The emergence of sarcopenia as an important entity in older people

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ABSTRACT

Sarcopenia refers to the loss of muscle mass and strength seen with advancing age. The pathophysiology is multifactorial, with loss of muscle satellite cells, changes in hormonal systems, chronic inflammation, oxidative stress and anabolic resistance to protein utilisation all implicated. Older age, female sex and immobility are important risk factors. Sarcopenia is clinically important as it is a major risk factor for physical frailty, falls, prolonged hospitalisation, dependency and earlier death. Diagnosis requires evidence of reduced muscle mass measured by handgrip strength or walk speed, together with evidence of low muscle mass, measured by one of a variety of techniques such as bioimpedance analysis or dual X-ray absorptiometry. Resistance training is the only intervention of proven efficacy to treat sarcopenia, but a range of nutritional and pharmacological interventions are under test, including myostatin inhibitors, leucine and protein supplementation, angiotensin-converting enzyme inhibitors and allopurinol.

What is sarcopenia?

Sarcopenia is the loss of both muscle mass and function that occurs with advancing age. Sarcopenia, from the Greek meaning 'poverty of flesh', was first proposed in 1989 by Irwin Rosenberg as a term to describe the loss of muscle mass with age. The definition of sarcopenia has evolved since that time to incorporate our understanding of the importance of muscle function alongside muscle mass. In 2010, a landmark paper[1] described the European Working Group on Sarcopenia in Older People (EWGSOP) consensus guidelines on the definition and diagnosis of sarcopenia. They provided this comprehensive working definition:

> *Sarcopenia is a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.*

Why is sarcopenia important?

Sarcopenia is associated with multiple adverse outcomes,[2] which are of importance to older people, the health services they use and the wider health economy. Sarcopenia underlies many of the limitations in mobility and activities of daily living that older people suffer from; it is also a key pathophysiology underlying physical frailty. Sarcopenia is associated with an increased risk of death, with one cohort study demonstrating that participants aged 80–85 years with sarcopenia had double the risk of death during a 7-year follow-up compared with those without sarcopenia, after adjustment for multiple potential confounders.[3] Sarcopenia is also an independent risk factor for falls,[4] which in turn are a major risk factor for hip fracture, functional decline and future hospitalisation. Once in hospital, patients with sarcopenia have longer lengths of stay than those without sarcopenia.[5] Recovery in function after discharge is also poorer for those with sarcopenia.[6]

How common is sarcopenia?

Sarcopenia is common among older populations although the estimated prevalence varies greatly depending on both the population and the techniques used to diagnose the condition.

Key points

- Sarcopenia is the loss of both muscle mass and function that occurs with advancing age; it is associated with multiple adverse outcomes, including frailty, disability and death
- Older age, female sex and muscle disuse are known risk factors although the underlying pathogenesis is complex and not currently well understood
- Sarcopenia is diagnosed by demonstrating the presence of both a reduction in muscle function and muscle mass
- Sarcopenia can be effectively treated using resistance exercise and there is now a developing focus on how best to deliver this treatment across health services
- Treatments for sarcopenia are the subject of intensive research activity; the impact of dietary modification, and the role of new and existing drugs are all areas of active investigation

KEYWORDS: Diagnosis, older people, sarcopenia, treatment

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A 2014 systematic review, applying the EWGSOP definition, found a prevalence of 1–29% among older community-dwelling adults, 14–33% among those living in long-term care settings and 10% for those in acute hospital care.[7]

What causes sarcopenia?

The pathogenesis of sarcopenia is complex and not currently well understood. There are multiple risk factors involved and there are likely to be multiple pathophysiological processes contributing to its development.[8] Alongside older age and female sex, muscle disuse caused by low levels of physical activity or immobility is a well-described risk factor. At the cellular level, the age-related loss of muscle mass that occurs in sarcopenia is caused by a decrease in the size of muscle fibres (myofibres) and in their total number. Both of the main types of myofibre – type 1 (slow) and type 2 (fast) – are affected; however, type 2 muscle fibres are affected to a greater extent. Age-related oxidative damage, low-grade chronic inflammation, nutritional factors (including the anabolic resistance of older skeletal muscle to protein-based dietary stimuli), changes in hormonal systems (including IGF-1 and the renin-angiotensin system) and mechanisms related to loss of myofibre innervation have all been implicated in this process. Furthermore, there is potential for each of these factors to contribute to loss of muscle mass versus muscle function in different ways, offering a further dimension of complexity.

When considering aetiology, it is important to remember that sarcopenia is not the only type of skeletal myopathy affecting older people; for instance, those associated with chronic obstructive pulmonary disease and heart failure are distinct clinical entities that preferentially affect type 1 muscle fibres. These conditions may of course coexist with sarcopenia of age. It is also likely that within the accepted definition of sarcopenia there are subtypes that are yet to be characterised. There is much work to be done to further elicit the differences and commonalities between types and subtypes of skeletal myopathy and how they contribute to morbidity in older people.

How to diagnose sarcopenia

As well as providing a comprehensive working definition of sarcopenia, the EWGSOP consensus guidelines outlined an approach to diagnosis of sarcopenia that can be used in clinical practice.[1] Their algorithm (Fig 1) for case finding among older adults (age >65 years) suggests initially identifying the presence of reduced gait speed and then proceeding to test grip strength if gait speed is normal. If either one of these measures of muscle function suggests a deficit, the second stage in the diagnostic process is to measure muscle mass. The presence of both a reduction in muscle function and muscle mass is required to reach a diagnosis of sarcopenia.

Gait speed

Gait speed is assessed by asking the patient to walk a set distance, often 4 metres, at usual pace. Slow gait speed is known to be a risk factor for falls, institutionalisation and death.[9] A value of <0.8 m/s has been suggested in both European and US guidelines as a diagnostic threshold although this may vary by population.[1,10]

Grip strength

Grip strength can be measured in the clinical setting by a device such as a Jamar dynamometer. It has been found to be one of the most practical methods of measuring muscle strength and correlates with measures of physical performance in the lower limbs. Weak grip strength has been shown to be related to both incident disability and death.[11,12] Cutoffs vary between populations and guidelines, but for European populations, cutoffs of <20 kg (females) and <30 kg (males) have been proposed by the EWGSOP guidelines.[1] More recent guidelines from the USA stratify grip strength cutoffs by body mass index.[10]

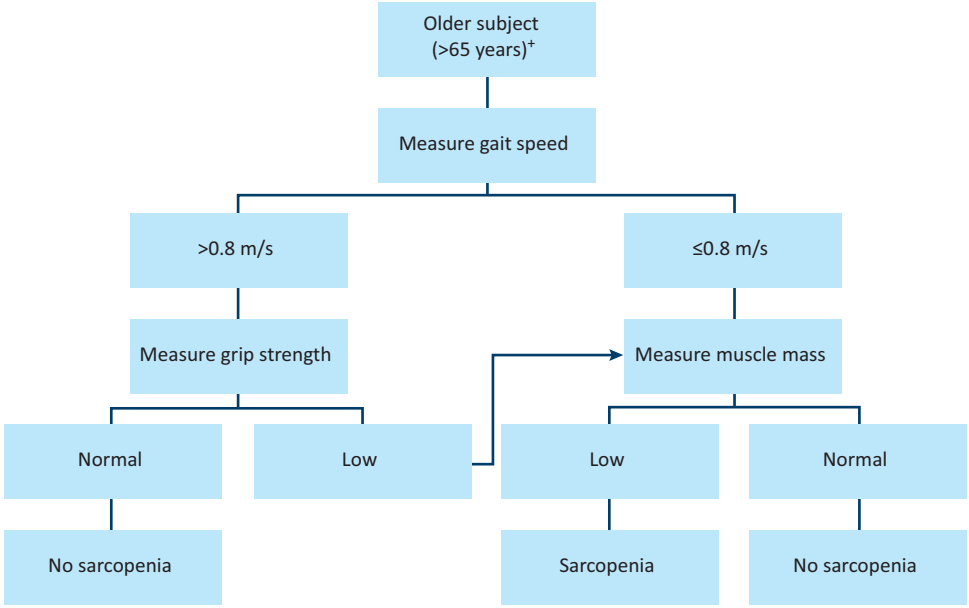

Fig 1. Algorithm for diagnosing sarcopenia. Comorbidity and individual circumstances that may explain each find must be considered. +This algorithm can also be applied to younger individuals at risk. Reproduced with permission from Cruz-Jentoft *et al.*[1]

Muscle mass

There are several ways to quantify muscle mass. Computerised tomography and magnetic resonance imaging are gold standard techniques for estimating muscle mass in research settings, but are often not easy to use in clinical practice. The European guidelines recommend dual energy X-ray absorptiometry as the preferred low-radiation alternative for routine measurement of muscle mass in clinical practice. However, this method is not portable and so may also be impractical for clinicians looking to diagnose sarcopenia at the point of assessment.

Bioimpedance analysis (BIA) is an inexpensive, portable and quick way to estimate body fat and lean muscle mass and has been validated for use in this context, with the European guidelines recommending it as an alternative to dual energy X-ray absorptiometry. Care needs to be taken to use a conversion equation that has been validated for both the bioimpedance analysis machine used and the population studied. Anthropometric measures, such as mid-arm circumference and skinfold thickness have previously been used to estimate muscle mass, but are no longer recommended as they have been validated by very few studies and are vulnerable to error. Similarly, although body mass index correlates with muscle mass, it is not sufficiently precise to allow diagnosis of low muscle mass and does not allow diagnosis of sarcopenic obesity – the combination of high body fat with low muscle mass.

Treatments for sarcopenia

Exercise

Resistance exercise remains the intervention with the most supporting evidence for effectiveness in the management of sarcopenia, and so is the current treatment of choice. Meta-analyses have shown improvements in physical performance and muscle strength with resistance exercise in the context of sarcopenia.[7] Outcomes vary between exercise studies, as does the nature of the exercise programme offered. This has led to difficulties in translating research findings into practice, and the focus now needs to be on producing resistance exercise programmes that are deliverable at scale within communities and across health services.

Diet

For those unable or unwilling to undertake resistance exercise, the management options are more limited, with the majority remaining in the experimental phase. Dietary modification and supplementation are areas of intense research activity, with interest in boosting protein, the impact of vitamin D supplementation and the effect of antioxidants and creatine. Supplementing bulk protein intake may be difficult for older people and evidence for effectiveness in sarcopenia is limited. However, supplementation with leucine or its metabolites may offer a more effective alternative and large scale trials are currently underway. Vitamin D supplementation has a small benefit on muscle strength but not muscle mass[13] and creatine may augment the effect of resistance training, at least on muscle mass.[14,15] The effects of supplementation in patients with sarcopenia as opposed to healthy older people require further study, however.

Medication

There is significant potential for drug development in the area of sarcopenia research although currently there is no recommended pharmacological treatment. Encouraging recent trial data suggest that inhibitors of the myostatin system may have a role in treating sarcopenia,[16] but phase III trials are awaited. Recent data from the TTT trials of testosterone did not show a useful improvement in physical function,[17] but large trials have not been conducted specifically in patients with sarcopenia. Other trials are examining the use of angiotensin-converting enzyme inhibitors, and also allopurinol as an antioxidant.

Conclusion

Sarcopenia is associated with multiple adverse outcomes, including frailty, disability, morbidity and mortality. It is an exciting, emerging area of geriatric medicine, highly relevant to the problems of functional impairment and dependency that affect large numbers of our ageing population. Recent efforts to achieve international consensus on the definition and diagnosis of sarcopenia have accelerated progress in sarcopenia research, and there are growing efforts within the specialty of geriatric medicine to translate research findings into clinical practice. For the front-line physician, techniques to measure muscle mass and function will ultimately add to the existing tools used for the assessment of older people presenting to hospital. Furthermore, our understanding of sarcopenia using a life-course approach could significantly broaden the opportunities to modify factors contributing to its development prior to old age, thus offering a way to improve the health and wellbeing of older people within the general population. ■

Conflicts of interest

The authors have no conflicts of interest to declare.

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