Annals of Clinical & Analytical Medicine
Review

Sarcopenia: A review of risk factors, diagnosis, and treatment methods

Sarcopenia

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Abstract
Sarcopenia is a geriatric syndrome characterized by not only the loss of muscle mass but also the deterioration of muscle function. Risk factors include advanced age, male gender, lifestyle, increased body fat mass, smoking, diabetes, and malignancies. For diagnosis, the SARC-F questionnaire (Strength, Assistance with walking, rising from a chair, climbing stairs, and Falls) is recommended for assessing specific symptoms of sarcopenia. Numerous studies have shown that sarcopenia is associated with various adverse health outcomes, such as functional decline, increased healthcare costs, falls, fractures, hospital admissions increase, longer hospital stays, and higher mortality rates in older adults due to loss of muscle strength. Since the etiology of sarcopenia is multifactorial, its treatment and management of sarcopenic patients are also multifactorial. We believe that further studies are needed due to the clinical importance of sarcopenia.

Keywords
Sarcopenia, Elderly Individuals, Muscle Function Limitation

DOI: 10.4328/ACAM.22426 Received: 2024-09-27 Accepted: 2024-11-11 Published Online: 2024-12-11 Printed: 2025-05-25 Ann Clin Anal Med 2025;16(Suppl 2):S132-136
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Introduction

Sarcopenia is a geriatric syndrome characterized by not only the loss of muscle mass but also the deterioration of muscle function. Sarcopenia is associated with various adverse health outcomes, including prolonged hospital stays, metabolic/cognitive disorders, and an increased risk of falls and fractures [1]. The word "sarcopenia" is derived from the Greek roots "sarx," meaning flesh, and "penia," meaning loss. It was first proposed by Rosenberg in 1989 to describe age-related loss of muscle mass. In the 1970s, it was referred to as losses in lean body mass associated with aging [2,3]. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP1) published a definition of sarcopenia aimed at advancing the identification and care of individuals with sarcopenia. In early 2018, they reconvened to update the original definition. To confirm the diagnosis of sarcopenia, the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) has employed the detection of low muscle mass and quality, in addition to low muscle strength, which is one of the key characteristics of sarcopenia. Poor physical performance is identified as an indicator of severe sarcopenia [4]. In this review, we aimed to summarize the epidemiological characteristics, risk factors, and management of sarcopenia.

Epidemiology

Differences in sarcopenia outcomes can be observed between the general population and patients. This is likely due to both the demographic variations of the study groups and the differences in study outcomes, which should be taken into consideration. The presence of heterogeneity between studies, the use of small sample sizes, and potential errors in anthropometric measurements may render certain relationships inconclusive and could make the results open to debate. The factors mentioned above explain the differing results encountered in studies related to sarcopenia [1]. Moreover, variations in definitions used in studies on sarcopenia prevalence have led to differing outcomes. For instance, the prevalence of sarcopenia varies between definitions, with estimates ranging from 5% based on the EWGSOP1 criteria to 17% according to the International Working Group on Sarcopenia (IWGS). According to the Asian Working Group for Sarcopenia (AWGS), the prevalence of sarcopenia is around 8%. In a study conducted in our country, the general prevalence of sarcopenia in individuals aged 65 and older was found to be 5.2% (4.1% in women and 6.7% in men) [5, 6].

Risk Factors

There are numerous studies addressing the risk factors for sarcopenia. There is a relationship between sarcopenia and demographic factors such as age and gender. As age increases, the incidence of sarcopenia also rises. Additionally, in males, the rate of muscle loss and the incidence of sarcopenia increases with age [7].

The relationship between body mass index (BMI) and sarcopenia may appear complex. There is a positive correlation between the increase in body fat mass, rather than muscle mass, and sarcopenia [8].

Lifestyle, diet, and physical activity appear to be associated with sarcopenia. Sarcopenia may develop as a result of insufficient energy or protein intake, which can be attributed to factors such as anorexia, malabsorption, limited access to healthy foods, or impaired ability to eat [4].

Smoking has been associated with an increased risk of sarcopenia in a meta-analysis of 29 studies. Excessive alcohol consumption impairs skeletal muscle protein synthesis, and the exposure of muscle tissue to ethanol leads to autophagy, contributing to the development of sarcopenia. Additionally, there is a positive relationship between both short and long sleep durations and sarcopenia [8,9].

Diabetes and its complications are not only associated with risk factors for sarcopenia but also with the complications arising from sarcopenia. Other comorbidities, such as heart diseases, cognitive impairments, respiratory diseases, depression, and anorexia, have also been positively associated with an increased risk of sarcopenia [9, 10].

Sarcopenia is also significantly associated with a poorer prognosis in digestive system cancers, head and neck cancers, lung cancers, urothelial cancers, hematological malignancies, breast cancers, and ovarian cancers [11].

Early sarcopenia is characterized by a reduction in muscle size. Over time, a decline in muscle tissue quality also occurs. This is characterized by the replacement of muscle fibers with fat, increased fibrosis, alterations in muscle metabolism, oxidative stress, and degeneration of the neuromuscular junction. This ultimately leads to a progressive loss of muscle function and increased frailty [12].

There are several mechanisms that may be involved in the onset and progression of sarcopenia (Figure 1).

Histological changes in muscle fibers reveal that sarcopenia predominantly affects type II (fast-twitch) muscle fibers, while

Table 1. SARC-F (Strength, Ambulation, Rising from a chair, Stair climbing and history of Falling [17]

Component	Question	Scroring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None=0 Some=1 A lot or unable=2
Assistance in walking	How much difficulty do you have walking across a room	None=0 Some=1 A lot, use aids, or unable=2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None=0 Some=1 A lot or unable whithout help=2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None=0 Some=1 A lot or unable=2
Falls	How many times have you fallen in the past year?	None=0 1-3 falls=1 4 or more falls=2

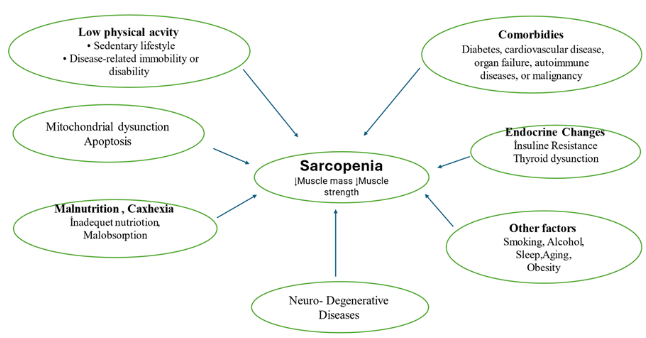

Figure 1. Mechanisms of sarcopenia

type I (slow-twitch) fibers are much less affected. It has been reported that there is a reduction in both the number and size of type II fibers [13].

Sarcopenia is classified into primary and secondary types based on its formation. While primary sarcopenia occurs due to old age, secondary sarcopenia occurs due to more than one cause. Unbalanced nutrition, decreased anabolic hormone levels, motor-neuron diseases, immobilization, apoptosis, and mitochondrial dysfunctions play a role in the formation of secondary sarcopenia [7].

According to EWGSOP2, sarcopenia consists of 3 stages

1-Probable sarcopenia: low muscle strength only

2-Confirmed sarcopenia: Low muscle strength + low muscle mass/quality

3-Severe sarcopenia: Low muscle strength + low muscle mass/ quality + low physical performance [4]. Sarcopenic obesity Changes in body composition occur with aging. Both the loss of skeletal muscle mass and the increase in adipose tissue are common characteristics observed with aging. The combination of these two conditions, known as sarcopenic obesity, increases the risk of adverse health outcomes. The prognosis is worse in the patient group with chronic disease along with sarcopenic obesity. The prolonged treatment process for this patient group also increases hospital costs. In addition, anthropometric measurements used in the diagnosis of sarcopenic obesity may yield incorrect results. Therefore, imaging modalities hold greater importance in this patient group [14]. There is a significant overlap between frailty and sarcopenia; most frail older adults have sarcopenia Frailty is a geriatric syndrome. Frailty is characterized by unwanted weight loss, fatigue, weakness, slow walking speed, and low physical activity. It is characterized by deterioration of the homeostatic reserve and decreased resistance capacity of the organism to stress. Frailty involves increased sensitivity to adverse health outcomes such as hospitalization, institutional care, and death [15, 16].

Diagnosis and Evaluation Methods

The 2018 European Sarcopenia Guidelines (EWGSOP2) recommend the use of the SARC-F questionnaire (Strength, Assistance with walking, rising from a chair, climbing stairs, and Falls) to assess specific symptoms of sarcopenia. SARC-F can be used as a screening test that is easily applicable in community healthcare services and other clinical settings. SARC-F is a 5-item questionnaire self-reported by patients to screen for the risk of sarcopenia. The responses are based on the patient's perception of their limitations in strength, walking ability, ability to rise from a chair, climbing stairs, and experiences with falls[4]. A score of 4 or above on the SARC-F questionnaire is considered significant for diagnosing sarcopenia (Table 1).

Muscle Strength

The handgrip test, also known as hand dynamometry, is used to provide a quantitative measure of muscle strength. Separate reference values are available for males and females in this test. In males, the handgrip strength should be 27 kg or higher, and in females, it should be 16 kg or higher. If the values fall below these thresholds, the individual is considered to have a lack of muscle strength, indicating possible sarcopenia [4]. Techniques such as knee flexion and extension, as well as peak expiratory flow methods, can also be used for the assessment of muscle strength. However, these two methods have disadvantages in terms of clinical applicability [7].

Muscle Mass Measurement

Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are considered the gold standards for the non-invasive assessment of muscle mass/quantity. However, these tools have several disadvantages, including high equipment costs, lack of portability, the need for highly trained personnel to operate the equipment, and increased overall costs. Additionally, the radiation exposure associated with CT scans has introduced limitations to its widespread use as a first-line diagnostic tool [4]. Dual-energy X-ray absorptiometry (DEXA) is a more commonly used tool for non-invasive measurement of muscle mass, such as total body lean tissue mass DEXA measurements may be affected by the patient's hydration status. The patient's hydration status should be considered before conducting measurements. Additionally, there is a direct correlation between an increase in height and muscle mass. Both skeletal muscle mass (SMM) and appendicular muscle mass (ASM) can be measured. Appendicular Skeletal Muscle (ASM) mass of 15 kg or more in women and 20 kg or more in men is considered normal. Another method used in the diagnosis of sarcopenia is the skeletal muscle mass index (SMI, skeletal muscle mass index, ASM/Ht2 (kg/m2), which is obtained by dividing SMM or ASM values by height squared. For ASMI, normal values are 7 kg/ m2 or higher in men and 5.5 kg/m²2 or higher in women [4,18]. Both skeletal muscle mass (SMM) and appendicular muscle mass (ASM) can be measured with Bioelectrical Impedance Analysis (BIA). BIA equipment does not directly measure muscle mass but instead derives a muscle mass estimate based on whole-body electrical conductivity. It operates based on the principle of quantifying the body's resistance to harmless alternating electrical currents sent through the body. BIA equipment, particularly single-frequency devices, is affordable, widely available, and portable. In addition, BIA measurements may also be affected by the patient's hydration status [4]. A definitive diagnosis of sarcopenia is made when both low muscle strength and low muscle mass are observed.

Anthropometric measurements are also used to estimate muscle mass. For this purpose, measurements of mid-upper arm circumference, skinfold thickness, and calf circumference can be performed. There is a positive correlation between calf thickness and muscle mass. One of the disadvantages of anthropometric measurements is the difficulty in obtaining accurate readings due to fat deposits and loss of skin elasticity that can occur with aging. On the other hand, due to the variability in measurements depending on the person performing them, anthropometric measurements are not recommended for routine diagnosis of sarcopenia on their own. However, it is suggested that they be combined with other tests for a more comprehensive evaluation [4, 19].

Physical Activity Evaluation

Physical performance assesses whole-body function, which is objectively measured in relation to movement. It is described as multidimensional, involving not only muscles but also many functions, including balance. Physical performance can be measured in a variety of ways, including gait speed, Short Physical Performance Battery (SPPB), and Timed-up andgo (TUG), among other tests. It may not always be possible to assess a patient's test performance. For example, this may not be possible for patients with dementia, Parkinson's, or gait deformity.

The walking speed of a person with normal muscle functions should be above 0.8 m/s. In the TUG test, the individual is asked to rise from a seated position without using their arms, walk 3 meters at a normal pace, turn around, and return to sit in the same spot. It is recorded in how many seconds the patient completes the specified activity. This time should normally be less than 20 seconds [4].

Stair Climbing Power Test: Primarily used for research purposes, this test involves asking the patient to step up and down on a platform of a certain height, with the time taken being compared to standard reference values [19].

When both muscle strength and mass are found to be low, and physical activity is also reduced, this condition is referred to as severe sarcopenia.

Alternative or new tests

The methods discussed here are used to assess muscle quantity and quality and their impact on the patient's quality of life. These diagnostic measurements are tested for validity, reliability, and accuracy, and they may play a significant role in the future. Factors such as cost, effectiveness, and standardization should be considered when using these methods.

Lumbar 3rd vertebra imaging with computed tomography

CT is considered the gold standard method for determining body composition because it distinguishes between fat and other soft tissues, has a strong correlation with total body muscle mass and fat mass, and provides a way to measure the cross-sectional area of tissue at the L3 vertebral level [20].

Specifically, CT images at a particular lumbar vertebral level (L3) have shown a significant correlation with total body muscle mass. This imaging method has been used to detect low muscle mass, even in patients with normal or high body weight. It can also be used to predict the prognosis of these patients [20]. It plays an important role in measuring muscle mass and detecting sarcopenia in the early stages [4, 21].

Mid-thigh muscle measurement

Mid-thigh imaging (with MRI or CT) has also been used in research studies. It is a good predictor of whole-body skeletal muscle mass. The mid-thigh muscle area is more strongly correlated with total body muscle volume compared to the L1–L5 lumbar muscle areas [21].

Psoas muscle measurement by computed tomography

Measurement of the psoas muscle with CT has also been used as a morbidity predictor in some studies, especially in conditions such as cirrhosis and colorectal surgery. However, since the psoas is a small muscle, some experts suggest that there are question marks about its use in the definition of sarcopenia. Further studies are needed to confirm or deny the reliability of this method [4].

Ultrasound Assessment of Muscle

Ultrasound is a non-invasive, radiation-free method with advantages such as bedside applicability by reliable and trained clinicians. It can be widely used to measure the amount of muscle, determine muscle loss, and also measure muscle quality. Assessment of pennate muscles, such as the quadriceps femoris, may detect a decrease in muscle thickness and cross-sectional area in a relatively short period of time [22].

Creatine dilution test

Creatine is produced by the liver and kidneys and is also obtained through a diet rich in meat. Creatine is taken up by muscle cells as phosphocreatine, converted into creatinine, and excreted in the urine. The rate of creatinine excretion is promising for estimating total body muscle mass. Total body creatine pool size and muscle mass are calculated from the enrichment of D3-creatinine in the urine. Creatine dilution test results show a strong correlation with MRI-based measurements of muscle mass and a moderate correlation with BIA and DEXA measurements. The creatine dilution test is currently primarily used in research settings, making its application in clinical environments impractical [23].

Specific Biomarkers

The development of a single biomarker could provide an easy and cost-effective means to diagnose individuals with sarcopenia and monitor treatment progress. However, due to the multifactorial pathophysiology of sarcopenia, it is currently not feasible to identify a single biomarker that can accurately characterize this condition across a heterogeneous population [20] Identifying a biomarker for sarcopenia would represent a significant advancement for diagnosis, treatment, and prognosis.

Outcomes and Complications of Sarcopenia

Numerous studies have demonstrated that sarcopenia is associated with various adverse health outcomes, including functional decline, loss of muscle strength, disability, healthcare costs, falls, fractures, increase in repeat hospitalizations, prolonged hospital stays, and increased mortality rates among older adults [9].

Sarcopenia is an increasingly prevalent global public health issue. It has been reported that sarcopenia affects 5-13% of individuals over 60 years old and 50% of those over 80 years old. In 2004, the total cost of sarcopenia to the American healthcare system was estimated to be approximately $18.4 billion [24]. In 2000, it was estimated that there were 600 million individuals aged 60 and above worldwide. This population is expected to rise to 1.2 billion by 2025 and 2 billion by 2050. This means that the elderly population is steadily increasing. With a more restrictive estimate, sarcopenia currently affects over 50 million people and could impact over 200 million individuals in the next 40 years [16].

Treatment and Management Strategies

Because the etiology of sarcopenia is multifactorial, its treatment and management of sarcopenic patients are also multifaceted. Early diagnosis and prompt initiation of treatment are of utmost importance. To manage sarcopenia, a multidisciplinary approach involving clinicians, physiotherapists, and dietitians is essential. The treatment can be divided into non-pharmacological and pharmacological approaches.

Non-pharmacological Approaches

Physical inactivity is directly associated with the loss of muscle strength and mass. One of the cornerstones of sarcopenia treatment is exercise under the guidance of a specialist. Short-term resistance exercise has been demonstrated to enhance the skeletal muscle's ability and capacity for protein synthesis.

Both resistance training and strength training have been shown to be effective interventions in the prevention and treatment of sarcopenia [2, 25].

Pharmacological Approaches

There are no agents approved by the Food and Drug Administration (FDA) for the treatment of sarcopenia in the United States. Dehydroepiandrosterone (DHEA) and human growth hormone have very limited effects. Growth hormone enhances muscle protein synthesis and increases muscle mass; however, it does not lead to significant gains in strength and function [26].

Testosterone and other anabolic steroids have positive effects on muscle strength and mass. However, their use is limited due to the increased risk of prostate cancer in men, virilization in women, and cardiovascular side effects [16, 26]

Among the compounds researched for sarcopenia treatment are myostatin inhibitors, vitamin D, angiotensin-converting enzyme inhibitors, eicosapentaenoic acid, thalidomide, OHR/AVR118, celecoxib, VT-122, omega-3 supplements, and anabolic agents such as ghrelin and its analogs, MT-102, BYM338, and ruxolitinib [16].

There is considerable interest in using herbal supplements to improve muscle mass and function in patients with sarcopenia. Some herbal compounds have shown positive effects on skeletal muscles in human studies. These include curcumin derived from Curcuma longa, alkaloids and steroidal lactones obtained from Withaniasomnifera (Solanaceae), catechins derived from Camellia sinensis, proanthocyanidins from grape seeds, and gingerols and shogaols derived from Zingiber officinale [27].

In the treatment of malnutrition-related sarcopenia, similar nutritional plans to those used for cachectic patients should be implemented. A daily protein intake of 1.2 to 1.6 g/kg/day is recommended to prevent age-related sarcopenia [28].

Conclusion

Sarcopenia is a significant health issue that negatively affects the quality of life and limits independence in the elderly population. Although progress has been made in the diagnosis and treatment of this condition, which requires a multidisciplinary approach, there are still important steps to be taken. Further clarification of diagnostic criteria and treatment approaches, development of personalized treatment strategies, and increasing awareness are crucial. Future scientific studies will contribute to the creation of more effective and comprehensive approaches to combating sarcopenia. This review aims to raise awareness of sarcopenia and support more effective management of this important geriatric problem in clinical practice.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

Funding: *None*

Conflict of Interest

The authors declare that there is no conflict of interest.

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How to cite this article:

Abdullah Ozdemir, Asiye Ozdemir. *Sarcopenia: A review of risk factors, diagnosis, and treatment methods. Ann Clin Anal Med 2025;16(Suppl 2):S132-136*