Sarcopenia: epidemiology, challenges and opportunities for multidisciplinary practice

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Sarcopenia, the loss of skeletal muscle mass, strength and function with age, is widely recognised as a major clinical problem for older people that is associated with serious health consequences in terms of frailty, disability, morbidity and mortality, as well as high health care costs. Recent diagnostic algorithms have provided a systematic approach to case-finding. This article reviews the epidemiology and pathogenesis of sarcopenia and presents an overview of comprehensive geriatric assessment (CGA) as a multidisciplinary-based approach to the assessment, management and follow up for the older patient.

LEARNING OUTCOMES
TO SUPPORT PHYSIO FIRST QAP

1 Be aware of the characteristics of sarcopenia.
2 Understand how sarcopenia affects our aging population.
3 Understand the challenges and opportunities presented.

Introduction

Demographic transformations across the world dictate that survival to older age is anticipated to be the norm for all of today's younger population (Chatterji *et al* 2015). While this is a cause for celebration, these cumulative demographic changes pose significant challenges for delivering health and social care to older people.

Sarcopenia is a particularly deleterious expression of aging that impacts on individuals across a range of health and social care settings, as well as on the consequent health economy (Fuggle *et al* 2017; Janssen *et al* 2004). Sarcopenia is characterised by generalised and progressive loss of muscle mass, reduction in muscle strength and resultant functional impairment. The condition is associated with poor health outcomes from disability and morbidity, e.g. diabetes, osteoporosis and consequent frailty (Gale *et al* 2007; Sayer *et al* 2005, 2007; Ferrucci *et al* 2014; Morley *et al* 2014). It is also predictive of mortality not only in older people, but also those who are middle aged (Cooper *et al* 2010; Studenski *et al* 2011). In 2016, sarcopenia was assigned an official disease classification based on the International Classification of Disease (ICD-10). This reflects the importance of recognising and managing this condition (Cao & Morley 2016).

Skeletal muscle across the life course

Skeletal muscle comprises 40-60% of total body mass, and plays an essential role in both physical and metabolic functioning, e.g. locomotion, thermoregulation, metabolism of glucose and amino acids (Sender *et al* 2016). Muscle is also a reservoir for proteins and energy that can be utilised in periods of stress or undernutrition, such as in any acute deterioration in health and / or hospitalisation.

Muscle development in humans begins at six weeks gestation and continues until approximately 24 weeks at which point the total number of Type I and Type II fibres is set. Any subsequent increase in muscle bulk occurs by hypertrophy (Maltin *et al* 2001; Brown 2014). Muscle mass increases during childhood and adolescence, remains relatively constant in early adulthood, and then is estimated to decline at 8% per decade after the age of 40 up to 70 years, followed by a more precipitous loss of 15% per decade thereafter (Janssen 2011). Loss of strength appears to be of a higher magnitude with a reported 10-15% loss of leg strength up to 70 years, followed by a greater decline of 25-40% per decade thereafter (Goodpaster *et al* 2006; Grimby & Saltin 1983; Hughes *et al* 2001). In this regard, direct proportionality between loss of muscle mass and impaired strength / function cannot be inferred as evidence from longitudinal, as well as cross-

"EXTRINSIC AND INTRINSIC FACTORS AFFECT MUSCLE QUALITY IN AN OLDER PERSON"

sectional studies show that younger individuals can be weaker, and older individuals stronger, than would be predicted by their muscle mass alone (Kallman *et al* 1990; Newman *et al* 2006). Consequently, the health of skeletal muscle in an older person is not only a result of the peak levels they may have attained in mass during their early to mid-life years, but also the extrinsic and intrinsic changes that affect muscle quality, the force generated per unit of muscle area, i.e. patterns of physical activity, nutrition, disease, disuse and hormonal changes that may have taken place during their middle years into old age.

Defining sarcopenia

Accepted definitions of sarcopenia in research, as well as in clinical practice include loss of muscle mass, strength and physical performance, collectively referred to as function (Cruz-Jentoft *et al* 2010). Diagnostic algorithms include those proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) (Cruz-Jentoft *et al* 2010), The Foundation for the National Institutes of Health (FNIH) Sarcopenia Project (Studenski *et al* 2014), and the Asian Working Group for Sarcopenia (AWGS) (Chen *et al* 2014).

The EWGSOP definition is most commonly used within the UK and Europe (figure 1). It incorporates slower walk speed (≤0.8m/s), or weaker strength (grip <30kg for men, <20kg for women) in combination with low muscle mass (defined as appendicular lean mass normalised by the square of body height [ALM/ht^2] ≤7.23 kg/m^2 for men and ≤5.67 kg/m^2 for women). From a clinical point of view, this and other algorithms facilitate sarcopenia case-finding, and can conceptually identify stages of sarcopenia that may allow early detection and intervention. For example, and as illustrated in figure 1, the pre-sarcopenia stage is characteristic of low muscle mass without impact on muscle strength or physical performance, the sarcopenia stage is characterised by low muscle mass, plus low muscle strength or poorer physical performance while severe sarcopenia is when all three criteria within the algorithm are met (Cruz-Jentoft *et al* 2010).

MEASURING MUSCLE MASS

The most common approach in measuring muscle mass is through portable bioimpedance scanning (BIA) and, where available, dual energy x-ray absorptiometry (DXA) scanning. Computerised tomography (CT) and magnetic resonance imaging (MRI) can also be used (Cooper *et al* 2012) but high operational costs and radiation in the case of CT, limits their use. Anthropometric measures such as skin fold thickness are prone to error, especially in hospitalised older people

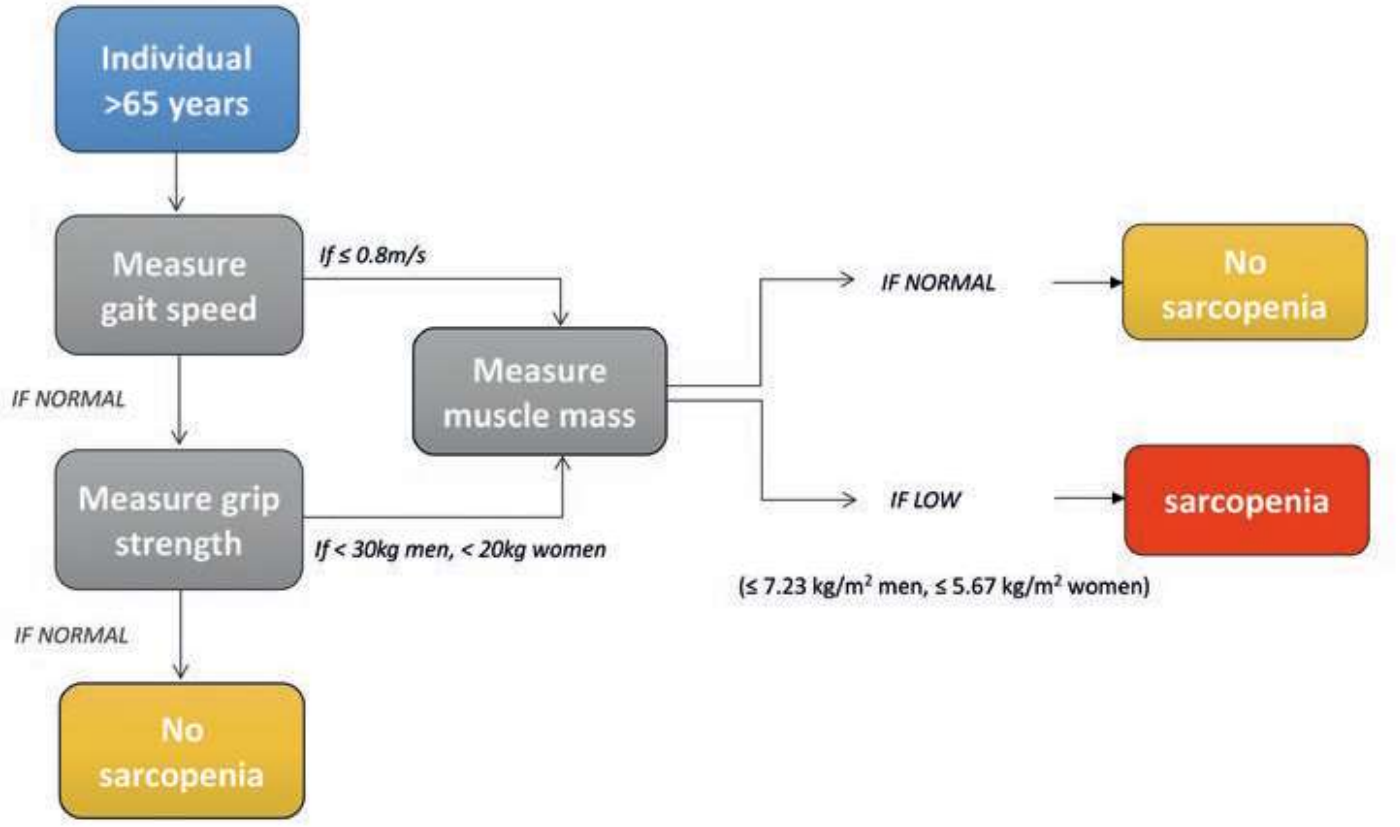

FIGURE 1: The European Working Group on Sarcopenia in Older People (EWGSOP) diagnostic algorithm for sarcopenia case finding adapted from Cruz-Jentoft *et al* (2010)

and are not suitable for assessing muscle mass in this population.

MEASURING MUSCLE STRENGTH

Hand-held dynamometry has gained wide acceptance, across healthcare settings, as a reliable and valid measure of muscle strength (Roberts *et al* 2011, 2012). Other methods include ascertainment of knee extensor power, isometric knee strength and quadriceps torque, but these require static and bulky equipment that can be impractical for use in routine practice.

MEASURING PHYSICAL PERFORMANCE

Slower gait speed is associated with risk of future morbidity and mortality and is therefore suitable for inclusion in diagnostic algorithms for sarcopenia (Vermeulen *et al* 2011). Measurement of gait speed requires intact co-ordination, and neural and joint control so may not be practical in context of acutely unwell, hospitalised older people. In this situation, grip strength measurements may have better predictive value and be more feasible (Roberts *et al* 2012; Ibrahim *et al* 2018).

Prevalence of sarcopenia

While it is clear that sarcopenia increases with age, estimates of its prevalence vary widely in different clinical settings, reflecting divergence in the approaches used for its definition, the ethnicity of the population studied, and the cut-off values for lean mass and function. In their systematic review Cruz-Jentoft *et al* (2014) reported rates of between 1% and 29% in community-dwelling populations and of 14-33% in long-term care residents. In the UK, the prevalence of sarcopenia, using the EWGSOP definition in the Hertfordshire Cohort Study was 4.6% in men and 7.9% in women, mean age of 67 years (Patel *et al* 2013).

QUESTIONNAIRES TO AID THE DIAGNOSIS OF SARCOPENIA

The SARC-F questionnaire was developed to predict poor muscle function (Malmstrom & Morley 2013; Cao *et al* 2014) and is based on five questions that ascertain how much difficulty an individual has in performing the following parameters:

- Ability to rise from a chair
- Walk assisted or unassisted
- Climb stairs
- Carry heavy loads (as a measure of strength).

It also contains an ascertainment on the number of falls a person has had over the previous 12-month period.

Each parameter is assigned a score: none (0); some (1); or a lot (2); the falls parameter score is none (0), 1-3 (1), 4 or more (2). A total score of ≥4 on a scale of 0-10 suggests that the subject is symptomatic of sarcopenia. While the SARC-F questionnaire has been shown to have excellent specificity, it has poor sensitivity for sarcopenia and so may be useful for case identification and subsequent diagnostic evaluation in a community-based setting rather than in hospital or care home based settings (Woo *et al* 2014), and therefore could be of practical value to therapists working in the community.

Despite the recent progress in refining and implementing criteria, at present no global consensus exists regarding the diagnostic criteria for sarcopenia based on cut-off values for skeletal muscle mass indices, grip strength and walking speed. However, ongoing collaborative efforts by the EWGSOP, FNIH and AWGS aim to harmonise the definition of sarcopenia for research and clinical use worldwide.

Pragmatic indicators of whether an individual is at risk of sarcopenia can be useful for the multi-discipline team (MDT), both in the hospital setting and within the community, and these can trigger a referral for more specialist assessment (Fielding *et al* 2011; Morley *et al* 2011):

- Measured gait speed < 1.0 m/s measured over a 6m course
- Post-hospitalisation as a consequence of disuse and deconditioning
- Recent weight loss
- Reduced levels of physical activity
- History of recurrent falls
- Self-reported functional difficulty, e.g. inability to get out of a bed or rise from a chair independently
- Decline in overall health
- Recent weight loss
- Presence of co-existent, comorbid conditions, e.g. Type 2 diabetes, heart failure, COPD.

> "DESPITE PROGRESS IN REFINING CRITERIA, NO GLOBAL CONSENSUS EXISTS REGARDING THE DIAGNOSTIC CRITERIA FOR SARCOPENIA"

Conditions such as malnutrition and cachexia can lead to muscle wasting and there can be considerable overlap in these entities with sarcopenia that can be difficult to disentangle, especially in hospitalised older people (Patel 2014). However, clues from the patient's history and examination can point to the predominant cause. Starvation leads to a loss on non-fat structures, as well as body fat, while cachexia is associated with severe muscle wasting as well as loss of body fat that is driven by a marked pro-inflammatory state, e.g. cancer or heart failure. Body fat in individuals with sarcopenia is often preserved or increased and while individuals with cachexia can be sarcopenic, individuals with sarcopenia are not considered cachectic (Malafarina *et al* 2012).

Pathogenesis of sarcopenia

Multiple intracellular cell signaling pathways execute environmental and cellular cues that determine myofibre size through protein synthesis or degradation. These include the insulin like growth factor -1 (IGF-I) signaling

pathways that promote protein synthesis, and pathways associated with protein catabolism that are mediated by inflammatory cytokines, e.g. tumour necrosis factor alpha (TNF) and interleukin 6 (IL-6), among others (Goodman *et al* 2011). While the acute inflammatory response can be beneficial to promote muscle repair and regeneration the persisting, chronic, low-grade production of inflammatory cytokines that appears to be present in older individuals can adversely impact on muscle mass and function and there is substantial evidence linking inflammation with sarcopenia (Beyer *et al* 2012).

Skeletal muscle aging is also characterised by a continuous cycle of denervation and reinnervation, as a consequence of the loss of alpha-motor neurones within the central nervous system (CNS). Withdrawal of nerve terminals from the neuromuscular junctions (NMJ) and axonal sprouting from neighbouring neurons collectively give rise to larger, inefficient motor units. Remodeling skeletal muscle tissue through neuropathic, neurohormonal and inflammatory pathways leads to a reduction in muscle cross sectional area, volume and a reduced rate of force generation (Hepple & Rice 2016). This is characterised by the presence of fewer Type I oxidative (slow twitch) and Type II glycolytic (fast twitch) myofibres, myofibre atrophy and concurrent increase in non-contractile material.

Challenges and opportunities for multidisciplinary practice

Sarcopenia is considered a core component of frailty, indicating loss of physiological reserve in the skeletal muscle system (Landi *et al* 2015). However, in the typical phenotype of frailty, the gradual decline in physiological reserves is accelerated and accumulates across multiple systems, including the brain, immune, endocrine, cardiorespiratory, renal and haematological systems, as well as skeletal muscle. This accelerated decline across multiple systems can lead to failure of homeostatic mechanisms which, in turn, leads to vulnerability to adverse outcomes following minor stressor events. There is strong evidence that individuals living with frailty have poorer outcomes and die sooner than expected (Clegg *et al* 2016, 2013). As weakness tends to be the first sign of frailty and given that slow walking speed and low physical activity typically precede weight loss and exhaustion, identification of sarcopenia may be an especially useful method of recognising those people at increased risk of progression in their frailty status.

INTERVENTIONS FOR INDIVIDUALS LIVING WITH SARCOPENIA

Nutrition

The synthesis of muscle fibres requires adequate protein. Physiological changes in the gastrointestinal system are associated with a blunted anabolic response to ingested proteins (Robinson *et al* 2012). As such, older people may require more protein to counteract the inflammatory and catabolic effects not only associated with the sarcopenic phenotype, but also with co-existent co-morbidities and their exacerbations (Wandrag *et al* 2015). Protein supplements vary in their composition and current evidence from trials is inconsistent to enable the development of evidence-based recommendations for protein supplementation in sarcopenia (Hickson 2015; Beaudart *et al* 2017). However, observational evidence does suggest that essential amino acids, i.e. leucine and beta-hydroxy-beta-methylbutyrate (a bioactive metabolite of leucine), stimulates muscle protein synthesis more than non-essential amino acids and may be useful for maintaining lean body mass and improving muscle function (Deutz *et al* 2013; Paddon-Jones *et al* 2004; Wu *et al* 2015; Flakoll *et al* 2004; Stout *et al* 2013). A recent consensus statement from the multinational PROT-AGE group recommend that older people have a protein intake of at least 1.2-1.5 grams per body weight (kg) per day to maintain muscle homeostasis (Bauer *et al* 2013). Low vitamin D levels are also associated with decreased muscle strength and vitamin D supplement,

> "COMBINING PHYSICAL ACTIVITY AND NUTRITIONAL INTERVENTIONS CAN BE ASSOCIATED WITH BETTER FUNCTION, STRENGTH AND REDUCED INFLAMMATION"

especially for those older individuals who are deficient, may have positive effects on muscle strength (Beaudart *et al* 2014). Ultimately, however, whole diet modifications rather than single agent supplementation may be more appropriate strategies when advising dietary changes in older people (Hickson 2015). At present there are no medicine-based treatments for sarcopenia.

Physical activity

Physical inactivity and sedentary behaviour are common among older people, and this can lead to an acceleration in muscle catabolism as well as reduced aerobic capacity. In conjunction with other personal, social and environmental factors, such as issues with access to food and social isolation, a decline in physical activity can create a spiral of further inactivity, muscle loss, weight gain, mobility problems and an increase in cardio-metabolic risk (Ford & Caspersen 2012; Ryan *et al* 2015).

Combining physical activity and nutritional interventions can be associated with better function, strength and less inflammation in older sarcopenic people (Rondanelli *et al* 2016; Churchward-Venne *et al* 2013; Naseeb & Volpe 2017). In terms of physical activity, progressive resistance and aerobic exercise have been shown to be the most beneficial for the prevention and 'treatment' of sarcopenia (Cruz-Jentoft *et al* 2014; Liu & Latham 2009; Pahor *et al* 2014; Valenzuela 2012). While progressive

resistance exercise improves lean mass, strength and function (Peterson *et al* 2011), optimising exercise capacity through aerobic activity improves metabolic control, reduces oxidative stress and insulin sensitivity, and can also stimulate a hypertrophic response on muscle fibres. Despite being shown to be safe and effective in older people (Fiatarone *et al* 1994; Liu & Latham 2009; Vincent *et al* 2002), implementing progressive exercise in clinical practice is not always readily achievable. However, recent evidence suggests even incremental elevations in habitual activity in older people may help decelerate age related declines in musculoskeletal fitness (Westbury *et al* 2018).

Falls are a serious, and sometimes fatal, complication of sarcopenia. A multicomponent approach that addresses balance and gait, flexibility and endurance, and lower limb strengthening is required to manage those susceptible to falls. These approaches are aimed at improving reaction time, gait, balance, strength co-ordination and physical and cognitive function (El-Khoury *et al* 2013; Stubbs *et al* 2015). Group- and home-based exercise programmes, which incorporate safety interventions, may reduce the rate and risk of falling (Robertson & Gillespie 2013). Moreover, targeted home-based or group-based exercise interventions can also improve mobility and functional outcomes for older people (Clegg *et al* 2012; Theou *et al* 2011).

Intervening earlier in the life course, before or at the onset of mild functional limitation, may have huge benefits for later skeletal muscle health. For example, Dodds *et al* (2013) ascertained that increased levels of leisure time physical activity in mid-life was associated with stronger grip strength in both men and women at age 60-64. This is consistent with optimising peak strength earlier on in life, thereby reducing the impact of sarcopenia. Regular physical activity in adulthood may, therefore, prevent a more precipitous decline in muscle strength in older age (Dodds *et al* 2013).

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Hospitalisation of older individuals is commonly associated with immobility and bed confinement, with a typical length of stay in hospital being between 7-10 days (Lim *et al* 2018). Studies have shown that during prolonged bed-rest there is significant reduction in muscle protein synthesis, loss of muscle mass, strength / function, and aerobic capacity (Coker *et al* 2015; Kortebein *et al* 2008). Rapid identification of these individuals and implementing interventions to maintain muscle function between periods of bed-rest should be a priority for the MDT and may provide opportunities for innovative ways of maintaining physical activity levels.

Comprehensive care planning

It is clear that the older person's care requirements are complex and that they often have co-existent functional, psychological and social needs. Ultimately, the treatment goals for an older person with sarcopenia revolve around improving physical function and maintaining independence and well-being. A useful method for planning the care of those living with sarcopenia and frailty is through a process of CGA, a multi-professional diagnostic process that involves medical, nursing, therapy, dietetics and social services, etc. It is focused on determining the psychological and functional capability of the older person in order to develop a co-ordinated, integrated and personalised care plan for treatment, and long-term follow-up (Ellis *et al* 2011). With the patient at the centre of their decision-making process, the purpose of CGA is to improve diagnostic accuracy, optimise treatment and minimise polypharmacy. Additionally, the aim is to improve outcomes and crucially, allow effective integrated case management that ensures that the care plan is enacted and remains continually responsive to the patient's needs. This involves effective communication between secondary and primary care and vice versa. The personalised care plan, both diagnostic and therapeutic, can be overseen by any member of the MDT. There is good evidence that CGA, when delivered to patients in the community and within the hospital setting, is associated with decreased mortality, and reduces the likelihood of the patient experiencing better function and cognition rather than a deterioration in health and / or being institutionalised (Ellis *et al* 2011; Stuck *et al* 2002; Cameron *et al* 2013). Equally, the CGA process can facilitate appropriate advanced care planning discussions with individuals who may be towards the end of their life.

Summary

Sarcopenia is a major health problem for older people. Clearly, early identification as well as a better understanding of mechanisms underpinning the development of sarcopenia will create a basis for clinical trials and therapeutic interventions. Physical activity and nutrition are currently the cornerstones of interventions as currently no drug is licenced for the treatment of sarcopenia.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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