The Value of Muscle in Improving Clinical Outcomes

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Skeletal muscle represents about 40% of the human body weight and is responsible for movement and postprandial glucose processing.[1, 2] It is the principal protein reservoir to replace blood amino acids,[3] the precursors for hepatic gluconeogenesis.[4] Adequate muscle mass is paramount to maintain plasma glucose concentration, conversely, depletion is incompatible with life. Warsaw ghetto studies suggest that death from starvation occurs when muscle protein breakdown becomes inadequate to maintain supply of gluconeogenic precursors.[5] Losing muscle occurs naturally with age and can lead to decreased strength and functionality. After 30 years of age, there is a shift towards degeneration, leading to a net loss of muscle mass and strength.[6] This muscle wasting in ageing, but otherwise healthy individuals, is referred to as sarcopenia.

The Impact of Sarcopenia on Clinical Outcomes

Sarcopenia has been defined as *"a progressive and generalised skeletal muscle disorder associated with increased likelihood of falls, fractures, physical disability and mortality."*[7] It is often associated with frailty, low grip strength and slow gait speed.[7] Sarcopenia has primary and secondary aetiology, developing through the ageing process or through chronic mediated inflammation respectively.[7] Secondary sarcopenia progresses through system cytokine-mediated inflammation present in chronic illnesses.[7] This shifts the body into a catabolic state, resulting in muscle net loss that is aggravated by ageing factors like inactivity, poor nutrition, and nausea.[8]

Sarcopenia is also associated with malnutrition,[9] and low muscle mass has been proposed in the definition of malnutrition.[10] Sarcopenia, has poorer prognosis impacting survival in chronic illnesses that are commonplace in older adults, such as cancer and chronic obstructive pulmonary disease (COPD).[11, 12] Sarcopenic cancer patients are at higher risk of complications like poorer tolerance to therapies, a greater incidence of infection, chemotherapy toxicity and perioperative problems that negatively affect prognosis[11] In COPD, emphysema severity, characterised by a loss of lung tissue, appears to be related to muscle mass and prognosis.[13] Therefore, it is vital to preserve muscle, and strategies to achieve this goal include nutritional intervention and physical activity.[14]

Practical Strategies Targeting Muscle Mass

Current trends towards the ageing population and increased prevalence of chronic diseases will continue rising in the next decades with complications such as sarcopenia, malnutrition, and frailty.[15] Body mass index (BMI) is commonly used for nutritional assessment, however, it has limitations in nutrition screening with a tendency to underestimate muscle mass.[16, 17] Thus, there is a need to use tools that provide more reliable muscle mass and strength assessments; low muscle mass is associated with a decreased strength.[18] Disappointingly, despite the wealth of research on the loss of muscle mass and its association with high mortality, nutrition experts still rely on screening tools that focus on weight loss and dietary intake.

1. Nutrition Interventions

Nutrition Screening

Body composition evaluation should be used for the screening, diagnosing and monitoring of malnutrition and sarcopenia. Reliable nutrition and muscle measurements will support the tailoring of multimodal therapy. The **R**emote – **M**alnutrition **APP** (R-MAPP), is a tool, also available as an App, for identifying nutritional risk and loss of muscle mass and function.[19] The R-MAPP consists of two simple validated clinical tools – Malnutrition Universal Screening Tool ('MUST') and SARC-F (5-item questionnaire: **S**trength, **A**ssistance with walking, **R**ise from a chair, **C**limb stairs and **F**alls). SARC-F has a low-to-moderate sensitivity and a high specificity to predict low muscle strength.[20] It is an inexpensive and convenient method that is self-reported by the patient and adaptable to telehealth services.

Assessment & Monitoring

Practical assessment tools for muscle strength includes handgrip strength and sit to stand (STS) testing. Gait speed, the 4 m walk test, is also part of sarcopenia diagnosis (**Table 1**). For those with physical disability, calf circumference, closely related to whole body muscle mass,[21] can be applied. This method can be utilised with a tape measure, or the individual can use their index finger and thumbs to create a finger circle, the yubi-wakka finger ring test.[22] (**Table 1**).

Nutrition Interventions

Nutrition intervention needs to ensure protein requirements are met for the maintenance or restoration of muscle. Protein recommendations for older adults are 1-1.2 g/kg body weight (BW), those with chronic illness up to 1.5 g/kg BW, increasing to 2 g/kg BW for severely malnourished.[24] Achieving protein requirements is a challenging task, where supplementation is crucial to reach adequacy. Timing, dose and quality are equally important as older individuals appear to have a higher per-meal protein threshold to promote anabolism. Suggestions for anabolism are for 20 g to 30 g for the older adult per dose.[25, 24] Subsequently, the use of oral nutrition supplements (ONS) is essential to ensure this high protein (HP) intake is achievable. Amongst the amino-acids, the branched-chain amino acids (BCAA) and their derivatives are of particular importance for building and maintaining muscle mass.[26] Leucine and its derivative, b-hydroxy-b-methylbutyrate (HMB), is an important regulator of muscle growth and a potent stimulator of protein synthesis whilst inhibiting protein breakdown.[27] The NOURISH study demonstrated the impact of a HP-HMB ONS in lowering the risk of mortality by 50% in malnourished older adults with heart or lung disease whilst improving nutritional parameters.[28] Additionally, a growing body of evidence suggests that HMB can help to slow or even reverse muscle loss in ageing, illness, or starvation,[29] whilst also improving clinical outcomes such as wound healing,[30] physical function,[31] and mortality.[28]

Other dietary interventions to also mitigate muscle loss is vitamin D adequacy. Vitamin D supplementation has been shown to improve muscle strength, particularly in those most deficient and within an older age group.[32]

2. Physical Activity

Undoubtedly, nutrition is key to muscle mass improvement, but anabolic potential can be maximised with exercise intervention. Exercise and resistance training (use of free weights, machines, and elastic bands, done in repetitions and in multiple sessions) are currently used to treat age-associated sarcopenia.[33] In cancer patients, structured resistance training programmes resulted in reduction in fatigue, decreased anxiety, weight gain and improved functional status.[34] Resistance training has been shown repeatedly to improve rates of protein synthesis and reverse muscle loss.[33]

Conclusion

The importance of muscle mass in improving clinical outcomes and quality of life is well established. There is a need to change the current malnutrition management approach from a focus on weight to targeting muscle mass. Treatment must target muscle mass from screening to assessment and interventions. Screening tools should include assessment of muscle mass and there exists a variety of tools to suits all clinical settings. Ultimately, a focus on the maintenance of muscle mass as a malnutrition management strategy will lead to improved clinical outcomes and quality of life.

Table 1: Sarcopenia diagnostic cut-off points[7, 22, 23]

Tests	Cut-off points
Grip strength	<27 kg for men <16 kg for women
Sit to stand	>15 s for five rises
Gait speed	≤0.8 m/s
Calf circumference (CC)	<33 cm
Finger ring test – use the ring to circle thickest part of the non-dominant calf, which is bent at a 90° angle. Check whether the CC is "bigger," "just fits" or "smaller" than the finger-ring circumference	CC "just fitting" and "smaller" is associated with sarcopenia. CC <30 cm in men and <27 cm in women predict long-term care and mortality.

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