Sarcopenia

Subjects: Pathology

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Sarcopenia, a geriatric disease characterized by a progressive loss of skeletal muscle mass and loss of muscle function, consists of a rising, often undiagnosed health problem.

Keywords: sarcopenia ; exercise ; nutrition ; supplements ; older adults ; muscle mass

1. Introduction

Sarcopenia is predominantly a geriatric condition, with a gradual loss of skeletal muscle mass and a loss of muscle function[1], first described by Rosenberg[2]. It is one of the leading health issues in the older adults, and it increases disability risk, falls as well as injuries related to falls, hospitalization, limitation of independence, and mortality[3]. Risk factors for sarcopenia include age, gender, level of physical activity, and the presence of chronic disease as well as human immunodeficiency virus (HIV)[4][5][6][7]. Its prevalence in elderly population is largely considered a variable, as it ranges from 5% to 50% depending on gender, age, pathological conditions as well as diagnostic criteria. There is no one unified approach of treatment or assessment, which makes sarcopenia even harder to assess. There is a pressing need to provide better diagnosis, diagnostics, prevention and individualized health care. Physical activity and nutrition are the main studied ways to prevent sarcopenia and they also offer better outcomes. In fact, there are several definitions for sarcopenia, with no consensus, hence its prevalence may vary widely[8]. This entry aims to report the prevalence of sarcopenia within the older adult age group, its etiology, prevention, and treatment techniques.

2. Pathophysiology

Sarcopenia is a multifactorial disease[9], with a few of its identified contributing factors being low levels of physical activity —likely being a contribution to muscle mass decline — [10][11], decreased caloric intake[12], progressive increase in fibrosis, muscle metabolism changes, chronic inflammatory state, oxidative stress, and neuromuscular junction degeneration[13].

The cellular and molecular mechanisms behind sarcopenia are well described by Riuzzi et al.[14].

Low levels of physical activity are among the main risk factors for sarcopenia, along with the muscle fiber decline[15] that begins in midlife. A gradual loss of muscle fibers begins at 50 years and approximately 50% of the fibers are lost by the age of 80, while the muscle fiber loss is also seen in athletes[15].

In addition to this, hormonal changes with age in growth hormone, testosterone, thyroid hormone, and insulin-like growth factor lead to muscle mass and muscle strength loss, in conjunction with catabolic signals by tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6)[13], which are in imbalance with the anabolic signals[16]. Furthermore, inadequate nutrient intake and low protein synthesis are common in older adults, while a buildup of lipofuscin and cross-linked proteins in skeletal muscles has been proposed as a factor for low muscle strength in people with sarcopenia[17]. Moreover, another cause of sarcopenia that has been proposed is the failure of satellite cell activation in the muscle[13].

From a histological point of view, it has been found that the sarcopenic state affects the type II muscle fibers with the effect of decreasing their amount, their size, and the number of their mitochondria[18][19]. Among older adults in particular, food consumption has been recorded to be reduced by 25%[20], with quality of food intake, being significantly compromised[21]. Reduced protein intake and low vitamin D levels have also been found to correlate with the diminished muscle strength[10][22][23]. Hormonal decline associated with aging is also likely to impact the loss of muscle mass, with reduced amounts of testosterone and estrogen in men and women, respectively[23][24][25][26].

Chronic inflammation is a contributing factor to almost every known disease[27][28][29]. Aging is characterized by an increase in inflammatory markers and its related factors. Aging-related inflammation in the absence of infection is characterized as low-grade, chronic, and systemic, resulting in responses that contribute to degeneration of tissues.

Aging-related inflammation is expected to result from a decreased immune response or lifelong exposure to antigenic stimuli[30][31], resulting in the development of reactive oxygen species and tissue damage via the release of cytokines mediated by the innate and acquired immune system[32]. In action, age-related inflammation is followed by age-related decrease in the number of T and B cells, along with a rise in natural killer cells[33], and tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1(IL-1), and C-reactive protein (CRP)[34][35]. Subsequently, it is proposed that such cytokines contribute to a predisposition to sarcopenia by triggering the ubiquitin–protease system[36][37]. This altered activation of the cell signaling pathway is known to promote the inflammatory state irrespective of tissue damage or antigenic exposure, further leading to one of the pathogenetic bases that underlie sarcopenia[38][39]. This state also leads to anabolic resistance, which is one of the major determinants of sarcopenia, suggesting that the skeletal muscle protein synthesis in response to physiological stimuli in the older population is below the level of muscle maintenance[40].

Furthermore, myostatin, a protein produced from and released by myocytes affects muscle cell function to inhibit myogenesis[41] by inducing the formation of the SMAD transcription altering protein complex (the main signal transducers for receptors of the transforming growth factor beta (TGF-β) superfamily, which are fundamentally important for adjusting cell development and growth)[42]. The effects of peroxisome proliferator-activated receptor-γ coactivator 1 α (PGC-1α), a transcriptional coactivator that enhances mitochondrial biogenesis as well as inhibits transcriptional activity of FoxO (a family of proteins crucial in regulating the expression of genes that play a role in cell growth, proliferation, differentiation, as well as longevity), are also suppressed by myostatin[42]. There is a correlation between elevated myostatin and reduced muscle mass in in both animal and human studies making it a potential mediator of sarcopenia as well as a therapeutic target[43][44][45].

Evidence shows that sarcopenia might be affected by a genetic predisposition. Large-scale genome-wide association studies evaluating the impact of genetic variation on gait speed, lean body mass, and grip strength discovered single nucleotide polymorphisms (SNPs) linked to synaptic function and neural maintenance, skeletal muscle fiber structure and function, and muscle metabolism[12].

There is also evidence connecting the molecular circadian rhythms with the maintenance of skeletal muscle. The circadian clock plays a critical role in many skeletal muscle physiological functions, and it is important to better understand the basic bio-physiological processes underlying those complex interactions. The significance of circadian expression for skeletal muscle structure, function, and metabolism becomes obvious when studying the muscle phenotype in models of molecular clock disruption. The loss of the *Bmal1* (brain and muscle Arnt-like protein 1) gene leading to sarcopenia and multiple pathological muscle disorders was observed to support this, including results such as decreased mitochondrial density and altered mitochondrial respiration, fiber-type changes, disrupted sarcomeric structure, and restricted function[46][47].

Epidemiological work into health and disease developmental origins has shown that early environmental effects on growth and development may have long-term impacts on human health[48]. Low birth weight is associated with decreased muscle mass and strength in adult life, a sign of a weak early climate[49][50]. One study showed that a substantial decrease in muscle fiber score is associated with lower birth weight, suggesting that developmental influences on muscle morphology may explain the association between low birth weight and sarcopenia[51].

3. Diagnosis

There are several diagnostic guidelines concerning sarcopenia. The major ones are the European Working Group on Sarcopenia in Older People (EWGSOP), the International Working Group on Sarcopenia (IWGS), the Asian Working Group for Sarcopenia (AWGS), and the American Foundation for the National Institutes of Health (FNIH)[52][53][54][55]. These guidelines suggest similar cutoffs for muscle mass, muscle strength, and physical performance for assessing and diagnosing sarcopenia[52].

In 2018, the Working Group (EWGSOP2) updated their initial definition of sarcopenia in order to take into account scientific and clinical evidence that came during the last 10 years. The new consensus (1) focuses on low muscle strength as a key characteristic of sarcopenia (cutoff points are: grip strength <27 kg for men and <16 kg for women and chair stand >15 s for five rises for both sexes), uses detection of low muscle quantity and to confirm the sarcopenia diagnosis (cutoff points are: appendicular skeletal muscle mass <20 kg for men and <15 kg for women), and identifies poor physical performance as indicative of severe sarcopenia (cutoff points are: gait speed ≤0.8 m/s); (2) updates the clinical algorithm that is utilized for sarcopenia case-finding, diagnosis and confirmation, and severity determination to (3) provide distinct cutoff points for measurements of indicators that identify and define sarcopenia[56].

The most accurate methods for assessing muscle mass in clinical settings are bioelectrical impedance analysis (BIA) and dual-energy X-ray absorptiometry (DXA), which is considered the gold standard, because of its accuracy, wide availability, and also because it is the only radiological tool with accepted cutoff values to diagnose sarcopenia[57][58]. There is evidence that measuring muscle mass through deuterated creatine (D3Cr) can reliably measure muscle mass otherwise obtained through DXA, and correlate better with physical activity[59][60]. In research settings, the EWGSOP2 advices the use of magnetic resonance imaging (MRI) and computed tomography (CT) as well as DXA[56].

Because of the variety of assessment techniques, cutoff points, and sarcopenia criteria, sarcopenia diagnosis can be difficult to understand. In addition, the significant variations in the prevalence of sarcopenia relative to the studied population (community dwelling, hospitalization, and living in nursing homes) make it much more difficult to develop preventive routines and therapeutic protocols and involve a more person-centered and focused approach[61].

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