

NUTRITION FOR SKELETAL MUSCLE HEALTH WITH AGING THE ROLE OF DAIRY PROTEIN

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Sarcopenia and the Graying of society

In the United States, the population over age 65 is increasing, parallel with an increasing human life expectancy (cdc.gov). Although people are living longer, quality of life is not necessarily improving; the number of years of impaired living may actually be increasing due to metabolic disease and physical impairments associated with obesity. Based on a publication in *Nature* in 2012 (Scully, 2012) as we age, the prevalence in impaired activities (≥ 1 activities) of daily living (e.g., getting dressed, bathing, transferring laundry, cooking, etc.) increases, suggesting increased physical dysfunction with aging and a larger window of diminished quality of life for older adults. This is in contrast to the decline in prevalence of metabolically related disease (e.g. cancer and diabetes) with increasing age. Overall, older individuals are faced with reduced ability to perform activities of daily living and loss of independence.

Skeletal muscle plays an important and necessary role in overall human health and independence. Skeletal muscle is essential for physical activity and exercise, skeleton support, metabolic processes and endocrine functions. The human body of a young adult is comprised of approximately 35-45%. However, as we age, skeletal muscle mass declines to approximately 25-30% of body weight by the age of 70 years. Loss of skeletal muscle mass begins as early as the third decade of life (Lexell J, 1988) and continues until death. Intriguingly, men lose skeletal muscle mass and strength and gain fat mass at a greater rate than women (Goodpaster et al., 2006; Janssen et al., 2000). Age-related changes in skeletal muscle, such as the involuntary loss of muscle mass (sarcopenia) and associated decrease in strength, increase the risk for falls and fractures as well as loss of mobility and independence (Bales and Ritchie, 2002; Doherty, 2003) and have been linked to physical disabilities in older adults (Rantanen et al., 1999). Concurrent with sarcopenia, fat and fibrotic tissue accumulation within and around skeletal muscle increase with age which combined likely increases one's risk for functional disability and metabolic dysregulation (Zoico et al., 2004).

There are many endogenous (e.g., muscle denervation, changes in autocrine, paracrine, and endocrine factors, inflammation, oxidative stress, mitochondrial dysfunction, and changes in protein metabolism) and exogenous factors (e.g. decreased physical activity and changes in dietary intake) that influence skeletal muscle deterioration. These effectors instigate muscle atrophy, functional decline, and metabolic dysfunction, which ultimately promotes weakness, loss of mobility, and metabolic disease, culminating in loss of independence.

Optimal therapies to maximize muscle health for older adults are essential. Unfortunately, optimal therapies for preventing or augmenting muscle deterioration have yet to be clearly defined. Dietary protein and branched chain amino acids, particularly leucine, are among the recommended therapies to attenuate muscle deterioration.

Dietary protein and amino acid requirements

Protein balance is important for maintaining muscle mass. Imbalanced protein metabolism from inadequate protein intake generally results in clinical manifestations such as muscle atrophy, impaired muscle (re)growth, and functional decline. Adequate dietary protein is essential for overall human health with recommendations differing throughout the human lifespan. As there are no true body stores for protein, insufficient protein intake to satisfy body requirements leads to a negative protein balance (i.e. protein synthesis lower than breakdown). The Recommended Dietary Allowance (RDA) for dietary protein is $0.8 \text{ g} \cdot \text{kg body weight}^{-1} \cdot \text{day}^{-1}$. However, in individuals with increased stress (e.g., infection, trauma, etc.), the dietary protein needs increase to minimize skeletal muscle atrophy from rapid degradation of skeletal muscle proteins. There is some consensus that older adults may also need a higher level of dietary protein intake.

Amino acids are the basic building blocks of endogenous proteins. Amino acids are provided from exogenous dietary protein and amino acid sources and from endogenous protein breakdown. On a daily basis, 300 g of endogenous protein are synthesized and degraded; approximately 3-4 % of our total body protein is turned over daily. The overall goal of daily protein consumption is positive protein balance. Protein balance is the balance of protein synthesis and protein breakdown. Amino acids are used for multiple purposes in the body including protein synthesis, energy production, and synthesis of glucose, non-protein derivatives, and non-peptide hormones. During the fed state, amino acids are provided through dietary sources. However, during the fasting state, skeletal muscle protein breakdown provides the amino acids necessary to complete body needs and functions.

Impaired skeletal muscle protein synthesis in old adults

Older adults have a blunted anabolic response to ingestion of dietary protein and leucine, a key essential amino acid for stimulating skeletal muscle protein anabolism. In relatively healthy, older adults, acute studies demonstrate that old (vs. young) adult skeletal muscle has an impaired protein synthesis response to dietary protein intake less than 20 g, but a comparable anabolic response is observed between younger and older adults following 25-30 g of protein in a single meal (Paddon-Jones and Rasmussen, 2009). Additionally, when compared to young adults, old adults have impaired or blunted anabolic responses to amino acid ingestion (7-10 g of EAA (Cuthbertson et al., 2005; Katsanos et al., 2005)). Additionally, research from our laboratory demonstrated that the skeletal muscle gene expression profile reflects an accommodative response to dietary protein in older males, such that older adults given the a diet containing dietary protein intake at and above the RDA had lower expression

of genes related to protein synthesis and modification, while consumption of a diet containing dietary protein at or below the RDA the older skeletal muscle had higher expression of genes related to protein catabolism (i.e. degradation) (Thalacker-Mercer et al., 2010).

Paddon-Jones et al., using the NHANES dataset demonstrated that the U.S. population is inclined to consume protein in a skewed dietary pattern, with more protein consumed at dinner and the least amount consumed at breakfast (Paddon-Jones et al., 2015). Mamerow et al. (Mamerow et al., 2014) demonstrated that consumption of dietary protein in the skewed pattern led to lower 24 h mixed muscle fractional synthesis rate compared to a diet containing dietary protein consumed in an even distribution (i.e. equal amount of dietary protein consumed at each meal throughout the day). Based on these and other studies, investigators have proposed a new pattern of dietary protein intake to maximally stimulate skeletal muscle protein synthesis in older adults, with the overarching goal of maximizing the anabolic response to dietary protein and/ or leucine intake. Researchers proposed older adults consume 30 g of dietary protein at breakfast, lunch, and dinner (90 g of protein consumed daily). The proposed 30:30:30 g protein diet for older adults has raised several concerns by clinicians, including how to get older adults to consume dietary protein at such a high amount, three times a day, when clinicians have a challenging time getting older adults to consume dietary protein.

Dairy protein for maximizing muscle protein balance in older adults

Although relatively few studies have investigated the long-term use of dairy products for skeletal muscle health, acute and short-term studies have demonstrated that dairy protein may provide the necessary substrate for maximal gains in skeletal muscle protein synthesis and muscle mass compared to other protein sources. Studies have demonstrated that milk and whey protein (vs. soy protein) yield better gains in lean body mass (a measurement of body composition containing skeletal muscle mass) when coupled with resistance exercise. Gains in lean body mass among younger adults are potentially due to greater stimulation of muscle protein synthesis and greater net protein balance following resistance exercise coupled with milk consumption (500 mL) compared to soy protein that is isonitrogenous, isoenergetic, and macronutrient matched (Wilkinson et al., 2007). Further, maximal stimulation of protein synthesis, in younger adults, could be attributed to the whey protein in milk products; whey protein stimulates greater protein synthesis and net protein balance after resistance exercise compared to casein and soy (Tang et al., 2009). Similarly, among older adults, whey protein stimulates muscle protein accretion more effectively than casein or casein hydrolysate (Pennings et al., 2011). In a review of studies examining the effects of protein source on changes in lean body mass, Phillips et al. (Phillips et al., 2009) demonstrated that milk and the milk protein whey resulted in greater gains in lean mass with resistance exercise training in both younger and older adults. The research is further supported by Radavelli-Bagatini et al. (Radavelli-Bagatini et al., 2014) who identified that older age women consuming ≥ 2.2 servings per day of dairy (1.5 servings per day of milk) had greater appendicular skeletal muscle mass than older women consuming ≤ 1.5 servings of dairy per day (0.8 servings per day of milk). While these

studies support the promising benefits of dairy products, particularly whey protein, for skeletal muscle protein metabolism and potentially mass, it is important to note that the leucine content of milk and whey protein is 77 and 108 mg leucine / g, respectively, compared to 62 mg leucine / g protein in soy protein; therefore, the beneficial effects of milk and whey proteins could come from greater leucine content in the milk and whey proteins. Never-the-less, research supports that dairy proteins could be beneficial for maintaining skeletal muscle mass in older adults.

Obesity in older adults—challenges faced and the role of dairy protein

Thirty-35% of older adults (65-85 years of age) are obese. Obesity and sarcopenia are both associated with increased risk for falls and immobility and sarcopenic obese older adults have decreased walking speeds and hand-grip strength compared to obese older adults without sarcopenia. Caloric restriction-induced weight loss is controversial for older adults as it initiates loss of lean body mass in conjunction with loss of fat mass. Therefore, there is the need for therapies to reduce fat mass among older adults while maintaining skeletal muscle mass (Smith and Mittendorfer, 2015). High calcium diets have been shown to promote adipocyte apoptosis. Additionally, high branched chain amino acid content in milk protein is an important factor in repartitioning dietary energy from adipose tissue to skeletal muscle. The high calcium and branched chain amino acid content of milk supports a potential dietary therapy that would minimize adiposity and maximize lean body mass (Zemel, 2004; Zemel and Miller, 2004; Zemel et al., 2004).

Milk and other dairy proteins are a promising protein product for older adults

In addition to adverse changes in skeletal muscle protein metabolism and body composition, older adults are challenged by a number of biological and social changes that affect their ability obtain and consume the necessary dietary protein to meet their needs. Challenges include but are not limited to changes in economic status; adverse changes in dentation (loss of teeth and sensitivity to foods); the inability or loss of desire to prepare food; and single serving food preparation.

Table 1. Protein content of common dairy products*

	Protein (g)	Lactose (g)
Greek yogurt, plain, nonfat, 150-170 g	15-17	4-7
Cottage cheese, 0.5 cup	15	3
Milk, 8 oz glass		
Whole (3.25% milk fat)	7.7	12-13
2% milk fat	8.1	12-13
1% milk fat	8.2	
Skim (nonfat)	8.3	12-13

*protein and lactose contents are approximations and will vary based on product and manufacturer.

Dairy products are a high quality protein source (Table 1) and address the observed dietary challenges faced by older adults, including affordability. Dairy protein comes in single servings that require no to minimal preparation and can be consumed despite dentation challenges faced by older adults due to the liquid or soft texture. With ongoing research regarding the balanced 30:30:30 g dietary pattern for protein intake, particularly among older adults, the common goal is to maximize skeletal muscle protein synthesis throughout the day with high quality protein. In general, commonly consumed dairy products offer a great food source of dietary protein for older adults given the dietary considerations faced by older adults.

There is some concern regarding the use of dairy products and higher protein in the diets of older adults. The common challenges and/ or concerns with consuming diets high in protein and/ or dairy products include lactose intolerance and chronic kidney disease. Lactose intolerance occurs as a result of fewer lactase enzymes, the enzymes required to digest lactose. There is a reported higher prevalence of lactose intolerance among African- and Native-Americans (~75 %) as well as Asian-Americans (~90%). However, the lactose content of dairy products varies (Table 1); dairy proteins can be chosen based on their lactose content or lactose-free products are also available. In addition to lactose, there is a general concern regarding the consumption of too much protein. Diets high in protein can lead to kidney stones and/or impaired function of the kidney due to extra metabolic stress. Patients with chronic kidney disease need to limit their protein intake. (http://www2.kidney.org/professionals/KDOQI/guidelines_ckd/p6_comp_g9.htm).

FUTURE DIRECTIONS

Studies have demonstrated dairy products are associated with greater skeletal muscle gains and/ or maintenance of skeletal muscle among older adults suggesting dairy enriched diets may be optimal for muscle health. However, there is insufficient evidence to determine whether gains in muscle anabolism and mass, due to a diet rich in dairy products, are associated with gains in skeletal muscle quality and function. Additionally, research up to this point has focused primarily on the impact of specific proteins or amino acids (i.e. leucine) on skeletal muscle protein synthesis. However, it is likely other bioactive compounds found in dietary protein sources are important for promoting skeletal muscle health and metabolism. Preliminary data from our laboratory suggest that other nutrients, aside from leucine, are essential for skeletal muscle health in older adults. Recognizing dairy products provide a unique nutrient profile associated with skeletal muscle health in older adults is essential for establishing a dairy-enriched diet as an optimal therapy for attenuating sarcopenia.

SUMMARY

In summary, the population over the age of 65 years is a growing demographic in the United States and globally. Older adults are challenged by impairments in activities of daily living and functional decline with advancing age; adverse physical challenges

related to skeletal muscle health. Appropriate therapies to attenuate skeletal muscle deterioration are necessary but have yet to be clearly defined. Dairy proteins offer a promising therapy for maximizing skeletal muscle protein metabolism and gains and potentially preserving muscle during energy restricted weight loss among obese older adults. The translation of acute studies to long-term improvements in skeletal muscle and overall metabolic health of older adults has yet to be addressed. Despite the need for additional research regarding dairy proteins for long-term muscle health, dairy products are an ideal source of dietary protein and other nutrients for older adults, particularly for overcoming physiological and sociological challenges faced with advancing age.

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