Unit No. 3

## ASSESSMENTS AND MULTIMODAL TARGETED INTERVENTIONS FOR MUSCLE HEALTH IN OLDER PERSONS

Adj Assoc Prof Samuel TH Chew

#### ABSTRACT

The populations in Singapore and worldwide are ageing rapidly and pose many challenges to patients, medical professionals and the healthcare system. Recent population-based research in communitydwelling older adults in Singapore suggests that after the age of 80, impaired physical ability and cognition are two major contributors to loss of independent living. Hence, there is an urgent need to raise awareness of the importance of muscle health in older adults as one of the modifiable factors to reduce and prevent disability in later life. Good muscle health is essential to facilitate independent living for as long as possible. The SARC-F questionnaire is an ideal screening tool in the community setting for sarcopenia in older adults. For screening of low muscle mass, calf-circumference can be used in the community as a surrogate measure. Bio-electrical Impedance Analysis (BIA) and Dual-Energy X-ray Absorptiometry (DEXA) can be used to assess appendicular skeletal muscle mass index (ASMI) in the community and hospital setting, respectively. Low ASMI with low muscle strength leads to the diagnosis of sarcopenia. Severe sarcopenia is diagnosed when all three of low muscle mass, low muscle strength and low physical performance are present. Muscle health is intimately linked with nutritional health and physical activity. The risk of malnutrition in older adults can be rapidly screened using Malnutrition Universal Screening Tool (MUST) in both inpatient and outpatient settings. For best outcomes, a combined multidisciplinary approach using targeted progressive resistance exercise training (RET) and provision of adequate protein, energy and replacement of any underlying Vitamin D deficiency is required. Efforts are urgently required to raise awareness and knowledge on the importance of muscle health, and its impact on function and clinical outcomes in older people.

Keywords: Muscle health, older adult, multidisciplinary, exercise, nutrition

SFP2021; 47(6): 19-28

## INTRODUCTION

Populations across the world continue to age at a rapid pace. In 2020, 15.2 percent of the Singapore population or about one in six was >65.<sup>1</sup> This is projected to increase to about

ADJ ASSOC PROF SAMUEL TH CHEW Senior Consultant Geriatrician Department of Geriatric Medicine Changi General Hospital one in four by 2030.<sup>2</sup> Similarly, in Asia, the population of people >65 is expected to more than double from about 409 million in 2017 to close to 996 million 2050.<sup>3</sup> This is worrying as the recent SIGN population study in Singapore suggest that one in two community-dwelling older adults will face difficulties in performing at least one instrumental activities of daily living which are required for independent living. The two common factors identified leading to these disabilities are loss of physical strength and cognition.<sup>4</sup> This ability to live independently has been defined by World Health Organisation (WHO) as functional ability. The pre-requisite for this defined as intrinsic capacity, which encompasses all the physical and mental reserves that the individual has to draw on.<sup>5</sup> There is a strong correlation between physical strength and muscle mass. It has been recognised that there is a progressive loss of muscle mass over time, especially after the fourth decade of life of about eight percent per decade. This then increases to about 15 percent per decade after the age of 70. This loss of muscle mass is then translated into the loss of muscle health and poor clinical outcomes.5-7

#### DEFINITION

Muscle health can be divided into two distinct components, namely muscle mass and muscle function. Muscle function in itself has another two components, muscle strength and physical performance. Low muscle strength or low physical performance in the presence of low muscle mass will fulfil the criteria for diagnosis of sarcopenia. In severe sarcopenia, all three features of low muscle strength, low muscle mass and low physical performance will be present.<sup>8-10</sup>

## EPIDEMIOLOGY

In terms of prevalence, sarcopenia was reported in about ten percent of the world's community-dwelling older adults11, 33 percent of older adults with frailty in long-term care institutions<sup>12</sup>, and ranges from 22 percent to 26 percent for inpatient older adults.<sup>13</sup> These numbers are reflected in a study of older adults in outpatient clinics in Singapore, which found that up to 44 percent were at risk for sarcopenia when screened with the SARC-F questionnaire.14 Two other local studies found the prevalence for sarcopenia of 25 percent in community-dwelling and functionally independent adults age >5015, and 27.4 percent in older adults with type-2 diabetes in a primary care setting.<sup>16</sup> In patients with type-2 diabetes, the presence of diabetic nephropathy increases the likelihood of developing sarcopenia by 2.5 times.<sup>16</sup> Lu et al similarly reported a prevalence of 46 percent for sarcopenia in a cross-sectional study of community-based Chinese subjects aged 65-90 in the Singapore Longitudinal Ageing Study Wave-2 (SLAS-2), and found a significant association

between sarcopenia and malnutrition. In this study, subjects at risk of malnutrition were almost 10-fold more likely to be sarcopenic compared with subjects with normal nutrition.<sup>17</sup>

This relationship between sarcopenia and nutrition was found again in the Strengthening Health In ELDerly through nutrition (SHIELD) study. The prevalence for low appendicular skeletal muscle mass index (ASMI) was 20.6 percent and 81.2 percent respectively in communitydwelling older adults in Singapore age >65 with normal nutrition versus those at risk of malnutrition. The risk of malnutrition was determined using the Malnutrition Universal Screening Tool (MUST). In nourished subjects, females had significantly lower ASMI than male subjects, and every ten years of age were correlated with 3.4 higher odds of having low ASMI.<sup>18</sup> In the cohort at risk of malnutrition, 70 percent also fulfilled the criteria for sarcopenia based on the Asian Working Group for Sarcopenia (AWGS).<sup>19</sup> These studies highlight the high prevalence of sarcopenia in seemingly well community-dwelling older adults, and strong correlations with age, diabetic nephropathy and those at risk of malnutrition.

## **CURRENT CHALLENGES**

In contrast, the screening and assessment for muscle health in general is still not a common practice and its' importance under-appreciated.<sup>20,21</sup> In an online international survey conducted by Bruyère O et al. of 255 physicians in 55 countries across five continents, only about half assessed at least one parameter of muscle health in older patients in their practices.<sup>22</sup> Although there are established guidelines on screening and assessment, there is still a need for integrated and targeted guidance on managing poor muscle health in older adults.<sup>8,9,23</sup> Fast and easy to apply physical and performance measures are also required.<sup>21</sup> There is also a great need to address the common misconception amongst the older patients themselves, the wider community and health care professionals that poor muscle and nutritional health is inevitable as one ages.<sup>5,24</sup> A population-based approach will be required to disseminate the current state of knowledge on the importance of muscle health, and how to achieve it for both practitioners and patients alike.<sup>25,26</sup>

## RECOMMENDATIONS

Muscle health plays a key role in determining functional and clinical outcomes for older adults in the community and hospital.<sup>27,28</sup> These include loss of physical function, loss of ability to live independently, increased risk for falls<sup>29-33</sup> and predicts mortality in the presence of sarcopenia.<sup>34-36</sup> Poor muscle health also increases the risk for nursing home placement, frequency and length of stay in hospitals, readmissions, polypharmacy<sup>37-40</sup> and health care costs.<sup>41-43</sup> Patient groups that would benefit from early screening are older adults with malnutrition, frailty, cognitive impairment, chronic illness, and recurrent falls<sup>44</sup>. A threeyear prospective study of older patients ( $\geq$ 60 years) admitted to acute geriatrics wards in China found that patients with or at-risk malnutrition and sarcopenia had a more than four four-fold likelihood of death compared with the group with normal nutrition and without sarcopenia. In comparison, non-sarcopenic patients at risk of malnutrition were found to have a more than two-fold likelihood of death, suggesting that the addition of sarcopenia to the risk of malnutrition in hospitalised older patients doubles the risks of death over three years for all-cause mortality.<sup>45</sup> Hence the presence of either sarcopenia or malnutrition in the older adult should trigger screening for one or the other.

MUST is a validated, reliable, fast, and easy to use screening tool for both inpatients and outpatients, with an integrated care plan based on the assessment outcome.<sup>46</sup> The use of MUST in the SHIELD study identified community-dwelling older adults at risk of malnutrition who were demonstrated to have a four-fold greater risk of having ASMI compared to those who were not at risk of malnutrition. In addition, 70 percent of the 811 older adults identified to be at risk of malnutrition was also sarcopenic<sup>19</sup>, based on AWGS 2014 cut-offs for ASMI using bio-electrical impedance analysis (BIA), handgrip strength (HGS) and gait speed, showing the utility of using MUST to rapidly identify older adults at risk of both malnutrition and sarcopenia.

The following are evidence-based recommendations on assessment and multimodal targeted interventions for muscle health in older adults.

#### Screening for sarcopenia

Lexell et al. report that loss of muscle mass as part of increasing age appears to start as early as 25 years of age.<sup>47</sup> After the fourth decade of life, there is a measurable loss of lean body mass (LBM) of about eight percent per decade. This accelerates to about 15 percent per decade after 70 years of age, potentially leading to loss of at least 30 percent of lean body mass at age 80.<sup>67,47,48</sup>

The International Clinical Guidelines for Sarcopenia recommends screening for sarcopenia in older adults >65 annually and after major health events<sup>23</sup>, as acute illness and prolonged immobilisation may lead to significant loss of muscle strength, muscle function and muscle mass.<sup>13,49</sup>

The SARC-F questionnaire is a validated rapid screening test for sarcopenia, with a cut-off of  $\geq$ 4 predictive of sarcopenia.<sup>50</sup> It is highly specific, reliable, and valid in Asian populations in both inpatient and outpatient settings.<sup>51-55</sup>

Both handgrip strength and 5-times chair stand test (5CST) can be used to assess muscle strength.<sup>9,44</sup> The AWGS Consensus Update 2019 cut-off values low HGS for males and females are <29kg and <18kg respectively.<sup>44</sup> For the 5CST, a cut-off of  $\geq$ 10s based on receiver operating characteristic (ROC) curve analysis predicts future disability in a large prospective cohort study of community-dwelling older people in Japan, and can be used as a surrogate measure for lower limb strength.<sup>56</sup>

The AWGS 2019 proposed a cut-off of 1.0 m/s in the 6-m walk test for gait speed as a marker for low physical performance in older adults in Asia.<sup>44</sup> Based on the work of Nishimura et al., this cut-off correlates with a cut-off of  $\geq$ 12s for the 5CST which can be easily and rapidly performed in the clinical and community setting.<sup>57</sup>

The AWGS 2019 and the European Working Group on Sarcopenia in Older People 2 (EWGSOP2)<sup>9,44</sup> guidelines both suggest that patients with a SARC-F score of  $\geq$ 4 and have low muscle strength would fulfil the criteria for possible/probable sarcopenia. In addition, the AWGS 2019 recommendations suggest that low physical performance can be interchangeable for low muscle strength for the diagnosis of possible/probable sarcopenia in the presence of low muscle strength.<sup>44</sup> This provides sufficient clinical grounds to initiate interventions in terms of nutrition and physical activity, and to trigger referral for further confirmatory assessment and diagnosis for sarcopenia.<sup>9,44</sup>

### **Diagnosis of sarcopenia**

A recommended approach to diagnosing sarcopenia can be summarised by the acronym FACS<sup>9</sup> (Find-Assess-Confirm-Severity). **Find** represents case-finding using the SARC-F tool or clinical features of sarcopenia such as recurrent falls, slow walking speed, and difficulty getting up from the chair. Assess refers to screening for muscle strength or physical performance as detailed above. Once the patient has a possible/probable diagnosis of sarcopenia, this diagnosis can then be Confirm-ed by measuring the appendicular skeletal muscle mass (ASM). This can be performed using bio-electrical impedance analysis (BIA) or whole-body dualenergy X-ray absorptiometry (DEXA). The former is more suited for use in the community and outpatient setting, with cut-offs <7.0 kg/m<sup>2</sup> in men and <5.4 kg/m<sup>2</sup> in women for the Asian population.<sup>44</sup> The latter is considered the gold standard for the clinical assessment of ASM<sup>58</sup>, performed in the hospital setting with cut-offs of  $<7.0 \text{ kg/m}^2$  for men and <5.7 kg/m<sup>2</sup> for women in Asia.<sup>44</sup> In terms of Severity, the diagnosis of severe sarcopenia requires the presence of all three factors low muscle mass, low muscle strength and low physical performance.9,44 The AWGS 2019 guidelines recommend the use of gait speed for 6-m walk test or Short Physical Performance Battery (SPPB) test as the measures of choice. The cut-off for the former is <1.0 m/s and for the latter is  $\leq 9.44$  As mentioned above, the 5CST can be used as a surrogate marker for gait speed with a cut-off of  $\geq 12s$ corresponding to the gait speed of 1.0 m/s.44,59

A summary of the recommended assessments and cut-offs can be found in table 1.

Parameter	Assessment	Recommended cut-off value for low muscle parameters	Reference
Physical activity related to muscle	SARC-F questionnaire	Score of ≥4 out of 10, indicative of sarcopenia	Malmstrom <i>et al.</i> , 2016 <sup>58</sup> ; AWGS 2019 <sup>2</sup>
Muscle strength	Handgrip strength	<b>Men</b> : <28 kg	AWGS 2019 <sup>27</sup>
		<b>Women</b> : <18 kg	
	5-times CST test (surrogate measure)	≥10s for 5 rises	Makizako <i>et al.</i> , 2017 <sup>61</sup>
Muscle mass	BIA (ASMI)	<b>Men</b> : <7.0 kg/m <sup>2</sup>	AWGS 2019 <sup>27</sup>
		<b>Women</b> : <5.7 kg/m <sup>2</sup>	
	DXA (ASMI)	<b>Men</b> : <7.0 kg/m <sup>2</sup>	AWGS 2019 <sup>27</sup>
		<b>Women</b> : <5.4 kg/m <sup>2</sup>	
	Calf circumference	<b>Men</b> : <34 cm	AWGS 2019 <sup>27</sup>
	(surrogate measure)	<b>Women</b> : <33 cm	
Physical performance	Usual gait speed	<1.0 m/s	AWGS 2019 <sup>27</sup>
	5-times CST test (surrogate measure)	≥12s as a proxy for low gait speed (<1.0m/s)	AWGS 2019 <sup>27</sup>

Table I. Assessments of muscle health with cut-off values for the Singapore population.

**Abbreviations:** ASMI: Appendicular skeletal mass index (ASM adjusted for height); AWGS: Asian Working Group for Sarcopenia; BIA: Bioimpedance analysis; DXA: Dual-energy X-ray absorptiometry; CST: Chair Stand Test.

#### **Targeted Interventions**

#### Resistance Exercise Training (RET)

Contrary to common misconceptions, older adults benefit from physical activity. The more in terms of frequency, duration and/or volume the better, as per WHO 2020 guidelines on physical activity.<sup>24</sup> In particular, progressive RET is recommended as the first-line intervention for older adults with sarcopenia by the International Clinical Practice Guidelines for Sarcopenia (ICFSR)<sup>23</sup>, and is recommended by the American College of Sports Medicine to increase strength and power in older adults.<sup>60</sup> Research suggests that RET programs of  $\geq$ three months duration with at least two sessions a week can lead to improvements of not only strength but also gait speed and muscle mass.<sup>12,61,62-64</sup>

1-repetition maximum (1-RM) is the gold standard used for the assessment of muscle strength in non-laboratory settings.65 1-RM is defined as the ability to lift or perform a movement one time and one time only, before muscle fatigue prevents lifting of the load or performing movement through a full range of motion.<sup>66</sup> The minimum muscle stimulus recommended in order to improve strength and function in untrained older adults is 60 percent of 1-RM, and this starting point intensity is recommended by the American Academy of Sports Medicine, the American geriatrics Society and the American Physiotherapy Association.<sup>66</sup> The literature on the dose-response relationship between RET and muscle health, including one recent systematic umbrella review by Beckwee et al 201967, further suggests that an increase in either RET volume (defined as total repetitions x weight used) or RET intensity (defined as a percentage of 1-RM), correlates with a potential increase of up to 0.5 kg of lean body mass with every additional ten sets of exercise performed per session, and about a 5.5 percent increase in strength for each higher intensity level achieved. Low intensity is defined as <60 percent 1-RM, low/moderate intensity as 60-69 percent of 1-RM, moderate/high intensity as 70-79 percent 1-RM and high intensity as >80 percent 1-RM respectively.<sup>62,63,67,68</sup>

In addition to strength training, task-specific functional and balance training are also important in preventing functional decline and falls<sup>69</sup>, and supported by WHO guidelines on integrated care for older people in the community and physical activity.<sup>5,24</sup> Task specific exercises may be even more important in older patients with limited functional reserves, frailty or lack of enthusiasm for formal exercise programs., Not only does it improve strength, but it may also achieve more functional gains than focusing on strength alone for these specific sub-groups.<sup>66</sup> A patient-oriented comprehensive guide on the basics for strength and power training for older adults, how to do it safely, including instructions and illustrations of recommended exercises, is available from Harvard Medical School publications.<sup>70</sup>

#### **Nutritional Interventions**

#### Energy

In general, older adults require on average 30 kcal/kg body weight/day to meet the total energy expenditure (TEE) needs. In underweight and malnourished older adults, up to 45 kcal/kg body weight/day may be required. This takes into account the resting energy requirements (REE) which makes up about 70 percent of the TEE, and is related to the amount of fat-free body mass and gender. REE is higher in men, and in older adults with low body mass index (BMI) and malnutrition.<sup>71</sup> Physical activity levels may add another 20-30 percent to the TEE and about another ten percent of TEE is required for thermogenesis. Under normal physiological conditions with sufficient diet and fat stores, the energy requirements are met by metabolism of carbohydrates (55-60 percent), fats (25-30 percent) and protein (5-10 percent).<sup>72</sup> In patients with protein energy malnutrition with no fat stores, breakdown of muscles into amino acids, which are then converted to glucose via gluconeogenesis to sustain vital functions occurs.<sup>72</sup> This highlights the importance of meeting energy requirements, particularly in vulnerable older adults with/at risk of malnutrition in order to optimise muscle health. Adequate energy intake is required to maintain a neutral nitrogen balance even in the absence of malnutrition or disease states.

## Protein

In older adults, there is a higher requirement in terms of daily protein requirements of 0.8-1.2 g/kg body weight per day in order to maintain good muscle health.<sup>73</sup> This is due to the presence of *anabolic resistance*, where a higher amount of dietary protein is required in order to stimulate the same level of muscle protein synthesis compared to a young adult. The per-meal protein requirement to optimally stimulate muscle protein synthesis is about 0.4 g/kg body weight per day, or about 24g of protein for a 60 kg individual.74 Patients with malnutrition, chronic illness or taking part in resistance exercise training/leading an active lifestyle may require 1.2 to 1.5 g/kg body weight per day. In the setting of severe illness or injury or severe malnutrition, up to 2.0g/kg body weight/day may be required.<sup>73</sup> For older patients with chronic kidney disease (CKD) stage 4 and 5 not on dialysis, the recommendations are for up to 0.8 g/kg body weight per day when well. This may increase to 0.8 to 1.0 g/kg body weight per day in the setting of acute illness or injury.73,75 The challenge for these CKD patients not on dialysis is in avoiding excess dietary protein to optimise renal health and taking enough protein to avoid malnutrition.75,76

When food intake alone, after dietary counselling and food fortification, are unable to meet the targeted requirements for energy and protein as detailed above, oral nutritional supplements (ONS) are recommended in older adults with or at risk of malnutrition based on WHO 2017<sup>15</sup> and European Society for Clinical Nutrition and Metabolism (ESPEN) Guidelines 2018.<sup>71</sup> Recent findings from large multicentre randomised placebo-controlled double-blind clinical trials suggest that the use of ONS with  $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) in older adults can improve leg and handgrip strength in community-dwelling at risk of malnutrition cohort<sup>77</sup>, and handgrip strength in hospital inpatient and post-discharge cohort with malnutrition.<sup>78</sup> It would follow from the discussions above that assessment of the daily protein and energy intake is an important part of the decision-making process in determining the level of nutritional intervention required. Healthcare professionals (HCP) in Singapore can make use of the online tool from Health Promotion Board (HPB), which includes a database of local food items<sup>79</sup> to do this.

A quick reference list of the estimated protein content of common food items based on this tool is provided in table 2. Table 3 shows a summary of commonly available ONS and protein content per one bottle of serving.

# Table 2. Estimated Protein Content Common FoodItem HPB

Food Item	Amount (grams)	Protein Content (grams)
Fish Fillet	100g	20g
Lean Chicken Breast	100g	22g
Egg	100g (2 large egg)	12g
Tofu	100g	8g
Peanut	100g (dry roasted)	25g
Cooked White Rice	100g (1/2 rice bowl)	3g
Plain Rice Porridge	100g	1.2g
Soyabean Milk	100g (1/2 cup)	4.2g
Whole Milk	100g (1/2 cup)	3.2g
Natural Yoghurt	100g	5g
Cheddar Cheese	100g (6 slices)	26g

# Table 3. Average Protein Content in OralNutritional Supplements

Oral Nutrition Supplement (ONS) Type	Serving Size 1 Bottle (average)	Protein Content (grams)
Standard ONS	250 mls	8 to 9 g
High Protein ONS	250 mls	16 to 20 g
Compact ONS	118 mls	9 g

## Leucine and HMB

Leucine is a branched-chain amino acid that has been shown to be a potent muscle protein synthesis stimulator in-vitro.<sup>80</sup> Meta-analysis of clinical trials shows that leucine supplementation can significantly improve lean muscle mass, but not muscle strength in older adults with sarcopenia<sup>81,82</sup>, particularly when co-supplemented with Vitamin D.<sup>82</sup> Of note, the benefits from leucine supplementation does not seem to extend to healthy well-nourished older adults.<sup>83,84</sup>

HMB is the active metabolite of leucine and is produced in small amounts in the body. About 5-10 percent of leucine is metabolised to produce 0.2 to 0.4 g of HMB per day in an adult. HMB stimulate muscle protein synthesis via activation of the mechanistic mammalian target of rapamycin (mTOR), and inhibits muscle breakdown by inhibiting the ubiquitin proteosome and capsaicin pathways. It also plays a part in the repair of muscle damage and is required for optimal muscle mitochondrial function.<sup>85</sup> A systematic review in 2019 of three randomised controlled clinical trials suggests that the use of up to 3g of HMB in older adults ( $\geq$ 60 years) with sarcopenia or frailty, led to significant improvements in lean muscle mass, and prevented further loss of muscle strength and function compared to the control group.<sup>86</sup>

## <u>Vitamin D</u>

Two recent studies in community-dwelling older adults in Singapore with normal nutrition as well as those at risk of malnutrition found prevalence for Vitamin D deficiency (<20  $\mu$ g/L)<sup>87,88</sup> of 13.5 percent and 18 percent respectively.<sup>18,77</sup> The prevalence for Vitamin D insufficiency (20-30  $\mu$ g/L)<sup>87,88</sup> were even higher at 38.5 percent and 41 percent respectively.<sup>18,77</sup> These findings are important as treatment of Vitamin D deficiency may be beneficial in the context of sarcopenia.

In a post-hoc analysis of a randomised controlled doubleblind clinical trial involving older adults with sarcopenia, lower serum Vitamin D levels at baseline was associated with lower muscle mass, strength and function than subjects with a serum Vitamin D level of >20  $\mu$ g/L<sup>89</sup>, In addition, even after adjusting for other factors, patients with serum Vitamin D levels of >20  $\mu$ g/L at baseline had higher gains in ASM in the nutritional intervention arm, suggesting adequate Vitamin D levels may be required in patients with sarcopenia to respond to nutritional interventions.<sup>89</sup> In a large systematic review of randomised clinical trials involving over 5615 children and adults, Vitamin D supplementation showed a small but significant effect on muscle strength. This beneficial effect muscle strength was found to be significant in individuals who had a serum Vitamin D level of <12 µg/L (<30 nmol/L or <12 ng/mL), and in adults  $\geq$ 65-years of age.<sup>90</sup>

Dzik and Kaczor reported in a recent literature review how Vitamin D deficiency can contribute to a reduction in muscle protein synthesis (via the mechanistic target of rapamycin pathway), and increase muscular atrophy (via the ubiquitin-proteasome pathway) and lead to mitochondrial dysfunction (via increase oxidative stress and reduction of mitochondria metabolism). Impaired mitochondrial function has been associated with symptoms of myopathy and fatigue. This has been shown to be reversible in adult patients with severe Vitamin D deficiency with a mean value <11  $\mu$ g /L by replacement of the deficiency to a mean serum Vitamin D value > 40  $\mu$ g/L, with direct correlations between clinical improvements and laboratory measures of improved mitochondrial function.<sup>91</sup> Vitamin D deficiency can also contribute to muscle weakness via impairment of calcium ion reuptake into sarcoplasmic reticulum, leading to prolonging the relaxation phase of muscle contraction.<sup>92</sup>

Although routine screening for Vitamin D deficiency is not recommended due to lack of availability of the assay in some settings and non-reimbursement of the high costs of testing, it should be performed in patients at risk of Vitamin D deficiency.93 In terms of management of Vitamin D deficiency, the Institute of Medicine recommends 600-800 IU of Vitamin D2 per day to maintain a target serum level of 20  $\mu g/L.^{94}$  Another recommendation by the Endocrine Society is for supplementation of 1000-2000 IU per day of Vitamin D2 to aim for a target serum level of 30-40 µg/L where maximum benefits of supplementation are expected.93 Rapid replacement can be achieved by using 50,000 IU of oral cholecalciferol weekly for eight weeks until the serum level is above 30  $\mu$ g/L, and then changing to a daily maintenance dose of 1000-2000 IU of cholecalciferol per day.88

#### **Integrated RET and Nutritional Interventions**

One of the earliest randomised placebo-controlled clinical trial examining the benefits of combining high intensity (80 percent 1-RM) RET (knee and hip extensor muscles) with nutrition (oral nutritional supplement, 360 kcal, 15g protein) was in nursing home residents (n=100, mean age 87 years old) performed by Fiatarone et al. in 1994 as part of the Frailty and Injuries: Cooperative Studies of Intervention Techniques (FISCIT) study. The study found significant improvements in muscle strength, muscle cross-sectional area and physical activity in the RET plus nutrition group, compared with RET alone, nutrition alone or control group.95 A more recent randomised controlled trial of independent community-dwelling older adults with sarcopenia or low muscle strength in Japan comparing RET plus nutrition (protein plus Vitamin D), RET alone, nutrition alone (protein plus Vitamin D) and control found significantly greater improvements in knee extension strength in the combined intervention group.96

A meta-analysis by Liao et al. 2017 suggests that protein supplementation with RET has a stronger effect in preventing ageing related loss of muscle mass and leg strength in older people compared with protein supplementation alone.<sup>97</sup> Antoniak et al. 2017 found similar significant improvements in lower limb muscle strength when Vitamin D supplementation was added to RET in older adults compared to RET alone.<sup>98</sup> This combination strategy of using RET and nutrition (adequate energy and protein) is recommended by both the ICFSR 2018 and ESPEN 2019 guidelines on clinical nutrition in geriatric patients as an effective treatment for sarcopenia and to improve muscle health in older adults at risk of or with malnutrition.<sup>23,71</sup>

# Multidisciplinary Approach, Patient and Family Education

A multidisciplinary team approach has been recommended in order to facilitate the development of individualised patient-centred care combined with treatment plans.<sup>23</sup> As detailed above, the optimisation of muscle health often requires assessment and targeted intervention in multiple domains (i.e., resistance exercise training, protein energy requirements, supplementation of significant Vitamin D deficiency, management of pre-existing morbidities), which can be best achieved in a multidisciplinary model of care.<sup>99,100</sup> In addition, it is important to educate patients and carers how RET and adequate protein can help improve muscle health, and that there are no prescription medications required.<sup>23</sup> For patients and families concerned with using weights for the first time, they can be further reassured that the use of light weights at higher velocity can also be beneficial<sup>101</sup>, and that muscle strengthening exercises are recommended by WHO for older adults. Pre-emptive counselling on delayed onset muscle soreness and how to manage is also important in sustaining long-term adherence to RET.66 Last but least, it would also be important for patients and families to know that sarcopenia is a medical diagnosis<sup>23</sup>, with specific investigations available for assessment and monitoring of progress over time is possible.

## SUMMARY

Muscle health is important for health and functional independence in the older adult. Loss of muscle strength, poor physical performance, and low lean muscle mass lead to a diagnosis of sarcopenia. Malnutrition and sarcopenia are intimately linked, and the presence of one should trigger the screening for the other. MUST can be used to identify community-dwelling older adults at risk of malnutrition in this context. This is important because the presence of both malnutrition and sarcopenia leads to a more than 4-fold increased risk of death in older adults discharged from hospital. A protein-focused dietary framework for muscle health to delay the onset of sarcopenia and attenuate its' adverse effect on function is important. Consumption of an adequate amount of protein at all three meals of the day, in combination with adequate provision of energy and progressive resistance exercise training is essential. The addition of Vitamin D and HMB supplementation in selected patients can further improve outcomes for lean muscle mass and muscle strength in older patients with sarcopenia, frailty and Vitamin D deficiency. Due to the

multidomain nature of muscle health, we recommend a multidisciplinary approach for the best outcomes. Raising awareness and education of patients, carers and healthcare practitioners is key.

### LIST OF ABBREVIATIONS

1-RM: 1-repetition maximum; 5CST: 5-times chair stand test; ASM: appendicular skeletal muscle mass; ASMI: appendicular skeletal muscle index; AWGS: Asian Working Group for Sarcopenia; BIA: bioimpedance analysis; CKD: chronic kidney disease; DEXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; FISCIT: Frailty and Injuries: Cooperative Studies of Intervention Techniques; HGS: handgrip strength; HCP: healthcare professional; HMB: β-hydroxy β-methylbutyrate; HPB: Health Promotion Board; ICFSR: International Clinical Practice Guidelines for Sarcopenia; LBM: lean body mass; MDT: multidisciplinary team; mTOR: mechanistic mammalian target of rapamycin; ONS: oral nutritional supplements; REE: resting energy requirements; RET: resistance exercise training; RM: repetition maximum; ROC: receiver operating characteristic; SPPB: Short Physical Performance Battery; TEE: total energy expenditure; WHO: World Health Organisation.

## REFERENCES

- Department of Statistics Singapore. Elderly, Youth and Gender Profile [Internet]. Singapore: Department of Statistics Singapore [cited 25 Apr 2021]. Available from: https://www.singstat.gov.sg/ find-data/search-by-theme/population/elderly-youth-and-genderprofile/latest-data
- 2. National Population and Talent Division. Population Trends: Overview [Internet]. Singapore: Strategy Group in the Prime Minister's Office [cited 25 Apr 2021].Available from: https://www. population.gov.sg/our-population/population-trends/overview
- Department of Economic and Social Affairs. World Population Ageing 2019: Highlights [Internet]. United Nations: Department of Economic and Social Affairs [updated 2019; cited 25 Apr 2021]. Available from: https://www.un.org/en/development/desa/ population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf
- 4. Chan A, Malhotra R, Manap NB, et al. Transitions in Health, Employment, Social Engagement And Intergenerational Transfers In Singapore Study (THE SIGNS Study) – I: Descriptive Statistics and Analysis of Key Aspects of Successful Ageing. 2018 [Internet]. Singapore: Centre for Ageing Research and Education, Duke-NUS Medical School [cited 29 Apr 2021]. Available from: https://www. duke-nus.edu.sg/docs/librariesprovider3/research-policy-briefdocs/the-signs-study---i-report.pdf
- World Health Organization. Integrated care for older people: guidelines on community-level interventions to manage declines in intrinsic capacity [Internet]. Geneva:World Health Organization [updated 2017; cited 20 Apr 2021]. Available from: https://apps. who.int/iris/handle/10665/258981
- Grimby G, Saltin B. The ageing muscle. Clin Physiol. 1983 Jun;3(3):209-18. doi: 10.1111/j.1475-097x.1983.tb00704.x. PMID: 6347501.
- Vandewoude MF, Alish CJ, Sauer AC, Hegazi RA. Malnutritionsarcopenia syndrome: is this the future of nutrition screening and assessment for older adults? J Aging Res. 2012;2012:651570. doi: 10.1155/2012/651570. Epub 2012 Sep 13. PMID: 23024863;

PMCID: PMC3449123.

- Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014 Feb;15(2):95-101. doi: 10.1016/j.jamda.2013.11.025. PMID: 24461239.
- Cruz-Jentoft AJ, Bahat G, Bauer J, et al; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16-31. doi: 10.1093/ageing/afy169. Erratum in: Age Ageing. 2019 Jul 1;48(4):601. PMID: 30312372; PMCID: PMC6322506.
- Arai H, Wakabayashi H, Yoshimura Y, et al. Chapter 4 Treatment of sarcopenia. Geriatr Gerontol Int. 2018 May;18 Suppl 1:28-44. doi: 10.1111/ggi.13322. PMID: 29745462.
- Shafiee G, Keshtkar A, Soltani A, et al. Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies. J Diabetes Metab Disord. 2017 May 16;16:21. doi: 10.1186/s40200-017-0302-x. PMID: 28523252; PMCID: PMC5434551.
- Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing. 2014 Nov;43(6):748-59. doi: 10.1093/ageing/ afu115.Epub 2014 Sep 21.PMID:25241753;PMCID:PMC4204661.
- Welch C, K Hassan-Smith Z, A Greig C, et al. Acute Sarcopenia Secondary to Hospitalisation - An Emerging Condition Affecting Older Adults. Aging Dis. 2018 Feb 1;9(1):151-164. doi: 10.14336/ AD.2017.0315. PMID: 29392090; PMCID: PMC5772853.
- 14. Tan LF, Lim ZY, Choe R, et al. Screening for Frailty and Sarcopenia Among Older Persons in Medical Outpatient Clinics and its Associations With Healthcare Burden. J Am Med Dir Assoc. 2017 Jul 1;18(7):583-587. doi: 10.1016/j.jamda.2017.01.004. Epub 2017 Feb 24. PMID: 28242192.
- Tay L, Ding YY, Leung BP, et al. Sex-specific differences in risk factors for sarcopenia amongst community-dwelling older adults. Age (Dordr). 2015 Dec;37(6):121. doi: 10.1007/s11357-015-9860-3. Epub 2015 Nov 25. PMID: 26607157; PMCID: PMC5005859.
- 16. Fung FY, Koh YLE, Malhotra R, et al. Prevalence of and factors associated with sarcopenia among multi-ethnic ambulatory older Asians with type 2 diabetes mellitus in a primary care setting. BMC Geriatr. 2019 Apr 29;19(1):122. doi: 10.1186/s12877-019-1137-8. PMID: 31035928; PMCID: PMC6489356.
- Lu Y, Karagounis LG, Ng TP, et al. Systemic and Metabolic Signature of Sarcopenia in Community-Dwelling Older Adults. J Gerontol A Biol Sci Med Sci. 2020 Jan 20;75(2):309-317. doi: 10.1093/gerona/ glz001. PMID: 30624690.
- Tey SL, Chew STH, How CH, et al. Factors associated with muscle mass in community-dwelling older people in Singapore: Findings from the SHIELD study. PLoS One. 2019 Oct 9;14(10):e0223222. doi: 10.1371/journal.pone.0223222. PMID: 31596873; PMCID: PMC6785067.
- Chew STH, Tey SL, Oliver J, et al. P289 Prevalence of sarcopenia and associated characteristics in community-dwelling older adults who are at risk of malnutrition in Singapore. J Frailty Aging 2020;9(S1):S46–179.
- Nakahara S, Wakabayashi H, Maeda K, et al. Sarcopenia and cachexia evaluation in different healthcare settings: a questionnaire survey of health professionals. Asia Pac J Clin Nutr. 2018;27(1):167-175. doi: 10.6133/apjcn.032017.15. PMID: 29222895.
- Deutz NEP, Ashurst I, Ballesteros MD, et al. The Underappreciated Role of Low Muscle Mass in the Management of Malnutrition. J Am Med Dir Assoc. 2019 Jan;20(1):22-27. doi: 10.1016/j. jamda.2018.11.021. PMID: 30580819.
- 22. Bruyère O, Beaudart C, Reginster JY, et al. Assessment of muscle mass, muscle strength and physical performance in clinical practice: an international survey. European Geriatric Medicine. 2016 Jun 1;7(3):243-6.
- Dent E, Morley JE, Cruz-Jentoft AJ, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): Screening, Diagnosis and Management. J Nutr Health Aging. 2018;22(10):1148-1161. doi: 10.1007/s12603-018-1139-9. PMID: 30498820.

- Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020 Dec;54(24):1451-1462. doi: 10.1136/ bjsports-2020-102955. PMID: 33239350; PMCID: PMC7719906.
- Giuffre S PT, EdD, Domholdt E PT, EdD, Keehan J PT, PhD. Beyond the individual: population health and physical therapy. Physiother Theory Pract. 2020 May;36(5):564-571. doi: 10.1080/09593985.2018.1490364. Epub 2018 Jul 18. PMID: 30019979.
- 26. World Health Organization. Global action plan on physical activity 2018–2030: more active people for a healthier world [Internet]. Geneva: World Health Organization [updated 2018; cited 22 Feb 2021]. Available from: https://www.who.int/ncds/prevention/ physical-activity/global-action-plan-2018-2030/en/
- Prado CM, Purcell SA, Alish C, et al. Implications of low muscle mass across the continuum of care: a narrative review. Ann Med. 2018 Dec;50(8):675-693. doi: 10.1080/07853890.2018.1511918. Epub 2018 Sep 12. PMID: 30169116; PMCID: PMC6370503.
- Beaudart C, Zaaria M, Pasleau F, et al. Health Outcomes of Sarcopenia: A Systematic Review and Meta-Analysis. PLoS One. 2017 Jan 17;12(1):e0169548. doi: 10.1371/journal.pone.0169548. PMID: 28095426; PMCID: PMC5240970.
- Tanimoto Y, Watanabe M, Sun W, et al. Association between sarcopenia and higher-level functional capacity in daily living in community-dwelling elderly subjects in Japan. Arch Gerontol Geriatr. 2012 Sep-Oct;55(2):e9-13. doi: 10.1016/j. archger.2012.06.015. Epub 2012 Jul 12. PMID: 22795189.
- Tyrovolas S, Koyanagi A, Olaya B, et al. The role of muscle mass and body fat on disability among older adults: A cross-national analysis. Exp Gerontol. 2015 Sep;69:27-35. doi: 10.1016/j. exger.2015.06.002. Epub 2015 Jun 3. PMID: 26048566.
- 31. Tanimoto Y, Watanabe M, Sun W, et al. Sarcopenia and falls in community-dwelling elderly subjects in Japan: Defining sarcopenia according to criteria of the European Working Group on Sarcopenia in Older People. Arch Gerontol Geriatr. 2014 Sep-Oct;59(2):295-9. doi: 10.1016/j.archger.2014.04.016. Epub 2014 May 4. PMID: 24852668.
- Yamada M, Nishiguchi S, Fukutani N, et al. Prevalence of sarcopenia in community-dwelling Japanese older adults. J Am Med Dir Assoc. 2013 Dec;14(12):911-5. doi: 10.1016/j.jamda.2013.08.015. Epub 2013 Oct 3. PMID: 24094646.
- Tanimoto Y, Watanabe M, Sun W, et al. Association of sarcopenia with functional decline in community-dwelling elderly subjects in Japan. Geriatr Gerontol Int. 2013 Oct;13(4):958-63. doi: 10.1111/ ggi.12037. Epub 2013 Mar 3. PMID: 23452074.
- Landi F, Cruz-Jentoft AJ, Liperoti R, et al. Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from iISIRENTE study. Age Ageing. 2013 Mar;42(2):203-9. doi: 10.1093/ ageing/afs194. Epub 2013 Jan 15. PMID: 23321202.
- Yuki A, Ando F, Otsuka R, Shimokata H. Sarcopenia based on the Asian Working Group for Sarcopenia criteria and all-cause mortality risk in older Japanese adults. Geriatr Gerontol Int. 2017 Oct;17(10):1642-1647. doi: 10.1111/ggi.12946. Epub 2017 Mar 5. PMID: 28261905.
- Yalcin A, Aras S, Atmis V, et al. Sarcopenia and mortality in older people living in a nursing home in Turkey. Geriatr Gerontol Int. 2017 Jul;17(7):1118-1124. doi: 10.1111/ggi.12840. Epub 2016 Jul 20. PMID: 27436345.
- Yang M, Hu X, Wang H, et al. Sarcopenia predicts readmission and mortality in elderly patients in acute care wards: a prospective study. J Cachexia Sarcopenia Muscle. 2017 Apr;8(2):251-258. doi: 10.1002/jcsm.12163. Epub 2016 Nov 28. PMID: 27896949; PMCID: PMC5377397.
- Keevil V, Mazzuin Razali R, Chin AV, et al. Grip strength in a cohort of older medical inpatients in Malaysia: a pilot study to describe the range, determinants and association with length of hospital stay. Arch Gerontol Geriatr. 2013 Jan-Feb;56(1):155-9. doi: 10.1016/j. archger.2012.10.005. Epub 2012 Oct 29. PMID: 23116975.
- Tang TC, Hwang AC, Liu LK, et al. FNIH-defined Sarcopenia Predicts Adverse Outcomes Among Community-Dwelling Older People in Taiwan: Results From I-Lan Longitudinal Aging Study. J Gerontol A Biol Sci Med Sci. 2018 May 9;73(6):828-834. doi:

10.1093/gerona/glx148. PMID: 28977377.

- Zhang X, Zhang W, Wang C, et al. Sarcopenia as a predictor of hospitalization among older people: a systematic review and meta-analysis. BMC Geriatr. 2018 Aug 22;18(1):188. doi: 10.1186/ s12877-018-0878-0. PMID: 30134867; PMCID: PMC6103964.
- Cheung JTK, Yu R, Wu Z, Wong SYS, Woo J. Geriatric syndromes, multimorbidity, and disability overlap and increase healthcare use among older Chinese. BMC Geriatr. 2018 Jun 25;18(1):147. doi: 10.1186/s12877-018-0840-1. PMID: 29940868; PMCID: PMC6019236.
- Lo YC, Wahlqvist ML, Huang YC, et al. Medical costs of a low skeletal muscle mass are modulated by dietary diversity and physical activity in community-dwelling older Taiwanese: a longitudinal study. Int J Behav Nutr Phys Act. 2017 Mar 14;14(1):31. doi: 10.1186/s12966-017-0487-x. PMID: 28288651; PMCID: PMC5348879.
- Sousa AS, Guerra RS, Fonseca I, et al. Financial impact of sarcopenia on hospitalization costs. Eur J Clin Nutr. 2016 Sep;70(9):1046-51. doi: 10.1038/ejcn.2016.73. Epub 2016 May 11. PMID: 27167668.
- Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. J Am Med Dir Assoc. 2020 Mar;21(3):300-307.e2. doi: 10.1016/j.jamda.2019.12.012. Epub 2020 Feb 4. PMID: 32033882.
- Hu X, Zhang L, Wang H, et al. Malnutrition-sarcopenia syndrome predicts mortality in hospitalized older patients. Sci Rep. 2017 Jun 9;7(1):3171. doi: 10.1038/s41598-017-03388-3. PMID: 28600505; PMCID: PMC5466644.
- 46. Stratton RJ, Hackston A, Longmore D, et al. Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the 'malnutrition universal screening tool' ('MUST') for adults. Br J Nutr. 2004 Nov;92(5):799-808. doi: 10.1079/bjn20041258. PMID: 15533269.
- Lexell J, Taylor CC, Sjöström M. What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. J Neurol Sci. 1988 Apr;84(2-3):275-94. doi: 10.1016/0022-510x(88)90132-3. PMID: 3379447.
- Beaudart C, Rizzoli R, Bruyère O, et al. Sarcopenia: burden and challenges for public health. Arch Public Health. 2014 Dec 18;72(1):45. doi: 10.1186/2049-3258-72-45. PMID: 25810912; PMCID: PMC4373245.
- English KL, Paddon-Jones D. Protecting muscle mass and function in older adults during bed rest. Curr Opin Clin Nutr Metab Care. 2010 Jan;13(1):34-9. doi: 10.1097/MCO.0b013e328333aa66. PMID: 19898232; PMCID: PMC3276215.
- Malmstrom TK, Miller DK, Simonsick EM, et al. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle. 2016 Mar;7(1):28-36. doi: 10.1002/jcsm.12048. Epub 2015 Jul 7. PMID: 27066316; PMCID: PMC4799853.
- Cao L, Chen S, Zou C, et al. A pilot study of the SARC-F scale on screening sarcopenia and physical disability in the Chinese older people. J Nutr Health Aging. 2014 Mar;18(3):277-83. doi: 10.1007/ s12603-013-0410-3. PMID: 24626755.
- Ida S, Murata K, Nakadachi D, et al. Development of a Japanese version of the SARC-F for diabetic patients: an examination of reliability and validity. Aging Clin Exp Res. 2017 Oct;29(5):935-942. doi: 10.1007/s40520-016-0668-5. Epub 2016 Nov 10. Erratum in: Aging Clin Exp Res. 2019 Aug 19;: PMID: 27832470; PMCID: PMC6702187.
- Tanaka S, Kamiya K, Hamazaki N, et al. Utility of SARC-F for Assessing Physical Function in Elderly Patients With Cardiovascular Disease. J Am Med Dir Assoc. 2017 Feb 1;18(2):176-181. doi: 10.1016/j.jamda.2016.10.019. Epub 2016 Dec 31. PMID: 28043805.
- Woo J, Leung J, Morley JE. Validating the SARC-F: a suitable community screening tool for sarcopenia? J Am Med Dir Assoc. 2014 Sep;15(9):630-4. doi: 10.1016/j.jamda.2014.04.021. Epub 2014 Jun 16. PMID: 24947762.
- Ida S, Kaneko R, Murata K. SARC-F for Screening of Sarcopenia Among Older Adults: A Meta-analysis of Screening Test Accuracy. J Am Med Dir Assoc. 2018 Aug;19(8):685-689. doi: 10.1016/j. jamda.2018.04.001. Epub 2018 May 31. PMID: 29778639.

- Makizako H, Shimada H, Doi T, et al. Predictive CutoffValues of the Five-Times Sit-to-Stand Test and the Timed "Up & Go" Test for Disability Incidence in Older People Dwelling in the Community. Phys Ther. 2017 Apr 1;97(4):417-424. doi: 10.2522/ptj.20150665. PMID: 28371914.
- Nishimura T, Arima K, Okabe T, et al. Usefulness of chair stand time as a surrogate of gait speed in diagnosing sarcopenia. Geriatr Gerontol Int. 2017 Apr;17(4):659-661. doi: 10.1111/ggi.12766. Epub 2016 Apr 27. PMID: 27120799.
- Buckinx F, Landi F, Cesari M, et al. Pitfalls in the measurement of muscle mass: a need for a reference standard. J Cachexia Sarcopenia Muscle. 2018 Apr;9(2):269-278. doi: 10.1002/jcsm.12268. Epub 2018 Jan 19. PMID: 29349935; PMCID: PMC5879987.
- Argilés JM, Campos N, Lopez-Pedrosa JM, et al. Skeletal Muscle Regulates Metabolism via Interorgan Crosstalk: Roles in Health and Disease. J Am Med Dir Assoc. 2016 Sep 1;17(9):789-96. doi: 10.1016/j.jamda.2016.04.019. Epub 2016 Jun 17. PMID: 27324808.
- American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, Salem GJ, Skinner JS. American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc. 2009 Jul;41(7):1510-30. doi: 10.1249/MSS.0b013e3181a0c95c. PMID: 19516148.
- Steffl M, Bohannon RW, Sontakova L, et al. Relationship between sarcopenia and physical activity in older people:a systematic review and meta-analysis. Clin Interv Aging. 2017 May 17;12:835-845. doi: 10.2147/CIA.S132940. PMID: 28553092; PMCID: PMC5441519.
- Peterson MD, Rhea MR, Sen A, Gordon PM. Resistance exercise for muscular strength in older adults: a meta-analysis. Ageing Res Rev. 2010 Jul;9(3):226-37. doi: 10.1016/j.arr.2010.03.004. Epub 2010 Apr 10. PMID: 20385254; PMCID: PMC2892859.
- Peterson MD, Sen A, Gordon PM. Influence of resistance exercise on lean body mass in aging adults: a meta-analysis. Med Sci Sports Exerc. 2011 Feb;43(2):249-58. doi: 10.1249/ MSS.0b013e3181eb6265. PMID: 20543750; PMCID: PMC2995836.
- Yoshimura Y, Wakabayashi H, Yamada M, et al. Interventions for Treating Sarcopenia: A Systematic Review and Meta-Analysis of Randomized Controlled Studies. J Am Med Dir Assoc. 2017 Jun 1;18(6):553.e1-553.e16. doi: 10.1016/j.jamda.2017.03.019. PMID: 28549707.
- Levinger I, Goodman C, Hare DL, Jerums G, Toia D, Selig S. The reliability of the IRM strength test for untrained middle-aged individuals. J Sci Med Sport. 2009 Mar;12(2):310-6. doi: 10.1016/j. jsams.2007.10.007. Epub 2007 Dec 19. PMID: 18078784.
- Avers D, Brown M. White paper: Strength training for the older adult.J Geriatr Phys Ther. 2009;32(4):148-52, 158. PMID: 20469563.
- Beckwée D, Delaere A, Aelbrecht S, et al. Exercise Interventions for the Prevention and Treatment of Sarcopenia. A Systematic Umbrella Review. J Nutr Health Aging. 2019;23(6):494-502. doi: 10.1007/s12603-019-1196-8. PMID: 31233069.
- Law TD, Clark LA, Clark BC. Resistance Exercise to Prevent and Manage Sarcopenia and Dynapenia. Annu Rev Gerontol Geriatr. 2016;36(1):205-228. doi: 10.1891/0198-8794.36.205. PMID: 27134329; PMCID: PMC4849483.
- Clemson L, Singh MF, Bundy A, et al. LiFE Pilot Study: A randomised trial of balance and strength training embedded in daily life activity to reduce falls in older adults. Aust Occup Ther J. 2010 Feb;57(1):42-50. doi: 10.1111/j.1440-1630.2009.00848.x. PMID: 20854564.
- 70. Harvard Medical School. Strength and Power Training for Older Adults, a Special Health Report [Internet]. Harvard Health Publishing [updated 2019; cited 16 Apr 2021]. Available from: https://www.health.harvard.edu/exercise-and-fitness/strengthand-power-training-for-older-adults
- Volkert D, Beck AM, Cederholm T, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr. 2019 Feb;38(1):10-47. doi: 10.1016/j.clnu.2018.05.024. Epub 2018 Jun 18. PMID: 30005900.
- Demling RH. Nutrition, anabolism, and the wound healing process: an overview. Eplasty. 2009;9:e9. Epub 2009 Feb 3. PMID: 19274069; PMCID: PMC2642618.
- 73. Bauer J, Biolo G, Cederholm T, et al. Evidence-based

recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc. 2013 Aug;14(8):542-59. doi: 10.1016/j. jamda.2013.05.021. Epub 2013 Jul 16. PMID: 23867520.

- 74. Moore DR, Churchward-Venne TA, Witard O, et al Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. J Gerontol A Biol Sci Med Sci. 2015 Jan;70(1):57-62. doi: 10.1093/gerona/glu103. Epub 2014 Jul 23. PMID: 25056502.
- Fiaccadori E, Sabatino A, Barazzoni R, et al. ESPEN guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease. Clin Nutr. 2021 Apr;40(4):1644-1668. doi: 10.1016/j.clnu.2021.01.028. Epub 2021 Feb 9. PMID: 33640205.
- Cano NJ, Aparicio M, Brunori G, et al; ESPEN. ESPEN Guidelines on Parenteral Nutrition: adult renal failure. Clin Nutr. 2009 Aug;28(4):401-14. doi: 10.1016/j.clnu.2009.05.016. Epub 2009 Jun 17. PMID: 19535181.
- 77. Chew STH, Tan NC, Cheong M, et al. Impact of specialized oral nutritional supplement on clinical, nutritional, and functional outcomes: A randomized, placebo-controlled trial in communitydwelling older adults at risk of malnutrition. Clin Nutr. 2021 Apr;40(4):1879-1892. doi: 10.1016/j.clnu.2020.10.015. Epub 2020 Oct 15. PMID: 33268143.
- Matheson EM, Nelson JL, Baggs GE, et al. Specialized oral nutritional supplement (ONS) improves handgrip strength in hospitalized, malnourished older patients with cardiovascular and pulmonary disease: A randomized clinical trial. Clin Nutr. 2021 Mar;40(3):844-849. doi: 10.1016/j.clnu.2020.08.035. Epub 2020 Sep 5. PMID: 32943241.
- 79. Health Promotion Board Singapore. Energy & Nutrient Composition of Food [Internet]. Singapore: Health Promotion Board [updated 14 Mar 2011; cited 23 Apr 2021]. Available from: https://focos.hpb.gov.sg/eservices/ENCF/
- Kimball SR, Jefferson LS. Signaling pathways and molecular mechanisms through which branched-chain amino acids mediate translational control of protein synthesis. J Nutr. 2006 Jan;136(1 Suppl):227S-31S. doi: 10.1093/jn/136.1.227S. PMID: 16365087.
- Komar B, Schwingshackl L, Hoffmann G. Effects of leucine-rich protein supplements on anthropometric parameter and muscle strength in the elderly: a systematic review and meta-analysis. J Nutr Health Aging. 2015 Apr;19(4):437-46. doi: 10.1007/s12603-014-0559-4. PMID: 25809808.
- Martínez-Arnau FM, Fonfría-Vivas R, Cauli O. Beneficial Effects of Leucine Supplementation on Criteria for Sarcopenia: A Systematic Review. Nutrients. 2019 Oct 17;11(10):2504. doi: 10.3390/ nu11102504. PMID: 31627427; PMCID: PMC6835605.
- Verhoeven S,Vanschoonbeek K,Verdijk LB, et al. Long-term leucine supplementation does not increase muscle mass or strength in healthy elderly men. Am J Clin Nutr. 2009 May;89(5):1468-75. doi: 10.3945/ajcn.2008.26668. Epub 2009 Mar 25. PMID: 19321567.
- 84. Murphy CH, Flanagan EM, De Vito G, et al. Does supplementation with leucine-enriched protein alone and in combination with fish-oil-derived n-3 PUFA affect muscle mass, strength, physical performance, and muscle protein synthesis in well-nourished older adults? A randomized, double-blind, placebo-controlled trial. Am J Clin Nutr. 2021 Apr 19:nqaa449. doi: 10.1093/ajcn/nqaa449. Epub ahead of print. PMID: 33871558.
- Holeček M. Beta-hydroxy-beta-methylbutyrate supplementation and skeletal muscle in healthy and muscle-wasting conditions. J Cachexia Sarcopenia Muscle. 2017 Aug;8(4):529-541. doi: 10.1002/jcsm.12208. Epub 2017 May 10. PMID: 28493406; PMCID: PMC5566641.
- Oktaviana J, Zanker J, Vogrin S, Duque G. The Effect of β-hydroxyβ-methylbutyrate (HMB) on Sarcopenia and Functional Frailty in Older Persons: A Systematic Review. J Nutr Health Aging. 2019;23(2):145-150. doi: 10.1007/s12603-018-1153-y. PMID: 30697623.
- Holick MF. Vitamin D deficiency. N Engl J Med. 2007 Jul 19;357(3):266-81. doi: 10.1056/NEJMra070553. PMID: 17634462.
- Holick MF, Binkley NC, Bischoff-Ferrari HA, et al; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin

Endocrinol Metab. 2011 Jul;96(7):1911-30. doi: 10.1210/jc.2011-0385. Epub 2011 Jun 6. Erratum in: J Clin Endocrinol Metab. 2011 Dec;96(12):3908. PMID: 21646368.

- Verlaan S, Maier AB, Bauer JM, et al. Sufficient levels of 25-hydroxyvitamin D and protein intake required to increase muscle mass in sarcopenic older adults - The PROVIDE study. Clin Nutr. 2018 Apr;37(2):551-557. doi: 10.1016/j.clnu.2017.01.005. Epub 2017 Jan 17. PMID: 28132725.
- 90. Beaudart C, Buckinx F, Rabenda V, et al. The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. J Clin Endocrinol Metab. 2014 Nov;99(11):4336-45. doi: 10.1210/jc.2014-1742. Epub 2014 Jul 17. PMID: 25033068.
- 91. Sinha A, Hollingsworth KG, Ball S, Cheetham T. Improving the vitamin D status of vitamin D deficient adults is associated with improved mitochondrial oxidative function in skeletal muscle. J Clin Endocrinol Metab. 2013 Mar;98(3):E509-13. doi: 10.1210/ jc.2012-3592. Epub 2013 Feb 7. PMID: 23393184.
- Dzik KP, Kaczor JJ. Mechanisms of vitamin D on skeletal muscle function: oxidative stress, energy metabolism and anabolic state. Eur J Appl Physiol. 2019 Apr;119(4):825-839. doi: 10.1007/ s00421-019-04104-x. Epub 2019 Mar 4. PMID: 30830277; PMCID: PMC6422984.
- Kimball SM, Holick MF. Official recommendations for vitamin D through the life stages in developed countries. Eur J Clin Nutr. 2020 Nov;74(11):1514-1518. doi: 10.1038/s41430-020-00706-3. Epub 2020 Aug 20. PMID: 32820241.
- Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011 Jan;96(1):53-8. doi: 10.1210/jc.2010-2704. Epub 2010 Nov 29. PMID: 21118827; PMCID: PMC3046611.
- Fiatarone MA, O'Neill EF, Ryan ND, et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med. 1994 Jun 23;330(25):1769-75. doi: 10.1056/ NEJM199406233302501. PMID: 8190152.

- 96. et al Yamada M, Kimura Y, Ishiyama D, et al. Synergistic effect of bodyweight resistance exercise and protein supplementation on skeletal muscle in sarcopenic or dynapenic older adults. Geriatr Gerontol Int. 2019 May;19(5):429-437. doi: 10.1111/ggi.13643. Epub 2019 Mar 13. PMID: 30864254.
- 97. Liao CD, Tsauo JY, Wu YT, et al. Effects of protein supplementation combined with resistance exercise on body composition and physical function in older adults: a systematic review and metaanalysis. Am J Clin Nutr. 2017 Oct; 106(4):1078-1091. doi: 10.3945/ ajcn.116.143594. Epub 2017 Aug 16. PMID: 28814401.
- 98. Antoniak AE, Greig CA. The effect of combined resistance exercise training and vitamin  $D_3$  supplementation on musculoskeletal health and function in older adults: a systematic review and meta-analysis. BMJ Open. 2017 Jul 20;7(7):e014619. doi: 10.1136/bmjopen-2016-014619. PMID: 28729308; PMCID: PMC5541589.
- Tieland M, Trouwborst I, Clark BC. Skeletal muscle performance and ageing. J Cachexia Sarcopenia Muscle. 2018 Feb;9(1):3-19. doi: 10.1002/jcsm.12238. Epub 2017 Nov 19. PMID: 29151281; PMCID: PMC5803609.
- 100. Kokura Y, Wakabayashi H, Maeda K, et al. Impact of a multidisciplinary rehabilitation nutrition team on evaluating sarcopenia, cachexia and practice of rehabilitation nutrition. J Med Invest. 2017;64(1.2):140-145. doi: 10.2152/jmi.64.140. PMID: 28373612.
- 101. Claflin DR, Larkin LM, Cederna PS, et al. Effects of high- and low-velocity resistance training on the contractile properties of skeletal muscle fibers from young and older humans. J Appl Physiol (1985).
  2011 Oct;111(4):1021-30. doi: 10.1152/japplphysiol.01119.2010. Epub 2011 Jul 28. PMID: 21799130; PMCID: PMC3191797.

#### LEARNING POINTS

- Malnutrition and sarcopenia are intimately linked in older adults. The presence of one on screening should trigger the screening for the other.
- Sarcopenia can be diagnosed using the Find-Assess-Confirm-Severity (FACS) approach. The risk of malnutrition can be rapidly determined by the Malnutrition Universal Screening Tool (MUST) in both inpatient and outpatient settings.
- Progressive resistance exercise training (RET) can improve muscle mass, strength and function in older adults with sarcopenia. The use of I-RM is an important and reliable method to quantify the intensity of RET.
- Adequate dietary protein and energy are required for optimal muscle health in older adults. The total required per day for each macronutrient is dependent on health status and physical activity level.
- Oral nutritional supplements are recommended when nutritional requirements cannot be met by dietary intake and fortification of foods in older adults with or at risk of malnutrition in both the community and hospital settings.
- The use of leucine or HMB in older adults with sarcopenia or frailty can lead to improvements in lean body mass, and can help prevent further loss of muscle strength and function.
- Vitamin D deficiency is prevalent in community-dwelling older adults and treatment of deficiency can improve muscle function, muscle mass, and muscle strength, particularly in the setting of sarcopenia managed with combined RET and nutritional interventions.
- Combining RET with nutritional interventions is strongly recommended in the management of older patients with sarcopenia and at-risk or with malnutrition.
- A multidisciplinary team approach is recommended in order to comprehensively assess and individualise the management plan for muscle health in older adults.
- It is important to counsel patients and carers on the importance and role of RET and nutritional interventions in the management of sarcopenia in older adults.