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The Mechanistic Interplay Between Sarcopenia and Hypertension in Older Adults: A narrative review

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ABSTRACT: Background: Sarcopenia and hypertension are common conditions in older adults and are associated with reduced physical function, increased morbidity, and loss of independence. Recent studies suggest a potentially bidirectional relationship between these conditions; however, the underlying mechanisms remain incompletely understood. **Objective:** This narrative review examines the relationship between sarcopenia and hypertension in older adults, focusing on shared mechanisms and the potential bidirectional interaction between skeletal muscle and vascular function. **Methods:** A non-systematic literature search was conducted to identify relevant studies and reviews in order to address the association between sarcopenia and hypertension and the potential underlying mechanisms using PubMed and Google Scholar. The available evidence was narratively synthesized. **Results:** The reviewed evidence suggests an association between sarcopenia and hypertension in older adults, but its strength and direction vary across populations and according to the diagnostic criteria used for sarcopenia and hypertension. Several observational studies reported significant associations, including one study in which hypertension was independently associated with sarcopenia, with approximately 2.4-fold higher odds in men (OR 2.403) and 1.9-fold higher odds in women (OR 1.906) (1). The association has been reported independently of obesity, although obesity may modify the relationship in some populations. Potential shared mechanisms include chronic low-grade inflammation, insulin resistance, oxidative stress, mitochondrial dysfunction, renin–angiotensin–aldosterone system dysregulation, vascular dysfunction, and physical inactivity. A recent Mendelian randomization study suggested potential causal relationships between sarcopenia-related traits and hypertension, with insulin resistance identified as a possible mediator. However, most available evidence is observa-

tional, and evidence that treating sarcopenia can improve blood pressure control is limited. **Conclusion:** Sarcopenia and hypertension appear to be associated in older adults, with multiple underlying shared and potentially bidirectional mechanisms. However, variation in diagnostic criteria and the predominance of observational studies limit the conclusion about whether one condition causes the other. More longitudinal and interventional studies are needed to clarify this relationship and its underlying mechanisms; also to address whether interventions targeting skeletal muscle health can improve blood pressure control and clinical outcomes.

KEYWORDS: Sarcopenia, Hypertension, Older adults, Muscle strength, Inflammation, Oxidative stress, Insulin resistance, Vascular dysfunction.

1. INTRODUCTION

Human longevity has been significantly increased over recent decades, owing to improvements in healthcare and medical advance. According to the World Bank Group, individuals aged 65 years and older are about 830 million, around 10% of the global population by the end of 2024, and this number is expected to reach 1.7 billion by 2054 [2]. Age-related diseases such as cardiovascular, musculoskeletal, neurodegenerative, and oncological diseases are expected to increase in burden as the population ages [3].

Given that skeletal muscle is one of the largest organs of the human body, age-related decline in skeletal muscle should be carefully monitored and early detected. Characterized by progressive and generalized loss of quality and quantity of skeletal muscles, sarcopenia is a common condition among older adults. Its prevalence varies depending on the studied population and diagnostic criteria applied. Sarcopenia among individuals aged ≥60 years is estimated from 10% to 27% across different diagnostic systems [4]. Using the European Working Group on Sarcopenia in Older People 1 (EWGSOP1), the prevalence rates range from 5% – 13% in those aged 60- 70 years to 11% – 50% among those ≥80 years. Among hospitalized older adults, it has been reported as high as 46.4%, highlighting sarcopenia as an important condition in the older population. [5]

According to the revised European consensus on the definition and diagnosis of sarcopenia (EWGSOP2), low muscle strength is the primary indicator of probable sarcopenia. The diagnosis of sarcopenia is confirmed when reduced muscle strength is accompanied by low muscle quantity or quality, and the presence of reduced physical performance in addition to these criteria indicates severe sarcopenia [6]. Using the same criteria, the prevalence of sarcopenia ranges from 10% to 27%, and the prevalence of severe sarcopenia is 2% to 9% [4]. Despite increasing consensus in the definition of sarcopenia, differences in diagnostic cut-offs and assessments such as bioelectrical impedance analysis (BIA) or dual-energy X-ray absorptiometry (DXA) contribute to the variation in its reported prevalence [7].

Hypertension, meanwhile, is one of the most Acommon chronic diseases among older individuals. According to the World Health Organization (WHO), about 33% of the population worldwide aged 30–79 years had hypertension in 2024. This prevalence is higher among the older group, estimated at 70% of adults aged ≥60 years according to recent National Health and Nutrition Examination Survey (NHANES) data [8].

Increasing evidence that shows an association between sarcopenia and hypertension (HTN), and this relationship is possibly bidirectional, although findings differ according to population characteristics, study design, and sarcopenia diagnostic criteria used. Older adults with sarcopenia may have a higher prevalence and risk of developing HTN [9,10], and those with HTN have also been more likely to suffer from sarcopenia [11,12]. Although the association between these two conditions has been recognized lately, underlying mechanisms linking them have not been completely understood. Early identification and proper management of both conditions may help preserve physical functions and reduce complications, supporting a better quality of life and more independence in older people. Consequently, this narrative review examines the association of the two conditions, mainly focusing on

their intertwined mechanisms and possibly bidirectional relationship between sarcopenia and HTN among older adults. Relevant literature was identified in PubMed and Google Scholar to find evidence on the association and potential underlying pathophysiological mechanisms linking them, using keywords: "sarcopenia", "muscle loss", or "muscle weakness"; "hypertension" or "high blood pressure"; "elderly" or "older adults"; and "mechanism", "insulin resistance", "inflammation", "oxidative stress", "mitochondrial dysfunction", "vascular dysfunction", or "endothelial dysfunction".

2. EVIDENCE OF THE ASSOCIATION BETWEEN SARCOPENIA AND HYPERTENSION

Several observational studies have shown the association between sarcopenia and HTN, as summarized in Table 1. The strength of the relationship and its direction vary according to population characteristics, sex, age, obesity status, and diagnostic criteria used for sarcopenia and HTN. Some studies also showed that obesity amplified this correlation. In contrast, two original studies showed no correlation between sarcopenia and HTN. Du et al. conducted a prospective cohort study in 7301 adults, using the Asian Working Group for Sarcopenia (AWGS) criteria, and reported no association between sarcopenia and HTN, but obesity and sarcopenic obesity were associated with a higher risk of HTN. Pasdar et al. researched 4021 adults, using low or moderate waist circumference tertile and low muscle mass and strength as the sarcopenia definition, and found that only obesity was related to HTN; sarcopenia and sarcopenic obesity were not.

This association has also been examined in several systematic reviews and meta-analyses, as shown in Table 2. Quan et al. and Bai et al. both reported an association between sarcopenia and HTN, although the association varied across the included studies.

TABLE 1. Studies investigating the relationship between Sarcopenia and Hypertension

Author	Year	Population	Study design	Sarcopenia definition	Hypertension definition	Main findings
Zou et al.[13]	2025	183,091 participants aged 40-70 years	Prospective cohort study	Low muscle mass + low muscle strength; Using BIA and Janssen's equation to calculate muscle mass; Low muscle mass: SMM <37.7% in men and <26.7% in women and low muscle strength: handgrip strength	incident HTN: hospital record, ICD-10: I10	Sarcopenia was associated with increased risk of HTN; the association was strongest among those with sarcopenic obesity.
Masik et al.[14]	2025	180 stage II hypertensive patients aged 63.8 ± 6.2 years	Prospective cohort study	EWGSOP2; handgrip, sit-to-stand, calf circumference, walking speed	BP ≥140/90 mmHg	Sarcopenia prevalence was 38.3% among hypertensive patients
Kim et al.[15]	2024	2,237 Koreans ≥60 years BMI 18.5-<25 kg/m²	Population-based cross-sectional study	Sarcopenia index 1–2 SD below young reference mean; moderate ≤ -1 SD, severe ≤ -2 SD	SBP ≥130 mmHg, DBP ≥85 mmHg; or antihypertensive medication	Sarcopenia severity is associated with arterial stiffness and HTN in older Korean adults without underweight or obesity
Murat et al.[1]	2023	2,613 participants aged 61 ± 9.5 years; 1,775 with HTN	Multicenter, cross-sectional study	ISarcoPRM algorithm: low muscle function + low anterior-thigh muscle mass (STAR index); severe sarcopenia additionally required mobility limitation.	Office blood pressure and/or antihypertensive medication use.	HTN was independently associated with sarcopenia. The odds of sarcopenia were approximately 2.4-fold higher in men (OR 2.403) and 1.9-fold higher in women (OR 1.906) with HTN.
Xing et al.[16]	2022	165 Chinese adults ≥60 with HTN	Retrospective clinical study	AWGS	Self-reported physician diagnosis of HTN; or use of antihypertensive medication.	Sarcopenia has high prevalence among hypertensive older individuals.
Ata et al.[11]	2021	272 community-dwelling adults	Cross-sectional study	Low STAR + Low muscle strength and/or low muscle performance	–	High prevalence of sarcopenia among hypertensive older adults.

Han et al.[17]	2020	132,324 Korean adults	Prospective cohort study	SMI (%) = total skeletal muscle mass (kg) / body weight (kg) × 100 Divided into four quartiles (Q1–Q4)	Incident HTN: during follow-up	Low muscle mass was associated with HTN in Korean men, but not in women.
Han et al.[18]	2014	4,846 Koreans ≥60 years	Cross-sectional study KNHANES 2008–2010	ASM/weight <1 SD below young-adult sex-specific mean	SBP≥140 mmHg, DBP≥90 mmHg or self-reported current use of antihypertensive medications.	HTN prevalence was 49.7% in the non-obese non-sarcopenia group, and 60.9% in the non-obese sarcopenia group. The adjusted odds ratios for HTN were 1.5 in the non-obese sarcopenia group and 3.0 in the obese sarcopenia group.
Du et al.[19]	2025	7,301 participants aged 58 ± 8.8 years	Prospective cohort study	AWGS in 2019	Self-reported diagnosis from the doctor Incident HTN: based on diagnostic report during follow-up.	Sarcopenia had no association with HTN, but obesity and sarcopenic obesity were associated with a higher risk of HTN.
Pasdar et al.[20]	2022	4,021 adults aged 47.9 ± 8.4 years Ravansar, Iran	Population-based cross-sectional study	Low muscle mass + low muscle strength (sex-specific tertiles); BIA for muscle mass and handgrip strength for muscle strength.	BP ≥140/90 mmH and/or antihypertensive medication use	Obesity was associated with HTN; sarcopenia and sarcopenic obesity were not.

KNHANES, Korea National Health and Nutrition Examination Survey; **BIA,** bioelectrical impedance analysis; **SMM,** skeletal muscle mass; **SMI,** skeletal muscle mass index; **ASM,** appendicular skeletal muscle mass; **EWGSOP2,** European Working Group on Sarcopenia in Older People 2; **HTN,** hypertension.

Note: Sonographic thigh adjustment ratio (STAR) was calculated by dividing the anterior thigh muscle thickness (mm) by body mass index (BMI).

TABLE 2. Existing reviews on Sarcopenia and Hypertension

Author	Year	Type	Main findings
Toba & Ishikawa (10)	2024	Mini review	Sarcopenia is a risk factor for HTN
Quan et al. (9)	2023	Systematic review, meta-analysis	Significant relationship between sarcopenia and HTN among older people, with sarcopenic obesity amplifying this risk
Bai et al. (21)	2020	systematic review, meta-analysis	Sarcopenia was significantly associated with HTN

3. SHARED COMMON MECHANISM BETWEEN SARCOPENIA AND HYPERTENSION

Several studies have identified the potential mechanisms linking sarcopenia and hypertension, including chronic low-grade inflammation, insulin resistance, oxidative stress, mitochondrial dysfunction, vascular dysfunction, renin-angiotensin-aldosterone system dysregulation, and physical inactivity. [9,10,21–23]

3.1. LOW-GRADE CHRONIC INFLAMMATION

Aging is accompanied by immune dysfunction, accumulation of senescent cells with senescence-associated secretory phenotype (SASP) rich in pro-inflammatory cytokines, changes in adipose tissue [24], and alterations in gut microbiome[25]; together, it may contribute to chronic low-grade inflammation, also referred to as inflammaging [26]. Characterized by elevated circulating concentrations of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP), even in the absence of acute infection, this persistent systemic inflammation can cause progressive tissue injury and organ damage. [27–29]. Several studies have reported an association between chronic low-grade inflammation and sarcopenia [30–37]. Similarly, chronic inflammation has also been linked to HTN [38–41], suggesting that inflammaging may contribute to age-related sarcopenia and HTN through shared inflammatory pathways.

Chronic low-grade inflammation can contribute to the disruption of the balance between protein synthesis and degradation [42–44]. Although IL-6 has physiological myokine functions during acute exercise,

such as regulating energy metabolism, chronically elevated pro-inflammatory cytokines, particularly IL-6 and TNF-α, during aging may promote muscle protein breakdown. These inflammatory signals can activate pathways involved in muscle atrophy, including NF-κB and FOXO-related signaling, which increase the expression of muscle-specific E3 ubiquitin ligases such as MuRF1 and atrogin-1, and consequently increase ubiquitin–proteasome system (UPS)–mediated protein degradation, contributing to skeletal muscle loss [43,45]. Meanwhile, chronic low-grade inflammation can suppress Protein kinase B/Mechanistic Target of Rapamycin/Insulin-like Growth Factor 1(Akt/mTOR/IGF-1) pathways, partly by compromising IGF-1 activity and mTOR expression, leading to reduced skeletal muscle protein synthesis [43,46]. Besides, TNF-α can increase the expression of cell death receptors and the caspase-dependent apoptotic pathway in skeletal muscle, particularly in type II muscle fibers (fast-twitch), contributing to muscle atrophy and weakness [37,43]. Moreover, while basal autophagy removes damaged proteins and cellular structures, and mitophagy eliminates dysfunctional mitochondria under normal circumstances, their function may be compromised with age and chronic inflammation, leading to the accumulation of damaged mitochondria and organelles, exacerbating mitochondrial dysfunction and oxidative stress, and further aggravating chronic inflammation, creating a vicious cycle of muscle damage [43].

In addition, chronic inflammation may contribute to more muscle loss by reducing satellite-cell numbers and function. Satellite cells are considered muscle stem cells, which play a vital role in maintaining muscle homeostasis and supporting regeneration after injury, and they are normally inactive in adult skeletal muscle [47]. Aging is associated with reductions in satellite-cell quantity and function, reducing their ability to repair or regenerate new muscle fibers. Some studies also demonstrate that there is a reduction of satellite cells per myofiber in both genders, more prominent in older females [48]. Persistent inflammatory signaling during aging may change satellite-cell activity and its regenerative capacity. Activation of pathways such as JAK/STAT3 and NF-κB has been involved in impaired satellite-cell function and depletion of its reserve [49]; together, compromise skeletal muscle cells' ability to regenerate, leading to progressive muscle loss in aging [44]. Also, chronically elevated cytokines promote mitochondrial dysfunction and oxidative stress in skeletal muscle, contributing to insulin resistance, which further accelerates sarcopenia [50].

Beyond its effects on skeletal muscle, age-related chronic inflammation is also associated with HTN [39,41], potentially through impaired vascular homeostasis, endothelial dysfunction, increased arterial stiffness, and vascular remodeling, while also contributing to renal dysfunction [40]. Persistent low-grade pro-inflammatory states may decrease nitric oxide (NO) bioavailability by reducing the expression and activity of endothelial nitric oxide synthase (eNOS), limiting NO production. It may also promote mitochondrial and NADPH-derived reactive oxygen species (ROS), supporting a potential link between chronic inflammation, mitochondrial dysfunction, and oxidative stress, creating a vicious cycle that may further reduce NO bioavailability [51–53]. On the other hand, chronic low-grade inflammation can increase endothelial-derived endothelin-1 (ET-1) and other vasoconstrictors [54]. Together, it shifts vascular homeostasis to decrease vasodilators and increase vasoconstrictors, leading to enhanced vascular tone and resistance, increasing blood pressure.

In addition, age-related pro-inflammatory processes may activate NF-κB in vascular endothelial cells, expressing more adhesion molecules and chemokines and recruiting more monocytes and their transformation into macrophages, further leading to vascular inflammation and endothelial damage [55]. Similarly, recent evidence suggests that aging may be related to increased migration of immune cells, such as T cells, monocytes, and macrophages, which can release more cytokines and ROS, exacerbating inflammation and oxidative damage in the arterial wall, especially around small resistance arteries [56]. Chronic inflammation may also stimulate vascular smooth muscle cell growth, enhancing collagen deposition and elastin degradation in the vascular wall, contributing to vascular fibrosis and remodeling [57], leading to increased systolic blood pressure and increased pulse pressure. Beyond that, age-related inflammation may act on the kidneys, resulting in elevated blood pressure. More specifically, immune cells infiltrate the renal interstitial and perivascular zones, releasing cytokines and ROS, promoting fibrosis and loss of functional nephrons. These inflammatory signals may further change renal sodium transporter activity, favoring sodium and water retention, which can increase blood volume and contribute to elevated blood pressure [58]. Apart from its effects on the vasculature and kidneys, chronic low-grade inflammation may contribute to enhancing blood pressure by acting on the brain. In detail, chronically increasing cytokines can activate cardiovascular regulatory regions in the brain

and increase sympathetic nervous system outflow [59], which further increases vascular resistance and promotes more sodium and fluid retention in the kidneys. Collectively, age-related systemic inflammation is associated with increased blood volume, vascular remodeling, vascular tone, and vascular resistance, therefore contributing to the development and persistence of HTN over time. Taken together, chronic low-grade inflammation may play a pivotal role in developing and sustaining sarcopenia and HTN during aging.

3.2. INSULIN RESISTANCE

Insulin resistance (IR) has been reported as another shared mechanism between sarcopenia and hypertension [9,22,60]. With advancing age, insulin sensitivity and the ability to regulate glucose in the body are likely to decline, possibly due to reduced insulin-stimulated Akt activity and decreased expression of glucose transporter 4 (GLUT4) in skeletal muscle, leading to impaired insulin signaling and consequently reduced glucose uptake and glucose homeostasis [61]. As insulin signaling is compromised, skeletal muscle glucose uptake and intracellular energy production decline, contributing to reduced muscle contraction.

In addition to its role in glucose metabolism, insulin is also involved in maintaining protein homeostasis. It helps preserve muscle mass by regulating the balance between protein breakdown and synthesis through the PI3K/Akt pathway, mTORC1, and FoxO transcription factors [62,63]. Therefore, age-related IR may contribute to increased muscle loss by promoting muscle protein degradation and reducing protein synthesis; however, this contribution may vary among individuals depending on other factors, such as adiposity, inflammation, physical activity, and comorbidities. Moreover, IR may activate caspase-3 and the UPS in the skeletal muscle [64], accelerating muscle protein breakdown [5], and further leading to sarcopenia. In addition, IR may diminish muscle contraction in older individuals by decreasing intracellular calcium uptake, along with decreased expression of L-type calcium channels in aging muscle, which may contribute to the decline in muscle strength [63]. These modifications impair skeletal muscle metabolism, protein homeostasis, and contractile function, contributing to the development and progression of sarcopenia. Because skeletal muscle is the major tissue responsible for glucose uptake and it constitutes 40-50% of lean body mass in adults, age-related skeletal muscle loss, as occurs in sarcopenia, may further contribute to IR [60], suggesting the potentially bidirectional relationship between IR and sarcopenia.

Apart from its role in skeletal muscle decline, IR is also associated with HTN, through mechanisms involving endothelial dysfunction, arterial stiffness, and neurohormonal activation [65–67]. Consistent with this, a population-based study reports that IR is associated with elevated systolic and diastolic blood pressure in adults, including those without obesity or with normal weight, and this association was observed even before established diabetes [68]. Another study in non-diabetic, hypertensive older people also revealed a relationship between IR and arterial stiffness independent of glucose tolerance status [69]. Together, they support that the relationship between IR and HTN may occur independently of obesity or diabetes [68,70]. Alongside its metabolic effect, insulin stimulates endothelial NO production via activating endothelial PI3K/Akt/eNOS signaling [66]. However, insulin signaling may become selectively impaired with aging and IR. Consequently, signaling through the PI3K/Akt/eNOS pathway is impaired while the MAPK pathway is relatively preserved or may become more active in the presence of compensatory hyperinsulinemia. This imbalance can reduce NO-mediated vasodilation and increase ET-1 production, favoring greater vasoconstriction and contributing to elevated blood pressure [71]. Age-related IR may contribute to increased oxidative stress and reduced NO bioavailability, impairing endothelial function and promoting arterial stiffness and remodeling. An experimental study in rats also demonstrated that aging diminishes insulin-stimulated arterial vasorelaxation through endothelial dysfunction, marked by reduced eNOS expression and insulin-stimulated eNOS phosphorylation, while enhancing inducible nitric oxide synthase (iNOS) and $gp91^{phox}$ expression in the vasculature [72]. As arteries become stiffer with age, the association between IR and HTN becomes more pronounced. In addition, IR may contribute to HTN through neurohormonal activation, marked by increased Renin-Angiotensin-Aldosterone system (RAAS) and sympathetic nervous system (SNS) activity [68,73]. IR develops in skeletal muscle, liver, and adipose tissues, while insulin sensitivity may remain relatively preserved in the kidneys, particularly in the renal proximal tubule, which plays an important role in sodium transport [74]. As a result, compensatory hyperinsulinemia may enhance sodium and water retention in the kidneys, potentially leading to increased blood volume; however, the role of renal insulin signaling in the development of HTN is complex and remains incompletely understood

[67,68]. Besides, this compensatory hyperinsulinemia may also activate SNS activity, increasing sympathetic nervous system outflow, and activate RAAS, promoting systemic vasoconstriction and fluid retention; together, increasing blood volume, vascular tone, and vascular resistance, further contributing to elevated blood pressure [73,75]. These findings suggest that IR may be a key biological mechanism linking age-related sarcopenia with HTN.

3.3. OXIDATIVE STRESS

Oxidative stress may play a critical shared mechanism of pathogenesis underlying both sarcopenia and hypertension in the elderly [9]. Reactive oxygen species (ROS) are produced at low concentrations in multiple cellular compartments such as mitochondria, cytosol, membranes, etc. [76,77], but mainly in the mitochondria during normal respiration. Additional ROS are generated by enzyme systems such as NADPH oxidases (Nox) under growth factor and inflammatory cytokine stimulation [76,78]. Excessive ROS are normally neutralized by the antioxidant defense system, which includes several important enzymes such as superoxide dismutase, catalase, glutathione peroxidase, vitamins like Vitamin C and E, and minerals like zinc, copper, and iron, etc. [78,79]. Oxidative stress happens when there is an imbalance between ROS production and the antioxidant defense system in the body, resulting in oxidative damage to cellular macromolecules such as proteins, lipids, and nucleic acids, leading to cell injury and death [77,79,80]. During aging, this imbalance may become more pronounced for several reasons, mainly because of the accumulation of damaged mitochondria [81] or a weakened defense system [5]. Excessive ROS may disrupt redox homeostasis and promote oxidative stress, contributing to oxidative damage in neurons and skeletal muscle fibers [82].

Skeletal muscle uses abundant oxygen to produce ATP to function; consequently, age-related muscle generates a greater amount of ROS [79]. Excessive production of ROS may directly damage skeletal muscle proteins, lipids in the cell membrane, DNA, and muscle contractile structures, leading to loss of muscle mass and function. Additionally, oxidative stress may contribute to anabolic resistance in skeletal muscle through Akt/mTOR signaling, reducing protein anabolism in response to stimuli, and promote muscle proteolysis via the UPS and autophagy pathway. When degradation of protein exceeds its synthesis, progressive muscle loss occurs, potentially leading to sarcopenia [83,84]. In addition, even though physiological ROS are required for satellite-cell signaling and activation, chronic oxidative stress may activate pro-inflammatory NF-kB in satellite cells, increasing inflammatory cytokines, inhibiting myogenesis through lower expression of Myogenic Differentiation (MyoD) and reducing myoblast differentiation; consequently, impairing protein synthesis of muscle fibers and increasing protein degradation [83]. Oxidative stress may also promote changes at the acetylcholine receptor endplate and loss of innervation at the neuromuscular junction, which further contributes to motor neuron loss and its innervated muscle fibers, compromising muscle strength and motor function. Although both type I and II muscle fibers can be affected by oxidative stress, type II (fast-twitch) muscle fibers appear more susceptible to age-related denervation; subsequent reinnervation by surviving motor neurons can drive a shift toward a more Type I-like, or slow-twitch, fiber phenotype. This muscle fiber remodeling and the preferential loss of type II muscle fibers, important for rapid and high force contraction, may contribute to reduced muscle strength, contractility, and physical performance [79,82]. More importantly, toxic effect from excessive ROS will be neutralized normally by the antioxidant defense systems, but they may be impaired with aging; also because of nutritional deficiency and inactivity [78,79], together exacerbating loss of muscle mass and function. Additionally, oxidative stress contributes to diminished excitation-contraction coupling and Ca2+ homeostasis, leading to reduced muscle contractility, force, and strength [82]; together, promoting sarcopenia.

Along with the deleterious effects of excessive ROS on skeletal muscle, oxidative stress may be responsible for the initiation and progression of several diseases, including cancer, diabetes, cardiovascular diseases, atherosclerosis, and HTN [77]. Excessive ROS, particularly superoxide, can reduce NO availability by quickly reacting with NO to form peroxynitrite (ONOO-). This may promote endothelial damage and dysfunction, contributing to increased vascular resistance and elevated blood pressure [80]. Additionally, oxidative stress can promote inflammation through NF-kB and cytokine pathways. Specifically, it may trigger redox-sensitive transcription factors, likely through NF-kB and hypoxia-inducible factor 1 (HIF-1), regulating cytokine expression, promoting vascular inflammation and fibrosis, further contributing to increased vascular resistance. It can also activate the NLRP3 (NOD-, LRR- and pyrin domain-containing protein 3) inflammasome through the Nox and redox-sensitive pathway, exacerbating vascular inflammation and fibrosis, contributing to vascular remodeling [77,80]. Moreover, excessive ROS can

increase Matrix Metalloproteinases (MMPs) by activating MMP genes, resulting in elastin breakdown and increasing vascular stiffness. It can also promote the infiltration of macrophages, T and B cells into the vessel wall, increasing the release of pro-inflammatory cytokines (TNF-α, IL-17, and IFN-γ), driving collagen deposition, thickening of arterial walls, and thereby leading to vascular stiffness, reduced compliance, and fibrosis [38,85]. Excessive ROS (especially H_2O_2) can induce vasoconstrictor pathways by enhancing ET-1, a potent vasoconstrictor, by increasing ET-1 gene expression and release by vascular endothelial cells and kidney mesangial cells [86]. There is also evidence of reciprocal interaction between oxidative stress and angiotensin II (Ang II) signaling. Ang II can stimulate Nox activity and increase ROS generation in endothelial and smooth muscle cells, while elevated ROS can amplify Ang II signalling. This interaction can reinforce oxidative stress, endothelial dysfunction, and vascular remodeling, contributing to persistent high blood pressure [87]. Excessive ROS in the cardiovascular control center in the brain may increase sympathetic nervous system (SNS) activity by removing the inhibitory effect of NO on SNS, increasing Ang II activity, and enhancing excitatory synaptic transmission in autonomic neurons [88,89]. Oxidative stress in the kidney may affect its function, decreasing renal blood flow, promoting sodium reabsorption, increasing fluid retention, and activating RAAS [80]. Collectively, oxidative stress may contribute to elevated blood pressure through its influence to kidneys. Overall, oxidative stress is related to sarcopenia and hypertension.

3.4. MITOCHONDRIAL DYSFUNCTION

Mitochondria are not only the cell's energy producer, it is the major source of reactive oxygen species (ROS). Healthy mitochondria are crucial for cellular functioning, as they regulate energy production, cell metabolism, calcium signaling, redox balance, and cell survival [5,81].

Aging contributes to a decrease in mitochondrial number and function by reducing mitochondrial biogenesis, accumulating damaged mitochondria, and impairing respiratory capacity. Consequently, age-related mitochondria may produce less energy through oxidative phosphorylation and more ROS leaking from the electron transport chain, further leading to increased oxidative stress and apoptosis signaling [5,40,90].

While skeletal muscle cells need a large amount of ATP to contract, a reduction in mitochondrial quantity and quality in age-related skeletal muscle can compromise ATP production, resulting in reduced muscular contractility. Low energy levels may also impair muscle protein synthesis, reducing its ability to repair and regenerate [91]. Besides, mitochondrial dysfunction may activate FOXO3 in skeletal muscle, promoting autophagy and proteolytic pathways, contributing to increased muscle protein degradation [5]. In addition, mitochondrial dysfunction may also promote cellular apoptotic signaling by opening the mitochondrial permeability transition pore, releasing pro-apoptotic proteins, and DNA fragmentation, resulting in deteriorating muscle fiber nuclei [91]. Skeletal muscle cells normally eliminate damaged mitochondria through mitophagy, a mitochondrial quality-control mechanism; however, this process may become impaired with age, leading to accumulating damaged mitochondria, creating a vicious cycle between dysfunctional mitochondria and its effection on age-related skeletal muscle, leading to progressive sarcopenia [5]. Mitochondrial dysfunction also contributes to reduced muscle capacity for repair and regeneration by affecting satellite-cell function, as reduced ATP production and poor mitochondrial quality control can limit satellite-cell activation or proliferation [47]. Moreover, mitochondrial dysfunction and excessive mitochondrial ROS may promote age-related muscle fiber remodeling and the preferential loss of type II muscle fibers, leading to reduced muscle strength and physical performance [91]. Collectively, mitochondrial dysfunction is associated with the development and progression of sarcopenia.

Along with its effects on skeletal muscle, mitochondrial dysfunction may contribute to elevated blood pressure in aging by promoting vascular aging and endothelial dysfunction, also changing sympathetic nervous system (SNS) activity and kidney function. Thoroughly, healthy endothelium depends on mitochondria for intracellular signaling and cellular homeostasis. Age-related dysfunctional mitochondria can promote endothelial dysfunction by increasing oxidative stress and reducing NO production and bioavailability, resulting in decreased vasorelaxation and increased vascular stiffness [92], further contributing to increased blood pressure. Besides, low ATP and excess mitochondrial ROS contribute to reduced vascular smooth muscle cell contraction in small arteries, promoting peripheral resistance and further leading to elevated blood pressure [93]. As a mitochondria-rich organ, age-related mitochondrial dysfunction in the kidneys can contribute to diminished function. Particularly, while renal tubular cells need a large amount of ATP for active sodium transport, less ATP and elevated

mitochondrial ROS can lead to cell senescence and tubular cell dysfunction, promoting renal failure, increasing sodium and fluid retention, and further contributing to elevated blood pressure [94]. Collectively, age-related mitochondrial dysfunction may contribute to the development and progression of both sarcopenia and HTN.

3.5. RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM DYSREGULATION

Growing evidence shows that renin-angiotensin-aldosterone system (RAAS) dysregulation as a shared mechanism associating to sarcopenia and hypertension in older adults [11]. Although systemic RAAS components are likely to reduce with age [95], local RAAS activity, or the classic pathway, such as Angiotensin II (Ang II) and Angiotensin II type 1 receptor (AT1R), is upregulated in several tissues, including skeletal muscle, kidneys, heart, vasculature, and the brain [96], but the protective pathway through angiotensin-[1-7] [Ang-[1–7]] and Mas receptors (MasR) diminishes during aging [97]. This shift may cause a greater imbalance between the harmful and protective actions of RAAS.

Ang II has primary effects through AT1R, inducing vasoconstriction, releasing aldosterone and vasopressin, and increasing sodium and fluid retention in the kidneys [98]. Additionally, brain RAAS dysregulation increases autonomic nervous system activity, affects the hypothalamus-pituitary axis, enhances vasopressin release, impairs the baroreflex, and increases thirst and salt intake. Together, they increase vascular resistance and blood volume, leading to elevated blood pressure [99]. In addition, Ang II acting on AT1R and aldosterone acting on mineralocorticoid receptors on vascular endothelial cells can increase vasoconstriction, activate pro-inflammatory and profibrotic pathways, and increase extracellular matrix deposition, contributing to vascular fibrosis, arterial remodeling, perivascular inflammation, and hyperreactivity [96]. Collectively, age-related RAAS dysregulation can lead to vascular stiffness, fibrosis, and high blood pressure.

Excess local RAAS activity in skeletal muscle may also contribute to sarcopenia [100]. Specifically, Ang II acts on AT1R, which can stimulate the UPS and increase skeletal muscle protein degradation [100–102]. Ang II can directly induce the production of cytokines, activating NF-kB and promoting chronic inflammation and further muscle protein loss. Besides, Ang II may promote extracellular matrix accumulation, including collagen deposition, by increasing the expression of transforming growth factor beta (TGF-β) and connective tissue growth factor (CTGF); it may also increase myostatin, which inhibits muscle growth. Excessive local RAAS activity may contribute to reduced skeletal muscle capacity to regenerate via impaired IGF-1 signaling and inhibited satellite-cell proliferation through enhanced TGF-β signaling [101]. Additionally, reduced expression of orexin and neuropeptide Y in the hypothalamus caused by dysregulated RAAS may suppress appetite and anabolic signaling, which further worsens muscle loss [100]. Collectively, excess RAAS activity contributes to impaired muscle quality and its ability to repair [100].

Moreover, Ang II may increase oxidative stress and impair mitochondrial function by stimulating Nox activity and promoting ROS production [100]. This potentially provides a link between RAAS dysregulation and the oxidative stress and mitochondrial dysfunction discussed above, further aggravating muscle loss and vascular injury, reinforcing the development of sarcopenia and hypertension. More importantly, AT2R and Ang-[1–7]/MasR pathways generally oppose the effects of Ang II/AT1R signaling [96]. Ang-[1–7] is produced from the cleavage of Ang II by angiotensin-converting enzyme 2 (ACE2) or from Ang I by endopeptidase. It binds to MasR in various cells, activating eNOS and stimulating endothelial NO release, leading to peripheral vasodilation. This pathway is also associated with anti- inflammatory, anti-fibrotic, and muscle-regenerating effects on satellite cells; however, its activity is attenuated in aging [96,97,101], further shifting the balance toward the harmful effects of RAAS. Overall, aging may promote RAAS imbalance and weaker protective signaling, promoting dysfunctional vasculature and progressive loss of skeletal muscle mass and function, contributing to sarcopenia and HTN.

3.6. VASCULAR DYSFUNCTION

Vascular dysfunction, particularly endothelial dysfunction and microvascular dysfunction, has been proposed as a shared mechanism between sarcopenia and hypertension. The endothelium, which forms the inner surface of blood vessels, is an active, heterogeneous, multifunctional organ that plays a pivotal role in maintaining vascular homeostasis and ensuring adequate blood flow to end organs [103,104]. In addition to regulating vascular tone and permeability, it is involved in hemostasis, inflammatory response, leukocyte movement, angiogenesis, and metabolism [103]. During aging, there are multiple factors that may compromise endothelial and vascular integrity, such as increased oxidative stress and chronic low-grade inflammation, reduced NO bioavailability, and endothe-

lial cell senescence that reduces repair capacity [105,106]; contributing to endothelial dysfunction.

Aging is accompanied by reduced NO bioavailability, which may result from the dysfunctional endothelium, increased oxidative inactivation of NO, and changed endothelial NO synthase (eNOS) regulation by chronic low-grade inflammation [51,52]. At the same time, endothelial production of vasoconstrictor mediators such as ET-1 may increase with age due to upregulation of prepro-ET-1 transcription and enhanced proteolytic maturation of ET-1, which are amplified by age-related oxidative stress and chronic inflammation [107,108]. Together, these changes can favor vasoconstriction and increase vascular resistance. Additionally, endothelial dysfunction, oxidative stress, and chronic inflammation in aging are associated with arterial stiffening, potentially due to increased collagen deposition, elastin degradation, and vascular calcification [105], contributing to HTN. Age-related changes in endothelial vasodilator pathways may extend beyond impaired NO signaling. Endothelium-derived hyperpolarizing factors (EDHFs) promote vascular relaxation through EDHF-mediated relaxation, which can become less effective with aging, further contributing to increased vascular resistance. Besides, in aging vessels, endothelium-derived contracting factors (EDCFs), mainly constrictor prostanoids such as thromboxane A_2 and prostaglandin $F_2\alpha$, can act on vascular smooth muscle cells and promote contraction [109]. Over time, endothelial dysfunction shifts vascular tone to persistent vasoconstriction and drives vascular remodeling [110].

Along with its influence on blood pressure, vascular dysfunction may relate to sarcopenia. Skeletal muscle is highly vascularized, maintaining an adequate blood supply to skeletal muscle with continuous delivery of oxygen, nutrients, hormones, insulin, etc., to keep it well functioning. During aging, endothelial dysfunction may promote impaired microvascular perfusion, contributing to compromised muscular metabolism and reduced the delivery of nutrients required for muscle protein synthesis and tissue regeneration [111]. Moreover, older people may exhibit a blunted muscle protein synthetic response, owing to an ineffective response to anabolic stimuli compared to younger adults, especially to insulin and muscle contraction. Repeatedly insufficient anabolic response over time, together with impaired perfusion in skeletal muscle, may further reduce muscle mass and strength, contributing to sarcopenia [112]. Besides, interaction between endothelium and satellite cells can be relevant to maintaining muscle; changes in vascular dysfunction may affect satellite-cell activity, contributing to reduced muscle mass and its ability to repair and regenerate [48].

In addition, aging is associated with reduced vascular density, referred to as microvascular rarefaction, and altered vascular distribution and remodeling, particularly in skeletal muscle and resistance arteries. This microvascular dysfunction further promotes elevated peripheral vascular resistance and impaired perfusion, potentially contributing to elevated blood pressure and sarcopenia in aging [113,114].

More importantly, physical inactivity, which is common in older people, may further exacerbate vascular dysfunction and promote increased oxidative stress [23,78,115], contributing to the development of sarcopenia and HTN.

Collectively, age-related endothelial and microvascular dysfunction may contribute to both conditions through vascular homeostasis dysregulation, increased vascular resistance, compromised skeletal muscle perfusion, and reduced muscle anabolism and regeneration.

3.7. BIDIRECTIONAL RELATIONSHIP

The relationship between sarcopenia and hypertension in aging may be bidirectional [9,22]. Mechanistically, chronic HTN may contribute to the development of sarcopenia through vascular dysfunction and microvascular rarefaction, RAAS dysregulation, inflammation, oxidative stress, increased arterial stiffness and pulse pressure; together, these mechanisms may impair muscle perfusion and increase muscle catabolism. In a cross-sectional comparative study in older men, reduced skeletal muscle capillarization was observed among those with HTN, correlating with lowered muscle mitochondrial oxidative capacity [116], which may contribute to sarcopenia. In contrast, sarcopenia may promote HTN through worsened insulin resistance with compensatory hyperinsulinemia, chronic inflammation, and physical inactivity. These changes may impair endothelial function and increase SNS and RAAS activity, consequently promoting arterial stiffness and vascular resistance, contribute to HTN. Shared mechanisms such as inflammaging, oxidative stress, mitochondrial dysfunction, RAAS dysregulation, and vascular dysfunction, as discussed above, create a reinforcing cycle that potentially accelerates both conditions in aging [9]. A recent bidirectional two-sample Mendelian randomization study suggests genetic evidence consistent with a causal relationship between HTN and sarcopenia traits, with insulin-related measures as a possible mediator [22].

4. DISCUSSION

The studies included in this review suggest that sarcopenia and hypertension are associated in older adults, although this relationship has not been consistent across different populations [1,14,15,22]. Available evidence suggests that several interconnected mechanisms may contribute to the development and progression of both conditions in aging. Mitochondrial dysfunction and increased oxidative stress may impair endothelial function [80,92], while RAAS dysregulation may further promote oxidative stress and inflammatory signaling [100]. Additionally, chronic low-grade inflammation and IR may adversely affect both vascular and muscular function [55,72]. Physical inactivity may further aggravate these processes by accelerating muscle loss and contributing to vascular dysfunction [78,115], suggesting a potential vicious cycle between skeletal muscle dysfunction and cardiovascular dysfunction. However, the underlying mechanisms linking the two conditions remain incompletely understood, and it is unclear whether any specific mechanisms have predominant roles.

The reported association between sarcopenia and hypertension varies across studies, probably owing to the differences in the diagnostic criteria used to define sarcopenia, as well as the differences in age, sex, physical activity, obesity, comorbidities, and antihypertensive treatments [1,11,13–15,18–20]. Although evidence supports a potentially bidirectional relationship between sarcopenia and HTN, most of the available studies are observational, which limits conclusions about causality between them. A recent bidirectional Mendelian randomization study suggests potential causal effects between sarcopenia traits and HTN, in which insulin resistance is identified as a possible mediator [22], but these findings should be cautiously interpreted alongside evidence from observational studies, given the methodological assumptions and limitations inherent to Mendelian randomization.

From a clinical perspective, recognizing the interplay between sarcopenia and HTN can be beneficial in assessment and management of older patients with either condition. Specifically, among those with HTN, low muscle strength is associated with higher mortality [117]. This suggests that along with blood pressure assessment, evaluating muscle strength and physical function may provide additional information about the patient's overall health and functional status, and the presence of sarcopenia should be considered when managing HTN in older adults. A secondary analysis of the SPRINT trial suggested that intensive blood pressure control in older hypertensive adults with sarcopenia was associated with lower risks of cardiovascular events, without a significant increase in adverse events compared with standard blood pressure control [118]. However, its intensity and blood pressure target should be determined based on the individual's health status and risks rather than applying the same target to everyone [119]. Additionally, in treating hypertensive patients with sarcopenia, some evidence suggests that angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers may have better effects beyond reducing blood pressure, including potential benefit for improving muscle mass and physical function; however, this needs to be further confirmed with more longitudinal studies, particularly with regard to potential sex differences [1,11]. Moreover, assessment of muscle strength, physical performance, or physical activity could benefit patients with poorly controlled blood pressure or multiple cardiovascular risk factors. Existing evidence suggests that a 10% higher appendicular muscle mass-to-body-weight ratio was associated with approximately 6.4 mmHg and a 7.8 mmHg lower systolic blood pressure in men and women, respectively [120]. In the INERTIA study, 71 adults aged ≥60 years with low muscle strength were randomized to 12 weeks of progressive resistance training or a control group with assessment only. The training program significantly improved muscle strength and was associated with a greater reduction in diastolic blood pressure (DBP) compared with the control group (between-group difference: −4.2 mmHg; 95% CI: −8.3 to −0.1), while the difference in DBP in the control group was not statistically significant [121]. Nutritional interventions may be relevant, given that inadequate protein intake may contribute to reduced muscular anabolism. In a 2025 study of 126 older women with sarcopenia, protein intake of 1.2 g/kg/day improved muscle composition and function over 12 weeks compared with 0.8 g/kg/day [122]. Interestingly, a 2025 systematic review and meta-analysis of 65 randomized controlled trials found that milk-protein supplementation was associated with a modest reduction in systolic blood pressure, with a pooled difference of −1.99 mmHg (95% CI: −3.16 to −0.82) [123]. However, evidence directly examining whether treatment of sarcopenia can improve blood pressure in older adults with both conditions remains limited. Further interventional and longitudinal studies are needed to determine whether improving muscle strength, physical function, and nutritional status can influence blood pressure control, and to clarify whether particular mechanisms play a more prominent role in the relationship between sarcopenia and hypertension.

5. CONCLUSION

Current evidence suggests that sarcopenia and hypertension may be interconnected through several shared and potentially bidirectional mechanisms, including oxidative stress, mitochondrial dysfunction, RAAS dysregulation, chronic inflammation, insulin resistance, and vascular dysfunction. Although observational and emerging Mendelian randomization evidence supports an association between the two conditions, the causal pathways remain incompletely established. From a clinical perspective, assessment of muscle strength and physical function may provide additional information when managing older adults with hypertension, especially in the presence of sarcopenia. Regarding interventions targeting sarcopenia, evidence that they can directly improve blood pressure control remains limited. Consequently, more longitudinal and interventional studies to clarify the underlying mechanisms and determine whether improving muscle health can contribute to cardiovascular risk reduction and better blood pressure management in older adults are needed in the future.

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