Identification and treatment of older persons with sarcopenia

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Abstract

In the last decades, sarcopenia in older persons has been operationalized by the assessment of lean body mass, muscle strength and/or physical performance. Several definitions of sarcopenia, using different parameters and cut-offs, have been proposed. However, which is the best definition to describe and to assess is still matter of debate. Hand grip strength has been suggested as better predictor of incident mobility impairment and mortality, than skeletal muscle mass. In the light of the current knowledge, we sought to propose an operative approach for identifying and treating sarcopenic older persons according to main categories of sarcopenia: the age-related or primary sarcopenia and disease-related or secondary sarcopenia. We suggest that a quantitative assessment of grip strength alone might be sufficient to identify patients with primary sarcopenia. When chronic diseases accompany the ageing process, the combined assessment of muscle strength plus a balance test could be more appropriate. The identification of tests and pathological relevant cut-offs that facilitates the entry of sarcopenia into the clinical practice, could step forward researchers and physicians. This could be important for planning multidisciplinary models to maximize the maintenance of locomotive abilities especially in older persons affected by chronic diseases such as Parkinson’s disease.

Keywords

Definition, older persons, sarcopenia

To define sarcopenia in older persons: what is the best approach?

Sarcopenia is a geriatric syndrome originally described in 1989 by Rosenberg as the age-related decrease of muscle mass [1]. According to gender-specific cut point based on a young male and female reference group, sarcopenia was firstly defined by Baumgartner and colleagues [2], as appendicular skeletal muscle mass divided by body height squared in meters (skeletal muscle index, SMI) two standard deviations below the mean SMI of young, healthy individuals measured with dual X-ray absorptiometry (DXA). Janssen and colleagues [3], by converting absolute skeletal muscle mass (kg) to percentage of weight (muscle mass/body mass \( \times 100 \)), described sarcopenia as the percentage of skeletal muscle mass that was more than one standard deviation below reference values for young adults. More recently, Clark and coworkers argued that the age-related loss of muscle strength could only be partially explained by the reduction in muscle mass and that other physiologic factors might account for muscle mass weakness in older adults [4]. Therefore, the authors suggested to separately naming muscle strength and muscle mass loss. Thus, the term “sarcopenia” was proposed to describe the age-related decline of muscle mass and “dynapenia” was coined to indicate the age-related loss of muscle strength and power [4]. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) for the first time defined sarcopenia by the presence of low muscle mass and low muscle function (either strength or physical performance) [5]. Interestingly, by using the EWGSOP criteria, Cherin et al. in a study-population of healthy ambulatory subjects, underlined that sarcopenia is a condition occurring even in those middle-aged [6], ranging from 9% at 45-year-old to 64.3% at 85-year-old. Since then, different diagnostic criteria based on various combinations of measures of muscle strength, function and physical performance with muscle mass have been proposed. In particular, the Society of Sarcopenia, Cachexia and Wasting Disorders developed diagnostic criteria for a diagnosis of “Sarcopenia with limited mobility” syndrome [7], which occurs in subjects with an habitual gait speed \(<1.0 \text{ m/s}^{-1}\), or who walk under 400 m in a 6-minute walk test, in conjunction with an appendicular fat-free mass \(>2\) SD below that of healthy 20–30 year olds of the same ethnic group. According to new
consensus definitions of sarcopenia, the International Working Group on Sarcopenia [8] recommends to consider a diagnosis of sarcopenia in all older patients with decreased physical function, strength, or overall health. In particular, the authors suggest to specifically assess bedridden older subjects, that cannot independently rise from a chair, or with a measured gait speed less than 1.0 ms\(^{-1}\). In these patients a diagnosis of sarcopenia was proposed to be consistent with a gait speed of less than 1 ms\(^{-1}\) and an objectively measured low muscle mass (e.g. appendicular mass relative to h\(^2\) that is \(\leq 7.23\, \text{kgm}^{-2}\) in men \(\leq 5.67\, \text{kgm}^{-2}\) in men) [8]. Malmstrom et al. [9], in a cohort of late middle-aged, African Americans showed as the contemporary presence of low appendicular skeletal muscle mass (ASM) and limited mobility (4-m gait walk \(\leq 1\, \text{ms}^{-1}\) or 6-min walk <400 m) was associated with poor health outcomes.

However, it should be acknowledged that the above-mentioned criteria for identifying sarcopenic older persons, consider different parameters and cut-offs for each test. As consequence of lack of standardized and reproducible criteria to diagnose sarcopenia, the prevalence of this condition enormously varies in relation to the method used to estimate the cut-off values for low muscle mass. This data was recently confirmed in a study of older Australian individuals investigating the prevalence rate of sarcopenia by EWGSOP criteria, using different SMI cut points derivation with a low grip strength (<30 kg for men and <20 kg for women) [10].

In this study, low muscle mass was identified using (a) Baumgartner’s method based on gender specific cut-off values for low muscle mass derived from a younger reference group [2], (b) the 20% gender specific method where cutoffs were derived for the lowest 20% of a predictive older study population [11] and (c) the linear regression method where the lowest 20% of residual of the linear regression models of ASM was adjusted for fat mass and height in both sexes [11]. Interestingly, the authors found a high discordance in the estimated prevalence of sarcopenia when Baumgartner’s definition was compared with the other two methods (2.5% versus 6.2% and 6.4% in men, and 0.3% versus 9.3% and 8.5% in women, respectively). By posing serious doubts on the use of gender specific cut-offs for low muscle mass derived from a younger reference group, they underlined the need of consensus about the best method to estimate sarcopenia [10].

We would acknowledge that low muscle strength, has been shown to be a better clinical marker of muscle quality and function and a better predictor of adverse outcomes than low muscle mass [12]. Therefore, quantitative grip strength assessment in the elderly could circumvent the need to assess muscle mass, helping in a more rapid and consistent identification of sarcopenic older persons or those with intermediate weakness. Lauritani and colleagues [12], have proposed low grip strength cut-offs <30 kg for men and <20 kg for women, derived from receiver operating characteristic (ROC) curves predicting walking speeds slower than 0.8 ms\(^{-1}\). Recently, The Foundation for the National Institutes of Health (NIH) Sarcopenia Project using data from nine sources of community-dwelling older persons worldwide [13] have confirmed that low grip strength is a more powerful independent predictor of mobility-limitation and mortality than low muscle mass [14]. Evidence-based handgrip cut-off points of 26 kg for men and 16 kg for women were proposed for the identification of sarcopenic older persons and those with pathological grip strength [15]. In accordance to what has been reported by Lauritani and colleagues [12], the authors also suggested grip strength cut-offs values of 26–32 kg in men and 16–20 kg in women for classifying older persons with intermediate weakness [15]. The role of low muscle strength in predicting mobility impairment and in conferring a higher risk of mortality has also been confirmed in prospective analyses [16,17].

### How to identify sarcopenic older persons

The objective assessment of physical performance of the lower extremities, as well as muscle mass and strength evaluation, is part of most recent criteria to identify sarcopenic older persons. Physical performance has been shown to be a strong predictor of frailty, all-cause mortality, incident mobility disability, hospitalization and risk for nursing-home admission in the elderly [18–21]. This is of importance because of the known overlap between sarcopenia with other syndromes associated with prominent muscle wasting. In particular, sarcopenia is frequently featured with frailty, even if the general concept of frailty goes beyond physical factors to encompass psychological and social dimensions as well, including cognitive status, social support and other environmental factors [22]. By using EWGSOP criteria, Henwood et al. [23] in a very old cohort residing in a residential aged care setting, have described in detail not only the time-intensive challenge of assessing sarcopenia but also how this approach is feasible into clinical practice. In contrast, Malmstrom and Morley [24] suggest more of an initial rapid screening of sarcopenia, which could then be followed up by the three-tiered assessments of muscle mass, strength and performance if required. To that end, the author recently developed and validated the SARC-F questionnaire [24,25] in older population, which investigate the ability to carry a heavy load, walking, rising from a chair, climbing stairs, and falls frequency. The SARC-F questionnaire, by obviating the need for measurement of muscle mass, has been shown to be a suitable community screening tool for a rapid and easy identification of sarcopenic older persons and those with impaired physical function into clinical practice [26,27].

Gait speed, sit-to-stand time and standing balance are the most used measures of functional performance in the elderly which rely on strength and motor control, and muscle power (with the exception of standing balance) [28]. The role of each of these tests in the prediction of adverse outcomes is also known [29,30].

In particular, timed walking speed at patient’s usual pace has been the most used measure in clinical and epidemiological research, because it is simple, quick, reproducible and inexpensive measure of functional and health status in the elderly [31]. Measured 4-m walking speed also allows a diagnosis of dysmobility, which is distinct from other terms related to poor mobility, recently defined by The Mobility Working Group as a gait speed lower than 0.8 ms\(^{-1}\) in both sexes [32]. Gait speed (timed 4-m walk), static balance and timed chair rises also constitute the main items of the Short Physical performance Battery (SPPB), which is the most used...
objective assessment tool for evaluating lower extremity functioning in older persons [18].

However, many of these tests such as walking speed and grip strength, walking speed and muscle mass and grip strength, being quite correlated could capture similar information regarding mobility-limitation in older persons. Additional information is also provided by total SPPB score. In the InChianti study population, we have already demonstrated that minor neurological signs are independently associated with mobility limitation and falls in older persons who have no clear history of neurological disease [33]. In older population, neurological diseases are particularly common and frequently coexist with other clinical conditions, influencing balance and mobility disability [34]. Standing balance test could be considered a surrogate marker of the neurological competence of the subject, and a combined assessment of balance stand test and muscle strength might powerfully integrate the muscular and neurological competence in this specific sub-population of older individuals.

At this regard, we sought to propose in Figure 1 with different schematic approaches for identifying sarcopenic older persons with primary and secondary sarcopenia, which might be useful into clinical practice [35]. Sarcopenia can be considered “primary” (or age-related) when no other cause is evident but ageing itself [5]. Primary sarcopenia is especially associated with physical inactivity, both derived by a reduction of the physical exercise during leisure time or work-related. In our opinion, the quantitative grip strength assessment could be sufficient to capture patients with primary sarcopenia. Secondary sarcopenia usually occurs when one or more identifiable causes coexist [5]. This condition is a proxy of chronic or acute diseases that are highly prevalent in older persons, such as Parkinson’s disease, depression, diabetes, chronic heart failure, COPD, stroke and hip fracture. When a secondary sarcopenia is suspected, a combined evaluation of muscle strength and physical performance could more appropriately capture the mixed effect of age and diseases on muscle efficiency. In this specific population, we propose to perform at least an assessment of the grip strength plus a balance test (e.g. those included in SPPB: the standing balance test, side-by-side, semi-tandem, and tandem positions). This approach has been shown to be extremely important in patients with acute diseases (e.g. after catastrophic events such as hip fracture or stroke) [36] and those affected by chronic conditions such as Parkinson’s disease or COPD [37,38].

However, it should be acknowledge that in older persons other causal factor might account for the reduced muscle mass and strength in the elderly. In particular, during the aging process, a simultaneous anabolic hormonal deficiency with “multiple hormonal dysregulation” is observed [39]. All

Figure 1. The algorithm depicts the diagnostic process and tools to assess primary sarcopenia sarcopenia or age-related sarcopenia (e.g. reduced physical activity, age-related malnutrition or age-related reduced hormonal levels) and secondary sarcopenia or diseases-related sarcopenia. Since other causal factor might account for the reduced muscle mass in the elderly, we also describe the diagnostic process to assess both sarcopenia related to low protein intake and sarcopenia related to low hormonal levels. Based on our diagnostic algorithm for the identification of sarcopenic older persons, we also proposed specific treatments targeting the main causes of sarcopenia.
together the anabolic hormones influence the anabolic nutrition status, the satellite cell activation and together with exercise and other mechanical stimuli have a strong influence on muscle hypertrophy [40]. In particular, testosterone plays a key role in the maintenance of muscle mass and strength in the ageing men [41,42]. Testosterone levels progressively decreased during ageing, and approximately 50% of men over 80 years have serum testosterone concentration below the normal range of young men [43]. Interestingly, older subjects with late-onset hypogonadism [44] often exhibit a vitamin D deficiency [45]. On the other hand, it is also very well known that vitamin D deficiency represent an important potential public health issue, affecting more than one-half of women and one third of middle-aged and older men living in US [46]. There is growing evidence that vitamin plays a role on several tissues including skeletal muscle [47], and low vitamin D status has been associated with greater muscle mass and mobility limitation in the elderly [48]. However, its role at muscular level is still unclear as well as the effectiveness of vitamin D supplementation in improving skeletal muscle strength, muscle mass and muscle power [45]. From our point of view, if one of these conditions is suspected, serum levels of total testosterone in 2 different days and/or 25(OH) vitamin D should be measured.

Finally, it should be acknowledged that malnutrition and/or a shortfall of protein supplies relative to needs are very frequent phenomena in older persons [49]. As a result, older people are at considerably higher risk for sarcopenia related to low protein intake. Therefore, dietary intake and nutritional status should be evaluated in all patients potentially malnourished or in case of starvation. Validated nutrition screening and assessment tools, such as the Mini Nutritional Assessment (MNA), could allow a rapid identification of geriatric patients who are malnourished or at risk of malnutrition [50]. Moreover, nutritional status according to mini nutritional assessment score, has been recently related to functional status in geriatric patients independent of health status [51]. Nutritional assessment should be conducted especially in vegans where the assumption of animal proteins is known to be generally reduced (Figure 1).

How to treat older persons with sarcopenia

Based on our diagnostic algorithm and tools for the identification of sarcopenic older persons, we are also proposing specific treatments targeting the main causes of sarcopenia including physical activity, hormonal therapy (testosterone and vitamin D), caloric and protein supplementation (Figure 1).

In case of age-related physical inactivity, resistance training should be increased. Bautmans [52] and colleagues elegantly showed that high-resistance training leads to a higher increase in one repetition maximum (1RM) strength than low-resistance training (20% of 1RM). Interestingly, this difference disappeared when a mixed low-resistance protocol in which the resistance was intensified within a single exercise set (40% of 1RM). Consistently, a recent systematic review in older adults showed that high-intensity progressive resistance strength training of the lower limb might be more effective in improving strength than moderate or lower intensities of strength training. The authors also underlined that training volume should be considered as it has an important effect on the strength gains achieved [53]. These findings support the need for more research on low-resistance programs in older age. In particular, long-term training studies focusing on residual effects after training cessation are needed.

When low total testosterone levels are observed lower than 230 ngdL\(^{-1}\), we can identify the real class of older men severely hypogonadal [44]. In this group of subjects, hormonal replacement treatment should be considered. However, in prostate cancer patients, especially those on androgen deprivation therapy (ADT), exercise may represent a way to offset many of the ADT side effects on body composition, physical fitness, functional performance, quality of life, as suggested by a recent systematic review [54].

With regard to vitamin D deficiency, it is not quite established whether or not vitamin D serum levels above 30 ngdL\(^{-1}\) is able to maximize the extra-skeletal effects of this “hormone” on physical performance in older persons [45]. However, given the extra-skeletal effects of Vitamin D on several tissues including skeletal muscle, we suggest Vitamin D supplementation and the monitoring of vitamin D levels.

Finally, recent metabolic and epidemiological studies suggest that the current recommendations of protein intake may not be adequate for the maintenance of physical function and optimal health in older adults [55]. Guidelines have traditionally advised a similar intake for all adults, regardless of age or sex, equal to 0.8 g of protein per kilogram of body weight each day (g kg\(^{-1}\) BW d\(^{-1}\)) [56]. In fact, these recommendations do not consider age-related changes in metabolism, immunity, hormone levels or progressing frailty, occurring during ageing. New evidence shows that higher dietary protein ingestion is beneficial to support good health, promote recovery from illness, and maintain functionality in older adults [57,58]. Recently, the PROT-AGE study group have recommended an average daily intake at least in the range of 1.0–1.2 g protein gkg\(^{-1}\) BW d\(^{-1}\) in older people in order to maintain and regain lean body mass and function [57]. Some authors have also suggested a dietary plan that includes 25–30 g of high-quality protein per meal to maximize muscle protein synthesis in older persons [59].

Conclusions

The assessment of muscle strength could be an important and useful measure to identify patients with age-related muscle deficit. When chronic disease coexist, muscle strength evaluation should be accompanied by balance test, which is part of the Short Performance Physical Battery (SPPB). Both of these tests should be included in the comprehensive geriatric assessment (CGA). The routine use of these measures could contribute to develop prognostic muscle index, taking into account the mixed effect of age-related and disease-related muscle efficiency.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.
References


