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Impact of heart failure on skeletal muscle: an overview

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ABSTRACT Heart failure (HF) is a complex clinical syndrome that promotes high morbidity and multi-systemic damage. Skeletal muscle can be directly affected by HF through a loss of physical capacity and various inflammatory, hormonal, and metabolic mechanisms observed in this cardiac condition, which collectively contribute to a high prevalence of sarcopenia in HF patients. Therefore, the aim of this review was to compile the main recent clinical and epidemiological data on muscle health in HF patients. Nine studies were selected from systematic reviews and clinical trials, which demonstrated a high prevalence of sarcopenia in patients with HF, particularly in males, hospitalized patients, the elderly, and those with HF with reduced ejection fraction. Oxidative stress markers and higher levels of natriuretic peptides were also observed in HF patients who exhibited damaged muscle parameters. Furthermore, the overall deterioration of prognosis in HF was associated with criteria defining sarcopenia, such as low muscle strength and lean mass loss. These findings reinforce the importance of evaluating skeletal muscle in HF patients, which can provide improvements in morbidity and functionality.

Heart failure (HF) is a complex syndrome, characterized by structural or functional heart impairment, which generates elevated intracardiac pressures or inappropriate cardiac output, culminating in a set of typical signs and symptoms, such as dyspnea, fatigue, and peripheral edema.[1-3]

The HF can be classified in different ways. From the left ventricular ejection fraction (LVEF), the HF is divided into: HF with preserved ejection fraction (HFpEF), when LVEF ≥ 50%; HF with mildly reduced ejection fraction (HFmrEF), if LVEF is 41%–49%; and HF with reduced ejection fraction (HFrEF), when LVEF ≤ 40%.[1,2] The New York Heart Association functional classification is used to assess the severity of the symptoms of HF. It is also common to categorize HF into chronic or acute.[1,3]

Sarcopenia is characterized by loss of mass and skeletal muscle function, which tends to progress with age and is associated with various adverse health effects, including loss of functionality and increased morbidity.[4,5]

Due to the heart's inability to supply adequate oxygen to the tissues, HF can generate a cardiac cachexia picture involving loss of muscle, bone, and adipose tissue.[6,7] The impairment of skeletal muscle in HF involves structural, metabolic, and functional changes that favor catabolism.[6]

This review aims to assess the impact of HF on skeletal muscle health by compiling the main current clinical and epidemiological data on the subject.

The present study consists of an integrative review that maps the state of the art on the consequences of HF on skeletal muscle health, based on scientific evidence developed over the last decade.

For data selection, the databases of PubMed and the Cochrane Library were consulted. In each one, three advanced searches were conducted, using the Boolean operator "AND", from the following descriptors, taken from the Medical Subject Headings (MeSH): 'heart failure' AND 'skeletal muscle', 'heart failure' AND 'sarcopenia', and 'heart failure' AND 'muscle strength'. We included clinical trials (randomized or not), meta-analyses, and systematic reviews, all published in the last 10 years (considering the end of the first half of 2024), that dealt with epidemiological data on the defining parameters of sarcopenia and other potential characteristics that indicate loss of function and muscle quality in HF patients, as well as those that sought to elucidate biomolecular mechanisms involved in its etiology and progression. Studies addressing sarcopenia therapy in HF were excluded, as were those that fell outside the proposed topic, that did not have their text available, or that were duplicated. In both databases, the filters were included with the period and types of studies mentioned ab-

ove, such as the presence of the descriptors selected in the title, abstract, or keywords.

Two researchers independently conducted the qualitative selection of the articles in a blinded manner, reading their titles, abstracts, and, if necessary, the full text, while evaluating their suitability to the topic. To do this, we used the application Rayyan® QRCI (Rayyan Systems Inc., Cambridge, MA, USA) with the blind mode enabled. After the initial selection, the cases of disagreements were evaluated and resolved with the help of a third author.

In Figure 1, there is the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart, with the detailed process of inclusion and exclusion of articles.

Initially, 153 articles were found, of which 21 articles were excluded by duplicity. The remaining 132 articles were first evaluated by title and abstract, which excluded 122 more studies. The remaining 10 articles were read in full by the two reviewers, with the exclusion of one article for not fully agreeing with the thematic proposal, and nine articles were finally selected. Table 1 brings together the baseline characteristics of the nine studies included.

Four of the selected studies addressed the prevalence of sarcopenia in patients with HF, providing general prevalence data along with stratifications by gender, ejection fraction, continent of origin, and follow-up (inpatient or outpatient).[8-11]

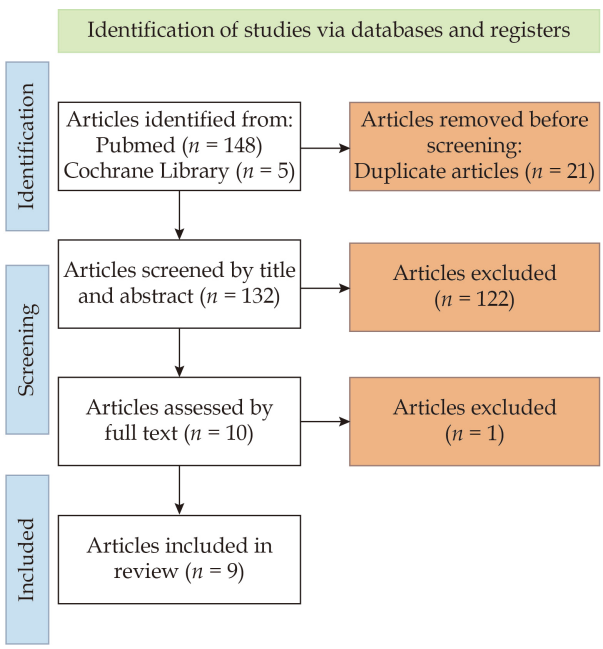

Figure 1 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) fluxogram with the selection process of articles for composition of the literature review.

Systematic review and meta-analysis by Zhang, *et al*.[8] demonstrated a variation in the prevalence of sarcopenia in patients with HF of 10% to 69%, with a grouped general prevalence of 34% (95% CI: 22%–47%, $I^2 = 96.59\%$, $P < 0.001$). A meta-analysis form Chen, *et al*.[9] revealed a combined prevalence of 31% (95% CI: 24%–39%, $I^2 = 98\%$, $P < 0.01$). Chandrashekhar Iyer, *et al*.[10] found similar grouped prevalence data: 33.96%, with a range between 10.1% and 68%. Zuo, *et al*.[11] evaluated the prevalence of sarcopenia in patients with cardiovascular diseases, stratified into subgroups according to the presented clinical condition, where the combined prevalence of sarcopenia was 32% (95% CI: 23%–41%) in chronic HF patients and 61% (95% CI: 49%–72%) in patients with acute decompensated HF. Table 1 shows the aggregated prevalence data from the four studies above.

Comparative analysis showed a higher prevalence of sarcopenia in men than in women. The meta-analyses by Chen, *et al*.[9] and Zhang, *et al*.[8] obtained similar pooled data: in the former, sarcopenia was present in 34% of men (95% CI: 23%–45%, $I^2 = 97\%$, $P < 0.01$) and 32% of women (95% CI: 20%–43%, $I^2 = 96\%$, $P < 0.01$); in the latter, 37% in men (95% CI: 26%–49%, $I^2 = 93.65\%$, $P = 0.803$) versus 33% in women (95% CI: 13%–58%, $I^2 = 95.45\%$, $P = 0.803$). The findings of Chandrashekhar Iyer, *et al*.[10] pointed to a greater discrepancy between the sexes (66% of sarcopenia in men versus 34% in women, $I^2 = 84\%$, $P < 0.0001$).

The prevalence of sarcopenia in hospitalized patients with HF was approximately twice that found in patients with outpatient follow-up, according to the data from two meta-analyses.[8,9] The study by Zhang, *et al*.[8] indicated the presence of sarcopenia in 55% of hospitalized patients (95% CI: 43%–66%, $I^2 = 87.17\%$, $P < 0.001$) and in 26% of outpatients (95% CI: 16%–37%, $I^2 = 92.45\%$, $P < 0.001$), while the meta-analysis of Chen, *et al*.[9] found a prevalence of 39% among inpatients (95% CI: 29%–50%, $I^2 = 99\%$, $P < 0.01$) and 20% in outpatient settings (95% CI: 12%–28%, $I^2 = 90\%$, $P < 0.01$). Chen, *et al*.[9] also analyzed the prevalence among different age groups, observing a higher presence of sarcopenia in patients aged 65 years or older [31% (95% CI: 22%–41%, $I^2 = 99\%$, $P < 0.01$) *vs*. 25% (95% CI: 13%–36%, $I^2 = 97\%$, $P < 0.01$) in younger patients]. Zuo, *et al*.[11] conducted an analysis of HF stratification in two categories based on the ejection fraction, demonstrating a difference between patients with HFpEF (15%) and HFrEF (21%).

Furthermore, two studies conducted a regional epidemiological stratification.[9,10] In the study by Chen, *et al*.[9] the grouped prevalence reached 35% in the Asian population (95%

Table 1 General characteristics of the nine selected studies and the main findings related to muscle health in patients with HF.

Study	Objective of the study	Type of study	Population	Considerations /Findings
Zhang, *et al.*[8]	Estimate the overall prevalence of sarcopenia in patients with HF	Systematic review and meta-analysis	Men and women ≥ 18 years with HF (n = 1.742)	Group prevalence of sarcopenia of 34% (95% CI: 22%–47%, I^2 = 96.59%)
Chen, *et al.*[9]	Investigate the epidemiological characteristics of sarcopenia in the population with HF and explore its association with poor prognosis in HF	Systematic review and meta-analysis	Men and women ≥ 18 years with HF (n = 68.556)	Combined prevalence of 31% (95% CI: 24%–39%, I^2 = 98%, P < 0.01), higher in subjects ≥ 65 years (31% *vs.* 25%) and with HFrEF (28% *vs.* 18%)
Chandrashekhar Iyer, *et al.*[10]	Investigate the general prevalence of sarcopenia in HF	Systematic review	Men and women ≥ 18 years with HF (n = 2.052)	Combined prevalence of 33.96%, ranging from 10.1% to 68%, being more common in men (66% *vs.* 34%, I^2 = 84%, P < 0.0001)
Zuo, *et al.*[11]	Investigate the prevalence of sarcopenia in patients with CVD compared to the general population	Systematic review and meta-analysis	Men and women ≥ 18 years of age, with (n = 4.327) and without CVD (n = 9.541)	Combined prevalence of 35% (95% CI: 28%–42%) in patients with CVD, being 32% (95% CI: 23%–41%) in chronic HF patients and 61% (95% CI: 49%–72%) in acute HF. Combined prevalence in the general population of 13% (95% CI: 9%–17%)
Yokota, *et al.*[12]	Evaluate whether systemic oxidative stress, indicated by TBARS levels, is associated with exercise intolerance and muscle abnormalities in the HF	Clinical screening	Men with (n = 17) and without HF (n = 13)	Significantly higher TBARS levels in HF carriers (5.1 ± 1.1 μmol/L *vs.* 3.4 ± 0.7 μmol/L, P < 0.01), with worse muscle aerobic and anaerobic capacity associated with systemic oxidative stress
Prokopidis, *et al.*[13]	Evaluate the association between sarcopenia and BNP/NT-proBNP levels in patients with HF	Systematic review and meta-analysis	Samples from 16 observational studies of patients with HF and mean age ≥ 50 years. Different samples for each analysis. BNP levels in patients with (n = 372) and without (n = 816) sarcopenia; NT-proBNP levels in patients with (n = 500) and without (n = 852) sarcopenia; BNP levels in patients with (n = 836) and without (n = 2190) low ALM; NT-proBNP levels in patients with (n = 382) and without (n = 425) low ALM	Sarcopenia associated with higher levels of BNP (mean differences: 87.76, 95% CI: 20.74–154.78, I^2 = 61%, P = 0.01) and NT-proBNP (mean differences: 947.45, 95% CI: 98.97–1795.93, I^2 = 35%, P = 0.03). Low ALM associated with higher levels of BNP (mean differences: 118.95, 95% CI: 46.91–191.00, I^2 = 93%, P < 0.01) and NT-proBNP (mean differences: 672.01, 95% CI: 383.72–960.30, I^2 = 2%, P < 0.01)
Konishi, *et al.*[14]	Investigate the association between blood kynurenine and chagnes in skeletal muscles in patients with HF	Clinical screening	Men and women with (n = 249) and without (n = 45) HF	Higher kynurenine levels in HFpEF and HFrEF carriers than in the control group 3.5 ± 1.5 μmol/L, 3.4 ± 1.3 μmol/L and 2.4 ± 1.1 μmol/L, P < 0.001). In patients with HF, there was an inverse correlation between kynurenine levels with handgrip strength (r = −0.26, P < 0.01), maximum oxygen consumption (r = −0.29, P < 0.01) and walking distance of 6 min (r = −0.23, P < 0.01)
Saied, *et al.*[15]	Determine whether sarcopenia is linked to the administration of specific HF-related medicines	Systematic review and meta-analysis	Men and women ≥ 50 years with (n = 334) and without (n = 640) sarcopenia	Lower ALM was associated with lower use of ACEI/ARBs (OR = 0.68, 95% CI: 0.50–0.90, I^2 = 12%, P < 0.01). No differences were found in the use of beta-blockers (OR = 0.84, 95% CI: 0.63–1.12, I^2 = 7%, P = 0.24) and loop diuretics (OR = 1.19, 95% CI: 0.87–1.63, I^2 = 0, P = 0.27)
Prokopidis, *et al.*[16]	Evaluate sarcopenia and its components as prognostic factors in HF	Systematic review and meta-analysis	Men and women ≥ 18 years with HF	There was no association between sarcopenia and prediction of mortality in 1–2 years (HR = 1.35, 95% CI: 0.76–2.38, I^2 = 54%, P = 0.31). Low muscle mass of psoas (HR = 2.20, 95% CI: 1.26–3.83, I^2 = 87%, P < 0.01) and low speed (HR = 1.45, 95% CI: 1.20–1.74, I^2 = 0, P < 0.01) were associated with higher mortality for all causes

ACEI: angiotensin-converting enzyme inhibitor; ALM: appendicular lean mass; ARBs: angiotensin II receptor blockers; BNP: B-type natriuretic peptide; CVD: cardiovascular disease; HF: heart failure; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; NT-proBNP: N-terminal pro B-type natriuretic peptide; TBARS: thiobarbituric acid reactive substances.

CI: 0.22–0.48, I^2 = 98%, P < 0.01), 31% in the European population (95% CI: 0.17–0.45, I^2 = 96%, P < 0.01) and 25% in the American population (95% CI: 0.14–0.37, I^2 = 96%, P < 0.01). Chandrashekhar Iyer, *et al*.[10] demonstrated a combined prevalence of 29.47% in Latin America and the Caribbean (based on three studies), 37.84% in East Asia and the Pacific (seven studies included), and 22.60% in two distinct regions of the Middle East and Europe (including one study from each region).

Biochemical changes and their relationship with structural and functional changes in skeletal muscle were evaluated in four of the nine studies included in this review.

Serum levels of thiobarbituric acid reactive substances (TBARS), a marker that points to lipid peroxidation, were significantly higher in patients with HF when compared to the control group (5.1 ± 1.1 μmol/L *vs.* 3.4 ± 0.7 μmol/L, P < 0.01), while the serum activity of superoxide dismutase, which has antioxidant action, was lower in HF patients (9.2 ± 7.1 units/L *vs.* 29.4 ± 9.7 units/L, P < 0.01).[12] The same study also analyzed the energetic metabolism of skeletal muscle through magnetic resonance spectroscopy. The data obtained revealed that the one-repetition maximum load of the plantar flexion exercise was significantly lower in the HF group than in the control group (35 ± 6 kg *vs.* 40 ± 6 kg, P = 0.02), and there was also a greater loss of muscle phosphocreatine during exercise in individuals with HF. In addition, the content of intramyocellular lipids (IMCL) in the resting leg muscle, one of the markers used in the evaluation of myosteatosis, was significantly increased in the HF group (4.0 ± 2.1 mmol/kg/moist weight *vs.* 1.6 ± 0.9 mmol/kg/moist weight, P < 0.01).[12]

Systematic review and meta-analysis of Prokopidis, *et al*.[13] showed that in individuals with HF there was an association between the presence of sarcopenia and higher levels of B-type natriuretic peptide (BNP) and its derivative N-terminal fragment (NT-proBNP) (mean differences: 87.76, 95% CI: 20.74–154.78, I^2 = 61%, P = 0.01; 947.45, 95% CI: 98.97–1795.93, I^2 = 35%, P = 0.03, respectively). As an additional finding in the study of Zhang, *et al*.[8] an association between higher levels of BNP was also observed in three of four studies that evaluated these biomarkers.

Plasma kynurenine was evaluated in the study by Konishi, *et al*.[14] They observed higher levels of this muscle metabolite in HF patients, as well as a negative correlation between kynurenine and muscle parameters, such as handgrip strength (r = -0.26, P < 0.01), peak oxygen consumption (r = −0.29, P < 0.01), and the 6-minute walk distance (r = −0.23, P < 0.01).

One included study evaluated a possible association between the pharmacological treatments for HF and the presence of sarcopenia.[15] The systematic review and meta-analysis of observational studies found no association between sarcopenia and the use of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blockers (ARBs) (OR = 0.78, 95% CI: 0.54–1.13, I^2 = 45%, P = 0.19), beta-blockers (OR = 0.95, 95% CI: 0.57–1.57, I^2 = 61%, P = 0.83), loop diuretics (OR = 1.09, 95% CI: 0.73–1.63, I^2 = 47%, P = 0.68), and statins (OR = 0.80, 95% CI: 0.48–1.34, I^2 = 61%, P = 0.40). However, when evaluating different sarcopenia criteria individually, an association was observed between low appendicular lean mass and a lower use of ACEI/ARBs (OR = 0.68, 95% CI: 0.50–0.90, I^2 = 12%, P < 0.01). The isolated evaluation of strength and physical performance was not sufficient for inclusion in the meta-analysis, but in one of the studies included, the presence of low handgrip strength was associated with a higher percentage of statin use (63% *vs.* 43%), loop diuretics (88% *vs.* 82%), as well as a lower percentage of ACEI/ARBs use (44% *vs.* 54%).[15]

Three of the nine included studies evaluated the impact of sarcopenia on HF prognosis.

The systematic review and meta-analysis by Prokopidis, *et al*.[16] evaluated sarcopenia and its components in isolation as potential prognostic factors in patients with HF. Sarcopenia was not a significant predictor for all-cause mortality at 1–2 years (HR = 1.35, 95% CI: 0.76–2.38, I^2 = 54%, P = 0.31). Regarding sarcopenia components, low psoas muscle mass (HR = 2.20, 95% CI: 1.26–3.83, I^2 = 87%, P < 0.01) and slow gait speed (HR = 1.45, 95% CI: 1.20–1.74, I^2 = 0, P < 0.01) were significant prognostic factors for mortality in HF, while low handgrip strength was not (HR = 1.24, 95% CI: 0.94–1.62, I^2 = 0, P = 0.13). When evaluating the association between reduced handgrip strength and mortality at 1–3 years, after excluding a study that evaluated mortality at 8.7 years, this sarcopenia parameter was found to be a predictor of mortality (HR = 1.47, 95% CI: 1.04–2.07, I^2 = 0, P = 0.03). Furthermore, improvement in appendicular lean mass and gait speed was observed to significantly reduce mortality.

Similarly, the study by Chen, *et al*.[9] showed that sarcopenia was associated with a poor prognosis in HF, with a pooled hazard ratio of 1.64 (95% CI: 1.20–2.25, I^2 = 94.0%, P < 0.01). Subgroup analysis of adverse outcomes showed that sarcopenia was mainly associated with an increased risk of all-cause mortality (HR = 2.06, 95% CI: 1.52–2.80, I^2 = 40.0%, P < 0.01) and hospitalization (HR = 1.52, 95% CI: 1.40–1.65, I^2 = 0, P < 0.01). Furthermore, phenotypic sub-analysis dem-

onstrated that sarcopenia was associated with an increased risk of poor prognosis in patients with HFrEF (HR = 2.77, 95% CI: 1.29–5.95, I^2 = 48.0%, P = 0.01), but not in those with HFpEF (HR = 1.61, 95% CI: 0.82–3.16, I^2 = 81.0%, P = 0.17).

The study by Konishi, *et al*.[14] although not directly evaluating the prognosis of HF in patients with and without sarcopenia, assessed prognosis according to plasma kynurenine levels, a marker associated with muscular health deterioration. They observed that patients in the highest kynurenine tertiles had a worse prognosis, with multivariate analysis demonstrating that higher kynurenine levels were predictors of death regardless of age, gender, body mass index, and hemoglobin (HR = 1.46, 95% CI: 1.15–1.86 for 1 μmol/L increase in kynurenine, P < 0.01).

The high prevalence of sarcopenia in HF patients can be attributed to a combination of factors. These two conditions share pathogenic pathways, including increased oxidative stress, chronic inflammation, endothelial dysfunction, reduced peripheral blood flow, hormonal changes, and malabsorption/malnutrition.[7] Functional impairment is commonly observed in HF patients and is associated with increased risk of death and hospitalization.[17] Physical inactivity, which often results from this functional limitation, is an important risk factor for sarcopenia.[18] Key pro-inflammatory cytokines in the pathophysiology of HF, such as interleukin-6 and tumor necrosis factor-alpha, potentiate the proteolysis and apoptosis of skeletal muscle.[7] Furthermore, HF leads to liver congestion, edema, and intestinal hypoperfusion, which contribute to poor nutrient absorption. This condition, coupled with high resting energy expenditure due to impaired myocardial function, causes catabolic activity to predominate, resulting in loss of muscle mass and strength.[7,19,20] Figure 2 compiles the main pathophysiological mechanisms that explain the high prevalence of sarcopenia in patients with HF.

There is no well-established cause for the higher incidence of sarcopenia in men with HF compared to women, as consistently observed in systematic reviews and meta-analyses.[8-10] One possible explanation is an association between male hypogonadism and HF, whereby lower endogenous testosterone synthesis leads to a more intense loss of muscle mass in men affected by this heart condition.[9,21] Low testosterone levels have been associated with worse cardiovascular, metabolic, and musculoskeletal outcomes.[21]

Regarding LVEF, Zuo, *et al*.[11] reported that the higher incidence of sarcopenia in HFrEF compared to HFpEF may be due to the greater volume of available data (in terms of both the number of studies and sample size) from HFrEF patients. However, it is hypothesized that the decrease in LVEF culminates in lower blood flow to skeletal muscle, which could lead to higher sarcopenia prevalences. Further studies focusing on muscle health in HFpEF are needed to fill this

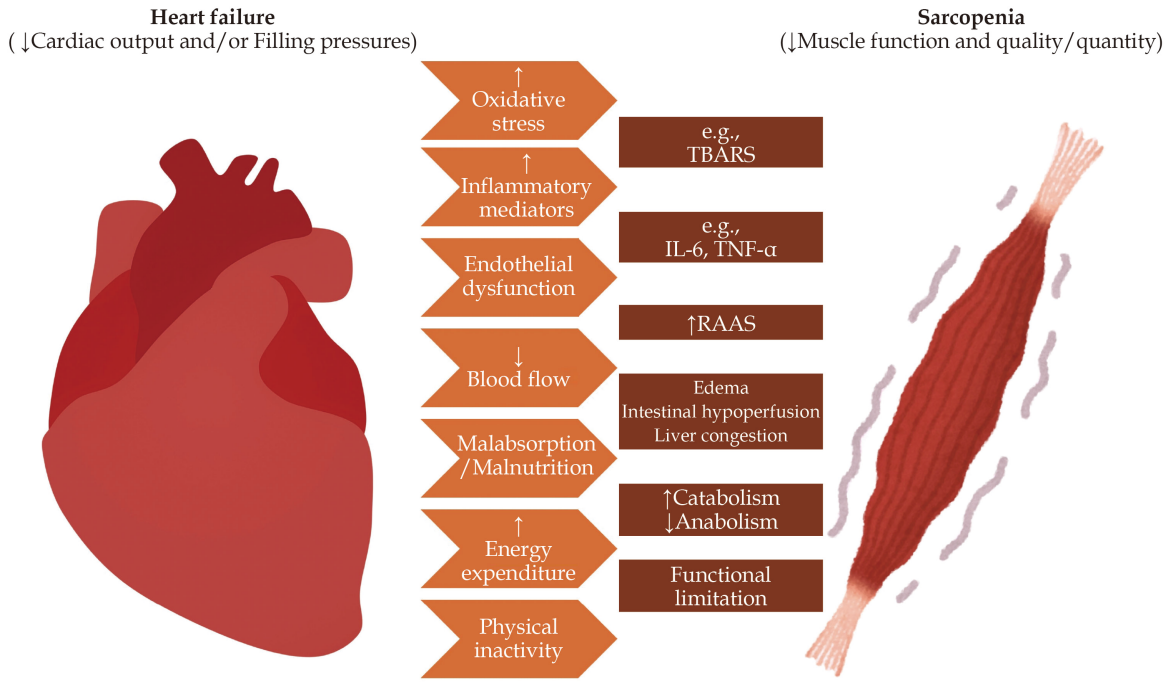

Figure 2 Main pathophysiological mechanisms of skeletal muscle deterioration in heart failure patients. IL-6: interleukin-6; RAAS: renin-angiotensin-aldosterone system; TBARS: thiobarbituric acid reactive substances; TNF-α: tumor necrosis factor-alpha.

gap in epidemiological data and confirm this hypothesis.

Increased oxidative stress, defined as an imbalance between the production of reactive oxygen species and the antioxidant defense mechanisms, is one of the factors contributing to the development and progression of HF through myocardial remodeling, altered electrophysiology, and damage to the contractile machinery.[22] Mitochondrial dysfunction, stimulated by the morphofunctional changes observed in HF, promotes an exacerbation in the generation of free radicals and elevates oxidative stress, thereby feeding a vicious cycle.[23] The study by Yokota, *et al*.[12] corroborates these mechanisms by demonstrating increased TBARS and decreased superoxide dismutase in HF patients, which characterizes the imbalance between reactive oxygen species and antioxidant components. In addition to these findings, the same study also demonstrated deterioration of muscle function, evidenced by reduced strength and greater phosphocreatine loss during exercise in HF patients, along with higher IMCL, which reinforces the deterioration of muscle energy metabolism in patients with HF.[12] The imbalance between the intramuscular absorption and oxidation of fatty acids increases IMCL, promoting myosteatosis, which further deteriorates muscle quality. Since the apparent loss of strength is stimulated by the loss of quality earlier than by the loss of muscle quantity, myosteatosis may be one of the early manifestations of skeletal muscle involvement in HF patients and is associated with the deterioration of energy metabolism.[22,25] Further studies are needed to provide more conclusive findings.

Natriuretic peptides, such as BNP and NT-proBNP, are increased in HF because they exhibit antagonistic effects on the prolonged activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system, which are typical mechanisms in the pathophysiology of HF. This antagonism provides natriuretic, vasodilator, and aldosterone-inhibiting actions.[26] Serum measurements of BNP and NT-proBNP have diagnostic value, and their degree of elevation is associated with short- and long-term adverse outcomes in HF patients.[1,2] The associations between BNP/NT-proBNP and changes in body composition have been little explored thus far, but an analysis of 9134 adults without cardiovascular disease demonstrated that the amount of lean mass was inversely associated with NT-proBNP levels.[7] These findings align with the meta-analysis by Prokopidis, *et al*.[13] which proposes the following possible explanations for the combined presence of increased BNP/NT-proBNP and sarcopenia in HF patients: the reduction of sexual steroids, the increase in pro-inflammatory cytokines involved in muscle loss, and substantial weight loss due to cardiac cachexia.

The kynurenine pathway is the main route for tryptophan metabolism, and its metabolites are involved in the pathophysiology of cardiovascular diseases.[28] Kynurenine accumulation contributes to an increased inflammatory response and muscle loss,[28] which may explain the higher levels of this metabolite in HF patients and its association with deteriorated muscle parameters found in the study by Konishi, *et al*.[14] Another recent study also highlighted this pathway, finding higher kynurenine levels in patients with HF, which was an independent predictor for reduced muscle endurance.[29]

Drug-related sarcopenia is a field that remains underexplored, often masked by age-related or disease-related muscle health deterioration.[30,31] Polypharmacy further complicates the identification of potential sarcopenia-causing drugs.[31] In the context of HF, we highlight the meta-analysis by Saied, *et al*.[15] which demonstrated a potential protective role for ACEI/ARBs use, alongside likely harm associated with statins and loop diuretics. However, these identified associations do not indicate causality, and further studies are needed to identify the direct role of these medications in the muscle health of HF patients.

Sarcopenia is associated with increased risks of adverse health outcomes, such as postoperative complications, prolonged hospitalization, falls, fractures, metabolic disorders, cognitive impairment, and lower survival.[32] Even low handgrip strength alone, which is a simple and affordable measurement, has been associated with an increased risk of cardiovascular and all-cause death.[33] The deterioration of prognosis provided by sarcopenia extends to patients with HF, as demonstrated in the meta-analyses by Prokopidis, *et al*.[16] and Chen, *et al*.[9] Since low muscle strength is already sufficient to characterize probable sarcopenia, according to consensus,[4,5] and handgrip strength can be introduced starting from primary care,[5] this assessment could be adopted more universally in HF patients, serving as a prognostic tool and defining the need to assess muscle quantity.

The high levels of kynurenine, evaluated by Konishi, *et al*.[14] also proved to be a strong predictor of mortality in HF. This finding converges with the pathophysiological mechanisms of this metabolic pathway and coincides with the worse prognosis associated with kynurenine in the context of acute coronary events,[34] and after cardiac arrest.[35]

The high heterogeneity among sarcopenia prevalence data in HF constitutes one of the main limitations of this study. Most studies included in the systematic reviews and me-

ta-analyses[8-11] that assessed sarcopenia prevalence use consensus criteria to define this muscle disease, particularly those from the Asian Working Group for Sarcopenia (AWGS)[5] and the European Working Group on Sarcopenia in Older People (EWGSOP).[4] These consensuses differ regarding certain cut-off points, as is the case for handgrip strength (low if < 28 kg for men and < 18 kg for women in the Asian consensus,[5] and < 27 kg for men and < 16 kg for women in the European consensus[4]). There are also distinct methods for assessing low muscle strength, low muscle quantity, and low physical performance.

Although dual-energy X-ray absorptiometry and bioelectrical impedance analysis are the most frequent methods for assessing muscle quantity, magnetic resonance imaging and computed tomography can also be used,[8-11] with muscle biopsy even being an inclusion criterion in one of the meta-analyses selected in this study.[10] Thus, the absence of universally adopted criteria for the diagnosis of sarcopenia hinders the estimates of prevalence and incidence of this condition in a global context, leading the Global Leadership Initiative in Sarcopenia (GLIS) to propose a unified global definition of sarcopenia.[36-38] There is an expectation regarding the publication of criteria that can be universally adopted, similar to what occurs with other prevalent chronic diseases.

Another limitation of this study refers to the pattern of comorbidities that can influence sarcopenia prevalence, given that conditions such as chronic kidney disease and diabetes mellitus are also associated with a higher occurrence of sarcopenia,[4,5] and are frequent in patients with HF.[1-3] Detailed data on renal function, glycemic status, and serum albumin levels were inconsistent or not uniformly reported in the studies, which limits a precise comparative analysis. This clinical variability underscores the complexity of the HF population and serves as a crucial context for interpreting the discrepancies in sarcopenia prevalence.

The findings of this review demonstrate a high prevalence of sarcopenia in HF, particularly in hospitalized patients, males, the elderly, and those with HFrEF. Biochemical changes, such as elevated TBARS, BNP/NT-proBNP and kynurenine, have been associated with the deterioration of muscle parameters and function in HF patients. Regarding HF treatment, the non-prescription of ACEI/ARBs was associated with low appendicular lean mass. Furthermore, there are indications that reduced handgrip strength was associated with the higher use of statins and loop diuretics and a lower use of ACEI/ARBs. Additionally, systematic reviews and meta-analyses have consistently shown that the presence of sarcopenia is associated with a poor prognosis in HF patients. These findings reinforce the need for skeletal muscle evaluation in HF patients, as potential combined interventions could improve functionality and reduce morbidity and mortality.

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REFERENCES

[1] Heidenreich PA, Bozkurt B, Aguilar D, *et al*. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2022; 145: e895–e1032.

[2] McDonagh TA, Metra M, Adamo M, *et al*. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021; 42: 3599–3726.

[3] McDonagh TA, Metra M, Adamo M, *et al*. 2023 Focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2023; 44: 3627–3639.

[4] Cruz-Jentoft AJ, Bahat G, Bauer J, *et al*. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019; 48: 16–31.

[5] Chen LK, Woo J, Assantachai P, *et al*. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc* 2020; 21: 300–307. e2.

[6] von Haehling S. The wasting continuum in heart failure: from sarcopenia to cachexia. *Proc Nutr Soc* 2015; 74: 367–377.

[7] Curcio F, Testa G, Liguori I, *et al*. Sarcopenia and heart failure. *Nutrients* 2020; 12: 211.

[8] Zhang Y, Zhang J, Ni W, *et al*. Sarcopenia in heart failure: systematic review and meta-analysis. *ESC Heart Fail* 2021; 8: 1007–1017.

[9] Chen R, Xu J, Wang Y, *et al*. Prevalence of sarcopenia and its association with clinical outcomes in heart failure: an updated meta-analysis and systematic review. *Clin Cardiol* 2023; 46: 260–268.

[10] Chandrashekhar Iyer L, Vaishali K, Babu AS. Prevalence of sarcopenia in heart failure: a systematic review. *Indian Heart J* 2023; 75: 36–42.

[11] Zuo X, Li X, Tang K, *et al*. Sarcopenia and cardiovascular diseases: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle* 2023; 14: 1183–1198.

[12] Yokota T, Kinugawa S, Hirabayashi K, *et al*. Systemic oxidative stress is associated with lower aerobic capacity and impaired skeletal muscle energy metabolism in heart failure patients. *Sci Rep* 2021; 11: 2272.

[13] Prokopidis K, Morwani-Mangnani J, McDowell G, *et al*. Sarcopenia is linked to higher levels of B-type natriuretic peptide and its N-terminal fragment in heart failure: a systema-

tic review and meta-analysis. *Eur Geriatr Med* 2024; 15: 893–901.
[14] Konishi M, Ebner N, Springer J, *et al*. Impact of plasma kynurenine level on functional capacity and outcome in heart failure: results from Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF). *Circ J* 2016; 81: 52–61.
[15] Saied S, Prokopidis K, Adenaya A, *et al*. Is sarcopenia an associated factor of increased administration of specific medications in patients with heart failure? A systematic review and meta-analysis. *Front Cardiovasc Med* 2024; 11: 1293537.
[16] Prokopidis K, Triantafyllidis KK, Kechagias KS, *et al*. Are sarcopenia and its individual components linked to all-cause mortality in heart failure? A systematic review and meta-analysis. *Clin Res Cardiol* 2025; 114: 532–540.
[17] Manemann SM, Chamberlain AM, Roger VL, *et al*. Multimorbidity and functional limitation in individuals with heart failure: a prospective community study. *J Am Geriatr Soc* 2018; 66: 1101–1107.
[18] Hämäläinen O, Tirkkonen A, Savikangas T, *et al*. Low physical activity is a risk factor for sarcopenia: a cross-sectional analysis of two exercise trials on community-dwelling older adults. *BMC Geriatr* 2024; 24: 212.
[19] Yin J, Lu X, Qian Z, *et al*. New insights into the pathogenesis and treatment of sarcopenia in chronic heart failure. *Theranostics* 2019; 9: 4019–4029.
[20] Fernández-Pombo A, Rodríguez-Carnero G, Castro AI, *et al*. Relevance of nutritional assessment and treatment to counteract cardiac cachexia and sarcopenia in chronic heart failure. *Clin Nutr* 2021; 40: 5141–5155.
[21] Di Lodovico E, Facondo P, Delbarba A, *et al*. Testosterone, hypogonadism, and heart failure. *Circ Heart Fail* 2022; 15: e008755.
[22] van der Pol A, van Gilst WH, Voors AA, *et al*. Treating oxidative stress in heart failure: past, present and future. *Eur J Heart Fail* 2019; 21: 425–435.
[23] Aimo A, Castiglione V, Borrelli C, *et al*. Oxidative stress and inflammation in the evolution of heart failure: from pathophysiology to therapeutic strategies. *Eur J Prev Cardiol* 2020; 27: 494–510.
[24] Correa-de-Araujo R, Addison O, Miljkovic I, *et al*. Myosteatosis in the context of skeletal muscle function deficit: an interdisciplinary workshop at the National Institute on Aging. *Front Physiol* 2020; 11: 963.
[25] Kim HK, Kim CH. Quality matters as much as quantity of skeletal muscle: clinical implications of myosteatosis in cardiometabolic health. *Endocrinol Metab (Seoul)* 2021; 36: 1161–1174.
[26] Kuwahara K. The natriuretic peptide system in heart failure: diagnostic and therapeutic implications. *Pharmacol Ther* 2021; 227: 107863.
[27] Echouffo-Tcheugui JB, Zhang S, McEvoy JW, *et al*. Body composition measures and N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) in US adults. *Clin Chem* 2023; 69: 901–914.
[28] Yang Y, Liu X, Liu X, *et al*. The role of the kynurenine pathway in cardiovascular disease. *Front Cardiovasc Med* 2024; 11: 1406856.
[29] Bekfani T, Bekhite M, Neugebauer S, *et al*. Metabolomic profiling in patients with heart failure and exercise intolerance: kynurenine as a potential biomarker. *Cells* 2022; 11: 1674.
[30] Kuzuya M. Drug-related sarcopenia as a secondary sarcopenia. *Geriatr Gerontol Int* 2024; 24: 195–203.
[31] Zhang Z, Yao L. Drug risks associated with sarcopenia: a real-world and GWAS study. *BMC Pharmacol Toxicol* 2024; 25: 84.
[32] Yuan S, Larsson SC. Epidemiology of sarcopenia: prevalence, risk factors, and consequences. *Metabolism* 2023; 144: 155533.
[33] Leong DP, Teo KK, Rangarajan S, *et al*. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet* 2015; 386: 266–273.
[34] Eussen SJ, Ueland PM, Vollset SE, *et al*. Kynurenines as predictors of acute coronary events in the Hordaland Health Study. *Int J Cardiol* 2015; 189: 18–24.
[35] Ristagno G, Latini R, Vaahersalo J, *et al*. Early activation of the kynurenine pathway predicts early death and long-term outcome in patient resuscitated from out-of-hospital cardiac arrest. *J Am Heart Assoc* 2014; 3: e001094.
[36] Kirk B, Cawthon PM, Arai H, *et al*. The conceptual definition of sarcopenia: Delphi consensus from the Global Leadership Initiative in Sarcopenia (GLIS). *Age Ageing* 2024; 53: afae052.
[37] Kirk B, Cawthon PM, Cruz-Jentoft AJ. Global consensus for sarcopenia. *Aging (Albany NY)* 2024; 16: 9306–9308.
[38] Alhmly HF, Fielding RA. A critical review of current worldwide definitions of sarcopenia. *Calcif Tissue Int* 2024; 114: 74–81.

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