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Bone Health Following Sleeve Gastrectomy versus Roux-en-Y Gastric Bypass Surgery

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ABSTRACT

Introduction: *Bariatric surgery may have detrimental effects on bone health. We investigated the long-term effects of bariatric surgery on bone health to delineate whether they differed by procedure type.*

Methods: *The records of patients who had undergone either sleeve gastrectomy (SG) or Roux-en-Y Gastric Bypass (RYGB) surgery with a follow up period of 2 years were reviewed. Comparison was made between blood assays (vitamin D, parathormone, calcium, phosphate and magnesium) and aerial bone mineral density (aBMD) measured at baseline with measurements made at 6, 12, 18 and 24 months post-operatively. History of fractures was also recorded.*

Results: *There were 1309 in the SG group and 1132 patients in the RYGB group. There was a gradual decrease in vitamin D, calcium, phosphate and magnesium and increase in parathormone levels peaking at 18 months in both groups ($P<0.05$). There was also reduction in aBMD over time being greater at 24 months and most marked in the total hip and full body measures ($p<0.05$). This correlated to amount of weight loss. All changes were more in RYGB ($p<0.05$) where there was also a higher number of post-operative fractures ($p<0.05$).*

Conclusion: *Bariatric surgery is associated with gradual decline in bone health and increased fracture risk peaking at 18 months after surgery. This effect is more prominent with RYGB (combined restrictive and malabsorptive) procedures as opposed to SG (restrictive only) surgeries. It is imperative to counsel patients about increased bone fragility and fracture risk prior to making the choice of bariatric surgery.*

Keywords
Bariatric surgery, Sleeve gastrectomy, Roux-en-Y Gastric Bypass Surgery, Bone health.

List of Abbreviations
aBMD: Aerial bone mineral density, BMD: Bone mineral density, BMI: Body mass index, DAF: Dar Al-Fouad Hospital, DEXA: Dual energy X-ray absorptiometry, OPD: Outpatient department, PTH: Parathormone, RYGB: Roux-en-Y Gastric Bypass Surgery, SG: Sleeve gastrectomy.

Introduction
Obesity and increased body mass index (BMI) are associated with significant comorbidities such as diabetes, cardiovascular diseases, stroke and cancer, which have serious consequences on public health [1-3]. It is estimated that worldwide, more than 600 million adults are obese [4]. In the Middle East region, approximately 33.14% of the population is overweight (BMI > 25 kg/m^2) and the prevalence of obesity (BMI >30 kg/m^2) is reported to be 21.17% [5]. This high rate is mainly related to lifestyle patterns in the region including unhealthy eating habits and physical inactivity as

well as cultural, social, and economic factors [3,5].

There are two main forms of bariatric surgeries. "Restrictive surgeries" which limit food intake by reducing the size of the stomach. Sleeve gastrectomy (SG) is one of those procedures though it may also induce functional malabsorption by altering nutrient transit time. The other form is "combined restrictive and malabsorptive surgeries" such as Roux-en-Y gastric bypass (RYGB) which limit the absorption of food and nutrients by bypassing sections of the small intestine in addition to their restrictive component [6]. These procedures are becoming increasingly popular worldwide because of their established efficacy for long-term weight loss as well as improving the various comorbidities associated with obesity leading to substantial benefits in quality of life and longevity [7-12]. There is however, mounting evidence suggesting that bariatric surgery adversely affects bone health [6]. There are reports that bariatric surgery leads to undesirable effects on bone health by increasing bone resorption markers [13-16] which leads to reduction in bone mineral density (BMD) and changes in bone histomorphometry parameters [17-20]. It is assumed that these effects are due to nutritional deficiencies, changes in mechanical loading and alterations in various gastrointestinal and fat-associated hormonal factors [21-24]. In addition, there are also several reports suggesting that high BMI has protective effects on the skeleton and that the loss of excessive body weight may actually result in decreases in BMD [25-29] though this is contested by the studies showing increased rates of fracture among those with greater levels of central obesity and in postmenopausal women with obesity [30-32].

The true effect of bariatric surgery on skeletal fragility remains unknown. A limited number of studies have investigated the risk of bone fracture after bariatric surgery [33-36] but the results are inconsistent and sometimes even conflicting [16,34,37]. Those discrepancies are likely due to the limited follow-up after surgery, a limited number of participants, and differences in surgical procedures [33,34,36,38-40].

The aim of the present study is to investigate the difference in the long term effect of SG (restrictive) vs RYGB (combined restrictive and malabsorptive) surgeries on bone health in a large group of patients in Egypt.

Methods

This is a retrospective observational study carried out on the patients attending the outpatient department (OPD) of Dar Al-Fouad Hospital (DAF) between the 1st of January 2008 to the 31st of December 2023 for follow up after bariatric surgery. The DAF is the largest hospital in Western Cairo with over 1000 patients attending the OPD on a daily basis. The OPD utilizes a database that is linked to the medical record system of the hospital. It includes patients' demographic information as well as all details pertaining inpatient and outpatient procedures including the results of all laboratory and radiological investigations. The records of patients aged 18 years or older who underwent SG or RYGB surgery within the 15-year study period were obtained from the database based on the procedure coding system implemented by the hospital in a de-identified fashion.

The study protocol was approved by the Hospital Ethics Committee. Informed patient consent was waived as the study involved the analysis of the existing patient information that was collected in a de-identified fashion. There was no risk of breach of confidentiality of any of the patients.

Study Design and Patient Populations

Only the patients who had the procedures in the same center (DAF) were included. This was to ensure that they all received the same pre-operative care which included abdominal ultrasound, bone densitometry, functional respiratory tests, upper gastrointestinal endoscopy, and blood analysis including nutritional parameters. It was verified that all procedures were performed laparoscopically using identical skin incisions and that all patients had the same level of care both during hospitalization and after hospital discharge.

The patients were divided into two main groups:

Sleeve Gastrectomy (SG Group): The procedure involved resection of the greater curvature including the complete fundus, which was resected from the distal antrum (6 cm proximal to the pylorus) to the angle of His over a 32-French bougie.

Roux en-Y Gastric Bypass (RYGB Group): The procedure involved stapling off a non-banded pouch together with a transmesocolic and retrogastric gastrojejunostomy with building of a 120-cm alimentary limb and a 40-cm biliopancreatic limb.

Inclusion Criteria

The patients had to be ≥ 18 years old and abided by the post-operative assessment protocol implemented by the hospital at 1, 3, 6, 12, 18, and 24 months after surgery. This protocol consists of abdominal ultrasound in the initial visit and blood analysis including nutritional parameters at each visit, with adaptation of the vitamin supplementation protocol according to the results. In addition, bone densitometry is performed 12 and 24 months after the surgery.

Exclusion Criteria

(a) malignancy, (b) previous major abdominal surgery, (c) severe medical conditions associated with increased risk of complications such as end stage liver or renal disease, (d) received chemo or immunotherapy, (e) drug or alcohol addiction, (f) pregnancy, (g) severe gastroesophageal reflux disease, and (f) long-term systemic corticosteroid use.

Postoperative Weight loss and Dietary Supplementation

Weight was measured and amount of weight loss was recorded in each visit. All the patients were asked to follow the same dietary protocol and were prescribed identical vitamin and mineral supplementations, including daily oral supplementation with 2 multivitamin/mineral tablets, 1000 mg calcium carbonate, 800 IU vitamin D3, and 100 mg ferrous sulphate (in premenopausal women), and intramuscular injections of 1 mg vitamin B12 every third month. This was carried out by registered dietitians based on the validated food frequency questionnaire during each follow up visit after the surgery.

Blood Analysis
Serum blood levels of all nutritional parameters were documented at baseline and at every postoperative visit (6,12,18 and 24 months) but for the purposes of this study only bone health related measures were recorded. This included vitamin D (normal: 75-125 nmol/l), parathormone (PTH, normal: 1.6-6.9 pmol/l), calcium (normal: 2.25-2.62 mmol/l), phosphate (normal: 1.12-1.45 mmol/l) and magnesium (normal: 0.80-1.05 mmol/l).

Bone Mineral Density
Areal bone mineral density (aBMD) (g/cm^2) was measured at baseline and then twice postoperatively (12 and 24 months) using Dual energy X-ray absorptiometry (DEXA) scans. Lumbar spine (L2–L4), femoral neck, total hip, and whole-body aBMD were measured independently. Results were considered normal when the Standard Deviation (SD) was < 1 of the T-score. Low bone mass or osteopenia was defined as a T-score between 1 to 2.5 SD and weak, porous and fragile bones or osteoporosis was defined as T-score of ≥ 2.5 SD.

Data Collected
Demographics
Age, sex, height, weight, and BMI and smoking history.

Pre-surgical Data
Comorbidities including diabetes, hypertension, gastro-esophageal reflux, osteoarthritis and sleep apnea, history of fractures, bone mineral density and blood analyses as described above.

Post-surgical Data
Weight, and BMI, history of fractures, and blood analyses as described above. These parameters were collected at four time points: 6, 12, 18, and 24 months after surgery. Bone mineral density was measured at two time points only 12 and 24 months.

Data Analysis
The primary endpoints were post-surgical changes in blood assays, reduction in aBMD or occurrence of a fracture at any of the 4 follow up time points recorded after surgery.

Descriptive statistical analysis was used and the results are presented as mean ± SD. Descriptive analysis was done using SPSS version 26, which computed simple descriptive analysis including frequencies for categorical data, mean & standard deviation for numerical data. Cross tabulation was done for some of the categorical data using Chi-Square, Fisher's Exact, and Cramer's V to test when there was a statistically significant difference between the groups. Correlations between quantitative variables were done using Spearman correlation coefficient. 95% CI was computed for all independent variables. P-values less than 0.05 were considered as statistically significant.

Results
3672 patients had bariatric surgery between January 2008 and December 2023. The 2441 patients who fulfilled the inclusion criteria and had regularly attended all follow up appointments in the OPD for at least 24 months postoperatively are presented in the current report. Of those, 1309 had SG and 1132 had RYGB.

Demographic Data and Baseline Measures
As displayed in table 1, there were no inter-group differences in any of the demographic data or comorbidities. Average serum vitamin D levels were low in both groups in a similar fashion and there were no presurgical significant differences in serum PTH, calcium, phosphate or magnesium levels between the two groups (Figure 1).

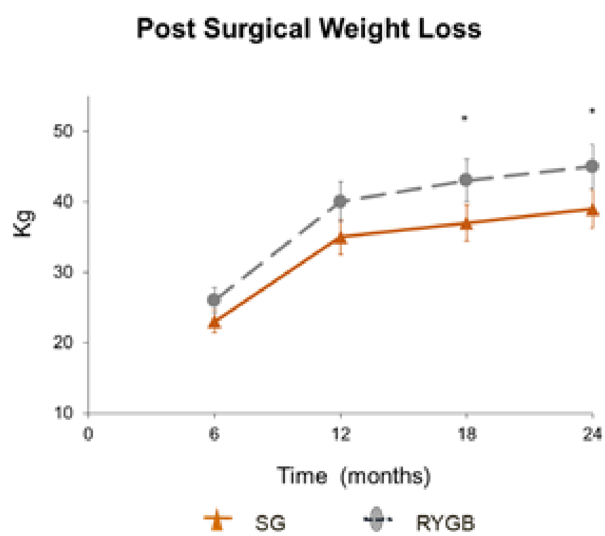

Figure 1: Average amount of weight loss in kilograms measured in each group at the four time points (6,12,18 and 24 months) of the post-surgical follow up period. Bars indicate 95% confidence intervals. * = $p < 0.05$.

There was evidence of osteopenia in most patients in both groups with average baseline BMD T-scores ranging between 0.9 to 1.5 SDs being least in the femoral neck however there were no between-group differences (Table 1). Sixty-eight (5.2%) of the SG and 55 (4.9%) of the RYGB group had a history of fractures before surgery (Table 2). These fractures were in the following anatomical locations: foot (n = 21 and 16 respectively), tibia/fibula (n = 12 and 11 respectively), femur (n = 2 and 1 respectively), hand (n = 6 in each group), radius/ulna (n = 14 and 10 respectively), humerus (n = 9 and 7 respectively), clavicular (n = 1 in the SG group), rib (n = 4 and 3 respectively) and face (n = 1 in the RYGB group). there were no significant differences between the two groups.

Post-Surgical Data
Weight Loss and Vitamin/Mineral Supplementation
Figure 1 demonstrates the average amount of weight loss at each time point for each group at each of the time points of the follow period. There was a similar rate of progressive weight reduction in both groups plateauing between 12-24 months post-surgery

		SG Group: (*n* = 1309)	RYGB Group: (*n* = 1132)
Demographics	Age (years)	46.1 ± 11.5	49.8 ± 12.6
	Gender M/F (n)	353/956	281/851
	Menopausal	38.3%	34.3
	Weight (kg)	136.3 ± 21.5	129.4 ± 29.7
	BMI (kg/m^2)	46.6 ± 6.7	46.1 ± 8.8
	Physical activity score (x/20)	9.7 ± 4.5	10.1 ± 5.8
	Smoker (%)	24	21
Comorbidity	Hypertension (%)	42.6	41.8
	Diabetes (%)	27.9	29.3
	Osteoarthritis (%)	28.6	30.6
	Sleep Apnea (%)	23.5	21.9
	Gastroesophageal reflux (%)	26.4	29.6
aBMD (g/cm^2)	Lumbar spine	1.281 ± 0.125	1.324 ± 0.151
	Femoral neck	0.939 ± 0.102	0.995 ± 0.112
	Total hip	1.164 ± 0.133	1.136 ± 0.135
	Whole body	1.237 ± 0.115	1.269 ± 0.121

Table 1: Patient demographics and baseline measures.

and it was always more in the RYGB group though the difference was only significant at 18 and 24 months ($p < 0.05$). There was no significant change in physical activity after surgery and it continued to be in the low to moderate range. This was similar in both groups. Adherence to vitamin and mineral supplementation was high (>90% of patients) in both groups throughout the follow up period with a significant increase in nutrient intake especially vitamin D and calcium in both groups during the follow up period. It was slightly more in the RYGB group but there were no significant differences between the two groups at any of the time points.

Serum Levels

As shown in Figure 2, there was a significant gradual decrease in changes in serum vitamin D, calcium, phosphate, and magnesium associated with an increase in serum PTH levels peaking at 18 months ($p<0.05$). The most significant drop was in vitamin D levels which started off in the low normal range at baseline in both groups and was low throughout the follow up period. With respect to all other measures the changes were smaller. In all measures the change (decrease in vitamin D, calcium, phosphate and magnesium and increase in PTH levels) was always more in the RYGB group though significant differences were only observed at 18 months continuing to 24 months post-surgery. There was a positive correlation between the amount of weight loss and the change in the serum levels of all measures in each group (r values ranging between 0.615 and 0.681 for the SG group and 0.631 and 0.694 for the RYGB group; $P<0.05$). This was most marked for PTH followed by magnesium in both groups.

Bone Mineral Density

Mean aBMD at the lumbar spine, femoral neck, total hip, and whole body were approximately 1.2 to 2.1 SDs of the T-scores above the mean aBMD in both groups, being significantly higher in the RYGB group at 24 months ($p<0.05$) especially in the total hip and whole body measures. The yearly drop in aBMD was significant compared to baseline in both groups ($p<0.05$; figure 3) and was also most prominent in the total hip, and the whole body measures. The percentage of this decrease in aBMD was always more in the RYGB group (both at 12 and 24 months), however intergroup differences were only significant 24 months after surgery. There was a positive correlation between the amount of weight loss and the percentage of aBMD loss in each group (r values ranging between 0.634 and 0.668 for the SG group and 0.652 and 0.691 for the RYGB group; $P<0.05$). Again, this was most prominent in the total hip and the whole body measures.

	SG Group: (*n* = 1309)	RYGB Group: (*n* = 1132)
Baseline (Presurgical)	68	55
6 months	0	0
12 months	1	3
18 months **	3	8
24 months *	2	5

Fractures

As shown in table 2, fractures occurred in 7 patients of the SG group and 16 patients of the RYGB groups at a mean time of 14.2 ± 9.4 months after surgery. Inter-group differences were significant at the18 and 24 months' time points of the follow up period. Of those, 10.7% of the SG and 21.9% of the RYGB group experienced multiple different fracture events and 12.3% of the SG group and 28.6% of the RYGB suffered from multiple fractured bones following a single event. Most fractures in both groups were in the hip (33.3% and 36.1% respectively) followed by the upper (31.5% and 29.3% respectively) and lower (23.2% and 26.3% respectively) limbs. Other sites included fractures of the ribs, pelvis and face/skull (12.0% and 9.2% respectively).

Discussion

This is the first study investigating the long-term effects of bariatric surgery on bone health compared to baseline and throughout a two year follow up period after surgery in a large cohort of Middle East (Egyptian) patients. We have shown that there is a postoperative

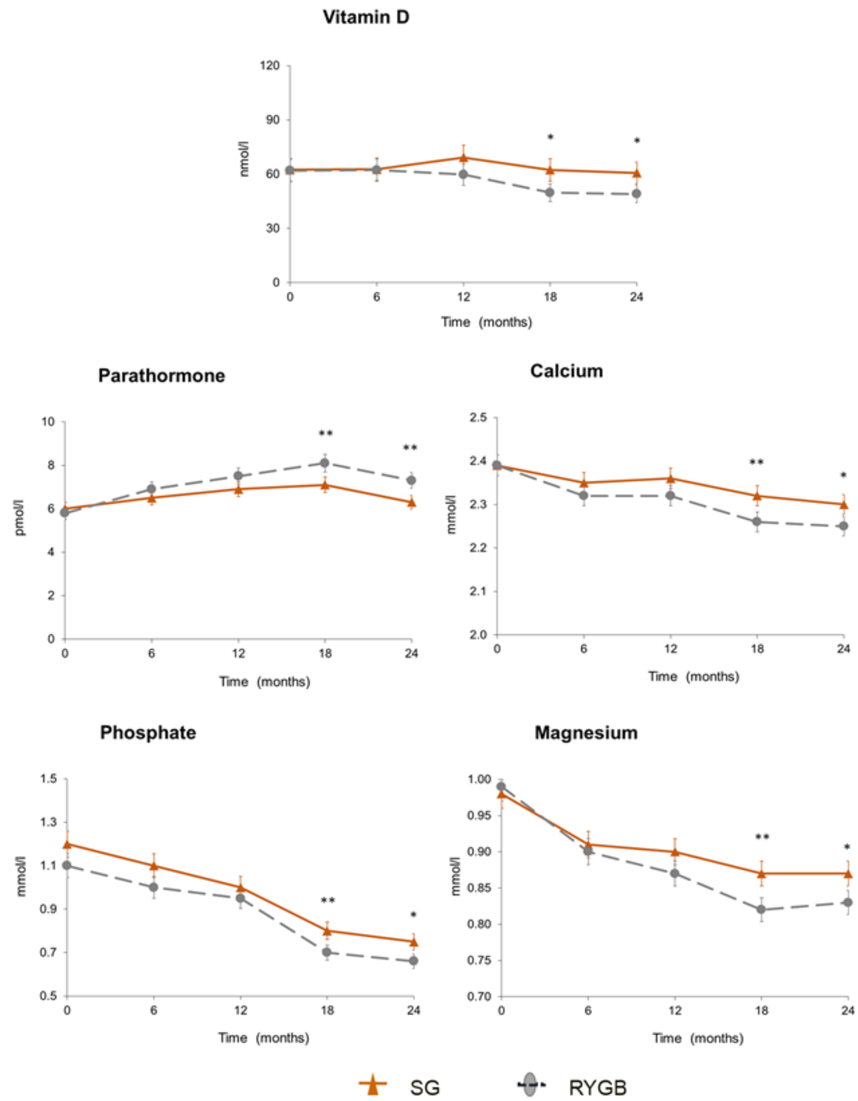

Figure 2: Serum Levels of Vitamin, minerals and hormones measured in each group at baseline and then the four time points (6,12,18 and 24 months) of the post-surgical follow up period. Bars indicate 95% confidence intervals. * = p< 0.05, ** = p < 0.01.

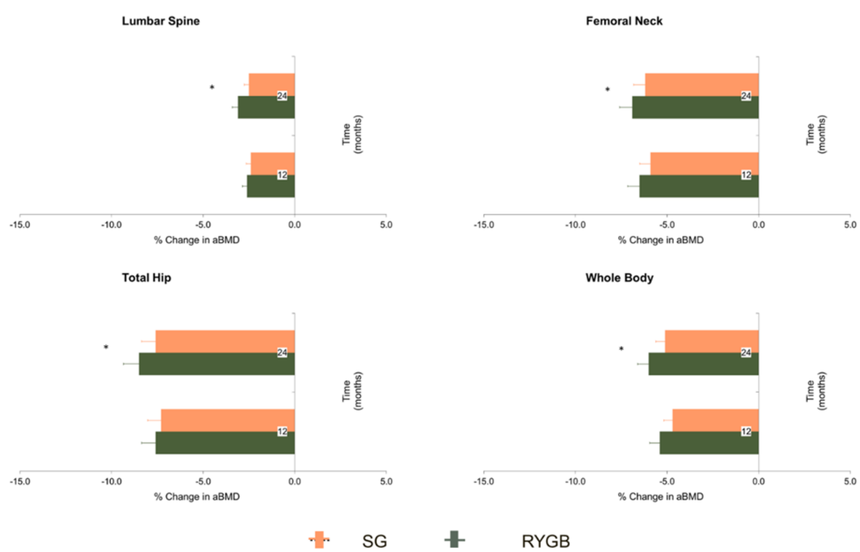

Figure 3: Mean percent change in areal bone mineral density (aBMD) measured in each group at the two time points (12 and 24 months) of the post-surgical follow up period. Bars indicate 95% confidence intervals. * = p< 0.05.

decline in bone health peaking at 18 months with increased risk of fracture especially at non-vertebral sites including the limbs. In addition, we found that this decline and increased risk are more prominent following combined restrictive and malabsorptive surgeries (RYGB) as opposed to restrictive only (SG) procedures.

In our study we found gradual decrease in vitamin D, calcium, phosphate and magnesium and increase in PTH levels peaking at 18 months and then plateauing. The change was small in all the parameters but it was always more in the RYGB group and was significant at18 and 24 months after surgery. This difference was not found in other studies [41-48]. This may be due to small sample size [42,44,48,49-51], short follow up periods [41] or high degree of between study heterogeneity. We also found evidence of gradual aBMD reduction and bone loss over time being greater at 24 months. These results are in agreement with most studies with a follow-up from 1 to 4 years [42-44,48]. Also similar to those studies, we found a greater aBMD reduction at the total hip [41,43,44] and the femoral neck [42,44,48] as well as the total body [41,43,45] and to a lesser extent the lumbar spine [41] after RYGB than after SG. There are however studies which did not find any differences between the two procedures in total hip and femoral neck aBMD [45,46,50-52] or lumbar spine aBMD [42-46,48,50-52].

The changes we observed in our study correlated positively with weight loss but were not affected by physical activity or adherence to vitamin and mineral supplementation protocols. Weight change has been shown to correlate with changes in femoral neck, total hip, lumbar spine, total body aBMD [41,43-45,51], and with changes in the bone turnover markers P1NP and CTX-1 [41,47,49] after gastric bypass and sleeve gastrectomy. The most widely accepted explanation for these findings is that the greater weight loss that occurs with bariatric surgeries that involve a malabsorptive component is probably more likely to be associated with various nutritional deficiencies when compared to purely restrictive procedures [21-23]. Gastric bypass induces malabsorption by bypassing the first part of the small intestine [53], which is particularly applicable to nutrients known to affect bone health [54] leading to greater bone loss and greater bone turnover after RYGB than after SG. But this does not explain why despite the significant increased vitamin and mineral intake throughout the follow up period in both groups which was corrected to secure that the levels were within the recommended range (normal to minimal change) based on the results of blood analyses performed at each visit there was still a significant decline in bone health in both groups with time even if less in SG. It could be that there are also alterations in gastro-intestinal hormones induced by these procedures [55], which could also affect bone health [56]. Another explanation is that weight loss may induce mechanical unloading of the skeleton leading to bone loss and an increase in bone turnover [57]. But this is not supported by the lack of an association between level of physical activity and bone loss. It is also undermined by studies reporting that gastric bypass, and not weight loss, is associated with a greater reduction in femoral neck and lumbar spine aBMD [41,48] or the increased bone turnover independent of surgical procedure found by Dag Hofso el al. [41]. Clearly there are more complex means involved leading to the increased bone loss associated with gastric bypass other than a physiological adaption to a lower body weight.

Even though the number of fractures reported during the follow up postoperative period was small in both groups, it was still significantly more after 18 months in the RYGB group. This is in keeping with all the other findings indicating increased risk of bone loss and fractures in patients undergoing malabsorptive procedures [21-23,34,35,58,59]. A discrepant finding was reported in a single study that did not observe any difference in overall fracture risk between the various types of bariatric procedures [35]. But they studied a small number of patients the majority of whom had undergone gastric banding and only 29% underwent RYGB. This could be the reason for this seeming disparity. As with previous reports, both groups had an increased risk for fractures at any site but were more common in the limbs and non-vertebral sites [60]. This may be attributed to the increased risk of falling that has been reported after bariatric surgery, which is associated with a higher chance of limb fractures [31]. Another possible explanation is that there is a difference in the effect of postoperative secondary hyperparathyroidism, caused by vitamin D and calcium deficiencies on bone resorption and formation at vertebral and non-vertebral sites. This may also account for the increased risk that seemed to peak after 18 months post-operatively and is in accordance with other reports that show increased risk of fractures within the first 2 years after surgery [60]. It also explains why the risk increases with mixed restrictive and malabsorptive procedures more than with restrictive only surgeries.

The main strength of our study is that we studied a large homogenous population and ensured that all baseline preoperative and postoperative data was available for all the included patients. All our results were collected from patients in one hospital with standardization of surgical techniques, which removed any confounding factors related to difference in surgeon expertise or follow up protocol. There are however several limitations. The most important is the retrospective nature and therefore only the data collected for the routine follow up of patients was available. Bone turnover markers such as bone alkaline phosphatase (BALP), C-telopeptide of type I collagen (CTX-1) and procollagen type 1 N-terminal propeptide (P1NP) are not assessed routinely and this data would have been a valuable addition to our findings. In addition, the follow up period was only two years so long-term effects were not available. Finally, the small number of fractures that occurred during the follow up period prevented us from making accurate inferences related to the site of fractures and their relationship to weight loss or type of procedure.

In summary, our large retrospective study demonstrates that bariatric surgery is associated with gradual decline in bone health and increased fracture risk peaking at 18 months after surgery. This effect is more prominent with RYGB (combined restrictive and malabsorptive) procedures as opposed to SG (restrictive only) surgeries. While it is still important to further validate these findings in larger long-term studies the results underscore the importance of taking the increased bone fragility and fracture risk into account during the decision-making process involved in choice of bariatric surgery. This is particularly important in patients with baseline osteopenia or risk of osteoporosis.

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