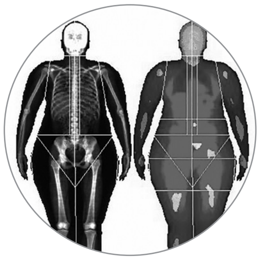

Changes in Bone Mineral Density and Body Composition in Obese Patients Undergoing Bariatric Surgery

Cambios en la densidad mineral ósea y en la composición corporal en pacientes obesos sometidos a cirugía bariátrica

Sara Jaimes Niño[1]
Sergio Valencia[2]
Gustavo Triana[3]
Javier Andrés Romero[3]

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Summary

Obesity is a public health problem that significantly affects the world population, increasing morbidity and mortality rates. Although there are multiple treatments for obesity, the most effective treatment in the long term is surgical. Bariatric surgeries, such as Y-de-Roux gastric bypass and gastric sleeve, have not only reduced body mass at the expense of reducing fat mass, but have also reduced the prevalence of comorbidities such as type 2 diabetes mellitus, dyslipidemia, arterial hypertension, among others. However, bariatric surgeries have also been shown to have negative effects on the musculoskeletal index and bone mineral density, variables that must be taken into account during pre-surgical assessment and post-surgical recommendations. From the results of the study, it can be inferred that bariatric surgery causes osteopenia / osteoporosis and sarcopenia in the long term based on the statistically significant decrease in bone mineral content (BMC) and fat-free lean tissue in the short term, which is why a long-term follow-up (longer than 12 months) of these patients is proposed.

Resumen

La obesidad es un problema de salud pública que afecta de forma significativa a la población mundial, aumentando los índices de morbilidad y mortalidad. A pesar de que existen múltiples tratamientos para la obesidad, el más efectivo a largo plazo es el quirúrgico. Las cirugías bariátricas, como el *bypass* gástrico en forma de Y-de-Roux y la manga gástrica, han logrado no solamente rebajar la masa corporal a expensas de la reducción de la masa grasa, sino que han disminuido la prevalencia de comorbilidades como diabetes *mellitus* tipo 2, dislipidemia, hipertensión arterial, entre otras. Sin embargo, las cirugías bariátricas también han demostrado tener efectos negativos sobre el índice musculoesquelético y la densidad mineral ósea, variables que deben ser tenidas en cuenta durante la valoración prequirúrgica y las recomendaciones posquirúrgicas. A partir de los resultados del estudio se puede inferir que la cirugía bariátrica ocasiona osteopenia/osteoporosis y sarcopenia a largo plazo basados en la disminución estadísticamente significativa del contenido mineral óseo (CMO) y del tejido magro libre de grasa a corto plazo, por lo cual se propone un seguimiento a largo plazo (mayor de 12 meses) de dichos pacientes.

1. Surgeon, Pontificia Universidad Javeriana. Radiology Resident, Universidad El Bosque. Bogotá, Colombia.

2 General practitioner, Universidad de los Andes. Master in Epidemiology, Universidad El Bosque. Bogotá, Colombia.

3 Radiologist and Master in Epidemiology, Pontificia Universidad Javeriana. Bogotá, Colombia. Department of Diagnostic Imaging, University Hospital Fundación Santa Fe de Bogotá. Bogotá, Colombia.

Introduction

Obesity is a public health problem that significantly affects the world's population, with high rates of morbidity and mortality. According to the World Health Organization (WHO), obesity has tripled worldwide since 1975. In 2016, 39 % of the adult population (people over 18 years of age) was overweight, while 13 % of this population was considered obese (1). Multiple treatments have been developed, of which bariatric surgeries have the highest rate of effectiveness for weight reduction and long-term comorbidities. However, these surgical procedures have shown side effects, such as osteopenia and sarcopenia, findings that are partially understood and have not been studied in depth.

The introduction of the study of body composition and osteodensitometry has made it possible to analyse these changes secondary to bariatric surgery, to evaluate the behaviour of the different body components - before and after the surgical procedure - and the relationship between them.

Multiple bariatric surgeries are performed at our institution with strict clinical and radiological monitoring before and after the procedure. Based on the data obtained from these patients, the behavior of the different body components is evaluated to establish the expected and side effects of these procedures.

1. Theoretical framework

Obesity is a multifactorial disease with genetic, nutritional and metabolic components (2). According to the WHO, it is classified according to the body mass index (BMI) - developed approximately 200 years ago by Quetelet - to describe the arithmetic relationship between body mass and patient's height (BMI = kg/m2) (2). However, it is now known that BMI is an imprecise mathematical estimate of adipose tissue, which ignores multiple associated factors, and is of little use in predicting patients' cardiovascular risk (2).

Adipose and musculoskeletal tissue are more than an energy reserve, they also produce adipocines and myocines, which actively participate in the metabolism of lipids and glucose as bioactive proteins (3). Due to the endocrinological function of adipose tissue, it is necessary to classify obesity according to the body composition of the patients, mainly according to their percentage of body fat (BFP) since this is strictly related to cardiovascular risk (3). However, it is not only the BFP that is decisive in defining the cardiovascular risk associated with obesity; the distribution of body fat is also important (3,4).

Visceral fat is found around the intra-abdominal organs and its increase is secondary to hypertrophy of existing adipose cells, associated with inadequate vascularization leading to fibrosis and secretion of pro-inflammatory cytokines (IL-1, IL-6, FNTα); this type of fat is related to ectopic adipose tissue. On the other hand, subcutaneous fat is the one found under the skin, its increase is secondary to preadipocytic cell hyperplasia associated with adequate vascularization that leads to expansion of adipose tissue with minimal fibrosis and minimal inflammation. It is vitally important to differentiate these two types of fat because it is the visceral fat that constitutes a risk factor for the development of dyslipidemia and insulin resistance, therefore, it is the one to be alert to. Accordingly, the android distribution of fat (central) increases cardiovascular risk compared to the gynecoid distribution of fat (peripheral), which also explains the metabolic abnormalities in normal weight patients (4,5).

As mentioned, muscle is also an endocrine organ that is affected by excess adipose tissue, and produces sarcopenia - loss of muscle mass, with subsequent weakness and limitation of movement. The concept of sarcopenic obesity was initially developed by Roubenoff, who discovered that the increase of inflammatory cytokines produced by excess adipose tissue, especially visceral fat, accelerates muscle catabolism through two pathways: direct -altering the amino acid balance of the muscle- and indirect -decreasing the sensitivity to insulin - which leads to sarcopenia (2,6).

Sarcopenic obesity is a public health problem associated with functional limitations and increased mortality, its incidence can be reduced by approximately 20 % with early diagnosis and appropriate treatment (1). Accordingly, judgement of obesity should be made using various diagnostic methods, including body composition. Prevention and treatment of obesity should include lifestyle changes (appropriate diet, increased exercise), behavioural therapy and pharmacotherapy; however, these measures are not sufficient for some patients, mainly those whose BMI is > 40 kg/m2. In these patients, surgical treatment should be additionally considered, which is very effective in long-term weight reduction and in decreasing comorbidities and mortality (7,8).

Bariatric surgery is recommended for patients with BMI > 35 kg/m2 (mainly patients with BMI > 40 kg/m2) who have associated comorbidities, such as metabolic syndrome and type 2 diabetes mellitus (2). There are several types of bariatric surgery: Y-de-Roux gastric bypass (YR-GB), gastric sleeve, gastric banding and duodenal switch. Patients submitted to the first two techniques (2,9) were included for this work.

The changes in the gastrointestinal tract mainly secondary to YR-GB are in the morphology of the intestinal mucosa and in its metabolic function. Intestinal hypertrophy is not only a post-surgical morphological change, but also a physiological response of the body to avoid malabsorption; however, it is to be expected that post-surgical intestinal absorption is not equal to pre-surgical intestinal absorption, secondary to deficiency in fat and caloric absorption. Because of this, bariatric surgeries are also called metabolic surgeries (10,11).

During the last decade, there has been a great deal of concern about bariatric surgery, since it not only reduces body mass, but also produces negative changes in bone mineral density (5). Calcium, the most abundant mineral in the human body, is mainly absorbed in the first portion of the small intestine (duodenum), which, after YR-GB, is isolated from the "active" or alimentary gastrointestinal tract (gastrointestinal tract in contact with food); as a consequence, there is a marked decrease in bone mineralization that negatively affects bone stability (12). The decrease in bone mineral density persists after the first post-surgical year, due to malabsorption of calcium and vitamin D (13,14). Additionally, lean body fat is decreased. However, the reduction in body weight is mainly at the expense of the decrease in fat mass (13,15).

Bariatric surgeries have been shown to adequately fulfill their main objectives: reduction of body mass, mainly at the expense of the fat component, and decrease in the incidence of comorbidities associated with obesity (arterial hypertension, type 2 diabetes mellitus, dyslipidemia, among others) (13). However, unexpected effects of the procedure have emerged that should be taken into account for the evaluation of patients prior to surgery and post-surgical recommendations: one of these events is the decrease in bone mineral density. For this reason, patients are currently given calcium (600-1200 mg/day) and vitamin D (400-800 IU/day) supplements to avoid this side effect and the increased risk of fractures (13,14).

Returning to what was discussed at the beginning, anthropometric measurements, such as body mass (weight), height and abdominal circumference, allow a moderate appreciation of the degree of obesity (according to BMI) and the cardiovascular risk of patients. However, the body composition obtained by means of Dual-energy X-ray absorptiometry (DEXA) allows a more precise observation of this information in a shorter time, since it shows the total body mass, body mass index (BMI), estimated visceral adipose tissue (eVAT), fat-free lean tissue (FFLT), android/gynoid ratio (A/G), resting metabolic rate, bone mineral density (BMD) and bone mineral content (BMC) (13,16). Additionally, the body composition provides partial information about the muscle mass represented in the relative musculoskeletal index (MSK index), which allows the definition of the state of sarcopenia of the patients, as well as the estimation of the appendicular muscle mass (lean mass in extremities) adjusted to the BMI of the patient; the trunk muscle mass is excluded from the analysis due to its difficulty in measurement. The established values of normality for the relative musculoskeletal index are < 0.789 in men and < 0.512 in women (6,15,17).

Some of the limitations of this diagnostic method are its inability to compare AVTF versus estimated subcutaneous adipose tissue (SAT), overestimating the values obtained and its incompetence to assess the body's water content, assuming that the soft tissues are hydrated (18). However, the high availability and low cost in comparison with other diagnostic methods with similar characteristics (computerized tomography [CT] and magnetic resonance imaging [MRI]), make DEXA the method of choice (18).

Osteodensitometry uses the same DEXA technology to get specific information about BMD and BMC in the column spine, hip and femoral neck; this way it can predict the patient's risk of fracture (patients between 40 and 90 years old), using specific mathematical algorithms such as FRAX (19).

2. Methods

A retrospective and descriptive study was conducted with patients who underwent bariatric surgery at the Hospital Universitario Fundación Santa Fe de Bogotá (HU-FSFB) between January 1, 2015 and May 31, 2017. As inclusion criteria, patients had to be older than 18 years, have a body mass index greater than 35 and pre- and post-surgical densitometry; patients with a history of previous bariatric surgery who were to undergo reoperation were excluded from the study, because, having a previous surgery, their metabolic state at the beginning of the study was altered.

After patient selection, medical records and diagnostic images were reviewed in order to collect their socio-demographic and clinical data according to the data collection format.

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3. Statistical analysis

The statistical analysis was performed in the univariate Stata 13® (Stata-Corp) program to establish the relative frequencies and proportions of the categorical variables. In addition, continuous variables were analyzed to obtain measures of central tendency (mean, median) and dispersion (interquartile range, standard deviation).

Finally, to evaluate the effect of surgery on variables such as body composition and bone mineral density, the Student t test of paired data or the Wilcoxon sign range test, according to normality. The Spearman correlation coefficient was used to evaluate the linear relationship between changes in composition body and bone mineral density, as well as on the clinical variables and demographics. Similarly, a regression model was carried out to assess in a multivariate way the association between the reduction of bone mineral density, body composition and the variables clinical and demographic.

4. Results

152 medical records of patients undergoing bariatric surgery between January 1, 2015 and May 31, 2017 were reviewed. The demographic characteristics and clinical outcomes of 22 patients were analyzed, 130 patients were excluded since they did not present pre-procedure measures and 6-12 months after the procedure. Of the 22 patients analyzed, 80.8% were women, the average age was 43.61 years, with a standard deviation of 10.49 years.

During the analysis, a statistically significant decrease in body mass index (BMI) was found to be 32.69 vs. 24.13 ($p = 0.001$), estimated visceral adipose tissue (VAT) 1174.26 g vs. 486.27 g ($p > 0.001$) bone mineral content (BMC) 2563.78 g vs. 2476.62 g ($p > 0.001$) fat-free lean tissue 44.85 g vs. 40.68 g ($p > 0.001$), fat tissue 46.08 % vs. 34.07 % ($p > 0.001$) and the android/gynoid ratio 1.03 vs. 0.87 ($p > 0.001$). Although the bone mineral density -(BMD) 1.24 g/cm² vs. 1.27 g/cm² (p 0.014)- and the musculoskeletal index relative -7.89 kg/m² vs. 6.53 kg/m² (p 0.68) - presented a decrease statistically not significant, we consider that this type of decrease is due to the short period of follow-up of the patients; since the statistically significant decrease in BMC and tissue fat-free lean predict a probable statistical decrease of BMD and the long-term musculoskeletal index, which is which would require a follow-up period of more than 12 months (Table 1)

Tabla 1. Registro del cambio en las variables de la composición corporal

Body Composition	Before		After		
Variables	Media	Standard deviation	Media	Standard deviation	*p* value
BMI	32.69	(2.68)	24.13	(2.84)	0.001
BMC (g)	2563.78	(356.92)	2476.62	(349.16)	> 0.001
BMD (g/cm²)	1.24	(0.09)	1.27	(0.36)	0.014*
FFLT (g)	44.85	(10.08)	40.68	(7.30)	> 0.001*
FT (%)	46.08	(5.41)	34.07	(7.61)	> 0.001
eVAT (g)	1174.26	(857.20)	486.27	(489.02)	> 0.001*
a/g	1.03	(0.17)	0.87	(0.26)	> 0.001
MSK index (kg/m²)	7.89	(1.19)	6.53	(0.86)	0.68*

BMI = body mass index. BMC = bone mineral content. BMD = bone mineral density. FFLT = fat-free lean tissue. FT = fat tissue. eVAT = estimated visceral adipose tissue. a/g = android/gynoid ratio. MSK = musculoskeletal index.

- *Non-normal distribution, estimated p-value with Wilcoxon test.

Subsequently, the Spearman correlation test, the which determines the correlation of association or interdependence between two random variables, whether continuous or discrete. During this test a significant correlation coefficient was established between multiple body composition variables (Table 2); the variable with the highest correlation was body mass index (BMI). One of the relationships among variables that it is important to emphasize is the coefficient of significant correlation ($p = <0.00$) between BMC and BMD (Figure 1), which establishes a strong partnership (Figures 2 and 3).

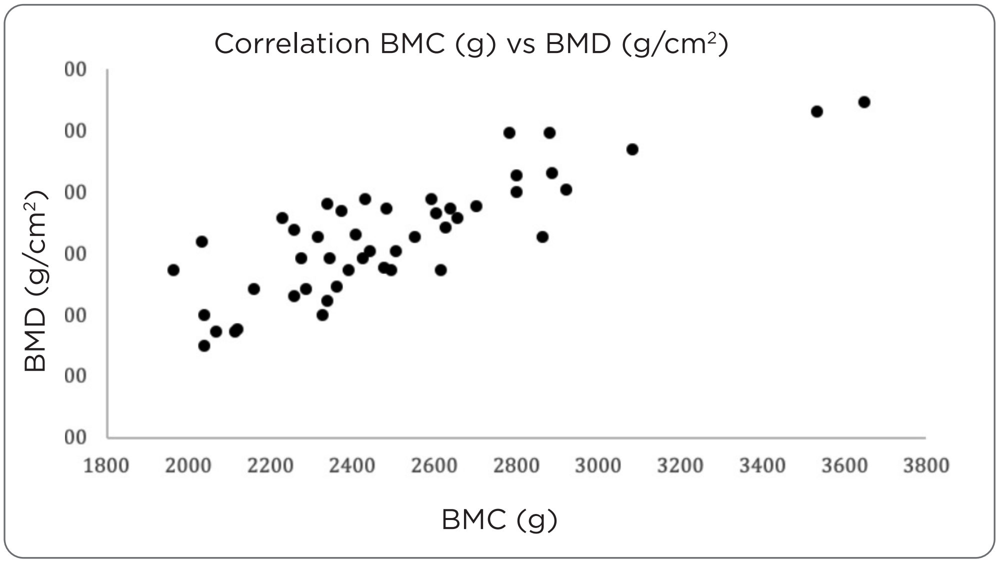
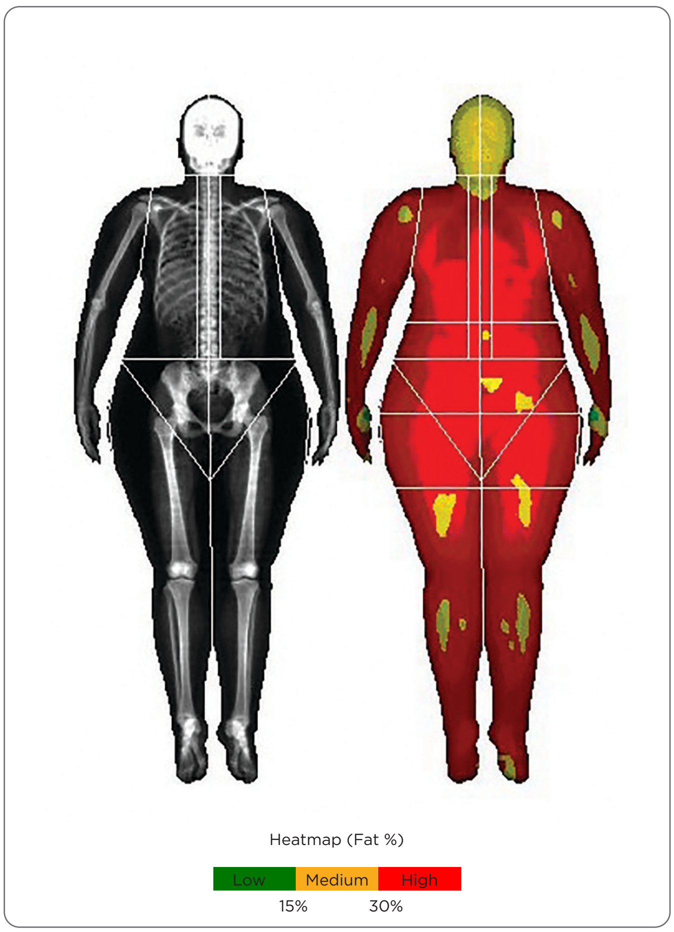


Figure 1. The correlation between BMC and BMD is observed, showing that when the BMC is increased/decreased, the BMD will behave in the same way.



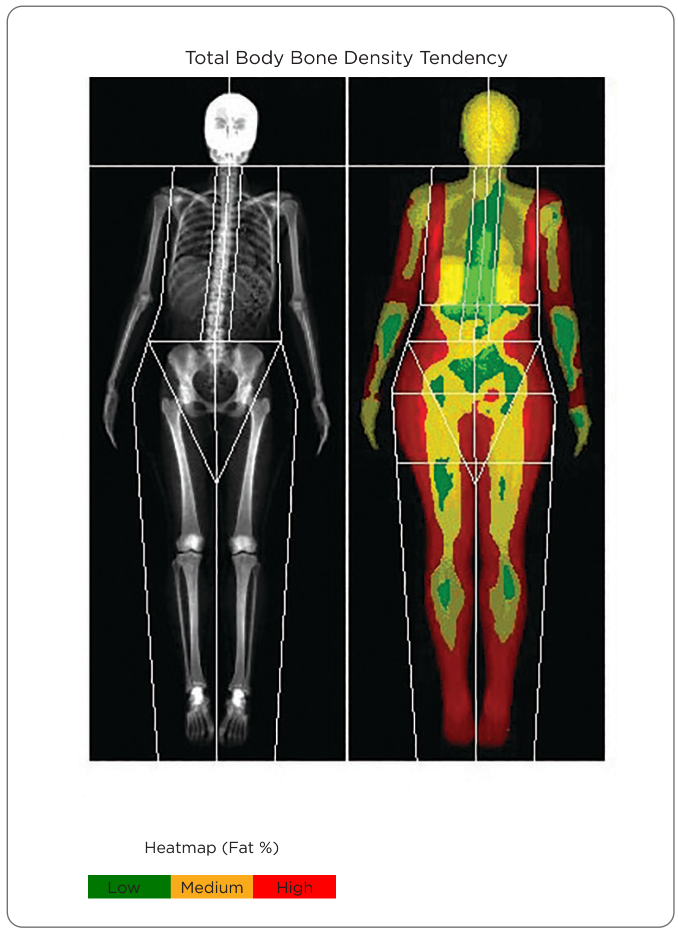


Figure 2. Body composition study prior to surgical procedure. A 30.1 year-old woman with a height of 161 cm, prior to surgical intervention with a total body mass of 93.5 kg, estimated visceral adipose tissue of 526 g, relative musculoskeletal index of 8.02 kg/m2, 52% fat tissue and bone mineral density of 1.609 g/cm2.

Figure 3. Body composition study after surgical procedure. A 31.5 year-old woman with a height of 161 cm, post-operative with a total body mass of 58.3 kg, estimated visceral adipose tissue of 61 g, relative musculoskeletal index of 6,23 kg/m2, fat tissue 30,5 % and bone mineral density of 1,471 g/cm2.

Table 2. Spearman's correlation between variables

		BMC	BMD	BMI	FFLT	FT	VAT	a/g	MSK Index
BMC	Correlation Coefficient	1.000	0.788**	0.150	0.807**	-0.172	0.207	0.077	0.464**
	Significance (bilateral)		0.000	0.315	0.000	0.237	0.153	0.601	0.001
BMI	Correlation Coefficient	0.788**	1.000	0.350*	0.491**	-0.012	0.219	0.175	0.435**
	Significance (bilateral)	0.000		0.015	0.000	0.936	0.127	0.225	0.002
BMD	Correlation Coefficient	0.150	0.350*	1.000	0.426**	0.743**	0.657**	0.610**	0.730**
	Significance (bilateral)	0.315	0.015		0.002	0.000	0.000	0.000	0.000
FFLT	Correlation Coefficient	0.807**	0.491**	0.426**	1.000	0.024	0.491**	0.341*	0.685**
	Significance (bilateral)	0.000	0.000	0.002		0.865	0.000	0.014	0.000
FT	Correlation Coefficient	-0.172	-0.012	0.743**	0.024	1.000	0.439**	0.307*	0.218
	Significance (bilateral)	0.237	0.936	0.000	0.865		0.001	0.029	0.137
eVAT	Correlation Coefficient	0.207	0.219	0.657**	0.491**	0.439**	1.000	0.731**	0.487**
	Significance (bilateral)	0.153	0.127	0.000	0.000	0.001		0.000	0.000
a/g	Correlation Coefficient	0.077	0.175	0.610**	0.341*	0.307*	0.731**	1.000	0.511**
	Significance (bilateral)	0.601	0.225	0.000	0.014	0.029	0.000		0.000
MSK Index	Correlation Coefficient	0.464**	0.435**	0.730**	0.685**	0.218	0.487**	0.511**	1.000
	Significance (bilateral)	0.001	0.002	0.000	0.000	0.137	0.000	0.000	

BMI = body mass index. BMC = bone mineral content. BMD = bone mineral density. FFLT = fat-free lean tissue. FT = fat tissue. eVAT = estimated visceral adipose tissue. a/g = android/gynoid ratio. MSK index = musculoskeletal index.

*Correlation is significant at the 0.05 level (bilateral).

**Correlation is significant at the level 0.01 (bilateral).

5. Discussion and conclusions

Bariatric surgery demonstrated a statistically significant decrease in body mass index (BMI) and estimated visceral adipose tissue (eVAT), adequately fulfilling its main objective. However, these were not the only variables with a statistically significant decrease; this type of change was also observed in fat-free lean tissue and bone mineral component (BMC).

The decrease in BMI relative to the decrease in fat-free lean tissue predicts a statistically significant decrease in the MSI over the medium/long term (>12 months), since this index represents the estimate of lean mass in extremities adjusted to the patient's BMI. When a statistically significant decrease in the musculoskeletal index occurs, bariatric surgery becomes a predictor of sarcopenia.

Additionally, the statistically significant decrease in BMC predicts a similar decrease in bone mineral density (BMD) in the medium/long term (> 12 months), as it shows a directly proportional relationship, which also makes bariatric surgery a predictor of osteoporosis.

The changes in body composition secondary to bariatric surgery represent a wide field of research, open to new proposals for analysis and eager to integrate knowledge. It is necessary to create and execute study protocols that clearly establish which examinations should be carried out before the intervention and their frequency in the post-surgical period, in order to carry out an adequate follow-up; taking into account that the duration of the follow-up should be greater than 12 months. Through these protocols, clear correlations can be established between the different variables of body composition, which will make it possible to predict changes before the procedure. In this way, recommendations on minimum bone mineral density, bone mineral content and musculoskeletal index can be defined pre-surgical treatments to prevent sarcopenia and osteoporosis in patients undergoing YR-GB or gastric sleeve.

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Correspondence

Sara Jaimes Niño
Carrera 7 # 111-64
sc.jaimesn@gmail.com

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