Not Just Calcium and Vitamin D: Other Nutritional Considerations in Osteoporosis

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Calcium and vitamin D are the mainstays of nutritional intervention for the prevention and treatment of osteoporosis. However, conditions that alter nutritional status as well as other nutrients should be considered when diagnosing and treating osteoporosis and osteopenia. Current research supports the early diagnosis and treatment of anorexia nervosa to prevent associated bone loss and increased risk of fracture. Weight restoration in patients with anorexia nervosa is central to bone mass stabilization. Other nutritional considerations include nutrients such as vitamin B-12 and vitamin K that may reduce fracture risk by increasing bone mineral density as well as the improvement of bone microarchitecture. Diets high in fruits and vegetables contribute nutrients such as magnesium associated with bone health and may also produce an alkaline environment, reducing calcium excretion and thus improving bone density.

Introduction

Osteoporosis is multifactorial disease, the appropriate management of which necessitates the recognition of other diseases and conditions that compromise nutritional status and thus contribute to low bone density. Eating disorders are psychiatric in nature but manifest as unhealthy eating behaviors that alter metabolic and hormonal pathways, alter body weight, and result in decreased bone density and increased fracture risk. The early identification and treatment of eating disorders, particularly anorexia nervosa, are crucial for preventing bone loss that leads to increased fracture risk often early in life.

Overall nutritional status and dietary patterns should also be considered in the clinical management of osteoporosis. Although calcium and vitamin D remain the mainstays of clinician nutritional management for optimal bone health, attention to B-12, vitamin K, and the nutrients associated with high intakes of fruits and vegetables such as potassium, magnesium, and vitamin C may be appropriate as well. This review discusses recent findings in these areas as well as recommendations for patient care.

Eating Disorders and Osteoporosis

The development of eating disorders in adolescence may threaten peak bone density accrual, which occurs largely during the adolescent years. Although low bone density in bulimia nervosa (BN) is not typical, it is well established that female patients with anorexia nervosa (AN) are at significantly greater risk of developing osteopenia, osteoporosis, and fragility fractures when compared to healthy controls. In a recent cross-sectional study of 214 women with AN, the prevalence of osteopenia, defined as a T-score between –1 and –2.5, was 51.7% [1••]. The prevalence of osteoporosis, defined as a T-score greater than or equal to –2.5, was 34.6%. The prevalence of women reporting a history of bone fractures was 30% [1••]. Grinspoon et al. [2] reported a 92% prevalence of osteopenia in young, female patients with AN, 38% of whom had osteoporosis. A sevenfold increase in the risk of nonspinal fractures has been reported in patients with AN when compared to age-matched controls [3].

Patients diagnosed with AN are undernourished and experience metabolic and hormonal abnormalities that interfere with bone resorption and formation [4,5]. However, clinical markers such as body mass index (BMI), duration of regular menses prior to diagnosis, and duration of amenorrhea may be the best predictors of bone mineral density (BMD) in patients with AN. Audi et al. [5] evaluated 73 female patients with AN classified according to the different stages of their illness (active, weight recovered but still amenorrheic, and fully recovered). Patients in the active phase presented with multiple hormonal and metabolic irregularities; however, none of these measurements predicted BMD. BMI and duration of

regular menses before amenorrhea were positively correlated with BMD, and duration of amenorrhea negatively correlated with BMI.

Similar results were found in a follow-up study of 47 patients with AN and BN. BMD of recovered AN patients was greater due to a net loss of bone mass in the nonrecovered patients after the 3.6-year study period [6]. BN patients had normal BMD with the exception of one patient. All patients who achieved a BMI of at least 18.5 kg/m^2 experienced no change or slight increases in BMD.

The bone loss that occurs in patients with AN appears to be greater than that in patients with amenorrhea but normal BMI. The BMD of 30 young, premenopausal women with AN was significantly lower than that of 19 age-matched women with hypothalamic amenorrhea, even though both groups had similar estradiol levels [7]. Duration of amenorrhea, age of menarche, and N-telopeptide levels were inversely correlated with BMD at all sites. BMI, insulin-like growth factor I, lean body mass, and fat intake were positively correlated with BMD, supporting the importance of nutritional factors, particularly BMI, on bone health in patients with AN.

Because of the relationship between estrogen deficiency and amenorrhea, many physicians prescribe estrogen/progestin medications for the treatment of low bone density in patients with AN. In a survey of physician members of the Society for Adolescent Medicine, 78% involved in the treatment of patients with AN prescribed hormone replacement therapy (HRT) [8]. However, little evidence supports the use of HRT in patients with AN. In a prospective observational study, patients with AN receiving estrogen-progestin therapy (mean age 17.5 ± 2.5 years) did not predict BMD change at the lumbar spine or the hip over the 1-year study period when compared to patients with AN receiving standard treatment (mean age 16.3 ± 1.9 years) [9]. Body weight was the greatest predictor of BMD at baseline and at follow-up. These findings are supported by other researchers who analyzed adults with AN (mean age 23.7 years) and found no benefit of estrogen therapy on bone density [10].

Other research findings support the importance of BMI, particularly lean body mass, in the restoration of BMD. Soyka et al. [11] prospectively compared changes in bone density, bone-related hormones, and bone turnover markers of 19 young females with AN (mean age 15 years) to healthy controls for 1 year. Bone turnover markers were significantly lower at baseline in subjects with AN compared to the controls but increased significantly in association with improvements in nutritional status after 1 year. Increases in bone-specific alkaline phosphatase and N-telopeptide were positively associated with lumbar spine BMD over the 1-year period; however, body mass and lean body tissue were the major predictors of changes in BMD. Subjects who resumed menstruation and gained weight were no more likely to increase BMD than subjects who gained weight only.

Bisphosphonate therapy in patients with AN has not been examined extensively. However, adolescent female subjects with AN (mean age 16.9 ± 1.9 years) receiving alendronate therapy in a small pilot study (n = 32) did experience increases in lumbar and hip bone density within the treatment group, but these increases were not significantly different than increases in the placebo group (4.4% ± 6.4% and 3.5% ± 4.6% in the alendronate group and 2.3% ± 6.9% and 2.2% ± 6.1% in the control group) [12]. Body weight was the single biggest determinant of bone density, accounting for 47.3% of the variance in the lumbar spine. However, only 17.2% of the patients at the end of the study period had bone densities within the normal range for their age.

In a more recent evaluation, risedronate therapy was found to increase bone density in young women with AN [13]. The BMD of 10 women (mean age 28.6 ± 2.6 years) with AN receiving 5 mg of risedronate daily was compared to baseline and to 14 controls (mean age 26.9 ± 1.5 years) with AN at 6 and 9 months. At 6 months, patients who had received risedronate experienced an increase in percent change in BMD at the lumbar spine compared to controls, who lost bone density (4.1 ± 1.6 vs –1.5 ± 1.0). At 9 months, the percent change was 4.9 ± 1.0 in the risedronate group compared to –1.0 ± 1.3 in the controls. Additionally, cross-linked N-teleopeptide of type I collagen (NTX) levels in the patients receiving risedronate were significantly lower than those of the controls at 1 and 3 months.

Both studies evaluating bisphosphonate use in young women with AN had very small sample sizes. Larger, randomized controlled trials should be conducted before definitive recommendations can be made for bisphosphonate use in premenopausal females with AN. Additionally, bisphosphonate therapy is not approved by the U.S. Food and Drug Administration in premenopausal women, with the exception of those receiving glucocorticoid therapy, so caution should be exercised with its use in this demographic.

Because anorexic bone loss is characterized by both increased resorption and decreased formation of bone, researchers have hypothesized that anabolic agents may be useful in treating bone loss. In a small, randomized intervention (n = 33), Miller et al. [14] hypothesized that short-term, low-dose (150 μg or 300 μg) testosterone administration would increase three markers of bone formation in young females with AN: C-terminal propeptide of type I collagen, osteocalcin, and bone-specific alkaline phosphatase. Baseline free testosterone levels correlated with L4 bone density (r = 0.51, $P < 0.001$) and BMI (r = 0.39, P = 0.02). After 3 weeks, type I collagen levels had increased (r = 0.50, P = 0.02), but no changes in osteocalcin or bone-specific alkaline phosphatase were observed in the group receiving testosterone when compared to the placebo group. The short-term duration and small study size warrant further investigation before testosterone can be recommended for treatment of low BMD in female patients with AN.

Table 1. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for anorexia nervosa

Criterion	Description
A	Refusal to maintain body weight at or above a minimally normal weight for age and height (eg, weight loss leading to maintenance of body weight less than 85% of that expected or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected).
B	Intense fear of gaining weight or becoming fat, even though underweight.
C	Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight.
D	In postmenarcheal females, amenorrhea (ie, the absence of at least three consecutive menstrual cycles). A woman is considered to have amenorrhea if her periods occur only following hormone (eg, estrogen) administration.
Specify type	
Restricting type	During the current episode of anorexia nervosa, the person has not regularly engaged in binge-eating or purging behavior (ie, self-induced vomiting or the misuse of laxatives, diuretics, or enemas).
Binge-eating/ purging type	During the current episode of anorexia nervosa, the person has regularly engaged in a binge-eating or purging behavior (ie, self-induced vomiting or the misuse of laxatives, diuretics, or enemas).

From American Psychiatric Association [41], with permission.

The consistent finding among the studies reviewed emphasizes the primary role of nutrition, specifically the recovery of a healthy body weight, as the major determinant of BMD restoration. However, a complete reversal of bone loss for most patients with AN is presently an unrealistic expectation. Few subjects in the studies reviewed regained bone density to normal levels. Longer study duration could reveal different outcomes; however, early diagnosis and treatment are critical to preventing long-term negative outcome, particularly in young patients. In a prospective study, Lantzouni et al. [15] found that 13 out of 16 premenarchal females with AN did not achieve their target height after 1 year postmenarche despite demonstrating catch-up growth with nutrition intervention [15].

Clinicians should be alert to early signs of AN prior to extreme weight and bone loss, in order to attenuate negative psychologic and physiologic effects. Dual-energy x-ray absorptiometry (DXA) is recommended in patients who develop eating disorders, the results of which can be helpful during the counseling process to raise awareness of the physiologic effects of eating disorders and motivate the patient to increase BMI [16••]. Osteopenia can develop in as little as 6 months after the onset of amenorrhea; therefore, early intervention is imperative. The diagnostic criteria for anorexia nervosa are shown in Table 1.

Vitamin B-12 and Homocysteine

Vitamin B-12 may play a role in increasing osteoblast proliferation possibly by stimulating alkaline phosphatase activity [17]. Furthermore, vitamin B-12 deficiency along with folic acide may increase homocysteine (hcy) levels, which may interfere with collagen cross-linking, thereby increasing bone fragility.

Two recent studies evaluated the relationship between high hcy levels and osteoporotic fracture risk in older men and women. In a prospective, population-based study using two nonoverlapping samples of subjects, van Meurs et al. [18] followed 2406 participants 55 years of age or older. A total of 191 subjects experienced osteoporotic fractures during the 11,253 person-years of follow-up. For every one standard deviation increase in hcy, the overall adjusted relative risk of fracture increased by a factor of 1.4 (95% CI, 1.2–1.6). Higher hcy levels were associated with a higher risk of fracture. Those in the highest quartile for hcy had a 1.9-fold increase in the risk of fracture (95% CI, 1.4–2.6). No association was found between hcy levels and BMD. The researchers speculate that elevated hcy levels interfere with bone microarchitecture and that its relationship to fracture risk is independent of BMD.

Data from subjects 59 to 91 years old enrolled in the Framingham study showed similar results [19]. The hip fracture risk for women in the highest quartile for total hcy increased by a factor of 1.92 (95% CI, 1.18–3.10) compared to the women in the first quartile. The hip fracture risk for men in the highest quartile for total hcy increased by a factor of 3.84 (95% CI, 1.38–10.70) when compared to men in the lowest quartile.

Although these findings suggest an association between low hcy levels and fracture risk, a direct, causal effect cannot be assumed. Hcy could simply be a marker for other causal factors, in which case, it could serve as a predictor of fracture in a clinical setting [20].

Low plasma vitamin B-12 was found to be associated with low bone mineral content and BMD in women but not men in a recent cross-sectional study [17]. Of the female subjects categorized as having normal B-12 levels (> 320 pmol/L), 6% had osteoporosis ($n = 34$). The prevalence of osteoporosis in the marginal group (210 < plasma vitamin B-12 ≤ 320 pmol/L) was 25% ($n = 48$) and 37% in the vitamin B-12 deficient group (≤ 210 pmol/L) ($n = 30$). The risk of osteoporosis increased by a factor of 6.9 (95%

CI, 1.2–39.4) for the women in the deficient group compared to women in the normal B-12 group. However, the large confidence interval is indicative of much variance and larger, longitudinal studies should be undertaken to better estimate population risk.

Researchers in Japan examined the effect of folate and mecobalamin (vitamin B-12) supplementation on hip fractures in 628 stroke patients 65 years of age or older in a double-blind, randomized controlled trial [21]. Patients in both the treatment and the placebo groups had elevated plasma hcy levels and low levels of serum cobalamin and folate at baseline. After two years of follow-up, hcy levels decreased by 38% in the treatment group and increased by 31% in the placebo group ($P < 0.001$). There were significantly more hip fractures in the placebo group than in the treatment group (27 vs 6, $P < 0.001$). The adjusted relative risk of hip fracture for the treatment group was 0.20 (95% CI, 0.08–0.05) compared to the placebo group and an absolute risk reduction of 7.1% (95% CI, 3.6%–10.8%). Although the risk of hip fracture decreased in the treatment group, their BMD did not differ from the placebo group at 1 or 2 years after baseline, suggesting that the positive effects of folate/mecobalamin supplementation may be due to improvement of bone microarchitecture. These data do not equivocally confirm the role of B-12 supplementation in treating osteoporosis and preventing fractures, but recommending a basic multivitamin in addition to foods high in vitamin B-12 and folate to assure adequate intake is low risk and possibly beneficial, particularly for elderly patients.

Vitamin K

Vitamin K is actually a group of compounds with similar function. Phylloquinones (vitamin K1) are found in vegetables, leafy greens, and other plant sources. Menaquinones (vitamin K2) are found in animal products such as meat, cheese, and fermented soy products such as miso, and they are also produced by bacteria in the large intestine. Poor vitamin K status may compromise bone matrix and increase the risk of osteoporotic fracture, but the effect of vitamin K supplementation on fracture risk is still a matter of debate. Results from studies vary, possibly due to the type of vitamin K evaluated. Three bone proteins (ie, osteocalcin, matrix Gla protein, and protein S) are vitamin K dependent [22]. The calcium-binding capacity of proteins such as osteocalcin is dependent upon the carboxylation of glutamic acid to γ-carboxyglutamic acid, which requires vitamin K [23]. As with vitamin B-12, vitamin K status may affect bone microarchitecture to a greater extent than bone density. However, BMD has been the major outcome measured in recent observational studies and clinical trials of vitamin K and osteoporosis.

Several studies have shown modest reductions in BMD loss with vitamin K supplementation and dietary intake. A cross-sectional study of 1112 men and 1479 women between the ages of 29 and 86 years old (mean 59 ± 9 years), researchers reported an association between dietary and supplemental vitamin K intake on BMD in women but not in men [24]. Women reporting the lowest total intakes of vitamin K (mean 70.2 μg/d) had significantly lower BMD at the femoral neck and the lumbar spine than those with the highest intake (mean 309 μg/d). No associations between vitamin K intake and BMD were found in men.

A more recent cross-sectional study evaluated the association between biochemical measures of vitamin K status and BMD at the hip and the spine in 741 men and 863 women with a mean age of 59 years [25]. Low plasma vitamin K was associated with low femoral neck BMD in men, but no association was found in the spine. In postmenopausal women not taking estrogen, high plasma levels of uncarboxylated osteocalcin (indicative of low plasma vitamin K) were associated with low BMD ($P < 0.10$). No significant relationships were found for premenopausal women or for postmenopausal women taking estrogen. Although these data suggest that estrogen status affects the relationship between plasma vitamin K levels and BMD, the cross-sectional designs of these studies limit their interpretation.

In a randomized, double-blind, placebo-controlled intervention study, Braam et al. [26] randomized 181 healthy postmenopausal women 50 to 60 years old to a placebo group, a mineral supplement containing calcium, magnesium, and zinc plus vitamin D (MD), and the MD supplement plus vitamin K1 (MDK). All three groups lost bone density in both the lumbar spine and the femoral neck over the 3-year study period, but the difference in the femoral neck between the MDK group and placebo was 1.7% (95% CI, 0.35–3.44) and between the MDK group and the MD group was 1.4% (95% CI, 0.10–3.41). No differences were found for lumbar spine BMD.

In another recent clinical trial, researchers compared the efficacy of HRT, etidronate, calcitonin, alfacalcidol, and vitamin K (menatetrenone 45 mg/day), on markers of bone turnover, BMD at the distal radius, and vertebral fractures in 396 postmenopausal Japanese women [27]. These outcome measures were assessed at baseline and every three months over the 2-year study period. BMD increased in the HRT and calcitonin groups and decreased in all other groups. However, compared to the placebo group, the decrease in bone density was less in the vitamin K group (-3.3% vs -1.9%, $P = 0.03$). The relative risk for new vertebral fractures in the vitamin K group was 0.44 (95% CI, 0.20–0.99); therefore, the risk of new vertebral fractures was reduced despite the lack of increase in BMD. The large confidence interval is indicative of the small sample size in the five intervention groups and the control groups thus limiting interpretation of the results.

Not all researchers have found positive results with vitamin K supplementation and BMD or other markers of bone health. An unpublished recent preliminary evaluation of 176 postmenopausal women without osteoporosis randomized to placebo, 1 mg of vitamin K1, or 45 mg of menatetrenone

Table 2. Composition of the DASH diet

Food Group	Servings	Examples	Nutrients
Grains (preferably whole grain)	7–8/day	1 slice whole wheat bread; 1/2 cup cooked rice, pasta, or cereal	Magnesium (in unrefined whole grains), fiber
Vegetables	4–5/day	1 cup raw leafy greens, 1/2 cup cooked vegetables, 1 cup raw vegetables, 6 oz vegetable juice	Potassium, magnesium, fiber
Fruits	4–5/day	6 oz 100% fruit juice; 1 medium piece of fruit; 1/4 cup dried fruit; 1/2 cup fresh, frozen, or canned fruit	Potassium, magnesium, fiber
Low-fat/fat-free dairy foods	2–3/day	8 oz low-fat or skim milk, 1 cup low-fat yogurt, 1.5 oz low-fat cheese	Calcium, potassium, phosphorus, protein, vitamin B-12
Lean meat, fish, poultry	2 or fewer per day	3 oz broiled sirloin, baked chicken without the skin, grilled fish	Protein, phosphorus, vitamin B-12
Nuts, seeds, starchy beans	4–5/week	1/3 cup almonds, walnuts, mixed nuts; 2 tablespoons sunflower seeds; 1/2 cup lentils, pinto beans, black beans	Magnesium, potassium, protein, fiber
Fats and oils	2–3/day	1 teaspoon soft margarine, 1 tablespoon mayonnaise, 1 teaspoon vegetable oil, 2 tablespoons light salad dressing	Essential fatty acids

DASH—Dietary Approaches to Stop Hypertension.
Data from [42].

daily found no differences among the groups in bone turnover markers or BMD at 1, 3, 6, and 12 months [28].

These studies suggest a possible modest effect of adequate vitamin K status and intake on reducing bone loss in older men and women. It is possible that vitamin K reduces the risk of fracture without significant improvement of bone density.

Dietary Patterns

Dietary patterns high in fruits and vegetables have been shown to have a beneficial effect on blood pressure and blood lipids, potentially lowering the risk for heart disease and stroke [29,30]. This dietary pattern may also have a beneficial effect on bone density and subsequent fracture secondary to effects on acid/base homeostasis favoring an alkaline environment that reduces bone resorption [31].

Several studies have found a positive association between bone density and dietary fruit and vegetable intake. Twelve-year-old girls with the highest fruit intake had significantly higher heel BMD than those with the lowest fruit intake ($\beta = 0.037$; 95% CI, 0.017–0.056) [32]. In a 4-year longitudinal study of elderly men and women ($n = 5209$), Tucker et al. [33] examined the association between potassium and magnesium from diet (ie, fruit and vegetable intake) and supplements on changes in BMD at three hip sites and one forearm site [33]. Potassium, magnesium, and fruit and vegetable intake were all positively associated with BMD at various sites for both men and women ($P < 0.05$), but not all sites. Nutrient intake and a diet high fruit and vegetables were associated with less BMD loss over time in men, but not in women.

Another cross-sectional study did not find associations between fruit and vegetable intake and BMD for women. Tucker et al. [34] examined the diets of 907 male and female subjects age 69 to 93 years. A high fruit and vegetable intake pattern was found to be protective for men but not for women. High candy consumption was associated with low BMD in both men and women at some but not all sites.

In a more recent longitudinal study, researchers examined nutrients associated with a high intake of fruits and vegetables in 891 women ages 44 to 55 years at baseline and 50 to 59 years after 5 to 7 years of follow-up [35••]. Magnesium intake was recently found to be associated with higher bone density in healthy older white subjects and may affect calcium metabolism because of its role in the actions of parathyroid hormone and vitamin D [36]. Higher intakes of potassium, magnesium, and vitamin C reduced BMD loss from baseline in pre- and perimenopausal women who had never taken HRT.

Prynne et al. [37] conducted a cross-sectional investigation of fruit and vegetable intakes and bone mineral status in five age and sex cohorts. Two particular strengths of this study were the dietary and BMD data collection methods. Seven-day food diaries were used to collect data on dietary intake. They recorded actual portion weights of fruits and vegetables consumed, reflecting more accurate measures of present instead of past fruit and vegetable intakes. Also, bone density was measured as size-adjusted bone mineral content (SA-BMC) as well as BMD. Positive associations were found between fruit intake and SA-BMC in the spine in adolescent boys and girls and older women. Both fruit and dietary vitamin C intakes were positively associated with femoral neck SA-BMC in boys. Vegetables alone were not associated with bone density measurements.

Other researchers have examined the effects of dietary intake of fruits and vegetables on bone turnover markers. In a recent randomized, feeding study of the Dietary Approaches to Stop Hypertension (DASH) diet, Lin et al. [38] evaluated two dietary patterns and three sodium levels on bone and calcium markers in 186 adults 23 to 76 years of age. The DASH diet (Table 2) is high in fruits and vegetables, low-fat dairy products, nuts, and seeds, and

Table 3. Bone-building nutrients

Nutrient	Daily value	Role in bone health	Best sources
Vitamin B-12	6 μg	May increase osteoblast activity; lowers elevated circulating homocysteine, which may increase fracture risk	Animal products (eg, meat, fish, poultry, eggs, milk, cheese), fortified cereals
Folic acid	400 μg	Lowers elevated circulating homocysteine	Fortified grains/cereals, leafy green vegetables, legumes, sunflower seeds, liver, orange juice, asparagus, tofu
Vitamin C	60 mg	Hydroxylation of collagen	Citrus fruits, cruciferous vegetables, dark green vegetables, cantaloupe, strawberries, lettuce, tomatoes, potatoes, papayas, mangoes
Vitamin K	80 μg	Bone protein synthesis; carboxylation of osteocalcin	Liver, leafy green vegetables, cruciferous vegetables, asparagus, soybeans, green tea, eggs, soybean oil, strawberries, lentils, chick peas, intestinal bacteria synthesis
Vitamin D	400 IUs	Calcium absorption	Synthesis from sunlight, cod liver oil, fatty fish, fortified foods such as milk, juice, and cereals
Magnesium	400 mg	Calcium metabolism, bone mineralization	Legumes, nuts, milk, yogurt, potatoes, halibut, artichokes, whole grains
Phosphorus	1000 mg	Bone mineralization, component of hydroxyapatite	Milk, yogurt, cheese, meats, fish, legumes, almonds, sunflower seeds, tofu
Potassium	3500 mg	Possible reduction in calcium excretion	Fruits, vegetables, milk, yogurt, cottage cheese, pinto beans, sunflower seeds, peanuts
Calcium	1000 mg	Bone mineralization, component of hydroxyapatite	Milk, cheese, yogurt, calcium-fortified orange juice

Data from Whitney et al. [43] and Pennington [44].

moderate amounts of lean meat, poultry, and fish and is high in magnesium, potassium, and calcium [29]. When compared to the subjects in the control group, the subjects on the DASH diet experienced 8% to 11% reduction in serum osteocalcin ($P < 0.001$) and 16% to 18% reduction in C-terminal telopeptide of type 1 collagen (CTX) ($P < 0.001$) over the 30-day study period. The researchers concluded that over time, this reduced bone turnover could have positive effects on bone health.

In a small, cross-sectional study of 62 healthy women ages 45 to 55 years, higher intakes of potassium and magnesium correlated with higher total bone mass ($P < 0.05$ to $P < 0.005$) [39]. BMD of the femoral neck was higher in women with the highest childhood fruit and vegetable intake compared to those whose consumption was classified as low to medium ($P < 0.01$). In a regression analysis, magnesium was inversely correlated with pyridinoline and deoxypyridinoline excretions, accounting for 12.3% and 12.0% of the variations, respectively. Potassium intake was positively associated with forearm BMD ($r = 0.30$; $P < 0.01$).

In a recent study, researchers used dietary potassium and protein intakes to approximate net endogenous acid production (NEAP) and markers of bone health in 5119 women ages 45 to 54 years [40]. Quartile comparisons showed that study subjects in the highest potassium intake group and the lowest NEAP group showed a 6% to 8% increase in free pyridinoline/creatinine and free deoxypyridinoline levels. The only associations observed between BMD and potassium intake were in premenopausal women, where a difference of 8% in BMD was observed in the highest quartile of potassium intake compared to the lowest. The researchers estimated this difference to equal one-half the standard deviation for this population. Hormonal influences could supercede dietary influences, which could explain the differences seen only in premenopausal women.

The relationship between fruit and vegetable intake and bone health is equivocal, but it is reasonable and of great potential benefit to recommend to the general populace a diet high in fruits and vegetables, such as the DASH diet.

Conclusions

Although individual dietary modifications may produce only modest effects on bone health, these modifications are generally low risk and potentially beneficial for general chronic disease prevention. Recommending a diet high in fruits and vegetables with moderate amounts of nuts, seeds. and low-fat dairy products is safe for most patients and can help reduce blood pressure and heart disease risk. A basic multivitamin can not only increase vitamin D intake but can add magnesium, vitamin K, and B-12 to the overall daily intake. Patients (with the exception of those taking warfarin) should be instructed to take a basic, daily multivitamin. However, none of the data presented here indicate that dietary changes alone are enough to prevent or increase bone loss independently. A summary of several nutrients, their function in bone health, and food sources are shown in Table 3.

Physicians should be aware of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, criteria for eating disorders, particularly anorexia nervosa, and identify clinical and subclinical cases as early as possible. Once bone mass is lost, complete recovery may not be possible, therefore early identification and intervention are essential.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1.•• Miller KK, Grinspoon SK, Ciampa J, et al.: **Medical findings in outpatients with anorexia nervosa.** *Arch Intern Med* 2005, **165:**561–566.

This article provides a comprehensive overview of the clinical characteristics of women presenting with anorexia nervosa and may aid clinicians in the treatment of patients.

2. Grinspoon S, Thomas E, Pitts S, et al.: **Prevalence and predictive factors for regional osteopenia in women with anorexia nervosa.** *Ann Intern Med* 2000, **133:**790–794.
3. Rigotti NA, Neer RM, Skates SJ, et al.: **The clinical course of osteoporosis in anorexia nervosa.** *JAMA* 1991, **265:**1133–1138.
4. Golden NH, Kreitzer P, Jacobson MS, et al.: **Disturbances in growth hormone secretion and action in adolescents with anorexia nervosa.** *J Pediatr* 1994, **125:**655–660.
5. Audi L, Vargas DM, Gussinye M, et al.: **Clinical and biochemical determinants of bone metabolism and bone mass in adolescent female patients with anorexia nervosa.** *Pediatr Res* 2002, **51:**497–504.
6. Zipfel S, Seibel MJ, Lowe B, et al.: **Osteoporosis in eating disorders: a follow-up study of patients with anorexia and bulimia nervosa.** *J Clin Endocrinol Metab* 2001, **86:**5227–5233.
7. Grinspoon S, Miller K, Coyle C, et al.: **Severity of osteopenia in estrogen-deficient women with anorexia nervosa and hypothalamic amenorrhea.** *J Clin Endocrinol Metab* 1999, **84:**2049–2055.
8. Robinson E, Bachrach LK, Katzman DK: **Use of hormone replacement therapy to reduce the risk of osteopenia in adolescent girls with anorexia nervosa.** *J Adolesc Health* 2000, **26:**343–348.
9. Golden NH, Lanzkowsky L, Schebendach J, et al.: **The effect of estrogen-progestin treatment on bone mineral density in anorexia nervosa.** *J Pediatr Adolesc Gynecol* 2002, **15:**135–143.
10. Klibanski A, Biller BM, Schoenfeld DA, et al.: **The effects of estrogen administration on trabecular bone loss in young women with anorexia nervosa.** *J Clin Endocrinol Metab* 1995, **80:**898–904.
11. Soyka LA, Misra M, Frenchman A, et al.: **Abnormal bone mineral accrual in adolescent girls with anorexia nervosa.** *J Clin Endocrinol Metab* 2002, **87:**4177–4185.
12. Golden NH, Iglesias EA, Jacobson MS, et al.: **Alendronate for the treatment of osteopenia in anorexia nervosa: a randomized, double-blind, placebo-controlled trial.** *J Clin Endocrinol Metab* 2005, **90:**3179–3185.
13. Miller KK, Grieco KA, Mulder J, et al.: **Effects of residronate on bone density in anorexia nervosa.** *J Cli Endocrinol Metab* 2004, **89:**3903–3906.
14. Miller KK, Grieco KA, Klibanski A: **Testosterone administration in women with anorexia nervosa.** *J Clin Endocrinol Metab* 2005, **90:**1428–1433.
15. Lantzouni E, Frank GR, Golden NH, Shenker RI: **Reversibility of growth stunting in early onset anorexia nervosa: a prospective study.** *J Adolesc Health* 2002, **31:**162–165.
16.•• Yager J, Andersen AE: **Clinical practice. Anorexia nervosa.** *N Engl J Med* 2005, **353:**1481–1488.

This article provides a comprehensive overview of the diagnosis and treatment of the patient with anorexia and will assist clinicians in managing patients with anorexia.

17. Dhonukshe-Rutten RA, Lips M, de Jong N, et al.: **Vitamin B-12 status is associated with bone mineral content and bone mineral density in frail elderly women but not in men.** *J Nutr* 2003, **133:**801–807.
18. van Meurs JB, Dhonukshe-Rutten RA, Pluijm SM, et al.: **Homocysteine levels and the risk of osteoporotic fracture.** *N Engl J Med* 2004, **350:**2033–2041.
19. McLean RR, Jacques PF, Selhub J, et al.: **Homocysteine as a predictive factor for hip fractures in older person.** *N Engl J Med* 2004, **350:**2042–2049.
20. Raisz LG: **Homocysteine and osteoporotic fractures—culprit or bystander?** *N Engl J Med* 2004, **350:**2089–2090.
21. Sato Y, Honda Y, Iwamoto J, et al.: **Effect of folate and mecobalamin on hip fractures in patients with stroke: a randomized controlled trial.** *JAMA* 2005, **293:**1082–1088.
22. Ferland G: **The vitamin K-dependent proteins: an update.** *Nutr Rev* 1998, **56:**223–230.
23. Vermeer C: **The vitamin-K dependent carboxylation reaction.** *Mol Cell Biochem* 1984, **61:**17–35.
24. Booth SL, Broe KE, Gagnon DR, et al.: **Vitamin K intake and bone mineral density in women and men.** *Am J Clin Nutr* 2003, **77:**512–516.
25. Booth SL, Broe KE, Peterson JW, et al.: **Associations between vitamin K biochemical measures and bone mineral density in men and women.** *J Clin Endocrinol Metab* 2004, **89:**4904–4909.
26. Braam LA, Knapen MH, Geusens P, et al.: **Vitamin K1 supplementation retards bone loss in postmenopausal women between 50 and 60 years of age.** *Calcif Tissue Int* 2003, **73:**21–26.
27. Ishida Y, Kawai S. **Comparative efficacy of hormone replacement therapy, etidronate, calcitonin, alfacalcidol, and vitamin K in postmenopausal women with osteoporosis: the Yamaguchi Osteoporosis Prevention Study.** *Am J Med* 2004, **117:**549–555.
28. Harke JM, Krueger D, Gremar D, et al.: **Vitamin K treatment reduces undercarboxlated osteocalcin but does not alter bone turnover or density in postmenopausal North American women.** *J Bone Miner Res* 2005, **20:**S288.
29. Lin PH, Ginty F, Appel LJ, et al.: **The DASH diet and sodium reduction improve markers of bone turnover and calcium metabolism in adults.** *J Nutr* 2003, **133:**3130–3136.
30. Obarzanek E, Sacks FM, Vollmer WM, et al.: **Effects on blood lipids of a blood pressure-lowering diet: the Dietary Approaches to Stop Hypertension (DASH) trial.** *Am J Clin Nutr* 2001, **74:**80–89.
31. New SA: **Nutrition Society Medal lecture. The role of the skeleton in acid-base homeostasis.** *Proc Nutr Soc* 2002, **61:**151–164.
32. McGartland CP, Robson PJ, Murray LJ, et al.: **Fruit and vegetable consumption and bone mineral density: the Northern Ireland Young Hearts Project.** *Am J Clin Nutr* 2004, **80:**1019–1023.
33. Tucker KL, Hannan MT, Chen H, et al.: **Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women.** *Am J Clin Nutr* 1999, **69:**727–736.
34. Tucker KL, Chen H, Hannan MT, et al.: **Bone mineral density and dietary patterns in older adults: the Framingham Osteoporosis Study.** *Am J Clin Nutr* 2002, **76:**245–252.

35.•• Macdonald HM, New SA, Golden MH, et al.: **Nutritional associations with bone loss during the menopausal transition: evidence of a beneficial effect of calcium, alcohol, and fruit and vegetable nutrients and of a detrimental effect of fatty acids.** *Am J Clin Nutr* 2004, **79:**155–165.
This study is a longitudinal evaluation of several dietary associations with bone mineral density. Clinicians may find this article helpful when answering patients' questions about lifestyle changes they can make to improve bone health.
36. Ryder KM, Shorr RI, Bush AJ, et al.: **Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects.** *J Am Geriatr Soc* 2005, **53:**1875–1880.
37. Prynne CJ, Mishra GD, O'Connell MA, et al.: **Fruit and vegetable intakes and bone mineral status: a cross-sectional study in 5 age and sex cohorts.** *Am J Clin Nutr* 2006, **83:**1420–1428.
38. Appel LJ, Moore TJ, Obarzanek E, et al.: **A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group.** *N Engl J Med,* 1997, **336:**1117–1120.
39. New SA, Robins SP, Campbell MK, et al.: **Dietary influences on bone mass and bone metabolism: further evidence of a positive link between fruit and vegetable consumption on bone health?** *Am J Clin Nutr* 2000, **71:**142–151.
40. Macdonald HM, New SA, Fraser WD, et al.: **Low dietary potassium intakes and high dietary estimates of net endogenous acid production are associated with low bone mineral density in premenopausal women and increased markers of bone resorption in postmenopausal women.** *Am J Clin Nutr* 2005, **81:**923–933.
41. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), 4th edn, Text Revision*. Washington, DC: American Psychiatric Association; 2000.
42. U.S. National Heart, Lung, and Blood Institute: **Your Guide to Lowering Blood Pressure.** Available at http://http://www.nhlbi.nih.gov/health/public/heart/hbp/hbp_low/hbp_low.pdf. Accessed December 5, 2006.
43. Whitney E, Rolfes SR: *Understanding Nutrition*. Belmont, CA: Thomson Wadsworth; 2005.
44. Pennington J: *Bowes and Church's Food Values of Portions Commonly Used*. Philadelphia: Lippincott-Raven Publishers; 1998.