ARTIGO ORIGINAL
ISSN 1677-5090

DOI: https://doi.org/10.9771/cmbio.v21i1.45171

Low bone mineral density in pre-menopausal women one year after gastric bypass

Baixa densidade mineral óssea em mulheres pré-menopausadas um ano após bypass gástrico

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Abstract

Introduction: *Nutritional deficiencies, hormonal changes and severe weight loss after Roux-en-Y Gastric Bypass (RYGB) can promote changes in bone metabolism which may lead to a reduction in bone mineral density (BMD).* ***Objective:*** *to investigate the prevalence of osteopenia/osteoporosis and factors associated with BMD in pre-menopausal women who underwent RYGB.* ***Methodology:*** *a cross-sectional study conducted with secondary data of patients followed-up in a specialized center for obesity treatment. Variables studied: biochemical and anthropometric data, body composition by multifrequency bioimpedance and BMD of the lumbar spine (LS), total femur (TF) and femur neck (FN) by dual-energy X-ray absorptiometry. For statistical analysis, the SPSS® software and a 5% significance level were utilized.* ***Results:*** *seventy-two (72) pre-menopausal women were evaluated. Mean age, BMI and mean post-surgery time was 38.7±6.5 years, 25.8±2.5 kg/m² and 13.1±1.7 months, respectively. The prevalence of osteopenia in at least one of the densitometry sites was 13.9%, with LS being the most frequent site. A lower LS BMD was associated with greater weight loss, higher percentage of body fat before surgery and lower post-surgery serum vitamin D levels. There was a positive correlation between skeletal muscle mass index adjusted for height in the pre-surgery period and LS BMD (r=0.361; p=0.010) and TF (r=0.404; p=0.004).* ***Conclusion:*** *a relevant prevalence of osteopenia was detected in pre-menopausal women after RYGB, mainly in the LS.*
Keywords: *Bariatric Surgery. Bone mineral density. Body composition. Vitamin D. Pre-menopause.*

Resumo

Introdução: o Bypass Gástrico em Y de Roux (BPGYR) pode promover mudanças no metabolismo ósseo decorrentes de deficiências nutricionais, alterações hormonais e perda severa de peso, podendo acarretar redução da Densidade Mineral Óssea (DMO). **Objetivo:** investigar a prevalência de osteopenia/osteoporose e fatores associados à DMO em mulheres pré-menopausadas submetidas à BPGYR. **Metodologia:** estudo transversal com dados secundários de pacientes acompanhadas em um serviço especializado no tratamento da obesidade. Variáveis estudadas: dados bioquímicos e antropométricos, composição corporal por bioimpedância multifrequencial e DMO de coluna lombar (CL), fêmur total (FT) e colo do fêmur (CF) por Absorciometria por Dupla Emissão de Raios X. Para análise estatística foi utilizado o programa SPSS®, com o nível de significância de 5%. **Resultados:** foram avaliadas 72 mulheres pré-menopausadas, com média de idade e de IMC de 38,7±6,5 anos e 25,8±2,5 kg/m², respectivamente, e tempo médio de pós-operatório de 13,1±1,7 meses. A prevalência de osteopenia em pelo menos um dos sítios densitométricos foi de 13,9%, sendo a CL o sítio mais frequente. Uma menor DMO na CL se associou a maior perda de peso, maior percentual de massa gorda antes da cirurgia e níveis séricos menores de vitamina D pós-operatória. Observou-se correlação positiva entre o índice de massa muscular esquelética ajustada pela altura no pré-operatório e a DMO da CL (r=0,361; p=0,010) e do FT (r=0,404; p= 0,004). **Conclusão:** detectou-se prevalência relevante de osteopenia em mulheres pré-menopausadas após BPGYR, principalmente na CL.
Palavras-chave: Cirurgia Bariátrica. Densidade Mineral Óssea. Composição Corporal. Vitamina D. Pré-menopausa.

INTRODUCTION

Roux-en-Y gastric bypass (RYGB) is one of the most performed procedures in the world for the treatment of severe obesity. It is a safe and effective method that promotes significant weight loss, improves patient comorbidities and quality of life. Despite the benefits, RYGB can be associated with surgical, metabolic and nutritional complications, including those related to bone metabolism [1-3].

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Studies have shown a reduction in Bone Mineral Density (BMD) [2,4-6] and an increased risk of fractures in patients who underwent bariatric surgery [7-9]. Numerous factors mediated by hormonal and anatomical changes caused by the surgery, such as calcium malabsorption, vitamin D deficiency, increased parathyroid hormone, accelerated weight loss, reduced mechanical load and loss of lean mass have been described as associated with the negative effects of bariatric surgery on bone mass [5,6,10].

In the literature, the association between changes in body composition due to bariatric surgery and bone mass loss has been explored [2,6], however studies focused on the relationship between skeletal muscle mass and BMD are scarce.

Thus, this study investigated the prevalence of osteopenia / osteoporosis and factors associated with BMD in non-menopausal women who underwent RYGB.

METHODOLOGY

A cross-sectional study based on data retrieved from records of patients of an obesity treatment clinic in Salvador-Bahia, after one year of bariatric surgery through the RYGB technique (between 2014-2015). The collected data were registered in a standardized questionnaire elaborated by the researchers.

The sample included pre-menopausal women older than 20 years, with preoperative BMI ≥ 35 Kg/m2 and associated comorbidities. Only women who have had a Dual Emission X-Ray Absorptiometry (DXA) scan around 12 months after surgery were included. From a total of 519 women operated between August 2014 and August 2015, applying the eligibility criteria described above, a sample of 72 medical records were selected for analysis.

The exclusion criteria were: self-reported menopause, being on medication that affects bone metabolism, diagnosis of collagen diseases, having consumptive diseases and pregnancy during one-year post-surgery.

This study was approved by the Human Research Ethics Committee of the School of Nutrition, Federal University of Bahia (nº 1.534.548/2016).

Definition of Variables

The dependent variable, BMD (g/cm²), was determined through DXA analysis of the Lumbar Spine (LS) (L1-L4), the Femur Neck (FN) and Total Femur (TF). The DXA was performed only one year after surgery once there was no recommendation for performing it on preoperative due to low prevalence of osteoporosis/ osteopenia in pre-menopausal women. This medical exam forms part of the health service protocol and can be done at the patient´s preferred clinic.

The diagnosis of osteopenia/osteoporosis was based on BMD classification[11] which considers normal to be T-score ≥ -1 standard deviation (SD), between -1.01 and -2.49 SD to be osteopenia and less than or equal to – 2.5 SD to be osteoporosis. Regarding Z-score, osteopenia (low bone mass for age and sex) was considered in patient with values below -2 SD. For women in the menacme phase, Z-score was used while for non-menopausal women over 40 years, T-score was utilized [12].

***Anthropometry**: The participants were weighed on a 300 kg capacity digital scale in light clothing and barefooted. Height was measured with a stadiometer (1 mm gradation) attached to a wall. Body Mass Index (BMI) was calculated and classified according to WHO (2000) standards [13].*

The following variables were calculated: ideal weight (ideal weight = 25 x height²); excess weight (pre-surgery weight – ideal weight) and, based on the current weight at one year post-surgery, percentage excess weight loss (%EWL) was obtained.

***Body composition**: Pre-surgery body composition in terms of skeletal muscle mass (SMM), fat mass (FM) and lean mass (LM) was estimated by Segmental Multifrequency Bioimpedance (Biospace®, model Inbody 720). All patients received guidance from trained staff on how to prepare for the examination according to protocol indicated by the equipment´s manufacturer (Biospace®).*

The percentage of fat mass (% FM) was calculated by the formula: % FM = fat mass (kg) / total weight (kg) x 100. Height-adjusted skeletal muscle index (HASMI) was defined by the formula [14]: HASMI = SMM (kg) / height (m)².

***Biochemical data**: Biochemical tests were requested by the center´s medical team and were carried out in laboratories of patients' preference. Serum parathormone (PTH) (pg/ml) and 25-OH vitamin D (ng/ml) values (measured by the chemiluminescence method) were retrieved from medical records before and after the bariatric surgery. The cutoff point of 30 ng/ml was adopted, considering obese and bariatric patients included in the risk groups for hypovitaminosis D and who benefit from the maintenance of values between 30 and 60 ng/ml. [15]*

Fracture risk: The FRAX® [16] online algorithm was used to calculate the risk of major fracture (spine, forearm, hip, and shoulder) and hip fracture in 10 years. This tool integrates femur neck BMD data combined with clinical risk factors investigated using the following variables: age, sex, weight and height, previous fracture history, parental fracture history, diagnosis of rheumatoid arthritis, current practice of smoking, use of glucocorticoids (current or previous for more than 3 months use of 5 mg or more of prednisolone or equivalent per day), consumption of 3 or more units of alcohol per day (1 unit = 10g of alcohol) and secondary causes of osteoporosis.

Statistical analysis

Qualitative variables were expressed as absolute and relative frequency and quantitative variables were *expressed as mean and standard deviation or median and interquartile range. For the analysis of associated factors, the patients were divided into groups considering median BMD (g/cm²) at each densitometry site analyzed. Independent variables were compared between groups using Student's t-test or Mann-Whitney test. Spearman or Pearson tests were used for correlation analysis according to the normality of the variables. Values with p <0.05 were considered statistically significant. All analyses were performed using the SPSS® version 22 statistical package.*

RESULTS

Seventy-two (72) pre-menopausal women were evaluated with a mean age of 38.7 ± 6.5 years and mean postoperative (RYGB) time of 13.1 ± 1.7 months. Regarding education and marital status, 53.8% had university degrees and 59.2% reported having a partner. As for the preoperative BMI, patients had grade 2 obesity (66.7%, n = 48) or grade 3 (33.3%, n = 24), and all had, at least, one comorbidity associated to obesity. The most prevalent comorbidities were hepatic steatosis (65.3%, n = 47), obstructive sleep apnea syndrome (51.4%, n = 37) and gastroesophageal reflux disease (43.1%, n = 31). Most patients (80.4%, n = 41) had vitamin D levels 25-OH <30 ng / ml before surgery. All patients showed excess weight loss greater than 60% one year after RYGB (Table 1).

Table 1 – *General, biochemical and body composition characteristics of pre-menopausal women undergoing RYGB.*

Characteristics	*Total n=72*	*Results*
Age (years)1	72	38.7 ± 6.5
Post-operative time (months)1	72	13.1 ± 1.7
Preoperative		
25-OH Vitamin D (ng/mL)2	51	26.0 (20.5-29.0)
25-OH Vitamin D <30ng/mL n (%)	51	41 (80.4)
PTH (pg/mL)2	35	27.0 (20.7-45.0)
BMI (kg/m²)1	72	38.9 ± 2.8
% FM2	50	46.5 (40-56.2)
% LM1	50	49.1 ± 8.9
SMM (kg)1	50	28.6 ± 2.9
HASMI (kg/m²)2	50	10.8 (10.4-11.4)
Postoperative		
25-OH Vitamin D (ng/mL)2	42	28.7 (24.2-38.9)
25-OH Vitamin D <30ng/mL n (%)	42	19 (45.2)
PTH (pg/mL)2	39	35.5 (28.3-45.0)
BMI (kg/m²)1	72	25.8 ± 2.5
% EWL2	72	95.5 (83.0-111.4)

[1] Mean ± standard deviation; [2] Median (interquartile range). PTH – Parathormone; FM – Fat mass; LM – Lean mass; SMM – Skeletal muscle mass; HASMI – Height-adjusted skeletal muscle index; BMI – Body Mass Index; EWL – Excess weight loss.

The prevalence of osteopenia in at least one of the analyzed densitometry sites was 13.9% (n=10), with LS being the most frequent site (Table 2). Three patients had osteopenia at all 3 sites and there was no case of osteoporosis. The average 10-year fracture risk estimated by the FRAX algorithm was low.

Table 2 – *Prevalence of osteopenia, BMD by densitometric site and risk of fractures by FRAX in pre-menopausal women undergoing RYGB.*

Variables	*Results*
Osteopenia n (%)	10 (14%)
Osteopenia in lumbar spine n (%)	8 (11%)
Osteopenia in total femur n (%)	5 (7%)
Osteopenia in femur neck n (%)	5 (7%)
Lumbar spine BMD (g/cm²)¹	1.20 (1.11-1.35)
Total femur BMD (g/cm²)¹	1.08 (0.97-1.15)
Femur neck BMD (g/cm²)¹	1.03 (0.96-1.09)
Risk of major osteophorotic fracture (%)2	2.3±1.1
Hip fracture risk (%)2	1.0±0.2

[1] Median (interquartile range). [2] Mean ± standard deviation. BMD – Bone Density mineral.

Table 3 shows the comparisons between the groups with the highest and lowest BMD, taking the median BMD for each site as a reference. A lower LS BMD was associated with a higher % FM before surgery, greater weight loss and lower levels of vitamin D one year after RYGB (p <0.05). TF BMD was associated only with preoperative HASMI (p = 0.008). FN BMD did not show associations with the analyzed variables (data not shown).

Table 3 – *Factors associated with BMD by densitometric site in pre-menopausal women undergoing RYGB.*

Variables	*Lumbar spine BMD*		*P-value*	*Total femur BMD*		*P-value*
	≤Median n=36	*>Median n=36*		*≤Median n=36*	*>Median n=36*	
Age (years)	*39.2 ± 6.2*	*38.2 ± 6.7*	*0.519*	*39.8 ± 6.5*	*37.8 ± 6.4*	*0.280*
Preoperative						
25-OH Vitamin D (ng/mL)	*25.0 (19.5-28.4)*	*27.2 (21.7-30.8)*	*0.239*	*25.9 (20.5-28.1)*	*26.5 (20.6-30.2)*	*0.854*
PTH (pg/mL)	*33.9 (20-49)*	*25 (20.8-29.5)*	*0.231*	*30.9 (23.7-54.4)*	*26 (19.5-36.1)*	*0.166*
BMI (kg/m²)	*38.6 (36.8-41.6)*	*38.1 (36.1-40.8)*	*0.398*	*38.5 (36.3-41.6)*	*38.3 (36.3-40.9)*	*0.943*
% FM	***49.5 (45.1-55.9)***	***45.1 (39.8-53.3)***	***0.026***	*49.2 (44-53.3)*	*46.6 (41.6-54.5)*	*0.617*
% LM	*48.7 ± 4.6*	*48.7 ± 4.7*	*0.285*	*47.8 ± 4.6*	*49.6 ± 4.4*	*0.464*
SMM (kg)	*28.6 ± 2.9*	*28.7 ± 3.0*	*0.970*	*28.1 ± 3.0*	*29.2 ± 2.7*	*0.163*
HASMI (kg/m²)	*10.8 ± 0.8*	*11.0 ± 0.7*	*0.252*	***10.6 ± 0.7***	***11.2 ± 0.7***	***0.008***
Postoperative						
25-OH Vitamin D (ng/mL)	***28.5 ± 8.5***	***34.4 ± 8.5***	***0.034***	*30.3 ± 8.6*	*32.4 ± 9.3*	*0.464*
PTH (pg/mL)	*42.1 ± 24.3*	*35.1 ± 10,7*	*0.312*	*39.7 ± 24.4*	*38.2 ± 10.0*	*0.822*
BMI (kg/m²)	*25.4 ± 2.6*	*26.2 ± 2.4*	*0.209*	*25.5 ± 2.5*	*26.1 ± 2.5*	*0.358*
Lost weight (kg)	***36.7 ± 6.9***	***32.3 ± 6.3***	***0.005***	*35.1 ± 7.5*	*33.7 ± 6.3*	*0.393*
% EWL	*97.0 (84.3-116.6)*	*92.0 (81.1-104.1)*	*0.195*	*97.0 (84.0-114.0)*	*91.3 (82.2-111.4)*	*0.376*

Data expressed in mean ± standard deviation or median (interquartile range). The groups were compared by Student's t-test or Mann-Whitney. BMD – Bone Density Mineral; BMI – Body Mass Index; PTH – Parathormone; FM – Fat mass; LM – Lean mass; SMM – Skeletal muscle mass; HASMI – Height-adjusted skeletal muscle index; EWL – Excess weight loss.

Table 4 shows the correlations between the BMD of each densitometry site and pre-surgery biochemical and body composition variables. There was a positive correlation between preoperative HASMI and LS BMD (r = 0.361; p = 0.010) and FT BMD (r = 0.404; p = 0.004). Postoperative vitamin D was positively correlated only with LS BMD (r = 0.343; p = 0.026).

Table 4 – *Correlation between biochemical and body composition variables with Bone Mineral Density by densitometric site.*

Variables	*Lumbar spine BMD*	*Total femur BMD*	*Femur neck BMD*
Preoperative			
25-OH Vitamin D (ng/mL)	*0.140 (0.327)¹*	*0.047 (0.744)¹*	*0.124 (0.391)¹*
PTH (pg/mL)	*-0.320 (0.061)¹*	*-0.276 (0.109)*	*-0.176 (0.313)¹*
% FM	*-0.188 (0.190)*	*-0.025 (0.863)*	*0.046 (0.755)*
% LM	*0.022 (0.877)*	*0.152 (0.291)*	*0.203 (0.162)*
SMM (kg)	*0.160 (0.266)*	*0.234 (0.103)*	*0.261 (0.070)*
HASMI (kg/m²)	***0.361 (0.010)***	***0.404 (0.004)***	*0.230 (0.112)*
Postoperative			
25-OH Vitamin D (ng/mL)	***0.343 (0.026)***	*0.206 (0.191)*	*0.164 (0.307)¹*
PTH (pg/mL)	*-0.116 (0.481)¹*	*0.081 (0.623)¹*	*0.045 (0.791)¹*
Lost weight (kg)	*-0.191 (0.108)*	*-0.155 (0.197)*	*-0.090 (0.457)*

¹ Spearman ρ (p-value). Others, Pearson r (p-value). BMD – Bone Density Mineral. PTH – Parathormone; FM – Fat mass; LM – Lean mass; SMM – Skeletal muscle mass; HASMI – Height-adjusted skeletal muscle index.

DISCUSSION

This study showed a relevant prevalence of osteopenia in non-menopausal women, mainly in the LS, one year after RYGB. It was observed that factors associated with lower BMD vary according to the evaluated densitometry site: LS BMD showed a negative association with preoperative % FM, weight loss and postoperative vitamin D level, while TF BMD showed positive association with HASMI.

The literature presents different results on the prevalence of osteopenia /osteoporosis in women who underwent bariatric surgery when considering menopausal status and post-surgery time. In non-menopausal women, the prevalence varied between 9.5%(7) and 13.3% 10, similar to the result obtained in our study sample. Studies that included pre – and post-menopausal women between one and three years after surgery observed higher prevalence of osteopenia, between 27% and 45.7% and 20% for osteoporosis [17,18].

Studies have shown a reduction in BMD at different sites in patients who underwent RYGB 4,17. From the prevalence analysis of osteopenia and osteoporosis according to densitometry site, LS seems to be the most frequent site at one year post-surgery 17 as observed in the present work and also at eight years post-surgery when the prevalence of osteopenia in the LS and FN can reach 67 % and 40%, respectively [19].

Low levels of 25-hydroxyvitamin D and the presence of secondary hyperparathyroidism are common in obese patients even before bariatric surgery. Several *factors are associated with hypovitaminosis D in obese individuals, such as inadequate intake of vitamin D food sources, insufficient sun exposure that reduces the skin's production, added to its sequestration by the adipose tissue and inflammatory profile [20]. A recent study[21] carried out in the Northeastern region of Brazil with severely obese individuals, mostly women indicated for bariatric surgery, found vitamin D levels <30ng/ml in 78.6% of the patients, similar to that evidenced in the present study.*

The anatomical and metabolic changes inherent to the procedure contribute to low serum vitamin D levels after surgery, contributing to the loss of bone mass [11,22,23]. Therefore, patients referred for bariatric surgery receive guidance on vitamins and minerals supplementation during the post-surgery period, including vitamin D. Maintaining adequate serum levels of vitamin D appears to be important in maintaining BMD after the procedure, as suggested by the positive correlation between postoperative vitamin D and LS BMD.

Other factors such as substantial weight loss and changes in body composition seem to play an important role in the pathophysiology of bone loss after bariatric surgery [7,11]. In the present study, greater weight loss in the first year after surgery was negatively associated with LS BMD; similar findings were found in prospective studies with follow-up periods between one and five years [6,7,24].

This can be justified by the composition of the spine, which has a higher proportion of trabecular bone, which is less dense, more porous and metabolically active compared to cortical bones. Consequently, the former is more sensitive to hormonal factors and changes in mechanical load, making it a preferential site for calcium reabsorption [6,7].

The reserves of lean and adipose mass in the body are independent determinants of bone mass. The physiological adaptation for more bone mass to support a greater mechanical load, in addition to higher levels of estrogen and insulin could justify greater bone mass in obese individuals [25,26]. However, these benefits seem to be limited by vitamin D deficiency, high PTH levels and the maintenance of a low-grade inflammatory state associated with excess adipose tissue, leading to bone fragility [25-27]. Accordingly, the % FM in the pre-surgery period was associated with a lower LS BMD after RYGB.

The maintenance of lean mass after surgery seems to be essential for the preservation of bone health due to its role in supporting the skeleton via the skeletal muscles[1]. In longitudinal studies, the greatest loss of lean mass was associated with a reduction in BMD at all bone sites[25] and a greater risk of osteopenia in women after RYGB[16]. The importance of physical activity after bariatric surgery is widely accepted to minimize muscle depletion during the period of intense weight loss and possibly help the maintenance of bone mass [26].

There was no difference between the groups in relation to % LM, however, the SMM adjusted by height^2 expressed as HASMI, reduced in the group with the lowest TF BMD and was positively correlated with the LS and TF BMD. In obese or patients who underwent bariatric surgery, no studies were found that assessed the association between bone mass and HASMI. In the present study, this indicator proved to be promising in assessing the association between SMM and BMD, given that it expresses a relative measure of muscle mass in relation to a fixed parameter, height, which does not change despite major changes in weight or hydration status.

Bariatric surgery has been associated with an increased risk of fractures 9. The probability of fractures by the FRAX® algorithm, a low-cost and easy-to-apply tool for estimating long-term fracture risk, was low and similar to a study 17, possibly because the studied samples were composed of young women with a short post-surgery time.

Among the limitations of the present study, the use of a convenience sample is highlighted, which makes generalization of the results difficult. However, the study sample is similar to that of many treatment centers for obesity and includes routine patient assessment protocols. Another limitation concerns the lack of data on BMD before the surgery. DXA is not a routine preoperative technique due to restrictions on equipment capacity and high cost. The use of T and Z-scores minimizes this limitation since they compare participants with reference populations of the same sex and age.

CONCLUSION

In conclusion, after one year of RYGB, a relevant prevalence of osteopenia in non-menopausal women was found, mainly in the LS. The factors associated with lower LS BMD after bariatric surgery were higher % FM and lowest HASMI before surgery, as well as greater weight loss and lowest 25-OH Vitamin D levels after surgery.

The findings reinforce the need for more accurate multidisciplinary evaluation before surgery which involves the analysis of nutritional status and body composition including BMD. Despite of methodological limitations, the association described between post-operatory BMD and the % FM and HASMI before surgery suggest that body composition might influence in bone mass after surgery, what justify the need of more studies.

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Submetido em: 23/06/2021
Aceito em: 22/11/2021