Bone, Body Weight, and Weight Reduction: What Are the Concerns?¹,²

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ABSTRACT Of the U.S. population, 65% is either overweight or obese, and weight loss is recommended to reduce co-morbid conditions. However, bone mobilization and loss may also occur with weight loss. The risk for bone loss depends on initial body weight, age, gender, physical activity, and conditions of dieting such as the extent of energy restriction and specific levels of nutrient intake. Older populations are more prone to bone loss with weight loss; in women, this is due at least in part to a reduced dietary Ca intake and/or efficiency of absorption. Potential hormonal mechanisms regulating bone loss during weight loss are discussed, including decreases in estrogen, leptin, glucagon-like peptide-2, growth hormone, and insulin-like growth factor-1, or an increase in cortisol. In contrast, the rise in adiponectin and ghrelin with weight reduction should not be detrimental to bone. Combining energy restriction with exercise does not necessarily prevent bone loss, but may attenuate loss as was shown with additional Ca intake or osteoporosis medications. Future controlled weight loss trials should be designed to further address mechanisms influencing the density and quality of bone sites vulnerable to fracture, in the prevention of osteoporosis. J. Nutr. 136: 1453–1456, 2006.

KEY WORDS: • bone • calcium • diet • osteoporosis • weight loss

A low body weight is associated with low bone mass (1) and an increased risk of fractures (2), whereas obesity is associated with increased bone mass (3) and reduced bone turnover (4,5) and loss (6,7). Although the additional bone mass in obese compared with lean subjects contributes only ~0.5 kg of total body weight or 1% of body weight (5), it is ~20% of total bone mineral content, thus making a substantial contribution to the higher risk of osteoporosis in lean compared with obese subjects. The reported higher risk of falling in the obese (particularly in those with greater abdominal fat) than in lightweight individuals (8) does not result in an increased risk of fracture due to higher bone density and the cushioning effect of the fat surrounding crucial areas such as the hip. The benefits of high bone density disappear when an individual successfully loses weight (9,10).

In overweight or obese individuals, weight reduction of ~10% is recommended because researchers found it is achievable and reduces co-morbid risk factors (11). However, studies show that a 10% weight loss results in ~1–2% bone loss at the various bone sites (12–16). In addition, Nguyen et al. (6) showed that there is greater bone loss (>1%) with weight loss in normal-weight (less than ~60 kg) compared with overweight or obese individuals (<1% bone loss). Importantly, weight loss and weight-cycling throughout adulthood and older age were shown to increase hip fracture risk (10,17). Losing as little as 5% of body weight increases the fracture risk in postmenopausal women, especially in those who are relatively thin in middle age (10).

Weight reduction and bone. The bone response to weight reduction also varies among different populations. Studies with mixed populations including pre-, peri-, and post-menopausal women, and/or men showed a loss of total body bone mineral density (BMD); 0–2.5% (4,5) and content (BMC; 3–4%) with weight loss, as well as variable losses at regional bone sites (1–13%) (15,18,19). In homogenous populations, studies have more consistent findings. For example, weight reduction (4–13%) in postmenopausal women led to bone loss of ~1–4% compared with a weight-stable group (14,20,21) and a rise in bone turnover (12). Older lean or overweight women who are close to menopause (~48 y) respond to weight reduction (~5%) in a manner similar to that described for postmenopausal women, showing bone loss (0.8% at the hip) (16). Weight loss studies in premenopausal women (<45 y) showed either a small decrease in total body and regional BMD and BMC of 0.5–1.8% (22–24), or no bone changes in controlled trials (25,26). It appears that greater weight loss (>14%) during a relatively short period of time (3–4 mo) results in significant bone loss (23,24), whereas a more moderate weight loss over a longer period of time (6 mo) results in little (<1%) (22) or no bone loss (25,26) in premenopausal women. In the only intervention study in men (middle-aged), in which only total-body bone mass was measured, moderate weight reduction (7%) resulted in a 1% bone loss (27). Epidemiologic studies of elderly men (~70 y) showed that weight loss (both voluntary and involuntary) is an important predictor of bone loss (28) and increased incidence of osteoporosis (29). Bone loss generally begins later in men compared with women due to a higher level of sex steroids until age (10).

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⁴ Abbreviations used: BMC, bone mineral content; BMD, bone mineral density; GLP-2, glucagon-like peptide-2; IGF, insulin-like growth factor; PTH, parathyroid hormone.
Calcium intake. Weight loss studies show that Ca intake typically decreases with energy restriction and that supplementation can suppress the expected rise in bone turnover during energy restriction (Table 1). These data are fairly consistent in the postmenopausal population (12,21). In premenopausal women, we found no bone loss, and Ca supplementation resulted in a slight increase in bone density during weight loss (26). Additionally, a shorter-term (<3 mo) study in a heterogeneous population showed a beneficial effect of Ca supplementation during weight loss (19). However, the decreases in bone mass observed with shorter-term weight loss may not reflect a true steady-state bone balance, but rather incomplete remodeling cycles, in which the resorbed space has not yet been filled in (30).

Calcium absorption. Calcium absorption is typically ~25% in healthy individuals. It is not only a vitamin D–dependent process, but is also mediated by estrogen. Calcium absorption will also vary as a function of dietary intake (31), age, menopausal status, and higher body weight (32). For example, severely obese women have higher true fractional calcium absorption (TFCA) values (35.9 ± 8.0%; unpublished data in our laboratory) than overweight women (27.0 ± 7.8%) (26,33), which is consistent with findings that height, weight, and surface area account for 4% of the variability in Ca absorption (32). It is possible that the higher estrogen levels (34) or greater mucosal surface in larger individuals (32) may contribute to the higher Ca absorption. Energy restriction due to dieting can attenuate Ca absorption (33,34) (Fig. 1), whereas severe chronic malnutrition may enhance absorption to maintain normal serum Ca levels (35). In addition, dieting often results in lowered amounts of Ca and vitamin D consumed (22,25), further compromising the total Ca absorbed. Energy restriction also reduces the intake of macronutrients, some of which enhance Ca absorption, i.e., protein, fat, and lactose. Several hormonal changes occur during weight loss, and it was shown that serum parathyroid hormone (PTH) and estrogen explain 36% of the variation in Ca absorption during weight loss in postmenopausal women (1 g Ca/d) (33). In addition, energy restriction (36) may increase cortisol levels and thereby lower Ca absorption. Although little is known about insulin-like growth factor (IGF)-I and Ca metabolism during weight loss, reduced levels due to energy restriction (37) may decrease Ca absorption (38). The reduced Ca intake and/or absorption during weight loss may contribute to increased bone mobilization and loss.

Other interventions. Extreme weight loss due to diet (39) or surgical intervention is expected to result in more extreme bone loss (40). The influence of varying specific micronutrients (other than Ca) or macronutrients on bone sites with higher fracture rate (i.e., hip or spine) during dieting has not been addressed in a controlled trial. Other studies examined the effects of exercise on bone during weight loss. Total body BMD was shown to decrease by 1–2%, despite the addition of exercise to a moderate weight loss (2–9 kg) regimen (Ca intake of ~700–900 mg/d) in postmenopausal women (13,14,41,42), but the same is not necessarily true for men (42). However, studies also showed that exercise may prevent regional BMD loss at some (13,41,42), but not at all (41,42) sites in postmenopausal women. A carefully controlled trial showed that the addition of osteoporosis medications can attenuate bone loss due to exercise-induced weight reduction (41).

Potential mechanisms for the influences of obesity and weight loss on bone. In obesity, there are a number of mechanisms that produce the higher bone mass, including the weight-bearing effect of excess soft tissue on the skeleton (43), the association of fat mass with the secretion of bone-active hormones (i.e., estrogens, leptin, and adiponectin) from the adipocyte, and the secretion of bone-active hormones from other organs such as the gut (i.e., ghrelin, which stimulates growth hormone), and the pancreas (including insulin and amylin). In addition, obese individuals have lower levels of serum 25-hydroxycholecalciferol (44), which is attributed to its deposition in adipose tissue (44). Secondary hyperparathyroidism is reported in the morbidly obese (45). Furthermore, the regional distribution of fat that influences circulating hormones may also alter bone mass independently of obesity, in which visceral fat is associated with both higher bone mass (46) and levels of estradiol.

During weight reduction, there is a decrease in circulating estrogen and other sex hormones that would be expected to

<table>
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<th>Reference</th>
<th>Population</th>
<th>BMI</th>
<th>Time</th>
<th>Group</th>
<th>Ca intake</th>
<th>Weight change</th>
<th>Total</th>
<th>Spine</th>
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<tr>
<td>Riedt (21)</td>
<td>Post</td>
<td>24–30</td>
<td>6</td>
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<td>+0.6*</td>
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<td>-1.2*</td>
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¹ Abbreviations used: FN, femoral neck; EnR, energy-restricted diet; Ca, Ca supplementation; HT, hormone therapy; NA, not available; PL, Placebo; Pre, premenopausal women; Post, postmenopausal; Ralox, raloxifene; Troch, trochanter; WL, weight loss; WM, weight maintenance.
² Exercise-induced weight loss, partial list of control groups.
³ BMC values (no BMD provided). *Differs from control group, P < 0.05 (WL-PL).
promote osteoclastic activity directly or indirectly due to increased levels of cytokines (i.e., IL-1, IL-6, tumor necrosis factor-α). In addition, there was a rise in the Ca-PTH axis during energy restriction in women consuming low/normal Ca (0.6–1.0 g/d), but not in those whose Ca intake was high (1.7 g/d); this could contribute to a rise in bone resorption. Although vitamin D intake is typically reduced (21) during moderate energy restriction, reduced serum levels were not observed. The adipocyte-derived hormones leptin and adiponectin may also play a role in bone metabolism during weight reduction. The anorectic effect of leptin is not apparent in obesity due to leptin resistance, whereas levels decrease with weight loss. The central effects of leptin inhibit bone formation (47), whereas leptin has direct effects on osteoblasts (48) and indirectly affects osteoclasts (49), possibly through sympathetic signaling (50). The relation between leptin and bone during weight reduction is likely dependent on a number of factors such as obesity, gender, age, ethnicity, and leptin resistance (51). Adiponectin is typically low in obesity and may increase with moderate weight loss (52). Because adiponectin suppresses osteoclast number and activates osteoblastogenesis (53), it is possible that a rise due to weight reduction would have a beneficial effect on bone mass. In addition, the gut-derived hormone, ghrelin, also increases with weight loss (to stimulate appetite) and stimulates osteoblastic proliferation and differentiation (54). However, severe weight loss due to gastric by-pass surgery decreases serum ghrelin levels to almost undetectable levels (55), which could have a detrimental effect on bone. Another gastrointestinal hormone, glucagon-like peptide-2 (GLP-2) increases bone mineralization and reduces bone resorption, yet decreases due to weight reduction (56). Serum IGF-1 is suppressed during energy or protein restriction, and the anabolic effect of IGF-I on bone is well established (57). Finally, serum cortisol may increase with acute fasting (58) or moderate weight loss (21), especially in low estrogen states (21) to increase osteoclast activity and/or decrease Ca absorption (59). Overall, weight reduction decreases serum estrogen, leptin, GLP-2, growth hormone, and IGF-I and/or will increase cortisol; these changes would be expected to have a detrimental effect on bone mass. However, the rise in adiponectin and ghrelin with moderate weight loss may prevent excessive loss of bone. The balance of hormonal changes during weight loss and their effect on bone depend on other factors such as age, gender and/or amount and type of weight loss.

In summary, the data support the occurrence of bone loss during energy restriction in postmenopausal women and possibly in older men. The risk for bone loss may depend on initial body weight, age, gender, physical activity, and conditions of dieting such as the extent of energy restriction or specific levels of nutrient intake. Mechanisms regulating bone due to weight reduction are not well understood at this time. Groups vulnerable to bone loss due to weight reduction likely will benefit from a higher Ca intake and/or possibly higher levels of vitamin D intake or other nutrients; however, to our knowledge, controlled trials designed to address the effect of other nutrients have not been conducted. The inclusion of osteoporosis medications for high-risk patients or during severe weight loss may be indicated. An individualized diet program to minimize bone changes is suggested for all persons, but especially for those ≥50 y old.

**LITERATURE CITED**


**FIGURE 1** The effect of weight loss (WL), weight maintenance (WM), and the level of Ca intake on estimated Ca absorbed in postmenopausal women. NL-Ca, normal Ca (NL-Ca, 1.0 g Ca/d); high-Ca, 1.8 g Ca/d. Values are means ± SEM, n = 57. *Differs from NL-Ca, P = 0.05. †Differs from NL-Ca group, P < 0.001. Adapted from (33).


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