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SARCOPENIA OF AGING

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Keywords: sarcopenia, aging, muscle loss.

Summary

Background. Sarcopenia is an age-related condition, defined by the muscle decline, impaired physical function, and deterioration in muscle tissue quality. The main cause for the interest of Sarcopenia is the apparent association of this disease with patient morbidity, mortality, prolonged hospitalization, and deterioration in the quality of life. The purpose of this review is to present a brief account of some age-related biological changes that may contribute to Sarcopenia.

Materials and methods. We reviewed the literature based on data from Medline (PubMed), Google Scholar, Science Direct, and CAIRN. The research was done on articles in English or French, published before the 31st of December 2019. The research was based on the following Mesh headings (Medical Subject Headings): "sarcopenia" AND "aging" OR "muscle loss".

Conclusions. A multitude of etiological factors influences the aging-associated deterioration of muscle mass and function that constitute Sarcopenia, such as imbalanced protein synthesis and degradation, decreasing anabolic hormones, inflammation, and age-related morphological changes, which are described in the review. In the future, research might be conducted for identifying specific biomarkers, which may lead to an opportunity to assess and monitor the disease non-invasively, granting possibilities for a more efficient therapeutic approach.

Introduction

Sarcopenia is the aging-associated gradual loss of muscle mass, strength and function (Fig.1), recognized as having an important role in adverse health-outcomes that are linked to advanced-age, including morbidity, mortality, frailty, and others (1). The etiology of Sarcopenia is multifactorial, with environmental causes, age-related decreases in anabolic hormones, active inflammatory-pathways, and morphological skeletal muscle changes, being a few of the contributing factors (2).

The aim of this review - to present a brief account of some age-related biological changes that may contribute to Sarcopenia.

Materials and methods

We reviewed the literature based on data from PubMed, Google Scholar, Science Direct, and CAIRN. The research was done on articles in English or French, published before the 31st of December 2019. The research was based on the following Mesh headings (Medical Subject Headings): "sarcopenia" AND “aging" OR “muscle loss".

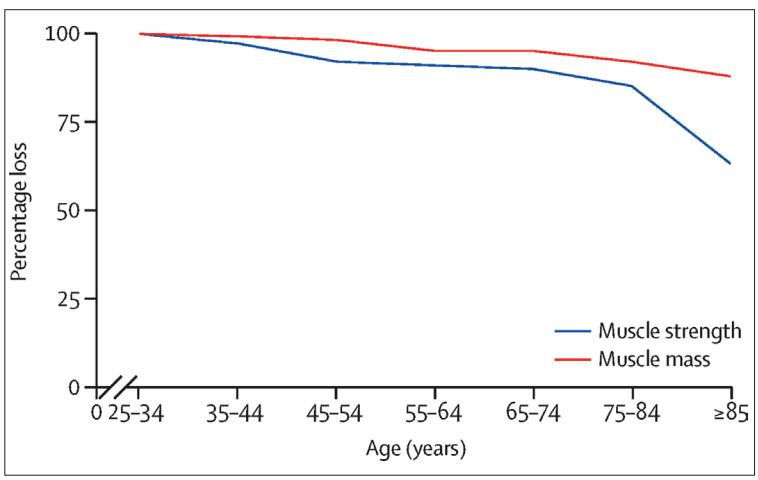

Figure 1. Muscle Mass and Strength Decline with Age.
Figure taken from Cruz-Jentoft et al. (3)

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Results

This literature review revealed the key factors of age-related biological changes that may contribute to Sarcopenia. 19 studies were used for this non-systematic review. These studies were either uncontrolled (N = 14) or reviews of the literature (N = 5). The quality of the methodology limited the interpretation of the results and their extrapolation. Another limitation was study designs which included animal trials. Future studies are necessary to conclude the correlation between animal and human trials with similar study design.

Epidemiology

Recent large-scale population studies have established that the incidence of Sarcopenia increases with advanced age (4,5,6). The average annual incidence rates were 1.6% for European men between the age of 40-79 (4), 3.1% in Chinese populations ≥65 years in age (5), and 3.6% among the very old (≥85 years) in the United Kingdom (6). Cognitive impairments, low body mass indexes (BMI), and low socioeconomic positions were some of the common risk factors associated with increased incidence. Importantly, patients with Sarcopenia have a 3.59% higher average mortality rate, and suffer from increased risks of falling, hospitalization, and overall functional decline (7). This has meant that the condition is now being linked to growing health-care costs (8).

Pathophysiology

Imbalanced Protein Synthesis and Degradation. A primary cause in the loss of skeletal muscle is the aging-associated imbalance of muscle protein synthesis and breakdown (9). Dietary intake of amino acids and proteins enhances muscle protein synthesis and reduces protein degradation; however, recent evidence has shown that the capability to respond to anabolic stimuli declines with age (9). One report (10) compared anabolic responses in 44 young and elderly men following ingestion of essential amino-acids, and found that young-people, on average, had a 1.5-fold higher rate of protein synthesis. This was associated with decreased expression and activation (by 30-50%) of key anabolic signaling pathway components – namely, mTOR, $p70^{s6}$ kinase and eIF4BP-1 in the elderly. Further support is provided by a recent study (11) that compared the *in vivo* postprandial muscle-protein synthesis using stable-isotope infusion, and found that older men had a 3-fold smaller capacity to elevate protein-synthesis following food-ingestion.

Decreasing Anabolic Hormones. Furthermore, aging-related reductions in anabolic-hormones, including testosterone and growth hormone (GH), and decreased levels of insulin-like growth factor 1 (IGF-1), are linked to declining muscle cell synthetic capacity and function (12). A longitudinal study in 221 men (71-86 years in age) found that testosterone levels decrease by 7% during a 4-year timespan (13), whilst another report showed that GH production decreases by approximately 14% per decade (14). An animal study (15) demonstrated that the injection of recombinant human GH in old mice, in conjunction with mild-exercise, efficiently inhibits Sarcopenic symptoms, including muscle atrophy and decreased protein synthesis. Of note, age-related decreases in cellular IGF-1 have been shown to adversely affect motor neuron function during aging (16). Transgenic mice were used to study the effects of sustained IGF-I overexpression during neuromuscular innervation, which showed that IGF-I prevents age-related alterations in nerve terminals and neuromuscular junctions (16).

Inflammation. Additionally, growing evidence suggests that age-related activation of inflammatory pathways is associated with elevated rates of muscle protein degradation, providing a mechanistic-link to Sarcopenia (17). Evidence suggests that the ubiquitin-proteasome pathway is instrumental for the induction of muscle-breakdown and is stimulated by inflammatory cytokines – tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) (18). One report (19) investigated the plasma cytokine profiles of 1411 participants (25-91 years in age) and found that IL-6 and TNF-α concentrations were 2.4-fold and 2-fold higher in the elderly, respectively. This link between age-related increase in inflammatory markers and Sarcopenia is supported by a study that used computed tomography (CT) to asses the changes in thigh muscle area in 2177 participants during a span of 5 years, and found a consistent association between elevated serum-concentrations of IL-6 and TNF-α and greater reductions in thigh muscle area (20). Furthermore, reinforcing this idea is an animal study (21), in which administration of an anti-inflammatory drug (ibuprofen) in old-mice significantly reduced muscle-mass loss during the span of 5-month treatment.

Age-Related Morphological Changes. Age-related muscle atrophy is associated with substantially decreased numbers and size of muscle fibers, and particularly, size-decrease of type II (fast-twitch) muscle fibers by 10-40% (22), which likely contributes to declining muscle-strength with increased age. An autopsy study (23) concerning two age-groups (72 ± 1 and 30 ± 6 mean ages) reported an 18% reduction in the muscle size of *m. vastus lateralis* and a 25% decrease in the number of muscle fibers in the older age-group. Additionally, accompanying type II muscle fiber atrophy is the aging-associated decrease of satellite cells contents and function (24). Satellite cells, otherwise known as muscle stem cells, are instrumental in muscle growth and regeneration; therefore, their age-rela-

ted decline is being increasingly linked to Sarcopenia (25).

Another age-related morphological change that occurs in skeletal muscle is the increased muscle fat infiltration (myosteatosis) – the elevated deposition of lipids within muscle fibers or adipocytes (26). This study (26) found that throughout a 5-year span, 30% and 50% increases in intermuscular adipose tissue (mid-thigh area) were observed for women and men (70-79 years old), respectively. Fat-accumulation in skeletal muscle is now considered as an important contributing factor for the impaired physical-capabilities and reduced-mobility observed in the elderly (27).

Conclusions

1. A multitude of etiological factors influences the aging-associated deterioration of muscle mass and function that constitute Sarcopenia, such as imbalanced protein synthesis and degradation, decreasing anabolic hormones, inflammation, and age-related morphological changes, which are described in the review.

2. In the future, research might be conducted for identifying specific biomarkers, which may lead to an opportunity to assess and monitor the disease non-invasively, granting possibilities for a more efficient therapeutic approach.

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SENĖJIMO SARKOPENIJA

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Raktažodžiai: sarkopenija, senėjimas, raumenų silpnumas.

Santrauka

Įvadas. Sarkopenija yra su amžiumi susijusi būklė, kuriai būdingas raumenų silpnumas, sutrikusios fizinės funkcijos ir raumenų audinių kokybės pablogėjimas. Susidomėjimo sarkopenija priežastis yra akivaizdus šios ligos ryšys su pacientų sergamumu, mirštamumu, ilgai trunkančiu hospitalizavimu ir gyvenimo kokybės pablogėjimu. Šios apžvalgos tikslas –pristatyti kai kuriuos su amžiumi susijusius biologinius pokyčius, galinčius sukelti sarkopeniją.

Medžiaga ir metodai. Literatūros apžvalga atlikta remiantis Medline (PubMed), Google Scholar, Science Direct ir CAIRN duomenimis. Tyrimas atliktas remiantis straipsniais anglų arba prancūzų kalbomis, paskelbtais iki 2019 m. gruodžio 31 d. Tyrimui buvo atrinkti medicinos mokslo straipsniai, kurių antraštėse rasti žodžiai: „sarkopenija“ ir „senėjimas“ arba „raumenų netekimas“.

Rezultatai. Literatūros apžvalga atskleidė pagrindinius su amžiumi susijusių biologinių pokyčių, galinčių sukelti sarkopeniją, veiksnius. Šiai nesisteminei peržiūrai buvo panaudota 19 tyrimų. Analizuotos literatūros apžvalgos (N = 5) ir nekontroliuojami tyrimai (N = 14). Metodikos kokybė ribojo rezultatų aiškinimą ir ekstrapoliaciją. Kitas apribojimas buvo tyrimai, apimantys bandymus su gyvūnais. Tolesni tyrimai yra būtini, norint nustatyti panašių tyrimų koreliaciją tarp bandymų su gyvūnais ir žmonėmis.

Išvados. Apžvalgoje aprašyta daugybė etiologinių veiksnių, sukeliančių su senėjimu susijusių raumenų masės ir funkcijos pablogėjimą, kurie konstatuoja sarkopeniją, pavyzdžiui, nesubalansuota baltymų sintezė ir skaidymasis, mažėjantys anaboliniai hormonai, uždegimas ir su amžiumi susiję morfologiniai pokyčiai. Ateityje gali būti atliekami tyrimai, siekiant nustatyti konkrečius biologinius žymenis, įgalinančius įvertinti ir stebėti ligą neinvaziškai, suteikiant galimybių efektyvesniam terapiniam gydymui.

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