Kerry Health and Nutrition Institute.

Muscle Ageing - Nutrition Interventions During Adulthood

Sara Llamas-Moya, M.Sc., Ph.D.

Ageing is an inevitable process affecting an increasing proportion of the world's population due to increasing life expectancy worldwide. Delaying and/or reducing the rate of muscle ageing has been identified as a key strategy to minimise frailty and maintain independence in the elderly, with the goal of maximising quality of life during the golden years.

Sarcopenia can be defined as the age-associated loss of skeletal muscle mass and function, which may be associated with increased fat mass[1]. In most instances, the term sarcopenia does not distinguish between loss of muscle mass *(sarcopenia)* and loss of muscle strength *(dynapenia)* Most of the knowledge around this condition has been gathered in populations over 65 years old. This research has identified nutrition as a contributing factor to the optimal balance between muscle protein synthesis (MPS) and breakdown[2]. The onset of this decline in muscle mass and muscle strength has been reported as early as 30-40 years of age[3]. Although the possible impact on frailty may not be evident until later years, nutritional strategies adopted during early adulthood may help to prevent an early onset and rapid progression of muscle ageing.

The Ageing Process: Influence on Muscle Metabolism

Over a person's lifetime, skeletal muscle mass is in a constant state of turnover, with the balance between MPS and breakdown determining the relevant gains or losses in muscle mass. Early life is characterised by rapid growth in muscle mass and strength, which peaks in early adult life[4]. It is from this point onwards that muscle mass and muscle strength decrease, the rate of which may determine whether individuals are at risk of becoming disabled (*Figure 1*). The clinical relevance of sarcopenia is inevitably dependent on the individual's total muscle mass prior to the condition and the rate at which this is reduced, which is determined by multiple factors.

In the ageing process, the number of muscle fibres decrease (hypoplasia) in conjunction with a reduction in their size (atrophy)[5]. These changes are more prevalent in type II muscle fibres, which are glycolytic, anaerobic fibres, mostly used for short burst of speed and power, and therefore, potentially required in preventing falls. Ageing also results in dynapenia, or reduced muscle strength.

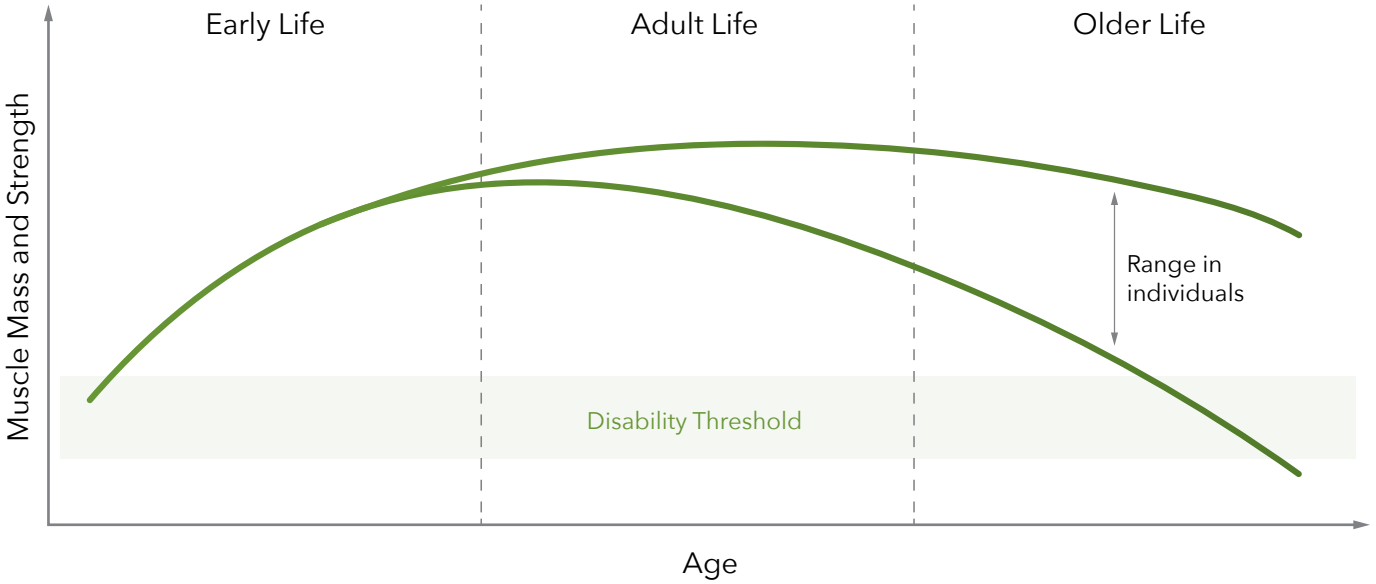
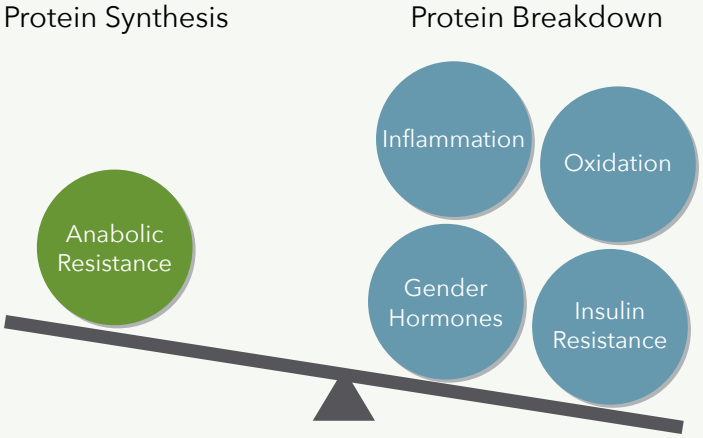


Figure 1: **Life course changes in muscle mass and muscle strength[4]. Source/adapted from: Kalache A, Kickbusch I. A global strategy for healthy ageing. *World Health*, 1997, 50(4):4-5**

Muscle synthesis is primarily regulated by strain on the muscle, such as muscle contractions during exercise, and by amino acid supply from the diet. Therefore, nutrition can play a critical role in the development or prevention of sarcopenia[2], especially when a person is obese[6]. As we age, our ability to synthesise protein decreases, often termed age-related anabolic resistance, which refers to the decreased ability of older muscles to uptake specific amino acids in order to stimulate MPS[7]. This reduced ability to utilise the muscle's building blocks, combined with low protein intakes typically seen in elderly populations[2], is a primary cause of muscle mass loss in ageing.

Muscle decline is exacerbated in older individuals by an age-related reduction in circulating levels of testosterone and estrogen, which are hormones that favour muscle growth[8]. In addition, the effect of insulin on promoting growth of older muscles declines with age, meaning more insulin is required[9]. 'Inflamm-ageing', a low-grade, chronic, and systemic inflammatory state typically seen in the elderly, has also been linked to decreases in muscle mass and/or functionality[10]. To find out more about inflamm-ageing, read our white paper, The Role of Food in Maintaining Immune Health in Ageing. Muscle ageing is influenced by oxidation and increases in reactive oxygen species (ROS)[11].

Factors influencing a negative balance in muscle protein synthesis and breakdown in the elderly



The Role of Dietary Protein in Muscle Health

Dietary protein has been the focus of many research studies, since protein and amino acids are integral to muscle physiology and metabolism. Essential amino acids (EAA) are involved in the anabolic (growth-promoting) pathways responsible for protein synthesis, namely the mTOR pathway, which is primarily regulated by the branched chain amino acid (BCAA), leucine[7]. However, as we age, EAAs do not provide a consistently strong stimulus for muscle growth, especially immediately after a meal[2]. This means that more protein intake at mealtimes is required for older muscles to provide an anabolic signal than for younger muscles.

These findings suggest that, to promote muscle health in ageing populations, additional protein should be consumed at mealtimes. This could be through additional food or supplementation. The benefits of additional protein seem to stop at around 30 grams of protein in one meal, meaning that for maximum muscle retention, healthy agers should try to consume up to 30 grams of protein at each meal. Spreading this intake throughout the day is beneficial so that each meal can provide an anabolic signal to the muscles. To read more about the importance of spreading protein intake throughout the day, read our blog Three Things You Need to Know about Protein for Exercise Performance.

The amino acid composition of proteins is important for muscle health because of the ability of specific amino acids, such as leucine, to provide a growth stimulus for muscles. However, the rate of digestion seems to have an effect on protein metabolism, as well. For example, whey protein is rapidly digested, due to its solubility in acid, and it results in a rapid increase in plasma post-prandial concentrations[12].

Soy has been considered the natural benchmark for traditional dairy proteins, due to its widely accepted high quality, which is associated with high protein digestibility corrected amino acid score (PDCAAS). Read our blog, Science Supports Soy for a Healthy Diet. Soy protein has been shown to improve MPS in young adults, either at rest or after resistance exercise training, albeit the impact

of whey following exercise was of greater magnitude[13]. Nonetheless, soy protein isolate was not able to stimulate MPS when compared to equal quantities of whey protein in older men. However, this could be overcome through additional soy protein intake or supplementation of soy protein with BCAA[14].

Other vegetable-based proteins have received lesser attention in relation to their potential effects on MPS, however rice protein hydrolysate has come to the fore as a hypoallergenic, non-dairy option. Read our blog, Nutritional Benefits of Plant Proteins Taking Root with Consumers.

Vitamin D Status and Muscle Ageing

Vitamin D deficiency is common in certain elderly populations and may have an impact on muscle health. Vitamin D supplementation has been shown to maintain the number and diameter of type II muscle fibres in women. Cross-sectional studies have also found a positive correlation between vitamin D status and muscle mass, although this association may be influenced by gender and age[15]. However, no relationship has been found between serum 25(OH)D concentration and lean body mass in a population of men with ages ranging between 30-79 years. Its potential positive effect on muscle mass and functionality may be confounded by baseline vitamin D status[15].

The lack of a more definitive influence coupled with seasonal and gender variations in levels of 25(OH)D in serum suggests that further research is needed. Serum concentrations of 25(OH)D should exceed 75 nmol/l in order to capitalise on the benefits of this vitamin on bone and muscle metabolism[16]. The National Adult Nutrition Survey in Ireland reported that the year-round prevalence rates for serum 25(OH)D below this cut-off value are in excess of 75% of the population surveyed (18-84 years of age)[17]. Furthermore, the incidence of vitamin D deficiency has been reported to increase significantly with age[18], which suggests that additional investigation on the effect of vitamin D in adulthood may warrant consideration as a prevention strategy to delay the onset of muscle ageing.

Acidosis and its Influence on Muscle Function

Acidosis has been known to have a direct impact on protein catabolism in the muscle, particularly in individuals with chronic kidney disease (CKD), in which the ability to maintain the blood acid-base system is impaired. Supplementation of potassium bicarbonate has been the object of research due to its potential to neutralise acidic conditions and its direct effect on lowering nitrogen excretion. However, certain dietary behaviours and food choices can also help to reduce mild acidosis in otherwise healthy individuals. Higher potassium excretion, which is a biomarker of dietary potassium intake, has been associated with the maintenance of muscle mass in elderly men and women[19]. Alkalinogenic foods (ability to reduce acid concentration), such as fruit and vegetables, may be paramount to reducing the rates of muscle mass and strength losses associated with ageing. The net dietary acid load has been identified as a critical factor on hip fracture risk following an evaluation encompassing results in 33 countries[20]. In a recent intervention study over 16 weeks, compliance with five portions/day of fruit and vegetables increased the measures of upper (e.g. hand grip) body physical strength when compared to two portions/day[21]. Considering the current high dietary protein intake and low compliance with fruit and vegetable recommendations in the general adult populations, it is plausible that dietary strategies

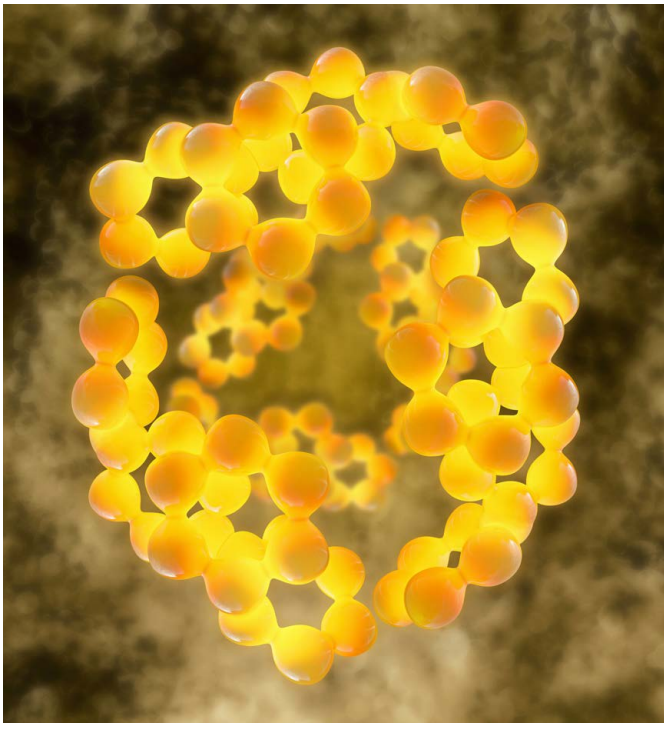
to reduce acidosis may have an impact in the onset of muscle ageing.

Dietary Fat Effect on Muscle Metabolism

Fatty acids originating from dietary fat are an essential energy source for muscle metabolism. Indirectly, dietary fat can exert an effect on muscle ageing[22]. Dietary fat composition is also known to have an influence on the inflammatory status of individuals; saturated fatty acids (SFA) and trans fatty acids exert a pro-inflammatory role, while poly-unsaturated fatty acids (PUFA) favour an anti-inflammatory state. Results from a randomised controlled trial comparing supplementation of corn oil or omega-3 fatty acids in individuals >65 years with a healthy weight showed that omega-3 fatty acids led to an increase in MPS. Similar results on muscle protein metabolism have been replicated in young adults (25-45 years) following PUFA supplementation[23]. No effect of PUFA supplementation was seen on the levels of inflammatory markers, which suggests that the anti-inflammatory properties of PUFA may not be the sole mechanism behind the enhanced protein synthesis in healthy individuals[23].

Metabolic Syndrome: Cross-talk Between Muscle and Adipose Tissue Pathways

Insulin plays a complex role in muscle metabolism primarily by promoting muscle protein synthesis independently of amino acid pathways[24]. This means that insulin resistant conditions, such as type 2 diabetes, can lead to impaired protein synthesis. Increased adiposity may in turn reduce the effectiveness of insulin and EAA to stimulate MPS, even in healthy young individuals[25].



As the prevalence of obesity increases in the general adult population, the frequency of excess body weight and sarcopenia together is increasing. This condition, known as sarcopenic obesity, has been recently quantified in the US as present in 18% of women and 42% of men aged >70 years[26]. It is well established that the risk of cardiometabolic disease is higher in older adults with sarcopenic obesity in comparison to those with either condition alone[6]. Risk factors associated with metabolic disease are already prevalent in the general middle-aged adult population, which can predispose individuals to an accelerated onset of muscle ageing. A recent study concluded that patients with sarcopenic obesity in older age had increased levels of cardiometabolic risk factors, such as fasting plasma glucose and type 2 diabetes, up to 30 years prior to being diagnosed with sarcopenic obesity[27].

Dietary Considerations for Adults to Mitigate Muscle Ageing

The primary message from all of this research is that, to promote muscle health in our ageing years, we must promote muscle health throughout life. Maintaining MPS during adulthood is essential for preserving metabolic health and may be an insurance against mobility issues and frailty in later life. Key nutritional strategies play a role in protecting muscle function; leucine-rich protein sources, such as whey, are widely accepted as facilitators of muscle growth in adults. As consumer demand for non-dairy and/or hypoallergenic products is on the rise, soy and rice protein could be good alternatives based on their effect on post-prandial aminoacidemia and MPS. Complying with recommendations for healthy eating, especially for fruit and vegetable intake, can also prevent the detrimental effect of acidosis and minimise skeletal muscle catabolism. This will also favour the consumption of dietary fats that facilitate muscle growth, such as PUFA, and reduce potential inflammatory pathways that ultimately can accelerate muscle ageing. Overall, a lifelong nutritional approach for the prevention of metabolic disease will have a positive impact in muscle ageing.

Sara Llamas Moya, M.Sc., Ph.D. - Global Applications Manager for Animal and Pet Nutrition

Sara is responsible for conducting clinical efficacy trials in target animal species and creating a scientific understanding of the technology's mode of action, from a nutrition and health perspective. Sara is also involved in product development and keeps up to date with new scientific findings that can be translated into innovative solutions to the human and animal nutrition industries.

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