Current clinical care of older adults with sarcopenia

Abbreviated title: Clinical management of sarcopenia

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Abstract

Sarcopenia, the reduction of skeletal muscle mass, strength and performance with age, is common in older people. Sarcopenia is recognised as a geriatric syndrome which often coexists with frailty, multiple comorbidities, polypharmacy, falls and reduced social networks. Importantly it is associated with increased risk of admissions to hospital and care homes, and of death. In clinical practice slow walking speed (longer than 5 seconds to walk 4 meters with or without a walking aid) can be used to identify people for further assessment of muscle strength (most simply assessed as grip strength) and muscle mass (measured using bioimpedance) to see if they fulfil the diagnostic criteria for sarcopenia.

Comprehensive Geriatric Assessment provides a useful method for clinicians managing older people with sarcopenia to assess risk factors and consequences of sarcopenia, and other factors that may impact on its management. Management is based on improving physical activity and diet. The strongest evidence is for progressive resistance exercise to be carried out 2-3 times weekly for at least 3 months, with a regular increase in physical activity such as walking. Lifestyle changes are important as benefits are lost if the exercise is not maintained. The evidence for dietary protein supplementation is limited but a dietary intake of 1.0-1.2 g/kg body weight/day is generally recommended. The involvement of a multidisciplinary team and support from friends and family is important to maintain these lifestyle changes to achieve long term benefits. Currently no pharmacological therapies are recommended for clinical use in people with sarcopenia.

**Introduction**

Sarcopenia, the reduction in skeletal muscle mass, strength and performance with age, is common in older adults. Importantly, it is associated with current and future risk of disability, falls, fractures, death, and admission to hospital and care homes. Thus busy clinicians should be aware of the risk factors and consequences of sarcopenia, and know how to identify people at high risk of developing the condition. Strategies for the clinical care of older adults with sarcopenia will be discussed.

**What is sarcopenia?**

Sarcopenia was first described in 1989 and was initially defined as a reduction in skeletal muscle mass. However increasing recognition of the importance of associated changes in muscle strength and quality has led to current expert consensus that the diagnosis is based on low muscle mass with poor muscle function (strength or performance). Muscle mass increases during childhood and early adulthood, remains stable until around 40 years of age, and then typically declines at a rate of 1-2% per year (Figure 1) ([1](#_ENREF_1)). Sarcopenia is termed primary, or age-related, when no other cause is present, but may also be secondary to a reduction in physical activity (eg bed rest, sedentary behaviour, zero gravity), poor nutrition (eg inadequate dietary intake of protein, malabsorption) or related to diseases such as malignancy, inflammatory disease, advanced organ failure or endocrine disease. In older adults the aetiology is often multifactorial, particularly among those in hospital or care home settings. This paper will focus on age-related sarcopenia.

Sarcopenia is considered to be a geriatric syndrome. These have been defined as common, complex and costly states of impaired health in older adults which result from poorly understood interactions of disease and age on multiple systems producing a constellation of signs and symptoms. Sarcopenia has considerable overlap with physical frailty in terms of definition and management, and indeed the criteria for the diagnosis of sarcopenia comprise three of the five criteria for the Fried Frailty Score. Frailty has been defined as a state of increased vulnerability to stressors due to reductions in physiologic reserve in multiple body systems. Most frail older people have sarcopenia and some older people with sarcopenia are frail.

Malnutrition and cachexia are also associated with muscle wasting and loss. However, starvation leads to a loss of both body fat and non-fat mass while body fat is preserved or even increased in sarcopenia. Cachexia is a complex metabolic syndrome characterised by severe muscle wasting (with or without loss of fat mass) and an underlying inflammation, and may be associated with cancer or advanced organ failure. Most people with cachexia will have sarcopenia but most people with sarcopenia will not be cachexic ([2](#_ENREF_2)).

**Why is sarcopenia in older adults important?**

Sarcopenia is associated with poor current and future health. Individuals with sarcopenia have an increased risk of physical disability, falls, poor quality of life, mortality and admissions to hospital and care homes. Sarcopenia also has significant personal and societal costs. The direct healthcare expenditure attributable to sarcopenia in the US was estimated to be $18.5 bn (equivalent to 1.5% total healthcare expenditure) in the year 2000. Thus the development of sarcopenia has significant consequences for both individuals and healthcare services worldwide.

**Risk factors for the development of sarcopenia**

Muscle mass is dependent on the peak muscle mass attained by early adulthood and the subsequent rate and duration of decline. Thus risk factors for sarcopenia include a low birth weight and poor growth during childhood and puberty. A healthy diet and appropriate exercise are essential to maintain muscle mass and function throughout the lifespan and older adults are at particular risk as they have a high prevalence of sedentary behaviour. Older adults may also have a low dietary protein intake, which is associated with a lower muscle mass. Comorbidities such as diabetes mellitus are more common with increasing age, as are obesity and low-grade inflammation, all of which are associated with an increased risk of developing sarcopenia.

It is important to note that there is a recognised transition from presarcopenia (defined as low muscle mass without a reduction in muscle strength or performance) to sarcopenia. The risk of transition is reported to be increased by the presence of pain or a high body mass index, and reduced in those individuals with a moderate level of physical activity.

**Diagnosis of sarcopenia**

***Diagnostic criteria***

The European Working Group on Sarcopenia in Older People (EWGSOP) consensus conference in 2010 proposed a diagnosis based on low muscle mass (appendicular lean mass (ALM)/height 2 ≤7.23 kg/ht2 for men and ≤5.67 kg/ht2 for women) with either low muscle strength (grip strength <30kg for men and <20kg for women) or low physical performance (gait speed <0.8 m/s) ([3](#_ENREF_3)). The International Working Group on Sarcopenia has similarly proposed a definition of sarcopenia based on low gait speed and muscle mass. The Foundation for the National Health Institutes of Health (FNIH) Sarcopenia Project has recently further analysed epidemiological and clinical trial data from 26,625 participants to identify clinically relevant cut points to define low muscle mass and strength, based on their relationship with mobility impairment. This project has recommended that low grip strength is defined as <26kg for men and <16kg for women, and low lean mass (appendicular lean mass adjusted for body mass index) is defined as <0.789 for men and <0.512 for women ([4](#_ENREF_4)). Thus while there is broad consensus on a definition of sarcopenia, the cut points to confirm the diagnosis are still unclear.

***Measurement tools***

Muscle mass can be assessed using dual-energy X ray (DXA), magnetic resonance imaging (MRI), computerized tomography (CT) or bioimpedance (BIA). MRI and CT assessments are costly and usually reserved for research studies. DXA scanning is more widely available but older people may have difficulty in physically accessing the scanner. BIA is a simple bedside assessment with portable equipment that can be conducted in a wide variety of healthcare or community settings. Muscle performance is usually assessed as timed gait speed over a 4-m course at a usual pace, but can be assessed as chair stands or in the Short Physical Performance Battery. Muscle strength can be assessed as knee extension strength or as grip strength but the handheld dynamometers used to assess grip strength are highly portable so more suited to a variety of settings. The use of BIA, grip strength and either gait speed or short physical performance battery are recommended as the most valid, reliable and feasible methods for the routine clinical assessment of older adults ([5](#_ENREF_5)).

***Identification of older adults with sarcopenia in clinical practice***

The EWSGOP has produced guidelines on the measurement of muscle mass strength and performance and a useful algorithm for use in practice (Figure 2). Case finding may take place within the general population aged over 65 years or within high risk groups, and in a variety of settings including both hospital and community settings. The EWSGOP recommends an initial gait speed assessment to identify those with a speed <0.8 m/s (ie who take longer than 5 seconds to walk 4m) who should then be further assessed for strength and muscle mass to see if they fulfill the criteria for a diagnosis of sarcopenia. However, the measurement of muscle mass can be operationally difficult in older people and the use of hand grip strength alone has been proposed as useful for people with walking difficulties.

The SARC-F scale is a newly developed tool to diagnose sarcopenia and obviate the need for measurement of muscle mass. The questions of SARC-F cover the ability to carry a heavy load, walking, rising from a chair, climbing stairs, and falls frequency, and a score of SARC-F ≥ 4 is defined as indicating sarcopenia. The scale has been evaluated in a prospective study of 4,000 community dwelling men and women in Hong Kong with direct measurement of muscle mass, strength and physical performance. The SARC-F had excellent specificity but poor sensitivity for the classification of sarcopenia, but it was comparable to the direct measurements in its predictive power for 4 year physical limitation ([6](#_ENREF_6)). Further research is directed at validating this tool in different populations and settings.

**The prevalence of sarcopenia**

The prevalence of sarcopenia depends on both the definition used to make the diagnosis, the type of assessments and the population being assessed. Among older community dwelling people in the UK Hertfordshire Cohort Study, the prevalence was 4.6% for men and 7.9% for women, using the EWGSOP definition ([7](#_ENREF_7)). Recently several operational criteria for sarcopenia have been compared among 10,063 participants of nine studies aged 65 years and older as part of the FNIH Sarcopenia Project ([8](#_ENREF_8)). The prevalence of sarcopenia was highest using the EWGSOP definition (5.3% men and 13.3% women) and lowest using the FNIH criteria (1.3% men and 2.3% women). Across the criteria there was good agreement for the absence of sarcopenia but poor positive agreement. This may reflect the difference in categorization of low muscle mass as ALM/ht2 (EWSGOP) or ALMBMI (FNIH) as well as the difference in cut off values for low grip strength.

The prevalence of sarcopenia also depends on the population or healthcare setting and has been reported to be 10% among hospital inpatients and over 30% among nursing home residents. Muscle strength has similarly been reported to vary with healthcare setting, with higher age-adjusted grip strength values among community-dwelling older people than those in hospital, and with care home residents having the lowest grip strength ([9](#_ENREF_9)).

**The clinical management of older adults with sarcopenia**

A lifecourse approach to the management of sarcopenia highlights the importance of successful early development to maximise peak muscle mass in adulthood, and then of minimising the rate of muscle loss with increasing age. Food intake and physical activity are important anabolic stimuli for muscle protein synthesis throughout life, thus risk factors such as exercise and diet should be addressed in order to reduce muscle loss.

***Exercise interventions***

The level of physical activity usually diminishes with increasing age, and sedentary behaviour in both mid-life and older age is associated with increased muscle loss. A recent epidemiological study of the leisure time physical activity undertaken by 1,645 community dwelling adults in the UK has demonstrated an association between increased activity between ages 36 and 60-64 years and stronger grip strength at age 60-64 years ([10](#_ENREF_10)). The impact of exercise on sarcopenia was evaluated in a recent systematic review which identified seven intervention studies ([11](#_ENREF_11)). The strongest evidence was for progressive resistance training which typically improved both muscle mass, strength and physical performance (chair rise, stair climb or 12 minute walk) when conducted over 3-18 months by older men and women. Combining high-intensity exercise interventions( such as aerobic, resistance, flexibility and/or balance training) improved muscle mass and function among 246 older community dwelling women in Germany but the results of smaller mixed gender studies with lower intensity in frail or sedentary individuals were inconclusive. Overall there appears to be a beneficial effect of exercise in community dwelling older people but the evidence is strongest for improvements in muscle strength and performance rather than for increase in muscle mass. Supervised resistance or composite exercise programmes lasting at least three months have been recommended for community dwelling older people, alongside a regular increase in daily physical activity such as walking.

***Nutritional interventions***

Older people often have a relatively low dietary protein intake and are also less responsive to the muscle development stimulated by protein intake compared to younger adults. While low muscle mass is recognised to be associated with lower protein intake, the evidence for the use of dietary protein supplements in older patients remains inconclusive. A recent systematic review identified five randomised controlled trials of protein supplementation in community dwelling older people (12). The only study without an associated additional exercise programme demonstrated an improvement in physical performance but no difference in muscle mass or strength compared to the control group. Four other studies combined differing protein supplementation with an exercise programme lasting between 24 weeks and 18 months. One study reported an increase in muscle mass, and one an increase in power: muscle strength and physical performance did not improve in any of the studies.

The administration of essential amino acids has also been evaluated, mainly using leucine which has been demonstrated to improve muscle protein synthesis in older men. However in controlled clinical trials there was limited evidence for any change in muscle mass and function. HMB (β-hydroxy β-methylbutyric acid), a bioactive metabolite of leucine, has also been assessed in small clinical trials either alone, in combination with arginine and lysine, or with resistance exercise. Again, there is only limited evidence for some improvement in muscle mass and function, and further larger trials are required.

The synergy between exercise and protein intake in older people may be important. There is some evidence that the timing of nutritional supplementation with exercise may impact on outcomes and this will be explored in future research. It is important to note that a dietary protein intake of 1.0 - 1.2 g/kg body weight/day has been recommended for adults of all ages, with 20-25g of dietary protein at each of the three main meals to facilitate post prandial muscle synthesis during the whole 24 hour period ([12](#_ENREF_12)).

Vitamin D receptors have been identified in skeletal muscle, and receptor polymorphisms are associated with variable muscle strength. Older patients with vitamin D deficiency are recognised to have an increased risk of frailty in epidemiological studies. However, there is no conclusive evidence for measureable improvements in muscle mass or performance with vitamin D supplementation, although there are recognised benefits of a reduction in falls and fractures. Foods with high antioxidant status and fish oils have been associated with improved muscle function in epidemiological studies but trials of supplements have again been inconclusive. In reality people have a mixed diet, and healthy ‘prudent’ diets containing fruit and vegetables, wholemeal cereals and oily fish have been associated with greater muscle strength in older adults ([13](#_ENREF_13)).

***Pharmacological interventions***

Currently no pharmacological therapies are recommended for clinical use in older people with sarcopenia. Studies of growth hormone were reported to demonstrate an increase in muscle mass but no improvement in muscle function and there are concerns about side effects including weight gain. Clinical trials with testosterone demonstrated increased muscle mass and strength but were discontinued because of adverse cardiovascular side effects. However, this has led to further research into the use of selective androgen receptor molecules. There is also current interest in angiotensin-converting enzyme inhibitors, typically prescribed for hypertension, which have been associated with improved muscle function during clinical trials in patients with sarcopenia. Myostatin is a muscle derived hormone that leads to muscle protein breakdown via the activin signalling pathway, and myostatin deficiency is associated with increased muscle mass in humans. Several myostatin inhibitors have been developed and have been reported to increase muscle mass and strength in mouse models. Small phase I and phase II studies of several inhibitors of the activin signalling pathway are currently underway in humans.

Importantly, there is evidence from large epidemiological studies that some medications in general use may have an adverse effect on muscle strength. Calcium channel blockers, used for the treatment of high blood pressure, and the diuretic furosemide have been shown to reduce grip strength in both older men and women. Thus the management of older people with sarcopenia should include a review of all current medications with the aim of stopping any that are not currently indicated.

***Comprehensive Geriatric Assessment***

Comprehensive Geriatric Assessment (CGA) is defined as ‘a multidimensional, interdisciplinary diagnostic process to determine the medical, psychological, and functional capabilities of a frail older person in order to develop a coordinated and integrated plan for treatment and long-term follow-up’. CGA has been demonstrated to improve healthcare outcomes for frail older people, including increased survival, cognition, quality of life and reduced length of stay, rates of readmission to hospital, long term care use and costs([14](#_ENREF_14)). Sarcopenia is recognised as a geriatric syndrome which is often associated with frailty, multiple comorbidities, polypharmacy, falls and reduced social networks. CGA provides a useful method for clinicians managing older people with sarcopenia to assess risk factors for sarcopenia, the consequences of sarcopenia, and other factors that may impact on its management. Thus treatment approaches for older people with sarcopenia may seek to address issues such as impaired mood and/or cognitive function both of which can impact self-care including nutrition, social isolation (leading to difficulty accessing food), comorbidities such as diabetes, review of medication including the need for bone protection, poor dietary intake, low habitual physical activity, and falls and balance impairment. Such an approach requires co-ordinated input from a multidisciplinary team including therapists, dietitians, social care agencies, as well as medical and nursing staff. Encouragement from friends and families to support lifestyle changes to improve dietary intake and physical activity levels is also important as these changes need to be maintained in the long term to achieve benefits.

**Conclusions**

Sarcopenia, the reduction of muscle mass, strength and performance with increasing age, is common and costly to both the individual and society. It is associated with poor health, disability, increased risk of admission to hospital and care homes, and death. Currently no pharmacological therapies are recommended for clinical use in people with sarcopenia and management is based on improving physical activity and diet. The strongest evidence is for progressive resistance exercise to be carried out 2-3 times weekly for at least 3 months, with a regular increase in physical activity such as walking. Lifestyle changes are important as benefits are lost if the exercise is not maintained. The evidence for dietary protein supplementation is limited but a dietary intake of 1.0-1.2 g/kg body weight/day is generally recommended. Older people living with sarcopenia are often frail with a range of medical and psychosocial issues. Comprehensive Geriatric Assessment enables the identification of an individual’s risk factors for sarcopenia, its consequences, and other factors that may impact on their clinical management. The involvement of a multidisciplinary team and support from friends and family is important to achieve long term benefits.

**Box with key messages**

* Sarcopenia is a common geriatric syndrome
* It is associated with poor current and future health, admission to hospital and care homes, and death
* Individuals with slow gait speed should be assessed for low hand grip and low muscle mass to confirm a diagnosis of sarcopenia
* Progressive resistance exercise and an increase in daily physical activity can be beneficial if sustained
* The evidence for dietary supplementation with protein or vitamin D is inconclusive
* No pharmacological interventions are currently recommended for sarcopenia
* Comprehensive Geriatric Assessment enables clinicians to identify the needs of these complex patients which should be addressed with the involvement of a multidisciplinary team

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Figure 1



Figure 2. EWGSOP-suggested algorithm for sarcopenia case finding in older individuals (3)

