Hindawi Cardiology Research and Practice Volume 2023, Article ID 7630594, 11 pages https://doi.org/10.1155/2023/7630594



Review Article

The Effect of High-Intensity Interval Training on Exercise Capacity in Patients with Coronary Artery Disease: A Systematic Review and Meta-Analysis

Siyi Li , Yan Li , Suankun Chen , Huachen Jiao , Yan Li , Guanghui Pan , and Xue Yitao , Suanghui Pan ,

Correspondence should be addressed to Xue Yitao; xytsdzydfy@126.com

Received 9 April 2022; Revised 10 November 2022; Accepted 25 November 2022; Published 3 April 2023

Academic Editor: Anwer Habib

Copyright © 2023 Siyi Li et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. The optimal exercise prescription for coronary artery disease (CAD) remains under debate. The aim of our metaanalysis is to investigate the efficacy of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) of coronary artery disease patients. Methods. Electronic databases were searched from their inception date until October 23, 2021, and the articles include randomized controlled trials. The mean differences and 95% confidence intervals were calculated, and heterogeneity was assessed using the I^2 test. Results. The study standards were met by seventeen studies. The pooled studies included 902 patients. HIIT resulted in improvement in peak oxygen uptake (1.50 ml/kg/min, 95% confidence interval: 0.48 to 2.53, n = 853patients, and low quality evidence) compared with MICT. There was no discernible difference between the individuals in the HIIT group and the MICT group in terms of systolic/diastolic blood pressure or peak/resting heart rate. Conclusion. This systematic review and meta-analysis reported the superiority of HIIT versus MICT in enhancing peak oxygen uptake in CAD patients.

1. Introduction

The main cause of death worldwide has been coronary artery disease (CAD) [1]. Cardiac rehabilitation (CR) based on exercise training is an approach to enhance cardiopulmonary capacity, metabolic parameters, and quality of life [2]. CR in patients with CAD decreases angina [3], hospitalizations [4], and mortality [5].

According to the intensity and method of training protocols, interrelated exercise rehabilitation can be divided into high-intensity interval training (HIIT) and moderate-intensity continuous exercise (MICT). MICT has shown some advantages in decreasing the cardiovascular risk and mortality [6]. Due to the exercise protocol of MICT, there

remains a low level of compliance with CR. In 2007, the American Heart Association recommended HIIT, which consists of repetition of quick and intense bursts of exercise, followed by short recovery periods [7].

In recent years, a growing amount of evidence proved that HIIT has beneficial effects on exercise capacity and cardiovascular function. However, these studies were limited by the small sample size and short follow-up period. Therefore, there is not sufficient clinical evidence to prove the efficiency of HIIT in CAD patients. Previous systematic reviews [8–10] also showed the superiority of HIIT on exercise capacity in patients involved with an exercise-based cardiac rehabilitation program. However, the most updated systematic review performed their literature search in

¹The First Clinical Medical School, Shandong University of Traditional Chinese Medicine, Jinan, China

²State Key Laboratory of Dampness Syndrome of Chinese Medicine,

The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China

³Key Unit of Methodology in Clinical Research, Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, China

⁴Department of Global Public Health, Health Systems and Policy, Karolinska Institutet, Stockholm 17177, Sweden

⁵Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan 250014, China

November 2016 [11]. The study has since been followed by the publication of new studies.

The objective of this systematic review with meta-analysis was to evaluate the benefits of HIIT compared with MICT. In addition, we evaluated for the effects of HIIT on exercise capacity, blood pressure, and heart rate in CAD patients.

2. Methods

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Supplementary Materials: PRISMA 2009 Checklist) [12] and the Cochrane Handbook for Interventional Reviews [13]. The study protocol has been published previously in INPLASY, the registration number is INPLASY202240036 (available in https://inplasy.com/inplasy-2022-4-0036/).

- 2.1. Search Strategy. The electronic databases PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, and CINAHL were searched from their inception until October 23, 2021. The searches were restricted to articles written in English. The search strategy details are provided in the Supplemental Materials—search strategy.
- 2.2. Study Selection. The full text was reviewed of all included articles. Two reviewers (S. L. and X. C.) independently screened the titles and abstracts. Furthermore, full-text screening was conducted according to the criteria for inclusion and exclusion. Disagreements for inclusion were discussed by the two reviewers and resolved by senior authors (Y. X.). Randomized controlled trials (RCTs) were included and the selection criteria are described below. The inclusion criteria were as follows: (1) RCTs comparing the effectiveness of HIIT with MICT in participants with CAD; (2) at least one of the following outcomes were measured—VO_{2peak}, peak heart rate (HRpeak), resting heart rate (HRrest), resting systolic blood pressure (SBP), and resting diastolic blood pressure (DBP); and (3) the language was restricted to English. The exclusion criteria were as follows: (1) single-arm research and animal experiment research; (2) conference papers, letters, or abstracts where the full text was not available; and (3) incomplete data.
- 2.3. Data Collection. The data extraction form was predefined and included the following: population characteristics, intervention duration, training protocols, and outcome measures. One reviewer (S. L) used a standardized form to extract data from the included articles, and the extracted data were checked by a second reviewer (X. C). Attempts were made to contact the original investigators regarding any missing data. Any discrepancies were resolved by agreement after rechecking the source papers and via further discussion with a third reviewer (Y. X.).
- 2.4. Risk of Bias Assessment. In accordance with the recommendations in the Cochrane Handbook, the trials' methodological quality was independently evaluated by two

reviewers (S. L. and X. C) using the Cochrane risk of bias assessment tool. Any discrepancies were resolved by agreement after rechecking the source papers and further discussion with a third reviewer (Y. X.). The following domains were considered: (1) random sequence generation, (2) allocation concealment, (3) blinding of the patients and personnel, (4) blinding of the outcome assessors for the primary outcomes, (5) incomplete outcome data, (6) selective reporting, and (7) other bias.

- 2.5. Quality of Evidence. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) [14] was used to assess the quality of evidence of outcomes, which criteria comprised the risk of bias, inconsistency, indirectness, inaccuracy, and publication bias. The quality of evidence was classified as high, moderate, low, or very low.
- 2.6. Statistical Analysis. Statistical analysis was performed with Review Manager (RevMan, Version 5.4.1 The Cochrane Collaboration, Copenhagen, Denmark) [15]. Given that all of the variables in the included studies consisted of continuous data, we used the mean difference (MD) when the same instrument was used, or the standardized mean difference (SMD) when different instruments were used, with 95% confidence intervals (CI) to analyze the outcomes. A p value < 0.05 was considered statistically significant. Heterogeneity was assessed with a chi-squared test (p < 0.10 was considered indicative of statistical significance) and the I^2 statistic (where $I^2 > 25\%$, 50%, and 75% indicated moderate, substantial, or considerable heterogeneity, respectively). When I^2 is less than 50%, it indicated low heterogeneity, and a fixed-effects model would be chosen; otherwise, a randomeffects model was adopted. Potential publication bias was evaluated by visual examination of funnel plot asymmetry and Egger's test (a p value < 0.05 was considered statistically significant). When the number of articles included in one analysis was limited (i.e., less than 10), the risk for publication bias was not assessed.

3. Result

- 3.1. Study Selection. The process of study selection is shown in Figure 1. The initial search identified 570 articles (560 from the database search and 10 from the manual search), of which 381 were eligible for title and abstract scanning following the exclusion of duplicates. Based on the inclusion and exclusion criteria, 321 studies were excluded with 60 remaining. After the full texts of 60 articles were completely read, 16 articles met the eligibility criteria and were included in the meta-analysis [16–31].
- 3.2. Characteristics of Included Studies. Table 1 lists the general characteristics of the included studies, and the studies consisted of seven RCTs and one retrospective cohort study. One study [16] had a three-arm parallel group design. A total of sixteen studies comprising 853 patients were included for the analysis, and 406 patients underwent HIIT.

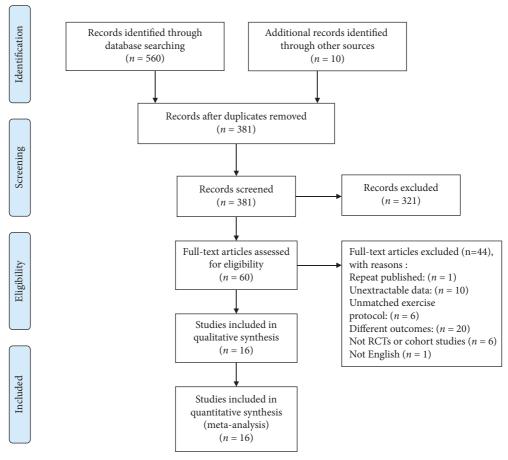


FIGURE 1: Flowchart of study identification and selection.

The number of participants included in each study in our meta-analysis ranged from 14 to 174, and the mean age of the included participants ranged from 55.9 to 68 years. In the included studies, MICT was applied for the intervention of the control group. The duration of the interventions ranged between 4 and 12 weeks.

3.3. Risk of Bias. The individual items on the risk of bias assessment are shown in Figure 2. Sixty percent of the included RCTs provided adequate random sequence generation but only four studies reported allocation concealment methods. As both HIIT and MICT are exercise trainings, designing an experiment with a credible placebo-control arm is challenging. Thus, all RCTs were open label. All studies claimed that the outcome assessors had been blinded to the patient treatment allocation. Four studies [21–23, 26] reported incomplete outcome data because the participants were lost to follow-up, and the reasons for loss or withdrawal were noted in the literature. Approximately 50% of the included studies were at unclear risk of selective reporting because neither their protocol nor trial registration information was available.

The risk of publication bias, as analyzed by funnel plots, showed only minor asymmetry (Supplementary Figure S1). Thus, a publication bias mechanism is not a major cause of concern.

3.4. Quality of Evidence. The GRADE system showed that the quality of evidence was low for VO_{2peak} because of unclear allocation concealment or lack of blinding. The quality of evidence was downgraded to very low for the SBP, DBP, and heart rate because of the large heterogeneity and risk of bias.

3.5. Meta-Analysis of Outcomes

3.5.1. Peak Oxygen Uptake. VO_{2peak} was measured in 16 studies [16–31] with a total of 853 patients. The pooled results showed that HIIT led to a statistically significant 1.50 mL/kg/min improvement in the patients' VO_{2peak} (95% CI, 0.48 to 2.53; I^2 = 59%; Figure 3(a)). A subgroup analysis was performed on the duration of intervention (<12 and ≥ 12 weeks) for HIIT versus MICT on VO_{2peak}. The short-term group (<12 weeks) showed a significant improvement in VO_{2peak} (MD = 2.75 mL/kg/min, 95% CI, 0.98, 4.52; I^2 = 36%; Figure 3(b)). The analysis long-term group (≥12 weeks) showed no significant effect on VO_{2peak} (MD = 0.58 mL/kg/min, 95% CI, −0.40, 1.57; I^2 = 50%; Figure 3(b)).

3.5.2. Blood Pressure. Blood pressure included SBP and DBP, which were measured in 9 studies [16, 18–23, 27, 30] with a total of 528 patients. The results of our meta-analysis

TABLE 1: Characteristics of included studies.

- 10	Sample size	Ages	Training	Training protocols	Program
Study	T/C (M/F)	$\tilde{T/C}$	HIIT	MICT	duration
Cardozo et al., 2015	23 (14, 9)/48 (34, 14)	$T: 56 \pm 12$ $C: 62 \pm 12$	10 bouts * 2 min (>90% HRpeak) Each interval: 2 min (<60% HRpeak)	30 min of continuous training (at 70 to 75% of HRpeak)	16 weeks
Choi et al., 2018	23 (21, 2)/21 (18,)	$T: 60 \pm 11$ $C:$ $C:$ 62.8 ± 11.9	4 bouts * 4 min (at 85–100% of the HRpeak) Each interval: 3 min (at 50–60% of the HRpeak)	28 min of continuous training (at 60 to 70% of HRpeak) 9-10 weeks	9-10 weeks
Conraads et al., 2015	85 (NA)/89 (NA)	NA	4 bouts * 4 min (at 85–90% of peak VO2 90–95% of HRpeak, 15–17 Borg scale, and shortness of breath) Each interval: 3 min (at 50–70% of HRpeak)	4 bouts * 4 min (at 85–90% of peak VO2 90–95% of HRpeak, 15–17 Borg scale, and shortness of 37 min of continuous training (at least 60–70% of peak VO2, breath) at least 65–75% of HRpeak) Each interval: 3 min (at 50–70% of HRpeak)	12 weeks
Currie et al.,2013	11 (NA)/11 (NA)	T: 63 ± 8 C: 66 ± 8	Part 1 (week 1–4): 10 bouts * 1 min (at 89% of PPO pre) Part 2 (week 5–8): 10 bouts * 1 min (at 102% of PPOpre) Part 3 (week 9–12): 10 bouts * 1 min (at 110% of PPOpre)	Part 1 (week 1–4): 10 bouts * 1 min (at 102% of PPO pre) Part1 (week 1–4): 30 min of continuous training (at 58% of Part 2 (week 5–8): 10 bouts * 1 min (at 110% of PPOpre) Part 2 (week 5–8): 40 min of continuous training (at 58% of PPOpre) Part 3 (week 9–12): 10 bouts * 1 min (at 110% of PPOpre) Part 5 (week 5–8): 40 min of continuous training (at 58% of PPOpre)	12 weeks
			Each interval: 1 min (at 10% of PPOpre)	Part 3 (week 9–12): 50 min of continuous training (at 58% of PPOpre)	
			Part 1 (month 1): 10 bouts * 1 min (at 85% of PPOpre) Part 2 (month 2): 10 bouts * 1 min (at 100% of PPOpre)	Part 1 (month 1): 30 min of continuous training (at 57% PPOpre)	
Currie et al., 2014	9 (9)/10 (9, 1)	$T: 62 \pm 11$	Part 3 (month 3): 10 bouts * 1 min (at 108% of PPOpre)	Part 2 (month 2): 40 min of continuous training (at 57% PPOpre)	24 weeks
		C: 68 + 8	Part 4 (month 4–6): 10 bouts * 1 min (at 121% of PPOpre)	Part 3 (month-3): 50 mm of moderate-intensity exercise (at 57% PPOpre)	
			Each interval: 1 min (at 10% of PPOpre)	Part 4 (month4–6): min of continuous training (at 78% PPOpre)	
Dunford et al., 2021	9/11 (Total: 18/ 2)	Total: 61 ± 7	3 bouts * 90 s stairs climbing Each interval: walking 90 s	30 min of continuous training (at 60–80% HRpeak)	12 weeks

TABLE 1: Continued.

	-		~	0 0000	1
Study	Sample size T/C (M/F)	Ages T/C	HIIT	Training protocols MICT	Program duration
Jaureguizar et al., 2016	36 (33, 3)/36 (28, 8)	T: 58 ± 111 C: 58 ± 111	Part 1 (week 1): HIIT: 15 bouts * 20 s (50% of the maximum load reached in the first SRT) Each interval: 40 s (10% of the maximum load reached in the first SRT) Part 2 (week 2): HIIT: 20 bouts * 20 s (50% of the maximum load reached in the first SRT) Each interval: 40 s (10% of the maximum load reached in the first SRT) Part 3 (week 3): HIIT: 25 bouts * 20 s (50% of the maximum load reached in the first SRT) Each interval: 40 s (10% of the maximum load reached in the first SRT) Part 4 (week 4): HIIT: 30 bouts * 20 s (50% of the maximum load reached in the first SRT) Each interval: 40 s (10% of the maximum load reached in the first SRT) Each interval: 40 s (10% of the maximum load reached in the first SRT) Part5 (week 5–8): HIIT: 30 bouts * 20 s (50% of the maximum load reached in the second SRT)	Part 1: MICT: 15 mins (at (VT1) Part 2 (2 w): MICT: 20 mins (at VT1) Part 3 (3 w): MICT: 25 mins at (VT1) Part4 (4 w): MICT: 30 mins at (VT1) Part 5 (5-8 w): MICT: 30 mins at (VT1+10%)	8 weeks
Keteyian et al., 2014	36 (33, 3)/36 (28, 8)	$T: 58 \pm 11$ $C: 58 \pm 11$	4 bouts of 4 min (at 80–90% of the heart rate reserve) Each interval: 3 min (at 60–70% of the heart rate reserve)	30 min of continuous training (at 60% to 80% of heart rate reserve)	2 weeks
Kim 2020	23 (18, 5)/24 (16, 8)	$T: 60 \pm 11$ C: 62.8 ± 11.9	4 bouts * 4 min (at 95–100% of the HRR) Each interval: 3 min (at 60% of the HRR)	First part: 3 bouts * 8 min (at 85% of the HRR) Each interval: 3 min (at 40% of the HRR)	6 weeks
Moholdt et al., 2009	28 (24, 4)/31 (24, 7)	T : 60.2 ± 6.9 C : 62.0 ± 7.6	4 bouts * 4 min (at 90% of the HRpeak) Each interval: 3 min (70% of the HRpeak)	46 min of continuous training (at least 70% of HRpeak)	4 weeks
Moholdt et al., 2012	30 (25, 5)/59 (49, 10)	T: 56.7 ± 10.4 C : 57.7 ± 9.3	4 bouts * 4 min (at 85–95% HRpeak) Each interval: 1 min (70% HRpeak)	Usual care exercise: 60 min of aerobic exercises	12 weeks
Pattyn et al., 2016	80 (76, 4)/83 (76, 7)	<i>T</i> : 57.4 ± 8.7 <i>C</i> : 59.9 ± 9.2	4 bouts of 4 min (at 85–95% of the HRpeak) Each interval: 3 min (50%–70% of the HRpeak)	37 min of continuous training (at least 70–75% of HRpeak)	12 weeks
Prado et al., 2016	17(14, 3)/18 (14, 4)	$T: 56.5 \pm 2.7$ $C: 61.3 \pm 2.2$	7 bouts * 3 min (at RCP) Each interval: 3 min (at VAT)	50 min of continuous training (at VAT)	12 weeks
Rocco et al., 2012	17(14, 3)/20 (15, 5)	$T: 56.5 \pm 3.0$ C: 62.3 ± 2.0)	7 bouts * 3 min (at RCP) Each interval: 3 min (at VAT)	50 min of continuous training (at VAT)	12 weeks
Rognmo et al., 2004	8(6, 2)/9(8, 1)	T: 62.9 ± 11.2 C : 61.2 ± 7.3	4 bouts * 4 min (at 80–90% oVO2peak (85–95% of HRpeak) Each interval: 3 min (at 50–60% of VO2peak)	41 min of continuous training (at 50-60% of VO2 peak)	10 weeks
Warburton et al., 2005	7(NA)/7(NA)	T: 55.9 ± 7 C: 57 ± 8	15 bouts * 2 min (at 90% of heart rate/VO2reserve (range 85% to 95%)) Each interval: 2 min (at 40% of heart rate/VO2reserve (range 35% to 45%))	30 min of continuous training (at 65% of heart rate/ VO2reserve)	16 weeks

indicated a small but significant benefit from HIIT on SBP (MD = 2.59 mmHg; 95% CI, 0.09 to 5.09; I^2 = 0%; Figure 4(a)). Moreover, the beneficial effect of HIIT on DBP was also small but significant (MD = 1.86 mmHg, 95% CI: 0.40 to 3.32; I^2 = 24%; Figure 4(b)).

3.5.3. Heart Rate. HRpeak was available for 13 [16, 18–25, 27, 28, 30, 31] studies with a total of 713 patients. The pooled results showed that HIIT led to a statistically significant increase in Hrpeak (MD = 5.51 bpm; 95% CI, 2.13 to 8.89), but the heterogeneity was considerable ($I^2 = 40\%$; Figure 4(c)). HRrest was available for 10 [18–22, 24, 26, 27, 30] studies with a total of 588 patients. The results of the meta-analysis indicated no significantly greater effect from HIIT on HRrest (MD = 0.19 bpm; 95% CI, -0.40 to 2.23; Figure 4(d)).

4. Discussion

The overall results of this study, which includes data from 16 RCTs and 853 patients, confirm a significantly larger effect size for ${\rm VO_{2peak}}$ (+1.50 ml/min/kg) in favor of HIIT. But the results of our meta-analysis found no significant effect on SBP and DBP, or HRpeak and HRrest. Although the meta-analysis of each outcome shows a certain degree of heterogeneity (I^2 <50%), we also used the random effect model, sensitivity analysis, and subgroup analysis to indicate the robustness of the results. Therefore, the results of our meta-analysis are relatively reliable.

Aerobic exercise has long been the cornerstone of cardiac rehabilitation programs for patients with CAD, and improving the aerobic exercise capacity of patients with CAD is its most significant benefit [31]. Aerobic exercise capacity is the strongest predictor of all cardiovascular morbidity and mortality and is the process of uptake, transport, and utilization of oxygen [5, 18]. In recent decades, MICT has been recommended for CAD patients according to the guidelines [32]. Several studies have already investigated the benefits of HIIT in exercise capacity [33].

 ${
m VO}_{2{
m peak}}$ is the gold standard method to assess the aerobic exercise capacity [31, 34]. In our meta-analysis of patients with CAD, HIIT showed a superiority compared with MICT in improving the ${
m VO}_{2{
m peak}}$ of patients. Given the significant heterogeneity found in the primary analyses due to the variance in exercise protocols (variable intensities and different durations of the exercise programs), caution is warranted when interpreting our results. Our finding showed that HIIT resulted in a larger gain of 1.50 mL/kg/min on ${
m VO}_{2{
m peak}}$ than MICT, and these results are in line with previous meta-analyses [8–10].

According to the duration of the total intervention, our research showed that <12 weeks group resulted in a greater improvement in VO_{2peak} by 2.75 mL/kg/min in MD than \geq 12 weeks group did, which is in line with Taylor et al.'s finding [35], which reported home-based HIIT and MICT had low rates of adherence features compared with the supervised stage. Only one included trial [21] stated the protocol consisted of 6 supervised sessions (4 weeks) and 24

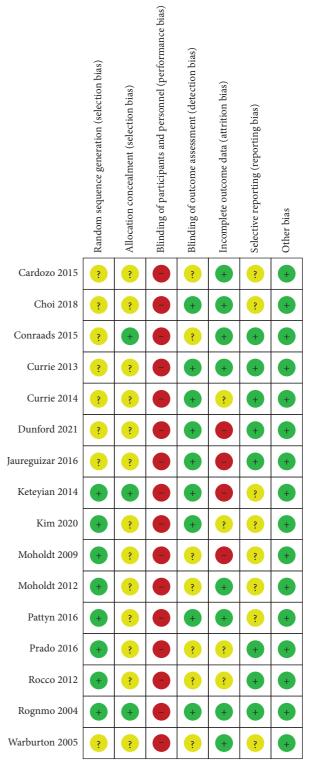
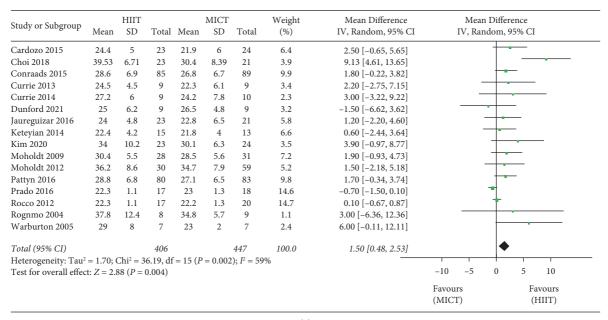


FIGURE 2: Risk of bias summary.

unsupervised sessions for an additional 8 weeks (12 weeks total). Therefore, higher patient acceptance of short-term exercise may have contributed to this outcome.

A meta-analysis involved one million adults suggested that 10 mmHg decrease of SBP and DBP could reduce the risk of premature death from stroke and ischemic heart

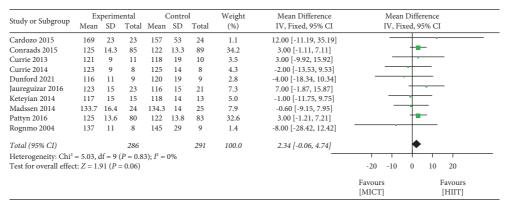


(a) HIIT MICT Weight Mean Difference Mean Difference Study or Subgroup SD Total SD Total IV, Random, 95% CI IV, Random, 95% CI Mean Mean (%) 2.4.1 <12weeks Cardozo 2015 24.4 5 23 21.9 6 24 6.4 2.50 [-0.65, 5.65] Choi 2018 30.4 9.13 [4.61, 13.65] 39.53 6.71 23 8.39 21 3.9 Currie 2014 27.2 9 24.2 7.8 10 2.3 3.00 [-3.22, 9.22] 6 Jaureguizar 2016 2.4 4.8 23 22.8 6.5 2.1 5.8 1.20 [-2.20, 4.60] Keteyian 2014 22.4 4.2 15 21.8 13 6.6 0.60 [-2.44, 3.64] Kim 2020 10.2 23 30.1 24 3.5 3.90 [-0.97, 8.77] 34 6.3 Moholdt 2009 30.4 28 5.5 28.5 5.6 31 7.2 1.90 [-0.93, 4.73] Rognmo 2004 37.8 12.4 8 34.8 5.7 9 1.1 3.00 [-6.36, 12.36] Subtotal (95% CI) 152 153 36.8 2.75 [0.98, 4.52] Heterogeneity: $Tau^2 = 2.20$; $Chi^2 = 10.86$, df = 7 (P = 0.14); $I^2 = 36\%$ Test for overall effect: Z = 3.05 (P = 0.002) 2.4.2 ≥12weeks 6.9 Conraads 2015 28.6 85 26.8 6.7 89 9.9 1.80 [-0.22, 3.82] Currie 2013 24.5 9 22.3 9 2.20[-2.75, 7.15]4.5 6.1 3.4 Dunford 2021 25 6.2 9 26.5 4.8 9 3.2 -1.50 [-6.62, 3.62] Moholdt 2012 36.2 34.7 7.9 59 1.50 [-2.18, 5.18] 8.6 30 5.2 Pattyn 2016 28.8 6.8 80 27.1 6.5 83 9.8 1.70 [-0.34, 3.74] Prado 2016 22.3 1.1 17 23 1.3 18 14.6 -0.70 [-1.50, 0.10] Rocco 2012 22.3 1.1 17 22.2 20 14.7 0.10 [-0.67, 0.87] 1.3 7 6.00 [-0.11, 12.11] Warburton 2005 29 8 23 2.4 Subtotal (95% CI) 254 294 63.2 0.58 [-0.40, 1.57] Heterogeneity: $Tau^2 = 0.73$; $Chi^2 = 14.12$, df = 7 (P = 0.05); $I^2 = 50\%$ Test for overall effect: Z = 1.16 (P = 0.25) Total (95% CI) 100.0 406 447 1.50 [0.48, 2.53] Heterogeneity: $Tau^2 = 1.70$; $Chi^2 = 36.19$, df = 15 (P = 0.002); $I^2 = 59\%$ -10 10 Test for overall effect: Z = 2.88 (P = 0.004) Test for subgroup differences: $Chi^2 = 4.40$, df = 1 (P = 0.04); $I^2 = 77.2\%$ Favours Favours (MICT) (HIIT)

(b) $\label{eq:Figure 3: Meta-analysis results for VO} Figure 3: Meta-analysis results for VO$_{2peak}$ (mL/kg/min).$

disease by 40% and 30%, respectively [36]. In patients with hypertension, both HIIT and MICT reduced ambulatory blood pressure, increasing the percentage of patients with normal ambulatory blood pressure values [37]. However, no significant changes were found in our meta-analysis of SBP and DBP after HIIT and MICT intervention. With the reason

for the significant heterogeneity among studies being unknown, whether there was a significantly greater effect on blood pressure in HIIT compared with MICT is still uncertain. This may be attributed to the inclusion of CAD patients rather than hypertensive patients in this metaanalysis. It seems that HIIT reduced SBP better than



(a) Mean Difference Control Weight Study or Subgroup IV, Fixed, 95% CI Mean SD Total Mean SD Total (%) IV, Fixed, 95% CI Cardozo 2015 22 3.00 [-6.54, 12.54] 32.2 2.7 74.7 Conraads 2015 8.4 85 72.5 8.2 89 2.20 [-0.27, 4.67] Currie 2013 79 11.00 [2.44, 19.56] 10 11 68 10 10 Currie 2014 6.7 -2.00 [-7.41, 3.41] 76 74 71 Dunford 2021 72 73 4.6 4.00 [-2.53, 10.53] 1.00 [-4.05, 6.05] -3.00 [-10.41, 4.41] Jaureguizar 2016 Keteyian 2014 23 21 7.7 74 11 15 13 3.6 24 8.0 1.80 [-3.14, 6.74] Madssen 2014 10 Pattyn 2016 74.8 8.4 80 72.5 30.9 2.30 [-0.22, 4.82] Rognmo 2004 73 10 8 79 14 9 1.5 -6.00 [-17.48, 5.48] 286 291 1.85 [0.45, 3.25] Total (95% CI) 100.0 Heterogeneity: Chi² = 10.55, df = 9 (P = 0.31); I² = 15% Test for overall effect: Z = 2.59 (P = 0.010) -20 -10 10 20 Favours Favours [MICT] [HIIT]

Ct . 1 C . 1		HIIT			MICT		Weight	Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	(%)	IV, Random, 95% CI	IV, Random, 95% CI
Cardozo 2015	133	24	23	128	19	24	5.8	5.00 [-7.41, 17.41]	
Conraads 2015	145	18.2	85	138	21.5	89	11.7	7.00 [1.09, 12.91]	-
Currie 2013	139	15	10	123	16	10	5.2	16.00 [2.41, 29.59]	
Currie 2014	146	16	8	128	29	9	2.5	18.00 [-3.95, 39.95]	
Dunford 2021	124	20	9	133	17	9	3.7	-9.00 [-26.15, 8.15]	
Jaureguizar 2016	126	14	23	119	21	21	7.1	7.00 [-3.65, 17.65]	 -
Keteyian 2014	151	17	15	135	26	13	3.9	16.00 [-0.55, 32.55]	-
Kim 2020	141	19.2	23	147.5	19.4	24	6.8	-6.50 [-17.54, 4.54]	
Madssen 2014	155.8	15.9	24	161.6	13.1	25	9.2	-5.80 [-13.98, 2.38]	
Moholdt 2012	156	17	30	154	16	59	10.1	2.00 [-5.33, 9.33]	
Pattyn 2016	146	18.4	80	139	21.8	83	11.4	7.00 [0.82, 13.18]	
Prado 2016	131	4.7	17	122	4.1	18	15.0	9.00 [6.07, 11.93]	-
Rognmo 2004	151	19	8	155	13	9	4.2	-4.00 [-19.67, 11.67]	*
Warburton 2005	155	19	7	159	15	7	3.4	-4.00 [-21.93, 13.93]	
Total (95% CI)			362			400	100.0	4.24 [0.51, 7.97]	•
Heterogeneity: Tau ²	= 21.88; 0	Chi ² = 1	28.67, d	f = 13 (F	0.0	$(07); I^2 =$	55%		
Test for overall effec									-20 -10 0 10 20
									Favours Favours
									[MICT] [HIIT]

Study or Subgroup	Mean	HIIT SD	Total	Mean	MICT SD	Total	Weight (%)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Conraads 2015	55.4	7.4	85	55.4	8.1	89	31.3	0.00 [-2.30, 2.30]	
Currie 2013	57	6	11	52	8	10	4.5	5.00 [-1.10, 11.10]	+
Currie 2014	57	4	8	55	7	9	5.8	2.00 [-3.35, 7.35]	
Dunford 2021	69	10	9	64	12	9	1.6	5.00 [-5.21, 15.21]	-
Jaureguizar 2016	64	10	23	59	8	21	5.8	5.00 [-0.33, 10.33]	
Keteyian 2014	66	13	15	64	10	13	2.3	2.00 [-6.53, 10.53]	
Kim 2020	62	8.5	23	65.1	8.3	24	7.2	-3.10 [-7.91, 1.71]	
Madssen 2014	65.7	11.6	24	63.2	11.1	25	4.1	2.50 [-3.86, 8.86]	
Moholdt 2009	66.4	8.7	28	63.9	8.8	31	8.3	2.50 [-1.97, 6.97]	
Pattyn 2016	56.3	7.7	80	55.8	8.5	83	26.8	0.50 [-1.99, 2.99]	
Rognmo 2004	63	7	8	63	11	9	2.2	0.00 [-8.67, 8.67]	
Total (95% CI)			314			323	100.0	0.98 [-0.31, 2.27]	*
Heterogeneity: Chi2 =	8.97, df =	10 (P	= 0.54)	$I^2 = 0\%$	ó			_	-
Test for overall effect:	Z = 1.49 (P=0.1	14)						-10 -5 0 5 10
									Favours Favours

MICT in our report. Our results are inconsistent with Du et al.'s [38], who reported MICT seemed to induce a larger reduction in both SBP and DBP than HIIT. Three [20, 23, 25] included trials reported changes in medications during the invention. This would make it difficult to interpret and discuss the underlying mechanisms. Factors associated with medications should be considered when making personalized prescriptions.

In resent epidemiological studies, Aboyans and Criqui [39] indicated that elevated HRrest is independently associated with atherosclerosis and increased cardiovascular morbidity and mortality in cardiovascular diseases. Our results suggested that HRpeak and HRrest are equally influenced by HIIT and MICT. It is suggested that vigorous exercise could increase the risk of sudden cardiac events in susceptible individuals [40]. According to the results of Rognmo et al.'s study [41], the risk of cardiovascular events is low after performing high-intensity exercise or moderate-intensity exercise in cardiovascular rehabilitation.

5. Strengths and Limitations

The strength of this systematic review provided an updated analysis of data from RCTs that compared HIIT to MICT in patients with CAD. Moreover, this study was conducted in compliance with the PRISMA checklist for clear reporting, registration on INPLASY platform with protocol, and applying the GRADE tool to assess the certainty of the evidence. The study has potential limitations. First, few trials reported in detail on randomization procedures to determine whether selection bias might have affected study outcomes. Another important limitation is the small number of studies comparing HIIT and MICT with isocaloric protocols. On the other hand, the pooled studies lack large-scale clinical RCTs, which may affect the objectivity and reliability of this meta-analysis. In addition, the duration of the training program ranged from 4 to 24 weeks. The long-term safety and effects of HIIT are still unknown.

6. Conclusion

This meta-analysis and systematic review reported the superiority of HIIT in improving VO_{2peak} in CAD patients compared with MICT. These findings suggest that HIIT is a promising alternative exercise protocol for improving cardiorespiratory function in patients with CAD. The duration of the intervention and the availability of supervision are further considerations for the exercise protocols. Moreover, there was no difference between the HIIT and MICT effects on SBP and DBP or peak and resting HR. In further studies, larger and longer-term studies are needed to address inadequate evidence.

Abbreviations

CAD: Coronary artery disease CR: Cardiac rehabilitation

HIIT: High-intensity interval training MICT: Moderate-intensity continuous exercise

VO_{2peak}: Peak oxygen consumption

HRpeak: Heart rate
HRrest: Resting heart rate
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
RCTs: Randomized controlled trials.

Data Availability

The data used to support the findings of this study are available from the authors upon request.

Disclosure

The authors have submitted in the INPLASY PROTOCOL "https://inplasy.com/wp-content/uploads/2022/04/INPLASY-Protocol-3118-1.pdf" and uploaded the updated manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors thank all the authors of the original studies included in this meta-analysis. The authors disclose that the following grant has been received for research, authorship, and publication of this article and thank the National Natural Science Foundation of China (no. 81774247) for its support.

Supplementary Materials

(1) Table S1: search strategy in English databases. (2) Figure S1: funnel plot of publication bias. (3) PRISMA 2009 Checklist. (Supplementary Materials)

References

- [1] G. B. D. Mortality, "Causes of Death C. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013," *Lancet*, vol. 385, no. 9963, pp. 117–171, 2015.
- [2] P. D. Thompson, R. Arena, D. Riebe, and L. S. Pescatello, "ACSM's new preparticipation health screening recommendations from ACSM's guidelines for exercise testing and prescription, ninth edition," *Current Sports Medicine Reports*, vol. 12, no. 4, pp. 215–217, 2013.
- [3] P. A. Ades, M. H. Grunvald, R. M. Weiss, and J. S. Hanson, "Usefulness of myocardial ischemia as predictor of training effect in cardiac rehabilitation after acute myocardial infarction or coronary artery bypass grafting," *The American Journal of Cardiology*, vol. 63, no. 15, pp. 1032–1036, 1989.
- [4] M. J. Haykowsky, K. M. Daniel, P. S. Bhella, S. Sarma, and D. W. Kitzman, "Heart failure: exercise-based cardiac rehabilitation: who, when, and how intense?" *Canadian Journal* of Cardiology, vol. 32, no. 10, pp. S382–s387, 2016.
- [5] L. Anderson, D. R. Thompson, N. Oldridge et al., "Exercise-based cardiac rehabilitation for coronary heart disease," *Cochrane Database of Systematic Reviews*, vol. 2016, no. 1, Article ID Cd001800, 2016.

- [6] A. Mezzani, L. F. Hamm, A. M. Jones et al., "Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European association for cardiovascular prevention and rehabilitation, the American association of cardiovascular and pulmonary rehabilitation and the Canadian association of cardiac rehabilitation," European Journal of Preventive Cardiology, vol. 20, no. 3, pp. 442–467, 2013.
- [7] G. J. Balady, M. A. Williams, P. A. Ades et al., "Core components of cardiac rehabilitation/secondary prevention programs: 2007 update: a scientific statement from the American heart association exercise, cardiac rehabilitation, and prevention committee, the council on clinical cardiology; the councils on cardiovascular nursing, epidemiology and prevention, and nutrition, physical activity, and metabolism; and the American association of cardiovascular and pulmonary rehabilitation," *Circulation*, vol. 115, no. 20, pp. 2675–2682, 2007.
- [8] A. D. Elliott, K. Rajopadhyaya, D. J. Bentley, J. F. Beltrame, and E. C. Aromataris, "Interval training versus continuous exercise in patients with coronary artery disease: a meta-analysis," *Heart Lung & Circulation*, vol. 24, no. 2, pp. 149–157, 2015.
- [9] K. Liou, S. Ho, J. Fildes, and S.-Y. Ooi, "High intensity interval versus moderate intensity continuous training in patients with coronary artery disease: a meta-analysis of physiological and clinical parameters," *Heart Lung & Circulation*, vol. 25, no. 2, pp. 166–174, 2016.
- [10] N. Pattyn, E. Coeckelberghs, R. Buys, V. A. Cornelissen, and L. Vanhees, "Aerobic interval training vs. Moderate continuous training in coronary artery disease patients: a systematic review and meta-analysis," *Sports Medicine*, vol. 44, no. 5, pp. 687–700, 2014.
- [11] M. Gomes-Neto, A. R. Durães, H. F. C. D. Reis, V. R. Neves, B. P. Martinez, and V. O. Carvalho, "High-intensity interval training versus moderate-intensity continuous training on exercise capacity and quality of life in patients with coronary artery disease: a systematic review and meta-analysis," *European Journal of Preventive Cardiology*, vol. 24, no. 16, pp. 1696–1707, 2017.
- [12] D. Moher, A. Liberati, J. Tetzlaff, and D. G. Altman, "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement," *PLoS Medicine*, vol. 6, no. 7, Article ID e1000097, 2009.
- [13] J. Higgins, J. Thomas, J. Chandler et al., Cochrane Handbook for Systematic Reviews of Interventions Version 6.3, Cochrane, Canada, 2022.
- [14] G. H. Guyatt, A. D. Oxman, G. E. Vist et al., "GRADE: an emerging consensus on rating quality of evidence and strength of recommendations," *BMJ*, vol. 336, no. 7650, pp. 924–926, 2008.
- [15] C. Cochrane, 2020, http://tech.cochrane.org/revman/download.
- [16] G. G. Cardozo, R. B. Oliveira, and P. T. V. Farinatti, "Effects of high intensity interval versus moderate continuous training on markers of ventilatory and cardiac efficiency in coronary heart disease patients," *The Scientific World Journal*, vol. 2015, Article ID 192479, 8 pages, 2015.
- [17] H. Y. Choi, H. J. Han, J. W. Choi, H. Y. Jung, and K. L. Joa, "Superior effects of high-intensity interval training compared to conventional therapy on cardiovascular and psychological aspects in myocardial infarction," *Ann Rehabil Med*, vol. 42, no. 1, pp. 145–153, 2018.
- [18] V. M. Conraads, N. Pattyn, C. De Maeyer et al., "Aerobic interval training and continuous training equally improve

- aerobic exercise capacity in patients with coronary artery disease: the SAINTEX-CAD study," *International Journal of Cardiology*, vol. 179, pp. 203–210, 2015.
- [19] K. D. Currie, K. J. Bailey, M. E. Jung, R. S. McKelvie, and M. J. MacDonald, "Effects of resistance training combined with moderate-intensity endurance or low-volume highintensity interval exercise on cardiovascular risk factors in patients with coronary artery disease," *Journal of Science and Medicine in Sport*, vol. 18, no. 6, pp. 637–642, 2015.
- [20] K. D. Currie, J. B. Dubberley, R. S. McKelvie, and M. J. MacDonald, "Low-volume, high-intensity interval training in patients with CAD," *Medicine & Science in Sports & Exercise*, vol. 45, no. 8, pp. 1436–1442, 2013.
- [21] E. C. Dunford, S. E. Valentino, J. Dubberley et al., "Brief vigorous stair climbing effectively improves cardiorespiratory fitness in patients with coronary artery disease: a randomized trial," Front Sports Act Living, vol. 3, Article ID 630912, 2021.
- [22] K. Villelabeitia Jaureguizar, D. Vicente-Campos, L. Ruiz Bautista et al., "Effect of high-intensity interval versus continuous exercise training on functional capacity and quality of life in patients with coronary artery disease: a randomized clinical trial," *Journal of Cardiopulmonary Rehabilitation and Prevention*, vol. 36, no. 2, pp. 96–105, 2016.
- [23] S. J. Keteyian, B. A. Hibner, K. Bronsteen et al., "Greater improvement in cardiorespiratory fitness using higherintensity interval training in the standard cardiac rehabilitation setting," *Journal of Cardiopulmonary Re*habilitation and Prevention, vol. 34, no. 2, pp. 98–105, 2014.
- [24] C. Kim and H. E. Choi, "The effect and safety of aerobic interval training according to exercise intensity in acute coronary syndrome," *Journal of Cardiopulmonary Rehabilitation and Prevention*, vol. 40, no. 3, pp. 178–182, 2020.
- [25] T. Moholdt, I. L. Aamot, I. Granøien et al., "Aerobic interval training increases peak oxygen uptake more than usual care exercise training in myocardial infarction patients: a randomized controlled study," *Clinical Rehabilitation*, vol. 26, no. 1, pp. 33–44, 2012.
- [26] T. T. Moholdt, B. H. Amundsen, L. A. Rustad et al., "Aerobic interval training versus continuous moderate exercise after coronary artery bypass surgery: a randomized study of cardiovascular effects and quality of life," *American Heart Journal*, vol. 158, no. 6, pp. 1031–1037, 2009.
- [27] N. Pattyn, L. Vanhees, V. A. Cornelissen et al., "The long-term effects of a randomized trial comparing aerobic interval versus continuous training in coronary artery disease patients: 1-year data from the SAINTEX-CAD study," *European Journal of Preventive Cardiology*, vol. 23, no. 11, pp. 1154–1164, 2016.
- [28] D. M. L. Prado, E. A. Rocco, A. G. Silva, M. T. Pacheco, P. F. Silva, and V. Furlan, "Effects of continuous vs. interval exercise training on oxygen uptake efficiency slope in patients with coronary artery disease," *Brazilian Journal of Medical* and Biological Research, vol. 49, no. 2, Article ID e4890, 2016.
- [29] E. A. Rocco, D. M. L. Prado, A. G. Silva et al., "Effect of continuous and interval exercise training on the PETCO2 response during a graded exercise test in patients with coronary artery disease," *Clinics*, vol. 67, no. 6, pp. 623–627, 2012.
- [30] Ø Rognmo, E. Hetland, J. Helgerud, J. Hoff, and S. A. Slørdahl, "High intensity aerobic interval exercise is superior to moderate intensity exercise for increasing aerobic capacity in patients with coronary artery disease," *European Journal of Cardiovascular Prevention & Rehabilitation*, vol. 11, no. 3, pp. 216–222, 2004.
- [31] D. E. Warburton, D. C. McKenzie, M. J. Haykowsky et al., "Effectiveness of high-intensity interval training for the

- rehabilitation of patients with coronary artery disease," *The American Journal of Cardiology*, vol. 95, no. 9, pp. 1080–1084, 2005.
- [32] M. F. Piepoli, U. Corrà, W. Benzer et al., "Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the cardiac rehabilitation section of the European association of cardiovascular prevention and rehabilitation," European Journal of Cardiovascular Prevention & Rehabilitation, vol. 17, no. 1, pp. 1–17, 2010.
- [33] U. Wisløff, A. Støylen, J. P. Loennechen et al., "Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study," *Circulation*, vol. 115, no. 24, pp. 3086–3094, 2007.
- [34] J. C. Quindry and B. A. Franklin, "Cardioprotective exercise and pharmacologic interventions as complementary antidotes to cardiovascular disease," *Exercise and Sport Sciences Reviews*, vol. 46, no. 1, pp. 5–17, 2018.
- [35] J. L. Taylor, D. J. Holland, S. E. Keating et al., "Short-term and long-term feasibility, safety, and efficacy of high-intensity interval training in cardiac rehabilitation: the FITR heart study randomized clinical trial," *JAMA Cardiol*, vol. 5, no. 12, pp. 1382–1389, 2020.
- [36] S. Lewington, R. Clarke, N. Qizilbash, R. Peto, and R. Collins, "Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies," *Lancet*, vol. 360, no. 9349, pp. 1903–1913, 2002.
- [37] E. G. Ciolac, G. V. Guimarães, V. M. D´Àvila, L. A. Bortolotto, E. L. Doria, and E. A. Bocchi, "Acute effects of continuous and interval aerobic exercise on 24-h ambulatory blood pressure in long-term treated hypertensive patients," *International Journal of Cardiology*, vol. 133, no. 3, pp. 381–387, 2009.
- [38] L. Du, X. Zhang, K. Chen, X. Ren, S. Chen, and Q. He, "Effect of high-intensity interval training on physical health in coronary artery disease patients: a meta-analysis of randomized controlled trials," *Journal of Cardiovascular Development and Disease*, vol. 8, no. 11, p. 158, 2021.
- [39] V. Aboyans and M. H. Criqui, "Can we improve cardiovascular risk prediction beyond risk equations in the physician's office?" *Journal of Clinical Epidemiology*, vol. 59, no. 6, pp. 547–558, 2006.
- [40] P. D. Thompson, B. A. Franklin, G. J. Balady et al., "Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American heart association council on nutrition, physical activity, and metabolism and the council on clinical cardiology," *Circulation*, vol. 115, no. 17, pp. 2358–2368, 2007.
- [41] "The effect of high intensity interval training on left atrial volume index in heart failure patients," *European journal of preventive cardiology*, vol. 26, p. S34, 2019.