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Sarcopenia and clinical presentation

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Abstract

Sarcopenia is characterized by the progressive generalized loss of muscle function, quality, strength and mass. Although it is known as a primary geriatric disease, it may also develop in younger individuals secondary to immobilization, malnutrion and cachexia.

The exact etiology is unknown, but the most commonly suggested contributory factors are a decrease in protein synthesis, mitochondrial dysfunction, reactive oxygen products, chronic inflammation, nutritional deficiency, loss of perfusion, age-related neuromuscular alterations, decrease in sex hormone, growth hormone (GH), insulin-like growth factor (IGF-1) and vitamin D levels together with physical inactivity.

There are severe negative effects on quality of life and the individual's socio-economic status and thus, sarcopenia is a significant public health problem. Sarcopenia is strongly correlated with the increased fragility that develops in the elderly and is a significant risk factor and also an indicator of disability and mortality.
The evaluation of muscle strength and physical performance is mandatory for the diagnosis of sarcopenia. Despite the lack of a definitive treatment method, the most commonly accepted approaches include physical activity, nutritional supplementation therapy, and hormonal and new pharmacological agents.
In this review sarcopenia, which is a common but sometimes misdiagnosed condition in clinical practice, is discussed in the light of current knowledge.

Keywords: Sarcopenia; Muscle Mass; Exercise.

The term 'sarcopenia' is a combination of the Greek words, 'sarx' meaning 'muscle' and 'penia' meaning 'loss'. It was first described by Rosenberg (1). The prevalence of sarcopenia has been reported to be 15%-24% in the 60-70 years age group and 50% in those over 80 years of age. Sarcopenia is primarily a disease of the elderly. However, it may also develop in young individuals in conditions of malnutrition, cachexia and immobility (2). Generally, sarcopenia is seen together with physical inactivity, reduced mobility, slow ambulation and reduced physical resistance. There are severe negative effects on quality of life and the individual's socio-economic status and thus, sarcopenia is a significant public health problem. Sarcopenia is strongly correlated with the increased fragility that develops in the elderly and is a significant risk factor and also an indicator of disability and mortality.

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Etiopathogenesis

The mechanism of sarcopenia is not fully understood (3). The development has been attributed to reduced protein synthesis, mitochondrial dysfunction, reactive oxygen species, chronic inflammation, malnutrition, reduced perfusion, age-related neuromuscular changes, reduced levels of sex hormones, reduced growth hormone (GH) and insulin-like growth hormone (IGF-I), reduced levels of Vitamin D and physical inactiivity (4).

Reduced Protein synthesis; for maintenance of the muscle mass, the destruction rate should not exceed the synthesis rate. With active synthesis of the new structural protein, maintenance not only of the muscle mass but also the muscle quality is achieved . Protein synthesis in the whole body decreases with age (5).

Mitochondrial dysfunction; mitochondria strengthen the muscle spasm. The age factor leads to a reduction in the muscle oxidative capacity. As people age, mitochondrial dysfunction develops and this is probably associated with the accumulation of oxidative damge. The hypothesis has been proposed that the number of mitochondria and reduced activity at the cellular level could be responsible for muscle fatigue, reduced resistance and probably losss of strength (6).

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Reactive oxygen species; these reactive species generally show harmful effects by leading to oxidative stress which disrupts cellular elements such as DNA, proteins and lipids and finally causes damage to cells and tissues (7).

Chronic inflammation; in previous studies it has been determined that levels of C-reactive protein (CRP), tumour necrosis factor alpha (TNF-α) and interleukine-6 (IL-6) are elevated in the elderly. A relationship has been observed between these increases and an increased risk of loss of muscle strength. In elderly males and females, high levels of IL-6 and CRP have been found to increease the risk of loss of >40% of muscle strength by 2-3 folds (8).

Malnutrition; there is increased insulin resistance and destruction of muscle protein in cachexia, which is a particular reason of malnutrition (3). Nutritional intake decreases with aging. Nutritional intake has complex regulation managed by central and peripheral mechanisms. Elderly individuals are quickly satiated. This is partially related to a decrease in gastric fundus relaxation and probably a reduction in the formation of nitric oxide in the fundus. Leptin, which is a hormone made in fat tissue, is influential in reducing nutritional intake and as there is a greater amount of fat tissue in the elderly, more leptin is synthesized. A reduced sense of taste and smell, inflammatory cytokines related to disease status, depression, concomitant chronic diseases and medications contribute to loss of appetite in the elderly. Insufficient calories and a negative nitrogen balance, especially in protein intake, leads to muscle destruction and loss (9).

Reduced perfusion; the resistance capacity of muscle is related to the oxidative energy metabolism and therefore the oxygen and response to the muscle tissue. Atherosclerotic plaque in the elderly prevents oxygen reaching the muscle (10).

Neuromuscular changes; it is thought that with ageing, the reduction in satellite cells, which function in muscle regeneration, may lead to sarcopenia (11). In a previous study, it was determined that after the age of 60 years, there is a reduction of up to 50% in motor neurons in some individuals compared to a young population (8).

Testosterone; Van den Beld et al showed a reduction of 3% in free testosterone level between the ages of 73-94 years. This rate is also in parallel with the loss of lean muscle mass and strength (12).

Growth hormone/IGF-1; the levels of GH and IGF-1, which is a peripheral mediator, decrease together with age. These anabolic hormones play an important role in the regulation of growth and skeletal muscle development (13).

Vitamin D; Vitamin D deficiency is common in the elderly, with reported rates of 80-100% in those living in care homes, and 36% in males and 47% in females living in the community. Vitamin D plays an important role in muscle and bone metabolism. Low levels of vitamin D have been related to atrophy in type 2 muscle fibres in particular. There is an established relationship between vitamin D and lower extremity functions, proximal muscle strength and physical activity

Vitamin D deficiency especially affects postural balance and the antigravity muscles of the lower extremities which are necessary for walking. A significant correlation has been found between falls and 25(OH) vitamin D levels in the elderly. Muscular strength and postural and dynamic balance can be increased with vitamin D supplementation (14).

Renin angiotensin aldosterone; it is thought that changes in this system may lead to sarcopenia (15).

Physical inactivity; this is a reason for a reduction in muscle power and strength (16).

Clinical Characteristics; In 2009, the European Union Geriatric Association formed a working group to establish diagnostic criteria and a report was published for the diagnosis and determination of sarcopenia. According to this report, when low muscle mass is determined together with reduced muscle strength and/or physical incapacity, this can be named as sarcopenia.

The European Working Group on Sarcopenia in Older People (EWGSOP) classified sarcopenia into 3 stages:

1. **Presarcopenia;** there is reduced muscle mass but muscle strength and physical performance are normal.
2. **Sarcopenia**; there is reduced muscle mass and reduced strength or physical performance.
3. **Severe sarcopenia;** there are reductions in all 3 criteria (17).

Methods used in the evaluation of sarcopenia

1) **Muscle mass evaluation**

Body imaging techniques, bio-impedance analysis (BIA), total body potassium and anthropometric measurements can be applied. Selections should be made taking applicability and cost into account (17).

Body imaging techniques; computed tomography (CT), magnetic resonance imaging (MRI) and dual energy x-ray absorptiometry (DEXA) can be used.

CT and MRI; anatomic details and musculo-skeletal volume can be evaluated with CT and MRI. CT and MRI are the only methods by which abdominal fat content can be evaluated. Due to the high costs, radiation exposure and difficulties in application, these methods are not used much apart from for clinical research (18).

Bio-impedance analysis; It can be used for both ambulatory and bed-ridden patients, as this method is both cheap and easy to apply. Measurements are made as estimates of fat volume and lean body mass. BIA can be an alternative to DEXA. However, the greatest handicap is that when oedema is present, there may be incorrect results in the measurement of muscle mass. To overcome this, several measurements should be taken at different times throughout the day (19).

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DEXA; this technique can be used easily in the clinic. Measurements are taken in a short time and radiation exposure is minimal. Fat, muscle and bone mineral tissue can be differentiated (20).

Total body potassium; skeletal muscle contains more than 50% of the total body potassium. Therefore, the determination of the total body potassium can be a classic method for the estimation of skeletal muscle. However, it is not used routinely (21).

Anthropometric measurement; this is a simple technique which can be used in clinical practice. Measurement of the thickness of skin folds provides information about the ratio of body fat. Measurements around the extremity provide information about the muscle mass and protein status in the extremity (22). Thigh circumference <31cm has been found to be correlated with disability status (23). This method of estimation is made more difficult by age–related fat deposits which form and the loss of skin elasticity. In addition, anthropometric measurements are highly dependent on the person taking the measurement and there may be measurement errors. Therefore, this method is not recommended in routine diagnosis (21).

2) **Muscle strength evaluation;**

Although walking and physical functions are much more related to the lower extremities than the upper extremities, the hand grip strength test is often used for this purpose (17).

Hand grip strength test; low hand grip strength has been shown to be better correlated to impaired mobility and unwanted clinical results than low muscle mass (24).

Knee flexion and extension techniques; these can be used for research but clinical use is limited because of the need for a special machine and training (25).

Peak expiratory flow; in those with no pulmonary disease, respiratory muscle strength is determined by peak expiratory flow. It is a technique which is cheap, easy to apply and has prognostic value, but research into its use in sarcopenia is limited (21).

3) **Physical performance evaluation;**

The tests used include the short physical performance battery, general walking rate, the 6-minute walking test and the stair climbing strength test.

Short physical performance battery; balance, walking, strength and endurance are measured in this test. In the evaluation of physical performance, this is a suitable test for use in both the clinic and practical research (26).

General walking speed; in previous studies, a linear relationship has been found between leg strength and general walking speed. The 6-metre walking speed test in partcular is thought to be a good determinant of results such as severe mobiity restrictions and mortality (27).

Timed 'up and go' test; this test is particularly important in respect of the evaluation of dynamic balance (28).

Stair climb power test; this test is used when leg muscle strength is insufficient and more often in research studies (29).

To be able to determine individuals with sarcopenia, an algorithm was developed by EWGSOP. According to this, the criteria of walking speed are recommended to be examined first in individuals aged over 65 years. If walking speed is <0.8m/sec, there is a risk of sarcopenia and further evaluation with the hand grip strength test is required. If the hand grip strength test is low, then muscle mass must be measured (17).

Treatment

Although there is no definitive treatment, the determination of individuals at risk and treatment are extremely important.

Exercises; Studies of exercise have shown this to be one of the most promising methods for both protection and treatment. It has been known for many years that aerobic exercise is beneficial to the cardovascular system and resistance capacity. Aerobic exercise contributes to muscle hypertrophy and increases the cross-sectional area of muscle fibrils. Following aerobic exercise, mitochondrial volume and enzyme activity increases. Regardless of age, muscle protein synthesis and muscle quality increases, and the body fat ratio decreases (30). In contrast to aerobic exercise, resistance exercises have much more evident effects on increasing muscle mass and muscle strength and reducing the development of sarcopenia. It has been shown that the application of resistance exercises even just once a week, improves muscle strength (31). Fiatarone et al showed that resistance exercises were clinically useful in individuals of advanced elderly age. In care home residents with an average age of 87 years, an increase was determined of more than 12.5% in muscle strength after a 10-week program of resistance exercises together with nutritional support, while the increase in the control group remained at 3%. In the group with additional exercises, there were improvements in walking speed, stair climb strength, and spontaneous physical activity (32). Resistance exercises are the primary treatment strategy in the prevention and treatment of sarcopenia (33).

Resistance exercises can be recommended to patients in the form of 2-3 times per week, 1-3 sets per day, 8-12 repetitions, up to 60%-80% of 1 RM (repetitive maximum), at warm-up cool-down speed and with 1-3 seconds resting time (34).

Nutritional support therapy

Many elderly individuals do not have sufficient protein intake in their diet, which causes lean body mass to reduce and increases functional disorders. In several studes it has been stated that it is necessary to increase daily protein intake to 1.2-1.3 gr/kg (35). In patients with very severe malnutrition, if there is no kidney failure, it is thought necessary to increase the protein intake up to 2gr/kg/day (36).

Distribution of daily protein intake at similar rates in 3 meals is seen to be important for the protection of

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muscle mass and functions (37). In previous studies, long-term essential amino acid supplementation has been observed to increase lean body mass and muscle protein synthesis in healthy elderly females. Of the essential amino acids, leucine in particular has been found to have a very positive effect on protein metabolism in muscle (35,37). Foods with the highest amount of leucine are sour milk, fish, chicken, sesame, groundnuts and lentils (38). In a study by Tieland et al of elderly patients, physical performance was seen to improve with nutritional support although muscle mass did not increase. In another study by Tieland et al, long-term resistance type exercises were found to be the most effective on muscle strength and physical performance. It was concluded that protein supplementation in the diet was necessary for elderly individuals to increase muscle strength in periods of exercise (39). Muscle loss in the young is associated with bedrest. Supplementation of essential amino acids and carbohydrates during bedrest in this group has been determined to protect muscle mass. Hyperinsulinemia which forms as a result of carbohydrate intake seems to have a greater anabolic effect on protein synthesis in the young compared to the elderly (40). From an extensive scan of literature including 17 studies of pateients aged over 65 years, it has been concluded that exercise therapy together with nutritional support increases muscle strength, power and physical performance (41).

Hormonal Treatments

Testosterone; together with declining serum testosterone levels with ageing, a relationship has been shown with reduced muscle mass, strength and functional status and reducing bone density (21). In longitudinal clinical studies, testosterone replacement in elderly hypogonadal males increases muscle strength, although only slightly. While this finding has been seen in some studies, in others it has not been determined. When testosterone treatment is combined with resistance exercises in the treatment of fragile elderly males, it has been reported that the addition of testosterone leads to a tendency to achieve greater muscle strength (42).

Oestrogen; no significant effect has been determined on muscle mass and muscle function of replacement therapy. It is not preferred in routine treatment because of the risk of breast cancer and cardiovascular disease (43).

Growth Hormone (GH); the effect of GH replacement in the elderly is debatable. In several studies, no positive effect has been shown of GH on muscle protein synthesis and strength even together with the application of resistance exercises (44). The only situation where it is recommended is in GH deficiency in young adults. The use of GH is not recommended for the elderly with sarcopenia as it may lead to unwanted results such as fluid retention, gynaecomastia, orthostatic hypotension and carpal tunnel syndrome (21).

Vitamin D; there is an evident improvement curve in muscle strength and physical performance with vitamin D replacement. The greatest effect of vitamin D replacement on increasing muscle strength has been seen in the group with the lowest serum vitamin D levels. Vitamin D replacement has been shown to significantly reduce the risk of falling in the elderly and this effect has been determined to be more pronounced with daily suplementation of 700-1000 IU vitamin D (45).

ACE inhibitors; these are thought to have positive effects on skeletal muscle function through various mechanisms, such as improvement in the endothelial function, and an improvement in skeletal muscle blood flow through angiogenesis regulation and the anti-inflammatory effect. ACE inhibitors can increase the number of mitochondria and levels of IGF-1. In observational studies, there has been seen to be less of a decrease in muscle strength and walking speed of those using long-term ACE inhibitors for antihypertensive purposes compared to those using other antihypertensive agents (46).

Statin group medications; it is thought that these have an effect on skeletal muscle through vascular and anti-inflammatory mechanisms. It has been reported that by preventing atherosclerosis, muscle nutrition is increased and as a result, muscle fatigue is reduced (47).

Creatinine; this may be effective on sarcopenia because of the anabolic and antioxidant effects. It has been determined to be more effective when applied together wiith resistance exercises. However, creatinine is not recommended in the routine treatment of sarcopenia because of various side-effects (48).

Other potential new agents; myostatin antagonists (follistatin), PPAR-gama agonisti and AICAR (5-aminoimidazole-4-carboxamide-1-beta-4-ribafuranoside) are drugs with which this research can be continued (30).

CONCLUSION

Sarcopenia is an important community health problem in terms of physical and functional levels in the elderly and healthcare costs. All individuals aged over 50 years, and all those with impaired general health and physical function should be assessed in terms of sarcopenia. If it is kept in mind that early diagnosis and treatment is extremely important in the elderly population with sarcopenia, cases should not be overlooked and diagnosis and treatment should be supported with new studies.

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