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# Sarcopenia: clinical consequences and management

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The term sarcopenia has Greek roots; “sarx” for flesh and “penia” for loss. Rosenberg in 1989 defined sarcopenia as “the process of loss of skeletal muscle mass and size” placing the sole emphasis on the quantity of skeletal muscle in the body [1, 2]. The later definitions, however, include other domains of skeletal muscle such as muscle strength and physical performance. The current definition states that Sarcopenia is a syndrome characterized by progressive loss of muscle mass, muscle strength and the physical performance with a risk of adverse outcomes such as physical disability, poor quality of life and death [3].

The prevalence of sarcopenia depends on gender, but in general, increases with age. Sarcopenia is seen in nearly 25% of those over 65 years and the prevalence increases to nearly 60% in people aged 80 years or more [4]. The prevalence of sarcopenia tends to vary between studies mainly due to the differences in the characteristics of study subjects including nutrition, physical activity and health and the criteria and methods used to diagnose the condition [5, 6].

Sarcopenia is classified as either primary which is age related or secondary when it is associated with an underlying cause. Age related decline of muscle mass is a part of complex body composition changes that occur with advancing age. Aging is associated with gradual increase in fat mass and reduction of body water content and lean muscle mass. Age related loss of lean mass is due to a multitude of causes and a detailed description of such changes is beyond the scope of this article. Apart from the reduced level of physical activities and inadequate nutrition [7], several molecular mechanisms operating at different levels of muscle physiology are responsible for the age related lean mass changes [8]. These mechanisms include the derangement of hormones (e. g. IGF-1 and Insulin), muscle fiber composition and neuro-muscular drive. In addition, abnormalities in myocyte cell differentiation and proliferation, inflammatory pathways and intracellular mechanisms in the processes of proteostasis and mitochondrial functions have been described [9, 10].

The onset of sarcopenia can be either acute (within 6 months of an illness) or chronic [11]. Sarcopenia can occur at any stage of an illness and clinicians should be aware of this possibility and rescreen patients with high risk of muscle loss when the initial screening is negative. Sarcopenia can be a consequence of an array of diseases or conditions. These include, but not

limited to, lifestyle-related factors, endocrine, metabolic and inflammatory diseases and malignancies. Malignancies and advanced end organ failure, however, can be associated with cachexia, which resemble sarcopenia but is considered a different condition. Unlike sarcopenia, cachexia leads to reduction of body fat content and loss of body weight. Although patients with cachexia have sarcopenia, patients with sarcopenia need not be cachectic [12].

Sarcopenic obesity, a subcategory of sarcopenia, is characterized by reduced lean mass together with increased body fat content, especially in intramuscular and visceral areas. The lack of a proper definition and diagnostic criteria has limited research related to this condition [13]. Similarly, osteosarcopenia where low muscle mass coexists with low bone mineral density is an ill-defined entity [14]. These two subcategories highlight that the loss of lean mass with age is not an isolated phenomenon but a part of complex derangement of body composition and shared metabolic pathways.

Reduced lean mass is linked with many adverse health outcomes such as increased mortality, recurrent falls, fracture [15], frailty, quality of life [16] and limitation of physical activities of daily living. The increased risk of mortality associated with sarcopenia has been seen among community-dwelling adults [17, 18] and those with specific diseases such as diabetes [19], chronic obstructive pulmonary disease [20] and cancer [21]. In addition, Bai *et al*, showed that sarcopenia is associated with cognitive decline among community-dwelling older adults [22]. This association has been observed in other analyses too [23, 24].

Despite robust evidence that sarcopenia is an independent determinant of poor clinical outcomes of many diseases, the application of such information in the clinical evaluation of patients is not clearly evident. This could partly be due to the lack of awareness of the condition and an operative definition that can be easily applied in busy clinical settings.

The unavailability of unambiguous criteria to diagnose sarcopenia has hampered research related to this condition until 2010. The first European Working Group on Sarcopenia among Older People (EWGSOP-1) met in 2010 classified sarcopenia as presarcopenia, sarcopenia and severe sarcopenia based on three domains related to skeletal muscles; muscle quantity, muscle strength and physical functions [3]. The deterioration of muscle mass without an involvement of either muscle strength or physical functions was considered as presarcopenia, while the diagnosis of sarcopenia required the deterioration of either muscle strength or physical performance in addition to low muscle mass. The diagnosis of severe sarcopenia required the deterioration of all three domains. Furthermore, the working group recommended a cut point, i.e. 2.5 standard deviation below mean based on local data, to determine abnormal values [3].

Although studies on sarcopenia steady increased following the EWGSOP-1 recommendations, the application of such knowledge in clinical decision making did not improve. The working group considered muscle mass as the mandatory criterion to detect sarcopenia and clinical settings were not equipped to measure this variable in their daily practice. As a result, the second European Working Group on Sarcopenia among Older People (EWGSOP-2) in 2019 made an attempt to address the major deficiencies of the previous recommendations [25].

Instead of muscle mass, the new guidelines consider the muscle strength as the main criterion required to detect sarcopenia. This is logical as there is no parallelism between muscle mass and muscle strength. Hughes *et al* in 2001 found that although changes in muscle strength is influenced by muscle mass changes over time, in some instances muscle strength declines in spite of the maintenance or gain of muscle mass [26]. Studies have shown that compared to muscle mass, muscle strength is a better predictor of mortality in community-dwelling older adults [27]. Isoyam *et al* observed that low muscle strength is more strongly associated with aging, physical inactivity and mortality, compared to low muscle mass, in patients on dialysis [28].

According to the new guidelines, the diagnosis of probable sarcopenia is made when muscle strength is abnormally low. The diagnosis of sarcopenia is made when this is combined with the low muscle mass and the diagnosis of severe sarcopenia requires the deterioration of all three elements; muscle strength, muscle mass and physical performance [25].

The SARC-F is a simple and practical tool to screen for sarcopenia in clinical practice. This is built on five bodily functions; strength, assistance in walking, ability to rise from a chair and climb stairs and history of falls during the previous 12 months [25]. Furthermore, the EWGSOP-2 recommends adhering to the F-A-C-S pathway for screening, confirming and the assessment of the severity of sarcopenia in clinical practice [25]. This allows clinician to diagnose probable sarcopenia at bedside using simple measures such as hand grip strength and chair stand test. The possibility of probable sarcopenia is sufficient to trigger further assessment for possible underlying causes and start interventions. In this approach, the confirmation of sarcopenia is not essential for the clinical management of patients.

The management of sarcopenia involves the control of underlying diseases, exercise and nutritional interventions [29, 30]. Clinical trials on sarcopenia are limited and have questionable quality due to methodological flaws [31, 32]. Furthermore, systematic reviews in this area have combined both randomized and non-randomized trials, hence the evidence on the efficacy of these interventions are not robust. Further, many studies have tested the effects of both exercise and nutritional interventions combined and it is difficult to ascertain the direct effects

of either nutrition or exercise on sarcopenia [33]. Based on the available evidence, a holistic approach including nutritional as well as physical activity modifications is more logical in the management of sarcopenia.

Studies have shown that protein intake can potentially enhance muscle mass, muscle strength and physical performance. In a systematic review involving clinical trials, Capitao *et al* have observed that protein intake above 1.4g/kg/day is required to maintain muscle mass in cancer patients with sarcopenia undergoing treatment. Protein intake below 1.2g/kg/day was associated with loss of muscle mass in these patients [34]. Furthermore, Deer *et al* report that the currently recommended protein intake for older adults (0.8g/kg/day) is inadequate to maintain muscle mass and apart from the quantity, the distribution of protein consumption throughout the day may also have an effect [35]. A meta-analysis in 2018 including six trials found that progressive resistance training improved knee extension strength, times up and go performance, appendicular muscle mass, and leg muscle mass. Although they concluded that exercise interventions significantly improved muscle mass, strength and balance, the small number of studies and the heterogeneity on exercise mode, duration and intensity between studies make the evidence weak [31]. Welch *et al* in 2021, assessing both pharmacologic and non-pharmacologic interventions among older adults highlight the gaps in the current knowledge in this area. They re-analyzed 27 studies on physical intervention, seven on nutritional interventions, three on neuromuscular electrical interventions, one on testosterone, two on growth hormone, one on nandrolone and another on erythropoietin. They found that these studies do not confirm treatment benefit in patients with sarcopenia. Furthermore, these studies had questionable quality and were inconsistent with regards to outcomes [32].

In summary, sarcopenia is a distinct clinical entity linked with many adverse clinical outcomes. Given the high prevalence of diseases and conditions that leads to the deterioration of lean mass, the prevalence of sarcopenia can be expected to be high. The SARC-F scoring system and F-A-C-S case finding pathway provide an easy and practical method to detect cases and trigger interventions. Current knowledge on the management of sarcopenia is limited and effective methods of prevention and treatment of sarcopenia need to be further evaluated.

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