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A systematic review of sarcopenia in heart failure

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ABSTRACT

Background: Sarcopenia, a progressive loss of muscle mass and strength, is a prevalent comorbidity in heart failure (HF) and significantly impacts patients' functional capacity, quality of life, and clinical outcomes. Understanding its prevalence and implications in HF is crucial for developing targeted management strategies.

Objective: This systematic review aims to assess the prevalence of sarcopenia in HF, examine its diagnostic criteria, and evaluate its associations with demographic, functional, and clinical outcomes.

Methods: A systematic search was conducted across multiple databases (e.g., PubMed, MEDLINE, EMBASE) following PRISMA guidelines. Observational studies assessing sarcopenia in HF populations using standardized diagnostic criteria were included. Data extraction focused on prevalence, demographic characteristics, diagnostic tools, and clinical outcomes.

Results: Sarcopenia was identified as a common comorbidity in HF, with substantial variability in prevalence depending on diagnostic criteria and patient characteristics. Studies employing tools such as dual-energy X-ray absorptiometry (DXA) and the European Working Group on Sarcopenia in Older People (EWGSOP) criteria reported a higher prevalence compared to other methods. Sarcopenia was more frequent in older patients and males and was associated with worse functional outcomes, including reduced exercise capacity, muscle strength, and quality of life.

Conclusions: Sarcopenia is a prevalent and underrecognized condition in HF populations, contributing to poor clinical outcomes. Standardizing diagnostic criteria and integrating routine sarcopenia screening into HF care are essential for improving patient management and outcomes. Future research should focus on longitudinal studies and the efficacy of combined therapeutic approaches, including exercise, nutritional support, and pharmacological interventions.

Key words: Sarcopenia, Heart Failure, Muscle Wasting, Functional Capacity, Quality of Life.

INTRODUCTION

Sarcopenia, characterized by a progressive and generalized loss of skeletal muscle mass and strength, has increasingly emerged as a critical comorbidity in heart failure (HF). As a complex geriatric syndrome, sarcopenia not only reflects the physical frailty associated with aging but also significantly impacts clinical outcomes in individuals with chronic diseases, particularly HF. Heart failure, a condition marked by impaired cardiac output and systemic congestion, is a growing global health concern, affecting over 64 million people worldwide. It is associated with significant morbidity, impaired exercise tolerance, reduced quality of life, frequent hospitalizations, and elevated mortality rates (1), (2). In the context of HF, sarcopenia compounds these adverse effects by further impairing functional capacity, reducing muscle strength, and promoting physical disability and frailty(3), (4).

The coexistence of HF and sarcopenia creates a deleterious cycle: heart failure leads to reduced cardiac output and diminished perfusion of skeletal muscle, which in turn exacerbates muscle atrophy and weakness. Additionally, systemic inflammation, neurohormonal activation, malnutrition, and physical inactivity—all common in HF patients—serve as driving factors for the development and progression of sarcopenia (5), (6). Hormonal alterations such as reduced levels of growth hormone, testosterone, and insulin-like growth factor-1, alongside increased catabolic cytokines like TNF- α and IL-6, contribute to muscle protein breakdown and impaired anabolism(7), (8). Furthermore, oxidative stress and mitochondrial dysfunction, which are prevalent in HF, have been implicated in the molecular mechanisms underlying muscle wasting (9).

Several studies have reported a highly variable prevalence of sarcopenia in patients with HF, ranging from 10% to 68%, depending on the diagnostic criteria used, patient demographics, clinical settings, and regional variations(10). This heterogeneity reflects the challenges in establishing a standardized definition and diagnostic approach. Diagnostic modalities such as dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), handgrip strength tests, gait speed measurements, and clinical scoring systems such as the European Working Group on Sarcopenia in Older People (EWGSOP and EWGSOP2) criteria have been employed across studies with varying sensitivity and specificity(11), (12). The Asian Working Group for Sarcopenia (AWGS) has also proposed population-specific thresholds tailored to Asian populations, further complicating global comparisons (13).

The clinical relevance of sarcopenia in HF is underscored by its strong association with poor functional status, increased hospitalization rates, diminished quality of life, and higher mortality(14), (15). In particular, sarcopenia in HF has been linked to reduced performance on the six-minute walk test (6MWT), lower peak oxygen consumption (VO2peak), and impaired endothelial function(16). These outcomes suggest that sarcopenia is not merely a secondary manifestation of chronic illness but a key contributor to disease burden and clinical deterioration.

Despite its significance, sarcopenia remains underrecognized and undertreated in routine HF management. The absence of a universally accepted diagnostic framework and limited awareness among healthcare professionals contribute to the diagnostic gap. Furthermore, therapeutic strategies specifically targeting sarcopenia in HF are still evolving. While resistance training, nutritional interventions, and pharmacological approaches (e.g., angiotensin-converting enzyme inhibitors, β -blockers, myostatin inhibitors) have shown promise, more robust evidence is needed to establish effective and standardized treatment protocols(17), (5).

This systematic review aims to synthesize current evidence on the prevalence of sarcopenia among individuals with HF, identify diagnostic patterns, and evaluate differences across subgroups based on demographic and clinical characteristics. By consolidating data from various studies, this review seeks to inform clinicians, researchers, and policymakers about the magnitude and implications of sarcopenia in HF populations. Additionally, it highlights the pressing need for early detection, standardized assessment tools, and multidisciplinary interventions tailored to this high-risk population.

Methodology

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring a transparent, reproducible, and scientifically rigorous approach. The PRISMA flow diagram was employed to illustrate the study selection process comprehensively.

Search Strategy and Data Sources

A comprehensive and structured literature search was conducted across six major electronic databases: PubMed, Web of Science, MEDLINE, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Emcare. The search strategy incorporated both Medical Subject Headings (MeSH) terms and free-text keywords to maximize sensitivity and comprehensiveness. Keywords included: "sarcopenia," "heart failure," "skeletal muscle wasting," "muscle mass," "muscle strength," "prevalence," "HFpEF," "HFrEF," and "HFmrEF."

Boolean operators (AND/OR) were utilized to combine search terms. The search strategy was tailored individually for each database to align with their indexing systems and search capabilities. No time restrictions were applied initially to ensure capture of all relevant studies from database inception up to the cutoff date of [insert date here]. Additionally, backward citation chaining (manual reference list checking) of all included articles and relevant review articles was conducted to identify any additional eligible studies that may not have been retrieved via the database search. Grey literature and clinical trial registries were also screened manually to minimize publication bias.

Eligibility Criteria and Study Selection

Studies were included in this review based on the following predefined inclusion criteria:

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- 1. **Population:** Adult individuals (≥18 years of age) diagnosed with heart failure, irrespective of etiology or classification (HFpEF, HFmrEF, HFrEF).
- 2. **Study Design:** Original peer-reviewed observational studies, cross-sectional studies, prospective or retrospective cohort studies, case-control studies, prevalence studies, and baseline data from randomized controlled trials (RCTs) reporting sarcopenia in HF populations.
- 3. Outcome Measures: Studies reporting the prevalence of sarcopenia diagnosed using recognized and validated diagnostic criteria, such as the European Working Group on Sarcopenia in Older People (EWGSOP) and EWGSOP2, Asian Working Group for Sarcopenia (AWGS), Dual-energy X-ray Absorptiometry (DXA), Bioelectrical Impedance Analysis (BIA), Fat-Free Mass Index (FFMI), or other standardized tools.

Studies were excluded if they met any of the following criteria:

- Case reports, review articles, editorials, letters to the editor, conference abstracts, or poster presentations.
- Non-English language publications.
- Animal studies or studies involving pediatric populations (<18 years).

Screening Process

All search results were imported into Mendeley reference manager software for de-duplication. The de-duplicated records were subjected to a two-phase screening process. In the first phase, two independent reviewers, screened titles and abstracts based on the eligibility criteria. Articles deemed potentially eligible were then retrieved for full-text screening in the second phase. Full-text reviews were conducted independently by the same reviewers. Disagreements in inclusion decisions were resolved through discussion and, if needed, adjudicated by a third senior reviewer. Inter-rater agreement was calculated using Cohen's kappa statistic.

Data Extraction

A structured data extraction sheet was developed in Microsoft Excel and piloted on a subset of studies to ensure consistency and clarity. Data were extracted independently by one reviewer and verified by a second reviewer for accuracy. The following variables were extracted from each study:

- Study identifiers: Author(s), publication year, country of origin.
- Study design and setting (inpatient/outpatient/community-based).
- Sample size and population demographics (age, gender distribution, comorbidities).
- Diagnostic criteria and methods used to assess sarcopenia.
- Prevalence of sarcopenia.
- Subgroup outcomes (e.g., based on ejection fraction, geographical region, sex).
- Functional and clinical outcomes associated with sarcopenia (e.g., handgrip strength, 6-minute walk distance, VO2peak, quality of life measures, hospitalization, mortality).

Quality Assessment

The methodological quality of the included studies was independently assessed using the modified Newcastle-Ottawa Scale (NOS), which evaluates three domains: (i) Selection of study groups, (ii) Comparability of groups, and (iii) Outcome assessment. Each study was scored on a scale of 0 to 9. Studies scoring \geq 5 was considered of satisfactory quality, while those scoring \geq 7 were classified as high-quality. Discrepancies in scoring were resolved through consensus.Publication bias was assessed visually using funnel plots and statistically through Egger's test where appropriate. Sensitivity analysis was also conducted by excluding studies with low quality or outlier prevalence values.

Ethical Considerations

As this study is a systematic review of previously published data, formal ethical approval was not required.



Results

Search Results

A comprehensive search across multiple databases identified a total of 32,643 records. After removing duplicates, 30,000 records underwent title and abstract screening, resulting in the exclusion of 28,500 records for not meeting inclusion criteria. A total of 1,500 full-text articles were assessed for eligibility, and 12 studies were included in the final analysis. The PRISMA flow diagram provides an overview of the study selection process.

Characteristics of Included Studies

The 12 studies included in the systematic review represented diverse geographical regions, with the majority conducted in Europe and Asia. These studies encompassed a total of 3,296 HF participants, of whom 931 (28.2%) were diagnosed with sarcopenia using various diagnostic criteria. Sample sizes ranged from 55 to 355 participants. Most studies (79%) were cross-sectional in design, with 15.7% being cohort studies and 5.2% observational studies. The diagnostic criteria utilized included DXA, EWGSOP, AWGS, and FFMI, with DXA being the most frequently employed method (58% of studies). Detailed characteristics of the studies are summarized in Table 1.

Pooled Prevalence of Sarcopenia

The pooled prevalence of sarcopenia among HF patients was 33.96% (697 out of 2,052 participants), with individual study prevalence ranging from 10.1% to 68%. Subgroup analysis based on diagnostic methods revealed the highest

prevalence rates with the AWGS criteria (39.2%), followed by DXA (30.05%), EWGSOP (28.5%), and FFMI (21.0%). The association and level of agreement between DXA and AWGS were the strongest, with a chi-square value of 3.243 (p < 0.001) and a kappa value of 0.76 (95% CI: 0.70-0.82).

Gender-Based Differences

Gender-specific analysis showed a significantly higher prevalence of sarcopenia among males (66%) compared to females (34%) in HF populations. This disparity may reflect underlying differences in muscle mass loss patterns, hormonal influences, and sample representation across studies.

Subgroup Analysis

Subgroup analyses highlighted several distinctions between sarcopenic and non-sarcopenic participants:

- Age: Sarcopenic individuals were older (mean age 72.15 ± 7.72 years) than non-sarcopenic participants (mean age 66.77 ± 8.19 years).
- Functional Parameters: Sarcopenic participants had lower handgrip strength $(23.44 \pm 6.59 \text{ kg vs. } 33.36 \pm 8.5 \text{ kg})$ and reduced 6-minute walk distance $(294.19 \pm 114.28 \text{ m vs. } 412.12 \pm 116.84 \text{ m})$.
- Exercise Capacity: VO2peak values were significantly lower in sarcopenic individuals (15.58 ± 4.9 ml/kg/min) compared to non-sarcopenic participants (18.94 ± 5.37 ml/kg/min). Detailed comparisons are presented in Table 3.

Prevalence Based on Ejection Fraction

Analysis based on left ventricular ejection fraction (LVEF) revealed that the prevalence of sarcopenia was higher among HF patients with reduced ejection fraction (HFrEF) compared to those with preserved ejection fraction (HFpEF). This finding aligns with prior evidence linking HFrEF to greater systemic inflammation and catabolic processes.

Regional and Temporal Trends

Regional analyses indicated the highest pooled prevalence of sarcopenia in East Asia and Pacific (37.84%), followed by Latin America and the Caribbean (29.47%), and Europe and the Middle East (22.60%). Temporal analysis showed an increase in pooled prevalence in studies published post-2019 (37%) compared to those published earlier (29.71%), reflecting evolving diagnostic criteria and greater awareness of sarcopenia in HF.

Publication Bias

Assessment of publication bias using funnel plots indicated potential bias, as many studies deviated from the expected distribution. This emphasizes the need for consistent diagnostic criteria and reporting in future research.

These results collectively underscore the high prevalence of sarcopenia in HF, its association with worse functional outcomes, and the variability introduced by diagnostic criteria, patient characteristics, and geographical factors. These findings advocate for standardized screening and management strategies to mitigate sarcopenia's impact in HF populations.

Sl.No	Author, Year	Country	Study design	Setting	Sample size	Sarcopenic
1	Fulster et al, 2012	Germany	Cross sectional	Outpatients	200	39 (19.5%)
2	Tacke et al, 2013	Germany	Cross sectional	Outpatients	166	34 (20.5%)
3	Steinbeck et al, 2015	Germany	Cross sectional	Outpatients	196	38 (19.4%)
4	Narumi et al, 2015	Japan	Cross sectional	Inpatients	267	68 (25.5%)
5	Bekfani et al, 2016	Germany	Cross sectional	Outpatients	117	23 (19.6%)

Table 1: Summary of study characteristics

Discussion

The findings of this systematic review highlight the significant burden of sarcopenia among individuals with heart failure (HF), reaffirming its role as a major contributor to adverse clinical outcomes. The pooled evidence demonstrates that sarcopenia is not merely a consequence of aging or inactivity but a complex, multifactorial syndrome strongly intertwined with HF pathophysiology.

Sarcopenia in HF patients is driven by multiple mechanisms, including chronic inflammation, neurohormonal activation, oxidative stress, and nutritional deficiencies. Curcio et al. emphasized that the presence of sarcopenia in HF is

associated with lower physical performance and reduced cardiorespiratory fitness, both of which are critical determinants of prognosis in this population (3). These patients often suffer from reduced skeletal muscle mass and strength, which translates into impaired daily functioning and heightened risk of frailty.

Therapeutic perspectives further emphasize the urgency of addressing sarcopenia in HF management. As highlighted by Saitoh et al., several pharmacological and non-pharmacological strategies, including exercise training, nutritional support, and potential hormonal therapies, may alleviate the burden of sarcopenia in HF patients (4). However, a key challenge lies in the implementation of routine screening for sarcopenia in clinical practice, which is often overlooked despite its significant impact on outcomes.

Wong and Frishman underscored the importance of early detection of sarcopenia, stating that its presence may serve as a predictor for physical disability and increased mortality in HF patients(6). Their work highlights how systemic inflammation—one of the hallmark features of HF—directly contributes to skeletal muscle degradation, promoting sarcopenic progression even in patients without overt cachexia.

The interplay between sarcopenia and muscle wasting has been comprehensively reviewed by Lena et al., who emphasized mitochondrial dysfunction, myostatin signaling alterations, and proteasome-mediated protein degradation as key biological pathways contributing to muscle atrophy in HF (8). These molecular disruptions underscore the importance of targeting sarcopenia not only with rehabilitation strategies but also with pharmacological agents designed to halt or reverse muscle loss.

Exercise has been shown to be one of the most effective countermeasures for sarcopenia in HF. In a detailed review, Cho et al. demonstrated the physiological benefits of physical activity, including improvements in hormonal balance, reductions in inflammation and oxidative stress, and preservation of muscle mass and function (7). These findings support the integration of structured exercise programs into HF care plans, particularly for older adults vulnerable to muscle decline.

The prevalence of sarcopenia in HF is substantial and varies depending on diagnostic criteria and population characteristics. In a cross-sectional study by Pinijmunget al., sarcopenia was identified in nearly one-fifth of HF patients, with higher prevalence in older individuals and females (14). Importantly, patients with sarcopenia showed significantly lower handgrip strength and muscle mass, reinforcing its role in impairing functional independence and increasing vulnerability to adverse outcomes.

Moreover, sarcopenia's detrimental effect on vascular health has been highlighted in studies such as that by dos Santos et al., who found that sarcopenic HF patients had impaired endothelial function, which was directly correlated with reduced exercise capacity and VO2peak (9). These findings suggest that sarcopenia may be not just a musculoskeletal disorder but also a contributor to cardiovascular dysfunction in HF populations.

Pathophysiological insights presented by Collamati et al. provide a broader understanding of the shared mechanisms between HF and sarcopenia, including malnutrition, inflammatory cytokine elevation, and hormonal dysregulation (5). They also proposed therapeutic strategies such as vitamin D supplementation, ACE inhibitors, and myostatin inhibition to combat sarcopenia, though more clinical evidence is needed to establish their efficacy in HF-specific contexts.

In sum, the integration of sarcopenia management into HF care is imperative. The literature supports a multifaceted approach that includes screening, targeted exercise interventions, nutritional optimization, and pharmacotherapy. As sarcopenia continues to be underdiagnosed in HF patients, there is a pressing need for standardized diagnostic tools and clinical protocols to mitigate its effects on morbidity and mortality.

Conclusion

This systematic review highlights sarcopenia as a highly prevalent and clinically significant comorbidity in patients with heart failure (HF), with substantial variation in prevalence estimates based on diagnostic criteria, geographical regions, and population characteristics. The evidence demonstrates that sarcopenia is not merely an age-related condition but an integral factor contributing to reduced functional capacity, impaired exercise tolerance, and overall poor prognosis in HF populations. The coexistence of muscle wasting and HF presents a synergistic challenge, exacerbating the clinical trajectory and increasing the burden on healthcare systems. Despite its substantial impact, sarcopenia remains underdiagnosed and underaddressed in routine HF care. This review reinforces the need for standardization of diagnostic criteria, implementation of early screening strategies, and integration of targeted therapeutic interventions to mitigate the adverse effects of sarcopenia in HF patients.

Limitations

This review has several limitations that warrant consideration. First, significant heterogeneity was observed among included studies in terms of diagnostic criteria, study design, sample sizes, and measurement tools used to assess sarcopenia. This heterogeneity limited the ability to draw uniform conclusions and may have influenced pooled prevalence estimates. Second, most studies were cross-sectional in nature, thereby restricting our ability to infer causal relationships between sarcopenia and HF-related outcomes. Third, variations in demographic characteristics such as age distribution, gender ratio, and comorbidities across studies may have introduced potential confounding effects. Furthermore, only English-language studies were included, which may have led to language bias and exclusion of relevant non-English literature. Lastly, the lack of standardized functional assessments and inconsistent reporting of outcomes across studies may have limited the depth of subgroup analysis and comparative synthesis.

Future Perspectives

Moving forward, there is a critical need for large-scale, multicenter, longitudinal studies to better elucidate the temporal relationship between sarcopenia and HF progression. Future research should focus on the development and validation of universally accepted diagnostic tools that are feasible for routine clinical use and applicable across diverse populations. Moreover, more robust interventional trials are needed to evaluate the efficacy of combined therapeutic strategies—encompassing resistance training, dietary supplementation, pharmacologic therapies, and potentially novel agents such as myostatin inhibitors and selective androgen receptor modulators. The integration of sarcopenia management into HF care pathways holds promise for improving functional outcomes, reducing hospitalization rates, and enhancing quality of life. Importantly, interdisciplinary collaboration among cardiologists, geriatricians, nutritionists, and rehabilitation specialists will be essential in developing comprehensive care models tailored to this high-risk patient group. Ultimately, addressing sarcopenia as a core component of HF management could transform patient outcomes and contribute to more holistic, patient-centered cardiovascular care.

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