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REVIEW ARTICLE

Sarcopenia, A Booming Concern of Ageing World: A Review

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Abstract:

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death. With the onset of advancing age, muscle tissue is gradually lost, resulting in diminished mass and strength, a condition referred to as sarcopenia. The sequelae of sarcopenia often contribute to frailty, decreased independence, and subsequently increased health care costs. This review article will introduce potential mechanisms that may contribute to sarcopenia, although no one mechanism has yet, and may not completely, define this process. Despite sarcopenia is an inevitable process of life, prevention and treatments are absolutely needed in order to improve the quality of life and quality adjusted life years. Adequate nutrition and structured exercises are essential components of treatment and prevention. However, even those individuals who maintain their fitness through exercise do not appear to be immune to sarcopenia.

Introduction:

The term *sarcopenia* (from the Greek *sarx* for flesh and *penia* for loss) was first coined by Rosenberg[1] in identifying the age-associated loss of muscle mass and function. Sarcopenia is determined by two factors: the initial amount of muscle mass and the rate at which it declines with age. The rate of muscle loss with age appears to be fairly consistent, approximately 1%–2% per year past the age of 50 years [2, 3]. With advancing age there are significant changes in body composition such that body fat increases while modest losses are observed in muscle mass [4, 5, 6]. This shift in body composition with advancing age is often masked by relative stability in overall body weight [3, 7]. Balagopal et al in a cross-sectional data demonstrates that young healthy men have a body composition of approximately 20% body fat at age 25, whereas in men aged 55 years, body fat was 30%, and greater than 35% in 75-year-old men[8]. Muscle mass was fairly stable between the 25- and 55-year-old men, but declined approximately 25% between 50 and 75 years of age[8]. Although physical activity and exercise status are important factors in the onset of obesity with age, the decline in muscle mass and gain in body fat are evident even in active older adults [3, 9, 10. 11]. In the New Mexico Elder Health Study[12], sarcopenia was defined as a muscle mass index [muscle mass (kg)/height (m) ^{2}] less than two standard deviations below the mean of a young reference population. Using this definition 10%–25% of persons under the age of 70 years were sarcopenic, whereas beyond the age of 80 greater than 30% of women and 50% of men were sarcopenic[12, 13].

Consequences of Sarcopenia

The consequences of sarcopenia include decreased strength[14, 15.], metabolic rate [16, 17, 18]and maximal oxygen consumption[19]. These physiologic decrements in maximal strength and fitness probably contribute to weakness and a loss of independence [20]. The loss of aerobic capacity with age is predominantly due to a loss of muscle mass [21]. This loss of fitness is also observable in highly active older adults, who continue to exercise regularly, yet display rates of decline are similar to their sedentary peers[22]. However, fitness remains greater at any age in those who exercise regularly as compared with those who do not.

Biology of Sarcopenia:Much like the underlying causes of aging, the biology of sarcopenia remains

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elusive. Two key observations associated with sarcopenia include a loss of skeletal muscle fiber number [23]and a change in the cross-sectional area (CSA) of the remaining fibers[24]. Various mechanisms have been put forth to explain the change in total muscle mass observed including:

(a) A lack of regular physical activity ("use it or lose it"),

(b) A change in protein metabolism (a deficit between protein synthesis versus degradation),

(c) Alterations in the endocrine milieu (decrease in growth hormone (GH) and testosterone and an increase in cortisol and cytokines),

(d) A loss of neuromuscular function (denervation versus reinnervation),

(e) Altered gene expression, and

(f) Apoptosis; other factors may also contribute in part to sarcopenia.

Skeletal muscle is a dynamic tissue constantly turning over its proteins to amino acids. For muscle to maintain its mass, the rate of protein synthesis must be in balance with the rates of degradation to amino acids in combination with dietary absorption maintaining the difference in amino acid utilization. For sarcopenia to occur, only small imbalances between synthesis and degradation over many years are necessary to eventually result in a significant loss of muscle mass[25]. In young adults, muscle mass accounts for approximately 30% of whole body protein turnover, whereas in elderly persons, muscle mass only represents approximately 20% or less of whole body protein turnover [26]. With advancing age, illness, trauma, or inadequate dietary intake of amino acids can all decrease the rates of protein synthesis and ultimately exacerbate the onset of sarcopenia. Alternatively, the oxidized proteins, which increase with advancing age, may not be as efficiently removed by the proteolysis system (ubiquitination and lysosomal degradation) resulting in the accumulation of lipofuscin and cross-linked proteins[27]. An age-related accumulation of nonfunctioning proteins that are not efficiently removed from the muscle could increase the amount of non-contractile material in muscle, which might explain why muscle strength declines to a greater degree than total muscle mass in sarcopenia.

Hormonal effects onSarcopenia:With advancing age, there is a well-documented increase in insulin resistance that contributes to diabetes. Insulin has long been considered anabolic, primarily by reducing protein degradation[28. 29]. A recent review of the topic has suggested that insulin can also stimulate protein synthesis[30]. One mechanism by which insulin signaling may facilitate amino acid transport into the cell is via stimulating nitric oxide synthase[31]. Therefore, insulin resistance with age may contribute to sarcopenia via an inhibition of the nitric oxide cascade resulting in less absorption of available amino acids for protein synthesis. As well, GH, liver-derived insulin-like growth factor (IGF)-I[32]and testosterone [33, 34]all decrease with age. Although GH-induced IGF-I production in the liver is the major source of circulating IGF-I, and mediates many GH metabolic effects, local IGF-I production within target tissues, under the influence of both GH and testosterone[35], accounts for greater than 50% of total IGF-I production and appears to be important for stimulating muscle growth and repair[36].Cortisol, a potent stimulus to protein catabolism[37], increases slightly with age and may contribute to the age-related increase in adiposity [38]. Circulating levels of these various hormones are altered by the aging process, all potentially contributing to sarcopenia[32. 39]. One molecular pathway of interest involves the suppression of myostatin, a recently discovered member of the transforming growth factor (TGF) superfamily. Myostatin is an autocrine factor that inhibits muscle development.[40]. However, we recently demonstrated that circulating hormone levels were not related to the expression of myostatin in skeletal muscle [41]. Therefore, how myostatin ultimately interacts in sarcopenia remains unclear.

Pathogenesis: Age-related reductions in muscle mass and strength are also accompanied by a reduction in motor unit (MU) number [42] and histological changes (angulated fibers, fiber-type clumping), which are suggestive of neuronal remodeling[43] in elderly people. The muscle appears to compensate for this reduction in MUs by hypertrophy of existing smaller and slower MUs that attempt to re-innervate faster fibers and transform them into slower myosin fiber types[43, 44] thus

partially explaining why slower muscle is preserved in aging. Urbanchek[45]recently assessed the issue of whether denervated fibers significantly contributed to the age-related loss of muscle strength and observed that only 11% of specific force decrements were due to denervated fibers.

The decline in $VO_{2\,max}$with age has been primarily attributed to sarcopenia and a reduced cardiac output[21]. However, available evidence suggests that mitochondrial metabolism is also adversely affected by age [46]and may contribute to a reduction in $VO_{2\,max}$. Aiken and colleagues, and others [47]have demonstrated that mitochondrial DNA mutations and deletions are increased in the single fibers of aged skeletal muscle, and the abundance of these abnormal mitochondrial regions increase with age in both rats and nonhuman primates[48]. The frequency of mutations is greater in muscles more prone to sarcopenia[47]. Human studies have also demonstrated increased numbers of mitochondrial point mutations in older versus younger participants[49].

Benefits of nutrition and exercise for the prevention of sarcopenia: Nutrition and especially amino acid intake are important to maintain protein turnover. Exercise is beneficial and will decrease body fat, improve reserve capacity, and increase muscle strength (and maybe muscle mass). It could be that sarcopenia has both physiologic factors, as has been discussed, in combination with social issues resulting in older persons not taking up exercise. Sarcopenia is a process whereby a loss of reserve capacity will result in an increased sense of effort for a given exercise intensity. If one avoids exercise, then future performance will continue to decrease, as cardiovascular function and $VO_{2\,max}$ will diminish, again feeding back to the increased perception of exercise effort, thus exacerbating sarcopenia.

As regular physical activity decreases with age, there is a down-regulation of physiological systems adapting to reduced exercise/stress levels. As cardiovascular and skeletal muscle reserve functions decline, this contributes to an increased relative perception of effort for a similar absolute task as compared to when an individual was younger. If tasks are perceived to be more difficult, this will increase the likelihood for avoidance of physical work. As more physical work is avoided, exercise performance will continue to decline, therefore contributing to additional physiological decrements in an individual's functional reserve capacity, thus leading to more sarcopenia.

Conclusion:

The physiological and psychological factors that contribute to the process of sarcopenia are multifactorial, occurring over a prolonged time period, possibly with no identifiable single cause or mechanism, potentially explaining this age-related loss of mass and strength in and of itself. Our goal as researchers should be to gain an improved understanding of the complex biological factors leading to age-related muscle loss beyond those attributable to a simple decrease in physical activity. Populations are rapidly ageing worldwide with major implications for health systems. This situation is more prevalent in low-income and middle-income countries. High-income countries show some evidence that a compression of morbidity (a reduction over time in the total lifetime days of disability) is taking place, as noted from trends of functioning and disability status. However, uncertainty remains about the health of future older generations in view of the different risk factor exposures in different cohorts and increases in the prevalence of chronic diseases. Low-income and middle-income countries currently have no reliable evidence of compression, and morbidity might even be expanding, driven by lifestyle risk factors and increasing prevalence of chronic diseases.

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