Endocrinología, Diabetes y Nutrición 70 (2023) 301–303

Endocrinología, Diabetes y Nutrición

www.elsevier.es/endo

EDITORIAL

Bariatric surgery: Effects on bone mineral density and fracture risk

Cirugía bariátrica: efectos sobre la densidad mineral ósea y el riesgo de fractura

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Current evidence regarding the long-term harmful effects of bariatric surgery (BS) on bone is increasingly compelling. However, the aetiopathogenesis is complex and not fully understood. Multiple factors have been implicated in the loss of bone mass, such as mechanical stress, changes in body composition, nutritional deficiencies, especially vitamin D, and changes in adipose tissue and gastrointestinal hormones.[1]

Weight loss after BS leads to a reduction in the body's mechanical load. This can increase the secretion of sclerostin, which negatively regulates the osteogenic Wnt/beta-catenin signalling pathway, and so decreases bone formation. After BS, an increase has been found in serum markers of bone remodelling, with a predominance of resorption and a decrease in bone mineral density (BMD) as large as 10.5% in the femoral neck (FN) and 7.4% in the lumbar spine (LS) one year after the procedure.[1,2]

Although more gradually, the loss of BMD continues over time despite the stabilisation of weight loss and, at the same time, the elevation of serum markers of bone resorption is maintained.[1,2] Although the evidence is scant, some studies have shown BMD loss at five years of 12–17% in the FN and 8–11% in LS, and in one of the few studies analysed at 10 years (following gastric bypass), bone loss was as high as 25% in the FN and 20% in the LS.[3,4] However, we have to bear in mind that these changes occur in a population that starts with high BMD values due to the mechanical effect of excess weight and that, depending on when it is analysed, they may have a higher-than-expected Z-score.[5] Although there is some discrepancy between studies (most of them non-randomised), loss of BMD is higher with the use of malabsorptive techniques (duodenal switch or biliopancreatic diversion), followed by mixed techniques (gastric bypass), and lower in restrictive techniques.[1,6]

There is now a large body of evidence from large retrospective cohort studies to suggest that the decrease in BMD is accompanied by a significant increase in the relative risk of vertebral and non-vertebral fractures from four to five years after BS, estimated by different studies from 1.20 (95% CI: 1.08–1.39) to 2.58 (95% CI: 2.02–3.31), compared to controls who did not have surgery.[7,8] The risk of fracture is highest in patients treated with malabsorptive techniques, followed by those operated on with mixed techniques, while in those treated with restrictive techniques

DOI of original article: https://doi.org/10.1016/j.endinu.2023.03.002
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the risk is lower and, in some studies, similar to the non-operated population.[9]

However, we should be aware that, in many of these studies, the most recently introduced surgical techniques with a malabsorptive component, such as the loop duodenal switch (single anastomosis duodeno-ileal bypass with sleeve gastrectomy [SADI-S]) or the mini-gastric bypass, are poorly represented. Moreover, the evidence comes mainly from non-randomised studies, with no control group of similar weight, and most of which lack clinical data relating to fracture risk factors, physical activity, adherence to vitamin supplementation and phosphorus and calcium metabolism and body composition parameters, all of which make it very difficult to interpret the results.

After BS, fractures occur in typical or major locations (spine, hip, distal forearm and humerus) and less frequently in atypical or minor locations (clavicle, scapula, sternum, femur and foot). In addition to factors such as age and menopause, the absolute or relative decrease in lean mass and the presence of sarcopenia can increase the risk of falls and fractures.[1] At the same time, protein, calcium and vitamin D deficiencies, and secondary hyperparathyroidism, which are highly prevalent in patients with obesity[10] and frequently worsen after surgery, could contribute to bone loss and the risk of fracture.[1]

Hormonal changes, such as an increase in adiponectin and a decrease in leptin and oestrogens, add to the predominance of bone resorption.[1] Variations in some gastrointestinal hormones, such as an increase in GLP-1, could enhance bone formation, while a decrease in ghrelin and an increase in peptide YY would stimulate resorption.[11,12] However, human studies have not shown changes in gastrointestinal hormones to be independent predictors of bone loss after BS. Other suggested aetiopathogenic mechanisms in bone loss after BS are infiltration of the bone marrow by adipose tissue or changes in the intestinal microbiota.[1]

One of the problems when studying BMD in patients treated with BS is that imaging techniques such as dual-energy X-ray absorptiometry (DXA) can be difficult to interpret in severely obese patients and only provide information on the bone mineral content and not on bone quality (bone microarchitecture). The trabecular bone score (TBS) is an indirect method of assessing bone microarchitecture and a predictor of the risk of vertebral fractures independent of BMD. As it is a non-invasive, cheap method, actually derived from DXA, it is increasingly being used in clinical practice. A study by our group found that 85% of patients who had metabolic gastric bypass, 66% of those who had sleeve gastrectomy and 58% of those who had tubular gastroplasty with plication had totally or partially deteriorated bone microarchitecture as measured by TBS at five years post-intervention.[6]

Calculation of the risk of fracture using the Fracture Risk Assessment Tool (FRAX) algorithm also has limited validity in patients treated with BS. The fact that obesity is considered to be a protective factor, the young age of the patients and the lack of previous fractures mean that the fracture risk is estimated as low in most cases. However, many patients operated on for BS have fractures without T-score values in the osteoporosis range. High-resolution quantitative computed tomography (HR-QCT) enables a more precise assessment of bone microarchitecture. A recent study demonstrated losses of up to 12% of the trabecular bone mass in the LS and both cortical and trabecular involvement of 20% in the radius and 13% in the tibia five years after gastric bypass.[3] A recent study evaluated the utility of analysing volumetric changes of cortical and trabecular bone in the proximal femur from 3D images obtained by DXA, which have a high correlation with HR-QCT.[13]

It is important to prevent bone loss through correct protein intake, calcium supplementation (1,200−1,500 mg/day in gastric bypass/sleeve gastrectomy and 1,800−2,400 mg/day in malabsorptive techniques) and vitamin D supplementation (2,000−3,000 IU/day) to maintain plasma calcidiol concentrations $\geq$30 ng/mL.[14] In addition, physical activity that includes resistance exercises has been shown to mitigate the harmful effects of BS on bone. A recent meta-analysis demonstrated the greater benefit of physical exercise on the FN, with a reduction of 0.7−3.7% in bone loss, compared to the standard medical intervention.[15]

Starting anti-resorptive therapy is recommended in menopausal women and men over the age of 50 if they have a history of fragility fractures before the age of 40, T-score $\leq$−2 in hip or LS or a FRAX score with risk of major fracture at 10 years >7.5% (corresponding to 20% in other countries) or hip fracture >3%.[16] Alendronate is considered the anti-resorptive therapy of choice, but oral administration can cause gastrooesophageal reflux and the development of anastomotic ulcers. In patients operated on with malabsorptive techniques, absorption of alendronate may be decreased, which is why zoledronate is sometimes used intravenously. However, parenteral administration of bisphosphonates and denosumab can lead to severe hypocalcaemia in patients without adequate calcium and vitamin D supplementation.[16]

There are currently several clinical trials underway to evaluate the effects of zoledronate (NCT04279392) and risedronate (NCT03411902) on patients undergoing sleeve gastrectomy, and of denosumab in the prevention of bone loss after gastric bypass (NCT04087096), so in the coming years we will have more evidence on this subject.[16]

In summary, BS leads to changes in body composition and nutritional and hormonal status that contribute to the decrease in BMD and increase the risk of fracture, which is greater when malabsorptive techniques are used. Therefore, when selecting a surgical technique, it is important to consider its potential effects on the bone and jointly and consensually assess the options with the patient, taking into account not only their body mass index and comorbidities, but also their fracture risk. Effective nutritional support, physical activity and long-term clinical monitoring are also necessary.

Funding

NV has received the following grants: Äjuts per a projectes de recerca clínica de l'Hospital Universitari de Bellvitge (2011-PR143/11)[Grants for clinical research projects at Bellvitge University Hospital (2011-PR143/11)], PI11/01960; PI14/01997 and PI17/01556from Instituto Carlos III [Carlos III Institute].

Conflicts of interest

The authors declare that they have no conflicts of interest.

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