Li *et al. BMC Cardiovascular Disorders* (2025) 25:217
https://doi.org/10.1186/s12872-025-04649-0

BMC Cardiovascular Disorders

SYSTEMATIC REVIEW Open Access

Impact of exercise training on exercise tolerance, cardiac function and quality of life in individuals with heart failure and preserved ejection fraction: a systematic review and meta-analysis

Hu Li[1*†], Yingxue Liu[2†], Yu Liu[1], Zhichao Xu[1], Pengchao Pan[1] and Lijun Zeng[1]

Abstract

Background Heart failure with preserved ejection fraction (HFpEF) is increasingly prevalent and poses significant treatment challenges due to its complex pathophysiology. Exercise training has emerged as a promising non-pharmacological intervention to improve outcomes in HFpEF patients. This study aims to evaluate the effect of exercise training on exercise tolerance, cardiac function and quality of life in HFpEF patients.

Method Through systematic review and meta-analysis, major databases were scoured for randomized controlled trials (RCTs) evaluating the influence of exercise training on HFpEF patients. Data on exercise tolerance, cardiac function parameters, and quality of life were extracted. The quality of the studies was assessed using the Cochrane Collaboration's risk of bias tool. Statistical analyses were performed using Review Manager 5.4, with mean differences (MD) or standardized mean differences (SMD) and 95% confidence intervals (CIs) calculated for continuous variables.

Results Seven RCTs encompassing 470 participants met the inclusion criteria. Exercise training significantly improved exercise tolerance as measured by the 6-Minute Walk Test ($P < 0.01$) and peak VO_2 ($P = 0.03$). No significant effects were observed on cardiac function parameters, including the E/A ratio, E/e' ratio, and LVEF. Total quality of life was similar between exercise and control groups, but significantly enhanced in physical components about quality of life was observed in the exercise group ($P = 0.03$). There were no significant differences between high-intensity interval training (HIIT) and moderate continuous training (MCT) in improving exercise tolerance, cardiac function, or quality of life.

Conclusion Exercise training effectively enhances exercise tolerance and physical quality of life in patients with HFpEF, without significantly impacting cardiac function parameters. HIIT and MCT has similar effect in HFpEF patients.

†Hu Li and Yingxue Liu contributed equally to this work.

*Correspondence:
Hu Li
lihu@medmail.com.cn

Full list of author information is available at the end of the article

These findings support the incorporation of exercise training into the management strategies for HFpEF patients to improve functional outcomes and quality of life.

Keywords Exercise training, Heart failure with preserved ejection fraction, Cardiac function, Quality of life, Meta-analysis

Introduction

Globally, heart failure (HF) stands as a significant public health challenge, detrimentally affecting patient quality of life and linked with elevated mortality rates [1]. According to the latest guidelines of Universal Definition and Classification of Heart Failure, HF is classified into four categories based on left ventricular ejection fraction (LVEF): HF with reduced EF (HFrEF) with an LVEF of ≤ 40%; HF with mildly reduced EF (HFmrEF) with an LVEF of 41–49%; HF with preserved EF (HFpEF) with an LVEF of ≥ 50%; and HF with improved EF (HFimpEF) [2]. Notably, data from the Framingham Heart Study over two decades indicate a more than 50% increase in HFpEF incidence between the periods 2000–2009 compared to 1990–1999 [3]. HFpEF has historically been considered a challenging condition to treat due to its complex pathophysiology [3]. Several recent pharmacological trials have shown positive results in managing HFpEF, particularly with agents such as sodium-glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists [4–6]. Alongside pharmacological approaches, exercise training has gained recognition as a critical non-pharmacological strategy in managing HF, particularly in enhancing cardiac health, physical endurance, and quality of life [7, 8]. In the context of HFpEF, aerobic and resistance training have shown potential benefits, including enhanced aerobic capacity and quality of life, indicate an enhancement in cardiorespiratory health and quality of life for HFpEF patients through exercise, without negatively impacting cardiac function [9, 10]. However, some recent studies suggest that combined aerobic and resistance exercises may not significantly benefit cardiac function in HFpEF patients [11]. Several meta-analyses have evaluated the impact of exercise training on patients with HFpEF, but a consensus regarding exercise tolerance, quality of life, and diastolic function has yet to be reached [10–14]. Moreover, since the concept of HFmrEF had not been established in earlier years, many previous meta-analyses included patients with HFpEF defined as an LVEF ≥ 45% instead of the current threshold of ≥ 50% [10]. Additionally, some meta-analyses included both original clinical trial publications and secondary sub-analyses of the same trial, potentially influencing the results [12].

Therefore, we conducted a systematic review and meta-analysis to comprehensively assess the impact of exercise training on exercise tolerance, cardiac function, and quality of life in patients with HFpEF (LVEF ≥ 50%). Additionally, we compared the efficacy of high-intensity interval training (HIIT) versus moderate continuous training (MCT). Our aim is to provide robust evidence to guide clinical practice and optimize rehabilitation strategies for patients with HFpEF.

Methods

This meta-analysis and systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15].

Search strategy

A comprehensive literature search was conducted in the following databases: PubMed, Embase, Cochrane Library, and Web of Science, from their inception until November 24, 2023. The search strategy was designed to include a combination of MeSH terms and free-text words related to “heart failure with preserved ejection fraction (HFpEF)” and “exercise training”, with the detailed search strategy presented in Table S1.

Eligibility criteria

Studies were included based on the following criteria:

- Study Design: Only randomized controlled trials (RCTs).
- Participants: Studies involving subjects diagnosed with HFpEF (LVEF ≥ 50%).
- Intervention: Studies examining the effects of exercise training, regardless of duration and frequency.
- Outcomes: Studies must report on exercise tolerance, cardiac function, and quality of life.
- Language: English.

Exclusion Criteria were as follows:

- Study Design: non-RCTs, such as case reports, commentaries, opinion articles, or reviews.
- Participants: Studies involving non-HFpEF patients or those with unclear diagnoses.
- Incomplete Data: Studies with incomplete data or unclear methodologies.
- Duplicate Publications: Studies that report on the same dataset or trial data analyzed and published more than once, unless the secondary publication includes additional outcomes not previously reported in the primary study.

Data extraction

Data was meticulously extracted by two independent reviewers using a pre-defined form. The gathered data encompassed aspects such as the general characteristics of the articles (including the author(s), publication year, study design, etc.), demographic details of the participants, specifics of the exercise interventions (covering the type, length, and regularity of exercises), as well as the outcomes measured and the findings of each study. In instances of disagreement between the two primary reviewers, a third reviewer was consulted to achieve a consensus.

Assessment of quality

The Cochrane Collaboration's bias assessment tool was utilized for evaluating the quality of the included RCTs.

Statistical analysis

The meta-analysis process was executed through the Review Manager (RevMan), version 5.4. Mean differences (MD) with 95% confidence intervals (CIs) quantified the effect size for continuous variables. For quality of life outcomes, the Standardized Mean Difference (SMD) was used to combine results from different quality of life measures, including the Short Form 36 Health Survey (SF-36), the Minnesota Living with Heart Failure Questionnaire (MLHFQ), and the Kansas City Cardiomyopathy Questionnaire (KCCQ). The SMD was calculated for the total quality of life scores, as well as for the physical and mental component scores of SF-36. Since the scoring for MLHFQ is inversely related to quality of life, we reversed the scoring for MLHFQ to ensure consistency in the interpretation of results across the different measures. Weights were automatically assigned by RevMan based on the combination of a large sample size and a small standard error. The I^2 statistic assessed heterogeneity across studies. A fixed-effect model was applied for low heterogeneity (I^2<50%), while significant heterogeneity (I^2≥50%) warranted the use of a random-effects model. Funnel plots were visually analyzed to detect any potential publication bias. A value of $P < 0.05$ was considered significant.

Results

Study selection process and characteristics

A PRISMA flowchart visually represented the methodology used for study selection. (Fig. 1). Initially, a search across various databases yielded 3943 records. After removing duplicates, 3427 records were screened, leading to 81 articles being thoroughly reviewed for their relevance. Finally, 7 RCTs involving 470 participants met the inclusion criteria and were included in the meta-analysis [16, 17]. The included RCTs predominantly conducted in the USA, focusing on middle-aged or older adults (≥ 40 years). Exercise training across these studies were diverse, mainly encompassing HIIT and MCT. The duration of these interventions was ranged from short-term programs of 4 weeks to longer interventions lasting up to one year. Some studies employed a combination of in-clinic and telemedically supervised home-based exercises. The comprehensive summary of included studies was detailed in Table 1.

Quality assessment

As depicted in Fig. 2, the majority of the analyzed studies were found to have a low bias risk in random sequence generation, blinding of outcome assessment, incomplete outcome data, as well as selective reporting. On the contrary, high risk of bias was observed in participant blinding. This could be attributed to the inherent characteristics of the study designs where the type of exercise intervention is inherently apparent to both the subjects and the investigators.

Effect of exercise training on exercise tolerance

The impact of exercise training on exercise tolerance was assessed using 6-Minute Walk Test (6MWT), peak VO_2, the ventilatory anaerobic threshold and VE/VCO_2 slope (Fig. 3). There was significant higher value in the 6MWT for HFpEF patients undergoing exercise training, with low heterogeneity (MD = 31.42, 95% CI: 19.35 to 43.49, $P < 0.001$; I^2=1%, $P = 0.39$) (Fig. 3A). In addition, exercise significantly increased peak VO_2 compared to the control group with random-effects model and high heterogeneity (MD = 1.53, 95% CI: 0.13 to 2.92, $P = 0.03$; I^2=70%, $P = 0.009$), while significant difference was not found between MCT and HIIT (MD = 1.60, 95%CI: -0.22 to 3.42, $P = 0.08$; I^2 = 19%, $P = 0.29$) (Fig. 3B and C). For the ventilatory anaerobic threshold, there were only two RCTs assessed, and significantly increased ventilatory anaerobic threshold was observed in HFpEF patients after exercise training (MD = 149.86, 95%CI: 42.07 to 257.64, $P = 0.006$; I^2 = 64%, $P = 0.09$) (Fig. 3D). For VE/CO_2 slope, No significant difference was found on VE/CO_2 slope in neither exercise compared to control (MD = 0.10, 95%CI: -0.80 to 1.00, $P = 0.83$; I^2 = 27%, $P = 0.25$; Fig. 3E) nor HIIT compared to MCT (MD = 2.23, 95%CI: -0.24 to 4.71, $P = 0.08$; I^2 = 0%, $P = 0.68$; Fig. 3F).

Effect of exercise training on cardiac function

To assess the influence of exercise training on cardiac function, parameters including the E/A ratio, E/e' ratio, and left ventricular ejection fraction (LVEF) were utilized (Fig. 4). There was no significant difference between exercise and control groups in E/A ratio (MD=-0.03, 95%CI: -0.10 to 0.04, P = 0.42; I^2 = 0%, P = 0.77), E/e' ratio (-1.12, 95%CI: -3.45 to 1.20; $P = 0.34$; I^2 = 82%, $P = 0.004$), and LVEF (MD = 0.92, 95%CI: -0.72 to 2.56, $P = 0.27$; I^2 = 0%,

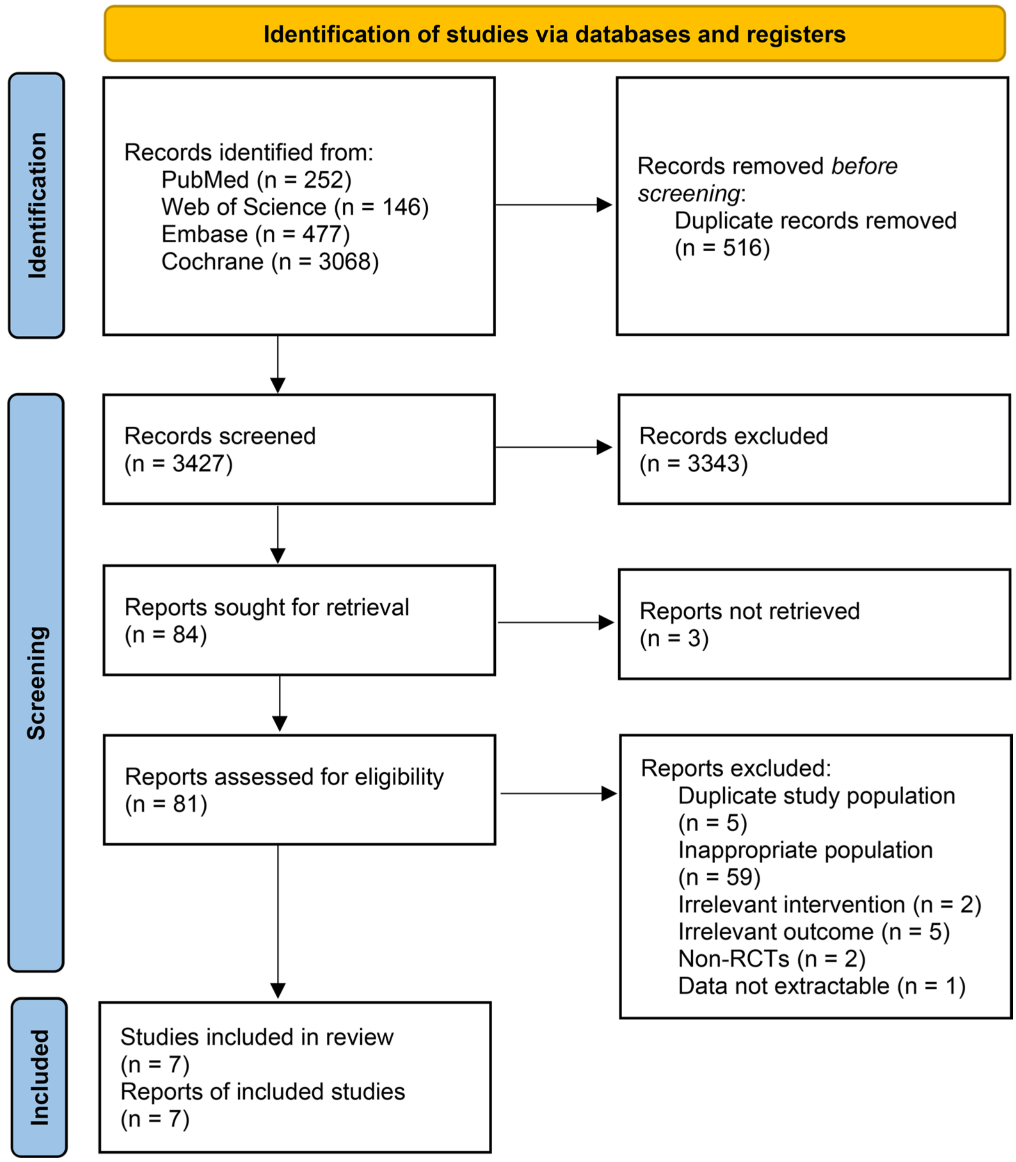

Fig. 1 PRISMA flow diagram

$P=0.64$) (Fig. 4A, C, E). Similarly, no notable distinction was observed between MCT and HIIT groups in E/A ratio (MD=-0.06, 95%CI: -0.24 to 0.12, $P=0.54$; $I^2=46\%$, $P=0.16$), E/e' ratio (MD=-0.96, 95%CI: -2.24 to 0.32, $P=0.14$; $I^2=37\%$, $P=0.20$) and LVEF (MD = 0.36, 95%CI: -1.83 to 2.55, $P=0.75$; $I^2=0\%$, $P=0.82$) (Fig. 4B, D, F).

Effect of exercise training on quality of life

The assessment of exercise training on quality of life was carried out through KCCQ, SF-36 Scale and MLHFQ (Fig. 5). Exercise group had similar total quality of life score compared to control group (MD = 0.14, 95%CI: -0.05 to 0.33, $P=0.15$; $I^2=0\%$, $P=0.99$) (Fig. 5A). Compared with control group, physical quality was significantly higher in exercise group (MD = 0.22, 95%CI: 0.02 to 0.42, $P=0.03$; $I^2=10\%$, $P=0.35$), whereas the emotional quality did not show a significant difference between the two groups (MD = 0.18, 95%CI: -0.31 to 0.66, $P=0.48$; $I^2=66\%$, $P=0.03$). Among them, both SF36 physical (MD = 0.31, 95%CI: 0.06 to 0.57, $P=0.02$; $I^2=34\%$, $P=0.21$) and emotional scores (MD = 0.51, 95%CI: 0.11 to 0.92, $P=0.01$; $I^2=0\%$, $P=0.58$) were significantly higher in the exercise group compared with the control group, but there was no significant difference in reverse MLHFQ physical (MD = 0.08, 95%CI: -0.24 to 0.39, $P=0.64$; $I^2=0\%$, $P=0.67$) and reverse emotional scores (MD=-0.16, 95%CI: -0.83 to 0.52, $P=0.65$; $I^2=65\%$, $P=0.09$) between the two groups. Subgroup analysis showed no significant difference in both scores ($P=0.25$ and 0.09, respectively) (Fig. 5B and C).

Table 1 General characteristics of the included studies

First author, Publication year	Setting	Age	Intervention, number	Duration of treatment
Kitzman DW et al. 2010 [40]	USA	60–82	Exercise training; *n* = 24 Attention control; *n* = 22	16 weeks
Edelmann F et al. 2011 [41]	Germany	≥ 45	Endurance/resistance training; *n* = 44 Usual care; *n* = 20	3 months
Kitzman DW et al. 2013 [42]	USA	70 ± 7	Endurance exercise training; *n* = 24 Attention control; *n* = 30	16 weeks
Angadi SS et al. 2014 [43]	USA	70 ± 8.3	HIIT; *n* = 9 MCT; *n* = 6	4 weeks
Kitzman et al. 2016 [44]	USA	67 ± 5	Exercise; *n* = 46 No Exercise; *n* = 46	20 weeks
Donelli da Silveira A et al. 2020 [16]	Brazil	60 ± 9	MCT; *n* = 9 HIIT; *n* = 10	12 weeks
Mueller, S et al. 2021 [17]	Europe	70	HIIT; *n* = 60 MCT; *n* = 60 Guideline control; *n* = 60	3 months in clinic followed by 9 months telemedically supervised home-based exercise

HIIT: high-intensity interval training; MCT: moderate continuous training

Publication bias

To explore potential publication bias across the studies, a funnel plot analysis was employed. The symmetry observed in the funnel plot suggested an absence of significant publication bias within the included studies (Figure S1).

Discussion

Earlier clinical trials targeting HFpEF often recruited patients with an LVEF > 40% or ≥ 45%, which may result in heterogeneous study populations and inconclusive treatment efficacy [18]. According to the latest definitions, LVEF of 41–49% is now classified as HFmrEF, which shares more clinical characteristics and therapeutic responses with HFrEF rather than HFpEF [2]. The inconsistent definitions of HFpEF in previous studies and meta-analyses have led to varied standards for inclusion, potentially confounding findings. To address this, this meta-analysis specifically focuses on patients with LVEF ≥ 50%, adhering to the latest definition of HFpEF, aiming to provide a more accurate assessment of the impact of exercise training on exercise tolerance, cardiac function, and quality of life in this HFpEF patients.

The analysis showed that exercise significantly improved peak VO_2, a key indicator of improved aerobic capacity in patients. This improvement is crucial as HFpEF patients typically exhibit reduced aerobic capacity, which significantly impacts their quality of life. The diminished peak VO_2 in these patients is linked to a mix of cardiovascular and muscular inefficiencies, which hampers oxygen's effective delivery and utilization by muscles during activity [7]. Evidence supports that endurance training, whether conducted independently or in conjunction with resistance exercises, provides a secure and effective strategy to enhance aerobic capacity in patients with HFpEF [19, 20]. The secondary analysis of OptimEx-Clin trial showed that peak O_2-pulse was a significant predictor of changes in peak VO_2 following exercise training, with baseline peak O_2-pulse explaining the variance in VO_2 improvements between exercise training and control groups [21, 22]. This meta-analysis also showed that exercise training led to significant higher value of the 6MWT for individuals diagnosed with HFpEF, indicating that exercise training can indeed translate to functional mobility improvements in daily life for these patients. Some research has shown that HFpEF patients can experience improvements in 6MWT outcomes following exercise training [12, 23]. These findings highlight the potential of exercise training to enhance both laboratory-based and real-world physical function in HFpEF patients. A secondary analysis of included OptimEx-Clin trial results shows that changes in circulating microRNA levels, such as miR-181c, were found to predict exercise training responses in HFpEF patients, effectively identifying low responders and high responders to exercise [24]. This suggests a potential biomarker-driven approach to tailoring exercise interventions. Therefore, the integration of more objective and personalized exercise measures, such as peak O2-pulse and miR-181c, in managing HFpEF patients.

Regarding cardiac function, MCT showed a significant decrease in the E/e' ratio, an echocardiographic measure of diastolic function, reinforcing the potential of MCT in ameliorating diastolic dysfunction in HFpEF [12]. However, neither MCT nor HIIT led to a significant improvement in the LVEF or the E/A ratio, suggesting limited effectiveness of exercise training on these specific indicators of heart function in HFpEF [10, 25]. It is important to note that previous meta-analys have shown conflicting results, with some indicating improvements in LVEF [26] and the E/A ratio [27] following exercise intervention in HF patients. This discrepancy may be attributed to the heterogeneity of the studies included in these meta-analyses. The current study focused solely on literature related to patients with HFpEF and did not include inspiratory muscle training in the exercise interventions.

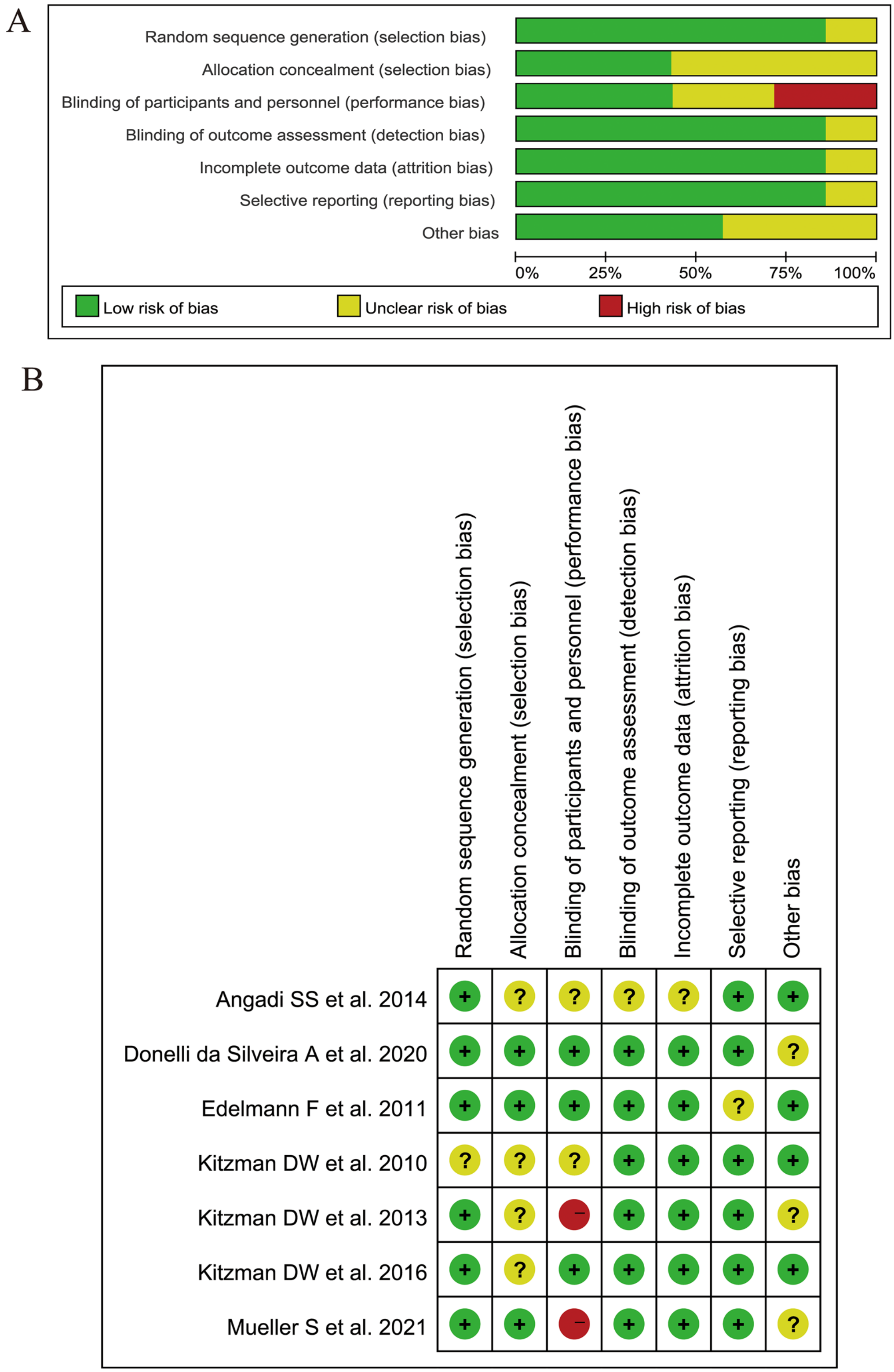

Fig. 2 Risk of bias assessment

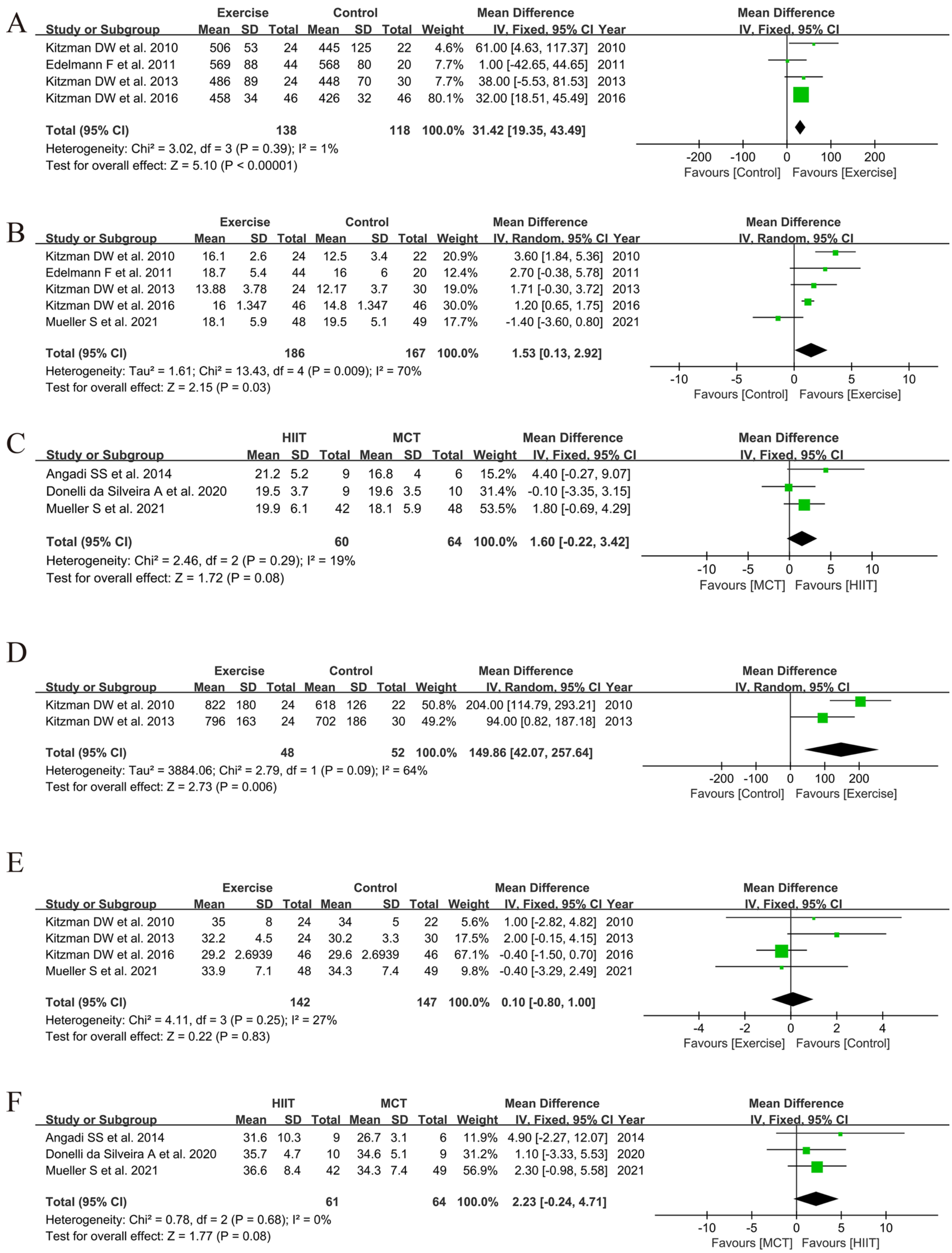

Fig. 3 Effect of exercise training on exercise tolerance. (**A**) 6-Minute Walk Test between exercise and control groups; (**B**) peak VO_2 between exercise and control groups; (**C**) peak VO_2 between HIIT and MCT groups; (**D**) ventilatory anaerobic threshold between exercise and control groups; (**E**) VE/VCO_2 slope between exercise and control groups; (**F**) VE/VCO_2 slope between HIIT and MCT groups

Following exercise training, there was a non-significant improvement in overall quality of life, as reflected in the total QoL score. This suggests that while exercise training may contribute to better functional well-being, the overall perceived quality of life improvement remains limited. When considering the overall quality of life scores categorized into physical and emotional domains, patients in the exercise group demonstrated a significantly higher physical quality of life score compared to those who did not undergo exercise intervention, reinforcing the role

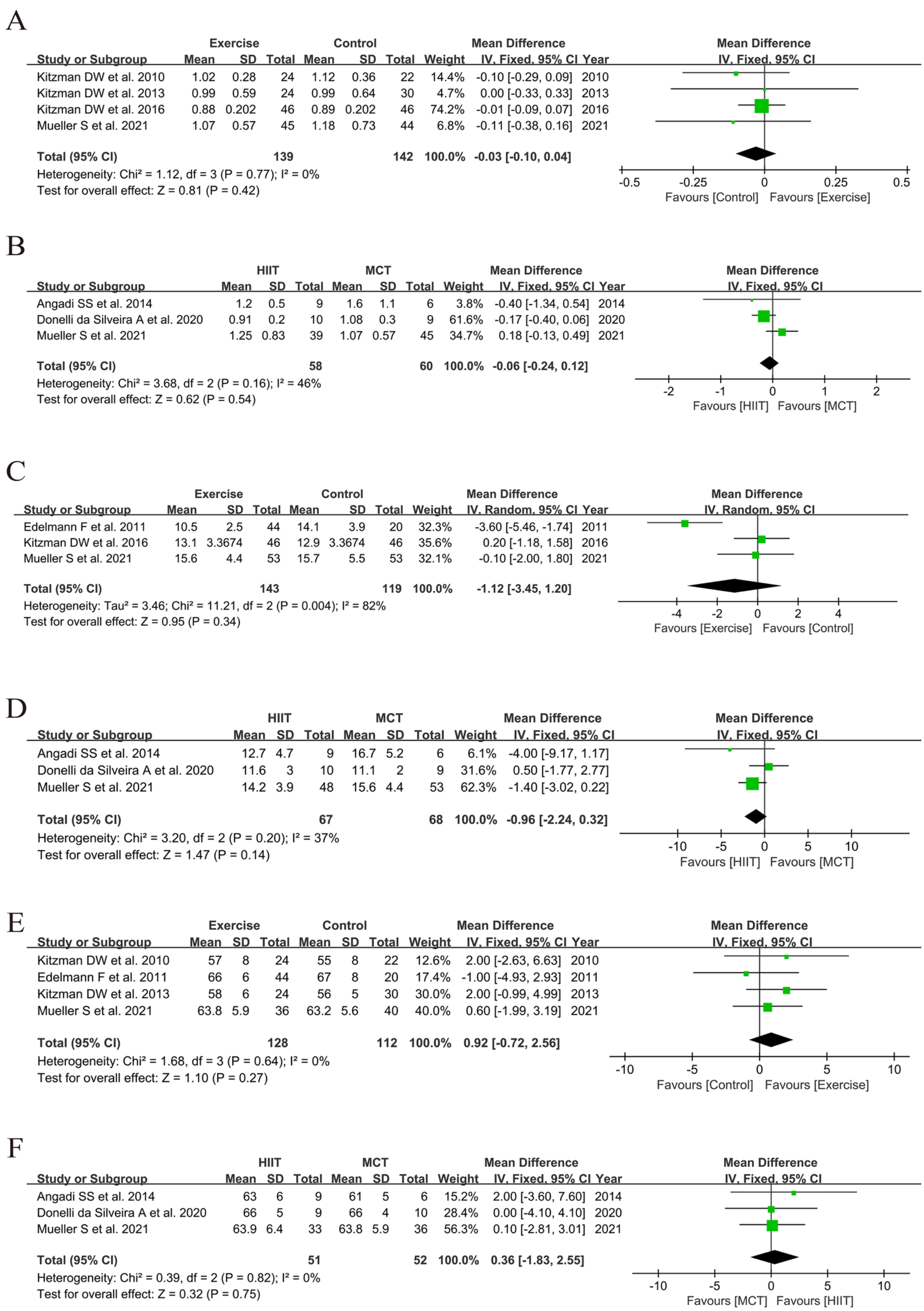

Fig. 4 Effect of exercise training on cardiac function. (**A**) E/A ratio between exercise and control groups; (**B**) E/A ratio between HIIT and MCT groups; (**C**) E/e' ratio between exercise and control groups; (**D**) E/e' ratio between HIIT and MCT groups; (**E**) LVEF between exercise and control groups; (**F**) LVEF between HIIT and MCT groups

of exercise training as an effective non-pharmacological strategy to improve functional capacity in HFpEF patients [10, 27, 28]. However, no significant differences were observed in emotional quality of life between the groups, which may be attributed to the multifactorial nature of emotional health in HFpEF patients. Emotional well-being is influenced by psychological, social, and economic factors that may not be as directly modifiable through exercise alone. These findings underscore the need for a more holistic approach to addressing

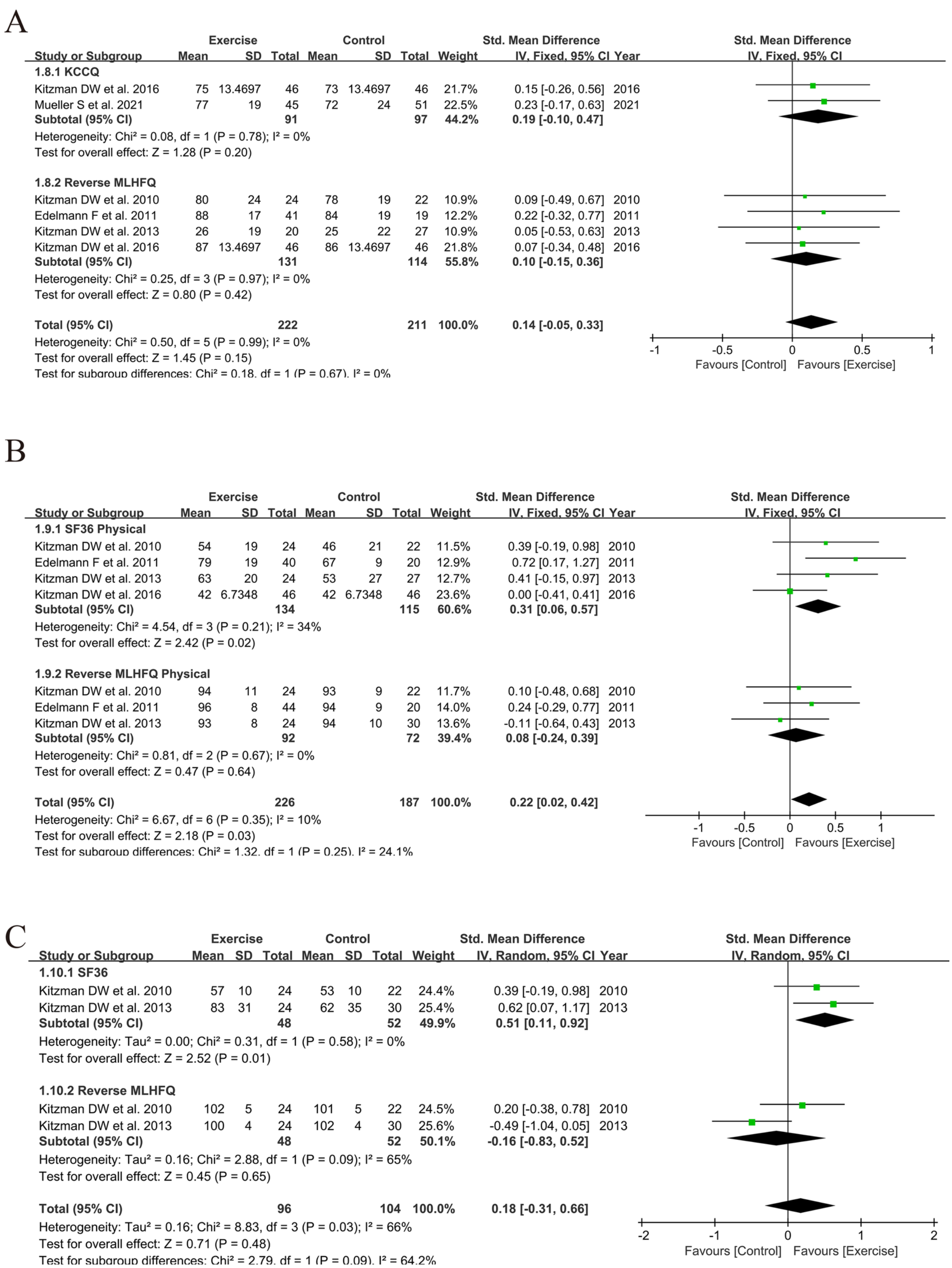

Fig. 5 Effect of exercise training on quality of life. (**A**) Total Quality of Life score between exercise and control groups; (**B**) Physical Quality of Life functioning score between exercise and control groups; (**C**) Emotional Quality of Life functioning score between exercise and control groups

emotional health in this population. Notably, the impact of exercise training appeared to vary based on the quality of life assessment tool used. In the SF-36 scale, both physical and emotional scores were significantly higher in the exercise group compared to the control group. Conversely, no significant differences were observed in either physical or emotional scores between the groups when assessed using the MLHFQ. This discrepancy may stem from differences in the design and focus of the two instruments [31]. The SF-36 is a generic quality of life measure that captures broader aspects of health and well-being, while the MLHFQ is more disease-specific and heavily weighted towards the physical and symptomatic burden of heart failure. It is possible that the benefits of exercise were not sufficient to translate into substantial changes in the domains emphasized by the MLHFQ. Nonetheless, previous meta-analyses have indicated that exercise intervention has a significant impact on MLHFQ scores. Specifically, in a meta-analysis conducted by Pandey et al. [10], it was found that exercise training contributes to better quality of life in individuals with HFpEF, based on measurements obtained from the MLHFQ. Additionally, another meta-analysis by Fukuta et al. [29] also found that exercise training improved MLHFQ total scores compared with usual care in HFpEF patients. A meta-analysis by Chan et al. [30] similarly supports this view. We hypothesize that the reason for this discrepancy may be due to the inclusion of studies on inspiratory muscle training in these meta-analyses, whereas our study only included physical exercise training. This difference is intriguing and warrants further exploration in future research to investigate the differences between inspiratory muscle training and physical exercise training in HFpEF patients.

Both MCT and HIIT have been shown to effectively increase exercise capacity and quality of life among patients suffering from a range of cardiovascular diseases [32]. However, the lack of significant differences between MCT and HIIT in most outcomes of our study suggested that, although previous studies have found HIIT to be more effective than MCT in some HF patients, this is not the case in HFpEF patients [33–35]. The key factor appears to be the regularity and consistency of the exercise rather than the specific type of training [36]. Sowa et al. reported that HIIT enhances HDL function, particularly its anti-oxidative properties and stimulation of eNOS activity in HFpEF patients, although these effects diminish with reduced training compliance [37]. Winzer et al. identified molecular changes in peripheral skeletal muscles, such as reduced markers of muscle atrophy (MuRF1 and Trim72) and increased mitochondrial enzyme activities, following 3 months of HIIT [38]. Though HIIT induces short-term molecular adaptations that may contribute to improvements in aerobic capacity, these effects were less pronounced or absent after 12 months of home-based training. In addition, the secondary analysis of the OptimEx-Clin trial found that increasing the frequency or duration of exercise training may be more effective in improving peak VO_2 than increasing exercise training intensity [22]. Therefore, long-term adherence is critical for maintaining these benefits of HIIT.

This meta-analysis has certain limitations that must be acknowledged. First, the reliance on follow-up values instead of changes from baseline could introduce potential biases due to baseline differences among study populations. For studies with slight baseline imbalances, we attempted to mitigate bias through the application of random-effects models. Despite these efforts, baseline differences could still influence the results. Future studies should aim to provide comprehensive baseline data and report changes from baseline to enhance consistency and reliability in meta-analyses. The significant risk of bias identified in allocation concealment and participant blinding in the included studies is also a notable limitation, potentially attributable to the inherent challenges in blinding exercise interventions. It is well recognized that blinding participants and personnel in exercise intervention studies is challenging, often leading to potential biases [39]. Third, the weight assigned to Kitzman et al. 2016 in the 6MWT analysis was notably high, which might disproportionately influence the overall effect size. Future studies with larger sample sizes from multiple sources are needed to reduce the impact of any single study on the meta-analysis results. Future studies should aim to address these methodological limitations, possibly through innovative blinding techniques or more rigorous allocation concealment, to strengthen the validity of their findings.

Conclusion

In conclusion, exercise training in HFpEF patients leads to significant improvements in exercise tolerance and select aspects of quality of life, particularly physical functioning, with modest effects on cardiac function. However, improvements in overall quality of life remain variable, and further research is needed to fully understand the multidimensional impacts of exercise interventions on HFpEF patient.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04649-0.

Supplementary Material 1: Fig. S1: Publication Bias. (A) 6-Minute Walk Test between Exercise and control groups; (B) peak VO_2 between exercise and control groups; (C) peak VO_2 between HIIT and MCT groups; (D) ventilatory anaerobic threshold between exercise and control groups; (E) VE/VCO_2 slope between exercise and control groups; (F) VE/VCO_2 slope between HIIT and MCT groups; (G) E/A ratio between eexercise and control groups; (H) E/A ratio between HIIT and MCT groups; (I) E/e' ratio between exercise and control groups; (J) E/e' ratio between HIIT and MCT groups; (K) LVEF between exercise and control groups; (L) LVEF between HIIT and MCT groups; (M) Total Quality of Life score between exercise and control groups; (N) Physical Quality of Life functioning score between exercise and control groups; (O) Emotional Quality of Life functioning score between exercise and control groups

Acknowledgements

Not applicable.

Author contributions

H.L. and Y.L. contributed equally to this work. H.L. conceptualized and designed the study, supervised data analysis, and drafted the manuscript. Y.L. conducted the literature search, data extraction, and performed the statistical analyses. Z.X. and Y.L. reviewed and verified the statistical analysis. P.P. and L.Z. assisted with data collection and manuscript drafting. All authors contributed to data interpretation, manuscript revisions, and approved the final manuscript for submission.

Funding
Not applicable.

Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
As this study was a systematic review and meta-analysis based on published data, ethical approval and patient consent are not required.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Cardiology, The First Naval Hospital, Southern Theater Command of PLA, No.10 Haibin Avenue Middle, Zhanjiang 524005, China
[2]Outpatient Department, The First Naval Hospital, Southern Theater Command of PLA, Zhanjiang 524005, China

Received: 9 October 2024 / Accepted: 10 March 2025
Published online: 25 March 2025

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