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Review Article

Utilization of Neuromuscular Electrical Stimulation as a Rehabilitation Strategy in Heart Failure with Reduced Ejection Fraction: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Heart Failure with Reduced Ejection Fraction (HFrEF) is associated with substantial functional impairment, and many patients are unable to participate in conventional exercise-based cardiac rehabilitation. Neuromuscular Electrical Stimulation (NMES) has been proposed as an alternative rehabilitation treatment, but its clinical effectiveness remains uncertain. This review aims to evaluate the effectiveness of NMES in improving cardiac function and exercise capacity in patients with HFrEF. A systematic review and meta-analysis of Randomized Controlled Trials (RCTs) was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies comparing NMES with standard medical therapy, exercise training, or no intervention in adult patients with HFrEF were identified through major electronic databases. Risk of bias was assessed using the Cochrane RoB 2.0 tool. Pooled effects were calculated as Mean Differences (MD) with 95% Confidence Intervals (CIs) using Review Manager (RevMan) version 5.4. Twelve RCTs involving 636 participants were included. NMES significantly improved peak oxygen uptake (VO_2 peak) (MD 2.03 mL/kg/min; 95% CI 1.21 to 2.84; $p < 0.00001$), systolic blood pressure (MD −2.02; 95% CI −3.97 to −0.06; $p = 0.04$), Left Ventricular Ejection Fraction (LVEF) (MD −1.38%; 95% CI −2.73 to −0.03; $p = 0.05$), and Heart Rate (HR) (MD 2.19 beats/min; 95% CI 0.44 to 3.95; $p = 0.01$). A borderline significant improvement was observed in the Six-Minute Walk Test (6MWT) distance (MD −11.40 m; 95% CI −23.04 to 0.24; $p = 0.05$). No significant effects were found for diastolic blood pressure (MD −0.12; 95% CI −3.30 to 3.06; $p = 0.94$) or Minnesota Living with Heart Failure Questionnaire (MLHFQ) scores (MD 1.97; 95% CI −9.06 to 13.01; $p = 0.73$). NMES is associated with meaningful improvements in exercise capacity and selected parameters of cardiac function in patients with HFrEF, supporting its role as a potential adjunct rehabilitation treatment.

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Keywords: Neuromuscular Electrical Stimulation, Heart Failure, Reduced Ejection Fraction, Cardiac Rehabilitation.

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Introduction

Heart Failure with Reduced Ejection Fraction (HFrEF) is a chronic clinical syndrome characterized by impaired left ventricular systolic function, resulting in insufficient cardiac output and markedly reduced exercise tolerance. Beyond central hemodynamic abnormalities, HFrEF is accompanied by significant peripheral skeletal muscle dysfunction, which contributes substantially to functional decline, reduced quality of life, and increased risk of recurrent hospitalization and premature mortality.[1-2]

Heart failure represents a major global health burden, affecting an estimated 64 million individuals worldwide.[3] Approximately 40–50% of these cases are classified as HFrEF, a subgroup associated with particularly high morbidity and mortality.[4] In developed countries, heart failure accounts for millions of hospital admissions annually, with readmission rates approaching one-third within a year.[5] Mortality among patients with heart failure remains substantial, ranging from 10–15% annually, while data from low- and middle-income countries suggest an even higher burden. In addition to its cardiovascular impact, HFrEF imposes profound functional limitations, with many patients experiencing difficulty performing daily activities such as walking, climbing stairs, and carrying loads, thereby reinforcing the need for effective rehabilitation strategies.[6-7]

Exercise-based cardiac rehabilitation is strongly recommended for patients with HFrEF and has consistently demonstrated improvements in exercise capacity, quality of life, and hospital readmission rates.[8] However, real-world participation in conventional rehabilitation programs remains suboptimal.[8] Advanced disease severity, frailty, fatigue, comorbid conditions, and limited exercise tolerance frequently prevent patients from initiating or completing structured exercise training. Consequently, a substantial proportion of patients with HFrEF are unable to access the established benefits of standard cardiac rehabilitation.[9]

Neuromuscular Electrical Stimulation (NMES) has emerged as a clinically relevant alternative rehabilitation strategy. By inducing involuntary skeletal muscle contractions through surface electrical stimulation, NMES enables peripheral muscle activation with minimal cardiovascular stress and without requiring active patient participation.[11] These characteristics make NMES particularly suitable for patients with advanced disease, severe deconditioning, or limited mobility. Despite increasing clinical interest and technological advances that have improved feasibility and safety, evidence regarding the effectiveness of NMES in HFrEF remains heterogeneous.[12] Therefore, this systematic review and meta-analysis aimed to evaluate the effectiveness of NMES in improving cardiac function and exercise capacity in patients with HFrEF.

Methods

Search Strategy

A comprehensive electronic literature search was independently conducted by two reviewers across PubMed, ScienceDirect, Google Scholar, the Cochrane Library, Taylor & Francis, and LILACS to identify Randomized Controlled Trials (RCTs) evaluating NMES as a rehabilitation intervention in patients with HFrEF. Search strategies were constructed using Boolean operators, combining intervention-related terms ("neuromuscular electrical stimulation" OR NMES), condition-related terms ("heart failure with reduced ejection fraction" OR HFrEF), and rehabilitation-related terms ("rehabilitation" OR "cardiac rehabilitation" OR "exercise therapy").

The search was limited to randomized or controlled clinical trials, with additional Boolean filters applied. The literature search covered studies published between January 2014 and May 2025, a period selected to capture evidence generated under contemporary guideline-directed management of HFrEF and clinically relevant NMES protocols. Standardized diagnostic criteria for HFrEF and widely accepted functional outcomes, including peak oxygen uptake and Six-Minute Walk Test (6MWT) distance, were established during this timeframe and remain applicable to current practice. The complete database-specific Boolean search strings are provided in Table 1. Only full-text articles published in English or Indonesian were considered eligible. This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the protocol was prospectively registered with PROSPERO (registration number: CRD420251235578).

Eligibility Criteria

Eligible studies were selected based on predefined criteria encompassing study design, participant characteristics, intervention, and comparator. Only RCTs were included, as they provide the highest level of evidence for evaluating intervention effectiveness. Eligible articles were required to be published in full text and written in English or Bahasa Indonesia.

The study population consisted of adult participants (≥18 years) of both sexes diagnosed with HFrEF, defined as a Left Ventricular Ejection Fraction (LVEF) <40%, and classified as New York Heart Association (NYHA) functional classes II to IV. Studies were excluded if they enrolled patients with implanted cardiac pacemakers, clinically significant arrhythmias, peripheral arterial disease, uncontrolled diabetes mellitus, unstable angina pectoris, or chronic pulmonary disease, as these conditions could interfere with the safety or interpretation of NMES outcomes.

Table 1. Search string.

Database	Search Field	Search String
PubMed	Title/Abstract + MeSH	("Neuromuscular Electrical Stimulation"[Mesh] OR "neuromuscular electrical stimulation"[Title/Abstract] OR NMES[Title/Abstract]) AND ("Heart Failure with Reduced Ejection Fraction"[Title/Abstract] OR HFrEF[Title/Abstract]) AND ("Rehabilitation"[Mesh] OR rehabilitation[Title/Abstract] OR "exercise therapy"[Mesh]) AND (randomized controlled trial[Publication Type] OR randomized[Title/Abstract])
ScienceDirect	Title, Abstract, Keywords	("neuromuscular electrical stimulation" OR NMES) AND ("heart failure with reduced ejection fraction" OR HFrEF) AND rehabilitation AND (randomized OR "controlled trial")
Google Scholar	All fields	"neuromuscular electrical stimulation" OR NMES AND "heart failure with reduced ejection fraction" OR HFrEF AND rehabilitation AND "randomized controlled trial"
Cochrane Library	Title, Abstract, Keywords	("neuromuscular electrical stimulation" OR NMES) AND ("heart failure with reduced ejection fraction" OR HFrEF) AND (rehabilitation OR exercise)
Taylor & Francis	All fields	("neuromuscular electrical stimulation" OR NMES) AND ("heart failure with reduced ejection fraction" OR HFrEF) AND rehabilitation AND (randomized OR trial)
LILACS	Title, Abstract	("Neuromuscular Electrical Stimulation" OR NMES) AND ("Heart Failure with Reduced Ejection Fraction" OR HFrEF) AND rehabilitation

Selection Process

The reviewers conducted a duplication check and screened titles and abstracts according to pre-defined criteria in Figure 1.

Risk of Bias Assessment

The methodological quality of the included RCTs was assessed using the Cochrane Risk of Bias tool version 2.0 (RoB 2.0). Overall, most studies were judged to have a low risk of bias across the evaluated domains. Some trials exhibited minor concerns, primarily related to deviations from intended interventions and selective outcome reporting. No study was considered to have a high risk of bias in multiple domains. The detailed risk of bias assessment for each study is presented in Figure 2.

Effect Measures

Continuous outcomes, including peak oxygen uptake (VO_2 peak), 6MWT distance, LVEF, systolic blood pressure, and Heart Rate (HR), were summarized as Mean Differences (MDs) with 95% Confidence Intervals (CIs). Dichotomous outcomes, such as all-cause mortality or hospitalization events, were analyzed using Risk Ratios (RR) with corresponding 95% CIs, where applicable. Statistical significance was assessed using two-sided p-values, and pooled estimates were presented graphically using forest plots, with diamond symbols indicating the overall effect across studies.

Synthesis Methods

Quantitative synthesis was planned using Review Manager (RevMan) version 5.4, applying the inverse variance method. A random-effects model was prespecified as the primary analytical approach, with fixed-effects models considered only in cases of low statistical heterogeneity. Heterogeneity was to be assessed using the I^2 statistic. Continuous outcomes were to be pooled as MD, and dichotomous

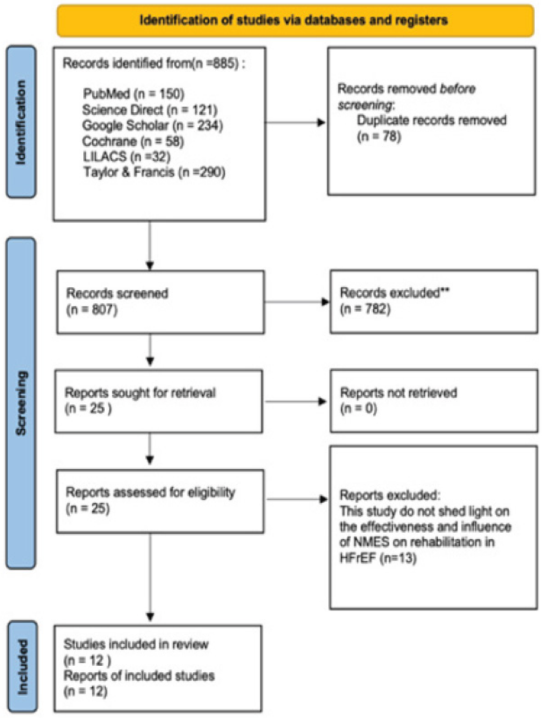

Figure 1. Flow of literature search.

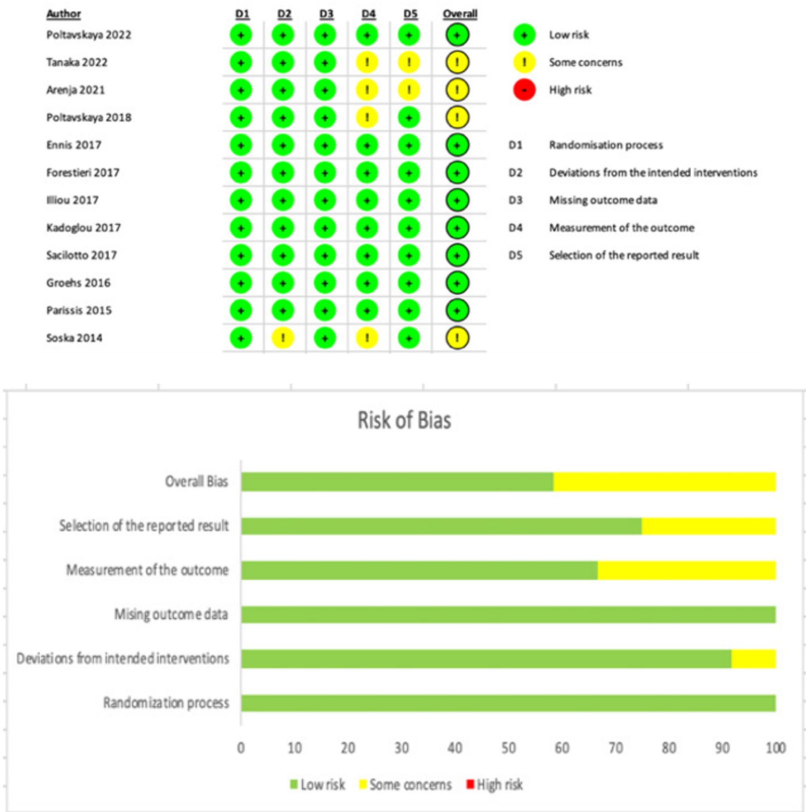

Figure 2. Assessment of the risk of bias score using the Cochrane Risk of Bias Tool 2.0 (RoB 2.0).

outcomes as RR, each with 95% CIs. Statistical significance was evaluated using two-sided p-values, and incomplete data were addressed by contacting study authors where feasible.

NMES interventions were evaluated according to predefined protocol characteristics, including target muscle groups, stimulation parameters, session duration, and intervention length. Control conditions were defined as standard medical therapy, exercise-based rehabilitation, sham stimulation, or no additional intervention. Outcomes of interest included measures of exercise capacity, cardiac function, health-related quality of life, and muscle strength, assessed according to the follow-up periods reported in each study.

Risk of Bias

The RoB 2.0 evaluation indicates that the majority of the included studies exhibited a low risk of bias across the majority of methodological domains. However, a number of studies have highlighted minor concerns in certain areas, particularly about deviations from intended interventions and selective reporting of outcomes, as illustrated in Figure 2.

Results

Study Selection

The systematic literature search identified a total of 885 records across six electronic databases: PubMed (n = 150), ScienceDirect (n = 121), Google Scholar (n = 234), the Cochrane Library (n = 58), LILACS (n = 32), and Taylor & Francis (n = 290). After the removal of 78 duplicate records, 807 articles were screened based on titles and abstracts. Of these, 782 records were excluded for failing to meet the predefined inclusion criteria.

The full texts of 25 articles were subsequently assessed for eligibility. Thirteen studies were excluded following full-text review due to irrelevance to NMES as a rehabilitation intervention in patients with HFrEF or insufficient outcome data. Ultimately, 12 RCTs met the eligibility criteria and were included in the final qualitative and quantitative synthesis. The study selection process is illustrated in the PRISMA flow diagram Figure 1.

Study Characteristics

The final analysis included 12 RCTs conducted between 2014 and 2022 across several countries, including the United Kingdom, Japan, Switzerland, Russia, Brazil, France, Greece, the Czech Republic, and the Netherlands. Sample sizes ranged from 15 to 120 participants per study, with most study populations consisting predominantly of older adults, generally aged over 60 years. Both male and female participants were included, and the severity of heart failure ranged from NYHA functional class II to IV.

Across all included trials, the intervention consisted of NMES applied primarily to lower limb muscle groups, most commonly the quadriceps femoris, hamstrings, tibialis anterior, and gastrocnemius muscles. The included studies evaluated a range of heart failure outcomes, including measures of exercise capacity, cardiac function, HR, and health-related quality of life. Detailed characteristics of the included studies are summarized in Table 2.

Meta-Analysis Results

A total of 12 RCTs were included in the quantitative synthesis. Meta-analysis demonstrated that NMES significantly improved exercise capacity in patients with HFrEF. NMES was associated with a significant increase in VO_2 peak compared with control interventions (MD 2.03 mL/kg/min; 95% CI 1.21 to 2.84; $p < 0.00001$; $I^2 = 47\%$). A borderline but clinically relevant improvement was also observed in the 6MWT distance (MD −11.40 m; 95% CI −23.04 to 0.24; $p = 0.05$; $I^2 = 23\%$).

Regarding cardiovascular parameters, NMES was associated with a modest yet statistically significant improvement in LVEF (MD 1.38%; 95% CI −2.73 to −0.03; $p = 0.05$). A significant reduction in systolic blood pressure was observed in the NMES group compared with controls (MD −2.02 mmHg; 95% CI −3.97 to −0.06; $p = 0.04$; $I^2 = 50\%$), whereas no significant difference was found in diastolic blood pressure (MD −0.12 mmHg; 95% CI −3.30 to 3.06; $p = 0.94$; $I^2 = 80\%$). HR was also significantly different between groups following NMES intervention (MD 2.19 beats/min; 95% CI 0.44 to 3.95; $p = 0.01$; $I^2 = 0\%$).

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Table 2. Characteristics study inclusion.

No.	Source	Country	Total Sample	Age	Gender	Treatment History	Frequency	Stimulation	Time	Frequency	Duration
1.	Poltavskaya, 2022.[12]	United Kingdom	n= 30 (intervention), n= 30 (control)	≥18 years old	M = 42, F = 18	Loop diuretics, ACE-I or ARBs, B-blockers, and MRA	25 Hz	The anterior and posterior muscles of the femur and tibialis in both legs were stimulated.	1 second of contraction, 2 seconds of relaxation	5 days a week	30-60 minutes per day
2.	Tanaka, 2022.[13]	Japan	n= 15 (intervention), n= 16 (control)	≥ 75 years	M = 14, F = 17	NR	20 Hz	Quadriceps femoris, hamstring, tibialis anterior, and triceps muscles	A 5-second contraction phase was followed by a 2-second relaxation period.	5 times a week	30-40 minutes per day
3.	Arenja, 2021.[14]	Switzerland	n= 9 (intervention), n= 8 (control)	≥ 60 years	M = 13, F = 14	Aspirin, anticoagulants, statins, ACE-I or ARBs, β-blockers, and MRA	25 Hz	The upper and lower portions of the anterior and posterior femoral and tibial muscles in both legs.	A 2-second contraction phase was followed by a 5-second relaxation period.	5 days a week for 6 weeks	30 minutes per day
4.	Poltavskaya, 2018.[15]	Russia	n=10 (intervention), n=16 (control)	> 18 years	M = 22, F = 4	ACE inhibitors/ ARBs, MCRAs, loop diuretics, beta-blockers	4 Hz	Anterior and posterior thigh and shin muscles	NR	for 3-7 weeks	30-240 minutes per day
5.	Ennis, 2017.[16]	United Kingdom	n= 30 (intervention), n= 30 (control)	59-80 years old	M = 42, F = 18	NR	4-5 Hz	Quadriceps and hamstring muscles	NR	5 times a week	60 minutes per day
6.	Forestieri, 2017.[17]	Brazil	n=24 (intervention), n=25 (control)	> 40 years	M = 8, F = 41	ACE-I, Diuretics	40 Hz	Quadriceps and gastrocnemius (calf) muscles	A contraction phase lasting 10 seconds was followed by a relaxation phase of equal duration.	2 times in 1 day for 2 weeks	60 minutes per day
7.	Iliou, 2017.[18]	Francis	n= 50 (intervention), n= 41 (control)	18-80 years old	M = 70, F = 21	NR	10 Hz	Bilateral Quadriceps femoral muscle	NR	for 4-8 weeks	30-60 minutes per day

8.	Kadoglou, 2017.[19]	Netherlands	n= 60 (intervention), n= 60 (control)	> 60 years	M = 68, F = 52	ACE-I, B-Blockers, Diuretics, MRAs	25 Hz	Quadriceps and gastrocnemius (calf) muscles	A contraction period of five seconds was succeeded by a relaxation period lasting two seconds.	5 days per week for 6 weeks	30 minutes per day
9.	Sacilotto, 2017.[20]	Brazil	n= 18 (intervention), n= 10 (control)	38-64 years	M= 24; F = 4	Diuretics, spironolactone, digoxin, beta-blockers, antiarrhythmics, antiplatelets, statins, CCBs, nitrates, ACE inhibitors	50 Hz	Bilateral femoral quadriceps	A contraction phase lasting three seconds was followed by a relaxation phase of nine seconds.	2 times a week for 7 weeks.	50 minutes per day
10.	Groehs, 2016.[21]	Brazil	n= 15 (intervention), n= 15 (control)	18-70 years old	M = 27, F = 3	B-blockers, ACE-I or ARBs, diuretics, anticoagulants, digitalis, statins, vasodilators, and antiplatelet agents.	10 Hz	Quadriceps and gastrocnemius (calf) muscles	A contraction period of twenty seconds was followed by an equal duration of relaxation.	8-10 consecutive days	60 minutes per day
11.	Parissis, 2015.[22]	Greece	n= 15 (intervention), n= 15 (control)	≥ 70 years old	M = 20, F = 10	ACE-I, B-Blockers, and Diuretics	25 Hz	Quadriceps and gastrocnemius (calf) muscles	A contraction phase of five seconds was followed by a relaxation phase lasting two seconds	5 days per week for 6 weeks	30 minutes per day
12.	Soska, 2014.[23]	Czech	n= 23 (intervention), n= 26 (control)	> 60 years	M = 29, F = 20	ACE-I, B-Blocker, Diuretic, Digoxin, Statin	10 Hz	Bilateral Quadriceps femoral muscle	A contraction phase lasting twenty seconds was followed by an equal twenty-second relaxation phase	2 times in 1 day for 12 weeks	60 minutes per day

Info : NR (Not Reported), M (Male), F (Female).

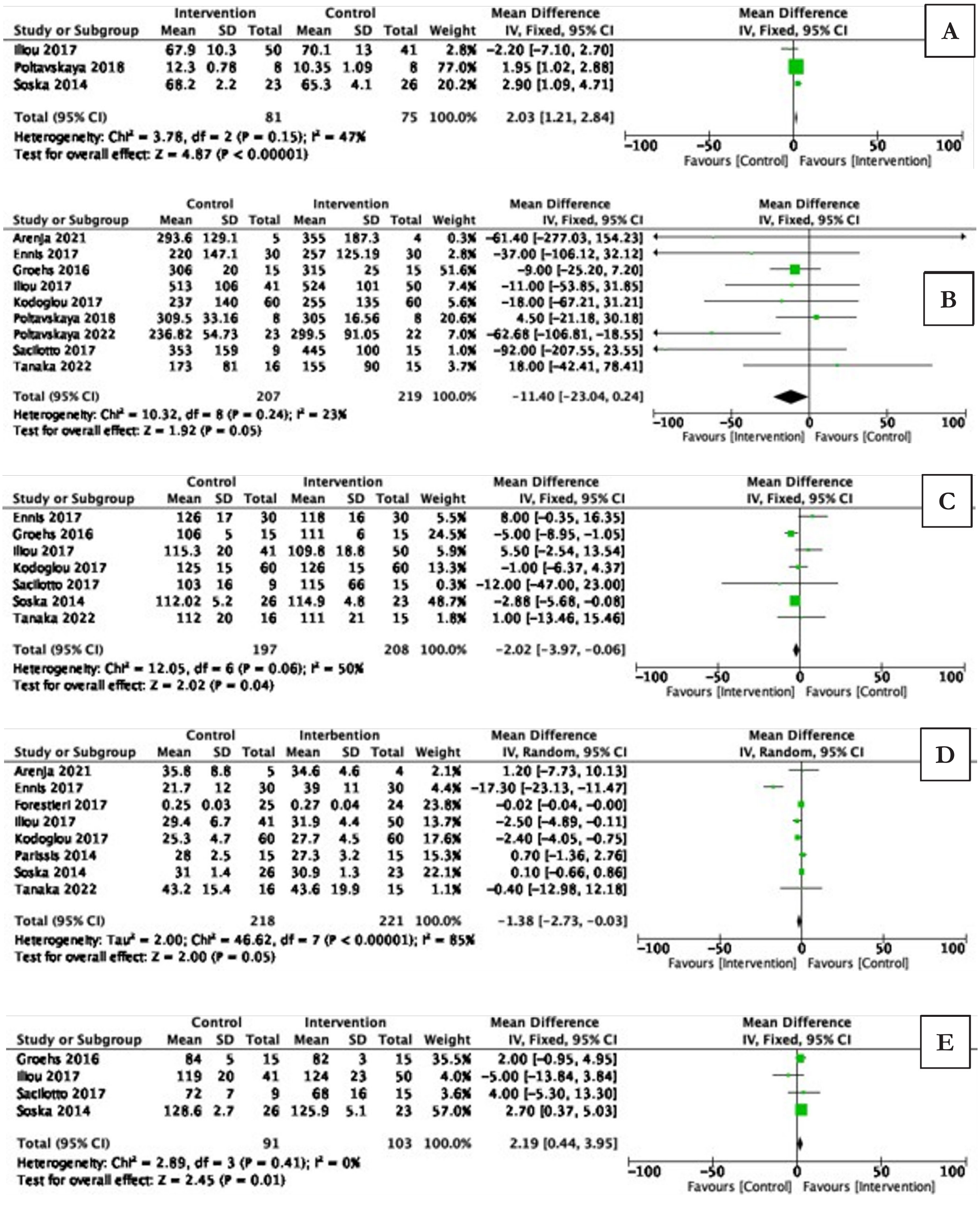

Figure 3. Results that have a significant effect of NMES on HFrEF rehabilitation. (A) VO_2 Peak, (B) 6 Minute Walking Test (6MWT), (C) Systolic Blood Pressure (SBP), (D) Left Ventricular Ejection Fraction (LVEF%), (E) Heart Rate (HR).

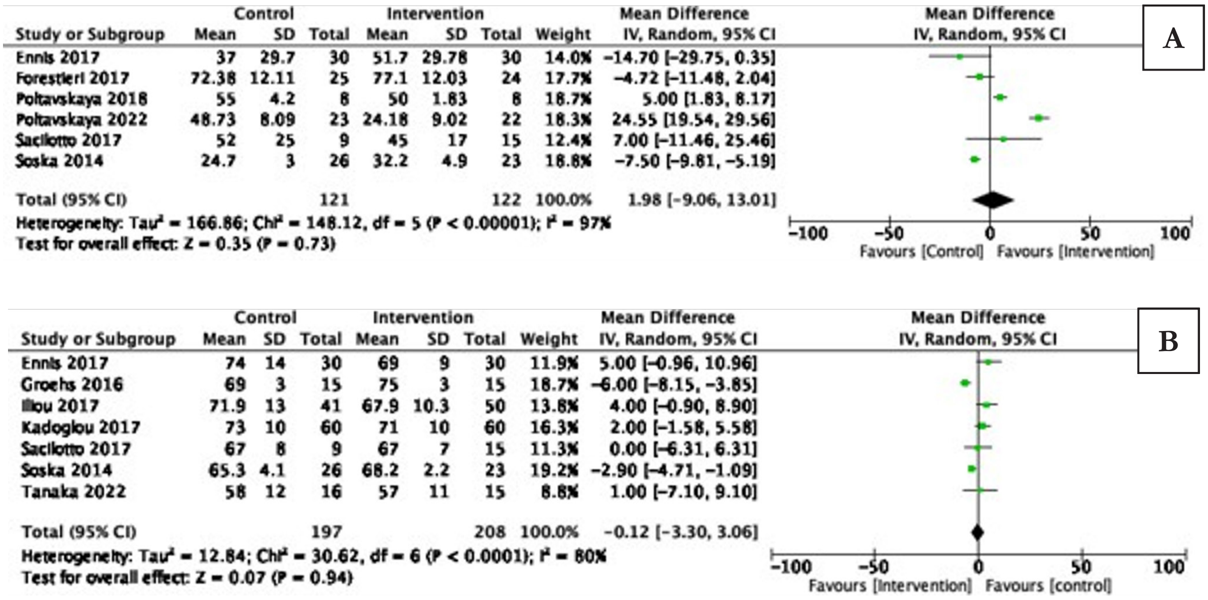

Figure 4. Results that have no significant effect of NMES on HFrEF rehabilitation (A) Minnesota Living with Heart Failure Questionnaire (MLHFQ) Score, (B) Diastolic Blood Pressure (DBP).

Discussion

NMES confers significant benefits on exercise capacity and selected cardiovascular parameters in patients with HFrEF. Pooled analyses showed a robust improvement in peak oxygen uptake and a borderline improvement in 6MWT distance, alongside modest but significant improvements in LVEF, systolic blood pressure, and HR. In contrast, no significant effects were observed on diastolic blood pressure or on health-related quality of life, as assessed by the MLHFQ. These findings indicate that NMES primarily improves objective physiological and functional outcomes rather than subjective patient-reported measures.[12-23]

The improvement in exercise capacity observed with NMES highlights its key advantage in addressing peripheral limitations that substantially contribute to exercise intolerance in HFrEF. Beyond impaired cardiac output, patients with HFrEF commonly exhibit skeletal muscle atrophy, reduced oxidative enzyme activity, and impaired peripheral perfusion, all of which limit functional performance.[24] NMES induces involuntary muscle contractions that enhance muscle fiber recruitment, increase local blood flow, and improve mitochondrial oxidative capacity, thereby improving aerobic efficiency without imposing excessive cardiovascular stress.[10] This peripheral mechanism provides a plausible explanation for the observed increases in VO_2 peak and walking capacity. It supports previous evidence suggesting that NMES can partially replicate the physiological benefits of exercise in patients unable to tolerate conventional training.[24-25]

In addition to its peripheral effects, NMES may exert favorable systemic and hemodynamic influences. The observed reduction in systolic blood pressure and modulation of HR suggest an improvement in autonomic balance, particularly through attenuation of heightened sympathetic nervous system activity, which is a hallmark of advanced heart failure.[25] Reduced sympathetic tone may lower systemic vascular resistance and cardiac workload, thereby indirectly supporting ventricular performance.[26] The modest improvement in LVEF observed in this analysis likely reflects these indirect neurohumoral and hemodynamic effects rather than a direct inotropic action on the myocardium. The absence of a significant effect on diastolic blood pressure is consistent with the primary action of NMES on muscle contraction and vascular tone rather than ventricular relaxation dynamics.[27]

From a clinical standpoint, the findings of this meta-analysis underscore the practical advantages of NMES as an adjunct rehabilitation strategy in HFrEF. NMES can be delivered with minimal physical effort, low cardiovascular strain, and high feasibility across inpatient, outpatient, and home-based settings. These characteristics make NMES particularly valuable for patients with advanced disease, frailty, or severe exercise intolerance populations that are frequently excluded from conventional exercise-based cardiac rehabilitation despite strong guideline recommendations.[25,27] While NMES should not be viewed as a substitute for comprehensive cardiac rehabilitation, its ability to improve objective functional and hemodynamic parameters supports its selective integration into individualized rehabilitation programs.[28]

Overall, this meta-analysis suggests that NMES offers meaningful physiological and functional benefits in patients with HFrEF, particularly in improving exercise capacity and selected cardiovascular measures. At the same time, its effects on quality-of-life outcomes remain inconsistent. These findings reinforce the role of NMES as a supportive and accessible rehabilitation modality that may help bridge the gap between guideline-based recommendations and the real-world limitations of rehabilitation in heart failure care.

Conclusion

NMES provides measurable benefits in patients with HFrEF. Based solely on pooled analyses, NMES was associated with significant improvements in peak oxygen uptake and a borderline improvement in 6MWT distance. In addition, modest but statistically significant improvements were observed in LVEF, systolic blood pressure, and HR. No significant effects were identified for diastolic blood pressure or health-related quality of life.

Taken together, these findings support the role of NMES as a beneficial adjunct rehabilitation intervention for patients with HFrEF, particularly for those who are unable to engage in conventional exercise-based rehabilitation.

List of Abbreviations

6MWT	Six-Minute Walk Test
CI	Confidence Interval
HFrEF	Heart Failure with Reduced Ejection Fraction
HR	Heart Rate
LVEF	Left Ventricular Ejection Fraction
MD	Mean Differences
MLHFQ	Minnesota Living with Heart Failure Questionnaire
NMES	Neuromuscular Electrical Stimulation
NYHA	New York Heart Association
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCTs	Randomized Controlled Trials
RR	Risk Ratio
VO_2	Oxygen uptake

Ethical Clearance

Not applicable.

Publication Approval

All authors consent to the publication of this manuscript.

Authors Contributions

All authors contributed substantially to the conception, design, and intellectual development of this systematic review and meta-analysis. BDA led the study conceptualization, literature search strategy, data extraction, statistical interpretation, and manuscript drafting. SA and DH contributed to data screening, risk-of-bias assessment, and verification of extracted datasets. R and I supported methodological validation and assisted in the synthesis and interpretation of pooled outcomes. H provided critical intellectual input, supervised the overall research process, and revised the manuscript for important scientific content and methodological rigor. All authors critically reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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Conflict of Interest

None.

Availability of Data and Materials

Not applicable.

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None.

Generative AI and AI-Assisted Technologies in the Writing Process

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