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Identifying the Optimal Respiratory Muscle Training Intervention for Heart Failure Patients:

A Network Meta-analysis of Randomized Controlled Trials

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Abstract

Background: Respiratory muscle training interventions have shown promising results in improving functional capacity, quality of life, and prognosis of heart failure patients. However, the optimal respiratory muscle training intervention for rehabilitation remains unclear.

Methods: A systematic review and network meta-analysis was conducted by searching PubMed, Embase, Scopus, and Cochrane Library until September 2025 for randomized controlled trials (RCTs) evaluating the effect of respiratory muscle training interventions on maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), six-minute walk test (6MWT), peak oxygen uptake (VO_2max), quality of life, and dyspnea. Random-effect network meta-analysis was used to estimate pooled mean differences. Interventions were ranked using the surface under the cumulative ranking curve (SUCRA).

Results: A total of 88 RCTs (5,757 participants) were included. Medium-intensity inspiratory muscle training (IMT) ranked highest for improving MIP (SUCRA: 89.8%). Combined aerobic and resistance exercise was optimal for MEP (SUCRA: 79.3%). Aerobic training showed the greatest benefit for FVC (SUCRA: 94.8%) and FEV_1 (SUCRA: 93.8%). Medium-intensity IMT was most effective for enhancing 6MWT performance (SUCRA: 81.6%). A combination of high-intensity IMT with aerobic training yielded the largest gains in improving VO_2max (SUCRA: 74.7%), quality of life (SUCRA: 81.4%), and reducing dyspnea (SUCRA: 89.3%).

Conclusion: Respiratory muscle training interventions provide different benefits across key rehabilitation outcomes in heart failure. Accordingly, rehabilitation strategies may be optimized by aligning exercise modalities with patients' rehabilitation needs, preferences, and clinical profiles, rather than adopting a uniform prescription.

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Introduction

Heart failure (HF) is a major cardiovascular disease affecting an estimated 40 million individuals worldwide (1). It is associated with mortality rates of 8% at 30 days and 25% at 1 year (2). HF also contributes substantially to the comorbidity burden and hospitalizations, accounting for 1–2% of all hospital admissions (3). By 2030, an estimated eight million adults in the USA alone are expected to be diagnosed with HF (4), highlighting the urgent need for more effective management strategies.

In recent years, non-pharmacological interventions such as respiratory muscle training programs have gained increasing attention as adjunctive therapies for HF. Respiratory muscle training interventions encompass a broad range of modalities, including respiratory muscle–targeted approaches such as inspiratory muscle training (IMT), as well as breathing-based interventions and broader exercise-based rehabilitation strategies, including aerobic exercise, combined aerobic and resistance exercise (CARE), high-intensity interval training (HIIT), tai chi, and yoga. These modalities do not all directly target the respiratory muscles, but they may influence overlapping rehabilitation outcomes through distinct mechanisms. Nevertheless, the effectiveness of different modalities varies across rehabilitation domains, making it challenging to identify the most appropriate approach in clinical practice.

Most analyses have been limited to pairwise comparisons of respiratory muscle training modalities, providing only partial insights into their relative efficacy. Network meta-analysis addresses these limitations by enabling both direct and indirect comparisons of multiple interventions and ranking them according to their effects (5). The present study aims to address

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these gaps by incorporating a broader range of respiratory muscle training modalities to evaluate their effects on different aspects of rehabilitation in patients with HF.

Methods

The study was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines, as provided in **Online Table 1** (6). The protocol for this systematic review and meta-analysis was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) (registration code CRD420251112968). As the analyses were solely based on summary data from previously published studies, no additional ethical approval was needed.

Search Strategy and Screening

We performed a comprehensive literature search across PubMed, Embase, Scopus, and Cochrane Library, from inception until September 5, 2025. The search strategy incorporated the following keywords ("Heart failure") AND ("Breathing Exercises " OR " Respiratory Training " OR " Pulmonary Rehabilitation "), along with their related terms, without language restrictions. The detailed search strategies for databases are listed in **Online Table 2**. Two reviewers (A.A. and E.A.) independently performed two rounds of screening, the first based on titles and abstracts and the second a full-text review. Any disagreements regarding study eligibility were resolved by discussion with a third author (K.T.). Additionally, two authors (E.S.M. and R.J.) manually screened the reference lists of included studies and relevant review articles to identify further eligible studies.

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Eligibility Criteria

We included randomized controlled trials (RCTs) that evaluated one or more respiratory muscle training, breathing-based interventions, or exercise-based rehabilitation modalities (aerobic exercise, CARE, IMT, HIIT, tai chi, yoga, and diaphragmatic breathing, or combination of them) compared either with each other or with a control group in patients with HF aged ≥18 years. Eligible interventions were required to be delivered at least twice per week for a minimum duration of three consecutive weeks. Given the differences in the effect of various IMT intensities on rehabilitation outcomes (7), we categorized the IMT into four intensities [none (<10% of maximal inspiratory pressure), low (10–15% of maximal inspiratory pressure), medium (30–40% of maximal inspiratory pressure), and high (>60% of maximal inspiratory pressure)] to minimize bias (8). Detailed descriptions of each respiratory muscle training intervention are provided in **Online Table 3**.

Studies were excluded if they were non-randomized, published only as abstracts, case reports, editorials, presentations, or review articles; if they lacked sufficient description of the respiratory muscle training interventions; if they did not report rehabilitation outcomes and the authors did not respond to data requests; or if the full text was unavailable. In cases where multiple publications from the same trial reported on one rehabilitation outcome domain, we included only the report with the most comprehensive outcome data.

Data Extraction

Four independent reviewers (A.A., E.A., E.S.M., and R.J.) extracted data from the eligible studies. Further information regarding the extracted data has been described in *Online Methods*. Any

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discrepancies in the extracted data were resolved after discussions with a third investigator (K.T.), who independently reviewed the data.

Outcomes

The outcomes of interest were various rehabilitation parameters assessed at the end of the intervention period, consisting of maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), six-minute walk test (6MWT), peak oxygen consumption during exercise (VO_2max), quality of life measured with the Minnesota Living with Heart Failure Questionnaire (9), and dyspnea assessed using the Borg or modified Borg scale (10). All outcomes were analyzed using mean difference (MD) with 95% confidence intervals (CIs), except for dyspnea, which was analyzed using standardized mean difference (SMD) with 95% CIs to account for differences between the Borg and modified Borg scales.

Risk of Bias Assessment

Two reviewers (A.A. and K.T.) independently assessed the risk of bias for each included study using the Cochrane Risk of Bias tool for randomized trials, version 2 (RoB 2) (11). Inter-reviewer agreement was evaluated, and any discrepancies were resolved through discussion and consensus.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation, and categorical variables as counts and percentages. Pairwise meta-analyses were first conducted using a random-effects model with the DerSimonian and Laird method to compare MDs or SMDs of respiratory muscle training subgroups from baseline to the end of intervention in each study. This approach enabled

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comparisons between interventions by evaluating differences in their corresponding MDs or SMDs (ΔMD/SMDs).

Subsequently, a random-effects Bayesian network meta-analysis was performed using the Markov Chain Monte Carlo method to estimate posterior distributions. The Markov Chain Monte Carlo model was run for 50,000 iterations, with a burn-in of 20,000, to ensure convergence and generate probability estimates. A network geometry plot was constructed to depict the evidence structure. In this graph, nodes represented different respiratory muscle training interventions, with node size proportional to the number of included studies. Connecting lines indicated direct comparisons between interventions, and line thickness was weighted by the inverse standard error of the random-effects model (12). Moreover, league tables were used to summarize the network meta-analysis results.

Heterogeneity was assessed using Higgins and Thompson's I^2 statistic and within/between-study variance (τ^2), with τ^2 estimated using the Sidik–Jonkman method. Consistency between direct and indirect evidence was examined with node-splitting analysis, where a p-value <0.05 was considered evidence of inconsistency. In addition, sensitivity analyses were conducted for all evaluated outcomes by restricting the analysis to studies that exclusively included patients with HF with reduced ejection fraction. To rank interventions, surface under the cumulative ranking (SUCRA) probabilities were calculated, with higher values indicating better effects on rehabilitation outcomes (13).

All statistical analyses were conducted using the *dmetar*, *meta*, *rjags*, and *gemtc* packages in R version 4.1.3 (The R Foundation, Vienna, Austria). All p-values were two-sided, and statistical significance was defined as $p<0.05$.

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Results

The initial database search identified 4,742 citations, among which 3,157 were reviewed based on the title and abstract. A total of 244 full-text articles were retrieved, and 93 articles representing 88 distinct RCTs were included in the final analysis (**Fig. 1**).

Baseline Characteristics

The studies were conducted across various regions of the world: 38 from Europe (14-54), 15 from North America (55-70), 12 from the Middle East (71-83), 11 from South America (84-94), 6 from East Asia (95-100), 2 from Australia (101, 102), 1 from South Asia (103), and 3 multi-regional trials (104-106). The included studies enrolled 5,757 participants with a mean age of 62.1 ± 8.4 years. Detailed study characteristics are summarized in **Table 1**.

MIP

A total of 24 studies evaluated the impact of respiratory training modalities on MIP (15, 21, 22, 28, 32, 38, 43, 51, 53, 63, 73, 74, 76, 79-81, 85, 88, 89, 91, 92, 94, 98, 100). High-intensity IMT and medium-intensity IMT were the most frequently evaluated interventions across the included studies (**Fig. 2A**). Medium-intensity IMT demonstrated the greatest improvement in MIP, whether performed alone (ΔMD: 31.2 cmH_2O; 95% CI: 21.4– 41.0), in combination with CARE (ΔMD: 30.6 cmH_2O; 95% CI: 15.6– 45.6), or with aerobic exercises (ΔMD: 29.3 cmH_2O; 95% CI: 5.5– 53.0) (**Fig. 3A** and **Online Table 4**). The SUCRA rankings also indicated that medium-intensity IMT alone (89.8%), combined with CARE (83.3%), or with aerobic exercises (83.1%) ranked highest in improving MIP (**Fig. 4A**).

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MEP

A total of nine studies compared the effect of respiratory training exercises on MEP (38, 73, 74, 76, 79, 80, 88, 89, 98). High-intensity IMT was the most frequently evaluated intervention (**Fig. 2B**). CARE showed the greatest improvement in MEP (ΔMD: 34.9 cmH_2O; 95% CI: 11.8– 58.1), followed by the combination of medium-intensity IMT with CARE (ΔMD: 29.0 cmH_2O; 95% CI: 12.9– 45.1), and high-intensity IMT (ΔMD: 26.5 cmH_2O; 95% CI: 13.9– 39.1) (**Fig. 3B** and **Online Table 5**). The SUCRA rankings identified CARE (79.3%), medium-intensity IMT combined with CARE (70.9%), and high-intensity IMT (69.1%) as the top-ranked interventions for improving MEP (**Fig. 4B**).

FVC & FEV_1

A total of nine articles compared the effect of respiratory training interventions on FVC and FEV_1 (**Fig. 2C** and **D**) (21, 32, 53, 73, 76, 80, 89, 93, 98). For FVC, aerobic exercise had the greatest improvement (ΔMD: 10.3%; 95% CI: 2.9– 17.8), followed by high-intensity IMT (ΔMD: 5%; 95% CI: -0.6– 10.7) and CARE (ΔMD: 4.7%; 95% CI: -0.7– 10.0) which showed modest but positive effects. Similarly, for FEV_1, aerobic exercise yielded the largest benefit (ΔMD: 19.0%; 95% CI: 9.0– 29.1), followed by CARE (ΔMD: 15.1%; 95% CI: 7.6– 22.6), and high-intensity IMT (ΔMD: 10.8%; 95% CI: 3.0– 18.7) (**Fig. 3C** and **D** and **Online Tables 6** and **7**). The SUCRA rankings also identified aerobic exercise (94.8% for FVC; 93.8% for FEV_1), high-intensity IMT (66.7% for FVC; 67.2% for FEV_1), and CARE (63.1% for FVC; 83.7% for FEV_1) as the highest-ranked interventions (**Fig. 4C** and **D**).

6MWT

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A total of 45 studies compared the effect of respiratory training interventions on the 6MWT (23, 26, 28, 30, 34-36, 41, 42, 46, 47, 51, 55, 56, 58-62, 67-69, 71, 73-76, 80, 82, 83, 87-90, 93-95, 97, 100, 103-106). Aerobic exercises and CARE were the most frequently investigated interventions (**Fig. 2E**). Medium-intensity IMT demonstrated the greatest improvement in 6MWT distance (ΔMD: 85.1 meters; 95% CI: 38.2– 131.9), followed by breathing technique exercises (ΔMD: 66.0 meters; 95% CI: 45.3– 86.7), and high-intensity IMT (ΔMD: 63.7 meters; 95% CI: 17.6– 109.8) (**Fig. 3E** and **Online Table 8**). The SUCRA rankings identified medium-intensity IMT (81.6%), high-intensity IMT combined with CARE (77.6%), and breathing technique exercises (70.2%) as the top-ranked interventions for improving 6MWT (**Fig. 4E**).

VO_2max

A total of 58 studies evaluated the effect of respiratory training interventions on VO_2max (14, 16-19, 21-25, 28-31, 33, 38-40, 42, 43, 45-54, 56-60, 65-67, 69, 70, 75, 77, 78, 81, 84-87, 90, 92, 93, 99-102, 105). Aerobic exercises and HIIT were the most frequently investigated modalities (**Fig. 2F**). The greatest improvements in VO_2max were observed with high-intensity IMT combined with CARE (ΔMD: 3.7 mL/kg/min; 95% CI: 1.8– 5.6), medium-intensity IMT combined with aerobic exercises (ΔMD: 3.7 mL/kg/min; 95% CI: 0.6– 6.7) and HIIT (ΔMD: 3.4 mL/kg/min; 95% CI: 2.7– 4.2) (**Fig. 3F** and **Online Table 9**). The SUCRA rankings identified the combination of aerobic exercises with high-intensity IMT (74.7%) or medium-intensity IMT (70.8%) and HIIT (70.6%) as top three interventions for improving VO_2max (**Fig. 4F**).

Quality of Life

A total of 40 studies compared the effect of respiratory training interventions on quality of life (18-20, 22, 26-30, 34, 35, 37, 39, 42, 51, 53, 58, 59, 62, 64, 67, 71, 75, 76, 78, 83, 85, 87-89, 91-93,

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97, 100, 102, 103, 105). Aerobic exercises, breathing technique exercises, and CARE were the most frequently investigated interventions (**Fig. 2G**). The combination of high-intensity IMT with CARE (ΔMD: -17.9; 95% CI: -27.9– -7.9), medium-intensity IMT (ΔMD: -16.9; 95% CI: -25.4– -8.4) and high-intensity IMT (ΔMD: -16.6; 95% CI: -22.8– -10.4) presented the most influence on improving quality of life (**Fig. 3G** and **Online Table 10**). Moreover, the SUCRA rankings identified high-intensity IMT, either in combination with aerobic exercises (81.4%), CARE (80.9%), or stand-alone (77.8%), as the top-ranked interventions for improving quality of life (**Fig. 4G**).

Dyspnea

A total of 12 studies compared the effect of respiratory training interventions on dyspnea (**Fig. 2H**). Significant improvement was observed only with high-intensity IMT combined with aerobic exercises (ΔSMD: -1.7; 95% CI: -2.9– -0.4) (**Fig. 3H** and **Online Table 11**). Consistently, the SUCRA rankings identified this combination (89.3%) as the most effective intervention for reducing dyspnea (**Fig. 4H**).

Data regarding sensitivity analysis and risk of bias assessment has been provided in *Online Methods.*

Discussion

By combining data from 88 RCTs, our analysis demonstrates that respiratory muscle training interventions exert differential effects across key rehabilitation outcomes in patients with HF. Medium-intensity IMT, either alone or combined with aerobic training or CARE, was most effective in improving MIP. For MEP, the most beneficial interventions were CARE, medium-intensity IMT with CARE, and high-intensity IMT. Pulmonary function parameters (FVC and

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FEV_1) improved most notably with aerobic exercise, high-intensity IMT, and CARE. Regarding cardiorespiratory fitness, medium-intensity IMT, the combination of high-intensity IMT with CARE, as well as breathing technique exercises, were superior for enhancing 6MWT performance. In contrast, the combination of aerobic exercises with medium or high-intensity IMT and HIIT were the optimal interventions for improving VO_2max. Quality of life showed the greatest improvements with high-intensity IMT, whether performed alone or in combination with aerobic training or CARE. Finally, the combination of high-intensity IMT and aerobic training yielded the greatest reductions in dyspnea (**Graphical Abstract**).

Previous studies have demonstrated that exercise-based cardiac rehabilitations improve exercise capacity, cardiorespiratory fitness, and quality of life, while also reducing hospitalizations in patients with HF (107-110). More broadly, rehabilitation-based interventions have been associated with improved clinical outcomes and reduced reliance on long-term care services (111). Accordingly, current guidelines recommend exercise-based cardiac rehabilitation for eligible patients with HF (112). Nevertheless, there are no standard recommendations regarding the optimal type of intervention. Different exercise modalities may exert their benefits through distinct biological mechanisms, including reversal of autonomic nerve remodeling, reduction in arterial stiffness and myocardial oxygen demand, improvement in endothelial function, and attenuation of adrenergic receptor sensitivity and expression. Exercise interventions may also mitigate chronic systemic inflammation while promoting anti-inflammatory responses (113, 114). Therefore, identifying the most effective rehabilitation strategies in each cardiac rehabilitation domain is essential to optimize outcomes in patients with HF.

In our meta-analysis, medium-intensity IMT, either alone or combined with aerobic training or CARE, was the most effective intervention for improving MIP, whereas CARE produced the

greatest improvements in MEP. These findings are consistent with previous studies reporting significant improvements in MIP while using IMT, whether applied as a standalone intervention or in combination with aerobic exercise or CARE (7, 51, 88). IMT addresses the respiratory muscle weakness by increasing inspiratory muscle endurance (73, 115). By providing progressive resistance loading, IMT reduces oxygen requirements during exercise, thereby facilitating improved oxygen delivery to peripheral muscles, which in turn enhances exercise tolerance, walking distance, and dyspnea (71). In contrast, our results indicate that CARE is more effective than IMT for improving MEP. This aligns with previous evidence suggesting that IMT exerts minimal influence on MEP, likely because IMT specifically targets the inspiratory rather than the expiratory muscles (7).

This study also revealed the aerobic exercises CARE and high intensity IMT were the most proficient interventions for improving FVC and FEV_1. Notably, reduced FEV_1 and FVC are independently associated with ventricular dysfunction beside higher mortality and cardiovascular events (116, 117). Interestingly, we found that the combination of IMT with CARE did not yield meaningful improvements in FVC or FEV_1. This is in line with the findings of previous studies demonstrating that the combination of IMT and CARE was not effective as using them alone in improving spirometry outcomes (32). One possible explanation is that the added respiratory load imposed by combined interventions increases respiratory muscle fatigue, thereby diminishing their overall efficiency.

In our study, medium-intensity IMT, the combination of high-intensity IMT with CARE, as well as breathing technique exercises were superior interventions for improving 6MWT. Additionally, the combination of aerobic exercises with medium or high-intensity IMT and HIIT demonstrated superiority for improving VO_2max. Previous studies have reported conflicting findings regarding

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the optimal intervention for improving 6MWT and VO_2max in patients with HF. A network meta-analysis of 31 RCTs identified high-intensity IMT as the most effective modality for both outcomes (8). However, they did not include more recently published trials and did not assess the effects of combining respiratory muscle training interventions. In contrast, a more recent network meta-analysis reported interval training and CARE as the most effective interventions for improving 6MWT and VO_2max, respectively (118). However, they did not stratify IMT by training intensity, which may have limited the specificity of their conclusions.

The clinical relevance of the observed improvements in exercise capacity should also be considered. For the 6MWT, proposed thresholds for a clinically meaningful improvement in patients with HF was approximately 30 m (119), although lower estimates have been reported in specific populations using patient-anchored methods (120). In our analysis, the largest improvements observed with medium-intensity IMT (85.1 m), breathing technique exercises (66.0 m), and high-intensity IMT (63.7 m) exceeded these commonly proposed thresholds, suggesting that these effects may be clinically meaningful. For peak VO_2, a universally validated minimal clinically important difference has not been established in HF. Nevertheless, an increase of approximately 1 mL/kg/min or 6% has been commonly used as a reference threshold based on the test–retest variability of cardiopulmonary exercise testing (119). The largest improvements observed in our analysis, reaching 3.7 mL/kg/min, exceeded this benchmark. However, these comparisons should be interpreted cautiously because the clinical significance of changes in 6MWT and peak VO_2 may vary according to baseline functional capacity, HF phenotype, patient characteristics, and the method used to derive clinically meaningful thresholds.

Cardiorespiratory fitness, which is typically assessed using the 6MWT and VO_2max, is a strong predictor of nonfatal cardiovascular events, rehospitalizations, and mortality, particularly in

patients with HF (121, 122). Moreover, these indices reflect not only peripheral muscle mass and muscle reflex regulation, but also integrated cardiovascular and respiratory responses, thereby serving as robust markers of patients' functional capacity and ability to perform daily activities (118). While VO_2max provides a more rigorous assessment of cardiorespiratory function, its measurement requires specialized hospital-based facilities. By contrast, the 6MWT is simple, inexpensive, and feasible in non-hospital settings, although its self-paced nature may underestimate true functional capacity (123). Consistent with previous findings, our study demonstrated that combining IMT with CARE yielded the greatest improvements in VO_2max (124). However, emerging evidence suggests that the optimal intervention may differ across HF phenotypes (125, 126), underscoring the need for further research to tailor rehabilitation strategies accordingly.

Our study also indicated that the combination of high-intensity IMT with CARE or aerobic exercises was the best approach for improving quality of life and alleviating dyspnea, highlighting their potential to address both the physical and symptomatic dimensions of HF. Likewise, previous studies have shown that combining IMT with either CARE or aerobic training yields greater improvements in quality of life and dyspnea compared with single-modality interventions (51, 118). Given that symptoms in patients with HF arise mainly from impairments in both peripheral and inspiratory muscle function (127), comprehensive rehabilitation programs that target multiple muscle groups may exert synergistic effects in reducing symptoms and enhancing quality of life.

Different studies have sought to identify the most effective rehabilitation interventions for patients with HF (7, 127, 128). However, there is no "one-size-fits-all" approach, as our findings underscore the differential benefits of various exercise modalities. Importantly, higher-intensity training does not necessarily translate into greater clinical gains. Clinicians must account for

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differences in HF pathophysiology, comorbidities, concomitant medications, and prior exercise experience when prescribing rehabilitation programs. Given that HF predominantly affects older adults, many of whom have reduced physical function and limited exercise capacity (118), using high-intensity exercise may compromise adherence, with patients often exercising below target thresholds and deriving limited benefit. Accordingly, exercise intensity and duration should be tailored to patient-specific conditions to optimize participation and adherence. Additional considerations include patient preferences, behavioral characteristics, and access to equipment and facilities.

Limitations

Our study has some limitations. First, variations in the frequency and duration of interventions across the included trials may have influenced the ranking outcomes. Although prior evidence suggests that intervention duration does not substantially affect results, this remains a potential concern (128). Second, we observed significant heterogeneity across studies, reflecting differences in patient demographics, HF pathophysiology, New York Heart Association classes, and comorbidities. Because this meta-analysis relied on study-level rather than patient-level data, we were unable to adjust for these potential confounders. Nonetheless, the inclusion of RCTs from diverse geographic regions enhances the generalizability of our findings. Third, although SUCRA provides a useful summary of the relative probability that an intervention is among the most effective treatments, a high SUCRA value does not necessarily indicate robust or high-certainty evidence. Some interventions in the network were represented by a limited number of studies and relatively small sample sizes, resulting in less precise effect estimates and greater uncertainty in

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their rankings. Therefore, the ranking results should be interpreted alongside the magnitude and precision of the estimated treatment effects, rather than as definitive evidence of the superiority of a particular intervention. Finally, although a broad range of interventions was examined, direct head-to-head comparisons between certain modalities were limited. Thus, despite performing node-splitting analyses to test the robustness of our results, these outcomes should be interpreted with caution.

Conclusion

Our findings support an outcome-oriented approach to rehabilitation in HF, with the selection of respiratory muscle training modalities guided by the predominant functional or symptomatic limitation. In patients with predominant inspiratory muscle weakness, medium-intensity IMT, either alone or combined with aerobic training or CARE may be particularly beneficial for improving MIP, whereas CARE may be preferable when impaired expiratory muscle strength is the primary limitation. Aerobic exercise may be prioritized in patients with impaired pulmonary function, while moderate/high-intensity IMT and breathing technique exercises may be considered for patients with reduced walking capacity. For patients with markedly impaired cardiorespiratory fitness, the combination of aerobic exercises with medium/high-intensity IMT and HIIT yielded the greatest improvements in VO_2max. In patients with impaired quality of life, high-intensity IMT, either alone or in combination with aerobic training or CARE may be beneficial, whereas dyspnea was most effectively alleviated by combining high-intensity IMT with aerobic training. Nevertheless, these findings should not be interpreted as evidence of treatment-effect modification by individual patient characteristics, because our analyses were conducted at the study level and

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did not directly evaluate interactions between intervention effects and age, sex, comorbidities, baseline functional capacity, or other patient-level characteristics.

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Declaration of Interest

None

Disclosure of AI Programs

We utilized AI tools, specifically ChatGPT 5, to aid in rephrasing portions of this article. The purpose was to improve clarity and readability only. Nevertheless, every piece of AI-generated content was carefully reviewed and verified by the authors to ensure accuracy and integrity.

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Authors' Contributions: All authors have made substantial contributions to the conception and design of the study, or acquisition of data, or drafting the article or revising it critically for important intellectual content beside final approval of the version to be submitted.

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Figure Legends

Graphical Abstract The effect of different respiratory muscle training modalities on rehabilitation outcomes in heart failure patients. The rankings were conducted using surface under the cumulative ranking (SUCRA) probabilities.

6MWT, six-minute walk test; CARE, combined aerobic and resistance exercise; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; HIIT, high-intensity interval training; IMT, inspiratory muscle training; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure; VO_2max, peak oxygen consumption during exercise.

Figure 1 PRISMA flow chart.

Figure 2 Network geometry graph for (A) maximum inspiratory pressure, (B) maximum expiratory pressure, (C) forced vital capacity, (D) forced expiratory volume in one second, (E) six-minute walk test, (F) peak oxygen consumption during exercise, (G) quality of life, and (H) dyspnea. The node size represents the number of studies, and the connecting line between nodes indicates direct comparison between predictors.

CARE, combined aerobic and resistance exercise; HIIT, high-intensity interval training; IMT, inspiratory muscle training.

Figure 3 Ranking plot representing ΔMD/SMD of respiratory muscle training interventions compared to no intervention in (A) maximum inspiratory pressure, (B) maximum expiratory pressure, (C) forced vital capacity, (D) forced expiratory volume in one second, (E) six-minute walk test, (F) peak oxygen consumption during exercise, (G) quality of life, and (H) dyspnea. CARE, combined aerobic and resistance exercise; HIIT, high-intensity interval training; IMT,

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inspiratory muscle training; MD, mean difference; RTI, respiratory muscle training intervention; SMD, standardized mean difference.

Figure 4 Surface under the cumulative ranking curve (SUCRA) for ranking respiratory muscle training interventions compared to no intervention in (A) maximum inspiratory pressure, (B) maximum expiratory pressure, (C) forced vital capacity, (D) forced expiratory volume in one second, (E) six-minute walk test, (F) peak oxygen consumption during exercise, (G) quality of life, and (H) dyspnea.

CARE, combined aerobic and resistance exercise; HIIT, high-intensity interval training; HIMT, high-intensity inspiratory muscle training; HIMTA, high-intensity inspiratory muscle training with aerobic exercises; HIMTC, high-intensity inspiratory muscle training with CARE; LIMT, low-intensity inspiratory muscle training; LIMTA, low-intensity inspiratory muscle training with aerobic exercises; LIMTC, high-intensity inspiratory muscle training with CARE; MIMT, medium-intensity inspiratory muscle training; MIMTA, medium-intensity inspiratory muscle training with aerobic exercises; MIMTC, medium-intensity inspiratory muscle training with CARE; NIMT, no-intensity inspiratory muscle training.

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Appendices

Online Figure 1 Ranking plot representing ΔMD/SMD of respiratory muscle training interventions compared to no intervention in patients with heart failure with reduced ejection fraction.

CARE, combined aerobic and resistance exercise; HIIT, high-intensity interval training; IMT, inspiratory muscle training; MD, mean difference; RTI, respiratory muscle training intervention; SMD, standardized mean difference.

Online Figure 2 Traffic light plot evaluating risk of bias of the included studies.

Online Figure 3 Summary plot evaluating risk of bias of the included studies.

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Study	Country	Total population (n)	Follow-up duration (years)	Number of sessions per weeks	Age	Male gender (%)	HFrEF (%)	DM (%)	HTN (%)	LVEF (%)	Intervention type
Adamopoulos 2014	Greece-Switzerland-Belgium	43	12 weeks	3	58±12	83.7	100	N/A	N/A	29.5±5	Supervised
Andryukhin 2010	Russia	75	24 weeks	4	67±5.2	30.6	0	N/A	N/A	N/A	Unsupervised
Angadi 2014	USA	15	4 weeks	3	70±8.3	80	0	26.6		±	Supervised
Antunes-Correa 2019	Brazil	33	16 weeks	5	56.3±2.8	48.5	100	21.2	72.7	27.4±3.1	Supervised
Arutyunov 2021	Russia	49	24 weeks	5	66.3±7.1	46.7	N/A	N/A	N/A	N/A	Supervised
Austin 2005	Wales	179	24 weeks	3	71.8±6.5	43	100	18.5	15.5	N/A	Unsupervised
Baldassarri 2018	Germany	62	12 weeks	3	65±7	44	0	N/A	N/A	67±7	Supervised
Barrow 2007	England	52	16 weeks	2	69.1±	80.7	N/A	N/A	N/A	N/A	Unsupervised
Beckers 2008	Belgium	58	24 weeks	3	58.5±10.9	72.4	100	N/A	N/A	24.4±8.1	Supervised
Belardinelli 1999	Italy	94	56 weeks	3	59±14	88.9	100	5	8	28.1±5.51	Supervised
Besnier 2019	France	31	4 weeks	5	59.2±12.3	70.9	100	13	39	36±7.4	Supervised
Bosnak-Guclu 2011	Turkey	30	6 weeks	7	67.7±9.3	80	100	N/A	N/A	34.7±7.4	Supervised
Caminiti 2010	Italy	60	12 weeks	4	73.8±6	85	100	46.6	70	33±9	Supervised

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Chen 2016	Taiwan	21	10 weeks	5	65.52±12.61	38.1	N/A	N/A	N/A	60.8±13.1	Supervised
Chrysohoou 2015	Greece	72	12 weeks	7	59.2±10.6	80	100	34.6	32.8	31.5±N/A	Supervised
DallAgo 2006	Brazil	32	12 weeks	7	56±3.2	68.7	100	N/A	N/A	38.5±3	Unsupervised
Dimopoulos 2006	Greece	24	12 weeks	3	60.5±9.4	95.8	N/A	4.1	N/A	32.1±10.6	Supervised
Dracup 2007	USA	173	24 weeks	3	54±12.5	71.7	100	25.6	45.3	26.4±6.8	Unsupervised
Edelmann 2025	Germany	322	48 weeks	3	69.6±7.2	40.4	0	21.1	83.5	61.2±5.4	Supervised
Ellingsen 2017	Belgium, Denmark, Germany, Luxembourg, Norway, Italy,	215	12 weeks	3	60±12.5	81.4	100	23.7	38.1	29±7.4	Supervised
Farghaly 2022	Egypt	40	12 weeks	3	55.7±7.7	N/A	100	N/A	N/A	33.2±4.5	Supervised
Feuerstein 2023	Germany	64	12 weeks	3	56±12	96.8	100	37.5	56.2	N/A	Supervised
Forestieri 2016	Brazil	18	3 weeks	3	46.6±10.6	82.3	100	N/A	N/A	34.5±3	Supervised
Freyssin 2012	France	26	8 weeks	5	55±11	50	100	31	N/A	29.3±5.2	Supervised
Fu 2013	Taiwan	45	12 weeks	3	67.2±2	64.4	N/A	N/A	N/A	38.3±3.8	Supervised
Gary 2004	USA	32	12 weeks	3	68±11	0	0	31.25	88	55.5±8	Unsupervised
Gottlieb 1999	USA	25	24 weeks	3	65.5±8.5	88	100	N/A	N/A	23.5±9	Supervised

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Hambrecht 1995	Germany	22	24 weeks	6	51±10	100	100	N/A	N/A	26.5±9.5	Unsupervised
Hambrecht 2000	Germany	64	24 weeks	6	54±8	100	100	N/A	N/A	27±9	Unsupervised
Haykowsky 2012	USA	40	16 weeks	3	70±6	87.5	0	15	77.5	N/A	Supervised
Iellamo 2013	Italy	36	12 weeks	3	67.8±7	86.1	100	N/A	52.7	34.8±6.5	Supervised
Jaarsma 2021	Germany, Netherlands and USA	605	48 weeks		67±12	29	47	27	44	N/A	Unsupervised
Johnsdottir 2006	Iceland	43	20 weeks	2	68±5.9	79	N/A	N/A	2.3	41±13.6	Supervised
Johnson 1998	UK	16	8 weeks	14	66.5±5.6	84.6	100	N/A	N/A	N/A	Unsupervised
Jones 2014	USA	90	12 weeks	3	66±11	74	100	38	58	26±8	Unsupervised
Katayifci 2022	Turkey	32	8 weeks	7	63.06±1.98	78.1	100	18.7	28.1	27.5±5.9	Unsupervised
Kawauchi 2017	Brazil	35	8 weeks	7	55.26±8.24	54.3	100	37.14	68.57	29±5.94	Unsupervised
Keteyian 1996	USA	29	24 weeks	3	56±11	100	100	N/A	N/A	21±7	Supervised
Kitzman 2010	USA	53	16 weeks	3	70±6	24.5	0	16.9	67.9	60±7	Supervised
Kitzman 2013	USA	63	16 weeks	3	70±7	23.8	0	23.6	89.1	57±5	Supervised
Kitzman 2016	USA	92	20 weeks	3	67±5	19	0	35	95	61±6	Supervised
Kitzman 2021	USA	304	12 weeks	3	72.2±8.1	52.4	47	52.1	92	N/A	Unsupervised

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Klecha 2007	Poland	50	24 weeks	3	60.1±9.2	76	100	N/A	74	28±5.4	Supervised
Koufaki 2014	UK	33	24 weeks	2	59.1±8.6	81.8	100	N/A	N/A	38.4±6.6	Supervised
Koukouvou 2004	Greece	26	24 weeks	3	52.5±9.6	100	100	N/A	N/A	N/A	Supervised
Krishna 2014	India	92	12 weeks	3	49.8±5.1	69.5	N/A	N/A	N/A	N/A	Supervised
Kulchu 2007	Turkey	44	8 weeks	3	59.3±10.7	72.7	N/A	N/A	N/A	N/A	Supervised
Laoutaris 2004	Greece	35	10 weeks	3	58.6±2.7	88.5	100	N/A	N/A	24.4±1.3	Supervised
Laoutaris 2007	Greece	38	10 weeks	3	58.6±2.7	88.5	100	N/A	N/A	24.4±1.3	Supervised
Laoutaris 2013	Greece	27	12 weeks	3	59±9	81.5	100	N/A	N/A	29±7	Supervised
Laoutaris 2020	Greece & Poland	74	12 weeks	3	66.1±2.67	93.2	100	N/A	N/A	28.3±2.8	Supervised
Lugo 2018	Colombia	37	24 weeks	2	55.5±12.3	53.1	100	N/A	N/A	32.5±12.5	Supervised
Mahmoodi 2025	Iran	76	8 weeks	3	68.2±4.8	80.3	100	26.3	59.1	30.4±4.9	Supervised
Martin 2017	Spain	47	16 weeks	3	N/A	12.7	0	N/A	N/A	N/A	Supervised
McKelvie 2002	Canada	181	48 weeks	2	64.8±1.1	89.5	100	25.5	39	27.9±0.8	Unsupervised
Mezzani 2012	Italy	30	12 weeks	3	64±7	100	100	N/A	N/A	29±6	Supervised
Moreno 2017	Brazil	26	8 weeks	6	61±14	61.5	100	N/A	N/A	36±8	Unsupervised

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Mueller 2020	Belgium, Germany and Norway	154	48 weeks	3	70±8	33.1	0	25.8	84.2	N/A	Unsupervised
Nechwatal 2002	Germany	50	3 weeks	6	46.5±7	94	100	N/A	N/A	27.5±4	Supervised
Nilsson 2008	Norway	80	16 weeks	2	70.1±7.9	78.7	N/A	N/A	12.5	31±8	Unsupervised
Nolte 2014	Germany	64	12 weeks	3	65±7	44	0	N/A	N/A	67±7	Supervised
Padula 2009	USA	32	12 weeks	6	74.7±15.7	37.5	100	N/A	N/A	N/A	Unsupervised
Palau 2013	Spain	26	12 weeks	14	71±11.8	50	0	57	96	72.5±10.4	Unsupervised
Palau 2018	Spain	28	24 weeks	2	74±9	39.2	0	35.7	96.4	67±10	Unsupervised
Papathanasiou 2020	Bulgaria	120	12 weeks	2	63.73±6.6	58.3	100	0	25.8	35.9±2.15	Supervised
Parati 2008	israel	24	10 weeks	2	64±9	0.75	100	N/A	N/A	32.8±5.4	Unsupervised
Passino 2006	Italy	85	36 weeks	3	60±1	87	100	N/A	N/A	33.8±1.9	Supervised
Peng 2018	China	98	8 weeks	4	66.3±10.5	59.2	N/A	N/A	N/A	34.05±6.65	Unsupervised
Piotrowska 2021	Poland	90	8 weeks	3	62.77±8.05	60	N/A	N/A	54.44	54±N/A	Unsupervised
Pullen 2008	USA	19	8 weeks	2	51.3±9.4	47.4	100	15.8	89.4	25.2±10.7	Supervised
Pullen 2010	USA	40	8 weeks	2	54.1±9.1	57.5	100	26.8	92.6	29.1±12	Supervised
Rahmati 2025	Iran	24	4 weeks	3	64±3.7	83.3	100	N/A	N/A	31.5±7	Supervised

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Roditis 2007	Greece	21	12 weeks	3	60±8	89.6	100	N/A	N/A	32.1±10.6	Supervised
Sadek 2021	Lebanon	60	12 weeks	3	53.5±10.8	100	50	N/A	N/A	37.3±6.5	Supervised
Sadek 2022	Lebanon	30	12 weeks	3	52.2±12.9	50	100	N/A	N/A	N/A	Supervised
Sadek 2024	Lebanon	30	12 weeks	3	52.2±12.9	50	100	N/A	N/A	N/A	Supervised
Selig 2004	Australia	39	12 weeks	3	64.5±11	84.6	100	N/A	N/A	27.5±6.5	Supervised
Seo 2016	USA	35	20 weeks	5	66±12.7	71.4	N/A	N/A	N/A	37.3±18.1	Unsupervised
Silveira 2020	Brazil	19	12 weeks	3	60±9	36.8	0	57.8	100	65±5	Supervised
Smart 2012	Australia	25	16 weeks	3	64±8	50	0	N/A	N/A	57±10	Supervised
Tang 2018	Taiwan	90	12 weeks	7	51.7±13.1	80	22.2	26.6	N/A	N/A	Unsupervised
Tanriverdi 2023	Turkey	34	8 weeks	3	63.1±7.8	76.4	100	35.2	79.4	30.4±6	Unsupervised
Trevizan 2021	Brazil	42	16 weeks	5	56±3	54.7	100	21.4	71.4	27.3±2	Unsupervised
Turri-Silva 2021	Brazil	22	12 weeks	3	56±10	72.7	36.4	36.4	54.5	46.7±15.3	Supervised
Ulbrich 2016	Brazil	23	12 weeks	3	54±7.5	100	100	9.1	63.6	33.9±7.7	Supervised
Wang 2025	China	80	12 weeks	N/A	57±2.4	52.5	N/A	N/A	N/A	42.8±4.5	Unsupervised
Weiner 1999	Isreal	20	12 weeks	6	68±6.2	90	100	N/A	N/A	23.8±2.1	Supervised

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Winkelmann 2009	Brazil	24	12 weeks	3	56.5±10.6	45.8	100	N/A	N/A	36.5±11.5	Supervised
Wisloff 2007	Norway	27	12 weeks	3	75.5±11.1	72.2	100	N/A	N/A	29±5.5	Supervised
Wu 2025	Taiwan	36	12 weeks	6	66.7±1.9	67	36.1	38.9	33.3	44±2	Unsupervised
Yeh 2008	Israel and USA	30	12 weeks	2	64±13	63.3	100	26.7	66.6	23±7	Supervised
Yeh 2011	Israel and USA	100	12 weeks	2	67±11	64	100	35	70	29±8	Supervised
Yeh 2013	Israel	16	12 weeks	2	66±12	50	0	18.7	75	63±8	Supervised

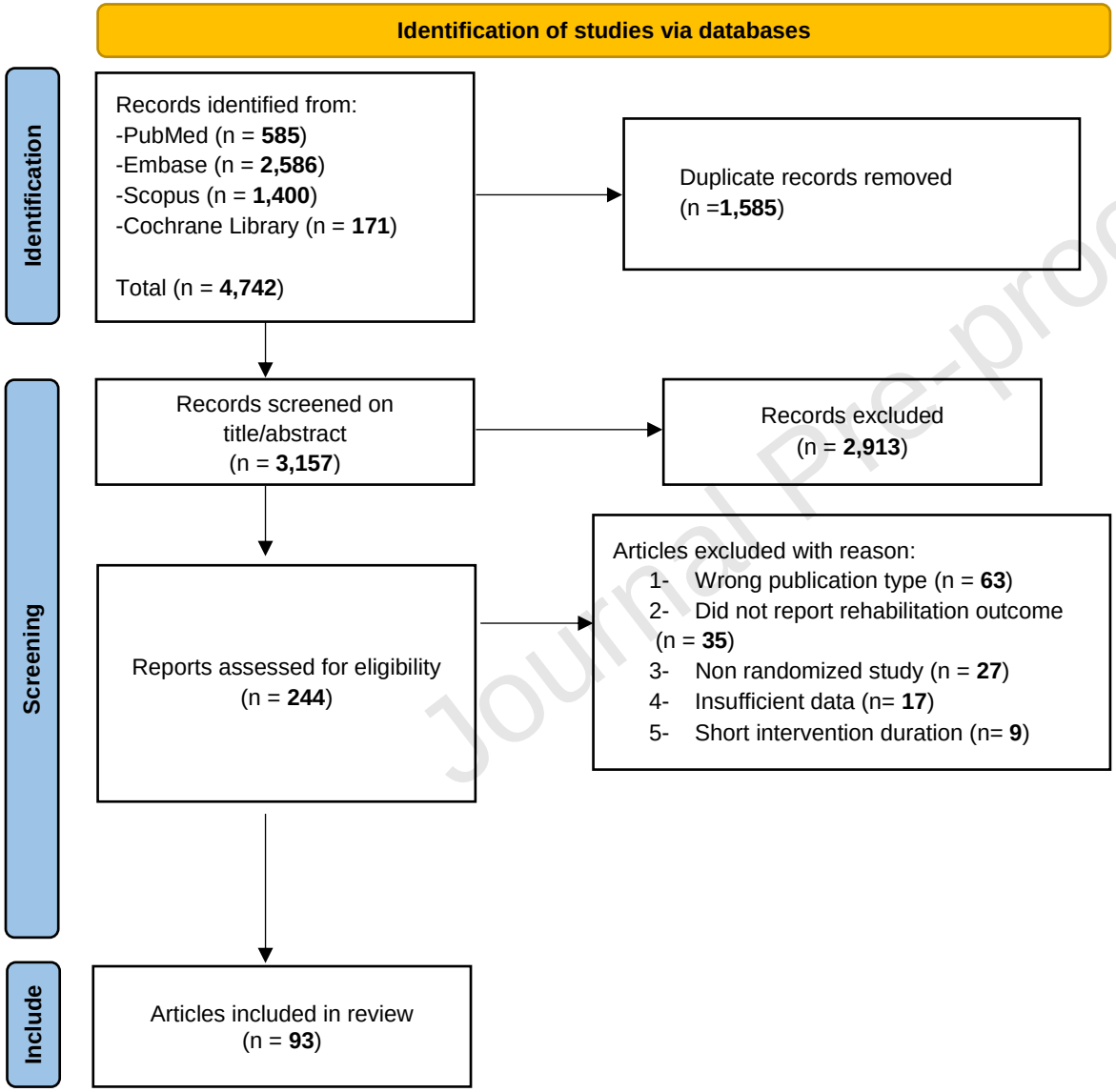
Data are presented as mean ± standard deviation for continuous variables, and as counts and percentages for categorical variables.

Table 1 Study characteristics.

DM, diabetes mellitus; HFrEF, heart failure with reduced ejection fraction; HTN, hypertension; LVEF, left ventricular ejection fraction.

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Figure 1



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Figure 2.

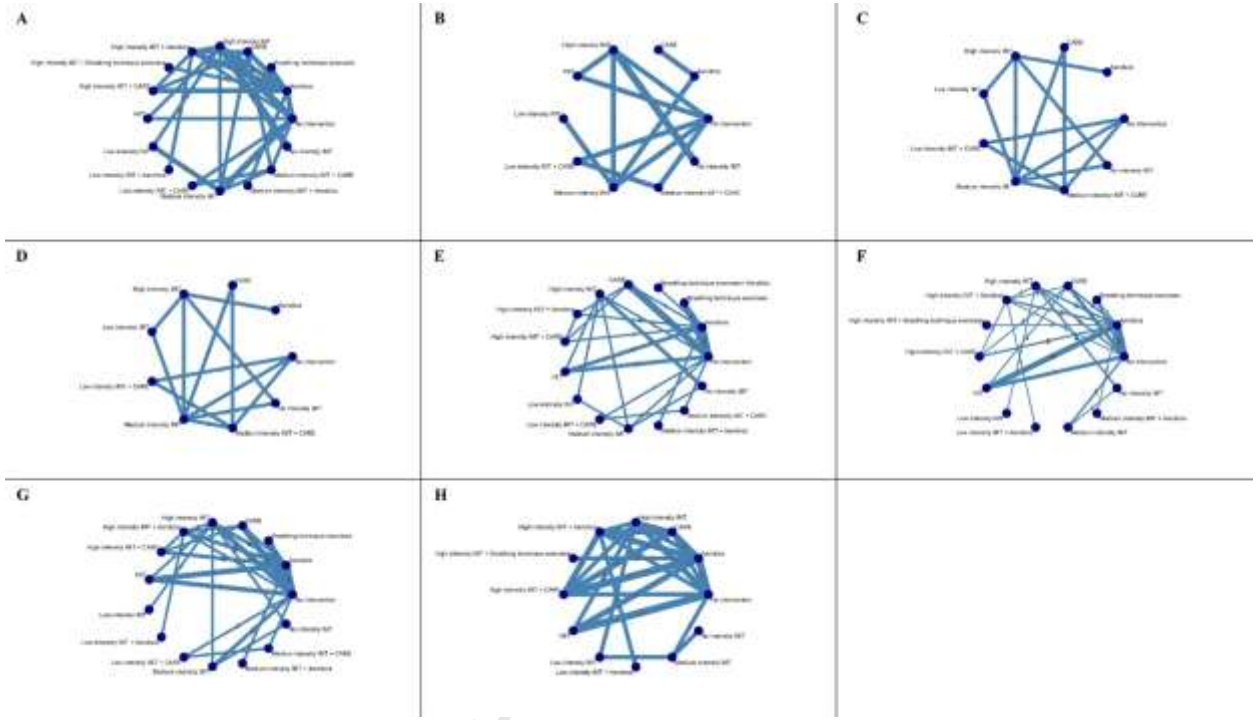


Figure 3.

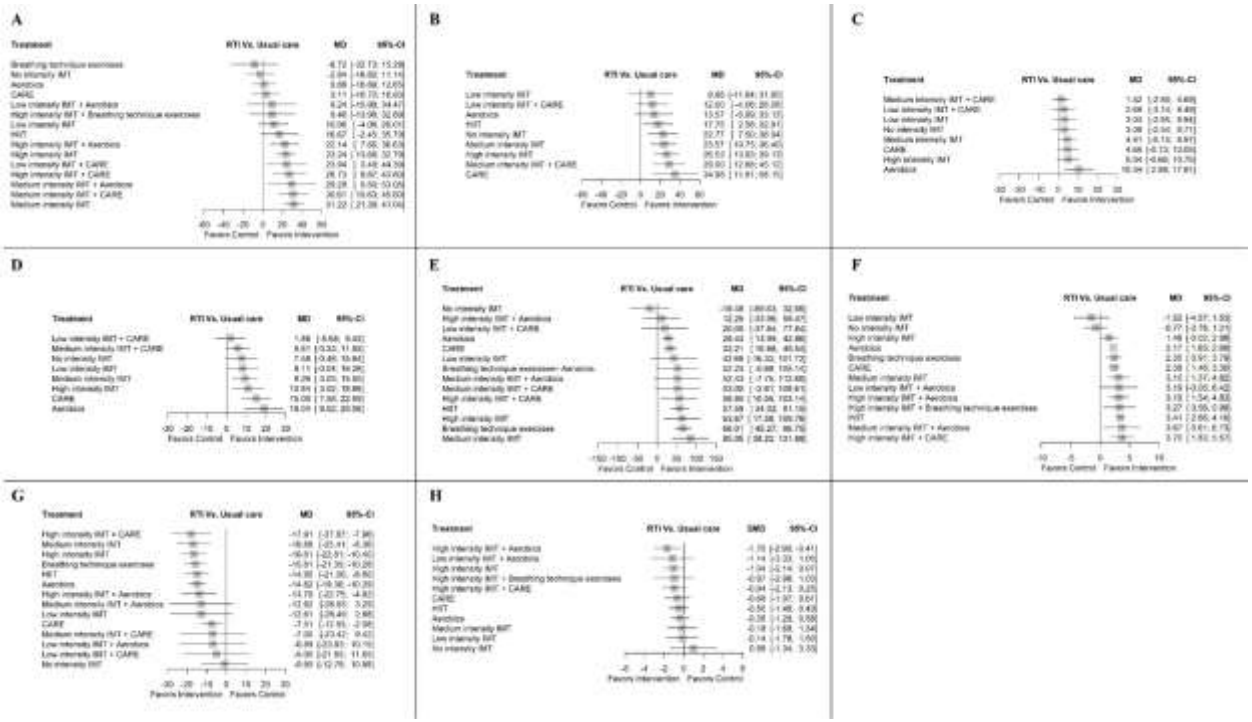
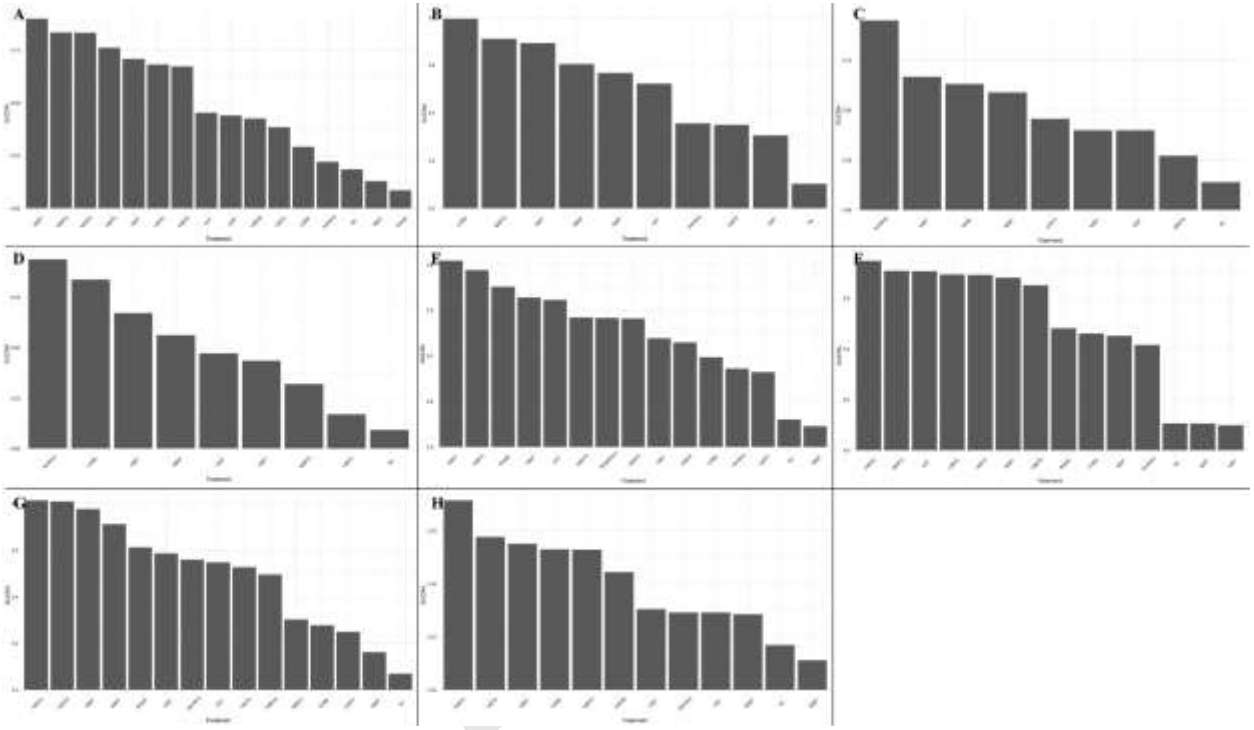
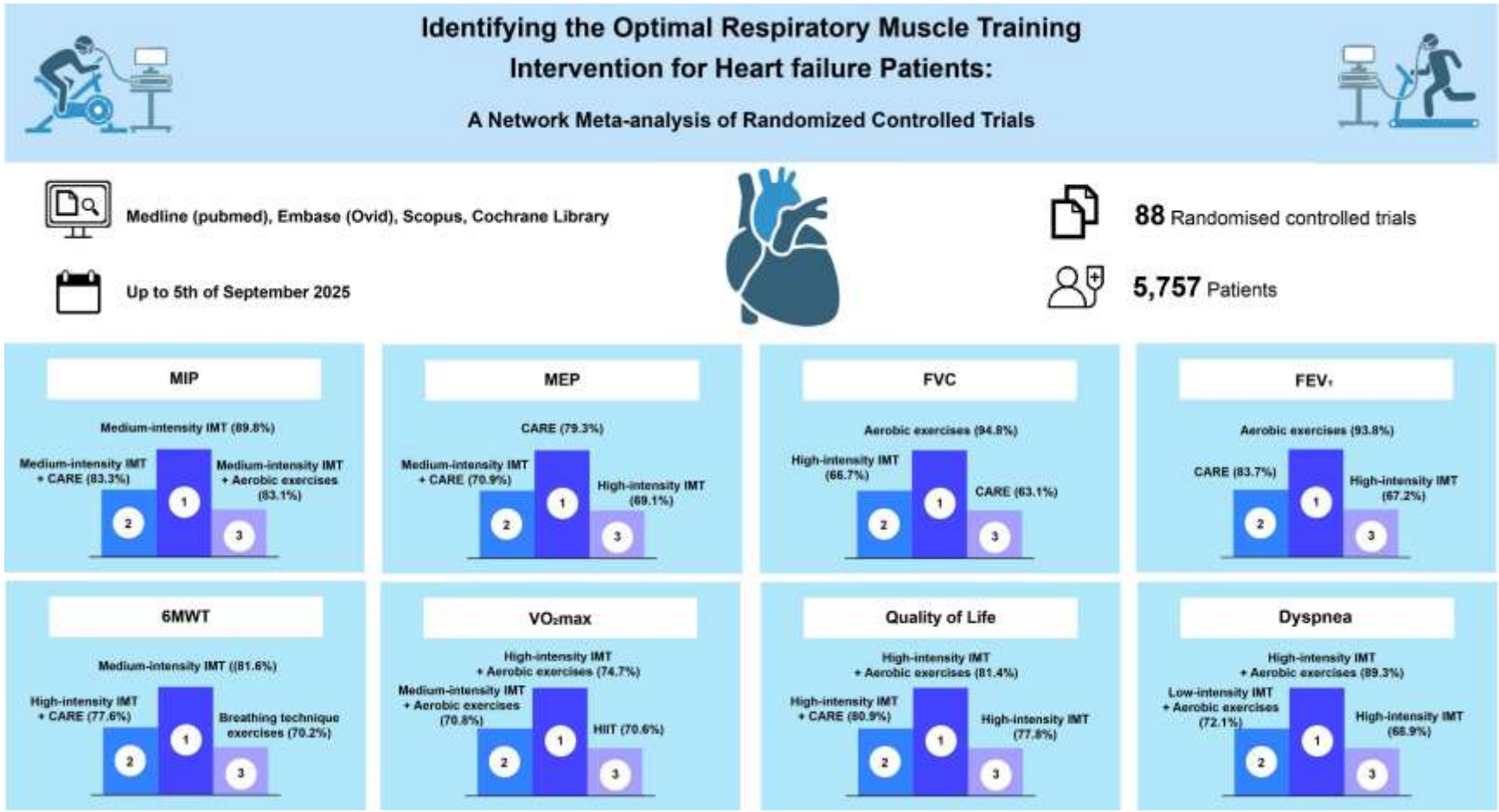


Figure 4.



Graphical abstract



Highlights

- We comprehensively evaluate respiratory muscle training strategies in HF.
- Medium-intensity inspiratory muscle training ranked highest for MIP improvement.
- Combined aerobic + resistance training had highest effect for MEP.
- Aerobic exercise gave largest gains in FVC, FEV1, and IMT improved 6MWD most.
- High-intensity IMT + aerobic best improved VO2 peak, QoL, and dyspnea.

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