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ORIGINAL CONTRIBUTIONS

Impact of Bariatric Surgery on Bone Mineral Density: Observational Study of 110 Patients Followed up in a Specialized Center for the Treatment of Obesity in France

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Abstract

Introduction Bariatric surgery is used to treat severe obesity. We aimed to investigate the incidence of clinically significant bone mineral density (BMD) loss at 6 and 12 months after bariatric surgery.

Methods Observational study performed in a specialized center for the treatment of obesity at the University Hospital of Reims, France. Surface BMD was measured by dual x-ray absorptiometry (DEXA). A reduction of > 0.03 g/cm^2 was considered clinically significant.

Results A total of 110 patients were included. A clinically significant reduction in BMD was observed in 62.1% of patients at 6 months, and in 71.6% at 12 months after surgery. No case of osteoporosis was observed. There were four cases of osteopenia and one fracture post-surgery. BMD loss was related by univariate analysis to the reduction in body mass index (BMI) ($p < 0.01$), weight loss ($p < 0.01$), fat mass ($p < 0.01$), and lean mass ($p < 0.01$). Multivariable analysis found a significant association between the reduction in BMD and the excess weight loss percentage (odds ratio 1.11, 95% confidence interval (1.05–1.18), $p < 0.001$).

Conclusion There was a clinically significant reduction in BMD at 6 months after surgery in over 60% of patients undergoing bariatric surgery. BMD loss is persistent over time and predominantly situated at the femoral level, and strongly associated with weight loss. Systematic vitamin and calcium supplementation, as well as follow-up by DEXA scan seems appropriate. Systematic DEXA scan pre- and post-surgery, and annually thereafter until weight has stabilized seems appropriate.

Keywords Bariatric surgery · Bone mineral density · Fracture, obesity · Bone densitometry

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Introduction

According to data from the World Health Organization (WHO), obesity has nearly tripled since 1975. In 2016, over 650 million (about 13%) of the world's adult population (11% of men and 15% of women) were obese in 2016 [1]. Over the last decades, obesity has become a health threat for the individual patient as well as a major socio-economic burden [1].

Bariatric surgery is a reference treatment for obesity, performed as second-line therapy after failure of medical management lasting at least 6 to 12 months [2]. Bariatric surgery leads to lasting, significant loss of 50 to 70% of excess body weight, making it one of the most effective therapeutic options [3]. According to the recommendations of the European guidelines for obesity management published in 2015 [2], bariatric surgery is indicated for patients with a body mass index (BMI) (weight/height^2) > 50 kg/m^2, or for patients with a BM ≥ 35 kg/m^2 associated with at least one comorbidity (psycho-pathological, cutaneous, orthopedic, cardio-respiratory, endocrine, metabolic).

The number of bariatric surgeries has been increasing in the last years. In 2013, 468,609 bariatric surgeries were performed worldwide. Bariatric surgery was performed most frequently in the USA, Canada, and France [4]. Surgical interventions to treat morbid obesity can be divided in two categories: interventions that restrict stomach capacity (including adjustable gastric banding and sleeve gastrectomy) and interventions that limit absorption: gastric bypass or biliopancreatic diversion.

Numerous studies have investigated the impact of bariatric surgery on bone mineral density (BMD) [3, 5–7]. The results are often based on the percentage variation in BMD before and after surgery, which only partially reflects the true processes. In rheumatology practice, the Smallest Detectable Difference (SDD) has been used to assess the reproducibility of BMD measurements in vivo between two different dual energy X-ray absorptiometry (DEXA) machines [8]. The SDD is estimated at 0.03 g/cm^2 [8]. This SDD corresponds to clinically significant bone loss, and BMD change has been shown to be an independent risk factor for fragility fractures [9].

In this context, the main aim of this study was to estimate the incidence of clinically significant BMD loss at 6 and 12 months after bariatric surgery. Secondary objectives were to study the prevalence and incidence of osteoporosis and occurrence of fractures in patients treated by bariatric surgery, and to identify factors associated with a clinically significant reduction in BMD.

Materials and Methods

Study Design

A national plan for obesity deployed in France from 2010 to 2013 created specialized centers for obesity management (COMs). These are centers that have a multidisciplinary team available to treat patients with obesity and are equipped with appropriate facilities for the management of severe obesity. There are currently 37 COMs in France.

We performed an observational, retrospective, single-center study in the University Hospital of Reims at the COM for the region of Champagne-Ardenne. We included patients aged 18 years and older, followed up at the COM of Champagne-Ardenne, who underwent bariatric surgery between January 2013 and December 2015, and who had at least one DEXA scan pre- and post-operative. Exclusion criteria were weight > 180 kg (maximum weight limit for bone densitometry scan) (Fig. 1).

Measurements

Surface BMD was measured by DEXA scan and expressed in g/cm^2. BMD was measured at three sites: the lumbar spine (L1-L4), the femoral neck, and the left total hip. Standard procedures for putting the patient in position for DEXA acquisition did not include manual retraction of the fatty panniculus covering the proximal femur during hip measurements.

The patients included had to have undergone at least one DEXA scan prior to surgery, in order to enable comparison between pre- and post-operative values. Given the current lack of consensus about the best time to perform DEXA scan for follow-up after bariatric surgery, some patients had a follow-up scan at 6 months, and others at 12 months. A small number of patients also had a DEXA scan more than 18 months after surgery.

All DEXA scans were performed using the same machine (Hologic Discovery, Hologic, Inc. Bedford, USA) by two experienced operators. BMD measurement by DEXA scan were

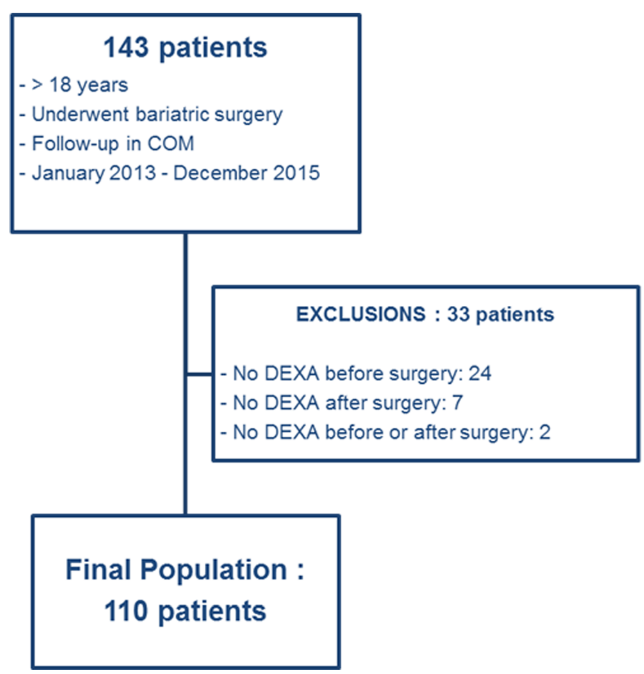

Fig. 1 Flow chart of the study population

coupled with whole-body DEXA scan to allow detailed analysis of the distribution of muscle mass (lean mass) and fat mass in different anatomical regions of the body [10]. In addition to fat mass, the quantity of lean mass and total body mass (in grams) were measured and the ratio of fat mass to lean mass was calculated.

Data Recorded and Endpoints

For all patients, we recorded the type of surgery, risk factors for osteoporosis (Table 1) (osteoporosis-inducing diseases and treatments, alcohol, and tobacco consumption), anthropometric measures (weight, height, and BMI), the level of self-reported physical activity, complications secondary to obesity, vitamin-calcium status, and the type of supplementation and compliance with vitamin-calcium supplementation, self-reported by patients during the medical history. The primary endpoint was the change in BMD measured at the three sites between pre- and post-operative DEXA scans using the same Hologic machine in comparison mode. A reduction in BMD > 0.03 g/cm^2 was considered clinically significant [8]. The *Z*-score and *T*-score indices for each patient were evaluated and compared. The WHO defines osteoporosis assessed by DEXA, as a *T*-score ≤ -2.5 and a *Z*-score ≤ -2, and osteopenia as a *T*-score ≤ -1 and > -2.5 [11–13].

Statistical Analysis

Quantitative variables were described with the mean ± standard deviation, or the median and interquartile range, and qualitative data as absolute frequencies and percentages. Qualitative variables (type of surgery, sex, hormonal status, physical activity) were compared using the chi-squared test or Fisher's exact test as appropriate. Quantitative variables were compared using Student's *t* test when they were normally distributed, and the Mann-Whitney *U* test otherwise. Associations between age, vitamin D concentration at the start of the study, weight loss, BMI loss, fat mass loss, lean mass loss, and the reduction in BMD at 6 and 12 months were evaluated using Student's *t* test. The association between pre-operative BMI, the percentage of excess weight loss, and the reduction in BMD at 6 and 12 months was evaluated by the Mann-Whitney *U* test.

A multivariable analysis was performed using logistic regression to identify factors associated with a significant BMD loss at 12 months. Variables with a p value < 0.20 in the bivariate analysis were included in the model. To avoid multicollinearity, only the most informative variable relating to weight was included in the multivariable model. p values < 0.05 were considered statistically significant. All analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, North Carolina, USA) and R version 3.3.2 [14].

Results

Patient Characteristics

A total of 110 patients followed up at the COM of Champagne-Ardenne met the inclusion criteria and were included in the study. The characteristics of the study population are shown in Table 1. In our population, 22 (20%) patients had a vitamin D level > 30 ng/mL before the bariatric surgery, 66 (60%) patients at 6 months, and 60 (54.5%) patients at 12 months. Compliance for calcium and vitamin D supplementation was considered adequate in 71 patients (64%).

BMD Change, *T*-Scores, and *Z*-Scores (Table 2)

All patients underwent DEXA scan before surgery; the majority performed at least two DEXA scans in the follow-up (i.e., 87 patients —79%). Only 23 patients achieved only one DEXA scan during follow-up (8 patients at 6 months, 13 patients at 12 months, and 2 patients at 18 months).

A clinically significant reduction in BMD (> 0.03 g/cm^2 on at least one site) was observed in 59 (62.1%) patients at 6 months after surgery, and 68 (71.6%) at 12 months. Five of the seven patients who had a DEXA at 18 months met the primary endpoint. BMD loss was more frequently observed at the level of the hip and femoral neck.

The percent variation in BMD (at 6 and 12 months) was respectively − 1.2% and − 3.4% at the femoral neck, − 2.0% and − 4.3% for the hip, whereas we observed an increase in BMD at the level of the lumbar spine (+ 5.8% at 6 and + 5.6% at 12 months).

Four patients developed osteopenia (*T*-score ≤ -1 and > -2.5). In the majority of cases, osteopenia occurred at the femoral neck (3/4). After 12 months, no patient had osteoporosis. One patient met the WHO criteria for DEXA osteoporosis before bariatric surgery and was therefore not included in the analysis.

Incidence and Prevalence of Fractures

In our study population, 41 patients (37.35%) had a personal history of fracture, and 10 (9.1%) had a family history of first-degree relatives with fractures, including one fracture of the femoral neck. Only one fracture (0.9%) occurred post-surgery. It was a fracture of the humeral head that occurred in a 38-year-old woman after falling from height 1 year after surgery.

Factors Associated with a Reduction in BMD (Table 3)

In bivariate analysis, only the extent of weight loss was associated with a significant reduction in BMD. Accordingly, at 12 months, there was a significant association between the occurrence of a clinically significant reduction in BMD and weight loss ($p < 0.001$), drop in BMI ($p < 0.001$), loss of fat

Table 1 Characteristics of the study population 110 patients prior to bariatric surgery

$N = 110$		Mean ± SD or n (%)
Age		44 ± 9.9 years
Sex	Men	28 (25.4%)
	Women	82 (74.5%)
Hormone status	Menopaused	19 (24.1%)
	Not menopaused	60 (75.9%)
Type of surgery	Sleeve	75 (68.2%)
	Gastric bypass	35 (31.8%)
Obesity-related complications	Rheumatological	84 (76.4%)
	Sleep apnea	65 (59.1%)
	Type 2 diabetes	35 (31.8%)
	Dyslipidemia	31 (28.2%)
Smoking status	Non-smokers	58 (52.7%)
	Former smokers	32 (29.1%)
	Smokers	20 (18.2%)
Alcohol consumption	None	71 (65.1%)
	Former	1 (0.9%)
	Occasional	37 (33.9%)
	Daily 0	0 (0%)
Physical activity	> 1 h/week	56 (52.3%)
	< 1 h/week	51 (47.6%)
Osteoporosis-inducing diseases	Family history of osteoporosis	7/110 (6.3%)
	Endocrine	7/110 (6.3%)
	Digestive	2/110 (1.8%)
	Renal	9/110 (8.2%)
	Cancer and leukemia	4/110 (3.6%)
	Deep vein thrombosis	7/110 (6.3%)
Osteoporosis-inducing treatments	Corticosteroids:	13/109 (11.8%)
	-Inhalation, asthma	7 (11.9%)
	asthma	1 (0.9%)
	-Local	5 (4.6%)
	-General	0 (0%)
	Barbiturates	5 (4.6%)
	Interferon treatment	0 (0%)
	Anti-osteoporosis treatment	
Bone status prior to surgery	Normal	89 (84.0%)
	Osteopenia (T-score ≤ − 1 and > − 2.5	16 (15.1%)
	Osteoporosis (T-score ≤ − 2.5)	1 (0.9%)
Biological vitamin/calcium status	- Corrected calcemia (mmol/L)	2.30 ± 0.12
	− 25(OH) vitamin D (ng/mL)	23.8 ± 9.95
	- Albumin (g/L)	41.1 ± 3.4

mass ($p < 0.001$), and loss of lean mass ($p < 0.01$). In multivariable analysis, the only factor found to be significantly related to BMD loss at 12 months was the percentage of excess weight loss (odds ratio for a change of 1% excess weight loss, 1.12; 95% CI 1.05–1.18; $p < 0.001$) (Table 3).

In the group that had a positive primary outcome at 12 months, 25 patients had a by-pass and 43 patients had a sleeve gastrectomy. In the group without significant mineral bone density loss, there were less patients with bypass surgery (7 patients).

Discussion

To our knowledge, this study reports the largest series to date of BMD follow-up in patients undergoing bariatric surgery [5,

Table 2 Variations in bone mineral density as assessed by dual energy X-ray absoptiometry (DEXA) scan before and after bariatric surgery overall, and by measurement site (lumbar spine, femoral neck, total hip)

	Pre-surgery	Post-surgery		
		M6	M12	M24
BMD reduction > 0.03 g/cm² at ≥ 1 site[a]	–	*59/95 (62.1%)*	*68/95* **(71.6%)**	*(5/7)*
Weight (kg)[b]	129.3 ± 21.8	101 ± 18.8	93.4 ± 16.9	98.1 ± 9.9
Weight (kg)[b]	129.3 ± 21.8	101 ± 18.8	93.4 ± 16.9	98.1 ± 9.9
Number of DEXA scans[a]	*110*	*95*	*95*	*7*
Lumbar spine				
BMD reduction > 0.03 g/cm²[a]	–	9/94 (9.6%)	7/92 (7.4%)	2/7
BMD (g/cm²)[b]	1.06 ± 0.1	1.13 ± 0.1	1.13 ± 0.1	1.07 ± 0.1
T-score[c]	0.32 ± 1.2	0.95 ± 1.3	0.92 ± 1.3	0.24 ± 1.3
Z-score[c]	0.72 ± 1.1	1.35 ± 1.3	1.27 ± 1.3	0.8 ± 1.2
Femoral neck				
BMD reduction > 0.03 g/cm²[a]	–	31/89 (34.8%)	40/88 (45.5%)	2/7
BMD (g/cm²)[b]	0.94 ± 0.1	0.93 ± 0.1	0.91 ± 0.1	0.90 ± 0.1
T-score[c]	0.58 ± 0.9	0.51 ± 0.9	0.37 ± 0.9	0.13 ± 0.6
Z-score[c]	1.15 ± 0.9	1.07 ± 0.9	0.98 ± 0.9	0.94 ± 0.6
Total hip				
BMD reduction > 0.03 g/cm²[a]	–	46/95 (48.4%)	57/93 (61.3%)	4/7
BMD(g/cm²)[b]	1.08 ± 0.1	1.05 ± 0.1	1.04 ± 0.1	1.06 ± 0.1
T-score[c]	0.83 ± 0.9	0.65 ± 0.9	0.54 ± 0.9	0.54 ± 0.9
Z-score[c]	1.16 ± 0.8	0.97 ± 0.9	0.85 ± 0.9	0.99 ± 0.7
25-OH-Vitamin D (g/mL)	23.8 ± 9.95	34.2 ± 2.86	32.3 ± 8.29	25 ± 7.35
Albumin (g/L)	41.1 ± 3.4	42.8 ± 2.9	43.1 ± 3.1	43.7 ± 2.2

[a] Number (percentage). [b] Mean ± standard deviation. [c] *T*-scores and *Z*-scores expressed as standard deviations (mean ± standard deviation)

BMD, bone mineral density; *BMI*, body mass index; *DEXA*, dual x-ray absorptiometry

15–19]. Our study found that more than 70% of patients had clinically significant BMD loss at 12 months after bariatric surgery. This loss of bone density was observed at the femoral neck and femur. At 12 months, the significant reduction in BMD was related by bivariate analysis to the extent of reduction in BMI, weight loss, and to loss of fat and lean mass. In the multivariable analysis, we found a statistically significant relationship between the reduction in BMD and the percentage of excess weight loss. No case of osteoporosis was observed at 12 months after surgery in our series.

Studies that evaluated the percent change in BMD report a reduction at the level of the femoral neck and femur ranging from 6 to 10% at 12 months after bariatric surgery [3]. The variation in our study was 4%. There are several possible explanations for this difference. The patients included in our study were highly selected, as they attended a COM, and were closely followed-up. Vitamin and calcium supplementation were prescribed systematically for all patients. However, vitamin and calcium supplementation were not prescribed uniformly across all studies [16] and are not systematically recommended [2 18], even though it has been shown that they slow the loss of BMD in patients undergoing bariatric surgery [19]. In addition, even when vitamin and calcium supplementation is prescribed, the duration of treatment varies widely between studies [20].

Secondly, the DEXA scans in our study were all performed by two experienced operators with specific training, in order to optimize reproducibility of the exams and to reduce measurement bias. Measuring bone metabolism in obese patients can be challenging [21]. The penetration of photons is reduced in soft tissue, and the substantial volume of fat can affect the interpretation of bone mineral density. The lack of accuracy in the measurement of BMD by DEXA scan increases with increasing BMI [6, 22]. To limit this potential bias, some studies have used high-resolution peripheral quantitative computed tomography to measure BMD; however, DEXA currently remains the gold standard [22–24].

Our study has several strengths, including the large number of patients included. Even if it is a study with a significant

Table 3 Factors related to a reduction in bone mineral density > 0.03 g/cm^2 at 12 months after bariatric surgery, by bivariate and multivariable analysis

	BMD reduction > 0.03 g/cm^2 at ≥ 1 site	No BMD reduction > 0.03 g/cm^2 at ≥ 1 site	Univariate analysis		Multivariate analysis	
			OR (95%CI)	*p* value	OR (95%CI)	*p* value
Patients[a,g]	68/92 (73.9%)	24/92 (26.1%)	–	–	–	–
Age[b]	42.2 ± 9.9	47.7 ± 9.1	–	0.02	0.93 [d] (0.83–1.02)	0.15
Women[a]	52/68 (76.5%)	16/24 (66.7%)	1.63 (0.59–4.49)	0.34	–	–
Menopausal status[a]	10/68 (14.7%)	5/24 (20.8%)	0.65 (0.20–2.16)	0.50	2.77 (0.38–20.05)	0.31
Physical activity[a] > 1 h/week	36/66 (54.5%)	13/23 (56.5%)	0.92 (0.35–2.4)	0.86	–	–
Type of surgery[a]						
- Gastric bypass	− 25/68 (36.8%)	−7/24 (29.2%)	1.41 (0.51–3.9)	0.50	1.85 (0.45–7.61)	0.39
- Sleeve gastrectomy	− 43/68 (63.2)	−17/24 (70.8%)				
Vitamin D level (ng/mL)[b]	23.3 ± 9.4	26.1 ± 11.4	–	0.27	0.94[e] (0.88–1.01)	0.07
Variation of vitamin D (ng/mL)[b]	9.3 ± 10.9	5.8 ± 15.5	–	0.38	–	–
Loss of excess weight (%)[c]	61.5% (54.1–75.4%)	43.3% (32.8%–52.0%)	–	< 0.0001	1.12[f] (1.05–1.18)	< 0.001
BMI prior to surgery (kg/m^2)[c]	46.5 (41.5–51.0)	45.6 (42.0–52.1)	–	0.74	–	–
Loss of BMI (kg/m^2)[b]	− 13.8 ± 4.5	− 9.8 ± 4.4	–	< 0.001	–	–
Weight loss (kg)[b]	− 37.9 ± 13.5	− 26.8 ± 11.1	–	< 0.001	–	–
Loss of fat mass (kg)[b]	− 23.6 ± 9.8	− 14.4 ± 10.4	–	< 0.001	–	–
Loss of lean mass (kg)[b]	− 11.0 ± 5.2	− 7.2 ± 4.5	–	< 0.01	–	–

[a] Number (percentage)

[b] Mean ± standard deviation

[c] Median (1st quartile–3rd quartile)

[d] Odds ratio for a change of 1 year

[e] Odds ratio for a change of 1 ng/mL

[f] Odds ratio for a change of 1% of excess weight loss

[g] Analyses about 92 patient with DEXA scan could be performed at the three sites (lumbar spine, femoral neck, and the left total hip)

BMD, bone mineral density; *OR*, odds ratio, *95% CI*, 95% confidence interval; *BMI*, body mass index

number of patients with regular bone monitoring (6 and 12 months) after bariatric surgery, our results should be confirmed by other studies with more patients. We chose to compare absolute values of BMD in g/cm^2, since percent change in BMD as used in other studies only partially reflects reality. There may be variations in BMD without their necessarily being clinically pertinent or significant. However, some limitations for this study should be noted. The duration of follow-up was short in this observational cohort, so fractures that would occur later after surgery were not considered. Indeed, only one fracture was observed in our series. In the literature, data are conflicting regarding the risk of fracture after bariatric surgery [25–28]. Studies with follow-up of less than 2 years do not report an increased risk of fracture [24, 26], whereas other studies with longer follow-up (6 to 12 years) report an increase in the relative risk of any fracture, ranging from a 1.2-fold increase (95% CI 1.02–1.43) [28] to a 2.3-fold increase (95% CI 1.8–2.8) [27]. Weight loss alone could explain the decrease in BMD; however, we could not easily identify a control group of patients with rapid weight who did not undergo surgery.

Likewise, our study cannot differentiate the respective contributions of weight loss and increased physical activity to BMD [26, 27].

The persistent nature of BMD loss has been demonstrated up to 24 months after surgery [22], confirming that BMD loss is prolonged over time. This raises the question of how to follow-up patients who undergo bariatric surgery, and the role of DEXA scanning during this follow-up. Whether the reduction in BMD is secondary to physiological adaptations by the bone metabolism to reduced mechanical constraints, or whether the bone loss is pathological in itself with increased fracture risk remains to be established [9]. In the future, we purport that DEXA scan monitoring should be pursued in these patients to monitor the progression of BMD and fracture risk over the long term.

The main data in the literature on change in bone mineral density after bariatric surgery concern gastric bypass. The reasons are a greater risk of vitamin D deficiency (vitamin D is absorbed by the jejunum and ileum and therefore procedures that bypass this part of intestine such as the RYGB exacerbate vitamin D deficiency), increased weight loss, and reduced food intake [3]. One case–matched study, compare the difference in bone mineral density after three different bariatric procedures [29]. Bone loss at the hips was observed on every patient even with adequate vitamin D supplementation. Laparoscopic Roux-en-Y gastric bypass causes significantly greater bone loss than the two other procedures [29]. In our study, the effect seemed to be consistent with the literature; however, it was not statistically significant probably because of the small proportion of patients with bypass surgery.

At present, there is no consensus regarding the indication for a DEXA scan in the follow-up of patients treated by bariatric surgery. DEXA scan is recommended before and either at 2 years after surgery [18], or on an annual basis at least until weight has stabilized [16, 18, 30]. Once weight has stabilized, scans could be repeated every 3 to 5 years, or every 2 years in case of osteoporosis or risk factors for fracture. Early- and long-term systematic calcium and vitamin D supplementation is indicated to avoid deficiency-related osteomalacia [31]. In case of osteoporosis on DEXA or severe fracture, osteoporotic treatment with intravenous bisphosphonates may be proposed in combination with vitamin D-calcium supplementation.

We found that bariatric surgery changes bone metabolism and is related to a clinically significant reduction in femoral BMD. This clinically significant reduction in BMD is significantly related to weight loss. The question remains open as to the clinical impact of this BMD loss. Our findings are reassuring in this regard, with a very low rate of fractures, but the length of follow-up was not long enough in our study to provide more information on this point. Prospective studies over a longer period are warranted to investigate this further, but systematic DEXA scans pre- and post-surgery, then annually until weight has stabilized appear to be appropriate.

Compliance with Ethical Standards

This retrospective study has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Formal consent was not required.

Conflict of Interest Dr. Marion Geoffroy, Dr. Jan Chrusciel, Dr. Isabelle Gaubil-Kaladjian and Dr. Ana Diaz-Cives have no commercial associations that might be a conflict of interest in relation to this article.

Dr. Charlot-Lambrecht reports personal fees from Amgen, outside the submitted work.

Dr. Eschard reports personal fees from Abbvie, personal fees from BMS, personal fees from Janssen, personal fees from Lilly, personal fees from MSD, personal fees from Novartis, personal fees from Pfizer, personal fees from Roche, personal fees from Sanofi, personal fees from UCB, outside the submitted work.

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