Amount and type of protein influences bone health[1–4]

Robert P Heaney and Donald K Layman

ABSTRACT

Many factors influence bone mass. Protein has been identified as being both detrimental and beneficial to bone health, depending on a variety of factors, including the level of protein in the diet, the protein source, calcium intake, weight loss, and the acid/base balance of the diet. This review aims to briefly describe these factors and their relation to bone health. Loss of bone mass (osteopenia) and loss of muscle mass (sarcopenia) that occur with age are closely related. Factors that affect muscle anabolism, including protein intake, also affect bone mass. Changes in bone mass, muscle mass, and strength track together over the life span. Bone health is a multifactorial musculoskeletal issue. Calcium and protein intake interact constructively to affect bone health. Intakes of both calcium and protein must be adequate to fully realize the benefit of each nutrient on bone. Optimal protein intake for bone health is likely higher than current recommended intakes, particularly in the elderly. Concerns about dietary protein increasing urinary calcium appear to be offset by increases in absorption. Likewise, concerns about the impact of protein on acid production appear to be minor compared with the alkalinizing effects of fruits and vegetables. Perhaps more concern should be focused on increasing fruit and vegetable intake rather than reducing protein sources. The issue for public health professionals is whether recommended protein intakes should be increased, given the prevalence of osteoporosis and sarcopenia. *Am J Clin Nutr* 2008;87(suppl):1567S–70S.

INTRODUCTION

Protein makes up roughly 50% of the volume of bone and about one-third its mass (1), and this bone protein matrix undergoes continuous turnover and remodeling. Because cross-linking of collagen molecules in bone involves posttranslational modifications of amino acids (including hydroxylation of lysine and proline), many of the collagen fragments released during proteolysis as part of remodeling cannot be reutilized to build new bone matrix. Accordingly, a daily supply of dietary protein is required for bone maintenance.

There are many factors that influence bone mass, but protein has been identified as being both detrimental and beneficial to bone health, depending on a variety of factors, including the level of protein in the diet, the protein source, calcium intake, weight loss, and the acid/base balance of the diet. Protein intake affects bone in several ways: *1*) it provides the structural matrix of bone, *2*) it optimizes IGF-1 levels, *3*) it is reported to increase urinary calcium, and *4*) it is reported to increase intestinal calcium absorption.

Moreover, loss of bone mass (osteopenia) and loss of muscle mass (sarcopenia) that occur with age are closely related. Factors that affect muscle anabolism, including protein intake, also affect bone mass. Bone health is not simply a skeletal issue; it is a musculoskeletal issue.

This review intends to briefly discuss several dietary and physiologic factors that affect bone health and to provide an overview of the current status of research in these areas. Suggestions for areas of further research and investigation are also provided.

LEVEL OF DIETARY PROTEIN

The high protein content of Western diets is often cited as a risk factor for osteoporosis or bone fractures (2, 3). High protein intakes have been shown to affect calcium homeostasis, resulting in increased calcium excretion, but findings regarding the effect of protein on calcium balance and bone health have been mixed. One study of 191 nuns who were studied over a 20-y period found that protein intakes ranging from 0.41 to 1.96 g/kg had no effect on calcium absorption efficiency (4). In a 12-wk study of 100 overweight and obese women, no differences in serum levels of osteocalcin, a marker of bone turnover, were found after 12 wk on either a high-protein (99 g/d) or high-carbohydrate diet (55.5 g of protein/d) (5).

Other studies suggest that, as a result of increased urinary calcium excretion with high protein intake, there is an increased risk of fractures or osteoporosis (2, 6). As protein intake increases, there is an increase in urinary calcium, with most subjects developing negative calcium balance (7–9). One estimate is that there is a 50% increase in urinary calcium associated with doubling protein intake or roughly 1 mg urinary calcium for every gram of dietary protein (1). However, the increase in urinary calcium observed with purified proteins or amino acid infusions is not readily observed with food sources of protein (1). Studies providing total parenteral nutrition found that urinary calcium output is a direct function of amino acid intake, at least under the unique circumstance of total parenteral nutrition (1).

[1] From Creighton University, Omaha, NE (RPH) and the Department of Food Science and Human Nutrition, University of Illinois, Urbana, IL (DKL).

[2] Presented at the conference "Protein Summit 2007: Exploring the Impact of High-Quality Protein on Optimal Health," held in Charleston, SC, May 24, 2007.

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[4] Reprints not available. Address correspondence to DK Layman, 437 Bevier Hall, University of Illinois, 905 South Goodwin Avenue, Urbana, IL 61801. E-mail: dlayman@uiuc.edu.

However, studies in which diets provided 30% of energy as protein (181–214 g/d) found no increase in calciuria (10–12). In healthy adults, when protein intake was increased from 0.7 to 2.1 $g \cdot kg^{-1} \cdot d^{-1}$, urinary calcium increased, but intestinal absorption increased as well (13).

Increased calciuria does not necessarily translate to calcium loss, negative calcium balance, and reduced bone mass (14). To the contrary, several studies have observed a positive association between dietary protein intake and increased bone mineral content or decreased risk of fracture (15–17). One study found that among premenopausal women, there was a significant positive association between protein intake and bone mineral content, suggesting that dietary protein intake actually may be a determinant of the peak bone mass (15). Among a group of 59 elderly patients hospitalized for femoral neck fractures, those given an oral nutrition supplement providing 20 g/d of protein had significantly better clinical outcomes (lower rates of complications and shorter hospital stays) compared with those not receiving the protein supplement (18).

Overall, however, there is general agreement that diets moderate in protein ($\approx$1.0 to 1.5 $g \cdot kg^{-1} \cdot d^{-1}$) are associated with normal calcium metabolism and do not alter bone metabolism (13). However, at low protein intakes ($<$0.8 $g \cdot kg^{-1} \cdot d^{-1}$) intestinal calcium absorption is reduced and levels of parathyroid hormone increase, causing the release of calcium from bone (13).

Another factor influenced by protein is insulin-like growth factor (IGF-1), which plays a key role in bone metabolism. Higher levels of IGF-1 are osteotrophic. As individuals age, there is a decline in serum concentrations of IGF-1 (19). Both the level and type of protein in the diet may have an effect on IGF-1 levels (20–22).

PROTEIN SOURCE

Data indicate that various protein sources may exhibit different effects on bone metabolism. Some, but not all (22), studies have found that meat as a protein source is associated with higher serum levels of IGF-1 (20, 21), which is in turn associated with increased bone mineralization and fewer fractures (23). Soy foods have been linked with lower levels of IGF-1 (21).

It has been suggested that animal protein–based diets might have a greater negative effect on skeletal health than do vegetable-based diets (24) because dietary animal protein induces a greater increase in urinary calcium excretion than vegetable protein. In a large group of middle-aged and elderly women in China, urinary excretion of calcium was correlated positively with intake of animal protein (25). However, in the Framingham Osteoporosis Study in which 391 women and 224 men, whose average age at baseline was 75 y, were assessed for bone mineral density and dietary intake, a higher intake of animal protein was not associated with a decrease in bone mineral density (17). Further, in a 3-y clinical study of 342 healthy men and women 65 y of age and older, those who consumed the most protein and were supplemented with calcium experienced the greatest improvement in bone mass density, and most of the protein consumed was animal protein (26).

Moreover, clinical studies do not support the idea that animal protein has a detrimental effect on bone health or that vegetable-based proteins are better for bone health (13, 27). Several studies examining the effect of meat have found no effect on either bone mineral density or markers for bone mineral density. A 16-wk randomized crossover study of healthy postmenopausal women found that consuming a high-meat diet (297 g/d of meat), providing 117 g of protein, did not adversely affect urinary calcium excretion, calcium retention, or clinical indicators of bone formation and resorption compared with a low-meat diet (45 g/d of meat and 68 g of protein) (28). In another study, 15 patients on a constant metabolic diet, including a constant calcium intake within each individual's diet, were given either 200 or 500 g/d of meat (29). The increase in meat intake resulted in no change in urinary calcium excretion.

CALCIUM INTAKE

The effect of protein on bone mass may also depend on calcium intake. Protein intake increases urinary calcium loss, but whether negative calcium balance results will depend on dietary calcium intake (4). In a study of changes in bone resorption markers, 15 young, healthy men and women participated in 3 randomly assigned 5-d diet periods (low-nitrogen, low-calcium; high-nitrogen, high-calcium; high-nitrogen, high-calcium). Levels of markers were compared with the subjects' average baseline dietary intake of 0.99 $g \cdot kg^{-1} \cdot d^{-1}$ protein and 152 mg of calcium/d. Bone resorption markers were decreased by an approximate 1 g·d increase in dietary calcium but were not affected by a dietary protein intake of 2.71 $g \cdot kg^{-1} \cdot d^{-1}$ (27). Similar findings have been observed in older subjects. In the study of 342 men and women cited earlier, associations between protein intake and changes in bone mass density were examined. The researchers identified a positive association between dietary protein intake and change in bone mass density in those with the highest intake of protein who were supplemented with calcium and vitamin D (26). There was no benefit from supplementation among those with lower intakes of protein.

ACID/BASE BALANCE

While protein seems to have a direct anabolic effect on bone, the relation between protein intake and bone is further complicated by the potential negative effect of overall dietary acid-base balance (30). A Western-type diet has been reported to be associated with osteoporosis and urinary calcium loss (31). Urinary calcium has been found to be increased with acid-forming foods, such as meat, fish, eggs, and cereal, and negatively associated with plant foods and is likely determined by the acid-base status of the total diet. Bone loss may be attributable, in part, to the mobilization of skeletal salts to balance the endogenous acid generated from acid-forming foods (32). In addition, net renal acid excretion can be predicted from the ratio of dietary protein to potassium because the dietary intake of potassium occurs mainly as salts of weak organic acids and therefore has an alkalizing effect (30, 33). This relationship may explain the reported beneficial influence of fruit and vegetables, the major dietary source of potassium, on bone health (25, 30, 34). The detrimental effect of dietary acidity on the skeleton is relatively small (35), but a small effect may have a large impact over time (36). The positive association sometimes observed between meat intake and bone loss may, in fact, be a reflection more of inadequate intake of fruits and vegetables than overconsumption of meat.

WEIGHT LOSS

Loss of bone mass often accompanies weight loss induced by calorie restriction (37–39). Self-reported weight cycling has also been found to be detrimental to bone mass (38). During weight loss, a higher protein diet (≈108 g/d) has been found to preserve bone mineral better than a lower protein diet (≈70 g/d) in overweight men and women, even after adjusting for the greater fat loss produced by the higher protein diet (40). In a study of obese women, those who lost weight as a result of bariatric surgery experienced significant loss of bone mass even at sites not influenced by loading caused by excess body weight. Hormonal factors, such as IGF-1, are associated with this process. Levels of IGF-1 were found to be significantly lower in those who underwent bariatric surgery compared with those who did not undergo surgery (41).

Exercise may offset the adverse effects of energy restriction on bone (42), though the research examining the effects of exercise on bone mass during weight loss is mixed (38, 43). One study found that moderate weight loss, even when accompanied by an increase in physical activity, resulted in greater loss of bone mass than among a group of control women who gained weight (39).

MUSCLE MASS

Changes in bone mass, muscle mass, and strength track together over the life span, making bone health a musculoskeletal issue, not just a skeletal issue (44, 45). Maintenance of adequate bone strength and density with aging is highly dependent on the maintenance of adequate muscle mass and function, which is in turn dependent on adequate intake of high-quality protein (46). It has been suggested that dietary proteins are as essential as calcium and vitamin D for bone health and osteoporosis prevention. The mechanisms responsible for bone loss with age, whether nutrient deficiencies, decreased hormone production, or a decrease in physical activity, may also be responsible for the loss of muscle mass (14, 44).

CONCLUSION

Despite a widely held belief that high-protein diets (especially diets high in animal protein) result in bone resorption and increased urinary calcium, higher protein diets are actually associated with greater bone mass and fewer fractures when calcium intake is adequate. Perhaps more concern should be focused on increasing the intake of alkalinizing fruits and vegetables rather than reducing protein sources. The issue for public health professionals is whether recommended protein intakes should be increased, given the prevalence of osteoporosis and sarcopenia. Currently, little or no attention is paid to ensuring adequate protein intake for elderly fracture patients. In the hospital setting, there should be nutrition protocols in place for hip-fracture patients that include higher protein and calcium intakes. Moreover, health professionals may need to be reeducated about the important role of protein in bone health.

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