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Bone Loss After Bariatric Surgery: Causes, Consequences and Management

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Abstract

Bariatric surgery is an effective and increasingly common treatment for severe obesity and its many co-morbidities. Among the side effects of these procedures are detrimental effects on bone and mineral metabolism. This review explores the skeletal response to bariatric surgery, potential mechanisms for these changes and strategies for management. Bone disease among bariatric surgery patients is influenced by pre-operative abnormalities in bone and mineral metabolism related to morbid obesity. Changes that occur after surgery are specific to procedure type, with the most pronounced abnormalities in calciotropic hormones and bone loss seen after procedures that result in the most malabsorption. The most consistent site for bone loss after all bariatric procedures is at the hip, although available BMD data are limited by issues associated with DXA technology, including artifact introduced by adipose tissue itself. The bone loss that occurs after bariatric surgery is likely multifactorial. Proposed mechanisms include skeletal unloading, abnormalities in calciotropic hormones, as well as changes in gut hormones. There are very limited data on fracture risk in the bariatric population, and this is a critical area for additional research. Current treatment should be geared toward correcting nutritional deficiencies and following BMD in high-risk patients.

Introduction

Bariatric surgery has become an increasingly common treatment for severe obesity[1, 2], as it results in significant, sustained weight loss [3], reverses many complications of obesity [4, 5] and decreases mortality [6, 7]. However, there are several detrimental effects of these procedures, among them deleterious effects on bone and mineral metabolism, including vitamin D deficiency, hyperparathyroidism and bone loss. The bone loss that occurs after

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bariatric surgery is likely multifactorial. Proposed mechanisms include skeletal unloading, abnormalities in calciotropic hormones, as well as changes in gut hormones. Increased bone turnover may be associated with physiological adaptation of the skeleton to unloading, or it may be associated with pathophysiological changes like increased parathyroid hormone (PTH). Whether the skeletal changes that occur after bariatric surgery are pathological and are associated with skeletal fragility remains to be seen. This review will explore the skeletal response to bariatric surgery, potential mechanisms for these changes and strategies for management. As other recent reviews have specifically explored the relationship between gut hormones and adipokines with bone, we will not address that topic in detail so as not to be duplicative of the recent contributions to the literature.

The rate of weight loss and resolution of co-morbidities after bariatric surgery varies by procedure [8]. The skeletal effects are similarly procedure specific(see Figure 1). Current surgeries involve reduction in stomach size (restriction), delayed mixing of food with bile salts and pancreatic juices (malabsorption), or a combination of both. Gastric banding (GB) is a purely restrictive procedure, in which a silicone band placed around the proximal stomach creates a pouch that holds only a small amount of food. In sleeve gastrectomy (SG), more than 80% of the stomach is transected. Nutrients rapidly pass through the gastric conduit, resulting in altered gut hormones and metabolism.[1] Roux-en-Y gastric bypass (RYGB) has both restrictive and malabsorptive features. Restriction occurs through the creation of a small gastric pouch from the proximal stomach, which is then anastamosed to the proximal jejunum to form an alimentary tract. Food content mixes with bile and pancreatic secretions in the distal jejunum. In biliopancreatic diversion with duodenal switch (BPD/DS), food bypasses most of the small intestine; agastric sleeve is anastamosed to the distal ileum where food mixes with digestive enzymes[8]. In RYGB and BPD/DS, the intestinal surface area available for caloric absorption is reduced, leading to malabsorption of minerals and fat-soluble vitamins. Hormonal changes that occur as a result of SG, RYGB and BPD/DS are important mediators of weight loss and may affect bone loss as well.

Search Strategy

We searched PubMed and Ovid MEDLINE using the search terms “bariatric surgery” and “bone”. We primarily selected publications from the past 5 years, but did not exclude commonly referenced and highly regarded older publications. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant. This review focused on prospective data when available, and on studies that reported bone mineral density (BMD) changes at sites used by the World Health Organization in their diagnostic criteria for osteoporosis, lumbar spine (LS), total hip (TH), femoral neck (FN) and 1/3 radius (1/3R). Other recent review articles are cited to provide readers with more details and references than can be accommodated in this manuscript.

Causes of Abnormal Bone Metabolism In Obese Individuals

Before discussing the effects of bariatric surgery on bone, it is important to review the skeletal consequences of obesity. Vitamin D deficiency is widespread[9, 10], with potential causes including inadequate dietary intake of foods and supplements containing vitamin D despite high overall caloric intakes [11], limited sunlight exposure [12], and decreased

bioavailability of vitamin D secondary to sequestration of the fat soluble vitamin in excess adipose tissue[13]. Individuals who are the most severely obese, African Americans and decreased sun exposure appear to be at greatest risk[9]. Hyperparathyroidism is common, and while this may be secondary to vitamin D deficiency, an independent relationship between PTH and obesity has been reported[14, 15]. Emerging data also support a direct relationship between bone and fat[16, 17]. One study found an inverse correlation between total fat mass and BMD.[18] Osteoblasts and adipocytes differentiate from the same mesenchymal precursor, and increased marrow fat is one proposed mechanism for low BMD among obese individuals[19]. Visceral fat in particular may have negative effects on bone formation, structure and strength, while subcutaneous fat may be protective[20, 21]. In a recent study of obese women had higher levels of PTH, bone specific alkaline phosphatase (BSAP), leptin, fibroblast growth factor-23 (FGF-23) and lower 1,25-dihydroxyvitamin D than controls[14]. Leptin levels predicted both PTH and FGF-23.

The relationship between body mass index (BMI) and fracture risk is complex, differs across skeletal sites[22]. Recent data question the long-held notion that obesity is protective of bone. Relative to body weight, microarchitecture and strength are lower in obese women compared to controls [23]. While data are limited, obese patients may be at increased fracture risk, particularly at peripheral sites[24-27]. This may relate in part to an increased risk of falls[24]. Increased intramuscular adipose tissue may result in impaired mobility and muscle strength[28]. In addition, these constraints on mobility in obese individuals may result in altered patterns of falling, with increased propensity toward backward and sideways falls. Men and women may be at risk for fractures at different anatomical sites[29].

Limitations of Bone Studies in the Bariatric Population

There are several limitations common to many studies of bone disease in the bariatric population. The majority of studies performed are small, and have substantial drop–out rates, particularly the few that follow subjects beyond one year post-operatively. There is a great deal of heterogeneity among studies relating to the age, sex and race of patients, surgical techniques, sites evaluated by DXA and DXA techniques. Supplementation of calcium and vitamin D is usually ancillary to the study protocol as part of clinical care and compliance is not assessed. In many studies, information on supplementation is not reported at all.

Limitations due to DXA technology include the fact that obesity itself and changes in fat mass introduce artifacts that may compromise accuracy and precision.[30-33] Measurements by QCT[34] and high resolution peripheral QCT (HR-pQCT)[35] may be less affected by changes in body fat. Although newer machines can accommodate patients up to approximately 200 kg or 450 pounds, the 136 kg or 300 pound weight limit of many DXA machines means that many studies were only able to perform axial DXA measurements (of the spine and hip) on a sub-set of patients, giving them less power and making the reported results less reliable.

Skeletal Consequences of Bariatric Surgery

Gastric Banding

After GB, patients typically lose 20-30% of initial body weight and 41-54% of excess body weight[36, 37]. However, weight regain is common [38, 39]. Although vitamin D deficiency has been documented prior to GB, post-operatively vitamin D remains stable or increases and PTH remains stable[40, 41]. Increased bone resorption, measured by C-Telopeptide (CTX), is evident by 6 months, and persists for at least 24 months after surgery[40]. Although it is beyond the scope of this review to discuss in detail, circulating estrogen and leptin levels decline, both related to decreased fat tissue.[42]

Bone density studies after GB are complicated by artifact in spine DXA measurements that may be introduced if the band overlies the spine. Spuriously high follow-up values occur if affected vertebrae are not properly identified and excluded. Studies have reported that LS BMD does not change, or increases slightly [40, 41, 43, 44]. Estimates of hip bone loss have been variable, from no change at 1 year in study of only premenopausal women, to 6% at 24 months[40, 41]. In vertical banded gastroplasty (VBG), another restrictive procedure, a decline of 9.9% at the FN was reported after one year [43], while in an older study there was no change.[45]

Sleeve Gastrectomy

Sleeve gastrectomy is becoming increasingly common, with weight loss falling between the purely restrictive and malabsorptive procedures (1 to 2 year weight loss: 20-30%; excess BMI loss: 45-80%).[36, 46-50]. Data on bone metabolism after SG are limited. In one study, where 95% of subjects had D deficiency, and 43% elevated PTH at baseline, 25OHD increased and PTH decreased post-operatively, although no information is available regarding supplement use or adherence[46]. A prospective study, with higher baseline levels found 25OHD increased but PTH did not change[48].

Data on skeletal outcomes are limited. Increased bone turnover markers have been reported at one year [48]. Bone loss has been reported as early as 6 months after SG (TH :-5.2% and FN :-7.0%, with had a small decrease at the LS)[51]. In a small prospective study, eight women who underwent SG had significant bone loss at the spine (4.6%) and hip(total hip 8.3% and FN 7.1%) at one year.[48] In contrast, a retrospective study in which most patients were vitamin D deficient pre-operatively, LS BMD increased over 2 years.[46] The contradictory findings in the latter study may be explained by its retrospective study design, selection bias in the subjects referred for DXA, and treatment of vitamin D deficiency. Larger, prospective studies are needed to elucidate the changes after SG.

Roux-en-Y gastric Bypass

The majority of available data on changes in bone after bariatric surgery comes from studies of RYGB. After RYGB, patients typically lose 35% of initial weight, or 62-75% of excess body weight[47, 52-54], significantly greater than with GB.[55, 56]. Calcium malabsorption has been documented as early as 3 months after RYGB[53, 54] with reduced true fractional absorption of calcium[57], and secondary hyperparathyroidism[52, 53, 58, 59]. Early studies

showed high rates of vitamin D deficiency[60, 61]. Although aggressive vitamin D repletion has led to less post-operative vitamin D deficiency, improvements have not been commensurate with supplementation, suggesting significant impairment in vitamin D absorption after RYGB. We found stable 25 OHD levels despite more than 200% increases in vitamin D intake (mean of 658 IU/d at baseline, 1698 IU/d at 12 months)[53], and no increase in 25OHD levels on doses of approximately 5000 IU daily[52]. Further reductions in 25OHD and increases in PTH have been reported at year 3 compared to year 1 after RYGB[62], but without information on compliance with supplements.

Bone turnover increases as early as 3 months after RYGB [53, 54]. Resorption markers increase steadily by up to 200% over the first 12-18 months [52, 63, 64]. Increases in bone formation markers are less exuberant[52, 53], and have not been uniformly reported[54]. There are no long-term longitudinal data elucidating the duration of the increased bone turnover. In one cross-sectional study, osteocalcin and BSAP were still elevated compared to obese controls 10 years after RYGB.[65]

While cross-sectional comparisons did not demonstrate consistent differences in BMD in RYGB patients compared to controls [65, 66], prospective studies have demonstrated clear declines in BMD in the first year following RYGB. Declines in hip BMD range between 8-11%[17, 52-54, 62, 67-69]. Few studies have evaluated changes beyond one year; in one study, hip BMD decreased by 3% between years 1 and 3 [62]. Changes at the spine are more variable, some studies report small decreases [24, 54, 63, 67-69], while others have not [52, 53, 65, 66]. One study reported that a further small decline between one and 3 years [62]. Some[66] but not all[52] studies have reported that menopausal status affects change in BMD after RYGB, with postmenopausal women losing the greatest amounts of bone.

BMD at the radius has only been measured in a few longitudinal studies, and most have found no change[34, 52-54] although one study did report a decline.[69] Other studies were limited by inclusion of patients who underwent other malabsorptive procedures.[70,71].

A recent study that followed subjects after RYGB with DXA and central QCT reported declines at the LS by both imaging modalities. However, the decline at the hip by DXA was not seen by QCT, raising the possibility that artifactual changes may significantly affect hip measurements.[63]. In other work, when bone mineral apparent density (BMaD) was calculated to compensate for potential artifact related to changes in bone size, BMaD did not decrease significantly at the spine.[53] As previously discussed, there is substantial artifact using any imaging modality in this population. Additional work is needed to clarify which modality is the most accurate.

Few studies have compared bone loss after RYGB with other procedures, and those that have are limited by small sample sizes. Typically, RYGB subjects lose more weight and more bone at the hip and FN at one year than those who undergo GB[44, 52] or VBG.[72]. The one study that found similar bone loss at the spine and hip after SG and RYGB also had similar excess weight loss and calciotropic hormone levels eliminating the differences in those factors that might be expected to affect bone density[73].

Biliopancreatic Diversion with Duodenal switch

BPD/DS is typically reserved for the super obese patients (BMI>50 kg/m^2). Mean excess weight loss is 70-80% [74-76]. After BPD/DS more than 50% of patients have vitamin D deficiency and estimates of secondary hyperparathyroidism range from 60-100% even with aggressive supplementation[75, 77-79]. Markers of bone turnover increase significantly[74, 80]. A randomized trial found more postoperative 25 OHD deficiency in BPD/DS versus RYGB, and while PTH levels did not differ, supplement use was far greater among BPD/DS patients[81]. Decreased bone formation and increased resorption by histomorphometry was reported after an early form of BPD [82]. The majority (73%) of subjects had defective mineralization. A small decrease in LS BMD and stable hip density was seen 4 and 10 years after BPD/DS[80], but results were very heterogeneous, with BMD increasing and decreasing in similar numbers of subjects. Another study that only measured only LS BMD found significant declines at one year, unattenuated by high dose calcium supplementation.[74]

Changes in Bone Quality and Microarchitecture After Bariatric Surgery

In addition to bone density and bone turnover, microarchitecture is an important property contributing to bone strength and fracture risk[83]. Evaluating changes in skeletal microarchitecture can better elucidate the nature of bone loss after bariatric surgery, but current data are limited. Bone biopsies at baseline and 4 years post-operatively in a group of patients who underwent BPD/DS demonstrated decreased cortical thickness, while trabecular bone volume increased [80]. Mineralization declined over the four year follow-up, with an increase in osteoid volume, and bone formation rate increased. These data raise the possibility that a decline in mineralization could explain some of the post-operative reduction in BMD. While this mechanism may play a role in the BPD/DS population, it is unlikely that defective mineralization plays a significant role in decreased BMD seen in recent studies of other procedures (GB, SG or RYGB), given that in response to robust supplementation the majority of subjects had 25OHD levels close to 20 ng/ml or 50 nmol/L. In our recent prospective study using HR-pQCT in 22 women (RYGB, SG, and GB), cortical area, density, thickness, and total density all decreased at the tibia one year after surgery. Declines in cortical bone were predicted by the increase in PTH. The sub-group of RYGB patients lost more weight, had more cortical bone loss than those with GB or SG and had declines in cortical load share estimated by finite element analysis[84]. Again, it is important to note that HR-pQCT may also be affected by changes in sub-cutaneous fat.

Mechanisms of Bone Loss After Bariatric Surgery

Unloading

Mechanical loading of bone is an important determinant of bone size, mass and biomechanical properties. Changes in loading can induce compensatory increases in localized bone remodeling[85], likely mediated through osteocytes and the sclerostin pathway. Bone loss has been observed in the setting of skeletal unloading in other populations, including patients with spinal cord injury[86], and bed rest [87]. Hip bone loss has been documented in individuals who lose even small amounts of weight from caloric restriction [88-92]. The hip typically carries a load approximately two to three times body

weight [93], therefore drastic weight loss after bariatric surgery may particularly affect this site. A strong association between extent of weight loss after bariatric surgery and amount of bone loss has been documented bymost[40, 45, 51-53, 62, 67] but not all studies.[63] We found that after RYGB, declines at the TH (r=0.65, p=0.02) and FN (r=0.90, p<0.0001) were associated with the extent of weight loss (Figure 2)[53]. Our HR-pQCT study demonstrating pronounced changes at the tibia but not the radius, suggests that there may be an interaction between PTH and weight bearing[52]. This hypothesis could explain the lack of change at the spine and radius observed in many studies.

Changes in calcium, vitamin D and PTH

Vitamin D deficiency in obese individuals may result in metabolic and skeletal abnormalities that antedate but are only detected after surgery. The variable rates of vitamin D deficiency at baseline, and marked disparities in repletion regimens also complicate our understanding of the impact of bariatric surgery on calciotropic hormones. In RYGB and BPD/DS, active absorption of calcium, 80% of which occurs in the duodenum and jejunum, is impaired. Additionally absorption of vitamin D which occurs in the jejunum and ileum is affected by delayed mixing of ingested nutrients with bile acids and pancreatic enzymes [57, 94]. Secondary hyperparathyroidism and bone loss may develop as a consequence [53, 66]. Also after SG and RYGB, gastric acid production is reduced, which may affect calcium absorption.[95] Calcium absorption may be further compromised by use of proton pump inhibitors, common in bariatric patients.[96]

Vitamin D levels are now routinely checked prior to surgery, and patients are supplemented with calcium and vitamin D post-operatively. Both observational [97] and randomized trials[98] have shown that despite extremely high supplementation doses, 25OHD levels are often in the lower end of the normal range, suggesting decreased absorption of vitamin D or increased distribution to the adipose tissue.

Many [52, 53, 60, 65, 66], but not all [54, 64] studies, have documented increased PTH following bariatric surgery. The decline in urinary calcium and rise in PTH that has been reported is consistent with calcium malabsorption, also despite aggressive supplementation. A significant rise in PTH levels, even within the normal range, can still have consequences. The differential effects of PTH on cancellous bone (anabolic) and cortical bone (catabolic), well described in primary hyperparathyroidism and osteoporosis therapy[99], may be evident after bariatric surgery[46, 52, 53]. In studies that found postoperative increases in PTH levels, lumbar spine BMD did not decline[52, 53, 65, 66]. Conversely, spine BMD declined in some[54] but not all[46] studies in which PTH was stable or decreased. These findings suggest that increased PTH may be protective of the predominantly cancellous bone at the LS. PTH may affect hip bone loss as well; with increased PTH associated with greater bone loss at the FN[53] and with cortical bone loss at the tibia [52] (Figure 3).

Changes in 25OHD have also been proposed to affect bone density. Subjects with increased or stable 25OHD had less bone loss at the FN than those whose 25OHD declined, suggesting that postoperative maintenance of 25OHD stores is important to hip bone preservation[52]. In another study, subjects randomized to high dose vitamin D had less hip bone loss than those who received only 800 IU daily[98].

Changes in other hormones

A detailed discussion of the complex and procedure specific hormonal changes that occur after bariatric surgery is summarized in other recent reviews.[47, 95, 100] Very little is known about the impact of these changes on bone metabolism following bariatric surgery. Declines in leptin after bariatric surgery[101], may be associated with increased osteoclast activity [102]. One study found the decrease in leptin after RYGB correlated with an increase in bone resorption measured by NTX [64]. A differential effect of leptin on cortical and trabecular bone has been proposed, and merits further exploration [47]. Adiponectin, an adipokine that is inversely associated with extent of fat mass, may also have an impact on post-operative changes in bone, although in vitro and animal studies have produced conflicting results[103]. In a prospective study, adiponectin levels almost doubled 12 months after RYGB and adiponectin levels were associated with a decrease in total body BMD.[67]

Gut hormones change substantially after SG, RYGB and BPD/DS and may also influence bone metabolism following bariatric surgery. Peptide YY (PYY), secreted by L-cells in the intestinal mucosa, inhibits food intake and helps regulate energy homeostasis. Levels of PYY increase following SG and RYGB but not GB [101] In animal studies, PYY was inversely related to osteoblast activity.[104] Ghrelin and GLP-1 may impact bone metabolism but there are no data relating changes in these hormones to altered skeletal metabolism following bariatric surgery. Lower levels of insulin and amylin after surgery could also result in increased osteoclast recruitment and inhibition of osteoblast activity [102].

Changes in gonadal hormones may also play a role in bone loss after bariatric surgery. Hypogonadism is common in obese individuals. As adipose tissue is the primary source of estrogen in postmenopausal women and men, decreased production after loss of adipose may lead to a relative increase in bone resorption. To date, some studies have shown reported increased bone loss in postmenopausal women [62], others have not[52]. Conversely, there is data to support normalization of gonadal hormones after bariatric surgery [105]. This topic merits further exploration. Sarcopenia could also play a role in bone loss, as lean body mass also declines after bariatric surgery.[52, 62] An association between decreased lean mass and femoral neck bone loss has been reported.[62]. The loss of muscle mass could potentially increase falls and fracture risk. Although there is one retrospective study that suggests an increase in falls after bariatric surgery,[106] additional data are needed.

Fracture Risk After Bariatric Surgery

There is very little data regarding the risk of fracture following bariatric surgery. A retrospective cohort study from the United Kingdom found no significantly increased risk of fracture in 2079 bariatric surgery patients compared to 10442 matched controls [84]. However, mean follow-up was only 2.2 years, and a trend toward increased fracture risk was noted in all patients after 3-5 years and in those with the greatest decline in BMI. Furthermore, the majority of subjects in this study underwent gastric banding, thus the results may not be representative of the risk for patients who undergo those types of surgery associated with greater bone loss. A historical cohort study (median follow-up: 7.7 years)compared fracture incidence in 258 subjects who underwent bariatric surgery, primarily RYGB, with expected incidence in a community based population[107]. Bariatric subjects had an increased incidence

of all fracture, fractures due to minimal or moderate trauma and specifically of fractures at the hip spine, wrist of humerus. Risk was greatest for appendicular fractures; half of all fractures occurred in the foot, leg or hand. Vitamin D deficiency and lower preoperative activity were predictors of fracture. Associations with PTH changes or physical activity after surgery were not examined. Both of these studies are limited by their retrospective design as well as potential difficulties in selecting appropriate controls. There are no prospective fracture data.

Management of Post-Operative Nutritional Deficiencies And Bone Loss

While there is evidence that vitamin D deficiency in obese patients prior to bariatric surgery can be effectively treated with cholecalciferol and ergocalciferol based regimens,[9] there are no interventional studies of vitamin D treatment that begin prior to surgery and continue post-operatively. After surgery, the separate effects of calcium and vitamin D on PTH levels cannot be discerned, making it difficult to determine whether calcium intake is adequate. The effects of vitamin D can be more readily assessed using 25OHD levels as an endpoint. Parent vitamin D in doses up to 800 IU daily have been shown to be inadequate in restoring vitamin D sufficiency after RYGB [66, 98, 108]. Patients randomized to 50,000 IU weekly of ergocalciferol after RYGB had higher 25OHD levels at one year than those who received 800 IU daily.[98] In another randomized trial 45 patients undergoing RYGB received vitamin D in doses of 800, 2,000, or 5,000 IU daily in addition to 2 grams of calcium. Levels of 25OHD increased in all subjects, and to a greater extent in the subjects receiving 2000 and 5000 IU compared to 800 IU daily. However, groups had significantly different baseline 25OHD and PTH levels, medication adherence was variable and almost half of all patients dropped out by the 24-month visit. Two subjects receiving 5000 IU daily developed hypercalciuria, measured by spot urine calcium collections[109]. Data from larger studies that include 24 hour urinary calcium measurements are needed to determine safe and effective regimen(s) for vitamin D repletion.

Earlier this year, AACE, TOS and ASBMS updated clinical practice guidelines for the peri-operative nutritional, metabolic and nonsurgical support of bariatric surgery patients [1]. These guidelines now address several issues pertaining to bone health (Table 1). While the guidelines are based on the best available data, many of the recommendations regarding bone health are not evidence-based. The Endocrine Society 2010 guidelines are similar; pre-operative and annual DXA are recommended until BMD stabilizes after RYGB, BPD and BPD/DS.[110]

It is important to note that despite significant declines, BMD remains in the normal range in the vast majority of patients. For patients found to have osteoporosis on the basis of a T-score below -2.5 or the presence of a low trauma fracture, a metabolic work-up including serum PTH, calcium, phosphorus, 25OHD and 24 hour urine calcium is advised.[1] The 2013 guidelines emphasize that adequate calcium and vitamin D intake are critical. It is important to recognize that compliance with supplementation decreases over time and subsequently the risk of inadequate calcium, vitamin D deficiency and secondary hyperparathyroidism increase. Pharmacologic therapy should only be administered after adequate replacement of calcium and vitamin D. The management guidelines recommend considering

bisphosphonate treatment for bariatric surgery patients with osteoporosis. Intravenous therapy is recommended given the associated risks and concerns about absorption with oral bisphosphonates.

There is no evidence supporting the use of antiresorptive therapy to treat the bone loss that occurs following bariatric surgery. In fact, use of these agents is associated with a high risk of adverse events in this population. Oral bisphosphonates are associated with risk of reflux and anastomotic ulceration. Hypocalcemia and tetany may complicate intravenous bisphosphonate use in patients with low calcium or vitamin D. Although not addressed in the guidelines, other parenteral therapies may have particular risks in this population, teriparatide because of the risk of secondary hyperparathyroidism and denosumab because of concerns about severe hypocalcemia.

Summary and Future Directions

Bariatric surgery offers an effective treatment of morbid obesity, and also its many comorbidities. As the prevalence of bariatric procedures increases, so does the need for more information about the potentially deleterious effects on bone. Bone disease among bariatric surgery patients is influenced by pre-operative abnormalities in bone and mineral metabolism related to morbid obesity. Changes that occur after surgery are specific to procedure type, with the most pronounced abnormalities in calciotropic hormones and bone loss seen after procedures that result in the most malabsorption. The most consistent site for bone loss after all bariatric procedures is at the hip, although available BMD data are limited by issues associated with DXA technology, including artifact introduced by adipose tissue itself. Potential mechanisms for bone loss after bariatric surgery include unloading, calcium and vitamin D deficiency and secondary hyperparathyroidism, and other hormonal changes. There are very limited data on fracture risk in the bariatric population. Current treatment should be geared toward correcting nutritional deficiencies and following BMD in high-risk patients.

The studies outlined in this review provide an important foundation for understanding metabolic bone disease in the bariatric population, and also highlight the many remaining gaps in our knowledge. Larger prospective studies are needed to validate existing data. Further, as SG becomes an increasingly prevalent procedure more studies are needed to elucidate the associated skeletal changes. The long-term skeletal changes after bariatric surgery are unknown: studies must address the question of whether bone loss continues after the first year or levels off as the velocity of weight loss slows. The effect on skeletal indices of weight regain, common after GB, is unknown.

As postmenopausal women may be at particular risk of bone loss following bariatric surgery, studies with larger groups of postmenopausal women are needed to quantify bone loss and fracture risk. Adolescent patients, who are now undergoing bariatric surgery in increasing numbers, are another population who may be at particular risk, since their skeletons are still achieving peak bone mass. Additional studies focusing on the role of lean mass, and changes in physical activity and falls will help elucidate the effects of sarcopenia on bone loss and potentially fracture risk in this population. Whether exercise regimens may

mitigate postoperative bone loss as has been shown in other populations undergoing weight loss remains to be seen. Finally, the most important question of whether the reported hormonal abnormalities and bone loss after bariatric surgery translate into increased fracture risk remains unanswered. Additional studies that address this question will be critical in determining the type of follow-up and treatment necessary for skeletal health in this burgeoning population.

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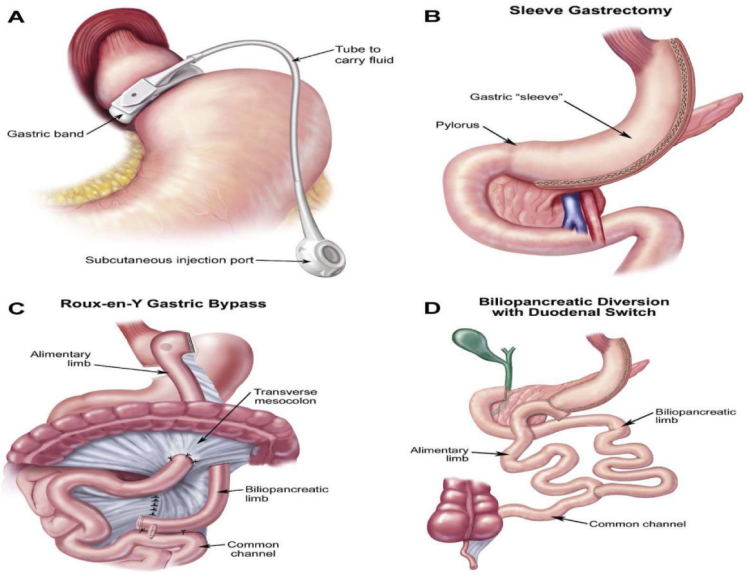

Figure 1.

Common Bariatric Surgery Procedures (from Atlas of Metabolic and Weight Loss Surgery, Jones et al. Cine-Med, 2010.[8]

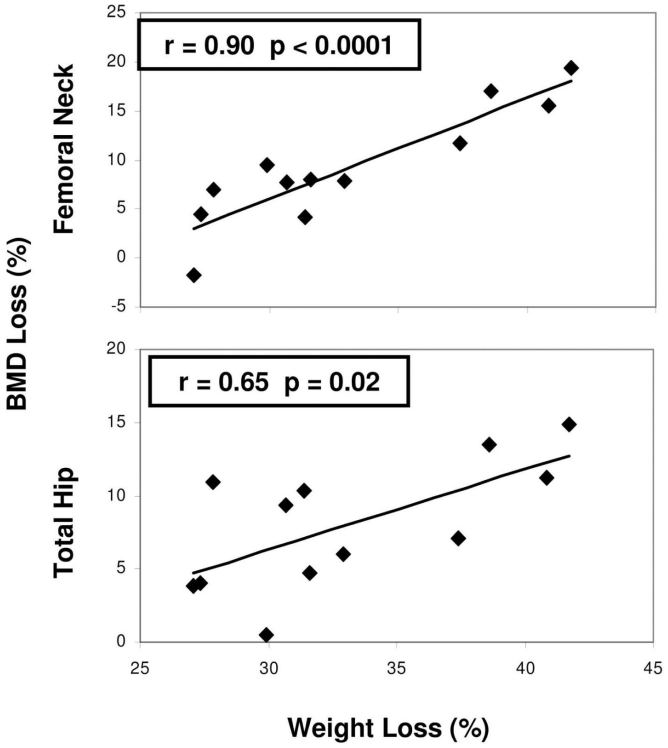

Figure 2.
Relationship between decline in BMD at the hip (FN and TH) and extent of weight loss at 1 year after RYGB. From Fleisher et al. JCEM 2008.[53]

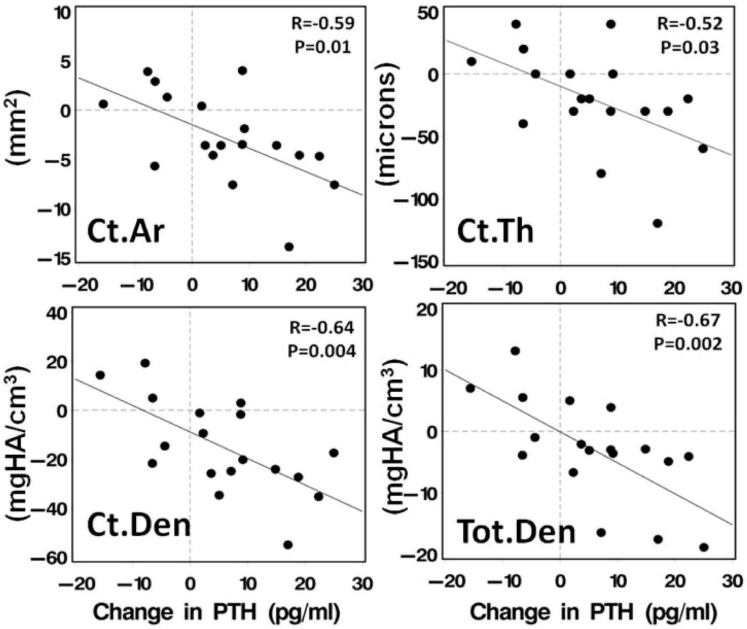

Figure 3.

Association between change in PTH and cortical area, cortical thickness, cortical density and total density by HR-pQCT at the tibia. From Stein et al. JCEM 2013.[52]

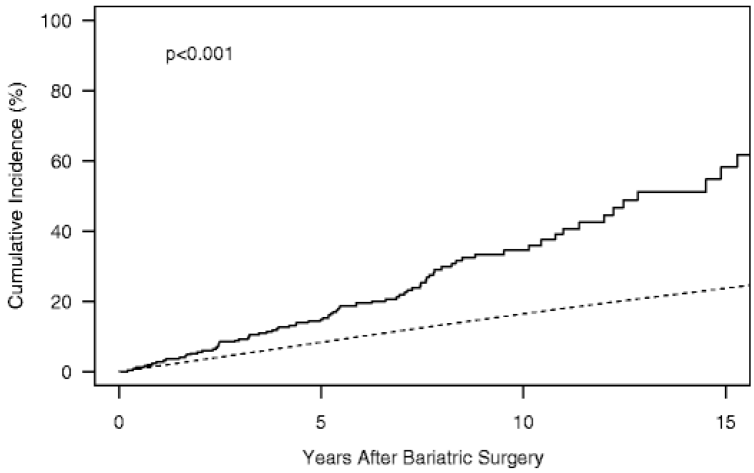

Figure 4.

Cumulative incidence of fracture among Olmsted County, Minnesota, residents following bariatric surgery in 1985–2004 (solid line) vs. expected incidence among community men and women (dashed line). From Nakamura et al. Osteoporosis Int 2013.[107]

Table 1

2013 AACE/TOS/ ASMBS Guidelines for Management of Bone Health in Patients after Bariatric Surgery[1]

	Prior to Surgery	After Surgery
All Patients	Measure 25OHD	• 1200-1500 mg of calcium citrate daily from diet and supplements • 3000 IU of vitamin D daily, dose titrated for 25OHD > 30 ng/ml • Check 24 hour urinary calcium at 6 months and then annually • Measure aBMD by DXA at 2 years
RYGB and BPD/DS (in addition to measures outlined above)	Measure areal BMD by DXA at spine and hip	• Measure 25OHD and PTH initially and then every 6-12 months • Follow-up DXA measurement at 2 years