

BRIEF REVIEW ΒΡΑΧΕΙΑ ΑΝΑΣΚΟΠΗΣΗ

Sarcopenia Literature update

Sarcopenia is a major health condition associated with aging, defined as loss of muscle mass and function. Its etiology is still poorly understood. Effective treatment options in the management of men and women with sarcopenia are focused on increasing activity (exercise) and providing adequate nutrition, but all options are under investigation. This is a review of current knowledge on the definition, etiology and consequences of sarcopenia, and effective intervention to help people with this condition.

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Σαρκοπενία: Νέα δεδομένα
από τη βιβλιογραφία

Περίληψη στο τέλος του άρθρου

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1. INTRODUCTION

Sarcopenia is recognized as a major health problem among older adults.¹ It is a syndrome characterized by loss of skeletal muscle mass and strength, with a risk of adverse consequences such as disability, development of frailty, poor quality of life and death.^{2–5} The term sarcopenia (from the Greek sarx for flesh and penia for loss) was first coined in 1989 by Irwin Rosenberg to describe this age-related decrease of muscle mass.⁶ Although primarily a disease of the elderly, its development may be associated with conditions such as dementia and osteoporosis.⁷

This overview is intended to outline the current understanding of sarcopenia and its consequences, and forms of intervention, with a view to helping clinicians to provide more accurate diagnosis and effective management.

2. DEFINITIONS OF SARCOPENIA

The term sarcopenia, derived from the Greek sarx (flesh)

and penia (loss), literally meaning poverty of flesh,⁸ was first coined by Irwin Rosenberg in 1989 to identify the age-associated loss of muscle mass and function.⁶ In 2009, sarcopenia was defined as the relative muscle mass of two standard deviations (*SDs*) below the mean of a large sex-specific reference population aged 18–40 years.⁹ Sarcopenia was subsequently classified according to its severity, with class I sarcopenia referring to a skeletal muscle index of between 1 and 2 *SDs*, and class II sarcopenia a skeletal muscle index of more than 2 *SDs* below the young adult reference values.¹⁰

Early definitions of sarcopenia were based solely on muscle mass in relationship to the range of muscle within a reference population. In recent years various other definitions have been proposed in an attempt to better characterize sarcopenia, to establish criteria for its definition and diagnosis, and to identify outcome measures in clinical practice and research.¹¹

Definitions of sarcopenia were included by the European Working Group on Sarcopenia in Older People (EWGSOP)

(based on gait speed, handgrip strength, muscle mass) and the International Working Group on Sarcopenia (IWGS) (gait speed, muscle mass).¹² In 2009, EWGSOP defined sarcopenia as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcome, including disability and poor quality of life,² and proposed as the criterion the coexistence of two factors: low muscle mass and low muscle function (handgrip strength, gait speed).¹³ In 2011, the International Group on Sarcopenia in Older People (IGSOP) defined sarcopenia as “the aged-associated loss of skeletal mass and function.”^{5,13}

3. DIAGNOSTIC CRITERIA

During the past two decades several diagnostic criteria have been proposed: Total or appendicular lean mass (ALM) as a percentage of body mass, absolute muscle mass defined as ALM corrected for height, i.e., ALM/height squared (ALM/ht²), or total lean mass, muscle strength, walking speed, or a combination of these criteria.¹⁴ In 2010, two articles were published that proposed diagnostic criteria,^{2,15} and in 2011 similar consensus diagnostic criteria were proposed.¹⁶ Diagnostic algorithms have been described by EWGSOP, IWGS and the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project.¹⁷

The EWGSOP diagnosis of sarcopenia is based on the criteria of low muscle mass (ALM ≤ 7.23 kg/ht² for men and ≤ 5.67 kg/ht² for women) and low muscle function, either low strength and or low physical performance. Low muscle strength is measured by grip strength (< 30 kg for men and < 20 kg for women) and low physical performance is measured by gait speed (< 0.8 m/s).^{2,17}

EWGSOP defined three clinical conditions: (a) Pre-sarcopenia (characterized by low muscle mass without impact on muscle strength or physical performance), (b) sarcopenia (characterized by low muscle mass, plus low muscle strength or low physical performance), and (c) severe sarcopenia (identified when all three criteria are met: low muscle mass, low muscle strength and low physical performance).^{11,13,17}

It has been recommended that sarcopenia should be evaluated in patients with decline in strength and physical function from the age of 50 years.¹³

4. ASSESSMENT TECHNIQUES

EWGSOP reviewed a wide range of assessment tools that can be used to measure the specific variables of muscle mass, muscle strength and physical performance.²

4.1. Muscle mass

Muscle mass or lean body mass can be determined by computerized tomography (CT), magnetic resonance imaging (MRI) and dual energy X-ray absorptiometry (DXA). DXA is a reliable method with minimal radiation exposure and therefore is the recommended option.^{13,18} Bioimpedance analysis (BIA) can be used to estimate fat and lean mass and is a good alternative to DXA.^{2,13,18} It is easy to operate, low cost, portable, and suitable for all patients. Under standard conditions, BIA measurements correlate well with MRI measurements.¹⁹

4.2. Muscle strength

Hand grip strength is a simple and reliable measure of muscle strength.^{13,17} Grip strength is related to limitations in the activities of daily living and represents a good marker of poor mobility.^{17,20} Knee extensor muscle strength can be also measured (isometric or isokinetic), which is suitable for research studies, although its use in clinical practice is limited by the need for special equipment and training.^{13,17}

4.3. Muscle-physical performance

The Short Physical Performance Battery (SPBB) test is recommended for use in clinical practice.^{13,17} This is a simple test that examines three areas: static balance, gait speed and getting in and out of a chair.^{13,21} Timed up and go test (TUG) is also recommended and can be used in geriatric assessment. TUG measures the time a person requires to rise from a chair, walk three meters, turn around, go back and sit down.^{13,17}

A brief, simple and inexpensive screening test for sarcopenia is a self-reported questionnaire (SARC-F). The SARC-F includes five items based on cardinal features or consequences of sarcopenia. SARC-F is a brief and inexpensive assessment tool which exhibits good internal consistency reliability and factorial, criterion related, and construct validity.²²

5. ETIOLOGY

Sarcopenia has a complex and multifactorial etiology. The causes may include loss of motoneurons, nutritional factors, inflammation, chronic diseases, insulin resistance, altered endocrine function, reduction in levels of sex steroids and impairment in the growth hormone (GH)/insulin-like growth factor (IGF-I) pathway.^{2,23} Molecular, cellular, nutritional and hormonal mechanisms are responsible

for progressive deterioration in skeletal muscle mass and function.²⁴ The causes can be classified as primary (age-related) sarcopenia and secondary sarcopenia from activity-, nutrition- and disease-related causes.^{17,25}

Muscle accounts for approximately 40% of the total body mass and 75% of the body's cell mass.²⁶ Aging is accompanied by changes in body composition, including a decrease in both muscle and bone mass.²⁷ After middle age, the fat mass gradually increases while the lean tissue mass decreases.^{27,28} Cross-sectional data demonstrate that healthy men have a body composition of approximately 20% body fat at the age of 25 years, 30% at 55 years and greater than 35% at 75 years.^{29,30} From 20 to 80 years of age, approximately 30% of muscle mass is lost.²⁴ In addition to loss of mass, there is a decline in muscle strength per unit of muscle mass (muscle efficiency).²⁶ The age-related loss of muscle mass results from both a reduction in the size and a decrease in the number of muscle fibers, particularly in individuals aged 70 years and above.²⁴ Cross-sectional studies have demonstrated a shift in muscle size composition with a higher type I/type II fiber ratio with advancing age.² Type I muscle fibers are recruited for most of the activities of daily living (ADLs) and during submaximal exercise (e.g., walking). Type II muscle fibers are recruited during high-intensity activities (e.g., rising from a chair, climbing steps or regaining posture after a perturbation of balance).^{13,31}

Obesity and fat infiltration into skeletal muscle also play an important role in sarcopenia.³² In the Framingham study, researchers highlighted the functional and mobility limitations in sarcopenic obesity.³³

Tendons are altered by aging and studies have shown that with aging there is a decrease in tendon stiffness.^{24,34} Tendon changes are important in altering muscle power with aging.^{2,24} Muscle power is defined as the product of force generation and speed of muscle contraction. Decrease in muscle efficiency is responsible for the decline in muscle power with aging.²⁶ Inability to develop muscle power is one of the causes of frailty.³⁵ Alteration in both muscle architecture and the mechanical properties of tendons may contribute to the loss of intrinsic muscle force with aging.¹³ Muscle strength and muscle power also decrease with advancing age, particularly in the lower body. The age-associated decline in isometric knee extensor strength has been estimated at between 55% and 76%.³⁶

At the molecular level, sarcopenia results from a decrease in skeletal muscle protein synthesis, and possibly an increase in protein breakdown.¹³

Environmental causes of sarcopenia are decline in activ-

ity and decrease in nutritional intake. The most prominent cause of sarcopenia is inactivity, and in general, elderly people are less active.³² Muscle contraction (exercise) causes the release of muscle growth factors which activate satellite cells and protein synthesis. With aging, there is a decrease in muscle protein synthesis, but in contrast exercise may lead to muscle regeneration.^{26,35} Loss of muscle may be caused by a decrease in anabolic factors (GH, androgens, estrogens, etc.), an increase in catabolic factors (i.e., inflammatory cytokines), or a combination of the two.²⁶ Studies have demonstrated an association between vitamin D deficiency and hyperparathyroidism and lowered muscle mass and muscle strength. Lower 25-OHD and higher PTH levels increase the risk of sarcopenia in old age.³⁷

There is a decrease in food intake in elderly people, who frequently consume less than the recommended daily allowance (RDA) of 0.8 g protein/kg.²³ Inadequate protein and calorie intake, but also over nutrition that results in sarcopenic obesity, play an important role in loss of muscle strength and function.³²

Other areas of research are related to the loss of myofiber innervation, which is a characteristic of aging muscles. Such changes occur at many levels, from the central and peripheral nervous system to cells in skeletal muscle tissue.³⁸ Oxidative stress, which is an imbalance in oxidant and antioxidant levels, chronic inflammation, and mitochondrial dysfunction also play an important role in age-related muscle atrophy.³⁹

Insulin, estrogens, androgens, GH, prolactin, thyroid hormones, catecholamines and corticosteroids are all involved in the etiology and pathogenesis of sarcopenia.³² The weight gain that frequently occurs during middle age results in a decline in the anabolic action of insulin, predisposing to sarcopenia. Clinical and experimental studies support the hypothesis that low testosterone predicts sarcopenia, as low testosterone levels result in lower protein synthesis and a loss of muscle mass. With aging the level of 25(OH) vitamin D declines and one recent longitudinal epidemiological study reported an independent association between low serum levels of vitamin D and sarcopenia.^{32,40}

The etiology of sarcopenia is multifactorial⁴¹ and all potential causes are summarized in table 1.

6. THE CONSEQUENCES OF SARCOPENIA

With lessening of the muscle mass, muscle strength and muscle function are greatly reduced.⁴² Sarcopenia is associated with reduction in muscle strength and walking

Table 1. The etiology of sarcopenia and its consequences.

Age	Potential causes → Consequences
20–40 years	Decreased type II fiber size and amount → sprinting capacity is reduced
40–60 years	Accelerated loss of motor units, increased body fatness, decreased androgens → decreased muscle protein synthesis, decreased aerobic and sprinting capacity, increased insulin resistance
60–70 years	Decreased physical activity. Reduced androgen and growth factor levels, menopause, chronic disease, increased total body and visceral fat, impaired appetite regulation → inflammation, nutritional deficiencies
70+ years	Decreased physical activity, depression, hospitalization, increased body fatness → fear of falling, inflammation, low functional capacity

speed.^{41,43} Compromised physical function, muscle weakness, decreased muscle density and a lowered specific force of muscle are all associated with an increased risk of hospitalization.⁴⁴ Sarcopenia is also associated with short- and long-term mortality in hospitalized patients.^{41,45}

Measures of strength, function, specific force and density may be more important than measures of lean mass alone in assessing health risks associated with sarcopenia in older adults. Low muscle strength, poor physical performance, and low muscle density (but not muscle size or lean mass) are associated with increased risk of hospitalization in adults aged 70–79 years.⁴⁴

Sarcopenia is associated with many comorbidities, including endocrine diseases, obesity, chronic kidney disease and osteoporosis, which have an impact on public health.⁴¹ Sarcopenia is also associated with serious health consequences in terms of frailty, disability, morbidity and mortality.⁴⁶ The consequences include decreased strength, metabolic rate and maximal oxygen consumption.³⁰ Loss of autonomy, poorer quality of life, altered functional status, increase of fatigue, falls and a higher mortality rate are well-known consequences of sarcopenia.⁴⁷ At the individual level, sarcopenia-related disability leads to reduced quality of life, while at the public health level, it leads to an increase in healthcare expenditure.⁴⁸

The loss of strength and muscle mass observed with aging is associated with increased health care costs.⁴⁴ The healthcare costs of sarcopenia have been estimated based on the effect of sarcopenia in increasing physical disability risk in older persons,⁴⁸ but economic data on sarcopenia are sparse.⁴¹

7. INTERVENTION

Most forms of intervention in the management of sarcopenia in men and women have focused on increasing activity (exercise) and providing adequate nutrition.^{32,49} The use of pharmaceutical agents such as myostatin inhibitor

and testosterone is still under investigation, with no clear evidence of benefit.⁴⁹

7.1. Exercise

7.1.1. Resistance training intervention. Resistance training intervention (lifting weights, stretching bands or using the individuals' weight, or exercise executed on resistance machines) is safe and effective for counteracting sarcopenia.^{13,49}

Resistance exercise (RE) programs improve muscle anabolism, muscle mass and muscle strength.^{18,50} RE alone improved muscle mass in 2 of 4 studies and muscle strength in 3 of 4 studies^{51–53} compared with control activities (low-intensity home exercise or standard rehabilitation).¹⁸ Three additional studies explored compound exercise intervention (with different blends of aerobic, resistance, flexibility and or balance training), which were performed for 3–18 months.^{18,54,55}

RE in older people should be performed 2 or 3 times/week with at least one set of 8–12 repetitions of the major muscle groups.^{49,56} To maximize strength development, a resistance (weight) should be used that allows 10–15 repetitions for each exercise.⁵⁶

7.1.2. Aerobic exercise. Aerobic exercise (AE) programs improve metabolic control, cardiovascular function, reduce oxidative stress and optimize exercise capacity, improve skeletal muscle insulin sensitivity,⁴⁹ and produce skeletal muscle hypertrophy.⁵⁷ AE stimulates muscle protein synthesis, increases maximal oxygen consumption (VO_{2max}) and improves muscle quality neuromuscular adaptation.³² Examples of aerobic exercise are jogging, cycling, brisk walking, swimming, dancing.^{13,32}

7.2. Nutritional intervention

Nutritional intervention may influence sarcopenia, and in particular diets rich in proteins, antioxidant nutrients and vitamin D or omega-3 fatty acids supplements.⁴¹ Increased age is associated with reduced appetite and therefore

protein supplements or essential amino acid supplements are recommended.⁴⁹ Current recommendations are that protein should be consumed at a rate of 0.8 g/kg/day, but only about 40% of persons above the age of 70 years reach this amount.⁸

7.3. Combination of exercise and nutrition

Exercise and nutrition in combination should be considered as an important intervention strategy in the prevention and or treatment of sarcopenia. The combination of exercise (regular resistance training) with protein supplementation or exercise with amino acid supplementation can be effective.⁴⁹

8. CONCLUSIONS

Sarcopenia presents a set of adverse outcomes, such as the loss of skeletal muscle strength and endurance, with loss of mobility and an increased risk of disability and mortality.³¹ Exercise intervention produces the most significant improvement in sarcopenia. Increased physical activity in daily life may also be recommended for these individuals. In the case of undernourishment or anorexia, nutritional support should also be considered.²³ The subject of this review is too broad to include every relevant study, but it is clear that further studies are needed to determine the effect of various different forms of intervention on muscle mass and function in subjects with sarcopenia.

ΠΕΡΙΛΗΨΗ

Σαρκοπενία: Νέα δεδομένα από τη βιβλιογραφία

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Η σαρκοπενία αποτελεί σημαντική πάθηση που σχετίζεται με τη γήρανση. Ορίζεται ως η απώλεια μυϊκής μάζας και λειτουργικότητας. Η αιτιολογία της σαρκοπενίας δεν είναι απόλυτα κατανοητή. Οι θεραπευτικές παρεμβάσεις για την αποτελεσματική αντιμετώπιση σαρκοπενικών ανδρών και γυναικών στοχεύουν στην αύξηση της φυσικής δραστηριότητας (άσκηση), καθώς και στην επαρκή πρόσληψη τροφής. Η επιλογή των παρεμβάσεων αποτελεί αντικείμενο μελετών. Ο σκοπός της παρούσας ανασκόπησης ήταν η καταγραφή πληροφοριών, οι οποίες σχετίζονται με τον ορισμό, τις κλινικές συνέπειες και τις αποτελεσματικές θεραπευτικές παρεμβάσεις που χρειάζονται οι ασθενείς με σαρκοπενία.

Λέξεις ευρητηρίου: Άσκηση, Γήρανση, Διαγνωστικά κριτήρια, Παρεμβάσεις, Σαρκοπενία

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