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COMMENTARY

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Sarcopenia definition, diagnosis and treatment: consensus is growing

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Abstract

Sarcopenia is a skeletal muscle disorder that commonly occurs with advancing age as well as with a number of long-term conditions. Recognition in clinical practice is relatively recent but important because of the association between sarcopenia and a range of adverse effects on health including impaired mobility, increased morbidity and mortality. Originally characterised as loss of muscle mass, the definition has evolved to focus on loss of skeletal muscle function, particularly strength, through a number of international definitions such as that of the European Working Group on Sarcopenia in Older People most recently revised in 2019. Progress in the decades ahead is likely to be seen with regard to use of routine health data, prescription of resistance exercise, translation of biology and epidemiology into first in man studies for new treatments, and focus on sarcopenia in low and middle-income countries. Immediate next steps include the newly formed Global Leadership Initiative on Sarcopenia to develop international consensus on definition and diagnosis.

Keywords: sarcopenia, older people, muscle function, muscle strength, skeletal muscle mass

Key Points

- Sarcopenia is a disorder involving the loss of skeletal muscle mass and function that commonly occurs with advancing age as well as with a number of long-term conditions.
- Recognition in clinical practice is relatively recent but important because sarcopenia has a range of adverse effects on health.
- Original definitions focused on muscle mass but emphasis is now on muscle function as illustrated in a number of international guidelines.
- Progress in the decades ahead is likely to be seen with regard to use of routine health data, prescription of resistance exercise, translation of biology and epidemiology into first in man studies for new treatments and focus on sarcopenia in low- and middle-income countries.
- Immediate next steps include an exciting Global Leadership Initiative on Sarcopenia (GLIS) to develop international consensus on definition and diagnosis.

Background

Sarcopenia is a progressive and generalised disorder of skeletal muscle that commonly occurs with advancing age and is associated with increased likelihood of a wide range of adverse outcomes including impaired mobility, increased morbidity and mortality. Coined only a few decades ago in the nutrition and body composition field [1], it was first widely used to describe low muscle mass, until it became evident that muscle function was a better predictor of outcomes [2, 3]. Around 2010, several definitions were

proposed adding muscle strength and physical performance to the concept of sarcopenia [3, 4]. Research in the field increased exponentially, showing that sarcopenia, with these definitions, was predictive of outcomes and responsive to treatment, and the research has expanded into a good number of medical and surgical disciplines. However, this growth is not yet translated, in most cases, into better patient care and improved outcomes such as reduced falls, fractures, hospitalisations and mortality.

In order to improve the clinical uptake of sarcopenia, some organisations have fostered coding of this condition in the clinical modification of the international classification of diseases that is used in the United States and other countries (ICD-10-CM, code M62.84) [5]. Recent definitions have incorporated simplified algorithms to be used in clinical practice [6, 7], clinical guidelines have been developed [8, 9] and research on screening tools is growing [10]. However, sarcopenia is not yet appropriately recognised in the World Health Organization latest version of the ICD (ICD-11) used by most countries. The most recent consensus definitions are the European Working Group on Sarcopenia in Older People (EWGSOP2) [6] (also supported by Australia and New Zealand) [11], the Asian 2019 Asian Working Group for Sarcopenia (AWGS) [7] and the American Sarcopenia Definitions and Outcomes Consortium (SDOC) [12].

Current practice

An 85-year-old woman was referred to the geriatric medicine outpatient clinic for suspected sarcopenia. She reported that she had been walking slower and had some difficulties rising from a chair, so her general practitioner performed a screening test for sarcopenia (SARC-F), which was positive. At the clinic, grip strength was found to be very low (11 kg). A dual-energy X-ray absorptiometry (DXA) scan was ordered to estimate muscle mass and reported an appendicular skeletal muscle mass of 10.3 kg (cut-off for women <15 kg). Sarcopenia was confirmed (with low muscle mass and strength) and was classified as severe as gait speed (a measure of physical performance) was 0.5 m/s (≤0.8 m/s). These steps followed the EWGSOP2 algorithm for case-finding, making a diagnosis and quantifying severity of sarcopenia in clinical practice [6]. However, this process most probably did not happen. A survey of healthcare professionals working in the National Health Service of the United Kingdom showed that only half of the respondents organisations identified sarcopenia, most did not use any formal criteria to diagnose the condition, and only one of the surveyed centres reported using a code for it [13]. Similar surveys in Australia, New Zealand and the Netherlands also showed that most practitioners do not make the diagnosis of sarcopenia and are unaware of diagnostic tools and instruments [14, 15]. In most settings, dynamometers are not widely available to measure muscle strength and access to DXA or other muscle mass measurement techniques is limited or restricted.

Interventions known to improve outcomes in sarcopenic patients like the one described are resistance exercise and optimising nutritional intake. An international guideline on sarcopenia released in 2018 gave a strong recommendation to resistance-based training and a conditional recommendation to increasing protein and calorie intake, with protein supplementation if needed [8]. Evidence on resistance exercise is strong for functional outcomes and weaker for body composition outcomes [16, 17]. A recent multicentre randomised controlled trial has shown that a multicomponent intervention comprised of moderate intensity exercise and personalised nutritional counselling can significantly reduce by 22% the incidence of mobility disability (defined as the inability to independently walk 400 m in <15 minutes) in patients with frailty and sarcopenia [18]. Evidence on nutrition interventions is still weak, partly due to the heterogeneity of interventions (proteins, full oral nutrition supplements with different composition, leucine, hydroxy-methyl butyrate [HMB]) and of inclusion criteria and outcomes in clinical trials [17]. The effect of nutraceuticals is inconclusive [19].

Sarcopenia was, and is still, used by many as a synonym for low muscle mass. However, this concept does not hold any more as low muscle mass is core to three related conditions: sarcopenia, cachexia and malnutrition. The most recent definitions of sarcopenia consider low muscle mass as a key diagnostic criterion even though discussion continues on how best to measure it [3, 6, 7, 12]. The most popular definition of cachexia lists having a low fat-free mass index as one of the seven diagnostic criteria [20]. In fact, cachexia includes low muscle mass and low muscle strength, so it can also be regarded as disease-associated sarcopenia [6]. And the Global Leadership Initiative on Malnutrition (GLIM) has proposed a worldwide definition of malnutrition that uses five criteria, one of them being low muscle mass [21]. A recent international consensus suggests how to measure muscle mass in clinical practice in the setting of malnutrition and recommends checking for coexisting sarcopenia in malnourished persons [22]. Sarcopenia, cachexia and malnutrition are therefore distinct with regard to what accompanies the low muscle mass (Figure 1).

Looking ahead

There is much interest in where the field of sarcopenia research will focus next, particularly with regard to how rapid progress in research can be translated into improved clinical care. A new area on the horizon is the use of routine data as well as research data to understand the burden of sarcopenia within healthcare systems. This is an important topic but one that has been to date fraught with difficulty because of the slow progress in recognising, recording and coding sarcopenia in clinical practice. The application of artificial intelligence may help. For example, natural language processing has been used to identify sarcopenia, frailty and cachexia patients in a US multisystem electronic health record database [23]. This approach could

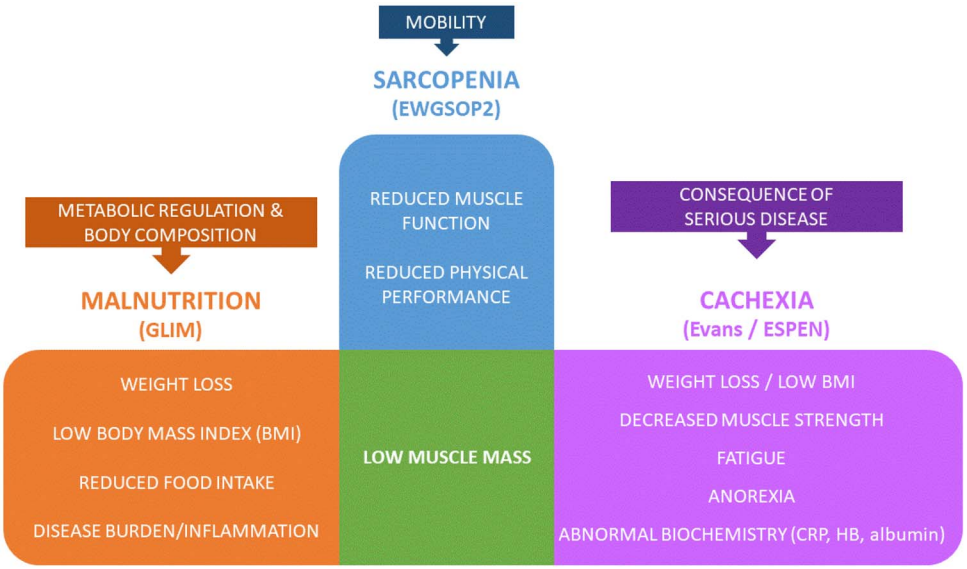

Figure 1. Low muscle mass in the definitions of malnutrition, sarcopenia and cachexia: conceptual crossroads.

also help identify sarcopenia where it co-exists with other long-term conditions or indeed with multiple long-term conditions [24].

The consensus on the benefit of resistance exercise for the treatment of sarcopenia within the research world has yet to translate into consistent provision of resistance exercise in clinical practice, something that has proved difficult and possibly expensive for other efficient exercise programmes. This is partly because guidance on standardised approaches is lacking and there has only been relatively recent recognition of the benefits of prescribing exercise as precisely as drug treatment. For example, a recent review on the prescription and delivery of resistance exercise for sarcopenia proposed a programme that consisted of two exercise sessions per week involving a combination of upper- and lower-body exercises performed with a relatively high degree of effort for 1–3 sets of 6–12 repetitions [25].

Progress in developing effective drug treatments has been slow [26, 27] and there are no licenced drugs for sarcopenia because initially promising avenues to date have not been supported by findings from well conducted randomised controlled trials [28]. Harnessing mechanistic insights from the rapidly growing fields of ageing skeletal muscle biology [29] and epidemiology for first in man studies of potential new treatments could provide an effective way forward if efficient infrastructure to support this translational ageing research pathway can be found [30]. For example, a study demonstrating that mitochondrial oxidative capacity and NAD+ biosynthesis were reduced in human sarcopenia [31] has informed a pilot experimental ageing medicine study using a drug that enhances NHAD levels to see if there may be beneficial effects in sarcopenia. In moving from single exemplars to a standardised platform approach, there are lessons to be learnt from the established field of experimental cancer medicine.

Developing depth in the field of sarcopenia research needs to be matched by developing breadth and this is starting to happen with increasing recognition of sarcopenia internationally. Nevertheless there remain areas of the world where research to date has been very limited. A systematic review and meta-analysis of normative data on global variation in grip strength (not sarcopenia directly) from 2016 revealed a preponderance of studies from high-income regions (with particularly poor representation from the African continent [32]). This is gradually changing and new work explicitly focused on sarcopenia and other ageing syndromes led by up and coming African researchers is starting to appear [33]. Studies from low and middle-income countries need to be encouraged for addressing local needs as well as for developing a global perspective on sarcopenia.

Immediate next steps

Many articles on sarcopenia start by complaining that there is no accepted definition of sarcopenia. This is not exactly true, as the Asian definition is widely used in Asia, the SDOC definition (and the former cut-off points recommended by the Foundation of the National Institutes of Health initiative) are increasingly implemented, and the European definition is used worldwide. These definitions have allowed better understanding of the epidemiology, clinical characteristics, outcomes and management of sarcopenia and have fostered basic research on underlying mechanisms. In addition, they have attracted the interest of drug companies. However, it has become evident that global agreement is needed on the conceptual definition of sarcopenia, the operational parameters that need to be used to diagnose it in clinical practice and research, and the key outcomes that are amenable to change with interventions.

To address this problem, a Global Leadership Initiative on Sarcopenia (GLIS) has been launched to produce an inclusive definition of sarcopenia that can be widely accepted. This initiative was led by all the current consensus groups that have proposed the last wave of definitions: Australian and New Zealand Society for Sarcopenia and Frailty Research, AWGS, EWGSOP and SDOC. It has now received support of more than 15 major organisations and international societies with interest in the field and has merged a large group of experts from all continents within the GLIS steering committee and GLIS group.

The first ongoing step is to agree on a definition for the general concept of sarcopenia by defining the core elements, even if available measurement instruments are not yet accurate enough to capture them. The low reliability of most measures or estimations of muscle mass has been one of the issues most difficult to tackle by current consensus definitions. A glossary of the terms used in the field will soon be published.

Once a global conceptual definition of sarcopenia becomes available, operationalisation of the elements involved will follow, including assessments, cut-offs, algorithms and outcome measures. After the boost in research brought about by the definitions released around 2010 that emphasised the importance of muscle function, the GLIS initiative will allow for a new boost that may finally allow sarcopenia to be incorporated into routine clinical practice and improve outcomes that matter to patients.

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