







Update: Sarcopenia

Atualização: Sarcopenia

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ABSTRACT | OBJECTIVES: To update on a sarcopenia literature review published in 2014 in this journal. According to the Working Group on Sarcopenia in Older People Consensus (EWGSOP2), sarcopenia was redefined as a muscular disease, characterized by muscular strength reduction, associated with a diminished muscular quantity and /or quality and /or low physical performance, being stratified as primary, secondary acute and chronic. Beyond physical consequences as a fall risk and daily activities, sarcopenia can promote a dysbalance between protein synthesis and degradation. Sarcopenia prevalence is higher with increasing age, especially after 60 years. Studies in six countries had found sarcopenia prevalence between 4.6% and 22.1%, but differences between definitions, diagnostic methods, and cutoff points to evaluate muscle mass and function are found. To improve sarcopenia risk detection, EWGSOP2 suggests the use of the SARC-F questionnaire. Muscle mass measurement recommended methods are Magnet Resonance Imaging, Computed Tomography, Double Energy X-Ray Absorptiometry, Electric Bioimpedance, and Anthropometry with variable accuracy and costs between these methods. To evaluate muscle strength, the handgrip strength test is the main method recommended. In addition, four Meter Gait speed is recommended to evaluate physical performance. Treatment options are progressive exercise, endurance training, and aerobic exercises, together with nutritional interventions. Sedentary lifestyle, obesity, and frailty are the main risks factors associated with muscle mass and function losses in the clinical setting.

KEYWORDS: Sarcopenia; Body composition; Muscular strength.

RESUMO | OBJETIVO: Fazer uma atualização da revisão de literatura sobre sarcopenia publicada em 2014 nesta revista. De acordo com o Consenso do *Working Group on Sarcopenia in Older People* (EWGSOP2), a sarcopenia foi redefinida como uma doença muscular, caracterizada pela redução da força muscular, associada à diminuição da qualidade/quantidade muscular e/ou desempenho físico, sendo classificada como primária, secundária, aguda e crônica. Além de consequências físicas como aumento da ocorrência de quedas e limitação para atividades cotidianas, pode promover alterações sistêmicas pelo desequilíbrio entre síntese e degradação proteica. A prevalência aumenta com a idade, sendo mais alta a partir de 60 anos. Estudos em seis países encontraram prevalência entre 4,6% e 22,1%, havendo oscilação de valores conforme definições utilizadas, métodos diagnósticos e os pontos de corte para índice de massa muscular (IMM). Como estratégia para refinar a detecção do risco da sarcopenia, o EWGSOP2 sugere aplicação do questionário SARC-F. Para mensuração da variável massa muscular, os métodos recomendados são Ressonância Magnética, Tomografia Computadorizada, Absorciometria de Raio-X de Dupla Energia, Bioimpedância Elétrica e Antropometria, existindo acurácias e custos variáveis entre eles. Na aferição da força muscular, a principal forma de mensuração é a força de preensão palmar. Já o desempenho físico pode ser quantificado através do teste de velocidade de marcha de quatro metros. As formas de tratamento são treino de exercícios de resistência progressiva e aeróbicos, além de uma nutrição adequada. O estilo de vida sedentário, obesidade e fragilidade são fatores desencadeantes de perda de massa e função muscular no ambiente clínico.

PALAVRAS-CHAVE: Sarcopenia; Composição corporal; Força muscular.

Summary of key actualization points

- Sarcopenia has been defined as a distinct disease and has received the CID-10-CM code.
- The EWGSOP2 revised, in 2018, sarcopenia diagnostic criteria and definition, characterized as muscle disease, with its main determinant being the reduced muscle force and its presence, even as an isolated condition, fulfills sarcopenia suspicion;
- Sarcopenia is present when reduced muscle strength is associated with a reduced muscle quality or quantity.
- Severe sarcopenia is present when reduced muscle strength is associated with reduced muscle quality or quantity and low physical performance.
- Time-associated substages were newly defined: acute sarcopenia substage (associated with lesions or acute diseases) and chronic sarcopenia when present ≥ 6 months (which tends to be related to higher mortality).
- The protocols included two screening tools: the decision-tree Find-Assess-Confirm-Severity (F-A-C-S); and the SARC-F sarcopenia risk screening questionnaire.

Introduction

The impairment of skeletal muscle function due to age and physical inactivity, malnutrition, and the presence of catabolic diseases, is an important public health problem.¹ This is related to increased risk of falls and fractures, mobility changes;² inability to perform daily activities;³ association with heart⁴ and respiratory⁵ diseases causing the decreased quality of life, social limitations and cognitive impairment^{6,7}, loss of independence or need for long-term care⁸, it can lead to death.⁹ Evidence is discussed that sarcopenia can occur at earlier stages of life, proposing its detection through low muscle strength. In this context, it is necessary to raise awareness about the disease and outline criteria, tools, and interventions to prevent, delay, treat and reverse sarcopenia when possible.¹

History and definition

Sarcopenia was initially described by Rosemberg as a reduction in overall muscle mass during aging. In 1998, Richard Baumgartner developed a way to measure sarcopenia, based on the determination of relative muscle mass or muscle mass index (MMI), by Dual Energy X-Ray Absorption (DEXA) methods, where muscle mass is divided by height squared, analogous to calculating the body mass index (BMI). Ian Jansen et al., in 2002, proposed a classification based on the severity after evaluation by the bioelectricity impedance method (BIA).¹⁰

The first Sarcopenia Consensus was published in 2010 by Working Group on Sarcopenia in Older People (EWGSOP) and expanded its definition to include, in addition to reducing muscle mass, decreased strength, and worse physical performance, the reduction in muscle mass being the main factor for identifying sarcopenia.¹¹

In 2016, sarcopenia became recognized as a distinct disease and received the CID-10-CM code. In 2018, the EWGSOP2 revised the definition and diagnosis, characterizing it as muscle disease, signaling that reduced muscle strength is the main determinant and the isolated presence evidence suspicion of sarcopenia.¹ When this reduced muscle strength is associated with decreased quality or quantity of muscle, it is possible to affirm the presence of sarcopenia. In situations where there is low muscle strength, low quality or quantity of muscle, and low physical performance, it is possible to affirm the presence of severe sarcopenia. Regarding the duration, the acute subcategories were also identified (associated with acute injuries or illnesses) and chronic, when equal or superior for six months, which is related to a higher risk of death.¹

Causes and consequences

The focal mechanism of the process of loss of mass, strength, and physical performance in sarcopenia

is oxidative stress, triggered by endogenous and exogenous factors, culminating in reduced protein synthesis, increased protein degradation, alteration of neuromuscular integrity, and increase in muscle fat content.¹²

Primary sarcopenia affects mainly the elderly people, there is no specific other evident cause, and its changes reveal the fragility, increased number of falls and fractures, the limitation for daily activities, which may influence adverse outcomes in hospitalization and result in a risk of death.¹⁰ For the secondary, physical inactivity is mentioned, which leads to the accumulation of visceral fat to activation of inflammatory pathways, interleukin-6 mediated, active in changes in muscle composition (reduction of myokines production from muscle contraction) and decreased functionality.¹³

Numerous diseases associated with progressive organ failure, inflammatory and endocrine disorders can promote catabolic effects through greater protein degradation¹⁴, the chronic diseases (obesity, chronic kidney failure, chronic obstructive pulmonary disease, type 2 diabetes, cancer, congestive heart failure); neurological diseases (dementia and depression), frailty and malnutrition may be associated with sarcopenia.¹³

Another crucial factor for secondary sarcopenia may be linked to nutritional aspects, as inadequate energy intake, macro, and micronutrients; gastrointestinal disorders (malabsorption); or use of medications that cause anorexia. Furthermore, conditions similar to sarcopenias such as sarcolemmic obesity, frailty, and malnutrition understand a cycle aggravating their adverse consequences.¹

Epidemiology of sarcopenia

Prevalence increases with age, and values fluctuate according to the definitions used in diagnostic methods for reduced muscle mass and cutoff points for the IMM.¹⁵ Data report that worldwide the prevalence is highest in the population over 60 years

old, despite the multifactorial causes present in its appearance and progression.¹⁶

In a study by Diz et al., which presented the prevalence in the elderly from six countries: The United States, United Kingdom, Brazil, Japan, South Korea, and Taiwan, the frequency ranged from 4.6% to 22.1%. There was a high prevalence in people aged 60 years and over, being the highest rates in Japan, corresponding to 22.1% for females and 21.8% for males. Brazil was the second country with a high proportion, in which women appeared with 16.1%, while men with 14.4%.¹⁷

In national investigations, a study conducted with elderly people in São Paulo found a prevalence of 4.8%. The relative hazard ratio was 3.32 for elderly people aged 70-79 years and 9.79 for 80 and over.¹⁸ A trial developed in Florianópolis verified the prevalence of sarcopenia and the association with changes in socioeconomic, behavioral, and health factors, noting a percentage of 17% in women and 28.8% in men.¹⁹ Already in Rio de Janeiro, the prevalence rate in pre-sarcopenia was 60% and in sarcopenia 77.5% in females; while for males, pre-sarcopenia 40% and sarcopenia 22.5%.²⁰

Shimokata et al.'s study on the epidemiology of sarcopenia with chronic non-communicable diseases demonstrated a high prevalence (39.5%) with type 2 diabetes. There was a positive association (odds ratio 5.5) in the metabolic syndrome with sarcopenia in men aged 65-74 years, being modified by sex and age; however, abdominal obesity was the main contributor. In people with chronic obstructive pulmonary disease, the prevalence was 14.5%; in those infected with HIV, 5-24.2%; with chronic kidney disease, 5.9-14% during pre-dialysis and 12.7-33.7% in dialysis.¹⁵

Regarding patients with neoplasms, it was reported that the percentage of pre-sarcopenia was 26-65% for gastric/esophageal cancer; 19-39% in colorectal cancer, 11-66% in hepatocellular carcinoma; 21-63% pancreatic cancer; 29-68% for kidney cancer; 60-68% bladder cancer; about 70% for non-small cell lung cancer; and approximately 55% in beta cell lymphoma.¹⁵

In a meta-analysis of prospective cohort studies, it was shown that individuals with sarcolemmic obesity had a 24% risk of mortality for all causes, especially men.²¹

Diagnostic instruments

There are many test options and tools used in clinical practice and research. The choice of instrument depends on the patient's mobility, the scope of application, technical resources, and whether there is a purpose for monitoring the patient's progression and/or treatment. The variables that establish the diagnosis are muscle strength, physical performance, and muscle quantity or quality. This was the relevant variable. However, muscle strength came to be highlighted, as sarcopenia is considered a muscle disease.¹

For clinical practice, complaints and apparent perceptions should be examined, paying attention to falls, weakness, slow walking, difficulty getting up from a chair, and weight and muscle mass reduction.¹ In this context, the SARC-F questionnaire is recommended for risk screening, as it is accessible, has low to moderate sensitivity, and has very high specificity to predict low muscle strength. It is self-reported and addresses limitations on strength, ability to walk, get up from a chair, climb stairs, and history of falls.^{1,3} The Ishii test can be used, as it calculates based on age, grip strength, and calf circumference.¹

The parameters for measuring sarcopenia are:

a) Muscle strength

The handgrip strength is the most used, obtained by manual dynamometry.²² In identifying muscle weakness, the reference values for women are less than 20kg and for men less than 30kg.¹ However, there are circumstances in which its application is

unfeasible, such as advanced arthritis and stroke, applying isometric torque methods to measure the strength in the lower limbs.²³

The stand-up test as a substitute for determining the strength of the quadriceps muscle group may be applied. It is necessary to get up five times, without the help of the arms, in a timed period. Also, the timed chair support test can be used, counting how many times the patient is able to get up and sit down in thirty seconds.²⁴

b) Muscle quantity

The amount of mass and muscle can be estimated by various techniques, requiring results to be adjusted for height or BMI. The recommendation is to measure the muscle quantity, the Body Skeletal Muscle Mass (BSMM), the Appendicular Skeletal Muscle Mass (ASMM), or Cross Section Area of Specific Groups of Muscles or Body Segments should be used.¹

Among the diagnostic evaluation methods are magnetic resonance imaging (MRI) and computed tomography (CT), considered the gold standard, DEXA, BIA, and anthropometry.²⁵ MRI and CT are the most accurate methods for BSMM quantification due to the advantage of determining muscle quality, fat mass, and fat infiltrated into the muscle; however, they have high costs, require trained personnel, and there are no well-defined protocols for low muscle mass.^{1,24}

DEXA determines the amount of muscle mass through total body lean tissue mass and ASMM.²⁵ The quantification of muscle mass, the absolute level of BSMM or ASMM, can be adjusted to body size by the equations – height² (ASMM/height²); weight (ASMM/weight) or BMI (ASMM/BMI).²⁶ However, it does not determine muscle quality due to reduced ability to differentiate between free lean mass, water, and bone mass, which may be influenced by hydration.^{1,27}

BIA assessment is a non-invasive, practical, reproducible, and relatively inexpensive method that estimates, in addition to body components, the distribution of fluids in intra-extracellular spaces, as well as the quality, size, and integrity of cells. It is based on the principle of electrical conductivity to estimate body compartments (fat and lean mass), but it does not determine muscle quality, and hydration can interfere with the results.²⁷

Anthropometry is a simple and inexpensive method, but it is less accurate than the others, as it is not accurate in measuring muscle composition and mass, although it is widely used to assess nutritional status in the elderly.²⁸ Robert Lee et al. developed predictive equations for muscle mass from anthropometric measurements and identified a high correlation with MR to estimate BSMM.²⁹ Robert Lee et al. developed predictive equations for muscle mass from anthropometric measurements and identified a high correlation with MR to estimate BSMM.³⁰ In this context, calf circumference can measure lean mass, which is important when there are no other access methods (cutoff point <31cm).²⁸

Muscle mass can also be obtained from the creatinine values of urinary excretion, as it originates almost exclusively from the muscle. The difficulty is to maintain a meat-free diet for several days and prolonged urine collection; however, the creatinine excretion rate is a promising protocol to estimate the BSMM.¹ The total or partial amount of potassium in the fat-free soft tissues is another measure of muscle mass. That is because skeletal muscle contains more than 50% of the body's potassium. Compared to other forms, it is a safe and cost-effective measurement, but it is little used in practice.³¹

c) Physical performance

Some tests are used to assess physical performance, which involves the aspect of locomotion, but as it is a multidimensional measurement, it involves muscles and nervous function (central and peripheral), including balance.³² One of these is the four-meter gait speed test, a fast, safe, and highly reliable method, with gait speed values $\leq 0.8\text{m/s}$ indicating reduced physical performance; it may indicate severe sarcopenia if the strength and mass variables are also reduced.¹

Other tests used to determine physical performance are "Time Up and Go" (TUG), which consists of leaving a sitting position in a chair, standing up, walking three meters, returning and returning to a sitting posture; the "Short Physical Performance Battery" (SPPB), composed of the gait speed tests, balance test and test of getting up from a chair; and the 400-meter walk test assesses physical performance, checking walking capacity and endurance. These tests may demonstrate limitations if the patient has pathologies such as dementia; gait, or balance disorders, as they make it unfeasible.^{1,10}

The EWGSOP2 proposed cutoff points supported by European populations of young and healthy adults³³, which are shown in Table 1.¹

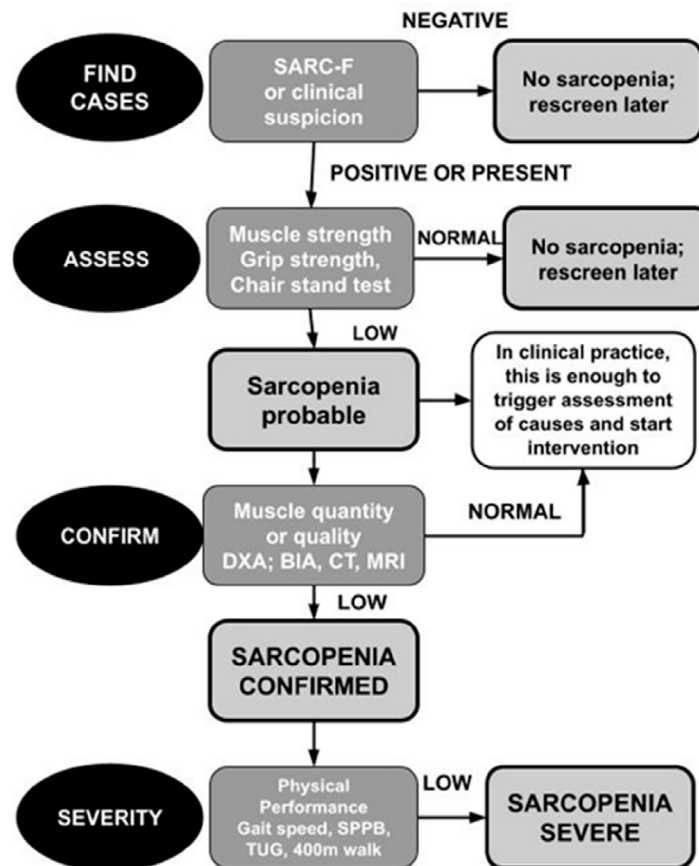
In order to screen patients at risk for sarcopenia, diagnose it and quantify its severity, the algorithm (Figure 1) becomes a simple and viable tool in clinical practice. Therefore, the decision tree is called Find-Assess-Confirm-Severity (F-A-C-S) or Find-Assess-Confirm-Severity.

Table 1. Sarcopenia test cutoff points suggested by the EWGSOP2

Test	Cut points	
	Man	Woman
Low strength by chair stand and grip strength		
→ Grip strength ³³	<27 Kg	<16 Kg
→ Chair stand ³⁴	>15s for five rises	---
Low muscle quantity		
→ ASM ³⁵	<20 Kg	<15 Kg
→ ASM/ height ^{2,36}	<7.0 Kg/m ²	<5.5 Kg/m ²
Low performance		
→ Gait speed ⁷	≤0,8m/s	---
→ SPPB ^{37,38}		
→ TUG ³⁹		
→ 400m walk test ⁴⁰	≤8 point score	
	≥20 s	
	Non-completion or ≥6 min for completion	

Source: Adaptation of sarcopenia test cutoff points suggested by EWGSOP2.¹

Figure 1. Adaptation of the suggested algorithm EWGSOP2¹



New tests for diagnosis

To detect sarcopenia, new tests (Table 2) are under development to measure the quantity and quality of the muscle, as well as its influence on the patient's quality of life.

Table 2. New tests for diagnosing sarcopenia

Test name	Use
Computed tomography image of the third lumbar vertebra (L3)	Used to detect reduced muscle mass, as the L3 muscle has been reported to portray that of the body.
Mid-thigh muscle measurement	Applied in research, as it is sensitive to changes and can deduce skeletal muscle mass throughout the body. It is done through magnetic resonance imaging or computed tomography.
Measurement of the psoas muscle with computed tomography	Although it has been described as a predictor of morbidity in some cases, experts debate that the psoas is a very small muscle that does not represent the general state of the disease.
Muscle quality measurement	Assessed using computed tomography and magnetic resonance imaging in the survey. For the purpose of verifying changes in muscle composition and functioning.
Creatine Dilution Test	Test used in research, in which a dose of creatine labeled with deuterium (D3-creatine) is ingested orally by the patient in a fasting state. After that, the types of creatine (marked, unmarked and in urine) are measured.
Ultrasound evaluation of muscle	Incorporated into clinical practice to support a diagnosis of sarcopenia in older adults. The EuGMS group suggested the assessment of muscle thickness, cross-sectional area, cord length, penetration angle and quality.
Specific biomarkers or biomarker panels	Creation and validation of a biomarker for diagnosis and monitoring of sarcopenia.
SarQoL Questionnaire	Easily applicable, which can foresee future complications of the disease that affected the patient's quality of life.

Source: Adapted from EWGSOP2.¹

Treatment

Among the forms of treatment for sarcopenia are physical exercise, nutrition, and hormone replacement, which are described below:

a) Exercise

The practice of physical exercise is one of the ways to mitigate the catabolic effects of inactivity and consequent sarcopenia. Among the different types of exercise, strength training has a great effect on increasing muscle mass and strength. Twelve weeks of strength training performed three times a week resulted in increased strength and muscle hypertrophy.¹⁰ However, some studies have demonstrated similar strength improvement with one set per week.^{12,41}

Strength training is progressively more used in the elderly. It consists of performing exercises with increased resistance to the greatest possible extent and is associated with increased muscle mass and physical function.⁴² The American College of Sports Medicine and the American Heart Association recommends performing 8 to 10 exercises for the largest muscle groups at least twice a week, with resistance that the individual can perform between 10 and 15 repetitions.¹⁰

Despite not contributing to hypertrophy, aerobic exercises can increase the cross-sectional area of muscle fibers, mitochondrial volume, and enzyme activity, promoting an improvement in the frequency of decline in muscle mass and strength. These reduce intramuscular fat, strengthen muscle functionality³² and reduce the loss of motor units.⁴³ The anabolic effects of aerobic exercise are related to the increased supply of nutrients to the muscle.⁴⁴

Among the studies showing the benefits of physical activity on sarcopenia in the elderly, one revealed that the elderly who practice it have a lower chance of developing sarcopenia. The other shows an improvement in the physical performance of sarcopenic elderly individuals undergoing a six-month exercise program.^{10,45,46}

a) Nutrition

Among the physiological changes of aging are changes in body composition, increased fat and visceral fat, and involuntary reduction in muscle mass.⁴⁷ Since nutrition is related to secondary causes of sarcopenia, such as low food intake, reduced nutrient bioavailability, high nutrient requirements; therefore, improving diet and nutrition can be effective in preventing and treating sarcopenia.¹

Certain nutrients and dietary patterns promote protective effects against aging processes.⁴⁸ An important anabolic stimulus for skeletal muscle is protein and amino acid intake. Among amino acids, branched-chain ones are directly stimulated by muscle protein synthesis, specifically leucine – activator of intracellular signaling proteins. And consumption alone, supplemented and associated with other amino acids or carbohydrates, are effective in stimulating muscle protein synthesis.⁴⁹

About micronutrients, the use of vitamins D, C, B6, B12, carotenoids, A, and E affects skeletal muscle and is related to metabolism and protein synthesis. Calcium, selenium, magnesium, potassium, phosphorus, iron, and zinc are the minerals used due to their association with regulatory signaling processes for muscle fibers, muscle protection against oxidative damage, related to physical activity, and muscle performance in the elderly, preservation of thin fabric, among others.⁴⁸

Other dietary and nutritional factors considered are antioxidant substances (omega-3 fatty acid), which can impact skeletal muscle systems; a combination of nutrients that are related to muscle strength or physical performance; food groups (dairy, tea, fruits, and vegetables); eating patterns; and the assessment of dietary factors; all can exert protective effects against sarcopenia and frailty, as well as play a role in the preservation of muscle mass and physical capacity.⁴⁸

b) Hormones

Considering the multifactorial genesis of sarcopenia, it is reasonable to believe that hormone supplementation is a good option to prevent or treat it. Therefore, several hormones have metabolic effects on muscle mass and function. Among them are sex hormones (testosterone, estrogens - estradiol and dehydroepiandrosterone), cortisol, growth hormone, IGF-1, ghrelin, insulin and oxytocin.⁴⁹

Closing remarks

Sarcopenia is a problem that affects individuals during senescence, may occur early and is defined as a muscle disease. It is recommended for diagnosis, the measurement of strength and skeletal mass, in addition to physical performance. However, data regarding frequency are quite divergent due to the various diagnostic instruments to measure muscle mass and the different cutoff points. Furthermore, it demands high costs for health systems, increased risk of hospitalization, and expenses during hospitalization.

The main strategy to treat it is progressive strength training, and aerobic exercise has positive effects on reducing muscle loss over the years and decreasing the loss of motor units. Optimal nutrition with an adequate amount of calories, macro, and micronutrients influences muscle function.

From future perspectives, there is a need to verify the impacts that can cause and worsen sarcopenia. In addition, the moment of intervention identifies

elderly people at high risk of sarcopenia and preventive actions. Finally, the accuracy of the strength and physical performance instruments must be evaluated to predict skeletal muscle mass reduction, as these are probably the most relevant variables for diagnosing sarcopenia.

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Author contributions

Martinez BP, Camelier FWRC, Camelier AA participated in the conception, design, data search, interpretation of results, writing of the scientific article, and final review. Santos NGS and Costa LVM da, Santana Neta LG, Sacramento JM, Santos NC participated in the data search, interpretation of results, and scientific article writing.

Competing interests

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