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Optimizing bone health in older adults: the importance of dietary protein

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Abstract

Age-related bone loss is progressive and can lead to osteoporosis. While it is accepted that both dietary calcium and vitamin D are important and beneficial for skeletal health, the impact of dietary protein on calcium metabolism and bone balance remains controversial. Contrary to the hypothesis that increasing dietary protein contributes to bone loss, research supports the notion that protein may play a pivotal role in maintenance of bone health by several mechanisms; for example, increasing dietary protein increases IGF-1, calcium absorption, muscle strength and mass, all of which could potentially benefit the skeleton. A moderate increase in dietary protein recommendations for the aging population (above the recommended dietary allowance of 0.8 g/kg) may be beneficial to bone health, while still falling within the safe and acceptable range for protein intake (as defined by the dietary reference intakes).

Keywords

bone; calcium; dietary protein; older adult; osteoporosis

An estimated 10 million people in the USA over 50 years of age suffer from osteoporosis, and an additional 34 million are at risk for the disease. Osteoporosis, characterized by low bone mass and quality, puts individuals at greater risk for often debilitating and sometimes fatal fractures. People experiencing low impact fractures secondary to osteoporosis are at significantly higher risk for death than their non-osteoporotic counterparts, and this persists for several years postfracture [1]. While the etiology of osteoporosis is multifactorial, alterations in lifestyle such as nutrition and physical activity play a key role in attenuating bone loss and preventing osteoporosis. Calcium and vitamin D are well known to be vital in the acquisition and maintenance of bone throughout all stages of life [2]. The role of dietary protein, however, is more controversial. Diets high in protein are thought to be detrimental to bone, because the resultant endogenous fixed acid load (resulting from amino acid

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metabolism) may not be completely neutralized by the aging kidney and requires buffering by bone. This, in turn, releases calcium from the skeleton causing bone loss. On the other hand, recent research suggests that dietary protein is an essential nutrient to bone health throughout the lifespan [3]. This review will outline the evidence supporting the hypothesis that dietary protein may work synergistically to support calcium metabolism and bone health. The recommended dietary allowance (RDA) for dietary protein may not be optimal to sustain normal calcium and bone homeostasis or muscle mass in the aging population. Throughout this discussion, we will generally define a 'high' protein diet as 1.5 g/kg protein or higher per day and a 'low' protein diet as less than 0.8 g/kg per day, although varying levels in individual research will be defined.

Protein requirements

The Food and Nutrition Board at the Institute of Medicine (IOM) of the US National Academy of Sciences set dietary reference intakes (DRI) for all of the nutrients in our diet. The DRIs include five different measures that can be used to evaluate the intake of each nutrient. The RDA is defined as the intake that is sufficient to meet the needs of 97.5% of the population and is perhaps the most commonly used reference value for protein. The RDA for protein in adults is 0.8 g/kg body weight. The estimated average requirement (EAR) is a second measure defined as "the average daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group" [4]. For protein, the EAR for individuals aged 14 years and over is 0.7 g/kg body weight. Adequate intake (AI), tolerable upper intake level (UL) and acceptable macronutrient distribution ranges (AMDR) are also contained within the report. The AI is used when the RDA cannot be determined and it is "the recommended average intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group of apparently healthy people that are assumed to be adequate" [4]. Dietary protein requirements do not have an AI level defined. The UL represents "the highest daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population" [4]. Finally, the AMDR is defined as "a range of intakes that is associated with reduced risk of chronic diseases while providing adequate intakes of essential nutrients" [4].

Both the current RDA (0.8 g/kg) and EAR (0.7 g/kg) for protein for adults were determined based on nitrogen balance studies [4]. Nitrogen balance represents the difference between nitrogen consumed and nitrogen excreted. Since dietary protein determines the amount of nitrogen consumed, balance studies are used to establish the amount of protein necessary to put an individual in zero nitrogen balance. For example, if we measure nitrogen excreted in the urine and gastrointestinal tract and estimate dermal losses, we can determine the amount of protein that should be in the diet in order to place the subject in nitrogen equilibrium. The RDA and EAR for protein place 97.5% and 50% of the adult population in zero nitrogen balance, respectively [4].

Unfortunately, the use of the nitrogen balance method has many limitations. The end point of nitrogen equilibrium is probably the most important limitation; this outcome is not directly related to bone mineral density (BMD) and increased muscle mass or strength [5]. The achievement of nitrogen equilibrium, where nitrogen input equals nitrogen output, does not necessarily equate with optimal health. Instead, it simply means that lean body mass is not lost. This deficiency prevention approach originated many decades ago when the RDAs were first defined, and micro- and macro-deficiencies were more prevalent than they are now. The amount of protein that is required in the diet to optimize bone and muscle health is quite different than the amount necessary to prevent a deficiency [6]. Unfortunately and all too frequently, the RDA for protein is misinterpreted by professionals and professional

organizations to be the optimal level to support health [7]. There is emerging evidence that dietary protein and amino acids are not solely required for synthesizing body proteins, but that they are also involved in cellular signaling, satiety, thermogenic and glycemic regulation in the body [7]. It is very likely that these other metabolic outcomes become important when protein intakes are above the minimum RDA levels [7]. The simple use of nitrogen balance as the only outcome for determining protein needs is crude at best and may not adequately address other potentially important functions.

Additionally, nitrogen balance studies really require long adaption times that are rarely conducted because of the expense. There is a tendency for nitrogen balance studies to overestimate nitrogen intake and underestimate nitrogen excretion. For practical purposes, we typically estimate skin and miscellaneous nitrogen loss (rather than measure directly), but they may vary greatly. Furthermore, many nitrogen balance studies were conducted in young men. Therefore, the inevitable changes in body composition related to fat, muscle and bone in aging are likely not fully represented by young subjects [6]. The authors of the DRI report acknowledge ‘serious shortcomings’ in using nitrogen balance, while justifying its use due to a lack of validated or acceptable alternatives [4].

The DRI report delineates an AMDR for adults to be 10–35% of calories coming from protein. This range does not necessarily match the RDA. In many cases, the RDA for protein (0.8 g/kg) represents less than 10% of calories, and therefore the AMDR does not even include this reference value [6].

The UL for protein (at which adverse effects may occur) has not been directly determined by the IOM due to a lack of sufficient data. Instead, the upper end of the AMDR range of 35% was calculated secondarily after the AMDRs for fat and carbohydrate were established. Therefore, the 35% was derived from the mathematical difference, not clinical trials. Nonetheless, the risk of adverse effects resulting from protein intake at the upper range appears very low [4]. Only a small fraction (<3%) of the population over 19 years consumes more than 35% of calories from protein [8]. If a 57 kg woman was consuming 2,000 calories per day with 35% coming from protein, she would be eating 175 g of protein or approximately 3.0 g/kg per day. This level is almost four-times the RDA for protein and is also well above what most people are consuming in the USA (Table 1). While no objective standard for a highest protein intake exists, a moderate intake of protein in the range of 1–1.5 g/kg easily falls within the acceptable protein intake range for most individuals [8].

Protein intake in the USA

Although it is often thought that Americans typically consume a high-protein diet, the 2003–2004 National Health and Nutrition Examination Survey (NHANES) dietary data do not support this notion for all age groups. Fulgoni *et al.* used the latest NHANES data to characterize protein intake according to age and sex categories [8]. The data show a trend toward decreased protein intake with age (Table 1). While 10% of women between the ages of 19 and 50 years had a protein intake at or below the RDA of 0.8 g/kg, 25% of the women over the age of 70 years were eating 0.8 g/kg or less protein. Men consume more protein than women at all stages of life. Overall, 10% of adults aged over 70 years did not meet the RDA for protein and 50% consumed 1 g/kg protein or less, an amount just above the RDA [8]. Therefore, to presume that all adults consume a high-protein diet would be an incorrect overgeneralization. The WHO’s 2007 Protein and Amino Acid Requirements in Human Nutrition report states that sedentary elderly are “most likely to be at risk from a protein deficiency”, and this fact combined “with the evidence of a beneficial effect of dietary protein on bone in elderly people, suggests that attention should be given to the provision of protein-dense foods to this particular population group” [9]. Clearly, the decrease in protein

intake that accompanies aging is of particular concern in a population that is already at risk for bone loss and osteoporosis.

Epidemiological studies

For the most part, epidemiological data support a positive association between protein intake and bone health. For instance, Hannan *et al.* evaluated the relationship between baseline protein intake and 4-year change in BMD in 615 subjects averaging 75 years of age [10]. The group consuming the lowest quartile of protein (ranging from 0.21–0.71 g protein/kg per day) also demonstrated the greatest loss in BMD. Whereas the highest quartile consumed 1.24–2.78 g/kg protein and demonstrated the least loss in BMD over the 4 years [10].

In a 5-year cohort study of 862 elderly women, food frequency questionnaires and dual energy x-ray absorptiometry (DXA) scans were used to examine the relationship between dietary protein and body composition at baseline and 5 years later [11]. After 5 years, there was greater bone mineral content (BMC) in those consuming the highest amount of protein (>87 g/day) than in those consuming a moderate- (66–87 g/day) or low- (<66 g/day) protein diet. Specifically, whole-body BMC and appendicular BMC were 5.3 and 6.0% greater in the highest versus lowest tertile of protein intake, respectively. BMD of the spine and hip were not reported. Subjects consuming the highest dietary protein also had significantly higher whole-body lean muscle mass than those consuming the moderate or low levels of protein. In total, these data support the hypothesis that protein intake may positively impact bone and muscle and are consistent with the theory that increased BMC may be due, in part, to an interaction between muscle and bone [11].

Darling *et al.* recently reported a systematic review and meta-analysis of protein intake and bone health [12]. These investigators initially collected over 2000 potential studies of which 61 met the inclusion criteria for the systematic review, because investigators measured both dietary protein and bone (BMD or BMC, bone turnover or fracture) in healthy adults. Overall, there was little support for a negative relationship between dietary protein and bone. In fact, from the cross-sectional surveys, the pooled r-values could not identify any negative association between protein intake and BMD or BMC at the clinically important skeletal sites. If anything, there was a slight positive association; dietary protein was able to account for 1–2% of BMD. In 19 randomized, placebo-controlled trials, Darling's group found there was an overall slightly positive impact of protein supplementation (from all different sources) on lumbar spine BMD. However, no association was observed between dietary protein and fracture rates. So, neither the qualitative review or the meta-analysis identified any significant association between protein intake and fracture incidence. It is important to note that this review and meta-analysis has limitations including heterogeneity in duration, supplement type, design and outcomes among the different studies included and potential publication bias toward positive findings [12].

While the meta-analysis found no association between dietary protein and fracture risk, in an earlier prospective study, Munger *et al.* observed an inverse relationship between protein intake and hip fracture risk [13]. This analysis was based upon data from the Iowa Women's Health Study, which included women aged 55–69 years. At baseline, a cohort of women completed a food frequency questionnaire. Incidence of hip fracture was determined and confirmed with follow-up questionnaires and physicians' reports 1 and 3 years later. Individuals sustaining a hip fracture had a significantly lower ($p = 0.01$) mean daily intake of protein. Furthermore, when protein intake was broken into quartiles, age-adjusted relative risk of hip fracture significantly ($p = 0.006$) decreased with increased protein intake. These

data suggest that increased dietary protein may be associated with decreased occurrence of hip fracture [13].

Although these epidemiological findings are important, they cannot establish a causal relationship between protein and bone. Clearly, the cross-sectional population studies justify well-designed, long-term, protein intervention trials to define the relationship between dietary protein, bone health and fractures.

Traditional hypothesis

It is generally well accepted that an increase in dietary protein results in greater calcium excretion in the urine [14]. The source of this urinary calcium is not perfectly clear. Several research studies published between 1932 and 1974 suggested that intestinal calcium absorption was modulated by dietary protein [15]. These data suggested that increased calcium absorption from the intestine occurred during a high-protein diet and was therefore, responsible for hypercalcuria. However, beginning in the mid 1970s, the majority of studies (primarily calcium-balance studies) failed to duplicate the original findings. If more calcium was being excreted than absorbed, calcium had to be coming from within the body. Since 99% of the body's calcium is found in bone, the skeleton became the suspected source of the extra urinary calcium. This led to the proposed hypothesis that intake of protein (particularly animal) would create a fixed metabolic acid load due to the high sulfur amino acid content. If the kidneys and lungs were not able to completely handle this diet-induced acid load, a source of additional buffer would be necessary. The large carbonate reservoir of the skeleton would be called upon to provide this buffer, and calcium would consequently be released with the carbonate [16]. This hypothesis is supported by cellular and animal studies (see review by Arnett [17]). Studies demonstrate that the addition of a base such as potassium bicarbonate or citrate suppresses bone resorption [18,19], further supporting the hypothesis. If this theory held true, a consistently high intake of animal protein would be detrimental to bone over time [16].

Several arguments have been raised against the above traditional hypothesis that dietary protein is 'bad to the bone'. There is little question that dietary protein is a major contributor to endogenous acid production; the American diet can generate 100 mEq of acid daily, primarily phosphate and sulfate [20]. The important question becomes: is this endogenous acid production from a high-protein diet of sufficient magnitude to impact bone? The lungs work to acutely regulate pH by expiring carbon dioxide, a metabolic byproduct, while the kidney helps with longer-term buffering by excreting excess hydrogen ions primarily as ammonium. The combined action of the kidneys and lungs efficiently regulates blood pH. This is a perfectly normal homeostatic response that allows the blood pH to remain constant [3]. In addition, dietary protein is typically consumed throughout the day, so that the acid generation also occurs gradually throughout the day, most likely leaving time for neutralization. The mechanism by which acidosis induces bone loss is through activation of osteoclasts by a fall in extracellular pH. However, the pH of extracellular fluid bathing cells is probably less than 7.36, and the initial activation of osteoclastic resorption requires an extracellular pH less than 7.2 [17]. It would seem improbable that such a low pH would occur following a high-protein meal, since blood pH is stable under changing protein conditions [3]. Therefore, it is unlikely that bone acts as a buffer for a protein-induced metabolic acid load [3].

In a recent meta-analysis, Fenton *et al.* examined whether a dose-dependent relationship between calcium balance and net acid excretion (NAE) in the urine exists [21]. The five studies included in the analysis had randomized, crossover designs, followed the IOM's recommendations for calcium balance studies, used an intervention altering acid-base intake

with food or supplemental salts and reported change in NAE and calcium balance. After conducting regression analysis, researchers observed a 0.3 mmol/day increase in urinary calcium for each 10-mEq increase in NAE. However, the researchers saw no relationship between changes in NAE and changes in calcium balance or between NAE and the bone marker, N-telopeptide. These findings are consistent with the theory that although urinary calcium is positively associated with NAE, NAE is not associated with measures of bone metabolism or calcium balance [21].

Isotopic studies

Calcium isotopic techniques are sensitive tools that are used to evaluate protein's impact on calcium homeostasis. Several recent short-term feeding studies used isotopes to evaluate calcium metabolism with different levels of dietary protein. Roughead *et al.* used a randomized crossover study of 15 healthy postmenopausal women and assigned participants to low (12% of energy) and high (20% of energy) meat protein diets each containing 600 mg calcium for 8-week periods [22]. Following a 4-week adjustment period on each diet, the food was labeled with ^{47}Ca and whole-body scintillation counting was performed over the subsequent 28 days. If the traditional hypothesis were correct, one would expect to see lower calcium retention when the women consumed the high-protein diet. However, no significant difference was seen in calcium retention between the groups, and in fact, a trend toward better calcium retention was observed on the higher protein diet. In addition, the high meat protein diet did not adversely affect biochemical markers of bone turnover [22].

In a follow-up randomized, controlled-feeding study conducted by this same team of investigators [23], 27 postmenopausal women were assigned to either a low- (675 mg) or high- (1510 mg) calcium diet. Subjects consumed low- (10% of energy) and high- (20% of energy) protein diets containing their assigned calcium level for 7 weeks. There was a 3-week washout period between interventions. After 3 weeks on each diet, 2-day diets were labeled with ^{47}Ca isotopes and whole-body scintillation counting followed. During the lower calcium diet, fractional calcium retention increased with the higher protein diet (in comparison with the low-protein diet). However, during the higher calcium diet this effect was not observed (Figure 1). The higher protein diet significantly increased serum IGF-1, an anabolic hormone that may be beneficial to bone, and also reduced urinary deoxypyridinoline, a marker of bone collagen breakdown [23].

Finally, dual stable isotopes were used to evaluate the effect of a 10-day dietary intervention containing a moderate- (1.0 g/kg) or high- (2.1 g/kg) protein diet and a low level of calcium (800 mg) in healthy women [24]. The high-protein diet resulted in a significant 42% relative increase (7.7% raw) in intestinal calcium absorption and a significant increase in urinary calcium (Figure 2). No differences were observed in kinetic measures of bone turnover between the moderate- and high-protein diets. However, the higher protein diet caused a significantly lower urinary fraction of calcium from bone origin. These effects were independent of subjects' postmenopausal status and were observed in both pre- and post-menopausal women. These data suggest that, at least acutely, hypercalcuria secondary to increased dietary protein is, in fact, the result of increased intestinal calcium absorption. Furthermore, there was a nonsignificant trend toward lower bone turnover in the high-protein group, which may positively impact bone [24]. It is important to note that in all of the above isotopic studies [22–24] where dietary protein had a positive effect on calcium and bone, dietary calcium was limited to 600–800 mg. At higher calcium intakes, the impact is less evident.

An earlier study using isotope methodology to look at protein intake and calcium absorption found no positive or negative association between the two [25]. This study was

observational and did not experimentally manipulate protein levels, and therefore interindividual variation in intestinal calcium absorption and uncontrolled dietary factors could have confounded the findings.

However, in a recent pilot feeding study, Ceglia *et al.* observed no change in intestinal calcium absorption during a high-protein (1.5 g/kg) versus low-protein (0.5 g/kg) diet using dual stable isotopes [26]. Because the investigators did not keep dietary phosphorus constant between interventions, the naturally high phosphorus load accompanying the high-protein diet may blunt any increase in calcium absorption [26]. In addition, the relatively high amount of elemental calcium (1200 mg) could potentially mask any changes in calcium homeostasis induced by dietary protein (as it may have in the Hunt *et al.* [23] study).

The aforementioned isotopic studies have strengths: the diets are controlled, the interventions are crossover and the isotopes are generally considered very sensitive and specific. Taken together, the isotopic studies are an important addition to the epidemiological data supporting a positive relationship between long-term (4–5 year) higher protein intake and calcium balance. Nevertheless, the dietary feeding studies are limited by their short-term nature and small sample sizes.

Potential explanations for discrepancies in the literature

If experimental diets contain high levels of calcium, the impact of protein on absorption may not be evident [23,26]. On the other hand, when dietary calcium is limited [23,24,27] the effect of protein on calcium absorption becomes apparent. Since dietary calcium is inadequate in many older individuals, inadequate dietary protein may compound the problem of calcium bioavailability while increasing protein may rectify it.

Variation in dietary phosphorus will also impact calcium absorption. Phosphorus has been shown to be hypocalciuretic, which may be due to its role in the modulation of endogenous calcium absorption [28]. In a study employing double isotope and balance method, dietary phosphorus was a strong determinant of total intestinal calcium (or the sum of proximal and distal intestinal calcium content) as each 1-mmol increase in dietary phosphorus was accompanied by a 0.037-mmol rise in endogenous intestinal calcium [29,30]. Inconsistent or uncontrolled levels of phosphorus and calcium may therefore modulate the effects of protein on calcium absorption within studies and may help to explain discrepant results among studies. It is not entirely understood if the effect of phosphorus accompanying dietary protein could negate benefits of protein to the calcium economy. Earlier studies by Spencer [31] failed to show that the increase in dietary protein induced renal calcium loss, and this was probably due to a concurrent rise in dietary phosphorus with dietary protein. However, shorter-term studies suggest that the relative ‘equalization’ of phosphorus across the different levels of protein likely enhances the changes seen in calcium absorption [24,27].

Potential mechanisms

There are several ways in which increasing the amount of protein in the diet could potentially benefit calcium and bone homeostasis including effects on calcium absorption, bone turnover, production of IGF-1 and lean body mass. It should be noted that these potential mechanisms are not mutually exclusive, and it is likely that all contribute (Figure 3).

Intestinal calcium absorption

Experimental feeding studies demonstrate that increases in dietary protein increase intestinal calcium absorption in at least at 1–7 weeks [23,24]. If more calcium is absorbed from the

intestine on a higher protein diet, parathyroid hormone would be expected to be lower, resulting in reduced rates of bone resorption. Over time, this could attenuate bone loss. A significantly lower level of parathyroid hormone observed in the trial with ten individuals on a 10-day high- (1.5 g/kg) versus low- (0.5 g/kg) protein diet supports this hypothesis [26]. In another short-term study, serum PTH was 1.6–2.7-times higher in women consuming a low- (0.7 g/kg) versus moderate- (1.0 g/kg) protein diet for 14 days [32].

One potential mechanism by which dietary protein increases intestinal calcium absorption is by an effect on gastric acid secretion. Calcium is thought to be absorbed in the ionized form in the small intestines. When ingested, calcium is in a food matrix or complexed with an anion and not in an ionized form. It is possible that adequate gastric acid is needed to facilitate the release of calcium from this complex and allow for its absorption. The typical fasting pH of the stomach is 1–3 and is conducive to the ionization of calcium. However, the clinical intervention trials addressing this question (usually using a proton pump-inhibiting drug to increase gastric pH) vary in their conclusions. For example, Recker was the first to observe that patients with achlorhydria absorbed less calcium (from calcium carbonate) when fasted, than control subjects with normal gastric acid production [33]. In agreement with this idea is a randomized crossover trial in which O'Connell *et al.* observed a significant decrease in fasting calcium absorption (from calcium carbonate) when ingested by elderly women who were given a proton pump-inhibiting drug to block gastric acid production [34]. On the other hand, during fed conditions, the blockage of gastric acid excretion by a proton pump-inhibiting drug did not impact calcium absorption [35]. Therefore, the impact of gastric acid on intestinal calcium absorption may be dependent on the fed or fasted state of the subject.

Bone turnover markers

The relationship between dietary protein and bone turnover is of considerable importance. Markers of bone resorption are released into the serum and urine as a result of the degradation of the mature, modified type I collagen. *N*-telopeptide and deoxypyridinoline (DPD) are two commonly used markers of bone resorption. In the controlled feeding study by Hunt *et al.* that provided 10 or 20% of calories from protein (mainly meat and milk protein sources), a significantly lower level of DPD was seen in the urine of subjects consuming 20% of calories from protein [23]. In another study, subjects with a daily protein intake of less than 0.85 g/kg were instructed to consume either a high-protein supplement (0.75 g/kg protein from meat sources) or a low-protein supplement (0.4 g/kg protein from mainly carbohydrate sources) in addition to their usual low-protein diet. Subjects were educated on how to reduce calories from carbohydrate to maintain an isocaloric diet. A significantly lower level of urinary *N*-telopeptide was observed in the urine of those on the high-protein supplement, consuming a total of 1.55 g/kg protein. These data support the hypothesis that high dietary protein may decrease resorption. The lack of change in PTH in the second study suggests that decreased resorption is not necessarily attributable to PTH [36].

Dietary protein & IGF in bone & muscle health

IGF-1 is a key mediator of bone growth [37], and dietary protein is an important regulator of circulating IGF-1 levels [38,39]. In both the Dawson-Hughes and Hunt studies, there were significantly greater levels of IGF-1 in subjects consuming the higher protein diets [23,36]. The anabolic effect of IGF-1 on muscle may help further explain a positive relationship between protein and bone. Thus, protein-induced increases in IGF-1 may directly benefit bone while also increasing muscle mass, which in turn is also beneficial to bone strength.

A frequently overlooked fact is that changes in bone mass and muscle strength tend to track together over the lifeSpan [40]. The relationship between dietary protein, muscle mass, strength and function, risk of falls and fracture, bone density and bone health is complex and not well understood. However, it is known that the maintenance of bone strength is dependent upon both the maintenance of muscle mass and the trophic effect of muscle contraction on bone anabolism [40].

Like bone, muscle mass decreases with age; after the age of 40 years, skeletal muscle loss occurs at a rate of approximately 0.5–1.0% per year [41]. Using food frequency questionnaire and DXA scan data from the Health, Aging and Body Composition Study, Houston *et al.* evaluated the association between protein intake and lean mass over a 3-year period in 2066 black and white individuals between the ages of 70 and 79 years [42]. Subjects with protein consumption in the highest quintile (median intake: 1.1 g/kg per day) had significantly lower rates of loss of muscle mass ($p < 0.05$) than those in the lowest quintile of protein intake (median intake: 0.7 g/kg per day) [42]. The relationship between protein intake and muscle mass in the aging population may be modulated by timing and frequency of intake, quality of protein, physical activity and consumption in the presence or absence of other macronutrients. While research continues to examine such modifying factors, a recent proposal suggests that the consumption of high-quality protein at each meal (25–30 g) will combat sarcopenia by slowing or preventing muscle loss in the aging population [43]. It is very likely that the maintenance of good skeletal health, including the avoidance of falls, with aging is very dependent on the maintenance of adequate muscle mass and function, which is, in turn dependent to some extent on adequate dietary protein.

Finally, 50% of bone volume is protein, and bone remodeling continuously occurs. Since protein plays a vital role in this remodeling process, inadequate intake of this macronutrient may impact bone remodeling and maintenance [44].

Potential safety concerns of a high-protein diet

While a higher protein intake may be beneficial to bone and muscle, there are persistent safety concerns regarding renal function, hydration, body weight and serum lipids. For the purposes of the following discussion, we will define a low-protein diet as containing less than 0.8 g/kg protein per day, while a high-protein diet is greater than 1.5 g/kg protein per day.

Glomerular filtration rate (GFR), a measure of renal function, rises with both acute and chronic increases in protein consumption [45]. Long-term elevations in GFR, resulting from a higher protein diet have been postulated to be damaging to the kidney. However, it is important to differentiate between individuals with healthy versus impaired kidney function when considering the impact of protein on the renal function.

For nondialyzed individuals with chronic kidney disease, the National Kidney Foundation's guidelines recommend a protein restriction of 0.6–0.75 g/kg per day [46,47]. In the Nurse's Health Study, a significant association was observed between protein intake and a decline in renal function in women with mild renal insufficiency [48]. In a cross-sectional study of adults with stage 3–5 chronic kidney disease (CKD), a high protein intake (>110% of the recommended 0.6–0.75 g/kg based on disease stage and Kidney Disease Outcome Quality Initiative Guidelines) was significantly correlated with a decrease in GFR when compared with a normal or low intake [49]. Clearly, a recommendation to increase protein intake in those with CKD is unwise. However, in individuals with normal kidney function, hyperfiltration, as evidenced by increased GFR, appears to be an adaptive mechanism to increased dietary protein and has not been linked to a decline in renal function [50].

Still, GFR decreases with age even in healthy individuals [47]. In a short-term 10-day study looking at the functional impact of a higher protein diet (3.0 g/kg fat-free mass [FFM]/day), GFR significantly increased in response to the high-protein diet in the younger group (24.3 ± 1.2 years), but did not change among the older individuals (70 ± 1.8 years) whose GFR was lower at baseline on the control diet [51]. The 3.0 g/kg FFM/day high-protein diet is equivalent to at least 1.2 g protein/kg total body weight [51]. More research should be conducted to better assess the impact of higher protein on GFR, especially in the older population, but a moderate increase in dietary protein to 1–1.5 g/kg appears to be safe for older individuals with age-appropriate kidney function. The use of screening tools such as the estimation of GFR from serum creatinine, hemoglobin A1C to screen for diabetes and urine dipstick for proteinuria may be useful in identifying individuals for whom supplemental protein may not be appropriate [41].

Concern has arisen over the impact of high-protein diets on hydration indices. This is important in older individuals who are susceptible to dehydration and its negative consequences [52]. One possibility is that the metabolism of a high-protein diet results in a greater renal solute load and the amount of water needed for excretion would increase with the solute load leading to dehydration. However, in a 12-week diet intervention study evaluating a low- (0.8 g/kg), moderate- (1.8 g/kg) and high- (3.6 g/kg) protein diet in healthy young men, only a minimal effect of increased dietary protein on hydration status was observed [53]. In another study of water balance, hydration status and FFM hydration in younger and older adults, subjects consuming an inadequate- (0.5 g/kg), marginal- (0.75 g/kg) and high- (1.0 g/kg) protein diet for 18 days per intervention, protein level did not appear to influence water input, output or balance in either the younger or older adults [52]. These findings support the notion that a moderate-protein diet does not influence hydration status in individuals with healthy kidney function.

Higher protein diets have also been proposed to increase risk of kidney stone formation, but experimental data are conflicting [54]. In a large prospective study of men, researchers observed a positive association between animal protein consumption and development of kidney stones [55]. However, in a 4-year randomized intervention trial in idiopathic calcium stone formers, the low-protein intervention did little to change stone reoccurrence risk [56]. It is unlikely that a dietary factor, such as higher protein intake, is an independent risk factors for development of kidney stones. Instead, dietary protein may become a concern when combined with inherited or underlying abnormalities associated with renal disease and formation of kidney stones [57].

The impact of protein on satiety, caloric intake and weight loss has been of increasing interest, given the present obesity epidemic [58]. Dietary protein was linked to weight loss, greater satiety and a decreased intake when compared with other macronutrients in short-term studies [59,60]. While the influence that protein has on weight loss and control may appear promising, one must also consider its potential effect on individuals for whom weight loss may be unfavorable. Sarcopenia and osteoporosis are prevalent among the older population in the USA. The elderly also face a variety of nutritional barriers including poor intake, nutrient deficiencies, poor access to wholesome food and reduced appetite. Such problems can lead to malnutrition, which can exacerbate sarcopenia and debilities that increase morbidity and mortality [61].

Calorie for calorie, protein is more satiating than the other macronutrients [2]. However, studies documenting the satiating effect of protein employed high levels of protein (25% of calories or greater) [62,63]. Because of the satiating impact of dietary protein, the short-term nutritional supplementation in elders may be offset by simultaneous reduction in voluntary food intake. That is, simply adding an oral protein supplement in elderly individuals may

actually function as a meal replacement with no net increase in total daily protein intake [64].

A final area of concern involves the relationship between protein intake, lipidemia and risk of cardiovascular disease. In the past, dietary protein was thought to be a potential risk factor for coronary heart disease due to higher saturated fat and cholesterol content in animal protein foods. However, recent work increasingly supports the notion that high-protein, low-carbohydrate diets reduce serum triacylglycerol, increase high-density lipoprotein (HDL) cholesterol, increase low-density lipoprotein (LDL) cholesterol size and reduce blood pressure, all of which may, in fact, reduce the risk of coronary heart disease [65].

In sum, a moderate increase in protein intakes above 0.8 g/kg does not appear, based on available evidence, to be associated with any serious risk of renal damage, dehydration or hyperlipidemia. The potential benefits of reducing sarcopenia of aging and attenuating age related bone loss seems to outweigh the risks in individuals with age appropriate renal function [41,66].

Practical suggestions for increasing protein in older individuals

A diet containing the RDA for protein or lower may not be able to support optimal bone and muscular health in older individuals. A diet slightly higher in protein appears beneficial to bone and strength and is safe for individuals with age appropriate renal function.

How can the aging population increase their protein intake? Protein is found in meat, dairy, vegetables and grains, with meat and dairy being the most concentrated sources of this macro-nutrient. Small increases in portion sizes of these foods will easily increase daily protein intake. Each ounce of meat, poultry or fish, contains 7 g of protein; milk products (1 cup milk or yogurt or an ounce of cheese) each contain approximately 8 g. Eggs are also an inexpensive and excellent source of protein and well accepted by many older people, providing approximately 7 g protein per egg. As an example, for a 70-kg individual, adding 2 ounces of meat (or egg) and a serving of dairy raises protein intake by approximately 21 g or 0.3 g/kg per day. In order to maximize protein synthesis [43], the distribution of the protein should be approximately a third at each meal, or a minimum of 25 g protein per meal.

In summary, recent evidence suggests that the current RDA of 0.8 g/kg protein may prevent a frank protein deficiency, but does not support optimal bone health in the elderly population. There is little evidence that a high-protein diet will increase bone loss. On the other hand, there are now significant clinical and population studies that support the hypothesis that a high-protein diet is good for calcium economy and potentially beneficial to bone health as well as muscle mass. The risks of increasing dietary protein in the elderly, as long as attention is paid to renal function, are small, particularly in relation to the potential benefits.

Future perspective

Before public health recommendations can be made, long-term clinical intervention trials in which dietary protein is increased in healthy individuals are needed to determine if these levels improve muscle mass, functional status, bone mass and affect fracture risk. To date, there are no known long-term dietary protein studies where fracture risk is an outcome. There are very few using BMD as the primary outcome variable. While conducting a nutrition intervention trial with a fracture outcome would be a difficult undertaking, the findings of such a study would be important, as dietary protein may reduce fracture risk

without changes in BMD. We also need to improve awareness of the healthcare professional of the importance of optimal dietary protein in the elderly.

Executive summary

Current protein recommendations & intake

- The current recommended dietary allowance of protein of 0.8 g/kg for adults was based upon nitrogen balance studies and was designed to provide the minimum amount of protein necessary to prevent a deficiency.
- The amount of protein that is required in the diet to optimize bone and muscle health is quite different and higher than the amount necessary to prevent a deficiency.
- The dietary reference intakes define a much wider acceptable protein intake range of 10–35% of caloric intake, although the upper limit has not been directly defined due to lack of sufficient data.
- In total, 25% of women over the age of 70 years consume 0.8 g/kg protein or less per day, and overall 10% of the population aged over 70 years does not meet the recommended daily allowance for protein.

Research findings support a positive relationship between protein intake & bone health

- Many epidemiological studies have found a significant positive relationship between protein intake and bone mineral density.
- Protein intake has also been inversely associated with hip fracture in postmenopausal women.
- Isotopic studies have demonstrated greater calcium retention and absorption among individuals consuming higher protein diets, particularly when the calcium content of the diet is limiting.

Protein may positively impact bone health by several mechanisms

- Experimental feeding studies have demonstrated that protein increases intestinal calcium absorption, and may positively affect bone turnover markers.
- Dietary protein is an important regulator of IGF-1, which is anabolic to bone and muscle.
- Maintenance of bone strength is dependent upon maintenance of muscle mass, which exerts a trophic effect on bone by the force applied during muscle contraction.
- Adequate dietary protein plays an important role in the continuous remodeling process that occurs in bone.

A higher protein intake is safe for the healthy aging population

- In healthy individuals, increased glomerular filtration rate accompanying increased protein intake appears to be an adaptive mechanism to increased dietary protein and has not been linked to decline in renal function. A moderate increase in protein intake appears to be safe.
- A moderate protein intake does not impact hydration indices in those with healthy kidney function.

Future perspective

- Long-term clinical intervention trials where dietary protein is increased in apparently healthy and well-nourished older individuals should be conducted in order to determine the impact on muscle, bone and fracture risk.

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•• of considerable interest

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Figure 1. Calcium whole-body retention from four experimental conditions in healthy postmenopausal women for 7 weeks

Data are presented as mean ($\pm$ standard error) from $n = 12$ for low-calcium and $n = 14$ for high-calcium diets.

© 2005, The Endocrine Society [23].

Figure 2. Urinary calcium and intestinal calcium absorption during moderate- (1.0 g/kg) and high-protein (2.1 g/kg) diets

Each line represents an individual subject where the dark circles represent the three postmenopausal women and the ten light circles represent the young women. The p-value identifies the statistical difference between levels of protein by paired t-test [24].

Figure 3. Potential mechanisms by which increased dietary protein positively impacts bone health

PTH: Parathyroid hormone. Modified with permission from [66].

Dietary protein intake (g/kg) in the US from the National Health and Nutrition Examination Survey 2003–2004 database.

Table 1

Age (years)	n	Protein intake (g/kg ideal body weight)										EAR	Percentage less than EAR
		Mean ± SD		Percentiles									
				5	10	25	50	75	90	95			
Males													
19-30	470	1.5 ± 0.4		0.9	1.0	1.2	1.4	1.7	2.0	2.2	0.7	<3	
31-50	624	1.4 ± 0.3		0.9	1.0	1.2	1.4	1.6	1.8	1.9	0.7	<3	
51-70	555	1.2 ± 0.3		0.8	0.8	1.0	1.1	1.3	1.5	1.7	0.7	<3	
71+	391	1.0 ± 0.3		0.7	0.7	0.9	1.0	1.2	1.4	1.5	0.7	<3	
Female													
19-30	393	1.2 ± 0.3		0.7	0.8	1.0	1.2	1.4	1.6	1.8	0.7	<3	
31-50	612	1.1 ± 0.3		0.7	0.8	0.9	1.1	1.3	1.5	1.6	0.7	4.0	
51-70	606	1.1 ± 0.3		0.6	0.7	0.9	1.0	1.2	1.5	1.6	0.7	7.2	
71+	406	1.0 ± 0.3		0.6	0.7	0.8	0.9	1.1	1.3	1.4	0.7	8.6	

Data from individuals with 2 days of reliable intake from the National Health and Nutrition Examination Survey 2003–2004. Body weights adjusted to nearest ideal body weight for both children and adults. Results generated using a Software for Intake Distribution Estimation program.

EAR: Estimated average requirement.

Adapted from [8].