Protein intake and muscle function in older adults

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Purpose of review
We provide an update on the recent advances in nutrition research regarding the role of protein intake in the development and treatment of sarcopenia of aging.

Recent findings
Specific muscle mass, strength and function cut-points for the diagnosis of sarcopenia have been identified. There is mounting evidence, as highlighted by multiple consensus statements, that the Recommended Dietary Allowance (0.8 g/kg body weight) may be inadequate to promote optimal health in older adults. Recent research indicates that in addition to total daily protein intake the timing of protein intake is also important to best stimulate muscle protein synthesis, and maintain muscle mass and function in older adults.

Summary
Recent evidence suggests that the Recommended Dietary Allowance for protein is inadequate, and that the timing and distribution of protein consumption throughout daily meals may be as important as the total quantity. Research has continued to advance our understanding of protein's effects on muscle metabolism; however, there remains a need for large, long-term, randomized clinical trials examining whether the positive effects of dietary protein on muscle metabolism seen in acute studies will translate over the long term into gains of muscle mass, function, and the overall health of older adults.

Keywords
aging, dietary protein, muscle strength, nutrition, sarcopenia

INTRODUCTION

As the older population (>65 years) continues to expand, the progressive loss of muscle mass and function with advancing age is becoming a greater concern. This condition – sarcopenia – is characterized by a gradual loss in skeletal muscle mass, strength, and function; and contributes substantially to frailty, disability, physical dependence, and mortality in older adults. Nutritional interventions, using protein supplementation, have been shown to have beneficial effects on muscle health. This brief review summarizes the current state of research regarding protein intake and skeletal muscle function in older adults.

LOSS OF SKELETAL MUSCLE MASS AND STRENGTH WITH AGING (SARCOPENIA)

Sarcopenia is a common clinical problem that is estimated to occur in at least one in 20 community-dwelling individuals, and as high as one in three in institutionalized frail older adults [1,2]. With advancing age, there is a loss of skeletal muscle strength and function, which affects physical performance and activities of daily living. This loss of strength is usually associated with decreased muscle mass or muscle quality. Debate is ongoing as how to best define and diagnose sarcopenia. Several operative definitions have been published by international consensus panels over the past few years [2,3▪▪,4,5]. The absence of a standard definition makes it difficult to determine the prevalence of sarcopenia and to compare the outcomes of clinical trials. Thus, research into the discovery of sarcopenia's causes and possible treatments has been hindered.

In order to address the existing inconsistencies, a set of articles was published in 2014 by the Foundation for the National Institutes of Health (FNIH) Sarcopenia group [3▪▪,6–10]. This series of articles used pooled data of primarily healthy older adults from a number of large cohort studies and clinical trials to provide evidence-based cut-points for the diagnosis of sarcopenia. Although this is a

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KEY POINTS

- Sarcopenia is a common clinical problem that is becoming of greater concern as the older population continues to grow.

- Mounting evidence suggests that the Recommended Dietary Allowance (RDA) for protein, designed to prevent deficiency, is inadequate to promote optimal health in older adults.

- New research has focused on the quantity, quality, and timing of protein intake to best stimulate muscle protein synthesis (MPS) in older adults.

- There remains a need for large, long-term, randomized clinical trials examining whether the positive effects of dietary protein on muscle metabolism seen in acute studies will translate over the long term into gains of muscle mass, function, and the overall health of older adults.

significant step in the right direction, additional research needs to be carried out to evaluate the specific contributions of skeletal muscle mass and function as it relates to functional outcomes. These thresholds should also be validated in more vulnerable older populations (with acute or chronic diseases, multiple comorbidities, etc.).

Sarcopenia is of great clinical interest because it has been shown to predict loss of independence, falls, and mortality. Recently, several studies have indicated that muscle strength and function effectively predicted mobility decline, disability, and mortality [9,11,12]. The FNIH sarcopenia project found that low grip strength and low lean mass strongly predicted incident mobility impairment [9]. A recent analysis of the Aging and Longevity Study – a prospective cohort study in community-dwelling frail older adults (aged 80–85 years) from the Sirente area – evaluated the impact of sarcopenia on the risk of all-cause death [11]. Twenty-two per cent of patients were found to have sarcopenia. Over the 7-year follow-up period, participants with sarcopenia had a higher risk of death for all causes (67 vs. 41%) as compared to nonsarcopenic patients [11].

Therefore, it is important to identify clinical therapeutic interventions that are able to enhance muscle mass and function in older adults. While exercise is a well known tool to improve muscle mass and function [2,13–15], in older adults, the capacity and/or ability to exercise is often limited. Malnutrition and undernutrition are also important contributing factors to sarcopenia [16–20]. Thus, nutritional interventions represent an important option to preserve muscle mass and function.

PROTEIN RECOMMENDATIONS FOR OLDER ADULTS

It is important to note that protein is the only macronutrient that does not have an inactive compound to serve as a reservoir and thus dietary amino acids must be incorporated into functional proteins. Skeletal muscle contractile proteins are the largest protein reservoirs that respond anabolically to feeding and can be rapidly utilized to supply amino acids to the entire organism during fasting or stress. Insufficient protein intake to satisfy daily requirements leads to negative protein balance and results in skeletal muscle atrophy, impaired muscle growth, and functional decline. Therefore, it is important that the proper amount of protein is consumed to prevent muscle wasting and maintain skeletal muscle mass and function.

What is the current recommendation for protein intake?

RDA is set to provide a sufficient quantity of a particular nutrient to prevent deficiency in the majority of the population. Currently, the RDA for protein (0.8 g protein/kg of body weight/day) is the same for all adults, regardless of age or sex. The Estimated Average Requirement (EAR) is the average daily protein intake level that meets the requirements of half of the healthy adults (0.66 g/kg body weight/day). In addition, the acceptable macronutrient distribution range (AMDR) specifies that protein should represent 10–35% of an individual's total daily energy intake. Interestingly, the RDA typically falls in the lower AMDR range (10–15%) for most adults.

The EAR and RDA recommendations were made based on studies using nitrogen balance as a proxy for protein balance. EAR is calculated using this methodology to be the average minimal amount of protein (nitrogen) intake to balance nitrogen excretion. In theory, if intake matches excretion, there will be no change in protein levels in the body over time. It is important to note that nitrogen balance studies are highly controlled, time-consuming, and difficult to run. Thus, very few well designed studies have been conducted. The results from the few studies done in older adults are conflicting, with some supporting the current protein RDA [21] and others indicating that higher intakes are necessary to prevent nitrogen loss [22]. An alternative method – the indicator amino acid oxidation technique – uses labeled tracer oxidation measured in expired air in response to different amounts of protein to determine the average minimal amount of protein necessary for nitrogen balance. Two recent studies using this technique

found that adults aged 65 years and older require protein intakes greater than the current RDA [23■,24]. These studies support the recent consensus reports that concluded that the current protein recommendation for older adults is too low and that older adults should consume 1.0–1.2 g/kg body weight/day [25,26■,27,28] for optimal health.

How much protein do older adults actually consume?

While many adults consume protein at or above the RDA, a significant proportion of older adults are consuming levels much lower than the RDA [25]. Data from the National Health and Nutrition Examination Survey (NHANES) 2005–2006 showed that 20–24% of older women and 5–12% of older men consumed less protein than the EAR of 0.66 g/kg body weight/day [29]. Thus, considering that the EAR is the mean protein intake sufficient for half of the healthy population, an even greater proportion of the aging population is at risk of inadequate protein intake.

Why do older adults require more protein than younger individuals?

The original RDA recommendations were made based on studies conducted in young healthy adults and do not take into account the many physiological changes that occur with aging. Additionally, these recommendations were based on the concept of preventing deficiency as opposed to promoting optimal health, which may be of greater importance in the elderly. There is mounting evidence that older adults need more dietary protein than their younger counterparts to support good health, promote recovery from illnesses, and maintain functionality.

The most common age-related causes of protein shortfall are inadequate intake of dietary protein (loss of appetite, gastrointestinal issues, reduced energy need, changes in food preference), a reduction in the utilization of available protein (anabolic resistance, insulin resistance, higher splanchnic extraction), and a higher basal requirement (acute and chronic diseases, inflammatory disease, increased oxidation of protein) [11,25,26■,30–34].

What amount of protein is needed to stimulate muscle protein synthesis in older adults?

Muscle growth is dependent upon protein consumption and the accompanying hyperaminoacidemia, which stimulates a marked rise in MPS and a mild suppression of muscle protein breakdown (MPB). Insufficient protein intake to satisfy daily requirements leads to a persistently negative protein balance (MPS is less than MPB) and results in skeletal muscle atrophy, impaired muscle growth, and functional decline. Thus, it is important to identify the quantity of protein that is necessary to optimally stimulate MPS in older adults in order to replenish the amino acids lost during fasting and stress.

Many metabolic studies have demonstrated that utilization of dietary amino acids for MPS is blunted or impaired in healthy older adults as compared to younger individuals. This anabolic resistance can be overcome by higher levels of protein/amino acid intake [14,32]. Recently, multiple studies have indicated that 25–30 g of a high-quality protein is necessary to reach the threshold for maximal stimulation of MPS in older adults [28,33,35■,36,37].

Is the meal pattern important for optimal utilization of dietary protein?

The total quantity of protein consumed daily is important, but recent research indicates that the distribution of dietary protein throughout the day's meals is just as important. For example, older Americans tend to consume a skewed meal pattern with the majority of protein intake occurring during the evening meal. The NHANES 2005–2006 survey data found that women aged above 51 years consumed 11–12 g of protein with breakfast, 15–18 g at lunch, 27–30 g at dinner, and an additional 6–7 g as snacks. Older men (aged >51 years) had a similarly skewed intake patterns (breakfast: 15–16 g, lunch: 18–23 g, dinner: 34–44 g, snacks: 7–11 g).

Three studies recently examined the anabolic efficacy of the quantity and distribution of protein throughout the day in elders. The first study is a cross-sectional analysis examining dietary patterns of German adults grouped into frail, prefrail, and nonfrail [38]. Interestingly, daily protein intake was similar in all groups (1.07 g/kg body weight/day), but the distribution varied by group. The elders in the nonfrail group had evenly distributed protein intake throughout the day, whereas those in the prefrail and frail groups ate a more skewed distribution of protein with higher protein consumption at lunch [38]. Consumption of an uneven distribution of protein was associated with frailty, slower walking speed, and fatigue [38].

The second study – a randomized clinical trial in hospitalized adults aged 85 years and older – grouped individuals into two diets that differed in the distribution of protein during four meals each day [39]. The spread protein diet had relatively evenly distributed protein over the course of four

meals (breakfast: 12.2 g; lunch: 21.0 g; snacks: 13.5 g; dinner: 21.1 g), whereas the pulse protein diet had a larger dose of protein at noon (breakfast: 4.5 g; lunch: 47.8 g; snacks: 2.3 g; dinner: 10.9 g). In this study, patients who were provided the pulse diet had significant increases in lean mass as compared to those on the spread diet [39].

While the results of these two studies seem contradictory at first, the amount of protein (12–21 g) in each of the spread diet meals may not have been adequate to maximally stimulate MPS. Thus, patients consuming the spread diet did not meet the threshold to maximally stimulate MPS at any of the four meals during the day, yet those in the pulse diet had one large dose of protein (48 g) capable of eliciting a robust anabolic response [25,28].

In agreement with this concept, the third study conducted in healthy middle-aged adults found that a diet providing enough protein (30 g) to maximally stimulate MPS at each meal (breakfast, lunch, and dinner) induced the largest 24-h MPS when compared to the same amount of daily protein (90 g) consumed in a skewed pattern (breakfast: 10.7 g; lunch: 16 g; dinner: 63.4 g), in which only the dinner contained enough protein to maximally stimulate MPS [35■].

Collectively, these data indicate that both the total daily protein and the patterns of intake are important to maximally stimulate MPS and maintain muscle mass in older adults.

Is there evidence that protein intake is associated with functional outcomes in older adults?

Several long-term observational studies examining the association of dietary protein intake with body composition and functional outcomes have shown that protein intake is positively associated with preservation of lean mass in older adults [40–44]. The Health, Aging and Body Composition (Health ABC) cohort study found that over a 3-year observation period, lower protein intake was associated with larger loss of lean body mass [40]. Consistently, another prospective cohort study using a subset of data from the Women's Health Initiative found that higher protein intake is associated with a reduction in the loss of muscle strength and function [41].

A recent prospective, nested, case-control study of healthy, community-dwelling adults aged 70 years and older found that the odds ratio (OR) of unhealthy weight loss in participants with low protein intake (<0.8 g/kg body weight/day) was 2.56 compared with participants with high protein intakes (>1.2 g/kg body weight/day). These results suggest that protein intake above 1.0 g/kg body

weight/day was protective against harmful weight loss in healthy elders [43]. A 6-year longitudinal observational study of a subset of women in the Women's Health Initiative population found that higher protein intake was associated with better physical function and with slower rates of functional decline in postmenopausal women [42]. In agreement with these findings is a cross-sectional observational analysis of the relationship between dietary protein on body composition and physical performance in older women aged 60–90 years. Patients were grouped based on protein consumption (below RDA = low protein, above RDA = high protein). Women in the high protein group had lower body mass, higher upper and lower extremity strength, higher short physical performance battery (SPPB) score, and higher physical performance test score, indicating higher muscle strength and physical function [44].

Although these findings are based on associations, they lend further evidence to suggest that older adults might benefit from higher protein intake than the current RDA.

Can we improve muscle mass and function in older adults by increasing protein intake?

A few intervention studies have been conducted to further examine the effects of protein intake on muscle mass and physical function. A recent long-term study in middle-aged adults (45–60 years old) found that patients consuming high protein meals (~35%) more frequently (six times a day) had lower abdominal fat and higher lean body mass as compared to patients consuming a more traditional dietary protein intake [45]. Similar findings were reported in a recent meta-analysis in which patients with higher protein diets (25–32%) had the greatest weight loss [46]. A third study in community-dwelling overweight middle-aged adults found that higher protein diets (1.4 g/kg body weight/day) allowed maintenance of lean body mass during weight loss as compared to diets based on the protein RDA (0.8 g/kg body weight/day) [47]. These studies suggest that high protein diets are beneficial in maintaining lean body mass during weight loss.

Recently, a 6-month intervention in mobility-limited older adults (70–85 years) indicated that protein supplementation (whey protein concentrate 20 g twice daily) in combination with resistance exercise tended to cause greater increases in lean body mass, mid-thigh cross-sectional area, and muscle strength as compared to exercise and an isocaloric nonprotein supplement [13]. These differences did not reach statistical significance perhaps

due to high variability in responses and low compliance.

A 12-week clinical trial in community-dwelling frail older adults examined the effects of protein supplementation (25 g twice daily) on physical function. In agreement with the previous study, patients in the protein supplement group had significant improvements in physical function (increase in physical function test, stable SPPB, improvement in gait speed) as compared to the control group [48]. When taken together, these studies support the notion that protein is beneficial in improving muscle mass and function in older adults.

CONCLUSION

Sarcopenia is a common clinical problem in older adults. Historically, research in this area has been hindered by the lack of a clear definition of sarcopenia. Evidence-based cut-points recently published by the FNIH for the diagnosis of sarcopenia will allow better coordination and comparison of future studies. Whereas exercise remains a fundamental tool for maintenance of muscle mass and function with aging, nutritional interventions involving protein intake patterns and supplementation have emerged as important approaches to managing sarcopenia. Research has continued to advance our understanding of protein's effects on muscle metabolism; however, many questions remain. Should we increase the RDA for older adults, and to what level? How can we incorporate in the RDA the evidence that daily protein intake patterns significantly impact dietary protein retention? How do we adjust protein intakes for ill older adults, considering that the RDA is specifically set for healthy adults yet most older adults have at least one chronic disease? Will the findings from recent acute studies indicating that 20–30 g of protein maximally stimulates MPS translate into improved muscle and functional outcomes?

Conflicts of interest
There are no conflicts of interest.

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