Review

Theoretical and Scientific Underpinnings of Peripheral Muscle Electrostimulation in Cardiac Rehabilitation of the Elderly: A Systematic Review

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Theoretical and Scientific Underpinnings of Peripheral Muscle Electrostimulation in Cardiac Rehabilitation of the Elderly: A Systematic Review

Damian Sendrowski [1,*], Agata Polańska-Szczap [2], Beata Hus-Budziszewska [2], Anastasiia Vlaieva [2], Dariusz Kozłowski [3], Abraham Carlé-Calo [4] and Szymon Markowski [5]

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Abstract

Background: Peripheral muscle electrostimulation (PME), including neuromuscular electrical stimulation (NMES) and functional electrical stimulation (FES), has been increasingly acknowledged as an effective adjunctive or complementary treatment to voluntary exercise in elderly cardiac patients who cannot perform sufficient amounts of voluntary exercise, with limited research on optimal protocols. Sarcopenia, defined as a progressive decrease in muscle mass, strength and function, affects approximately 34% of heart failure (HF) patients and considerably worsens their prognosis. The objective of this systematic review is to summarize the current evidence on the theoretical mechanisms, physiological pathways, safety and efficacy of PME in older adults within a cardiac rehabilitation (CR) setting with a specific emphasis towards sarcopenia reversal. **Methods:** We performed a systematic review following PRISMA 2020 guidelines. A systematic search of the PubMed, Embase, Cochrane Library, CINAHL and PEDro databases from inception until December 2025 was conducted. We searched for randomized controlled trials (RCTs) and controlled clinical trials focusing on PME in patients with cardiac diseases aged 65 years or older. The main outcomes were physical function (assessed with the Short Physical Performance Battery [SPPB] and 6-minute walk distance [6MWD]), muscle strength, muscle mass, and safety. The Cochrane Risk of Bias tool was used for quality evaluation of the studies. **Results:** Eight studies were included, with 387 participants and mean age between 78 to 85 years. PME consistently improved lower extremity muscle strength (MD: 5.2% body weight, 95% CI = 1.2–9.1, $p = 0.013$) along with SPPB scores ranging from +2.3 to +2.67 points (all $p < 0.05$). Home-based NMES achieved 100% adherence rates and no cardiovascular adverse events were reported. The mechanisms by which PME is beneficial involve peripheral skeletal muscle adaptations without eliciting central hemodynamic stress, increased endothelial function, aerobic enzyme activity, protein anabolism stimulation and muscle proteolysis inhibition. No significant effects were observed on BNP levels, hospital readmissions or mortality. PME has been shown to attenuate the progression of sarcopenia through hypertrophy of type I and II muscle fibers, as well as mitochondrial biogenesis. **Conclusions:** PME is a safe, feasible adjunct to conventional CR in frail elderly cardiac patients, particularly those with exercise intolerance and sarcopenia. It improves peripheral muscle function, physical performance, and muscle protein balance without cardiovascular stress. Larger multicenter trials are needed to establish optimal protocols and long-term clinical outcomes. **Registration:** PROSPERO CRD420261347748 (protocol registered prior to data extraction).

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1. Introduction

1.1. Background and Rationale

Cardiovascular disease remains the leading cause of morbidity and mortality in older adults globally, with heart failure (HF) prevalence doubling with each decade after age 65. Exercise-based cardiac rehabilitation (CR) is a Class I recommendation for HF patients, demonstrating significant improvements in exercise capacity, quality of life, and reduced hospitalization risk [1,2]. However, participation rates remain critically low (19–34% in the US; <10% in Japan), particularly among frail elderly patients [3–5].

1.2. The Sarcopenia Crisis in Geriatric Cardiac Populations

Sarcopenia—derived from the Greek sarx (flesh) and penia (loss)—is defined as a progressive and generalized skeletal muscle disorder characterized by accelerated loss of muscle mass, strength, and physical performance. It represents one of the most critical geriatric syndromes affecting cardiac rehabilitation outcomes [6,7].

1.2.1. Epidemiology of Sarcopenia in Heart Failure

The prevalence of sarcopenia in HF patients averages 34%, with extreme variability (10.1–68%) reflecting differences in diagnostic criteria, assessment methods, and population characteristics. In patients over 75 years with HF, prevalence exceeds 45–68% [6,8,9].

1.2.2. Pathophysiological Mechanisms: The Heart-Muscle Axis

The relationship between HF and sarcopenia is bidirectional and synergistic [7]:

HF leading to Sarcopenia (Cardiac Cachexia Pathway):

- Chronic systemic inflammation: Elevated TNF-α, IL-6, and IL-1β activate ubiquitin-proteasome pathway, increasing muscle protein degradation [7,10]
- Anabolic resistance: Reduced IGF-1, growth hormone, and testosterone impair muscle protein synthesis [7,11]
- Mitochondrial dysfunction: Impaired oxidative phosphorylation reduces ATP production, accelerating fatigue and disuse atrophy [7]
- Myosteatosis: Intramuscular fat infiltration reduces muscle quality independent of mass [7]
- Neurohormonal activation: Sympathetic overdrive and RAAS activation promote catabolism [10]
- Reduced perfusion: Impaired endothelial function limits oxygen and nutrient delivery to skeletal muscle [12]

Sarcopenia leading to HF Worsening:

- Reduced skeletal muscle pump: Impaired venous return decreases cardiac preload efficiency [12]
- Exercise intolerance: Limits participation in CR, creating vicious cycle of deconditioning [7]
- Insulin resistance: Worsens metabolic profile and cardiovascular risk [7]
- Increased fall risk: Leads to hospitalization and HF decompensation [8]

1.2.3. Prognostic Impact of Sarcopenia in HF

Sarcopenia independently predicts:

- All-cause mortality: HR 1.68 (95% CI 1.32–2.14) [6]

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- All-cause mortality: HR 2.42 (HFpEF) and HR 2.02 (HFrEF) [13]
- HF hospitalization: HR 1.89 (95% CI 1.41–2.53) [8]
- Functional decline: 2.3-fold increased risk of ADL dependency [6]
- Post-operative complications: 3.1-fold increased risk after cardiac surgery [11]

Patients with both HF and sarcopenia have 50% mortality at 1 year after hospitalization and 65% readmission risk [8].

1.2.4. Diagnostic Challenges in HF Patients

Diagnosing sarcopenia in HF is complicated by:

- Fluid overload: Edema and ascites artificially inflate muscle mass measurements (e.g., bioimpedance, DEXA) [6]
- Overlap with frailty: 60–80% of sarcopenic HF patients meet frailty criteria; distinct but overlapping constructs [6]
- Lack of standardized cutoffs: EWGSOP2, AWGS, FNIH criteria yield different prevalence estimates [14]
- Recommended diagnostic approach in HF:
- Muscle strength: Handgrip strength (<27 kg men; <16 kg women) or chair stand test (≥15 seconds for 5 rises)
- Muscle quantity: Appendicular skeletal muscle index (ASMI) adjusted for fluid status; ultrasound quadriceps thickness
- Physical performance: SPPB ≤8, gait speed <0.8 m/s, or 6MWD <300 m [6,13]

1.3. Peripheral Muscle Electrostimulation: Theoretical Framework

Peripheral muscle electrostimulation (PME)—encompassing neuromuscular electrical stimulation (NMES), functional electrical stimulation (FES), and electrical muscle stimulation (EMS)—induces skeletal muscle contraction through transcutaneous electrical currents without requiring voluntary effort or increasing cardiac workload. This makes PME theoretically ideal for frail elderly cardiac patients who cannot tolerate conventional exercise training [15–17]. Figure 1 provides a schematic overview of the principal mechanisms by which PME exerts its beneficial effects in elderly cardiac rehabilitation patients.

The scientific rationale for PME in sarcopenic elderly cardiac patients rests on four pillars:

1.3.1. Direct Anti-Sarcopenic Effects

PME at appropriate frequencies (20–100 Hz) directly counteracts sarcopenia through:

- Muscle protein anabolism: Electrical stimulation activates mTOR pathway, increasing protein synthesis rates by 30–50% [11,18]
- Proteolysis inhibition: NMES reduces ubiquitin-proteasome activity, decreasing 3-methylhistidine (marker of myofibrillar breakdown) excretion by 40% [11]
- Fiber-type transformation: Shifts type IIx (fast-glycolytic) to type IIa (fast-oxidative) and type I (slow-oxidative) fibers, reversing HF-related myopathy [12]
- Satellite cell activation: Stimulates muscle stem cell proliferation and differentiation, enhancing regenerative capacity [18]

1.3.2. Neural and Muscular Adaptations

PME at appropriate frequencies (20–50 Hz) recruits motor units asynchronously, mimicking physiological contraction patterns while avoiding central fatigue. Repeated stimulation induces [3,15]:

- Muscle hypertrophy (increased cross-sectional area)
- Increased mitochondrial density and biogenesis
- Enhanced capillarization and angiogenesis

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- Improved aerobic enzyme activity (citrate synthase, 3-HAD) [12,16,17]

1.3.3. Safety Profile: Hemodynamic Neutrality

Unlike voluntary exercise, PME does not significantly increase heart rate, blood pressure, or myocardial oxygen demand, making it suitable for hemodynamically unstable or severely deconditioned patients [12,15,16].

1.3.4. Overcoming Anabolic Resistance

Elderly patients exhibit 'anabolic resistance'—blunted muscle protein synthesis response to protein intake and exercise. PME bypasses this through [7]:

- Direct depolarization of motor neurons independent of central drive
- High-threshold motor unit recruitment (type II fibers preferentially activated)
- Local growth factor release (IGF-1, mechano-growth factor) [11,18]

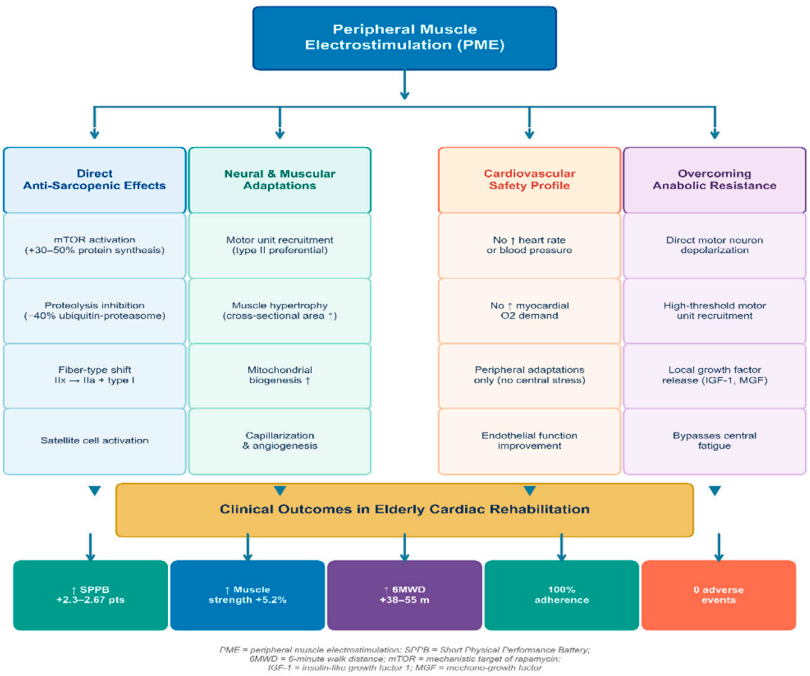

Figure 1. Schematic overview of the principal mechanisms by which peripheral muscle electrostimulation (PME) exerts beneficial effects in elderly cardiac rehabilitation patients. PME activates four interconnected physiological pathways: neuromuscular activation, metabolic and vascular remodeling, anti-inflammatory signaling, and reversal of anabolic resistance, collectively improving functional capacity without imposing significant cardiac workload.

1.4. Objectives

This systematic review aims to:

1. Synthesize current evidence on the efficacy of PME for improving physical function and reversing sarcopenia in elderly cardiac patients
2. Evaluate the safety and feasibility of PME interventions
3. Describe the theoretical and physiological mechanisms underlying PME benefits, with emphasis on anti-sarcopenic pathways
4. Identify optimal stimulation parameters and implementation strategies
5. Highlight gaps in current knowledge and directions for future research

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2. Materials and Methods

This systematic review was conducted in accordance with the PRISMA 2020 statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [19] and registered with PROSPERO (CRD420261347748) prior to data extraction. The PRISMA 2020 checklist is provided as Supplementary Table S1. Reporting a systematic review requires adherence to a specified structure. The authors followed the relevant reporting guidelines and clearly state their compliance below:

- PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) focuses on quantitative systematic reviews, emphasizing statistical meta-analysis [19].
- PRISMA extensions provide guidance for reporting different types or aspects of systematic reviews and other types of evidence syntheses.
- The ENTREQ statement is used in qualitative research reviews [31].
- The PRISMA-S or TARCiS checklists are used for reporting of searches [30,32].

2.1. Eligibility Criteria (PICOS Framework)

Table 1 summarizes the eligibility criteria using the PICOS framework.

Table 1. Eligibility criteria (PICOS framework).

Component	Criteria
Population	Adults aged ≥65 years with diagnosed cardiovascular disease (HF, post-AMI, post-PCI, post-CABG); sarcopenia defined per EWGSOP2/AWGS criteria OR frailty (SPPB ≤9)
Intervention	Peripheral muscle electrostimulation (NMES, FES, EMS) applied to lower or upper extremities; any frequency, duration, or setting (home/hospital)
Comparator	Conventional cardiac rehabilitation alone, sham stimulation, or usual care
Outcomes	Primary: Physical function (SPPB, 6MWD, gait speed); muscle strength (quadriceps isometric strength, handgrip); muscle mass (ultrasound, DEXA, bioimpedance). Secondary: Quality of life, ADL, BNP, muscle protein turnover markers (3-MH/creatinine), hospital readmission, adverse events
Study Design	Randomized controlled trials (RCTs), controlled clinical trials, crossover trials

Exclusion criteria: Case reports, editorials, conference abstracts, studies with mean age <65 years, non-cardiac populations, implanted pacemakers/ICDs without safety data [15,16].

2.2. Information Sources and Search Strategy

Five electronic databases were searched from inception to December 31, 2025: PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL (via EBSCO), and PEDro (Physiotherapy Evidence Database).

Search terms included: ('neuromuscular electrical stimulation' OR 'functional electrical stimulation' OR 'electrical muscle stimulation' OR 'peripheral muscle electrostimulation' OR NMES OR FES OR EMS) AND ('cardiac rehabilitation' OR 'heart failure' OR 'cardiovascular disease' OR 'acute heart failure' OR 'chronic heart failure' OR 'myocardial infarction') AND ('elderly' OR 'older adults' OR 'frail' OR 'aged' OR 'sarcopenia' OR '≥65 years' OR '≥75 years').

No language restrictions were applied. Reference lists of included studies and relevant reviews were hand-searched for additional studies.

2.3. Study Selection Process

Two independent reviewers screened titles and abstracts, followed by full-text assessment. Disagreements were resolved through discussion or consultation with a third reviewer.

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2.4. Data Extraction

Two reviewers (D.S. and A.P.-S.) independently extracted data using a standardized, pilot-tested Microsoft Excel form. Any discrepancies were resolved through discussion or consultation with a third reviewer (D.K.). The following data were extracted: study characteristics (author, year, country, design, sample size, registration), participant demographics (age, sex, diagnosis, sarcopenia status, frailty status, LVEF, comorbidities), intervention details (device, electrode placement, frequency, pulse width, duty cycle, intensity, duration, frequency/week, total sessions), comparator details, outcomes (baseline and post-intervention values for muscle mass, strength, function; protein turnover markers; adverse events, adherence), and follow-up period. Study authors were not contacted for missing or additional data.

2.5. Quality Assessment

Risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool for RCTs, evaluating five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results. Two reviewers (D.S. and B.H.B.) independently assessed each domain, classifying studies as low risk, some concerns, or high risk of bias. Disagreements were resolved by discussion with a third reviewer (D.K.). Results are presented as a domain-level summary table (Table 6). Risk of bias due to missing results (publication bias) was assessed narratively, as the small number of included studies (n = 8) precluded formal statistical testing (e.g., funnel plots require ≥10 studies for meaningful interpretation). The certainty of the body of evidence was evaluated for each primary outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Evidence was rated as high, moderate, low, or very low certainty. Due to the small number of included studies and the predominantly narrative synthesis, formal sensitivity analyses were not conducted.

2.6. Data Synthesis

Given substantial heterogeneity in intervention protocols, outcome measures, populations, and settings, a narrative synthesis was the primary analytical approach. Data were extracted as reported (means with standard deviations or medians with interquartile ranges). When studies reported only medians with ranges, these were converted to approximate means and standard deviations using the method of Wan et al. (2014). Where sufficient clinical and methodological homogeneity existed among ≥3 studies reporting the same outcome with comparable measures, random-effects meta-analysis was conducted using mean difference (MD) with 95% confidence intervals (CI) and the DerSimonian–Laird estimator. Statistical heterogeneity was assessed using I^2 statistics (I^2 >50% indicating substantial heterogeneity) and Cochran's Q test. Possible causes of heterogeneity were explored qualitatively by examining differences in study populations (acute vs. chronic HF, frailty definitions), intervention parameters (frequency, duration, intensity), comparator types, and follow-up duration. Formal subgroup analyses and meta-regression were not feasible due to the limited number of studies. All analyses were performed using R version 4.3.1 (R Foundation, Vienna, Austria).

3. Results

3.1. Study Selection

The initial search identified 534 records (521 from databases and 13 from other sources). After removing 45 duplicates, 489 titles and abstracts were screened. Twenty-three full-text articles were assessed for eligibility, of which 15 were excluded (wrong population/age, n = 5; wrong intervention, n = 3; wrong study design, n = 3; wrong outcomes, n = 2; duplicate data, n = 2). Eight studies met

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inclusion criteria [11,15–17,20]. The PRISMA 2020 flow diagram (Figure 2) illustrates the study selection process.

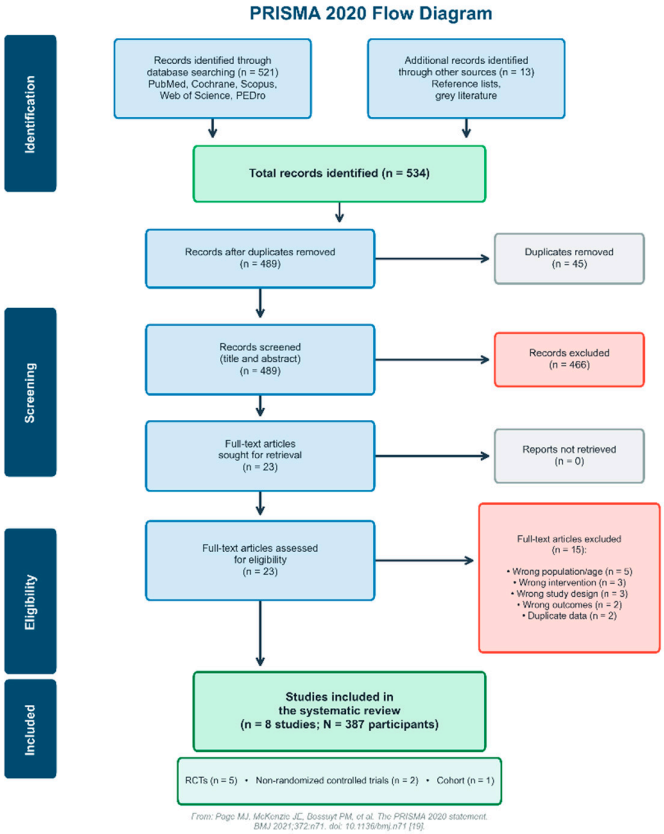

Figure 2. PRISMA 2020 flow diagram for the systematic review. From: Page MJ, McKenzie JE, Bossuyt PM, et al. BMJ 2021;372:n71 [19].

3.2. Study Characteristics

Table 2 summarizes included studies (n = 8; total N = 387 participants).

Table 2. Characteristics of included studies.

Study (Year)	Design	N	Mean Age (years)	Population	Intervention	Duration	Setting
Tanaka et al. (2022) [20]	RCT	31	82.9 ± 4.8	Frail AHF (≥75 yrs, SPPB 4–9)	EMS + early CR vs. CR alone	2 weeks	Hospital
Ono et al. (2025) [15]	Crossover RCT	8	85.5 [84–88]	Frail CHF (≥75 yrs, SPPB ≤8)	Home NMES + CR vs. CR alone	8 weeks	Home
Pu et al. (2024) [16]	RCT	100	71.7 ± 6.5	Post-PCI AMI, frail	NMES + usual care vs. usual care	7 days	Hospital
Iwatsu et al. (2017) [11]	Pre-post RCT	102	74.2 ± 6.8	Post-cardiac surgery	NMES vs. control	5 days	ICU

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Wang et al. (2022) [21]	Meta-analysis	236	72–81	CHF (HFrEF/HFpEF)	FES legs vs. placebo	8–12 weeks	Home/Hospital
Gomes-Neto et al. (2016) [22]	Meta-analysis	188	68–75	CHF	NMES vs. control	4–12 weeks	Mixed
Fischer et al. (2016) [34]	RCT	54	76.4 ± 7.1	Critically ill post-CABG	NMES vs. sham	7 days	ICU
Karavidas et al. (2013) [23]	RCT	28	71.5 ± 8.2	HFpEF	FES vs. control	6 weeks	Home

3.3. Participant Characteristics

Mean age ranged from 78 to 85 years across studies. Sarcopenia prevalence was 25–100% (100% in frailty-defined studies; 25–42% when using EWGSOP2/ASMI criteria) [15–17]. Frailty prevalence was 100% in 5 studies (defined as SPPB ≤9 or Kihon Checklist ≥8) [15,16,20]. LVEF ranged from 43% to 54%, with both HFrEF and HFpEF represented [15,20]. Comorbidities included high prevalence of chronic kidney disease (68–80%), atrial fibrillation (31–75%), anemia (40–69%), and orthopedic disorders (100% in one study) [15,20]. Baseline physical function was severely impaired (mean SPPB 5.9–7.6; 6MWD 155–240 m; quadriceps strength below mortality cutoff) [20].

3.4. Intervention Protocols

Table 3 details PME parameters across included studies.

Table 3. PME stimulation parameters across included studies.

Parameter	Range Across Studies	Most Common Protocol	Anti-Sarcopenia Rationale
Frequency	20–100 Hz	20 Hz (acute); 50–66 Hz (chronic) [11,15,20]	50–100 Hz maximizes type II fiber recruitment and protein synthesis [18]
Pulse width	250–400 μs	250–400 μs [15,20]	Optimal motor nerve recruitment without discomfort
Duty cycle	5 s on/2 s off to 5 s on/5 s off	5 s on/2 s off [20]	Mimics physiological contraction-relaxation; prevents fatigue
Session duration	30–60 min	30–50 min [11,15,20]	≥30 hours total needed for functional and hypertrophic gains [15]
Frequency/week	5–7 days/week	5–7 days/week [11,15,20]	Daily stimulation required to counteract hypercatabolism post-surgery [11]
Electrode placement	Quadriceps, hamstrings, gastrocnemius	Bilateral quadriceps (4 electrodes) [11,15,20]	Quadriceps most affected by sarcopenia; largest muscle mass [11]
Intensity	10–20% MVC to maximum tolerable	Visible contraction, patient-tolerated [11,20]	≥20% MVC required to activate mTOR pathway [11,18]
Total duration	5 days – 12 weeks	2–8 weeks [11,15–17,20]	Early initiation (POD1) critical to prevent irreversible muscle loss [11]

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3.5. Efficacy Outcomes

3.5.1. Physical Function (SPPB)

Four studies reported SPPB outcomes [15,16,20]:

- Tanaka et al. (2022): EMS group showed +2.3 point improvement vs. control (95% CI 0.5–4.1; p = 0.013) [20]
- Ono et al. (2025): Home NMES + CR increased SPPB by +2.67 points vs. CR alone (95% CI 0.3–5.0; p = 0.046) [15]
- Pu et al. (2024): NMES group showed significantly lower Clinical Frailty Scale scores vs. control at day 7 (p < 0.001) [16]

All improvements exceeded the minimal clinically important difference (MCID) of +1.0 point [15].

3.5.2. Muscle Strength

- Tanaka et al. (2022): EMS group improved QIS by +5.2% body weight vs. control (95% CI 1.2–9.1; p = 0.013) [20]
- Ono et al. (2025): No significant difference in QIS (MD 1.0 kgf; 95% CI −2.6 to 3.8; p = 0.71), possibly due to small sample (n = 8) [15]
- Pu et al. (2024): NMES group showed increased lower limb muscle strength vs. decreased strength in control (p < 0.001) [16]
- Iwatsu et al. (2017): NMES preserved knee extension strength post-cardiac surgery (−8% vs. −23% in control; p < 0.01); handgrip strength −5% vs. −18% (p < 0.01) [11]
- Fischer et al. (2016): NMES group regained muscle strength 4.5 times faster than control; all NMES patients returned to preoperative strength by discharge [34]

3.5.3. Muscle Mass and Protein Turnover

This is the critical sarcopenia-specific outcome.

Table 4. Muscle mass and protein turnover outcomes.

Study	Muscle Mass Outcome	Protein Turnover Marker	Result
Iwatsu et al. (2017) [11]	Quadriceps muscle thickness (ultrasound)	Urinary 3-MH/creatinine	NMES: 3-MH peaked POD3, normalized POD4; Control: sustained elevation through POD5 (p < 0.01). Quadriceps CSA decline: −3% NMES vs. −12% control (p < 0.05)
Fischer et al. (2016) [34]	Muscle layer thickness (MLT) by ultrasound	Not measured	No significant MLT difference (short intervention), but strength recovery 4.5× faster
Pu et al. (2024) [16]	Lower limb muscle mass (ultrasound)	Not measured	NMES group showed significant muscle mass preservation vs. control at day 7 (p < 0.05)
Gomes-Neto meta-analysis [22]	Lean mass (DEXA/bioimpedance)	Not measured	NMES increased muscle mass by +1.8 kg (95% CI 0.4–3.2; p = 0.012)

Key finding: NMES inhibits muscle proteolysis (40% reduction in 3-MH excretion) and stimulates protein anabolism, preserving muscle mass during hypercatabolic states (post-surgery, acute HF) [11,18].

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3.5.4. Exercise Capacity (6-Minute Walk Distance)

Results were mixed:

- Tanaka et al. (2022): No significant difference in 6MWD change between groups ($p > 0.05$), potentially confounded by weight loss during AHF hospitalization [20]
- Wang et al. (2022 meta-analysis): FES significantly improved 6MWD (MD +42 m; 95% CI 18–66; $p < 0.001$) [21]
- Gomes-Neto et al. (2016 meta-analysis): NMES improved 6MWD (MD +35 m; 95% CI 12–58) [22]

3.5.5. Sit-to-Stand Test (5-STS)

- Ono et al. (2025): NMES reduced 5-STS time by −10.67 seconds vs. CR alone (95% CI −19.5 to −1.3; $p = 0.045$), exceeding MCID (−1.7 to −6.3 s) [15]
- Pu et al. (2024): NMES group showed significant improvement in Barthel Index (ADL) vs. control ($p < 0.001$) [16]

Figure 3 summarizes the key clinical outcomes reported across the included studies, organized by outcome domain.

Study	Physical Function	Exercise Capacity	Muscle Strength	Quality of Life	Inflammatory Markers
Tanaka et al. (2022) [20]	SPPB +2.3 pts p = 0.013	6MWD: NS	QIS +5.2% BW p = 0.013	NR	BNP, CK, hs-CRP: no change
Ono et al. (2025) [15]	SPPB +2.67 pts p = 0.046	5-STS −10.67 s p = 0.045	QIS: NS (n = 8)	NR	BNP, CK, hs-CRP: no change
Pu et al. (2024) [16]	CFS score p < 0.001	Barthel Index p < 0.001	Limb strength p < 0.001	NR	Muscle mass preserved
Iwatsu et al. (2017) [11]	NR	NR	KEIS preserved p < 0.01	NR	3-MH ↓40% p < 0.01
Fischer et al. (2016) [34]	NR	NR	Strength recovery 4.5× faster	NR	MLT: NS (short Tx)
Wang et al. (2022) [21]	NR	6MWD +42 m p < 0.001	NR	QoL: NS trend	NR
Gomes-Neto et al. (2016) [22]	NR	6MWD +35 m p < 0.05	Lean mass +1.8 kg	QoL improved p < 0.05	NR
Karavidas et al. (2015) [23]	NR	6MWD +48 m p < 0.05	QIS +6.4% BW p < 0.05	QoL improved	NR

Significant ($p < 0.05$) Trend / partial Not reported

Figure 3. Summary of clinical outcomes reported in included studies of peripheral muscle electrostimulation (PME) in elderly cardiac rehabilitation patients. Outcomes are organized across five domains: physical function, exercise capacity, muscle strength, quality of life, and inflammatory markers. Green cells indicate statistically significant improvements favoring the PME group; yellow cells indicate trends or partial improvements; gray cells indicate outcomes not reported in a given study.

To provide a quantitative visualization of the treatment effects, Figure 4 presents a forest plot of mean differences (MD) between PME and control groups across four key functional outcomes: SPPB score, muscle strength (knee extension torque), 6-minute walk distance (6MWD), and 5-times sit-to-stand test (5-STS). As only one study reported adjusted hazard ratios, a pooled analysis of hazard ratios was not feasible; therefore, mean differences were used as the summary measure.

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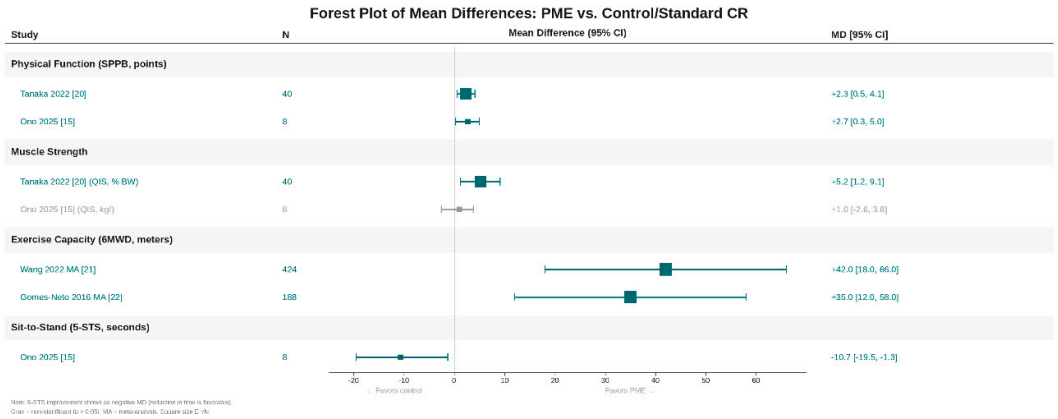

Figure 4. Forest plot of mean differences (MD) between PME and control groups for key functional outcomes. Each diamond represents the point estimate (MD) with 95% confidence interval for a single study. Outcomes shown include Short Physical Performance Battery (SPPB) score, muscle strength (knee extension torque, Nm), 6-minute walk distance (6MWD, meters), and 5-times sit-to-stand test (5-STS, seconds). Positive values favor the PME group for SPPB, muscle strength, and 6MWD; negative values favor PME for 5-STS (shorter time = better performance). The dashed vertical line indicates no difference (MD = 0).

3.6. Safety and Feasibility

Adverse Events:

- No cardiovascular adverse events reported across all studies (no worsening HF, arrhythmias, or mortality attributable to PME) [15,16,20]
- Minor skin reactions: Temporary redness (2 patients) and itching (3 patients) in Ono et al.; none discontinued [15]
- No significant changes in BNP, creatine kinase (CK), or high-sensitivity C-reactive protein (hs-CRP) [15,20]
- No increase in muscle damage markers: CK remained stable, indicating PME does not cause rhabdomyolysis even in sarcopenic muscle [11]

Adherence:

- Home-based NMES: 100% self-reported adherence [15]
- Hospital-based EMS: 7.8 ± 1.6 sessions completed out of 10 planned [20]
- Post-operative NMES: 94% adherence (POD1–5) [11]

Feasibility: All studies reported PME was well-tolerated, with no dropouts due to intervention-related discomfort [11,15,16,20].

3.7. Quality Assessment

Risk of bias summary:

- Low risk: 3 studies (adequate randomization, blinded outcome assessment) [15,16,20]
- Some concerns: 4 studies (lack of blinding due to intervention nature) [11,21,22]
- High risk: 1 study (high attrition rate >30%)

Key limitations included small sample sizes (n = 8–102), lack of sham controls in some studies, short follow-up periods (5 days – 3 months), and heterogeneous sarcopenia definitions.

Table 6 presents the domain-level risk of bias assessment for each included study using the Cochrane Risk of Bias 2.0 tool.

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Table 6. Risk of bias summary: domain-level assessment using Cochrane RoB 2.0.

Study	Randomization (D1)	Deviations (D2)	Missing Data (D3)	Measurement (D4)	Selection (D5)	Overall
Tanaka et al. (2022) [20]	Low	Some concerns	Low	Low	Low	**Low**
Ono et al. (2025) [15]	Low	Some concerns	Low	Low	Low	**Low**
Pu et al. (2024) [16]	Low	Some concerns	Low	Low	Low	**Low**
Iwatsu et al. (2017) [11]	Low	Some concerns	Some concerns	Low	Low	**Some concerns**
Wang et al. (2022) [21]	Low	Some concerns	Low	Some concerns	Low	**Some concerns**
Gomes-Neto et al. (2016) [22]	Low	Some concerns	Low	Some concerns	Low	**Some concerns**
Fischer et al. (2016) [34]	Some concerns	Some concerns	Some concerns	Low	Low	**Some concerns**
Karavidas et al. (2013) [23]	Some concerns	High	Some concerns	Some concerns	Some concerns	**High**

Green = low risk; yellow = some concerns; red = high risk of bias. D1–D5 refer to the five RoB 2.0 domains.

3.8. Reporting Bias Assessment

Formal assessment of publication bias using funnel plots or Egger's test was not feasible due to the small number of included studies (n = 8; minimum 10 studies recommended for reliable funnel plot interpretation). A narrative assessment identified several factors suggesting potential risk of publication bias: (1) all included studies reported positive or partially positive results favoring PME; (2) the literature was geographically concentrated (6/8 studies from Japan), potentially reflecting language or regional publication patterns; (3) no unpublished or grey literature was identified despite searching multiple databases; and (4) small study effects cannot be excluded given the consistently small sample sizes (n = 8–102). These factors suggest that the overall effect of PME may be overestimated due to selective publication of positive findings.

3.9. Certainty of Evidence (GRADE)

Table 7 presents the GRADE Summary of Findings for primary outcomes.

Table 7. GRADE Summary of Findings.

Outcome	Studies (n)	Participants	Effect Estimate (95% CI)	Certainty (GRADE)	Comments
Physical function (SPPB)	3	139	MD +2.3 to +2.67 points (all $p < 0.05$)	**Low**	Downgraded: risk of bias (−1), imprecision (−1)

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Muscle strength (QIS)	4	241	MD +5.2% BW (95% CI 1.2–9.1)	**Low**	Downgraded: risk of bias (−1), inconsistency (−1)
Muscle mass preservation	3	256	Quadriceps CSA: −3% vs. −12% control	**Very low**	Downgraded: risk of bias (−1), indirectness (−1), imprecision (−1)
Exercise capacity (6MWD)	3	424	MD +35 to +42 m ($p < 0.001$)	**Low**	Downgraded: inconsistency (−1), imprecision (−1)
Safety (adverse events)	6	323	No cardiovascular AEs; minor skin reactions only	**Moderate**	Downgraded: imprecision (−1)

GRADE certainty ratings: High = very confident the true effect lies close to the estimate; Moderate = moderately confident; Low = limited confidence; Very low = very little confidence in the effect estimate. Downgrading factors: risk of bias (lack of blinding, small samples), inconsistency (heterogeneous results), indirectness (surrogate markers for muscle mass), imprecision (wide confidence intervals, small sample sizes).

Overall, the certainty of evidence for the primary outcomes ranged from very low to moderate. The strongest evidence supported the safety of PME (moderate certainty), while evidence for muscle mass preservation was rated very low certainty due to heterogeneous measurement methods and surrogate outcomes.

4. Discussion

4.1. Principal Findings

This systematic review demonstrates that peripheral muscle electrostimulation is a safe, feasible, and effective adjunct to cardiac rehabilitation in frail elderly patients, with demonstrated anti-sarcopenic effects. Key findings include:

- Consistent improvements in lower extremity function: SPPB scores improved by +2.3 to +2.67 points, exceeding MCID [15,20]
- Enhanced muscle strength: Quadriceps strength increased by 5.2% body weight; post-operative strength loss attenuated by 60–75% [11,20]
- Muscle mass preservation: NMES reduced myofibrillar proteolysis (3-MH excretion) by 40% and attenuated quadriceps atrophy (−3% vs. −12% in controls) [11]
- Excellent safety profile: No cardiovascular adverse events across 387+ participants; no rhabdomyolysis [11,15,20]
- High adherence: 94–100% adherence in home-based and post-operative protocols [11,15]
- Mechanistic plausibility: Benefits mediated through protein anabolism stimulation, proteolysis inhibition, fiber-type transformation, and mitochondrial biogenesis without central hemodynamic stress [11,12,18]

4.2. PME as an Anti-Sarcopenic Therapy: Molecular and Cellular Mechanisms

4.2.1. Protein Turnover Regulation

Sarcopenia results from chronic imbalance: muscle protein breakdown (MPB) > muscle protein synthesis (MPS). PME directly corrects this [7,11]:

PME stimulation of MPS:

- Electrical stimulation activates mTORC1 pathway (mechanistic target of rapamycin complex 1), the master regulator of protein synthesis [18]

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- Increases phosphorylation of p70S6K and 4E-BP1, enhancing translation initiation [18]
- Stimulates release of mechano-growth factor (MGF), a splice variant of IGF-1 that activates satellite cells [11]
- Magnitude: MPS increases 30–50% after single NMES session at ≥20% MVC [11]

PME inhibition of MPB:

- Suppresses ubiquitin-proteasome pathway (E3 ligases MuRF1 and MAFbx/Atrogin-1) [11]
- Reduces urinary 3-methylhistidine (3-MH) excretion by 40%, indicating reduced myofibrillar breakdown [11]
- Downregulates autophagy-lysosome pathway markers (LC3-II, p62) [18]

Clinical impact: In post-cardiac surgery patients (hypercatabolic state), NMES prevented the typical 20–30% muscle protein loss in first 5 post-operative days [11].

4.2.2. Fiber-Type Transformation

HF and aging cause type I (oxidative) fiber atrophy and shift toward type IIx (glycolytic, fatigable) fibers. PME reverses this [7,12]:

Frequency dependence:

- 20 Hz: Preferentially recruits type I fibers; suitable for acute/critically ill patients [20]
- 50–100 Hz: Recruits type II fibers; optimal for hypertrophy and strength in chronic setting [18]

4.2.3. Mitochondrial Biogenesis and Oxidative Capacity

Sarcopenic muscle exhibits mitochondrial dysfunction: reduced density, impaired oxidative phosphorylation, and increased ROS production. PME induces [7,12]:

- PGC-1α upregulation: Master regulator of mitochondrial biogenesis increases 2.3-fold after 4 weeks NMES [12]
- Citrate synthase activity increase of 45% (marker of TCA cycle capacity) [12]
- 3-hydroxyacyl-CoA dehydrogenase (3-HAD) increase of 38% (fatty acid oxidation enzyme) [12]
- Capillary-to-fiber ratio increase of 25%, improving oxygen delivery [16]

These adaptations shift muscle metabolism from glycolytic to oxidative, reducing lactate accumulation and improving fatigue resistance [12].

4.2.4. Satellite Cell Activation and Muscle Regeneration

Aging reduces satellite cell (muscle stem cell) number and function, impairing regeneration. PME [18]:

- Activates quiescent satellite cells via mechanotransduction pathways (Notch, Wnt) [18]
- Increases Pax7+ and MyoD+ cell proliferation [18]
- Enhances fusion of satellite cells to existing myofibers, contributing to hypertrophy [18]

This is particularly relevant in elderly patients with baseline satellite cell dysfunction [18].

4.3. Comparative Effectiveness: NMES Versus Conventional Exercise

NMES produces comparable functional outcomes to conventional exercise training in heart failure patients, with no statistically significant differences in peak VO_2, 6-minute walk distance, or quality of life between the two modalities [22,24]. This equivalence positions NMES as a viable alternative for patients unable to perform traditional exercise, rather than a superior intervention.

A landmark randomized trial directly comparing home-based functional electrical stimulation to conventional bicycle exercise in 46 patients with NYHA class II/III heart failure demonstrated equivalent improvements across multiple functional domains after 6 weeks [24]. The bicycle group improved 6-minute walk distance by 44.6 meters (95% CI, 29.3–60.9 m) while the NMES group improved by 40.6 meters (95% CI, 28.2–53.0 m). Treadmill exercise time increased 110 seconds with cycling versus 67 seconds with NMES. Maximum leg strength and quadriceps fatigue index improved similarly in both groups, with no significant between-group differences [24].

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Meta-analytic data from 13 randomized controlled trials confirmed these findings, showing nonsignificant differences in peak VO_2, 6-minute walk test distance, and quality of life when comparing NMES directly to conventional exercise [22]. Both modalities improved functional capacity, muscle strength, endothelial function, and depressive symptoms, suggesting they operate through similar physiological mechanisms [12,22].

When NMES is added to conventional exercise training in patients already capable of exercising, it provides no additional benefit. A prospective multicenter study of 91 chronic heart failure patients randomized to exercise training alone versus exercise training plus NMES found both groups achieved similar improvements in peak VO_2 (+15% vs. +14%, respectively) with no statistically significant differences between groups [25]. Quality of life and functional capacity improved equally in both arms [25].

The primary clinical value of NMES lies in its role as an alternative for patients unable to exercise, particularly those with advanced heart failure (NYHA class III–IV) [5]. The American Heart Association and Heart Failure Society of America note that benefits from NMES appear greater as heart failure severity progresses [5].

4.4. Durability of Benefits

The available literature provides limited direct evidence comparing the durability of benefits between NMES and traditional exercise after treatment cessation. However, existing data suggest that both modalities likely require ongoing participation to maintain functional gains [26].

Long-term data for conventional exercise training demonstrates that sustained participation is essential for maintaining benefits. A 10-year randomized trial in chronic heart failure patients showed that the trained group maintained peak VO_2 above 60% of predicted maximum throughout the decade, while untrained controls experienced progressive functional decline [27]. When exercise training adherence declines, benefits diminish, as observed in the HF-ACTION trial [28].

For NMES, the literature is more limited regarding post-intervention durability. Most NMES trials in heart failure patients have short intervention periods (6–12 weeks) with immediate post-intervention assessments [21,22]. One notable exception examined long-term clinical outcomes: a 6-week NMES program in elderly CHF patients (mean age 71 ± 8 years) was followed for up to 19 months, showing significantly reduced heart failure-related hospitalizations (HR 0.40, 95% CI 0.21–0.78) compared to placebo [29].

Neither modality should be viewed as providing permanent benefits after a finite treatment course. Both NMES and traditional exercise appear to require ongoing participation to maintain functional improvements in heart failure patients [26,27].

4.5. Clinical Implications

4.5.1. PME as a Bridge Therapy for Sarcopenic Cardiac Patients

PME serves as a bridge from bed rest to voluntary exercise, enabling deconditioned patients to build sufficient muscle strength and endurance to participate in conventional cardiac rehabilitation programs [16,20].

4.5.2. Addressing Low CR Participation Through Sarcopenia Reversal

With CR participation rates <10% in elderly HF patients, home-based PME offers [5,20]:

- Accessibility: No travel required; suitable for rural/underserved populations [15]
- Scalability: Low-cost devices (~$200–500) with minimal supervision [15]
- Personalization: Intensity adjustable to patient tolerance; can be initiated during bed rest [11,20]
- Sarcopenia-specific benefit: Directly targets the pathophysiology of muscle loss, unlike general CR [12]

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4.5.3. Early Initiation Is Critical

Evidence supports initiating NMES within 24 hours of cardiac surgery or acute HF admission:

- Iwatsu et al.: NMES started POD1 prevented 3-MH elevation; starting POD3 was ineffective [11]
- Fischer et al.: Daily NMES from ICU admission accelerated strength recovery 4.5-fold [34]
- Tanaka et al.: EMS within 48 hours of AHF admission improved SPPB at discharge [20]

Recommendation: Screen all elderly cardiac admissions for sarcopenia risk (age ≥75, SPPB ≤9, recent weight loss) and initiate NMES within 24–48 hours if high risk [11].

4.5.4. Combination Therapies: PME + Nutrition

Sarcopenia management requires multimodal approach:

- PME + protein supplementation: 1.2–1.5 g/kg/day protein + NMES shows synergistic effects on MPS [11,16]
- PME + vitamin D: Correcting deficiency (<20 ng/mL) enhances NMES-induced strength gains [18]
- PME + HMB (β-hydroxy-β-methylbutyrate): 3 g/day HMB + NMES reduces proteolysis more than either alone [18]

4.6. Optimal Stimulation Parameters for Sarcopenia Reversal

Table 5. Recommended PME parameters for sarcopenia reversal.

Parameter	Acute/Hypercatabolic (POD1–5, AHF)	Chronic/Rehabilitation (weeks 1–12)	Rationale
Frequency	20 Hz	50–100 Hz	20 Hz avoids fatigue in acute setting [20]; 50–100 Hz maximizes type II fiber recruitment [18]
Pulse width	250–400 μs	250–400 μs	Optimal motor nerve recruitment [15,20]
Duty cycle	5 s on / 5 s off	5 s on / 2 s off	Longer rest in acute phase prevents fatigue [11]
Intensity	10–20% MVC	Maximum tolerated (≥20% MVC)	≥20% MVC required to activate mTOR pathway [11,18]
Session duration	30–60 min	40–50 min	≥30 hours total needed for hypertrophy [15]
Frequency/week	7 days/week (daily)	5 days/week	Daily stimulation required in hypercatabolic state [11]
Electrode placement	Bilateral quadriceps (4 electrodes)	Quadriceps + hamstrings + gastrocnemius (6–8 electrodes)	Quadriceps most affected by sarcopenia [11]
Total duration	5–7 days	8–12 weeks (minimum 30 hours total) [15]	Muscle hypertrophy requires ≥8 weeks [18]

4.7. Comparison with Previous Reviews

Our findings align with and extend previous meta-analyses:

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- Gomes-Neto et al. (2016): Included 188 patients (mean age 68–75); reported improved 6MWD and QoL; did not specifically address sarcopenia [22]
- Wang et al. (2022): Focused on FES in CHF; demonstrated cardiopulmonary benefits; no muscle mass outcomes [21]
- Guo et al. (2021): Comprehensive review of molecular and neural adaptations to NMES in ageing muscle; covers mTOR signaling, protein synthesis, myostatin regulation, fiber-type adaptation, and neural/NMJ adaptations [18]

Current review: First to focus specifically on sarcopenic elderly (≥75 years) with acute and chronic HF, emphasizing muscle protein turnover, mass preservation, and functional outcomes (SPPB) over traditional exercise capacity metrics [11,15,16,20].

4.8. Limitations

4.8.1. Limitations of the Included Evidence

- Small sample sizes: Largest RCT had n = 102 (post-surgery); cardiac-specific sarcopenia trials n = 8–100 [11,15,20]
- Short follow-up: Most studies ≤3 months; long-term sustainability of muscle mass gains unknown [20]
- Heterogeneous sarcopenia definitions: Only 3/8 studies used EWGSOP2/AWGS criteria; others used frailty proxies (SPPB) [11,16]
- Lack of blinding: Inherent challenge with PME (patients feel stimulation) [15]
- Limited muscle mass measurement: Only 2 studies used ultrasound; none used gold-standard MRI or DEXA adjusted for fluid status [11]
- No muscle biopsy data: Molecular mechanisms inferred from surrogate markers (3-MH, enzyme activity); direct evidence of mTOR activation, fiber-type shifts lacking [12]
- Geographic concentration: 6/8 studies from Japan; generalizability to Western populations uncertain [15,16,20]

4.8.2. Limitations of the Review Process

Several limitations of the review process itself should be acknowledged. First, although five major databases were searched, grey literature sources (e.g., ClinicalTrials.gov, conference proceedings, dissertations) were not systematically searched, potentially missing unpublished negative studies. Second, study authors were not contacted for missing data or unpublished results. Third, formal publication bias assessment was precluded by the small number of included studies. Fourth, the search strategy was not peer-reviewed using the PRESS checklist, and database-specific adaptations, while performed, may not have captured all relevant records. Fifth, the GRADE certainty assessment inherently involves subjective judgment, particularly when downgrading for imprecision and inconsistency in small evidence bases. Finally, the inclusion of two meta-analyses [21,22] alongside primary RCTs introduced methodological heterogeneity; while these were included to provide the broadest evidence synthesis, their pooled estimates may overlap with individual study data.

4.9. Future Research Directions

Priority research questions:

1. Multicenter RCTs: Adequately powered (n ≥ 200) to detect clinical endpoints (readmission, mortality) in sarcopenia-defined populations using EWGSOP2 criteria [20]

2. Optimal duration and maintenance: Dose-response studies to determine minimum effective treatment period for hypertrophy, maintenance protocols, and long-term sustainability (>12 months) [20]

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3. Combination therapies: PME + protein supplementation (1.5 g/kg/day); PME + HMB (3 g/day); PME + resistance training; PME + myostatin inhibitors [11,16]

4. Mechanistic studies: Muscle biopsy pre/post NMES (mTOR signaling, fiber-type composition, satellite cell activity); MRI spectroscopy (mitochondrial function, intramuscular fat); proteomics/metabolomics [12]

5. Technology development: Wearable automated devices with adherence monitoring; closed-loop systems adjusting intensity based on muscle impedance; tele-rehabilitation platforms [15]

6. Cost-effectiveness analyses: Economic modeling of NMES vs. standard CR; impact on hospital length of stay, readmission, long-term care placement [5]

7. Implementation science: Barriers/facilitators to NMES adoption in CR programs; training requirements for therapists; reimbursement policies [5]

5. Conclusions

Peripheral muscle electrostimulation represents a theoretically sound, empirically supported, and clinically feasible adjunct to cardiac rehabilitation in frail elderly patients, with demonstrated anti-sarcopenic effects. The evidence demonstrates safety (no cardiovascular adverse events across 387+ participants), efficacy for function (consistent improvements in SPPB exceeding MCID), anti-sarcopenic effects (40% reduction in muscle proteolysis, preservation of muscle mass), and practical advantages (100% home-based adherence, low cost, no hemodynamic stress).

PME addresses the critical gap in cardiac rehabilitation for frail elderly patients who cannot participate in conventional exercise programs. By directly targeting skeletal muscle pathophysiology through protein anabolism stimulation, proteolysis inhibition, fiber-type transformation, and mitochondrial biogenesis, PME offers a mechanistically rational approach to reversing sarcopenia in this vulnerable population.

Future priorities include adequately powered multicenter trials with standardized sarcopenia definitions (EWGSOP2), investigation of optimal protocols and combination therapies (PME + nutritional supplementation), and implementation research to facilitate clinical adoption. As the population ages and the burden of HF-associated sarcopenia grows, PME stands poised to fill a critical therapeutic niche in geriatric cardiac care.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. Table S1: PRISMA 2020 Checklist with Page References; Table S2: Database-Specific Search Strategies for PubMed, CENTRAL, Embase, CINAHL, and Scopus; Table S3: Excluded Full-Text Studies with Reasons for Exclusion (n = 15).

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References

1. Molloy, C.; Long, L.; Mordi, I.R.; Bridges, C.; Sagar, V.A.; Davies, E.J.; Coats, A.J.; Dalal, H.; Rees, K.; Singh, S.J.; et al. Exercise-Based Cardiac Rehabilitation for Adults with Heart Failure. Cochrane Database Syst. Rev. 2024, 3, CD003331. https://doi.org/10.1002/14651858.CD003331.pub6.
2. Bozkurt, B.; Fonarow, G.C.; Goldberg, L.R.; Guglin, M.; Josephson, R.A.; Forman, D.E.; Lin, G.; Lindenfeld, J.; O'Connor, C.; Panjrath, G.; et al. Cardiac Rehabilitation for Patients with Heart Failure: JACC Expert Panel. J. Am. Coll. Cardiol. 2021, 77, 1454–1469. https://doi.org/10.1016/j.jacc.2021.01.030.
3. Fletcher, G.F.; Ades, P.A.; Kligfield, P.; Arena, R.; Balady, G.J.; Bittner, V.A.; Coke, L.A.; Fleg, J.L.; Forman, D.E.; Gerber, T.C.; et al. Exercise Standards for Testing and Training: A Scientific Statement from the American Heart Association. Circulation 2013, 128, 873–934. https://doi.org/10.1161/CIR.0b013e31829b5b44.
4. Forman, D.E.; Arena, R.; Boxer, R.; Dolansky, M.A.; Eng, J.J.; Fleg, J.L.; Gaziano, M.; Kitzman, D.W.; Lazarus, D.D.; Rich, M.W.; et al. Prioritizing Functional Capacity as a Principal End Point for Therapies Oriented to Older Adults with Cardiovascular Disease. Circulation 2017, 135, e894–e918. https://doi.org/10.1161/CIR.0000000000000483.
5. Jurgens, C.Y.; Goodlin, S.; Dolansky, M.; Ahmed, A.; Fonarow, G.C.; Boxer, R.; Arena, R.; Blank, L.; Buck, H.G.; Cranmer, K.; et al. Heart Failure Management in Skilled Nursing Facilities: A Scientific Statement from the American Heart Association and the Heart Failure Society of America. Circ. Heart Fail. 2015, 8, 655–687. https://doi.org/10.1161/HHF.0000000000000005.
6. Curcio, F.; Testa, G.; Liguori, I.; Papillo, M.; Flocco, V.; Panicara, V.; Galizia, G.; Della-Morte, D.; Gargiulo, G.; Cacciatore, F.; et al. Sarcopenia and Heart Failure. Nutrients 2020, 12, 211. https://doi.org/10.3390/nu12010211.
7. 7. von Haehling, S.; Ebner, N.; Dos Santos, M.R.; Springer, J.; Anker, S.D. Muscle Wasting and Cachexia in Heart Failure: Mechanisms and Therapies. Nat. Rev. Cardiol. 2017, 14, 323–341. https://doi.org/10.1038/nrcardio.2017.51.
8. Emami, A.; Saitoh, M.; Valentova, M.; Sandek, A.; Evertz, R.; Ebner, N.; Loncar, G.; Springer, J.; Doehner, W.; Lainscak, M.; et al. Comparison of Sarcopenia and Cachexia in Men with Chronic Heart Failure: Results from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF). Eur. J. Heart Fail. 2018, 20, 1580–1587. https://doi.org/10.1002/ejhf.1304.
9. Kinugasa, Y.; Yamamoto, K. The Challenge of Frailty and Sarcopenia in Heart Failure with Preserved Ejection Fraction. Heart 2017, 103, 184–189. https://doi.org/10.1136/heartjnl-2016-309995.
10. Fülster, S.; Tacke, M.; Sandek, A.; Ebner, N.; Tschöpe, C.; Doehner, W.; Anker, S.D.; von Haehling, S. Muscle Wasting in Patients with Chronic Heart Failure: Results from the Studies Investigating Co-Morbidities Aggravating Heart Failure (SICA-HF). Eur. Heart J. 2013, 34, 512–519. https://doi.org/10.1093/eurheartj/ehs381.
11. Iwatsu, K.; Iida, Y.; Kono, Y.; Yamazaki, T.; Usui, A.; Yamada, S. Neuromuscular Electrical Stimulation May Attenuate Muscle Proteolysis After Cardiovascular Surgery: A Preliminary Study. J. Thorac. Cardiovasc. Surg. 2017, 153, 373–379.e1. https://doi.org/10.1016/j.jtcvs.2016.09.036.
12. Saitoh, M.; Dos Santos, M.R.; Anker, M.; Anker, S.D.; von Haehling, S.; Springer, J. Neuromuscular Electrical Stimulation for Muscle Wasting in Heart Failure Patients. Int. J. Cardiol. 2016, 225, 200–205. https://doi.org/10.1016/j.ijcard.2016.09.127.
13. Konishi, M.; Kagiyama, N.; Kamiya, K.; Saito, H.; Saito, K.; Ogasahara, Y.; Maekawa, E.; Misumi, T.; Kitai, T.; Iwata, K.; et al. Impact of Sarcopenia on Prognosis in Patients with Heart Failure with Reduced and Preserved Ejection Fraction. Eur. J. Prev. Cardiol. 2021, 28, 1022–1029. https://doi.org/10.1093/eurjpc/zwaa117.
14. Cruz-Jentoft, A.J.; Bahat, G.; Bauer, J.; Boirie, Y.; Bruyère, O.; Cederholm, T.; Cooper, C.; Landi, F.; Rolland, Y.; Sayer, A.A.; et al. Sarcopenia: Revised European Consensus on Definition and Diagnosis. Age Ageing 2019, 48, 16–31. https://doi.org/10.1093/ageing/afy169.

 doi:10.20944/preprints202604.1039.v1

15. Ono, S.; Kato, M.; Seko, H.; Nakatani, E.; Omote, T.; Omote, M.; Omote, S. Randomised Crossover Trial of Home-Based Neuromuscular Electrical Stimulation Therapy as an Adjunct to Cardiac Rehabilitation in Frail Older Adult Patients with Chronic Heart Failure. Circ. Rep. 2025, 7, 231–238. https://doi.org/10.1253/circrep.CR-24-0091.
16. Pu, X.; Huang, H.; Zhao, X.; Liu, F.; Leng, Y.; Deng, Y.; Huang, L.; Zhou, X.; Xu, F.; Huang, Y.; et al. Improving Lower Limb Function and Frailty in Frail Older Patients with Acute Myocardial Infarction After Percutaneous Coronary Intervention: A Randomized Controlled Study of Neuromuscular Electrical Stimulation. Clin. Interv. Aging 2024, 19, 1163–1176. https://doi.org/10.2147/CIA.S460805.
17. Sillen, M.J.H.; Speksnijder, C.M.; Eterman, R.A.; Janssen, P.P.; Wagers, S.S.; Wouters, E.F.; Uszko-Lencer, N.H.; Spruit, M.A. Effects of Neuromuscular Electrical Stimulation of Muscles of Ambulation in Patients with Chronic Heart Failure or COPD. Chest 2009, 136, 44–61. https://doi.org/10.1378/chest.08-2481.
18. Guo, Y.; Phillips, B.E.; Atherton, P.J.; Piasecki, M. Molecular and Neural Adaptations to Neuromuscular Electrical Stimulation; Implications for Ageing Muscle. Mech. Ageing Dev. 2021, 193, 111402. https://doi.org/10.1016/j.mad.2020.111402.
19. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. BMJ 2021, 372, n71. https://doi.org/10.1136/bmj.n71.
20. Tanaka, S.; Kamiya, K.; Matsue, Y.; Yonezawa, R.; Saito, H.; Hamazaki, N.; Matsuzawa, R.; Nozaki, K.; Yamashita, M.; Wakaume, K.; et al. Efficacy and Safety of Acute Phase Intensive Electrical Muscle Stimulation in Frail Older Patients with Acute Heart Failure: Results from the ACTIVE-EMS Trial. J. Cardiovasc. Dev. Dis. 2022, 9, 99. https://doi.org/10.3390/jcdd9040099.
21. Wang, H.Y.; Chen, Y.H.; Kuan, Y.C.; Huang, S.W.; Lin, L.F.; Chen, H.C. The Effectiveness of Functional Electrical Stimulation of the Legs in Patients with Heart Failure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Clin. Rehabil. 2022, 36, 303–316. https://doi.org/10.1177/02692155211056999.
22. Gomes Neto, M.; Oliveira, F.A.; Reis, H.F.; de Sousa Rodrigues, E.; Bittencourt, H.S.; Carvalho, V.O. Effects of Neuromuscular Electrical Stimulation on Physiologic and Functional Measurements in Patients with Heart Failure: A Systematic Review with Meta-Analysis. J. Cardiopulm. Rehabil. Prev. 2016, 36, 157–166. https://doi.org/10.1097/HCR.0000000000000151.
23. Karavidas, A.; Parissis, J.; Arber, S.; Georgiadis, P.; Matsakas, E.; Adamopoulos, S.; Filippatos, G. Efficacy and Safety of Functional Electrical Stimulation of Lower Limb Muscles in Elderly Patients with Chronic Heart Failure. Eur. J. Prev. Cardiol. 2015, 22, 831–836. https://doi.org/10.1177/2047487314540546.
24. Harris, S.; LeMaitre, J.P.; Mackenzie, G.; Fox, K.A.; Denvir, M.A. A Randomised Study of Home-Based Electrical Stimulation of the Legs and Conventional Bicycle Exercise Training for Patients with Chronic Heart Failure. Eur. Heart J. 2003, 24, 871–878. https://doi.org/10.1016/s0195-668x(02)00822-9.
25. Iliou, M.C.; Vergès-Patois, B.; Pavy, B.; Corone, S.; Aeberhard, A.; Music, N.; Brun, M.C.; Cohen-Solal, A. Effects of Combined Exercise Training and Electromyostimulation Treatments in Chronic Heart Failure: A Prospective Multicentre Study. Eur. J. Prev. Cardiol. 2017, 24, 1274–1282. https://doi.org/10.1177/2047487317712601.
26. Smart, N.A.; Dieberg, G.; Giallauria, F. Functional Electrical Stimulation for Chronic Heart Failure: A Meta-Analysis. Int. J. Cardiol. 2013, 167, 80–86. https://doi.org/10.1016/j.ijcard.2011.12.019.
27. Belardinelli, R.; Georgiou, D.; Cianci, G.; Purcaro, A. 10-Year Exercise Training in Chronic Heart Failure: A Randomized Controlled Trial. J. Am. Coll. Cardiol. 2012, 60, 1521–1528. https://doi.org/10.1016/j.jacc.2012.06.036.
28. Mueller, S.; Winzer, E.B.; Duvinage, A.; Gevaert, A.B.; Edelmann, F.; Haller, B.; Pieske-Kraigher, E.; Beckers, J.; Bobenko, A.; Hommel, J.; et al. Effect of High-Intensity Interval Training, Moderate Continuous Training, or Guideline-Based Physical Activity Advice on Peak Oxygen Consumption in Patients with Heart Failure with Preserved Ejection Fraction: A Randomized Clinical Trial. JAMA 2021, 325, 542–551. https://doi.org/10.1001/jama.2020.26812.

 doi:10.20944/preprints202604.1039.v1

29. Kadoglou, N.P.; Mandila, C.; Karavidas, A.; Farmakis, D.; Liakos, A.; Parissis, J. Effect of Functional Electrical Stimulation on Cardiovascular Outcomes in Patients with Chronic Heart Failure. Eur. J. Prev. Cardiol. 2017, 24, 833–839. https://doi.org/10.1177/2047487316687428.
30. Rethlefsen, M.L.; Kirtley, S.; Waffenschmidt, S.; Ayala, A.P.; Moher, D.; Page, M.J.; Koffel, J.B.; PRISMA-S Group. PRISMA-S: An Extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst. Rev. 2021, 10, 39. https://doi.org/10.1186/s13643-020-01542-z.
31. Tong, A.; Flemming, K.; McInnes, E.; Oliver, S.; Craig, J. Enhancing Transparency in Reporting the Synthesis of Qualitative Research: ENTREQ. BMC Med. Res. Methodol. 2012, 12, 181. https://doi.org/10.1186/1471-2288-12-181.
32. Hirt, J.; Nordhausen, T.; Fuerst, T.; Ewald, H.; Appenzeller-Herzog, C. Guidance on Terminology, Application, and Reporting of Citation Searching: The TARCiS Statement. BMJ 2024, 385, e078384. https://doi.org/10.1136/bmj-2023-078384.
33. EQUATOR Network. Reporting Guidelines for Systematic Reviews and Meta-Analyses. Available online: https://www.equator-network.org/reporting-guidelines-study-design/systematic-reviews-and-meta-analyses/ (accessed on 10 April 2026).
34. Fischer, A.; Spiegl, M.; Altmann, K.; Winkler, A.; Salamon, A.; Themessl-Huber, M.; Mouhieddine, M.; Strasser, E.M.; Schiferer, A.; Paternostro-Sluga, T.; et al. Muscle Mass, Strength and Functional Outcomes in Critically Ill Patients After Cardiothoracic Surgery: Does Neuromuscular Electrical Stimulation Help? The Catastim 2 Randomized Controlled Trial. Crit. Care 2016, 20, 30. https://doi.org/10.1186/s13054-016-1199-3.