Acta Cardiologica

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/tacd20

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To cite this article: Tong Li, Han Jiang & Jun Ding (2024) The role of exercise-based cardiac rehabilitation after percutaneous coronary intervention in patients with coronary artery disease: a meta-analysis of randomised controlled trials, Acta Cardiologica, 79:2, 127-135, DOI: 10.1080/00015385.2023.2266650

To link to this article: https://doi.org/10.1080/00015385.2023.2266650

Published online: 11 Mar 2024.

ACTA CARDIOLOGICA
2024, VOL. 79, NO. 2, 127–135
https://doi.org/10.1080/00015385.2023.2266650

ORIGINAL SCIENTIFIC PAPER

The role of exercise-based cardiac rehabilitation after percutaneous coronary intervention in patients with coronary artery disease: a meta-analysis of randomised controlled trials

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ABSTRACT

Background: this study was designed to analyse patient outcomes using a combination of PCI and exercise-based cardiac rehabilitation compared with PCI alone.

Methods: PCI can improve the survival rate of patients with coronary artery disease, but it can also cause vascular endothelial cell injury, thrombosis, and even restenosis. Early cardiac rehabilitation exercise is crucial for patients with coronary heart disease after PCI. Five databases were examined for randomised controlled trials involving early cardiac rehabilitation exercise and standard treatment in patients with coronary heart disease after PCI. The search period lasted from the creation of the database (2006) until December 2022. The outcomes including angina, arrhythmia, coronary restenosis, left ventricular ejection fraction, left ventricular end diastolic diameter, 6-min walk distance, total cholesterol, heart rate, systolic blood pressure and diastolic blood pressure. RevMan 5.3 was used to analyse the data, and the Cochrane Collaboration was used to assess the quality of evidence.

Results: A total of 1231 patients were enrolled in this study. Angina pectoris (RR = 0.24, 95% CI [0.10, 0.57], $p = 0.001$), Arrhythmia (RR = 0.17, 95% CI [0.05, 0.55], $p = 0.003$), Coronary artery restenosis (RR = 0.10, 95% CI [0.01, 0.76], $p = 0.03$).

Conclusion: Exercise after PCI improves LVEF, enhances 6MWD, lowers HR and minimises the risk of angina, arrhythmia and coronary artery restenosis in CHD patients. Exercise had no discernible effect on LVEDD, TC, SBP, or DBP.

ARTICLE HISTORY
Received 31 May 2023
Revised 25 August 2023
Accepted 29 September 2023

KEYWORDS
Exercise; cardiac rehabilitation; percutaneous coronary intervention; coronary heart disease

1. Introduction

Coronary Heart Disease affects about 11 million individuals in China and is still one of the main causes of death [1,2]. Percutaneous coronary intervention has been demonstrated to lower mortality and morbidity in CHD patients [3]. Exercise-based cardiac rehabilitation (CR) has been extensively researched, and current international recommendations strongly advocate CR to improve health outcomes and reduce modifiable risk factors following PCI [4].

Exercise-based CR is related with considerably lower odds of all-cause mortality, rehospitalization, and cardiovascular morbidity, according to a wide number of randomised controlled studies (RCTs) [5]. Another study found that exercise-based CR increased myocardial perfusion and coronary endothelial function in patients with chronic coronary syndrome [6]. As a result, the purpose of this systematic review was to evaluate patient outcomes using a combination of PCI and exercise-based cardiac rehabilitation versus PCI alone.

2. Participants and methods

RCTs were searched for in PubMed, Embase, the Chinese National Knowledge Infrastructure (CNKI), Wanfang Data, and the Cochrane Database of Systematic Reviews for this study. The following key words were used: exercise, “walking”, “jogging”, percutaneous coronary intervention, coronary heart disease, heart function, and meta-analysis

Inclusion criteria were as follows: (1) individuals with coronary heart disease who have undergone PCI; (2) a randomised controlled trial of exercise versus normal care without exercise; (3) Left ventricular ejection fraction, end-diastolic diameter of the left ventricle, 6-min walking distance, angina, arrhythmia, restenosis, heart rate, systolic and diastolic blood pressure. Exclusion criteria included: (1) studies unrelated to exercise or PCI; (2) participants with modifiable

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cardiovascular risk factors or major complications; and (3) patients with substantial problems. (3) insufficient reporting or lack to provide outcome measures; (4) observational studies or pathology reports

The risk of bias in the included literature was assessed using the criteria recommended by the Cochrane Collaboration. The evaluation was based on seven parameters. Review Manager (RevMan5.3) was used for the statistical analysis. The mean difference (MD) and 95% confidence interval (CI) of a meta-analysis including continuous outcomes were used to present the results. The meta-analysis results for binary data classification were shown using the risk ratio (RR) and 95% CI. The chi-square test was used to determine the degree of heterogeneity among all studies. A fixed-effect model was adopted if heterogeneity was not significant in all inclusive studies ($p > 0.1$, I[2] $\leq$ 50%). A random-effects model was used if the heterogeneity in all inclusive trials was statistically significant ($p \leq 0.1$, I[2] $>$ 50%).

3. Results

The search approach yielded 807 studies, of which 762 were evaluated and 732 were discarded due to incorrect citations. Finally, this meta-analysis comprised 13 published RCTs (Figure 1). including 610 patients in the exercise group and 621 in the control group. The characteristics of the trials and the patients were both unique. Table 1 summarizes the characteristics of the included studies (the essential medications and care, intervention strategies, follow-up length and clinical outcomes).

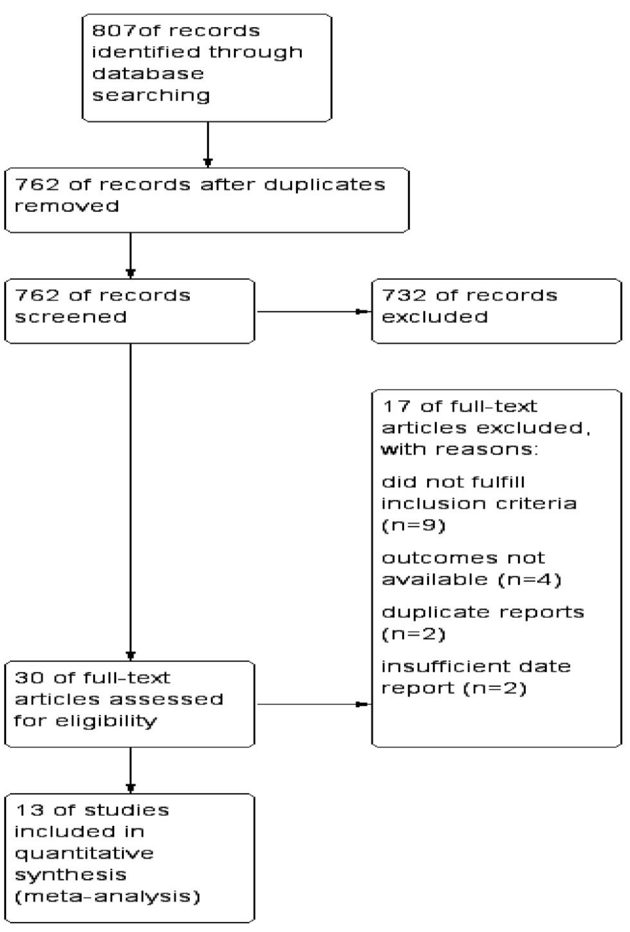

Figure 1. Flow diagram of the research strategy.

The trial findings are shown in Figures 2 and 3. For randomisation, two trials employed random number tables and computer-generated random sequences (Meiling Xiao et al. 2021; Yan Yang et al. 2021). In three trials, the allocation concealment was described in detail (Ya-JieShi et al. 2022; Yan Zou et al. 2022; Young-Hwa Lee et al. 2022). Four studies employed blinded procedures (Jiajia Li et al. 2022; Ya-JieShi et al. 2022; Yan Zou et al. 2022; Young-Hwa Lee et al. 2022). There was no evidence of incomplete or selective reporting in any of the trials included. Other potential causes of bias were not addressed in the experiments. The funnel plot was symmetrically distributed, and no publication bias was identified.

Three trials that included 176 and 175 patients who underwent PCI with or without exercise evaluated angina pectoris. The rate of angina pectoris differed statistically between the two groups (RR = 0.24, 95% CI [0.10, 0.57], $p = 0.001$, Figure 4).

The same three trials evaluated arrythmia. The rate of arrhythmia differed statistically between the two groups (RR = 0.17, 95% CI [0.05, 0.55], $p = 0.003$, Figure 4). Two trials that included 111 and 110 patients who underwent PCI with or without exercise evaluated coronary artery restenosis. The rate of coronary artery restenosis differed statistically between the two groups (RR = 0.10, 95% CI [0.01, 0.76], $p = 0.03$, Figure 4).

A statistically significant difference in the HR rate was found between the two groups (MD = −4.55,95% CI [-7.16, −1.94], $p < 0.05$, Figure 5). No statistically significant difference of SBP and DBP was found between the two groups (MD = −4.42, 95% CI [−11.47, 2.63], $p = 0.22$, Figure 5) and (MD = −1.60, 95% CI [−7.14, 3.93]), $p = 0.57$, Figure 5).

No statistically significant difference in TC was found between the two groups (MD = −0.99, 95% CI [-2.38, 0.40], $p = 0.16$, Figure 5). Five trials that included 296 and 299 patients who underwent PCI with or without exercise evaluated LVEF. A statistically significant difference in LVEF rate was found between the two groups (MD = 4.56, 95% CI [1.34, 7.78], $p < 0.05$, Figure 5).

Two trials that included 100 and 103 patients who underwent PCI with or without exercise evaluated

Table 1. Characteristics of randomised controlled trials included in this meta-analysis.

Study	Participants M/F	Age,	Surgical procedure	Exercise group	Control group	Follow-up	Outcome measures
Zhang et al. 2018 [7]	Exercise:65,59/ 6Control:65,54/11	70.3 ± 10.769.8 ± 10.4	PCI	Walking	usual care and conventionl drug therapy	6 months	recurrence angina readmission LVEF 6MWD
Yang et al. 2021 [8]	Exercise:53,34/ 19Control:53,33/20	45.3 ± 6.545.6 ± 6.3	PCI	Walking, limbjoint exerciseMeditation exercise	regular rehabilitation exercises	1 year	angina arrhythmia coronary artery restenosis
Ya-Jie Shi, 2022 [9]	Exercise:25,21/ 4Control:26,19/7	49.8 ± 7.751.3 ± 7.5	PCI	Multidisciplinar-y exercise management	routine care	2 months	6MWD
Meiling Xiao et al. 2021 [10]	Exercise:82,61/ 21Control:82,64/18	60.2 ± 9.258.7 ± 8.8	PCI	A 10-minute warm-up, 30 to 40 min of aerobic exercise (walking or bicycling), and a 10-minute cool-down period	conventional medical therapy	9 months	Revasculariz-ation, myocardial infarction and cardiac death, LVEF 6MWD total cholesterol triglyceride-s LDL cholesterol glucose
Minghui Jiang et al. 2021 [11]	Exercise:49,31/ 18Control:49,33/16	58.79 ± 9.3659.62 ± 8.96	PCI	Training of alternating between fast and slow breathing at the bedside, 5–6 times/min for 10 min. 3 types of stretching exercises for 5 min/time. squatting, weight-bearing exercises, and so on, 10 repetitions/set, 3 sets/d. upper and lower limb training.	routine care	6 months	LVEDV LVESV LVEF QOL
Fang Cui, 2012 [12]	Exercise:26,21/ 5Control:31,23/8	59.4 ± 5.958.3 ± 6.1	PCI	bicycling, boat rowing, hand and arm swing car, and treadmill exercise	conventional medical therapy	3 months	NST and ΣST of ECG and the frequency of anginal episodes ST segment depression time and emergence time of angina
Huan Zheng, 2008 [13]	Exercise:27Control:30	Not mentioned	PCI	CPET	routine care and lifestyle education	6 months	HRAT HRrest LVD diameter LVMI peak VO2 Powermax VO2AT tAT HRR LVEF LVDdiameter
Yan Zou, 2022 [14]	Exercise:39,35/ 4Control:39,34/5	61.6761.13	PCI	Slow breathing exercise (SBE)	routine care	12weeks	heart rate (HR) and blood pressure (BP)
Hye Young Lee, 2013 [15]	Exercise:37,30/ 7Control:37,31/6	58.8 ± 10.8 60.3 ± 8.7	PCI	a 10 min warm-up, a 40 min aerobic exer-cise on a treadmill or bicycle ergometer, and a 10 min cool-down phase.	routine care	9 months	coronary restenosis
Young-Hwa Lee, 2013 [16]	Exercise:26,22/ 4Control:29,22/7	54.3 ± 8.9 57.8 ± 7.5	PCI	scheduled gait exercise at home four to five times weekly 50 min each including flexibility exercise for 20 min (warm-up exercise for 10 min and cool-down exercise for 10 min) and main exercise of gait for 30 min. treadmill exercise once to twice while in hospital	routine care	12weeks	RPPsubma-x and RPEsubma-x QOL
Huaqin Yu, 2021 [17]	Exercise:58,41/ 17Control:57,39/18	60.22 ± 2.4860.18 ± 2.56	PCI	early home-based cardiac rehabilitation walk slowly indoors. walk outdoors. quick walk outdoors. jog outdoors	routine rehabilitation guidance	1weeks 3 months	angina pectoris coronary artery restenosis arrhythmia Cardiac function index LVEF LVESD LVEDD 6MWD Cardiac antioxidant index
Jiajia Li, 2022 [18]	Exercise:50,35/ 15Control:50,39/11	65.3 ± 8.767.7 ± 7.6	PCI	home-based online supervised exercise program (HOSEP). walking for 30–60 min, and STS exercise for 2–3 sets every day. 60–80% of maximum heart rate (HRmax) (HRmax = 220-age) calculated for intensity	conventional health education	6weeks	6MWT 30-s sit-to-stand test (30-s STS test) Timed Up and Go test (TUG test) and Hand Grip Strength (HG) total cholesterol (TC) triglycerides (TG)
Kourosh Soleimannejad et al. 2014 [19]	Exercise:73,53/ 20Control:73,43/30	58.05 ± 10.2756.76 ± 10.07	PCI	5 min of stretching and warm up, followed by treadmill, rowing, stepping, and ergometry	usual care	1-2weeks2-3 months6-12 months	LV diastolic function LVEF LVEDD LVESD RVEDD LAD

LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-diastolic dimension; RVEDD: right ventricular end-diastolic diameter; LAD: left anterior descending artery; 6MWD : 6 min walk distance; QOL: quality of life.

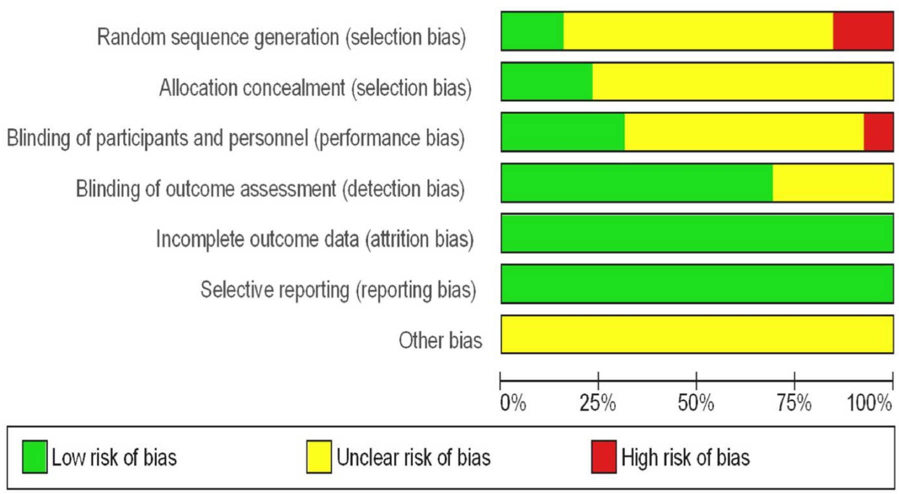

Figure 2. Quality assessment of the included papers in this review: Graph illustrating bias risk.

LVEDD. No statistically significant difference in LVEDD was found between the two groups (MD = −2.23, 95% CI[−5.57, 1.11], Figure 5).

Four trials that included 230 and 230 patients who underwent PCI with or without exercise evaluated 6MWD. A statistically significant difference in the 6MWD rate was found between the two groups (MD = 88.59,95% CI [58.08, 119.10], $p < 0.05$, Figure 5).

4. Discussion

This study included 1231 participants (610 in the experimental group and 621 in the control group). Early rehabilitation exercise combined with PCI was found to be more beneficial than normal care after PCI in lowering the risk of angina, arrhythmia, and coronary restenosis. It also decreased heart rate while increasing LVEF and 6MWD. However, no significant variations in LVEDD, cholesterol level, SBP, or DBP were seen between the two groups.

Plaque buildup in the coronary arteries, which reduces the heart's ability to receive blood, is referred to as CHD [20]. PCI is a clinical intervention used to dilate and maintain patency of narrowed coronary arteries with significant therapeutic efficacy [21]. Despite the fact that PCI is very effective in lowering symptoms and improving prognosis, patients continue to live with chronic heart disease and may face consequences. As a result, active secondary prevention of CHD is essential to enhance patient prognosis. CR exercise is an important part of the secondary prevention of CHD [22].

Cardiac function is critical in predicting long-term prognosis in PCI patients. CR exercise improves myocardial blood supply and myocardial function, enhances left atrial contractility, alleviates left ventricular remodelling, increases open coronary collateral circulation, strengthens cardiomyocyte vitality, improves myocardial glucose uptake and thus helps avoid cardiomyocyte injury [23]. The primary mechanism thought to improve coronary collateralization through exercise is increased pressure gradients between proximal and distal arteries. The metrics regularly employed to assess heart function are LVEF, LVEDD, and 6MWD. Minghui Jiang et al. found that the LVEF of the progressive exercise of kinetic energy (PEKE) group was higher than that the LVEF of the patients in the RI group [11]. Ya-Jie Shi et al. reported that 6MWD was improved after a period of 2 months of cardiac rehabilitation in 51 patients with CHD [9]. Elevated heart rate (HR) and blood pressure (BP) after PCI are modifiable risk factors associated with an increased risk of cardiac events [24,25]. Yan Zou et al. observed that the HR of patients receiving PCI in the experimental group fell noticeably [14] after conducting an RCT with 36 controls and 12 weeks of rehabilitation training. According to this study, the exercise group had increased LVEF, 6MWD, and HR. The exercise group's LVEDD, TC, SBP, and DBP numbers don't seem to indicate a better prognosis, though. More research is needed to identify how long the intervention should last in order to produce effective change in TC. Patients who undergo PCI often have diminished ventricular systolic and diastolic performance as a result of myocardial injury, which may result in a modest or no reduction in blood pressure. Meanwhile, when blood pressure is aberrant, slow breathing exercise (SBE) plays a function in stabilising it. As a result, the effect of SBE on decreasing blood pressure did not manifest. In CHD patients, the CR exercise

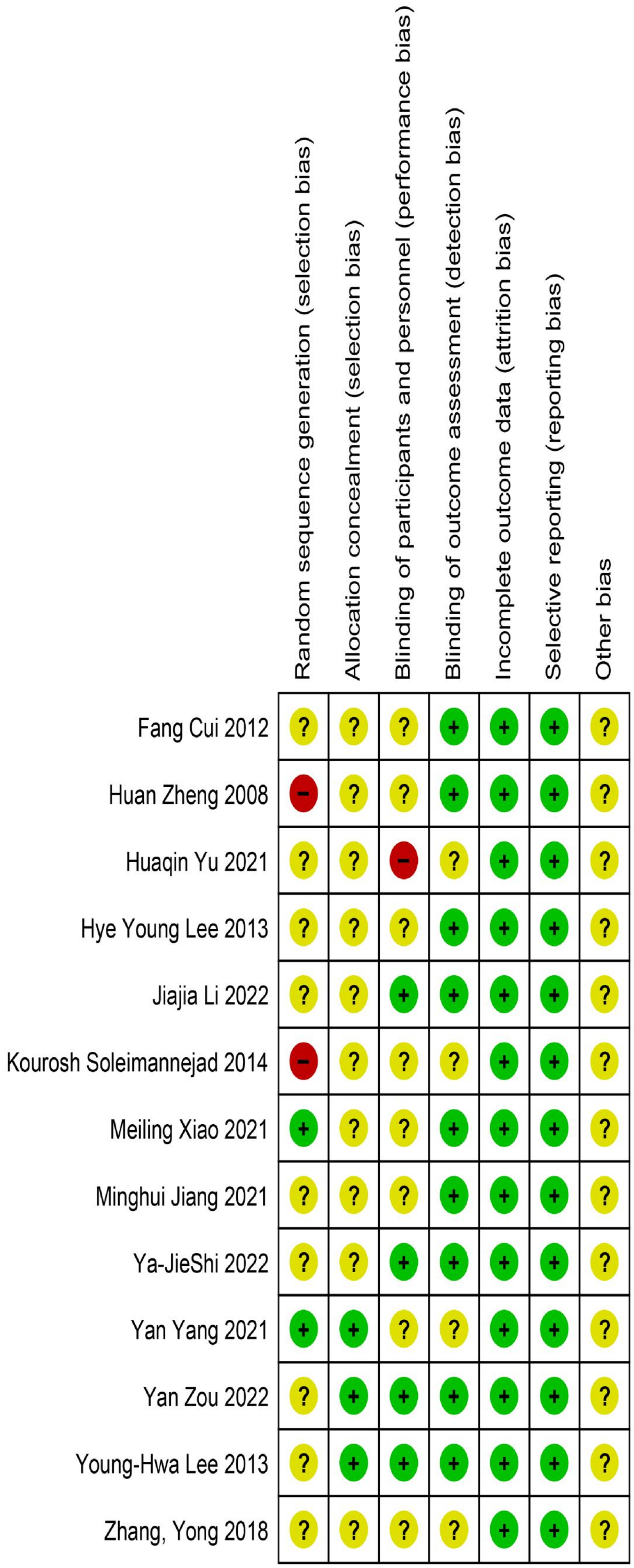

Figure 3. Quality rating of papers included in this review: Summary of the risk of bias.

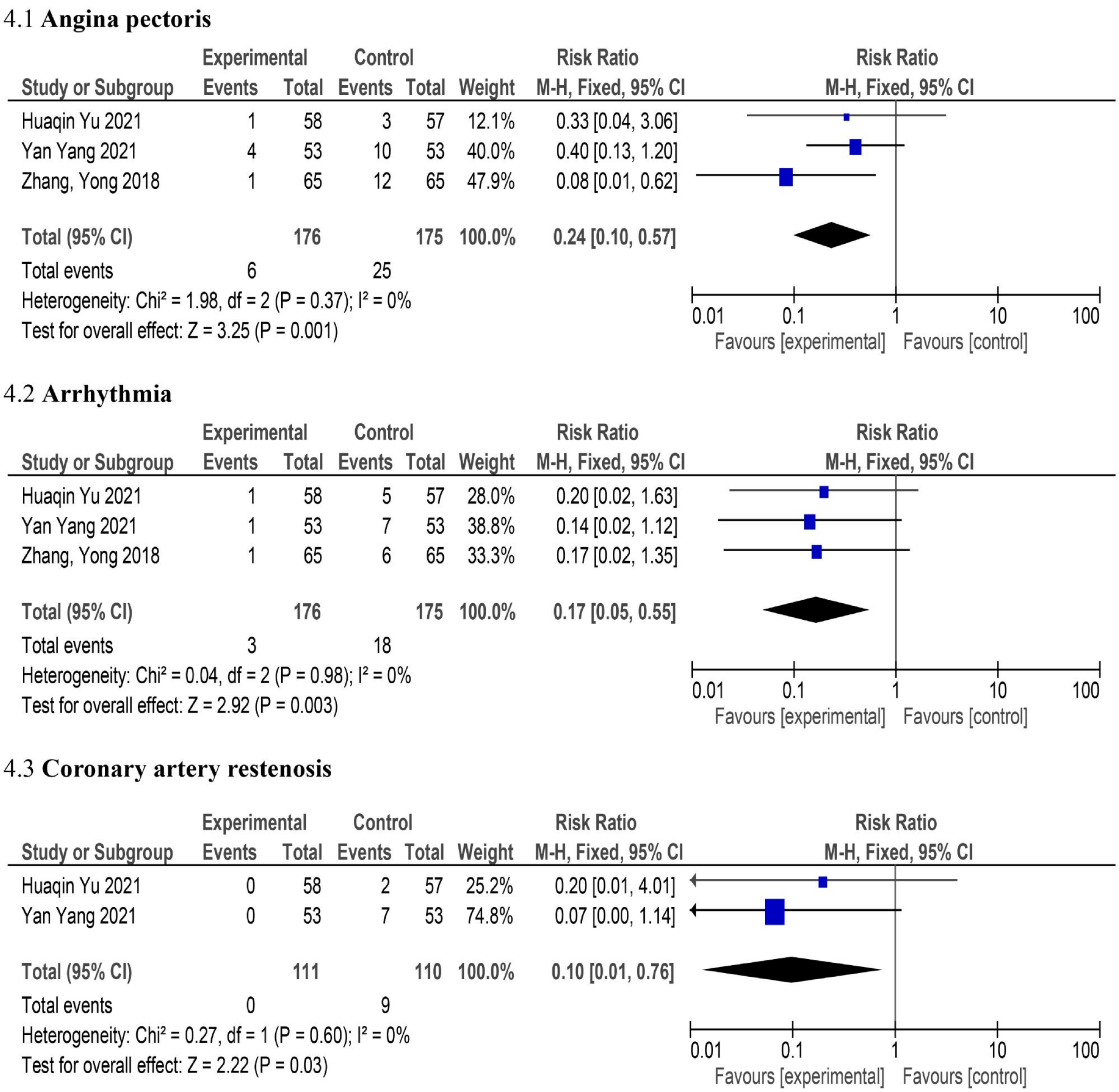

Figure 4. Comparison of adverse cardiovascular events in the activity and no-exercise groups.

program was helpful in improving LV diastolic dysfunction after PCI, with no significant changes in LV diameters.

Additionally, research has demonstrated that exercise in CHD patients following PCI is associated with a considerable decrease in hsCRP and inflammatory cytokines (TNF- alpha and IL-6), as well as a marked improvement in exercise tolerance and capacity [26]. Anxiety and depression are common symptoms in patients with CHD after PCI. The miRNAs play an important role in depression [27] and anxiety [28]. Tai Chi reduced anxiety, depression, and stress symptoms and increased miR-17-92 expression in CHD patients following PCI [29].

Coronary artery restenosis, angina, and arrhythmias are significant risk factors for post-operative CHD. cardiac rehabilitation exercise enhances blood supply and decreases arterial stiffness, lowers numerous risk factors for heart disease, and improves human vascular system regulation [30]. Implementing a 7-day gradual early functional exercise program following PCI in young and middle-aged patients with acute myocardial infarction increases compliance with functional exercise, daily activities and quality of life, while decreasing the incidence of sequelae [8]. Our study results revealed an improvement in angina, arrhythmia and coronary artery restenosis in the exercise group compared with the control group after PCI.

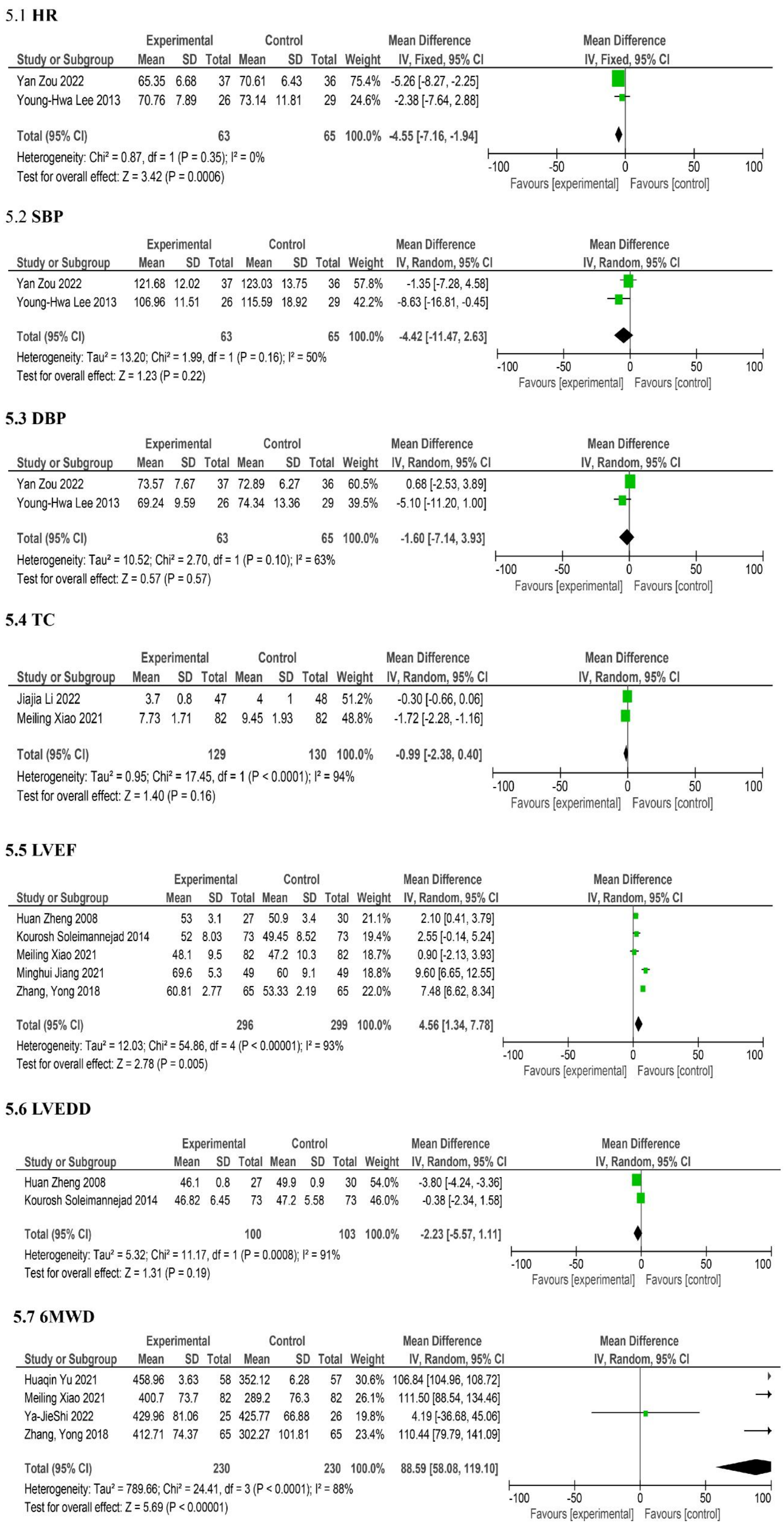

Figure 5. Cardiac function and secondary endpoint parameters were compared between the activity and no-exercise groups.

5. Conclusion

Exercise after PCI improves LVEF, enhances 6MWD, lowers HR, and minimises the risk of angina, arrhythmia and coronary artery restenosis in CHD patients. Exercise had no discernible effect on LVEDD, TC, SBP, or DBP. More research is needed to increase the sample size and enhance reporting quality.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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