

Research Article

Systematic Review and Meta-Analysis on the Rehabilitation Effect of Different Intensity Exercise on the Patients with Cardiovascular Diseases

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Background. Cardiovascular disease is a common disease with high prevalence, disability, and mortality. Exercise therapy can improve cardiac functional reserve and life quality of patients, but the benefits of different exercise intensities for cardiovascular patients are still controversial. In this study, literature search and meta-analysis were used to explore the effect of 2 intensities of exercise on the rehabilitation effect of cardiovascular patients. **Methods.** We searched Embase, Wiley online library, PubMed, Science Direct, and Clinicaltrials to look for randomized controlled trial (RCT) studies of high-intensity interval training (HIIT) versus moderate continuous training (MCT). After screening the inclusion criteria for the literature and assessing the risk of bias, a software analysis was performed using the R language toolkit to obtain forest plots and funnel maps. **Results.** 10 articles were included in this study into the quantitative analysis, and 520 patients participated in the study; meta-analysis results showed that after HIIT intervention, the VO₂ peak index of patients was higher than that of the MCT group (MD = 1.39, 95% CI (0.10, 2.68), $Z = 2.12$, $P = 0.0344$), the peak heart rate HR peak was higher than that of the MCT training (MD = 7.71, 95% CI (5.12, 10.30), $Z = 5.84$, $P < 0.0001$), the respiratory exchange rate (maximum RER) was higher than that of the MCT training (MD = 0.02, 95% CI (0.00, 0.04), $Z = 2.36$, $P = 0.0184$), and the quality of life was higher than that of the MCT training (MD = 0.39, 95% CI (0.07, 0.71), $Z = 2.40$, $P = 0.0165$). **Discussion.** Compared with moderate continuous training, high intensity interval training is more conducive to improve the cardiopulmonary function of cardiovascular patients and improve their physical life quality.

1. Introduction

Cardiovascular disease is a heart blood vessel disease with the characteristics of high prevalence, disability rate, and mortality, which is an ischemic or hemorrhagic disease of the systemic tissues and heart caused by atherosclerosis, blood viscosity, hyperlipidemia, and hypertension. Cardiovascular disease is a common disease in the elderly over 50 years of age and a serious threat to the health of the elderly [1]. Exercise therapy is the main content of cardiovascular function training for patients, especially aerobic exercise, which can improve their cardiac functional reserve and quality of life [2, 3]. Traditional aerobic exercise such as walking, running, and cycling are moderate continuous training (MCT) (50-70% oxygen consumption). However, it remains unclear whether MCT training has the

greatest effect [4]. Clinical studies have confirmed that high-intensity interval training (HIIT) is also another effective method of rehabilitation, which usually refers to exercise with an oxygen consumption of 70-90%. Combined with a short period of intermittent exercise and a certain period of active recovery, the patient's physiological system can achieve higher motor adaptability [5]. At present, RCT literature is comparing MCT with HIIT. Some studies [6] believe that there is no significant difference in the benefits of MCT and HIIT for cardiovascular patients, and the study [7] believes that the effect of HIIT is superior to MCT. In order to solve these controversies, we implemented a meta-analysis of RCT studies. We systematically evaluated the effect of HIIT and MCT in the recovery period of cardiovascular patients to provide an evidence-based basis for exercise rehabilitation of patients.

2. Materials and Methods

2.1. Database and Search Strategy. We used a computer to search the literature in Embase, Wiley online library, PubMed, and Science Direct databases. Moreover, clinical experimental research in <http://Clinicaltrials.org> also has been searched. We set the search time to the database under construction to December 2021 and searched with the keyword combination (high-intensity interval training/HIIT) & (moderate continuous training|MCT) & (heart).

2.2. Literature Inclusion Criteria. (1) We only included randomized controlled trials (RCTs), the language is English, and RCTs are a means of testing the effects of a therapy or drug in health care, which is often considered the gold standard in clinical evidence. (2) All patients with cardiovascular disease, we have no restrictions on age, the disease types include acute (chronic) coronary heart disease, angina, arrhythmia, heart failure, and the causes of which are hypertension, hyperlipidemia, and atherosclerosis [8]. (3) Intervention types: the study needs to group the patients (for the sake of literature quality, we only accept the randomization method), including at least 2 groups, one of the exercise intervention mainly adopts HIIT, the other of the intervention adopts MCT, and there may be other control groups in the study (such as conventional exercise group), but its data will not be included in this meta-analysis. Exercise interventions may also include a combination of HIIT and MCT with anaerobic exercise (or resistance training), but the modalities of anaerobic exercise (or resistance training) must be the same to ensure comparability of final results. (4) The exercise intervention time of patients in the 2 groups needs to be more than 3 weeks. The peak oxygen consumption (VO_{2peak}), peak heart rate (HR_{peak}), and maximum respiratory exchange rate (maximum RER) before and after the intervention need to be recorded in detail in the literature. Other aerobic exercise indicators may appear in the literature, but we will not make statistics. Other indicators such as adverse reactions to exercise and quality of life will be included in the statistics as secondary outcome indicators. Since the scales used for evaluating the quality of life are inconsistent in literature, we only selected the physical scores in the scales for comparison

2.3. Literature Exclusion Criteria. (1) We excluded patients with severe heart disease (requiring bed rest), patients who were not suitable for immediate exercise after cardiovascular surgery, and patients with paralysis and musculoskeletal diseases who could not perform aerobic exercise; we excluded patients with only cardiovascular disease tendency (but no disease), such as diabetic patients, hypertensive patients, and severely obese patients; we also excluded studies with healthy subjects. (2) Patients with detailed description of intervention frequency and intervention methods will be excluded. (3) Patients with the nonrandomized controlled study will be excluded, and we also excluded all pilot study, cause the sample size included in the study is too small. (4) Patients lacking outcome indicators, or the data cannot be transformed into studies

2.4. Screening of Studies. All documents are imported into the software (Endnote X9) after the literature search and duplicate documents are excluded. 2 researchers read the title and abstract for further screening. If the original text is unavailable on the Internet, contact the author of the original text. 2 researchers cross-checked the results of their respective screens, and if there were inconsistencies, they were resolved after discussion and a third person could be introduced for discussion if necessary.

2.5. Literature Quality Evaluation and Bias Risk Assessment. We used the Joanna Briggs Institute Evidence-Based Health Care Center (JBI) in Australia [9] to evaluate the evaluation criteria for randomized controlled trials. The evaluation criteria included 6 aspects: randomization, allocation concealment, blind method, withdrawal and loss to follow-up, ITT analysis, and baseline comparison. The studies were divided into 3 levels: level A: meeting the evaluation in the above 6 aspects, with a small possibility of bias; level B: partially meeting the evaluation in the above 6 aspects, with a certain possibility of bias; level C: most of them did not meet the evaluation, with a high possibility of bias. We only included studies with quality level A or B and excluded studies with quality level C.

2.6. Data Extraction. 2 researchers independently extracted literature data: patient age, patient nationality, gender ratio, height, weight, disease, medication, grouping characteristics, number of grouping samples, and exercise intervention characteristics (intervention method, intensity, weekly exercise time, and exercise duration days). Two researchers cross-examined the results after data extraction and discussed the resulting differences.

2.7. Statistical Methods. (1) R language toolkit R Version 4.1.2 (released by The R foundation for statistically computing) was used as the analysis tool, and Meta package was loaded before software operation; (2) continuous variables take the inverse variance statistic, and mean difference (MD) and 95% CI were used to report statistics; (3) descriptive statistics of forest maps and comparisons; (4) I^2 analysis and Q validation were used for literature heterogeneity, $I^2 > 50\%$ or $P < 0.1$ was used to indicate heterogeneity of results, random-effects model was used to obtain OR values; otherwise, fixed effects were used to obtain OR values; (5) heterogeneity analysis shows that there is heterogeneity between the literature, and the source of heterogeneity needs to be investigated using a case-by-case exclusion method, which is generally described when the source of heterogeneity cannot be determined; (6) software's *Meta inf* command is used for sensitivity analysis; (7) funnel plot was used to represent publication bias, and *metabias* command of the software was used for quantitative analysis of publication bias

3. Results

3.1. Literature Screening Process and Results. The flowchart of literature selection was shown in Figure 1, and finally, 10 articles were included in the quantitative analysis (520 patients participating).

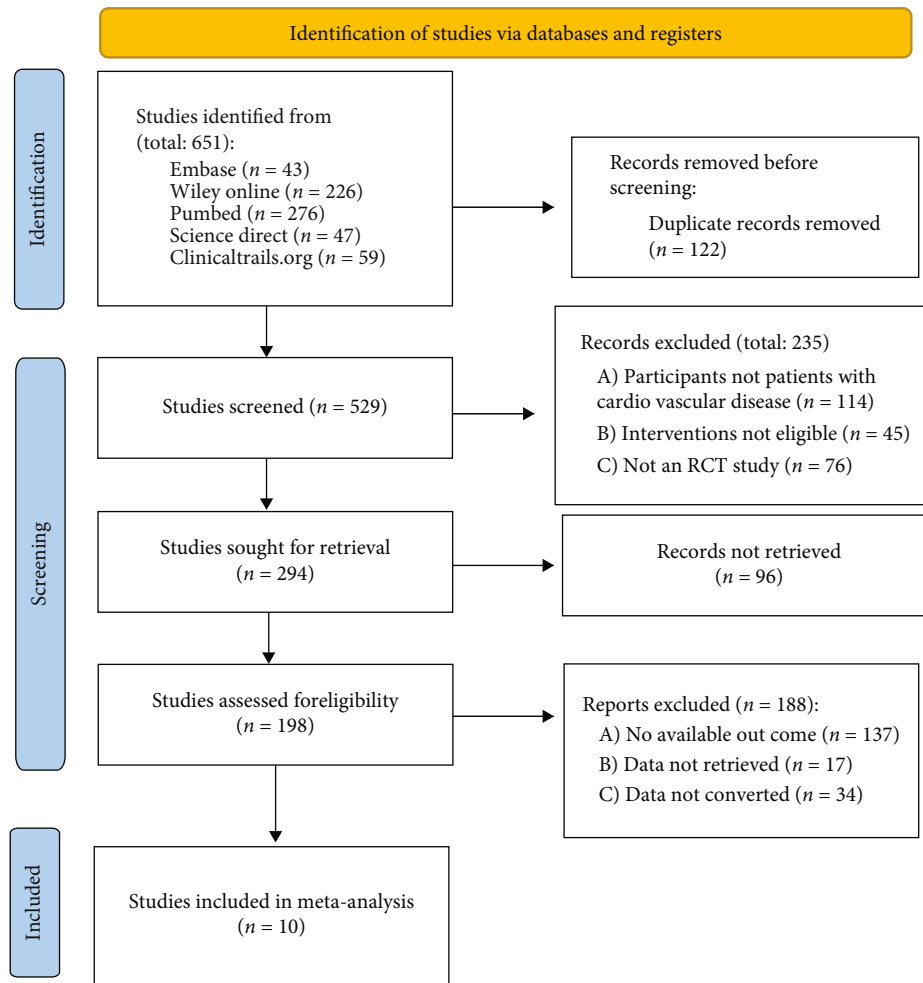


FIGURE 1: Literature selection flowchart.

3.2. Basic Characteristics of Studies. 10 studies were included in this study. 5 studies were conducted on patients with coronary heart disease, and 5 studies were conducted on patients with heart failure, as shown in Table 1.

3.3. Literature Quality and Bias Evaluation. All studies [6, 7, 10–17] were randomized controlled trials, all described blind method (single-blind or double-blind), and only studies [10] described allocation hide. All studies recorded drop out cases and baseline comparison in detail, using ITT analysis. The overall quality was good (Table 2).

3.4. Meta-Analysis

3.4.1. Effect of High-Intensity Interval Training (HIIT) and Moderate Continuous Training (MCT) on Peak Oxygen Consumption (VO₂peak) in Patients with Cardiovascular Disease after Intervention. All studies [6, 7, 10–17] reported oxygen consumption VO₂peak index after intervention (unit: mL/min/kg), with statistical heterogeneity in the studies ($I^2 = 78\%$, $P < 0.01$). Random effect model was used. Meta-analysis showed that VO₂peak index in patients after HIIT intervention was higher than that in MCT group (MD = 1.39, 95% CI (0.10, 2.68), $Z = 2.12$, $P = 0.0344$).

The studies were further analyzed according to the types of cardiovascular diseases. The studies were divided into 2 subgroups (coronary heart disease and heart failure). There still has heterogeneity in the internal studies. The statistics of VO₂peak index after the 2 interventions were ($Z = 2.07$, $P = 0.0433$) and ($Z = 2.35$, $P = 0.0297$) (Figure 2).

3.4.2. Effect of High Intensity Interval Training (HIIT) and Moderate Continuous Training (MCT) on Peak Heart Rate (HR Peak) in Patients with Cardiovascular Disease after Intervention. A total of 6 studies [6, 7, 11, 13, 15, 16] reported the peak heart rate (HRpeak) index of patients after intervention, without statistical heterogeneity between studies ($I^2 = 32\%$, $P = 0.20$). The fixed-effect mode was used. Meta-analysis indicated that the HRpeak of patients after HIIT training was higher than that after MCT training (MD = 7.71, 95% CI (5.12, 10.30), $Z = 5.84$, $P < 0.0001$) (Figure 3).

3.4.3. Effect of HIIT and MCT on Respiratory Exchange Rate (Maximum RER) in Patients with Cardiovascular Disease after Intervention. 9 studies [6, 7, 11–17] reported the statistical index of respiratory exchange rate (maximum RER), but there was no statistical homogeneity in the studies

TABLE 1: Basic characteristics, intervention measures, intervention time, and outcome indicators of the included studies.

Author and date of publication	Number of subjects	Number (HIIT/MCT)	Age (years)	Disease type	Intervention measures	Control group	Intervention time	Rehabilitation index
Trachsel et al. [6] 2020	41	23/18	63.6 ± 9.0	Coronary heart disease	Low volume HIIT	MCT/MICET	Weeks	1-4, 6
Villelabeitia et al. [7] 2017	73	37/36	58 ± 11	Coronary heart disease	HIIT	MCT	8 weeks	1-4, 6, 7
Mueller et al. [10] 2021	120	60/60	70 ± 7	Heart failure	HIIT	MCT	12 weeks	1, 7, 8
Donelli et al. [11] 2020	19	10/9	60 ± 9	Heart failure	HIIT	MCT	24 weeks	1-3, 6
Moholdt et al. [12] 2009	59	28/31	60.2 ± 6.9	Heart failure	HIIT	MCT	4 weeks	1, 6, 8
Wisløff et al. [13] 2007	18	9/9	75.5 ± 11.1	Heart failure	HIIT	MCT	3 weeks	1, 2, 6-8
Jaureguizar et al. [14] 2016	72	36/36	58 ± 11	Coronary heart disease	HIIT	MCT	8 weeks	1, 3-8
Cardozo et al. [15] 2015	47	23/24	64 ± 12	Coronary heart disease	HIIT	MCT	16 weeks	1-4, 6
Prado et al. [16] 2016	35	17/18	59.3 ± 1.8	Coronary heart disease	HIIT	MCT	12 weeks	1, 2, 6
Iellamo et al. [17] 2014	36	18/18	67.2 ± 6	Heart failure	HIIT	MCT	12 weeks	1, 6, 7

Outcomes: (1) VO₂peak, mL/min/kg; (2) HR peak; (3) maximum SBP, (mmHg); (4) maximum DBP, (mmHg); (5) maximum power (W); (6) maximum RER; (7) serious advert event; (8) QOL. Abbreviation: VO₂: volume of O₂ consumption; QOL: quality of life; PER: respiratory exchange ratio.

TABLE 2: Methodological quality assessment based on JBI.

Study	Random sequence generation	Classification hiding	Blind method	Withdrawal and lost to follow-up	ITT analysis	Baseline comparison	Quality level
Trachsel et al. [6] 2020	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Villelabeitia et al. [7] 2017	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Mueller et al. [10] 2021	Adopt	Described	Single-blind	Described	Adopt	Described	Level A
Donelli et al. [11] 2020	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Moholdt et al. [12] 2009	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Wisløff et al. [13] 2007	Adopt	Not described	Double-blind	Described	Adopt	Described	Level B
Jaureguizar et al. [14] 2016	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Cardozo et al. [15] 2015	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Prado et al. [16] 2016	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B
Iellamo et al. [17] 2014	Adopt	Not described	Single-blind	Described	Adopt	Described	Level B

($I^2 = 0\%$, $P = 0.63$). The fixed effect mode was used. Meta-analysis showed that the respiratory exchange rate (maximum RER) of patients after HIIT training was higher than that after MCT training (MD = 0.02, 95% CI (0.00, 0.04), $Z = 2.36$, $P = 0.0184$), as shown in Figure 4.

3.4.4. *Effect of HIIT and MCT on the Quality of Life of Patients with Cardiovascular Disease after Intervention.* 3 studies [10, 12, 13] reported the quality of life indicators of patients after intervention, and there was statistical heterogeneity in the studies ($I^2 = 57\%$, $P = 0.07$). The random-

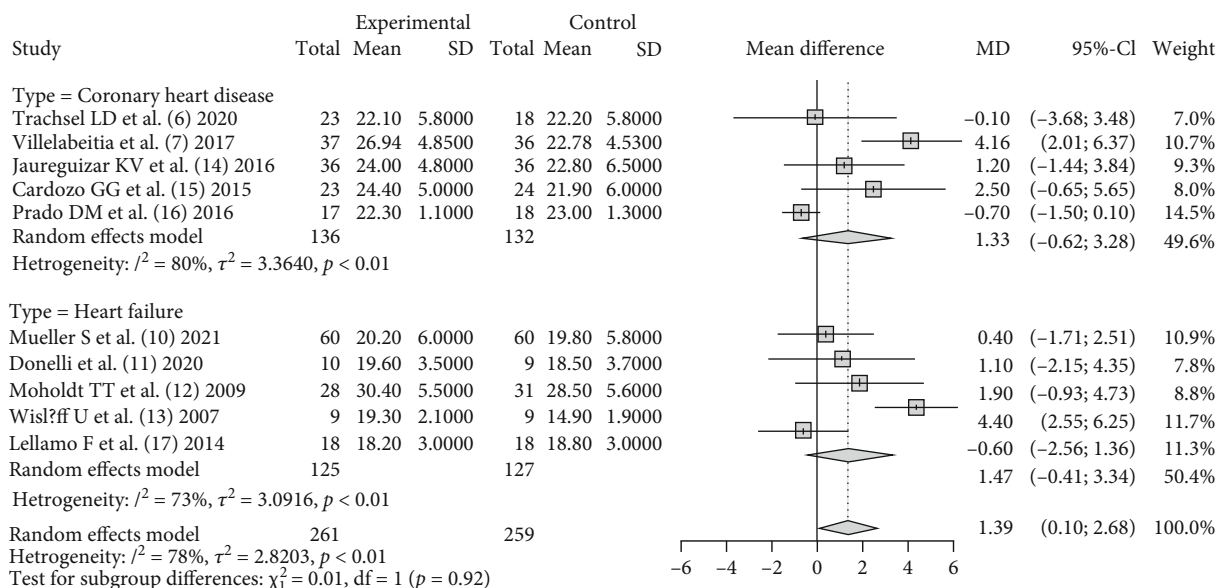


FIGURE 2: VO2peak in cardiovascular patients after HIIT and MCT intervention.

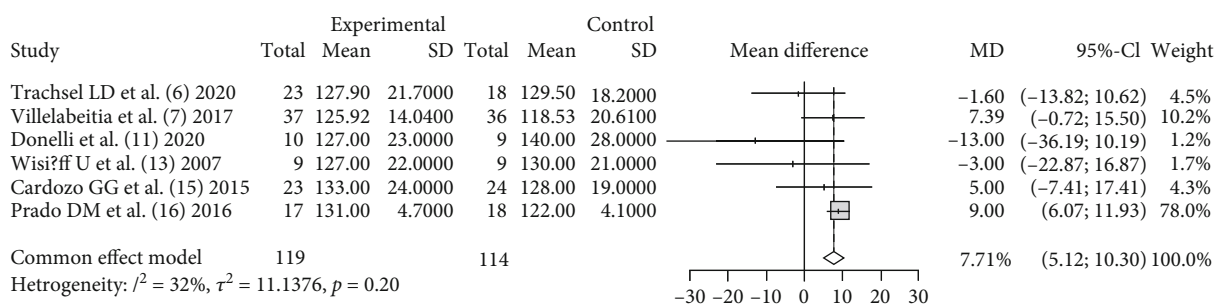


FIGURE 3: HRpeak of cardiovascular patients after HIIT and MCT intervention.

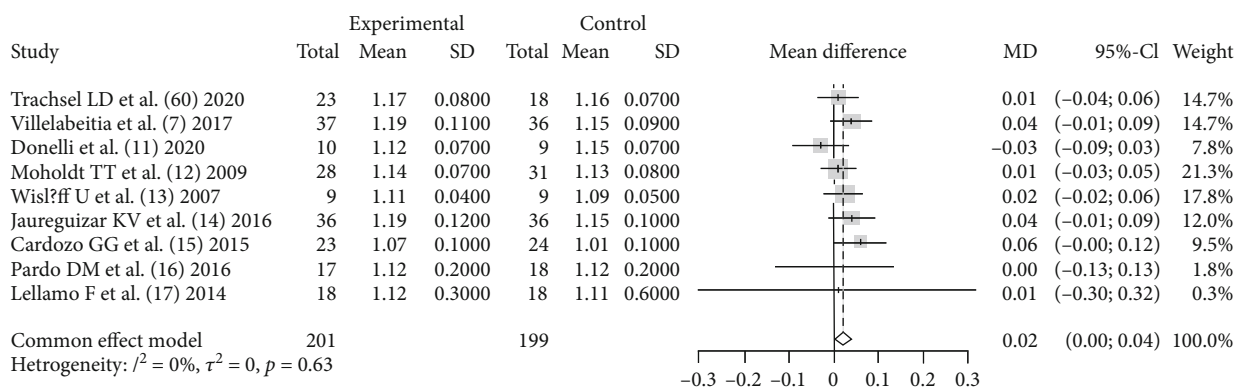


FIGURE 4: Maximum RER in patients with cardiovascular diseases after HIIT and MCT intervention.

effects model was used. Meta-analysis indicated that the quality of life of patients after HIIT training was higher than that after MCT training (MD = 0.39, 95% CI (0.07, 0.71), Z = 2.40, P = 0.0165) (Figure 5).

3.4.5. Analysis of Adverse Reactions of 2 Intervention Methods. It was reported in the studies [7, 13, 14, 17] that

no serious adverse reactions were found in the intervention of the 2 groups. However, it was reported in the studies [10] that there were 18 cases (31%) of serious adverse reactions of HIIT group and MCT group, of which the most common adverse reaction was acute coronary syndrome, followed by worsening heart failure, and then atrial fibrillation.

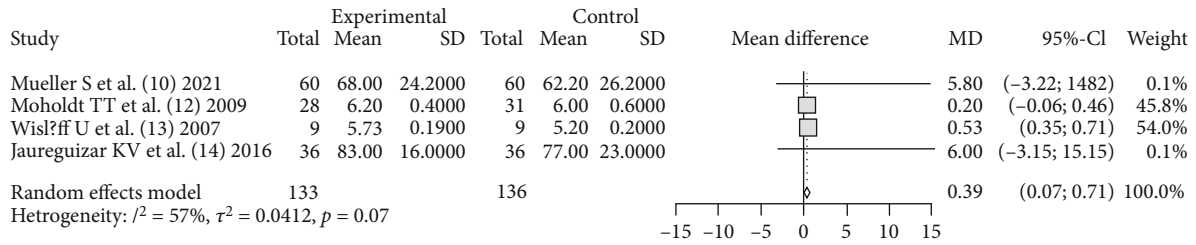


FIGURE 5: Life quality of scores of cardiovascular diseases patients after HIIT and MCT intervention.

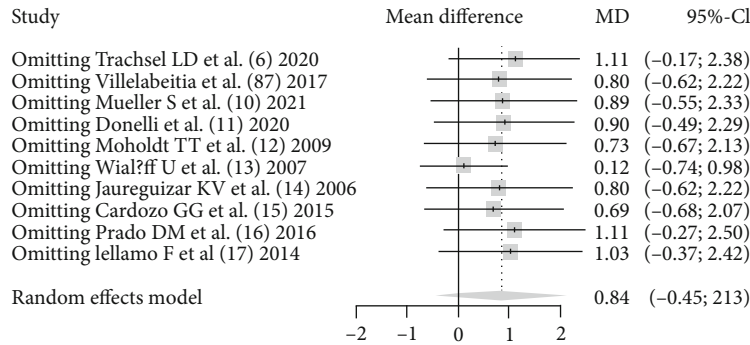


FIGURE 6: Stability analysis.

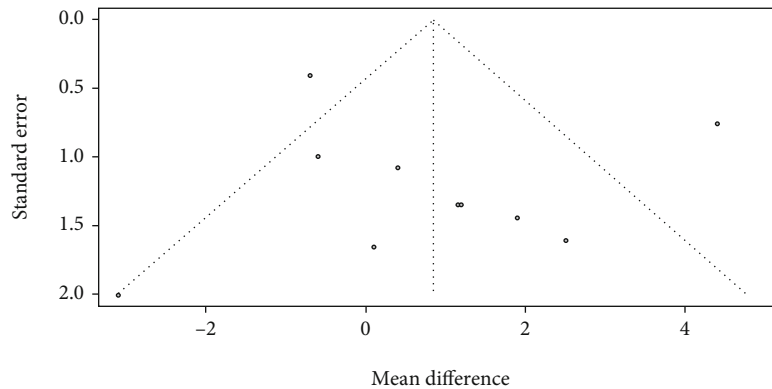


FIGURE 7: Funnel plot analysis.

3.4.6. *Heterogeneity and Sensitivity Analysis Source.* Analysis of the VO₂ peak index and quality of life index shows statistical heterogeneity between the literature ($I^2 = 79\%$, $P < 0.01$). After the studies were divided into 2 subgroups according to disease types, the internal heterogeneity was not eliminated. We speculated that the existence of heterogeneity may be related to multiple factors such as patient age level, disease type, and difference in intervention methods.

Influence factor analysis using *meta Influence* showed good stability (good sensitivity) of the results, as shown in Figure 6.

3.4.7. *Publication Bias Analysis.* In the analysis of VO₂ peak index, the funnel plot shows that the data are basically evenly distributed and the publication bias is small, as shown in Figure 7. Quantitative analysis using *Metabias* resulted in $t = 0.75$, $df = 8$, P value = 0.4748, and $P > 0.05$ suggesting no publication bias.

4. Discussion

10 RCT studies were in this study. 1 “level A” study was evaluated by JBI methodology, and the other 9 were all level B. The main reason why 9 articles were rated as level B was the concealment of literature description allocation, which may cause the imprecise design of study protocol and finally the risk of implementation bias.

Meta-analysis results showed that the peak oxygen consumption of cardiovascular patients after HIIT exercise intervention was higher than that of MCT exercise, the peak heart rate and respiratory exchange rate of patients were higher than the MCT exercise, and the quality of life of patients after HIIT exercise was higher than that of MCT exercise. Maximum oxygen consumption, peak heart rate, and respiratory exchange rate can reflect the pumping function and cardiopulmonary exchange function of individual

heart. The greater the oxygen consumption value, the better the individual cardiopulmonary function [18–21]. HIIT exercise is an explosive, rapid, and full exercise in a short period of time, which increases the body's demand for oxygen and creates a hypoxic state, and which increases the patient's cardiac pumping function and improves cardiopulmonary exchange function; in addition, the increase in exercise stimulation can better improve their cardiovascular fitness and exercise capacity, thereby promoting the outcome of the disease and improving the quality of life [22–25]. However, MCT exercise also has some limitations, which are more suitable for patients who cannot tolerate high-intensity training [26–29]. Clinical studies have found that cardiovascular diseases can bring physical pain or discomfort to patients [30], limit the patient's normal work and life, and easily cause patients to have negative psychology such as anxiety and depression. Exercise rehabilitation therapy can comprehensively improve the quality of life of patients. The meta-analysis of this study shows that the quality of life of patients after HIIT training is higher than that of patients after MCT training, but there is statistical heterogeneity in the literature, and more large-sample high-quality randomized controlled trials are expected to verify.

High-intensity intermittent training has been applied in the recovery of various diseases. Meta-analysis by Wewege et al. [31] compared the effect of HIIT and MCT exercise in obese people. The results showed that the 2 methods were equally effective for obese people, but the HIIT exercise was more efficient and time-consuming. In a study by Rolid et al. [32], cardiologists were trained on HIIT and MCT and compared for 3 years, and the results showed that in the first 1 year, the cardiorespiratory fitness of patients in the HIIT group was better than that in the MCT group, but the long-term effect did not differ significantly. This shows that in the long term, MCT can also achieve the same cardiopulmonary function as HIIT, and we cannot deny the long-term effect of MCT, but the efficiency of HIIT is higher compared with it. The results of a meta-analysis of the effects of HIIT and MCTs on blood pressure in adult patients with prehypertension [5] by Costa et al. showed that HIIT had a greater improvement with O₂max compared to MCTs. Another meta-analysis conducted by Ramos et al. [33] concluded HIIT is more effective than MCT in improving the vascular function of the brachial artery, which could be due to its tendency to positively reduce the risk factors of traditional cardiovascular disease, influencing oxidative stress, inflammation, and improving insulin sensitivity.

The study by Trachsel et al. [34] divided patients with chronic coronary heart disease into male and female groups and applied HIIT training. The results showed that the peak oxygen consumption was increased in both groups, with no significant difference. This suggests that HIIT training is as effective for men as it is for women. A study by Heinrich et al. [35] showed that HIIT participants spent less time exercising per week compared to MCT participants and can maintain exercise enjoyment; hence, HIIT participants were more likely to intend to continue the training and maintain good compliance.

Although studies [7, 13, 14, 17] reported that no serious adverse reactions were found in the 2 groups of intervention, study [10] reported that there were 18 cases (31%) of serious adverse reactions in HIIT group and MCT group, of which the most common adverse reaction was acute coronary syndrome, followed by worsening heart failure, and then atrial fibrillation. Therefore, we believe that although both HIIT and MCT trainings are beneficial for patients, the training process still needs to be carried out under the guidance of a therapist.

Patients were divided into 2 subgroups in this study by different disease types: the coronary heart disease group and the heart failure group. However, the heterogeneity was still shown in the 2 groups. Source of heterogeneity comes from multiple factors such as patient age level, disease type, and difference in intervention methods, which could not be further analyzed in depth. Funnel plots of the two-sided distribution indicate that publication bias is less likely. The quality of the studies included in this meta-analysis was high. However, the sample size in the studies was small on average. Therefore, the RCT study needs to be further deeply explored. But this study also has some shortcomings. The studies were divided into 3 levels. There would be a huge variation in level B and a big jump from level B to C based on the description. We will use a more detailed grading of the literature in the next further research. Differences between the two cardiovascular diseases are also mentioned in this study, but this issue has not been investigated further, which may be related to multiple factors, which we will examine separately in the next in-depth study.

5. Summary

520 patients in 10 articles were in this meta-analysis. The results of this study show that high-intensity intermittent training is superior to moderate-intensity training in terms of improving cardiorespiratory fitness and quality of life in cardiovascular patients. However, lower case number of literature included in this study is small, so randomized controlled studies still need to be further explored.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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