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Original research

Bone mineral density after bariatric surgery. A systematic review

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HIGHLIGHTS

- Bariatric surgery is the most effective weight loss therapy for morbid obesity.
- In the long-term nutritional deficiencies leading to further complications.
- Mixed surgery had significantly higher deterioration at one postoperative year.
- Monitoring lies in preventing or detecting subclinical disturbances prior to DXA.

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ABSTRACT

Purpose: Bone regulation system may be affected after bariatric surgeries, but procedures impact differently to bone mineral density (BMD) and measures restraining bone loss are frequently neglected until clinical consequences become manifest. This is a systematic review aimed to elucidate whether BMD loss is comparable after different bariatric surgeries. **Materials and methods**: A search of morbid obese adults, undergone to bariatric surgery, with BMD measured by dual-energy X-ray absorptiometry at baseline and after surgery studies was performed in several databases. Studies were assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement and COCHRANE Risk of Bias tool. The random model was selected for meta-analysis; heterogeneity was analyzed with T^2, inconsistency ($I^2 > 50\%$) and Chi^2 ($p < 0.10$). Level of evidence and strength of recommendations were summarized using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE System). **Results**: Twelve studies met the selection criteria. After one year, reduction in total BMD in patients with mixed surgical procedures was significant: -0.03 g/cm^2 (CI 95% 0.00 to -0.06, $p < 0.05$). BMD was reduced by -0.12 g/cm^2 (CI 95% -0.10 to -0.15, $p < 0.001$) in the hip, -0.07 g/cm^2 (CI 95% -0.03 to -0.11, $p < 0.001$) in the column, and -0.03 g/cm^2 (IC 95% -0.02 to -0.04, $p < 0.001$) in the forearm, but not in restrictive surgeries. Studies included showed high heterogeneity and low quality of evidence. **Conclusions**: Patients undergone to mixed bariatric surgery had significant higher BMD deterioration as demonstrated in this review, suggesting that more attention for preventing fractures is required.

1. Introduction

After years of debate, it was until recently that obesity was recognized as disease and not as risk factor only [1]. Despite overt evidence of its remarkable growing prevalence and its precedence to other metabolic diseases, with serious consequences on organs

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and systems, it had yet been seen as a lifestyle problem. Obesity is set under the interaction of genetics and environmental influences [1,2] and associates to main causes of mortality and disability around the globe [3]. Bariatric surgery has proved to be the most effective therapy available for weight loss in morbid obesity and provides additional benefits on improvement or complete resolution of comorbidities [4].

In the hands of experienced surgical teams, post-operative mortality accounts for less than 1% [5], but in the long term, nutritional deficiencies may be unnoticed and lead to further complications. Osteoporosis, Wernicke encephalopathy, anemia or peripheral neuropathy [6,7] are among the hazards that may develop if malabsorption importantly reduces nutrients flow through the intestinal wall.

In extremely obese subjects, mineral turnover is also affected, beginning with obesity driven increased bone mass until before operation and ending up with bone mass loss and increased risk of fractures after weight reduction surgical procedures [8], unfortunately, often are neither recognized nor treated [9]. Beside weight loss, other factors play a role on influencing the risk of bone mass loss: initial body weight, age, gender, physical activity, type 2 diabetes, Cushing disease or drug induced lipodystrophies [10]. Weight loss of any origin may trigger decline in bone mineral density (BMD), it results from lower bearing weight and forceful hormonal changes, that may be precipitated by low food intake and malabsorption of essential nutrients, as it follows after weight reduction surgical procedures [11]. Concomitantly, homeostasis of vitamin D and calcium [7] are disrupted in obese patients before surgery (often associated to secondary hyperparathyroidism) and also may be aggravated after the procedures. Other factors playing key roles on post-surgical bone loss are adipokines and gastrointestinal hormones peptide YY (PYY), glucagon like peptide 1 (GLP-1); these hormones, beside their effect on hunger-satiety regulation, influence bone homeostasis too [8].

Though dual-energy X-ray absorptiometry (DXA) is the standard tool accepted to assess BMD and the potential risk of fracture [12], major changes in fat mass distribution induced by weight loss may affect the precision of BMD measurements in these patients [8].

Based upon the aforementioned evidence, it is crucial to setup proper postsurgical monitoring protocols for these patients but controversies still remain. The AACE/TOS/ASMBS (American Association of Clinical Endocrinologists, The Obesity Society and American Society for Metabolic and Bariatric Surgery) sets forth that patients undergoing into mixed procedures should have their BMD monitored by axial hip and column (spine) DXA before and two years post-surgery, whereas in patients going into restrictive procedures DXA measurements can be taken after 2 years post-surgery, only [13]. However, other groups recommend to have DXA tests on a yearly basis [11]. Reports reviewing the relationship between bariatric surgery and bone metabolism are inconclusive as their sample sizes are small, the time length of follow up varies from 6 months to 2 years and are qualitative in essence. This systematic review is aimed to assess whether in morbidly obese patients, undergone to restrictive or mixed bariatric maneuvers, their BMD equally declined after one year of bariatric surgery.

2. Methods

Studies including both male and female patients with morbid obesity [preoperative Body Mass Index (BMI) $\geq$40 kg/m^2 or BMI $\geq$35 kg/m^2 associated to comorbidities], ages 18 years and over, who had a bariatric surgery upon, with BMD measured by DXA at baseline and one year post-operatory, were selected. The studies searched for the analysis were quasi-experimental, cohort or clinical trials. Articles in which BMD was measured with devices other than DXA or in which patients with restrictive surgery converted to a mixed procedure in less than a year were excluded. Duplicate articles and articles without clearly relevant data for our study were disregarded.

Eligible studies were searched across MEDLINE, EMBASE, Cochrane-CENTRAL, WHOLIS and LILACS databases using the following MeSH and entry terms: restrictive surgery [vertical banded gastroplasty (VBG); sleeve gastrectomy; gastric banding/adjustable gastric band, gastroplasty and laparoscopic gastroplasty]; mixed surgery [biliopancreatic diversion (BPD)/biliopancreatic diversion with duodenal switch, jejunoileal bypass, roux-in-y gastric bypass (RYGB)/gastric bypass/long limb roux in y gastric bypass]; BMD (bone mineral density, bone density, bone mass, bone loss, apparent bone mineral density, bone mineral content, osteopenia and osteoporosis). The most recent search was date March 2013.

Medline search strategy: *#1 Descriptor MeSH Bone mineral density. #2 Bone Density. #3 Bone mass. #4 Bone loss. #5 Osteoporosis. #6. Osteopenia. #7 Bone mineral content. #8 Apparent bone mineral density. #9 Gastroplasty. #10 Vertical banded gastroplasty. #11 Sleeve gastrectomy. #12 Gastric banding. #13 Adjustable gastric band. #14 Gastric bypass. #15 Roux-in-y gastric bypass. #16 Jejunoileal bypass. #17 Biliopancreatic diversion. #18 Biliopancreatic diversion with duodenal switch. #19 Long limb roux in Y gastric bypass. #20 Banded roux in Y gastric bypass. #21 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8). #22 (#9 OR #10 OR #11 OR #12 OR #13). #23 (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20). #24 (#21 AND #22). #25 (#21 AND #23). #26 (#21 AND #22 AND #23). #27 (#24 OR #25 OR #26).*

The analysis and evaluation of risk of evidence bias were performed by two separate reviewers and a third evaluator was included to solve discrepancies, reviewers used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement and COCHRANE Risk of Bias tool for the analysis [14]; the level of evidence and strength of recommendations were summarized using the Grading of Recommendations, Assessment, Development and Evaluation: (GRADE System). Data extraction was done independently by two reviewers using their own developed database at Microsoft Excel 2010 (Redmond, Washington: Microsoft). Selected variables included for the analysis were: type of surgery, BMD changes (g/cm^2 or percentage change) at total and different body regions (hip, column, and forearm), weight (kg) and BMI (kg/m^2) difference between baseline and 1 year post-surgery and whether supplements were used during the study period.

Data were entered into Review Manager Software [Computer program version 5.2. Copenhagen: The Nordic Cochrane Centre. The Cochrane Collaboration, 2012] and the data exploratory process was carried out by univariate analyses, appraising central tendency summaries and distributions behavior. Subsequently, the random effects model for the meta-analysis was selected to combine information and inspect heterogeneity among the studies. For continuous data, all participants from each study were included and mean differences were obtained. T^2, inconsistency (I^2, >50%) and Chi^2 ($p < 0.10$) tests were used to estimate heterogeneity. After a first assessment, subgroups were formed (type of surgery, study period, supplementation) to reduce variation among the studies. Statistical significance was set at $p < 0.05$ [Online review protocol does not exist, contact author for further information].

3. Results

We reviewed two hundred and fifty six titles from databases and another sources, fifty were disregarded due to duplication during the search. From the 206 articles identified, 167 were ruled out for not meeting inclusion criteria. From the remaining 39 articles, only twelve studies were included in the meta-analysis