https://doi.org/10.33591/sfp.51.3.u2

Unit No. 3

THE IMPORTANCE OF EXERCISE AND NUTRITION IN SARCOPENIA PREVENTION AND MANAGEMENT

A/Prof Samuel T H Chew

ABSTRACT

It has been said that sarcopenia is a condition whose time has come. Over the last two decades the importance of muscle health and how it impacts the health, functional ability, and quality of life of a rapidly ageing global population has become evidently clear. Poor muscle health defined as the presence of inadequate muscle mass and function are the hallmarks of sarcopenia. The prevalence of sarcopenia increases with age, with peak muscle mass reached in early adulthood, followed by measurable loss of both muscle mass and strength from mid-adulthood onwards. In spite of the accumulation of a large body of knowledge and significant research efforts, there is currently no licensed therapeutic agent for the prevention or treatment of sarcopenia. Regular moderate-intensity physical activity should be encouraged and adopted across all age groups as a preventative measure. Progressive resistance exercise remains the best evidence-based therapy for individuals with sarcopenia, supported by adequate nutrition. For best outcomes, an individualised targeted approach is required for both exercise and nutrition interventions. Efforts will also be required to tailor the interventions to the specific needs, capabilities, and other co-morbidities that might be present in order to make the interventions achievable, sustainable, and beneficial, particularly in older adults and those whom are frail. Despite being pervasive, sarcopenia can be prevented and reversed. However, a large gap exists between knowledge and day-to-day clinical practice.

Key words: Exercise, Management, Nutrition, Prevention, Sarcopenia

SFP2025; 51(3): 24-29

INTRODUCTION

The world population is rapidly ageing, with the number of people aged 65 and above expected to more than double from 703 million in 2019 to 1.5 billion by 2050.[1] Amongst those aged 80 and above, the numbers are expected to rise even faster, tripling to reach 426 million.[2] The percentage of older adults aged 65 and above in Singapore is also projected to rise from 12 percent to 33 percent by 2050,[1] highlighting the urgent need to identify and target reversible causes of disability such as poor muscle health. Sarcopenia is one high value target as the presence of sarcopenia is not just associated with increased risks of falls, fractures, and mortality, but also leads to increased overall healthcare utilisation and reduced quality of life.[3]

A/PROF SAMUEL T H CHEW
Associate Professor, Medicine, NUS, Duke-NUS
Senior Consultant Geriatrician
Changi General Hospital

The literature has reported that bidirectional transition from non-sarcopenic, possible/pre-sarcopenia, and sarcopenic states are possible in older adults. Individuals in the pre/possible-sarcopenic state are almost three times more likely to recover to a non-sarcopenic state than to progress to a sarcopenic state over a 3-year period of observations,[4] and are hence a high-value target group. However, assessments to identify those with sarcopenia and possible sarcopenia are still not performed routinely in clinical practice, even by physicians whom are aware of the importance and clinical significance of sarcopenia in Asia.[5] Recognising this, there have been numerous calls to action to implement evidence-based interventions that address this urgent need in Asia Pacific.[3,6-10]

Poor muscle health can be defined as inadequate muscle mass and muscle function. Muscle function can be further defined as the presence of inadequate muscle strength and physical performance.[9] The lack of muscle mass, muscle strength, and low physical performance are the hallmarks of sarcopenia and form the key components of diagnostic criteria for sarcopenia.[3]

Although previously associated only with the older and very old population, current research suggest that sarcopenia is prevalent in both the young and the old in the community based on conservative estimates (5-10 percent).[3,11] This is in keeping with the life course framework of how, after reaching peak muscle mass in early adulthood (approximately age 30),[3,12] there is measurable loss of both muscle strength and muscle mass over time from about age 40 onwards, which then accelerates further after the age of 60 (refer to **Figure 1**).[13]

There are numerous contributary factors underlying the aetiology of sarcopenia (refer to **Figure 2**).[14] However, the two chief modifiable risk factors are physical inactivity[12] and an increase in age-related anabolic resistance to the muscle protein synthesis stimulatory effect of protein in one's diet (refer to **Figure 3**).[13] It has been reported that between the ages of 18 and 80 in healthy individuals with similar physical activity levels, there is an average fat free mass loss of 8 kg. Between very sedentary and highly physically active individuals, the mean difference is about 4 kg or 50 percent of the loss over time due to the ageing process alone,[12] suggesting that adequate physical activity might potentially reduce this age-related in fat free mass. In addition to ageing, physical inactivity further compounds this anabolic resistance, which further increases the resultant net negative muscle protein turnover and muscle loss. This disuse-related atrophy from inactivity is age-independent and occurs rapidly with measurable loss of muscle mass within two days as a result of net negative protein balance.[13,15]

Figure 1 (adapted from Jung HN et al, 2023)[11]

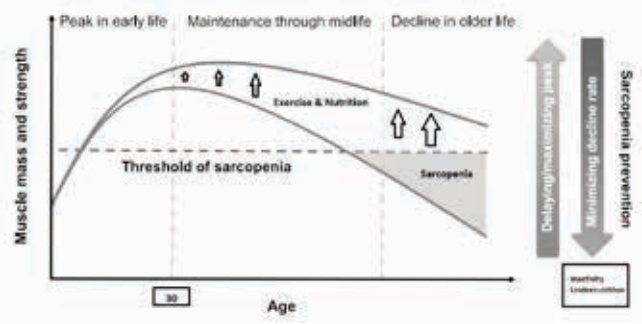


Figure 2 (adapted from Robinson S et al, 2023)[14]

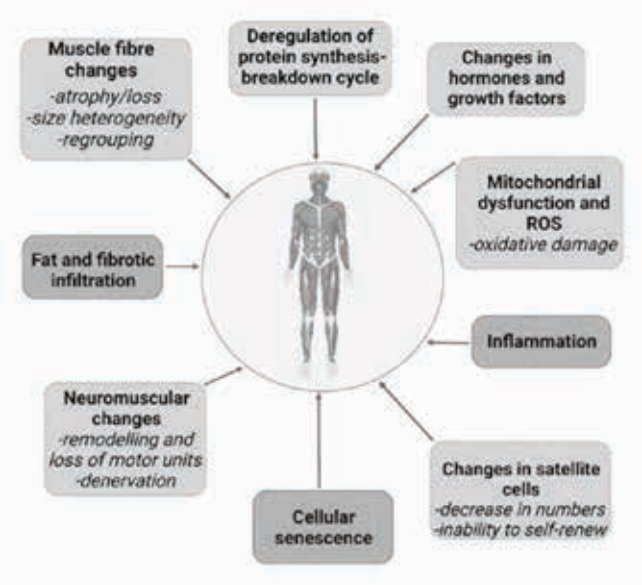
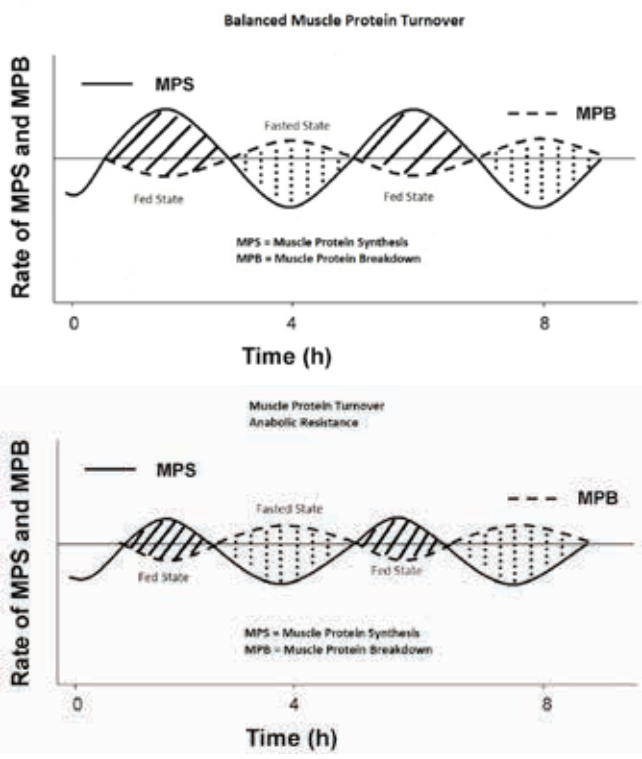


Figure 3 (adapted from Phillips SM et al, 2009)[15]



DEFINITION AND DIAGNOSTIC CRITERIA FOR SARCOPENIA

The word "sarcopenia" was first proposed by Irwin H Rosenberg in 1997 to describe the significant loss of muscle mass (poverty of flesh) observed with ageing and consequent adverse health outcomes.[16] Since then, this definition has been refined and revised by a number of working groups on sarcopenia,[3] culminating with the most recent global consensus conceptual definition by the Global Leadership Initiative in Sarcopenia in 2024.[17] In general, most diagnostic criteria include the three components of muscle mass, muscle strength, and physical performance, and localised cutoffs are required for each of the components measured to account for the known difference in the norms for body composition and physical performance in different populations.

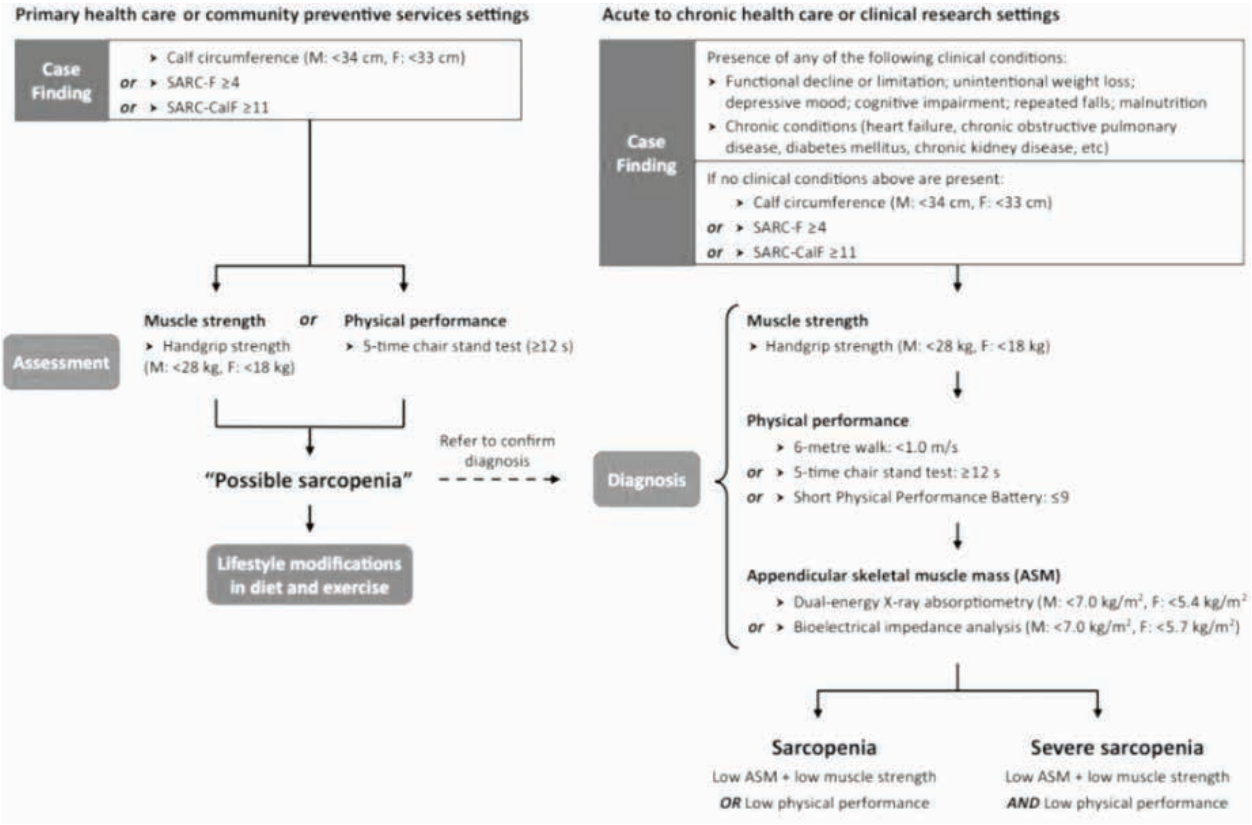
For the Asian context, the current diagnostic criteria and cutoffs are based on the Asian Working Group for Sarcopenia 2019 Consensus Update. In patients identified to be at risk of sarcopenia, muscle strength and physical performance measures such as handgrip strength and 5-chair stand test are recommended for the diagnosis of "possible sarcopenia", with further assessment of muscle mass to confirm the diagnosis of sarcopenia. The presence of all three components would fulfil the criteria for severe sarcopenia. Interventions are recommended once low physical strength or low physical performance are confirmed in the "possible sarcopenia" category in primary care or community settings (refer to **Figure 4**).[18]

AETIOLOGY OF SARCOPENIA

The main determinant of muscle health once peak muscle mass is achieved in early adulthood is a balanced net muscle protein turnover as there is no physiological reservoir for muscle protein in the human body. This process involves the stimulation of muscle protein synthesis, which is largely driven by physical activity and dietary protein, and muscle breakdown, which are mediated via a number of processes such as degradation of muscle protein via the ubiquitin-proteosome and calpain-mediated systems. Calpains and Caspases also play important roles in apoptosis of muscle cells, with Caspases further involved in degradation of the actin-myosin complex. Autophagy, another intrinsic process for muscle breakdown, plays an important role in maintaining muscle health by promoting the degradation and removal of misfolded muscle protein and dysfunctional organelles that would otherwise lead to a decline in both muscle quality and function.[19]

Other aetiologies for sarcopenia include: impaired neuromuscular integrity; reduction in number and function of muscle satellite cells, which are required for muscle regeneration; muscle mitochondrial dysfunction, which ultimately results in muscle cell apoptosis; inflammaging and cellular senescence; hormonal changes with ageing affecting testosterone; growth hormones and insulin-like growth factor-1; and activation of the classical pathway of the renin-angiotensin system.[19]

Figure 4 (adapted from Chen LK et al, 2019)[18]



On a macro level, a lack of physical activity and undernutrition are important causes of poor muscle health. Measurable loss of muscle mass occurs rapidly from either voluntary inactivity as a lifestyle choice or immobilisation as a result of illness or injury. This is due to the loss of muscle protein stimulatory effects of physical activity on muscles, and compounded by the concurrent increased anabolic resistance to protein intake in one's usual diet as a result of the physical inactivity. These adverse effects are greater in older adults and persist during period of recovery of mobilisation. Muscle mass might not return to normal levels even if mobility levels do.[13]

Adequate nutrition in the form of energy and protein is essential for muscle health. The relationship between malnutrition and sarcopenia has also been demonstrated in systematic reviews and meta-analyses of studies on the dietary intake of individuals with sarcopenia compared with those without.[14] In the early stages of severe undernutrition, energy requirements to sustain the physiological process necessary for life are derived from glycogen stores from the liver. When this energy store is depleted, energy is then obtained from body fat stores. Once this is also depleted, the only remaining source of energy muscle protein is then broken down and used to generate the energy required to sustain life, leading to severe muscle loss and wasting indistinguishable from cachexia.[20] It has been reported that in individuals with normal weight, fat free mass accounts for more than 35 percent of the total weight loss induced by intentional caloric restriction,[21] suggesting that muscle breakdown as a source of energy may occur even before the body fat store is depleted.

MANAGEMENT

Longitudinal population studies suggest that changes in grip strength over time mirrors the changes in lean body mass, peaking in early adulthood before a subsequent decline in late adulthood.[3,11] This suggests the possibility of preventative efforts in optimising peak muscle mass quantity between adolescent and early adulthood, and reducing the rate of muscle loss between mid-adulthood to late adulthood and beyond through targeted exercise and nutritional interventions.[3]

There is a lack of evidence to guide definitive preventative interventions for sarcopenia per se. However, Westerterp et al[12] reported that a highly physically active lifestyle can potentially reduce the loss of fat free mass by 50 percent over the course of a lifetime based on physical activity levels calculated using the doubly labelled water assessment method for energy expenditure. Hence, it is conceivable that adopting a lifestyle with regular moderate-intensity physical activity can help prevent or delay the onset of sarcopenia, particularly if muscle-strengthening exercise is incorporated at least twice a week. Both World Health Organisation and Singapore Health Promotion Board guidelines recommend at least 150 to 300 minutes a week,[22,23] and this should be encouraged and adopted across all individuals and age groups.

For individuals who are already sarcopenic, the aims of treatment would be to first stabilise, and then reverse, if possible, the loss of muscle strength and muscle mass.[3] In spite of extensive research efforts, there are currently no licenced therapeutic agent for the treatment of sarcopenia

either due to adverse side effects (e.g., testosterone, growth hormone, metformin), lack of efficacy (e.g., metformin, angiotensin converting enzyme inhibitors), or lack of significant improvements in muscle strength and/or physical performance in spite of improvements in muscle mass (e.g., myostatin and activin II receptor inhibitors).[3,19]

Resistance Exercise Training

Resistance exercise training remains the only evidence-based treatment for sarcopenia, supported by adequate energy and protein intake. To be effective, exercise prescription requires adequate intensity of at least 50 percent 1-repetition maximum, a frequency of at least two sessions a week with a duration of at least 12 weeks.[3,24] Increasing the intensity of the resistance exercises leads to additional improvement in muscle strength, while increasing the volume of resistance exercises leads to improvements in muscle mass,[3,24,25] highlighting the importance of the concept of progression when prescribing resistance exercise training.[26] Tailoring the frequency, intensity, and duration of resistance exercise training to each individual's abilities and needs is paramount in order to attain increases in strength, thus improving health, quality of life, functional capacity, and reducing risk of falls. Underdosing of strength training programmes does not lead to significant physiological or health benefits.[27]

The benefits of physical activity outweigh the risks, even in the presence of long-term medical conditions, as long as the activity is tailored to each individual patient's and caregiver's needs and ability, with education on what limits they should set for themselves in terms of intensity and symptoms. Prior counselling on why and how to manage the post-exercise symptoms such as delayed onset muscle soreness,[28,29] transient post-activity fatigue, and shortness of breath will go far in enabling and encouraging the individual to continue with regular physical routine for the long term.[30] The Physical Activity Readiness Questionnaire (PAR-Q)[31] is a simple tool that can be used to check if a medical review is required before embarking on an exercise programme or any moderate to high-intensity physical activity, and can be accessed via HealthHub.[32]

In very frail individuals with severe sarcopenia, the effort in standing up from a sitting position might sometimes be the equivalent intensity of 1-repetition maximum, defined as the amount of weight or resistance that can be lifted once and once only before fatigue sets in.[33] In this setting, a similar resistance exercise prescription can still be achieved by using one's own body weight as the resistance while performing a sit-to-stand exercise, focusing on improving the strength of the lower limbs. There is an inverse relationship between the intensity of the weight/resistance being moved and the number of repetitions possible with each level of intensity. As the intensity increases, the number of possible repetitions will decrease, leading to a relationship continuum between the two. By gradually increasing the number of repetitions over time, the individual can progress from one repetition per set (1-RM), to three repetitions per set (95% 1-RM), to five repetitions per set (90% 1-RM), to 10 repetitions per set (75% 1-RM), to 20 repetitions per set (60% 1-RM) over time.[34] If the individual can achieve 15 to 20 repetitions from a baseline of one repetition, this will mean that the lower limb muscle strength has improved over time as the individual is able to do more repetitions using the same body weight as the load.

Three randomised controlled trials have suggested that this simple resistance exercise for the lower limbs can increase knee extensor strength and lead to less effort required to perform this very important activity of daily living,[35-37] which can significantly reduce the burden of care and improve the quality of life for both the sarcopenic individuals and their caregivers.

Nutritional Intervention

For reasons described above, having sufficient energy and protein in the daily intake are the two most important nutritional interventions in prevention and management of sarcopenia.

For older adults aged 50 and above, the recommended energy intake per day is 1.5 times the resting energy expenditure or about 30 kcal/kg/day, and subject to requirements of physical activity. This is similar to the recommendations by the European Society of Clinical Nutrition and Metabolism of 20 to 30 kcal/kg/day for elderly patients, and 30 to 40 kcal per day for malnourished older adults.[38] These estimates can then be adjusted to achieve the targets of a stable weight and a BMI of above 20 for the Asian context as per the cutoffs recommended by the Global Leadership Initiative for Malnutrition.[39]

The PROT-AGE Study Group and the European Society of Clinical Nutrition and Metabolism Expert Group both recommend a protein intake of 1.0 to 1.2 g/kg/day for healthy older people. For older adults who are malnourished or ill, 1.2 to 1.5 g/kg/day are recommended.[13] Muscle protein turnover studies suggest that maximal effects of muscle protein synthesis occur with a dietary intake of 20-25 g of protein per meal,[15] which is in keeping with the previous daily recommended protein intake. Ingestion of a protein bolus leads to a peak in muscle protein synthesis in about 120 minutes before returning to baseline at 180 minutes even if there are still elevated serum levels of essential amino acids in circulation. This suggests that optimal anabolic effects of protein intake on muscle health may be best achieved with a protein intake of 0.4-0.6 g/kg/meal, 3-4 times a day.[13]

In terms of a conducting a rapid and simplified assessment of dietary protein and energy intake, one fish fillet or one palm-sized portion of lean chicken breast would provide approximately 20 g of protein. One large egg or one tofu square would provide approximately 6 g of protein. One cup (200 g) of cooked white rice is about 280 kcal and one slice of white bread is about 70 kcal. Five hundred millilitres of plain rice porridge is about 200 kcal. A very useful and comprehensive database on the energy and

nutrient composition of food in Singapore is available on the Singapore Health Promotion Board website.[40]

If the required protein and energy requirements cannot be met via normal dietary intake and food fortification, oral nutritional supplementation should be considered.

CONCLUSION

Sarcopenia is a prevalent and significant health burden that is preventable and reversible, especially in increasingly ageing populations. Regular moderate intensity physical activity across the life course may help prevent or delay onset and should be encouraged and adopted in all age groups. Evidence-based resistance exercise and nutritional interventions are known and available for those with sarcopenia. A progressive and treat-to-target approach are required respectively for best outcomes. However, a large gap exists between knowledge and day-to-day clinical practice. We know what to do; we just need to do it and do it right.

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LEARNING POINTS

- **The role of therapeutics is limited in the prevention and management of sarcopenia.**
- **Targeted nutrition and exercise interventions are key to muscle health.**
- **Recognition of the roles of adequate protein and energy in diet for muscle health needs to be promoted**
- **Strategies are needed to encourage and facilitate resistance exercises as part of daily life.**
- **Early intervention to maintain muscle health, diagnose sarcopenia, and slow down progression/reverse loss of muscle strength and muscle mass in individuals with sarcopenia are required.**