stroke volume, hence substantially improving organs' oxygenation and peripheral adaptation, which can lead to an increase in VO_2peak [30-32]. Prolonged exercise, as revealed by T. Moholdt et al.'s study, can elicit a significant enhancement in VO_2peak due to its positive effects on heart structure and cardiac output [33, 34]. Extended periods of high-intensity interval training improve cellular metabolism by altering mitochondrial density and augmenting the uptake of oxygen and glucose, hence reinforcing the effects [25, 26].

Functional ability is a significant predictor of mortality rates in patients with coronary artery disease (CAD) [41]. Reduced FC levels raise the chance of developing cardiovascular disease [42], as do cardiovascular risk factors [42]. According to prior research, decreased exercise ability is prevalent among CAD patients [43]. VO_2peak and METs are largely considered the most precise measures of assessing FC fitness [44]. Previous research has demonstrated a correlation between an increased VO_2peak and a diminished risk of all-cause death among patients with CAD [45]. A 1 mL/kg/min rise in the VO_2peak was associated with a 10-15% reduction in cardiac mortality in CAD patients [45]. Given the efficacy of HIIT programs in enhancing functional capacity, HIIT training may reduce mortality in post-CABG patients, suggesting an improvement in patient prognosis.

Another factor influencing the training programs' efficacy is commitment to cardiac rehabilitation programs which is a crucial element in elucidating and explaining the effect of exercise on cardiorespiratory fitness [37]. Our findings suggest that the HIIT program may enhance the functional capacity of post-CABG patients over long-term follow-ups, contingent upon the patients' sustained commitment to the training regimen. Similarly, several studies have demonstrated that HIIT may enhance patients' adherence to the CR program [38] more effectively than MICT [20, 39, 40]. The presence of recovery intervals during HIIT sessions could justify this. The incorporation of alternating training sessions and rest intervals elucidates the increased willingness and commitment of patients to engage in training over the long term [28]. Increased adherence to the HIIT program can significantly contribute to its enhanced efficacy, including increased functional capacity in the participants.

In our review study, the effects of exercise program types on echocardiography parameters were inconsistent throughout the trials examined. Ghardashi-Afousi et al. demonstrated that the HIIT program had a greater effect on ejection fraction (EF) and end-systolic volume (ESV) which was contrary to T. Moholdt et al.'s study findings [20, 22]. The trial conducted by Ghardashi-Afousi et al. [22] provided participants with a 6-week plan, which was longer than the 4-week duration in the T. Moholdt et al.'s study; that various programs' length can explain the variation in their effectiveness in remodeling-related parameters, including LVEF changes [20]. According to previous research, cardiac remodeling modification typically requires an extended duration. Consequently, extended durations of exercise can enhance cardiac remodeling and left ventricular compliance, resulting in improved echocardiography parameters. The Tucker et al.'s study revealed that after 6 months, exercise training had the greatest effect on heart remodeling regulation [27]. Besides, regular physical activity improves cardiac output, stroke volume, and LVEF by enhancing ventricular compliance and reversing pathological changes [28]. Researchers deem this training program to induce more significant ventricular remodeling than MICT, due to the pronounced impact of HIIT on these parameters [29]. However, additional clinical studies with appropriate matching and randomization are required to evaluate the efficacy of MICT and HIIT programs on cardiac remodeling.

The Ghardashi-Afousi et al.'s study found that the HIIT program significantly improved heart rate variability (HRV) parameters [22]. HRV is defined as the fluctuation in R-R intervals of the heartbeats and is indicative of the function of the heart's autonomic nervous system (ANS). Exercise can increase HRV in patients with CAD [32]. HRV variations correlate with vagal tone and the parasympathetic system. Although the exact process by which HIIT can influence the cardiac autonomic system is unknown, previous research has revealed that HIIT can raise the bioavailability of Nitric Oxide (NO), which at first lowers levels of angiotensin II, catechol amines, and beta-adrenergic receptor density, all of which modulate autonomous nervous system [33, 34]. Based on previous studies, low HRV is accompanied by cardiovascular complications like arrhythmias and hemodynamic dysfunction, and it is attributed to a higher rate of morbidity and mortality [30]. In addition, Belichick et al. revealed that a 10-millisecond increase in HRV reduced mortality in CVD patients [31]. Another study conducted by Besnier et al. on the patients with heart failure showed that the HIIT program caused a greater and earlier improvement in HRV compared to the MICT program. In the mentioned study, improvement in the HRV parameters was observed after 3.5 weeks of HIIT. Therefore, cardiac autonomic function enhancement can be expected after only several HIIT sessions [32].

The study by Zare Karizak et al. found that the HIIT program lowered $BNP_{1\text{-}32}$ and $NT\text{-}PROBNP_{1\text{-}76}$ blood levels at a greater rate compared to the MICT program (HIIT-MICT difference: P = 0.01, P = 0.013) [23]. Rebecca Martland et al. also reported the efficacy of HIIT in reducing BNP-associated markers in a meta-analysis study [33]. These blood markers display ventricular wall stress due to cardiac muscle dysfunction in heart failure, which can be a complication after CABG surgery and is considered a risk factor for mortality. Reduced levels of the BNP-related markers owe a great impact on decreasing angiotensin II, and endothelin, as well as an increase in vasodilator agents, such as NO and prostaglandins; these physiologic alterations can increase parasympathetic activity and diminish volume overload and adverse remodeling [34, 35].

Two studies indicated that HIIT can attenuate blood pressure (BP) in post-CABG patients [22, 23]. Previously, the HIIT program was shown to decrease volume overload by renin-angiotensin-aldosterone system inhibition [36] and improve oxygen delivery to the myocardium by increasing the quality and number of heart microvessels [37], both of which can lower blood pressure. However, contradicting results were also reported. A meta-analysis on CAD patients by Du et al. looked at the results of twenty-five studies with 1272 participants and found that the MICT program was better at blood pressure regulation (-3.61 mmHg, $P < 0.01$) [38]. This inconsistency in the results may stem from the subject's heterogeneous characteristics [39, 40]. BP regulation being dependent on many factors, including antihypertensive medication, which was not considered in Zare Karizak et al.'s study results' analysis [41]. Additionally, the study done by Zare Karizak et al. was conducted on the patients who underwent CABG surgery. This surgery can increase cardiac blood circulation and oxygenation. Conversely, the aforementioned meta-analysis focused on patients with CAD who may have coronary artery occlusions. Considering HIIT and MICT programs, if the patient's cardiac muscle suffers from a hypooxygenation, which is mostly seen in CAD patients, high-intensity exercise can even worsen this problem due to inducing higher demand in cardiac muscle and stimulating the sympathetic nervous system and norepinephrine secretion, which, in turn, increases blood pressure. Therefore, the ability of the coronary artery to deliver oxygen determines BP regulation in patients undergoing rehabilitation programs, and it is important to warn patients with coronary disease about high-intensity exercise [42].

One study evaluated the effectiveness of HIIT and MICT on body fat reduction. According to Zare Karizak et al.'s results, the HIIT program was more effective in subcutaneous fat reduction. From a physiological aspect, exercise with high intensity is effective on fat oxidation [29] and consumes more fat during the active sessions in the body. While moderate-intensity exercise should use more oxygen than fat to produce calories, it can also continue to burn fat after exercise. However, further studies are necessary to compare the effectiveness of various training programs in fat consumption among post-CABG patients in the future.

Conclusion

In summary, post-CABG patients can benefit from both HIIT and MICT programs. Previous studies have shown that after CABG surgeries, rehabilitation programs that focus on high-intensity interval training are more likely to improve heart rate variability, volume and overload pressure, as well as functional capacity (VO_2 max and METs). Also, high-intensity training can reduce the participants' percutaneous fat percentage and blood pressure. Regarding moderate versus high-intensity training effects on ventricular function, there are conflicting results, and more clinical studies are needed in the future.

Limitation

Due to the limited number of original studies presenting identical outcomes, we were unable to do a meta-analysis of the results. Future research should address the gap in clinical trials comparing the advantages of HIIT and MICT regimens in post-CABG patients.

Disclosure of conflict of interest

None.

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Supplementary Table 1. PRISMA 2020 checklist

Section and Topic	Item #	Checklist item	Locations where item is reporte
TITLE			
Title	1	Identify the report as a systematic review.	title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Eligibility criteria and study selection
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Search strategy
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Table 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Eligibility criteria and study selection
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Data extraction
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	no
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	no
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Evaluation of bias
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	no
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Not applicable
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Not applicable
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Effects of HIIT versus MICT on cardio-metabolic indices and quality of life
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	no
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	no

RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Prisma flow, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	no
Study characteristics	17	Cite each included study and present its characteristics.	Tables 1 and 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Risk of biases assessment (Results)
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Effects of HIIT versus MICT on cardio-metabolic indices and quality of life
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	no
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	no
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	no
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	discussion
	23b	Discuss any limitations of the evidence included in the review.	discussion
	23c	Discuss any limitations of the review processes used.	discussion
	23d	Discuss implications of the results for practice, policy, and future research.	Conclusion section
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	methods
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	references
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	methods
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	funding
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data availability

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P and Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71. doi: 10.1136/bmj.n71.

Supplementary Table 2. Search strategy

Search engine	Search strategy	Time	Results
Pubmed	((High-Intensity Interval Training[MeSH Terms]) OR (High Intensity Interval Training[Title/Abstract]) OR (High-Intensity Interval Trainings[Title/Abstract]) OR (Interval Training, High-Intensity[Title/Abstract]) OR (Interval Trainings, High-Intensity[Title/Abstract]) OR (Training, High-Intensity Interval[Title/Abstract]) OR (Trainings, High-Intensity Interval[Title/Abstract]) OR (High-Intensity Intermittent Exercise[Title/Abstract]) OR (Exercise, High-Intensity Intermittent[Title/Abstract]) OR (Exercises, High-Intensity Intermittent[Title/Abstract]) OR (High-Intensity Intermittent Exercises[Title/Abstract]) OR (Sprint Interval Training[Title/Abstract]) OR (Sprint Interval Trainings[Title/Abstract]) OR (high-intensity interval training[Title/Abstract]) OR (high-intensity intermittent exercise[Title/Abstract]) OR (Interval Training, High-Intensity) OR (Interval Trainings, High-Intensity) OR (sprint-interval training[Title/Abstract]) OR (HIIT[Title/Abstract]) OR (HIT[Title/Abstract]) OR (HIIE[Title/Abstract]) OR (Anaerobic interval exercise[Title/Abstract]) OR (moderate continuous interval training[Title/Abstract]) OR (MCIT[Title/Abstract])) AND ((CABG[Title/Abstract]) OR (Coronary Artery Bypasses[Title/Abstract]) OR (Coronary Artery Bypass[Title/Abstract]) OR (Aortocoronary Bypass[Title/Abstract]) OR (Aortocoronary Bypasses[Title/Abstract]) OR (Coronary Artery Bypass[MeSH Terms]))	4/23/2023	126
Embase	#1 ‘sprint interval training’/syn OR ‘sprint interval training’:ab,ti,kw,cl,de OR ‘sprint interval training’/exp OR ‘high intensity interval training’/syn OR ‘high intensity interval training’:ab,ti,kw,cl,de OR ‘high intensity interval training’/exp OR ‘moderate continuous interval training’:ab,ti,kw,cl,de OR ‘moderate continuous interval training’ OR ‘mcit’:ab,ti,kw,cl,de OR ‘mcit’ #2 ‘coronary artery bypass’:ab,ti,kw,cl,de OR ‘coronary artery bypass’/syn OR ‘coronary artery bypass’/exp OR ‘cabg’:ab,ti,kw,cl,de OR ‘cabg’ OR ‘aortocoronary bypass’:ab,ti,kw,cl,de OR ‘aortocoronary bypass’/exp #1 AND #2	4/23/2023	35
Web of Science	(TS=(High-Intensity Interval Training) OR TS=(high intensity intermittent exercise) OR TS=(sprint interval training) OR TS=(High-Intensity Interval Trainings) OR TS=(high intensity intermittent exercises) OR TS=(sprint interval trainings) OR TS=(HIT) OR TS=(HIIT) OR TS=(HIIE) OR TS=(moderate continuous interval training) OR TS=(MCIT)) AND (TS=(Coronary Artery Bypass) OR TS=(CABG) OR TS=(Aortocoronary Bypass) OR TS=(Aortocoronary Bypasses))	4/23/2023	128
Scopus	(TITLE-ABS-KEY (high-intensity AND interval AND training) OR TITLE-ABS-KEY (high-intensity AND interval AND trainings) OR TITLE-ABS-KEY (high-intensity AND intermittent AND exercise) OR TITLE-ABS-KEY (high-intensity AND intermittent AND exercises) OR TITLE-ABS-KEY (sprint AND interval AND training) OR TITLE-ABS-KEY (sprint AND interval AND trainings) OR TITLE-ABS-KEY (hiie) OR TITLE-ABS-KEY (hit) OR TITLE-ABS-KEY (hiit) OR TITLE-ABS-KEY (moderate AND continuous AND interval AND training) OR TITLE-ABS-KEY (mcit)) AND (TITLE-ABS-KEY (cabg) OR TITLE-ABS-KEY (coronary AND artery AND bypass) OR TITLE-ABS-KEY (aortocoronary AND bypass))	4/23/2023	265
Google Scholar	(“high intensity training” OR “high intensity intermittent exercise” OR “sprint interval training” OR “moderate continuous interval training” OR “HIIT” OR “HIIE” OR “MICT”) AND (“coronary artery bypass” OR “CABG” OR “aortocoronary bypass”)	4/23/2023	34