

Increasing Dietary Protein Requirements in Elderly People for Optimal Muscle and Bone Health

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Osteoporosis and sarcopenia are degenerative diseases frequently associated with aging. The loss of bone and muscle results in significant morbidity, so preventing or attenuating osteoporosis and sarcopenia is an important public health goal. Dietary protein is crucial for development of bone and muscle, and recent evidence suggests that increasing dietary protein above the current Recommended Dietary Allowance (RDA) may help maintain bone and muscle mass in older individuals. Several epidemiological and clinical studies point to a salutary effect of protein intakes above the current RDA (0.8 g/kg per day) for adults aged 19 and older. There is evidence that the anabolic response of muscle to dietary protein is attenuated in elderly people, and as a result, the amount of protein needed to achieve anabolism is greater. Dietary protein also increases circulating insulin-like growth factor, which has anabolic effects on muscle and bone. Furthermore, increasing dietary protein increases calcium absorption, which could be anabolic for bone. Available evidence supports a beneficial effect of short-term protein intakes up to 1.6 to 1.8 g/kg per day, although long-term studies are needed to show safety and efficacy. Future studies should employ functional measures indicative of protein adequacy, as well as measures of muscle protein synthesis and maintenance of muscle and bone tissue, to determine the optimal level of dietary protein. Given the available data, increasing the RDA for older individuals to 1.0 to 1.2 g/kg per day would maintain normal calcium metabolism and nitrogen balance without affecting renal function and may represent a compromise while longer-term protein supplement trials are pending. *J Am Geriatr Soc* 57:1073–1079, 2009.

Key words: sarcopenia; osteoporosis; dietary protein; nutrition; aging

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DOI: 10.1111/j.1532-5415.2009.02285.x

Sarcopenia is the loss of muscle mass that frequently occurs during aging and can be defined using the skeletal muscle mass index (SMI). A SMI between 1 and 2 standard deviations (SDs) below young adult values is termed Class I sarcopenia, and a SMI more than 2 SDs below young adult values is Class II sarcopenia.¹ Muscle mass begins to decline at approximately age 45 to 55 after peak muscle mass is attained in middle adulthood. There are multiple causes of sarcopenia, and an understanding of the complex etiology is evolving. Sarcopenia is estimated to affect 30% of individuals aged 60 and older, and more than 50% of those aged 80 and older.² Chronic muscle loss is associated with disability; the likelihood of disability is three to four times as great in those with sarcopenia independent of age, sex, and a variety of other factors.³ Contributing factors to sarcopenia include impaired protein turnover rate, neurodegenerative processes, reduced anabolic hormone production and response, dysregulation of cytokines, inflammatory changes, sedentary lifestyles, and inadequate nutritional intake, including protein.⁴ Adequate dietary protein is important for attaining peak muscle mass in young adulthood, and increasing dietary protein may be important for preserving muscle mass in later years.

Osteoporosis is the loss of bone mineral density (BMD) that is also considered a consequence of aging. The World Health Organization defines osteoporosis as BMD of 2.5 SDs or more (T score) below normal peak values for young adults. Osteopenia refers to BMD T scores between -1 and -2.5. Osteoporosis and osteopenia affect almost 44 million Americans aged 50 and older. With the accelerating growth of the older population, it is estimated that 52 million people will suffer from osteoporosis or osteopenia by 2010.⁵ Rates of bone loss in women accelerate during the menopausal years, when estrogen levels decline rapidly, resulting in accelerated rates of skeletal catabolism. After the menopausal years, the rate of bone loss in women slows slightly and becomes more comparable to that seen in older men. Peak bone mass is obtained somewhere between the ages of 16 and 18 and remains relatively stable until age 35 to 40, after which bone mass, like muscle mass, begins to decline.⁶ Maximizing peak bone mass (PBM) is therefore an impor-

tant way to prevent osteoporosis. Although calcium and vitamin D are essential for bone health, recent evidence supports the hypothesis that dietary protein is also critical for bone health and fracture reduction.⁷ Bone is approximately 50% protein matrix, so it is not surprising that dietary protein is an essential nutrient for the development of maximum PBM, although recent evidence also suggests that dietary protein has an important role in skeletal health throughout adulthood.⁸⁻¹²

Given the debilitating and costly nature of sarcopenia and osteoporosis, preventing and treating these diseases is of great public health importance. The loss of muscle and bone tend to occur at approximately the same time, and changes in muscle and bone mass are correlated.^{13,14} Dietary protein is important for muscle and bone development. The original recommended requirement for dietary protein (that which was required to achieve nitrogen equilibrium) was 1.0 g/kg until the 1980 RDAs, when it was subsequently decreased to 0.8 g/kg, which is the current RDA for all adults aged 19 and older. Because energy requirements decline with age, 0.8 g/kg represents a larger percentage of energy in elderly than in younger adults. This review will outline the evidence supporting a role for increasing the RDA for dietary protein in the aging population to optimize muscle and bone mass and strength.

THE HISTORY OF THE CURRENT PROTEIN RECOMMENDATIONS

There is a growing body of evidence suggesting that the current recommendations for dietary protein in the elderly population (≥ 65) are inadequate for optimal muscle and bone health.^{4,10,12,15-17} The current recommendations were developed using a large body of literature employing nitrogen balance techniques to assess protein requirements. Using nitrogen balance to determine a protein requirement is vastly different from determining the optimal level of protein needed to prevent or attenuate a chronic disease such as sarcopenia or osteoporosis. Given concerns about sarcopenia and bone loss, it would be better to base recommendations for the optimal level of dietary protein on functional outcomes, including maintenance of bone and muscle mass. The following discussion details the current dietary protein recommendations and their limitations.

In 2002, the Food and Nutrition Board, in conjunction with the Institute of Medicine (IOM), the National Academies, and Health Canada, published the *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*.¹⁸ This comprehensive document provides a set of reference values for nutrient intakes for healthy U.S. and Canadian individuals and populations based on the best scientific data available at that time. The dietary reference intakes (DRIs) are composed of several reference values: the Estimated Average Requirement (EAR), RDA, Adequate Intake (AI), and Tolerable Upper Intake Level.

The RDA for protein for men and women aged 19 and older was set at 0.8 g of good-quality protein per kg body weight per day or approximately 56 g/d for men and 46 g/d for women when using the reference weights of 70 kg and 57 kg, respectively. This level of dietary protein corresponds to 10% of total caloric intake when energy needs approx-

imate 2,000 to 2,200 kcal/d. The RDA for protein was determined using meta-analysis of the short-term nitrogen balance studies rather than large-scale clinical studies and was therefore limited by short comings in nitrogen balance methodology. Nitrogen balance refers to the difference between the amount of nitrogen consumed (as dietary protein) and the amount excreted in urine and feces combined with losses via skin and hair. The purpose of a nitrogen balance study is to determine the minimum amount of protein required in the diet to place the individual at zero nitrogen balance. This level of dietary protein would theoretically prevent nitrogen deficiency, because it was assumed that zero balance equals the protein requirement. In contrast, the acceptable macronutrient distribution ranges (AMDR) set out an upper range for protein of 35% of calories once the levels of the other macronutrients were determined because there were insufficient data to establish a Tolerable Upper Intake Level for protein. Therefore, the recommended range of dietary protein is 10% to 35% of total caloric intake, with 10% representing 0.8 g/kg per day using the reference weights.

The well-known limitations of using nitrogen balance studies to determine protein requirements are discussed in the IOM report.¹⁸ Some are practical limitations, but others are methodological limitations that probably result in an underestimation of true protein requirements. There are three principal limitations of nitrogen balance studies. First, urea turnover in adults is slow, so several days of adaptation are needed to reach a new steady state. This represents a practical limitation because studies employing nitrogen balance need to include a long adaptation time, which may limit the number of protein levels tested in any given individual. Because nitrogen balance studies may not be conducted at a level of protein intake that results in zero nitrogen balance, individuals must be studied at several protein levels and the results interpolated to determine zero balance. Such studies would perforce be long. Second, the measurement of nitrogen intake and excretion is difficult and therefore tends to be relatively inaccurate. Specifically, intake is frequently overestimated, whereas excretion is frequently underestimated, so the net effect is a bias toward a more-positive nitrogen balance. For example, there have been many instances in which an unusually large positive nitrogen balance was observed in adults at higher protein intakes.¹⁹ Because adults do not normally accrue a large mass of protein, persistently positive nitrogen balance is biologically implausible and therefore probably explained by measurement error. Additionally, the magnitude of nitrogen balance and the stability of body weight are inconsistent with each other, probably because of the overestimation of nitrogen balance. In other words, if nitrogen balance was significantly positive, a proportional increase in total body weight, particularly lean body mass, would be expected, which has not been documented in the literature. Studies published after the 2002 DRIs were established indicate that individuals can adapt to low-protein diets by reducing nitrogen excretion, resulting in a disconnect between nitrogen balance and muscle mass or strength, which may help explain the observed inconsistency between body weight and nitrogen balance.²⁰ Finally, dermal and miscellaneous nitrogen losses are typically estimated and can vary greatly based on environmental conditions.

The majority of nitrogen balance studies used low levels of protein intake, which produced a negative nitrogen balance. The protein level required to reach zero balance was then extrapolated by plotting nitrogen balance against protein intake. Because adaptation occurs during low protein intake, and the efficiency of nitrogen use declines as zero nitrogen balance is approached, extrapolating to zero balance would probably result in an underestimation of the true requirement. In a study designed to examine nitrogen balance in older women consuming three levels of dietary protein for 3 weeks, nitrogen balance had still not reached steady state by 3 weeks, and the authors concluded that protein needs for elderly women were at or above the current RDA.²¹ Additionally, the relationship between nitrogen intake and balance is not likely to be linear, but linear interpolation had to be used in the IOM meta-analysis because the published studies do not include enough data points on each individual. With a larger number of data points, more-appropriate statistical analyses such as smooth nonlinear or two-phase linear models, which may better describe the relationship between nitrogen intake and nitrogen balance, could have been used. Furthermore, the majority of the nitrogen balance studies used for the IOM meta-analysis were conducted on younger men, and it is tenuous to extrapolate those results to older men and women.

The current RDA does not take into account the changes that occur with age, such as reduced muscle mass, increased fat mass, changes in food intake and physical activity, and more-frequent illness.²² Given the potential for the protein RDA to be insufficient for elderly people consequent to the limitations inherent to nitrogen balance studies, there are two logical questions to ask. First, are there more-accurate ways to measure protein status in elderly people, and what are the results of studies using these techniques? Second, what outcomes other than nitrogen balance can be used to evaluate protein status for optimal bone and muscle health in this population?

EPIDEMIOLOGICAL EVIDENCE SUPPORTS A POSITIVE RELATIONSHIP BETWEEN DIETARY PROTEIN AND BONE AND MUSCLE MASS

Although many Americans consume more than the RDA for dietary protein, research shows that a significant number of elderly people do not meet the estimated average requirement let alone the RDA;²³ between 32% and 41% of women and 22% to 38% of men aged 50 and older consume less than the RDA for protein.²⁴ Epidemiological studies show that protein intake is positively associated with preservation of muscle mass. For example, in a recent study, 38 healthy, normal-weight, sedentary women aged 57 to 75 were recruited to determine whether a higher muscle mass index was associated with animal or vegetal protein intake.²⁵ The investigators found that animal protein intake was the only predictor of muscle mass index of all variables studied. In a second study, 50 healthy men and women aged 60 to 75 were recruited for a study designed to examine the association between antioxidant and protein intake and class I sarcopenia, the earliest stage of muscle loss.²⁶ The prevalence of sarcopenia was 23.5% in the women and 25.0% in the men. Although the sarcopenic and

nonsarcopenic groups consumed more protein than the RDA, the investigators observed a positive relationship between protein intake and preservation of muscle mass. In the recent Health, Aging and Body Composition longitudinal study designed to assess protein intake and 3-year changes in lean mass (LM) and nonbone appendicular LM (aLM), changes in LM and aLM were associated with protein intake.²⁷ It was reported that individuals in the highest quintile of protein intake lost approximately 40% less LM and aLM than those in the lowest quintile. These findings suggest that protein intake above the RDA may be optimal for prevention or attenuation of sarcopenia.

The majority of observational studies support a positive association between protein intake and bone health. There are several epidemiological studies, both cross-sectional and longitudinal, that have reported an association between dietary protein and bone.⁸⁻¹⁰ These studies reveal that individuals who consume the most dietary protein have the highest BMD. In addition, prospective studies have observed that individuals with the highest protein intake have the slowest rate of bone loss.^{8,28} Another study with cross-sectional and longitudinal components found a dose-response relationship between the tertiles of dietary protein (<66, 66-87, and >87 g/d) and BMD in 1,077 women with a mean age of 75 ± 3 .²⁹ Although epidemiological studies cannot prove causality, they point to a beneficial effect of higher dietary protein on skeletal health and provide a basis for clinical intervention trials.

Other epidemiological studies have shown a positive association between dietary protein and additional outcomes (other than bone and muscle mass). In longitudinal studies, protein intake of 1 g/kg per day was found to maintain protein status in community-living elderly people as measured according to serum protein and upper arm mass.³⁰ In another 10-year longitudinal study in New Mexico, women with protein intake of 1.2 to 1.76 g/kg per day tended to have fewer health problems than women consuming 0.8 g/kg per day (the RDA).³¹

However, some cross-sectional studies report a positive association between dietary protein intake and hip fracture incidence, leading to the hypothesis that higher protein intake is detrimental to skeletal health.^{32,33} Unfortunately, the use of Per Capita Food Supplies to estimate individual dietary protein intake and inadequate control for lifestyle factors that affect BMD and fracture risk limited these studies. Another cross-sectional epidemiological study showed inconsistent associations between bone density and habitual protein intake, with varying results depending on the site measured,³⁴ whereas others found a positive association rather than a negative one.⁸⁻¹⁰

The epidemiological studies are intriguing, and the majority support the notion that protein intakes greater than the RDA are associated with better bone and muscle health in the older population. There are several clinical intervention trials whose findings are consistent with the epidemiological observation that higher-protein diets are associated with better muscle and bone health. Although these clinical studies support a causal relationship between dietary protein and bone and muscle health, longer trials are needed to confirm these findings and establish the magnitude of effect and relevance to different populations.

HIGHER PROTEIN INTAKE IS ANABOLIC FOR ELDERLY MUSCLE

Although protein appears to be anabolic for muscle in young and elderly adults, protein metabolism differs between age groups. Using isotope methodology, recent studies have characterized protein metabolism with various levels and types of protein and amino acid intake, as well as the presence or absence of other macronutrients (e.g., glucose).³⁵⁻⁴¹ One common isotope method employs ¹³C-leucine for the measurement of whole-body protein turnover, and another method uses ²H/¹⁵N-phenylalanine infusions in combination with arteriovenous catheterization and muscle biopsies for measurement of amino acid incorporation (protein synthesis) and release (protein breakdown) from proteins in a specific tissue.

Several studies designed to determine how intravenous or oral amino acids affect muscle protein synthesis in healthy elderly individuals have been conducted. In one study, the isotope method with femoral arteriovenous catheterization and muscles biopsies was used to investigate muscle protein synthesis and breakdown in response to amino acid infusion.³⁸ Amino acid infusion resulted in greater protein synthesis, with no change in protein breakdown, resulting in a net (net = protein synthesis - protein breakdown) anabolic effect. This study showed that increases in circulating amino acids are anabolic to muscle in healthy elderly people. It remains unclear whether the anabolic response to amino acids noted in elderly people is similar to that in younger individuals. Some studies have found that protein turnover is lower in older adults and that a greater proportion of turnover comes from visceral protein stores.³⁷ Others have shown that the anabolic response to protein in elderly people is not different,^{38,39} whereas others point to an impairment of the anabolic response with aging.^{36,40}

There are important differences between how elderly individuals and younger individuals metabolize protein, including the proportion of dietary amino acids extracted by the splanchnic bed and the postprandial concentrations of circulating amino acids. Specifically, a study using the arteriovenous catheterization method investigated the effect of an oral amino acid supplement on muscle protein turnover during the postabsorptive state; a 40-g oral amino acid supplement given in small boluses over a 3-hour period increased muscle protein synthesis and net balance to the same extent in healthy elderly volunteers (71 ± 2) as in young volunteers (30 ± 2).³⁹ While the splanchnic extraction of phenylalanine was greater in the elderly subjects, delivery of this amino acid to the periphery was not different. In contrast, when the anabolic response to an oral supplement containing amino acids and glucose was evaluated, the increase in arterial asparagine and histidine was blunted in elderly people, as was the anabolic response to the supplement.³⁶ A recent article also concluded that the anabolic response to a protein-rich meal was the same in elderly men and women (mean age 70.2 ± 5.1) as in younger adults (mean age 41.1 ± 8.0).³⁵ As measured according to stable isotope kinetics, feeding a 4-ounce portion of lean beef resulted in an approximately 51% increase in fractional synthetic rate in the younger and older groups. In both groups, plasma essential amino acid (EAA) concen-

tration increased after the beef meal, with a maximum increase 100 minutes after the meal. Nevertheless, the rate of increase and maximum increase were greater in the elderly group than in the younger group, suggesting that a larger precursor pool of amino acids was necessary to elicit the same anabolic response in muscles in elderly than in younger adults. The lower body weight, body mass index, and body muscle mass of the elderly subjects, which would result in greater protein intake per kg of body weight, may explain the larger precursor pool. In total, these findings suggest that higher protein intake may be necessary to insure adequate delivery of amino acids to the periphery in the setting of a mixed macronutrient supplement and perhaps to overcome an impaired insulin response (as discussed below).

Other studies have shown differences in whole-body protein and muscle protein synthesis between elderly and younger adults based on the rate of appearance of plasma amino acids. In elderly people, whole-body protein gain was greater in response to quickly digested proteins than to slow proteins, suggesting that, although elderly people can respond anabolically to dietary protein, the anabolic threshold may be higher in elderly people than in younger.⁴¹ In a nitrogen balance study in older women, a "pulse diet," in which 80% of the daily protein intake was provided in one meal, was associated with a more-positive nitrogen balance than in the "spread diet," in which the same daily protein was spread over four meals.¹⁶ The pulse diet was also associated with maintenance of fat-free mass and higher rates of protein turnover than the spread diet. Although plasma amino acids were not measured in these women, a greater increase in amino acids would be expected after the pulse diet than the spread meals. The protein level in this study was 1.6 g/kg of fat-free mass per day, which was equivalent to approximately 1.0 g/kg per day. This level is above the RDA for this age group, but the spread diet group still lost fat-free mass during the 2-week intervention. These results suggest that even 1.0 g/kg of protein per day may be insufficient to maintain muscle mass in elderly women, depending on the pattern of protein intake. This underscores the inadequacy of nitrogen balance as an endpoint to determine optimal protein intake, because both groups were in positive nitrogen balance. The above observations are significant to public health, given the implication that protein intake should be increased in elderly people and the pattern of intake possibly modified to optimize muscle mass.

Finally, the difference in the anabolic response to amino acids noted with aging could be due to decreased insulin production or sensitivity. Therefore, using a carbohydrate source along with the protein may lead to different outcomes. Decreased production or sensitivity to anabolic hormones, such as insulin, with age could explain the blunted anabolic response to a mixed meal.³⁶ For example, when an oral amino acid study was repeated with a mixture of amino acids (40 g) and glucose (40 g), the anabolic response was more attenuated in healthy elderly subjects (72 ± 1) than in the younger (30 ± 3) volunteers.³⁶ To answer the question of whether age-related loss of muscle protein may involve a decreased response to anabolic stimuli, a study investigated muscle protein synthesis in six young (25 ± 1) and eight elderly (72 ± 2) subjects during a

euglycemic hyperinsulinemic hyperaminoacidemic clamp using isotopic leucine infusion.⁴⁰ Although protein synthesis increased in the younger and older subjects, the increase was blunted in the older group. In a study of the hyperinsulinemic anabolic response in two groups of elderly individuals, one group was assigned to a bout of aerobic activity and the other to a nonexercise control group. It was found that the anabolic response to insulin was restored in the exercise group as measured according to mammalian target of rapamycin (mTOR) activity and net muscle protein balance.⁴² mTOR is a kinase involved in cell growth (as described in the Mechanisms section below). Cumulatively, the above studies show that, although elderly muscle can respond to the anabolic stimulus of dietary protein and amino acids, there is an impairment in the anabolic response to mixed meals containing dietary protein. Specifically, protein turnover is lower in the postabsorptive state, and splanchnic extraction of certain dietary amino acids is greater in elderly people.

HIGHER PROTEIN INTAKE IS BENEFICIAL FOR CALCIUM METABOLISM AND BONE HEALTH

Increasing dietary protein in humans results in higher urinary calcium.²⁴ Because previous calcium balance studies did not show an improvement in calcium absorption, the increase in urinary calcium was assumed to be of bone origin, which lead to the hypothesis that high protein diets are detrimental to the skeleton.⁴³ This formulation posits that increasing protein intake results in a fixed metabolic acid load that the large carbonate reservoir in the skeleton must buffer.⁴⁴ As a result of releasing carbonate, calcium would also be released. Over time the increase in bone resorption would lead to decreased BMD, but with the use of calcium isotopes, calcium handling can be much more precisely measured than with balance studies, and it appears that this hypothesis is incorrect. Recent studies show that the increase in urinary calcium excretion is due to improved intestinal calcium absorption, and high protein diets do not result in negative skeletal calcium balance.^{12,15}

Three recent diet-controlled studies employed calcium isotope methodology to evaluate the effects of increasing dietary protein on calcium metabolism.^{11,12,15} All three studies suggested that high-protein diets are not detrimental to skeletal health but rather are beneficial. The first study examined 15 healthy postmenopausal women during 8 weeks of a low- (12% of energy) or high-protein (20%) diet in a randomized crossover design.¹¹ Midway through each diet, calcium retention was measured by extrinsically labeling the diet with ⁴⁷Ca for 2 days. Twenty-eight days of whole-body scintillation counting followed the labeling phase. Although not significant, there was a trend toward better calcium retention during the high-protein diet. In a recent second trial, 27 healthy postmenopausal women were studied in a two-by-two factorial study under conditions of high and low dietary protein and high and low dietary calcium for 7 weeks each.¹⁵ When calcium intake was 675 mg, increasing dietary protein from 10% to 20% of total energy resulted in better calcium absorption. Using dual-stable calcium isotopes, we found that increasing dietary protein from moderate (1.0 g/kg per day) to high (2.1 g/kg per day) for 1 week in young and postmenopausal

women results in greater intestinal calcium absorption with no increase in bone resorption.¹² Greater calcium absorption would then be expected to decrease parathyroid hormone (PTH) secretion. PTH raises serum calcium in part by increasing bone resorption; therefore, long-term elevations in serum PTH would be detrimental to the skeleton. Because increasing dietary protein increases intestinal calcium absorption, over time this effect could be beneficial to the skeleton by suppressing PTH secretion. We also observed a trend toward lower bone turnover during the high-protein diet, which is thought to be beneficial to the adult skeleton.¹² The above studies show that increasing dietary protein for at least 1 to 8 weeks has beneficial effects on the skeleton. Long-term protein supplement studies are needed to determine whether the beneficial effect of dietary protein continues beyond 2 months. Epidemiological data currently support the hypothesis that a habitually high protein intake promotes bone health,⁸⁻¹⁰ but controlled intervention studies with BMD and fracture rates as the primary outcome variables are needed.

POTENTIAL MECHANISMS FOR THE FAVORABLE EFFECT OF DIETARY PROTEIN ON MUSCLE AND BONE HEALTH

There are several mechanisms by which dietary protein may improve muscle and bone mass and strength (Figures 1 and 2). Muscle synthesis is dependent on adequate quantities of EAAs. Leucine, one of the EAAs, has recently been recognized as particularly important as a signaling molecule and a building block for muscle. Rat studies show that leucine can directly stimulate muscle protein synthesis through increasing messenger ribonucleic acid translation and thus global protein synthesis.⁴⁵ Amino acids (especially leucine) and insulin are anabolic stimuli for muscle and share a

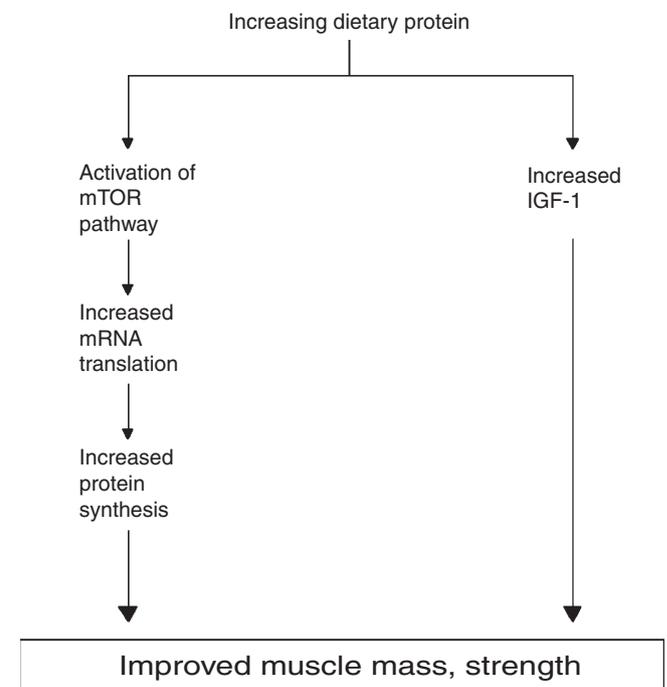


Figure 1. Potential mechanisms by which increasing dietary protein improves muscle health.

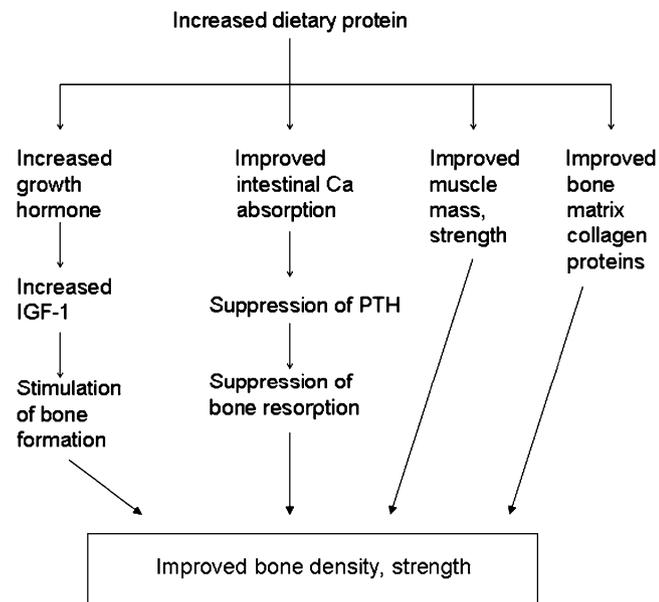


Figure 2. Potential mechanisms by which increasing dietary protein improves bone health.

common pathway of action via activation of a kinase known as mTOR.⁴⁶ mTOR is a master regulator of cell growth and exerts its actions by phosphorylating target proteins involved in mRNA translation. Because insulin sensitivity decreases with age, one possible mechanism by which amino acids might improve muscle mass is by providing another anabolic stimulus to activate the mTOR-controlled pathway. As reviewed elsewhere,⁴⁷ leucine-enriched amino acid supplements, along with exercise, may be a potential intervention to build muscle in elderly people.

Increasing dietary protein is also known to increase circulating levels of insulin-like growth factor 1 (IGF-1), and conversely, a low-protein diet decreases IGF-1.¹⁷ IGF-1 is a key mediator of bone growth but also has a role in the skeletal response to anabolic PTH therapy.⁴⁸ Increasing dietary protein from 0.85 to 1.55 g/kg per day resulted in lower markers of bone resorption and higher circulating levels of IGF-1 in healthy older men and women.⁴⁹ Additionally, IGF-1 and skeletal muscle fiber decrease in older women fed a low-protein diet, suggesting that increasing IGF-1 by increasing dietary protein intake may be beneficial to muscle.⁵⁰ Because circulating IGF-1 levels and muscle fiber cross-sectional area were significantly correlated, perhaps plasma IGF-1 can be used as a biochemical marker for changes in muscle histology.⁵⁰

ESTABLISHING FUTURE PROTEIN RECOMMENDATIONS

Increasing dietary protein frequently raises concerns about renal health, particularly in older adults. In particular, because chronic ingestion of a high-protein diet can increase glomerular pressure and filtration rate, there is concern that this will cause renal damage. On the contrary, high protein intakes are not associated with kidney damage in healthy individuals, and hyperfiltration is a normal adaptation to greater protein intake.⁵¹ There is evidence that restricting protein is beneficial for people with preexisting kidney dis-

ease, but there is no evidence that high protein intake is detrimental to renal function in healthy individuals.⁵²

Mounting evidence suggests that the RDA for protein of 0.8 g/kg per day is not optimal for muscle and bone health in elderly people. Reassessments of the nitrogen balance studies show that a protein intake of 1.0 to 1.3 g/kg per day is needed to offset the typically lower energy intake and impaired insulin response in elderly individuals.²² Given the limitations of nitrogen balance studies, functional outcomes such as greater muscle tissue synthesis and maintenance of bone and muscle mass and strength should be used to determine optimal levels of dietary protein intake. IGF-1 also has the potential to serve as a marker for these outcomes, but research is preliminary at this point.

The studies using muscle anabolism and maintenance of muscle tissue as outcome variables show that a protein intake of 1.6 to 1.8 g/kg per day supports anabolism at rest or after exercise in older men and women,²⁰ although small amounts of leucine-enriched amino acids have also been shown to stimulate muscle protein anabolism.⁵³ Moderate-protein diets of 1.0 to 1.5 g/kg per day are shown to be associated with normal calcium homeostasis without altering bone metabolism.¹² These data seem to indicate that doubling the RDA from 0.8 g/kg per day to 1.5 to 1.6 g/kg per day may result in better muscle and bone health in elderly individuals. Although this level is approximately twice the current RDA, it is still within the acceptable range of intake (10–35% of total calories). It remains unclear whether the relationship between dietary protein and muscle and bone health is linear in the range of 0.8 to 1.6 g/kg per day. In addition, it is not known whether type of protein (specifically high or low quality) or timing of intake significantly affect the anabolic actions of protein on muscle and bone. Given the available data, increasing the RDA to 1.0 to 1.2 g/kg per day (or approximately 13–16% of total calories) would maintain normal calcium metabolism and nitrogen balance without affecting renal function and still be well within the acceptable range according to the IOM.¹⁸ Therefore, increasing the RDA to 1.0 to 1.2 g/kg per day for elderly people may represent a compromise while longer-term protein supplement trials are still pending.

ACKNOWLEDGMENTS

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper. This work was supported by grants from the National Cattleman's Beef Association (Award AG070992), U.S. Department of Agriculture (Agreement 97-35200-4420; 00-35200-9579), National Center for Research Resources General Clinical Research Center (Grant RR00125).

Author Contributions: EGS, KLI, NRR, and JEK all participated in the preparation of the manuscript.

Sponsor's Role: The sponsors did not participate in preparation of the manuscript.

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