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25-OH-vitamin D and reversal of metabolic comorbidities associated with obesity after bariatric surgery

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Summary

Introduction: Obesity is a public health concern in which defects in the endocrine system occur, which may lead to metabolic diseases. Bariatric surgery (BS) has proved to be more effective in weight loss and reversal of comorbidities (especially inflammatory and metabolic). The underlying mechanisms related to the reversal of comorbidities are still poorly understood. Patients undergoing BS routinely receive vitamin D supplements, so its role in the reversal of comorbidities may be relevant.
Objectives: To determine the relationship between 25-OH-vitamin D levels, the prevalence of metabolic comorbidities before BS and 6 months post-op.
Results: 328 patients were evaluated, who showed significant loss of weight and lean mass 6 months after BS. Serum levels of 25-OH-vitamin D increased in parallel with an increase in supplementation. However, no correlations were observed with the presence of baseline metabolic comorbidities or at 6 months of BS. Serum levels of 25-OH-vitamin D were correlated with some parameters of body composition independently of the reversal of comorbidities.
Conclusions: Bariatric surgery was associated with a significant improvement in metabolic comorbidities in the patients studied independently of 25-OH-vitamin D serum levels.

Key words: vitamin D, obesity, metabolic comorbidities, reversal.

Introduction

Obesity is a chronic metabolic disease with an increasing incidence that is associated with the development of multiple metabolic and mechanical comorbidities, it has also been associated with a higher incidence of tumors, a worse evolution of autoimmune diseases (SEEDO/WHO)[1,2] and a increase in all-cause mortality[3,4]. According to Spain's Ministry of Health data, the prevalence of obesity in the adult population (25-65 years) is 14.5% (17.5% in women; 13.2% in men), with a parallel increase with people's age (21.6% and 33.6% in women and men over 65 years of age, respectively). This situation is a public health challenge, not only because of its prevalence, but also due to the increase in morbidity and mortality, accelerated aging, the economic costs and associated social implications[5,6].

To date, intensive medical treatment and lifestyle modifications in obese patients have not shown a significant decrease in the development of complications during follow-up (10-20 years)[7-9]. In contrast, bariatric surgery (BS) is an intervention that entails significant weight loss (25-58% at 10 years), associated with a significant improvement in comorbidities directly and indirectly related to the disease[7,10]. Additionally, BS reduces the risk of mortality by 51%[10]. Different meta-analyzes suggest reductions in cardiovascular mortality (OR, 0.58, 95% CI, 0.46-0.73), all-cause mortality (OR: 0.70, 95% CI, 0.59-0 ,84) and increased life expectancy of up to 7 years in patients with underlying cardiovascular disease[11].

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On the other hand, 25-OH-vitamin D levels have been closely related to the development of cardiovascular disease, specifically, its deficit has been associated with higher cardiovascular and all-cause mortality[12]. After BS, there is a significant reversal of metabolic comorbidities, as well as reduced cardiovascular risk and mortality from all causes in this population[10,13,14]. Likewise, the use of vitamin D supplements is carried out systematically during the follow-up of patients undergoing BS[15,16]. In this sense, it is not clear whether this supplementation can modulate the post-BS inflammatory response and that it could be related to the improvement of comorbidities in this patient group.

In this context, we analyze the levels of 25-OH-vitamin D in obese patients undergoing BS and its relationship with the reversal of metabolic comorbidities 6 months post op.

Patients and methods

Patients

The clinical variables of 328 patients undergoing BS at the Reina Sofía Hospital in Cordoba, Spain were analyzed. Our ethics committee, whose protocol was designed in accordance with the Declaration of Helsinki and with national and international guidelines for biomedical research approved the study. Each individual signed a written informed consent before taking part. Inclusion was carried out consecutively, all patients who underwent surgery and voluntarily decided to participate in the study. Bariatric surgery in our center is performed in men and women between 18 and 65 years old with BMI >40 Kg/m^2 or BMI >35 Kg/m^2 and at least one metabolic, mechanical or psychological comorbidity that indicates it, as established clinical practice guidelines[17-20]. A 6-month follow-up was carried out following the protocol of our hospital, which is based on international clinical practice guidelines. For this control, 260 patients of those initially evaluated were included. The general clinical characteristics of the included patients are summarized in the table 1.

The patients were treated according to the available clinical guidelines[15,17,19,21], an anthropometric assessment was also performed, with bioimpedance measurement (TANITA MC-780MA multifrequency impedance meter) and analytical. The determination of 25-OH-vitamin D was carried out by chemiluminescence with acridinium ester, with capture of streptavidin-biotin. The presence and disappearance of metabolic comorbidities was determined as part of the clinical history in the evaluation of the patient, and it was confirmed by analysis or determination of blood pressure in the consultation.

Statistic analysis

U-Mann Whitney tests were used to assess clinical associations. The xi-square test was used to compare categorical data, as well as Kruskal-wallis tests and ANOVA for multiple comparisons. Statistical analyzes were performed using the statistical software SPSS version 20 and Graph Pad Prism version 7. The graphs and tables present the data expressed as mean ± standard deviation or median ± interquartile range. The proportions were expressed as a percentage. In all analyses, p values <0.05 were considered statistically significant.

Table 1. Characteristics of the baseline population and 6 months after surgery

Characteristic	Baseline (n=328)	Post-BS (6 meses)	*p*
Age	47.54 ± 9.78		
Sex			
Female (%)	65.7		
Male (%)	34.3		
Metabolic comorbidities (%)	62.7	53.3	0.004
BMI (Kg/m^2)	47.5 ± 6.63	34.14 ± 5.55	<0.001
Fat mass (Kg)	59.09 ± 16.49	31.67 ± 11.86	<0.001
Lean mass (Kg)	58.29 ± 12.46	58.29 ± 2.45	0.639
Abdominal perimeter (cm)	131.18 ± 15.26	110.7 ± 14.80	<0.001
25-OH-vitamin D (ng/dl)	16.43 ± 9.95	30.08 ± 12.86	<0.001
Calcifediol supplementation (%)	26.2	93.8 (16/260)	<0.001
Supplementation dosage			
Calcifediol 0.266 mg every 30 days	5.2 (17/328)	31.2 (81/260)	
Calcifediol 0.266 mg every 21 days	4.9 (16/328)	33.8 (88/260)	
Calcifediol 0.266 mg every 15 days	12.8 (42/328)	23.8 (62/260)	
Calcifediol 0.266 mg every 10 days	2.4 (8/328)	0.8 (2/260)	
Calcifediol 0.266 mg every 7 days	1.2 (4/328)	3.1 (8/260)	

Results

The 328 operated patients presented a significant decrease in the presence of metabolic comorbidities at the sixth month after surgery, in parallel with the decrease in BMI and fat mass, but not in lean mass (figure 1A; table 1). Only 26.2% of the patients received calcifediol supplementation before surgery. This percentage increased to 93.8% 6 months after surgery (table 1). The presence of arterial hypertension (HT), dyslipidemia (DLP) and type 2 diabetes mellitus (DM2) were evaluated as metabolic comorbidities, which decreased from 62.7% to 53.3% (table 1). Supplementation at discharge from BC and at 6 months was significantly higher, as was the percentage and absolute number of patients with an increase in the dose interval (figure 1B).

Baseline 25-OH-vitamin D levels did not show differences between patients with or without metabolic comorbidities (figure 2A), both groups increased their serum levels in parallel (figure 2B) and the values did not affect the presence or absence of metabolic comorbidities. at the sixth month of BS (figure 2C). When analyzing metabolic comorbidities separately, no differences were observed between their presence and baseline 25-OH-vitamin D levels (figures 2 D-F); patients with HT had significantly higher levels of 25-OH-vitamin D at 6 months (figure 2H) while in patients with DM2 the increase was not significant (figure 2G); patients with DLP showed a trend that did not reach statistical significance (figure 2I).

From the anthropometric point of view, baseline BMI together with fat mass were negatively correlated with serum levels of 25-OH-vitamin D, while these values were positively correlated with baseline lean mass and at 6 months of BC. For its part, the determination of 25-OH-vitamin D at 6 months was only negatively correlated with pre-surgery abdominal girth and weight after BS (figure 3).

Discussion

This study is presented in which possible associations between 25-OH-vitamin D levels and the reversal of metabolic comorbidities after bariatric surgery are analyzed in a large cohort of patients undergoing this procedure. The aim is to determine the relationship between 25-OH-vitamin D levels, the prevalence of metabolic comorbidities before BS and 6 months post operative.

Vitamin D has been associated with an increased risk of developing DM2, HT, myocardial infarction, peripheral arterial disease, some types of cancer, autoimmune and inflammatory diseases, and even with increased mortality[22]. It also has an essential role in homeostasis and insulin secretion mechanisms[23]. After BC, there are numerous effects on mineral and bone metabolism, including calcium and/or vitamin D deficiency, secondary hyperparathyroidism, and loss of bone mass[24-27]. The changes in its metabolism seem to be influenced first by abnormalities in bone metabolism prior to surgery (related to morbid obesity), and later by changes in calciotropic hormones after BS and nutrient malabsorption. It is also unknown whether in the long term, these changes persist or stabilize after the body adapts to the new weight, hormonal secretion and environmental habits[28].

Likewise, calcidiol levels have been related to modulation of the inflammatory response in different diseases, conditioning their evolution and prognosis[29]. In this context, the mechanisms underlying the improvement in comorbidities are dependent and independent of the percentage of weight lost[30,31], and to a large extent are related to the improvement in insulin resistance and the improvement in β-cell function-pancreatic[32]. Vitamin D has been reported to improve insulin sensitivity and decrease the risk of developing diabetes, which is why it could have an additive (or essential) effect in the reversal of comorbidities[33]. However, in our cohort, no significant changes were observed in the evolution of metabolic comorbidities in the patients evaluated. This can be explained by the follow-up time of the patients, considering that, if there is no re-gain in weight, a greater reversion of comorbidities would be expected in these patients.

On the other hand, vitamin D deficiency is more common in obese patients, in this sense different mechanisms have been postulated, including a lower dietary intake, lower skin synthesis, decreased intestinal absorption and alteration in its metabolism[34]. There are

Figure 1. Clinical changes after BS. A) evolution of anthropometric changes 6 months after BS; B) interval of prescription of calcifediol supplementation after 6 months from the BS

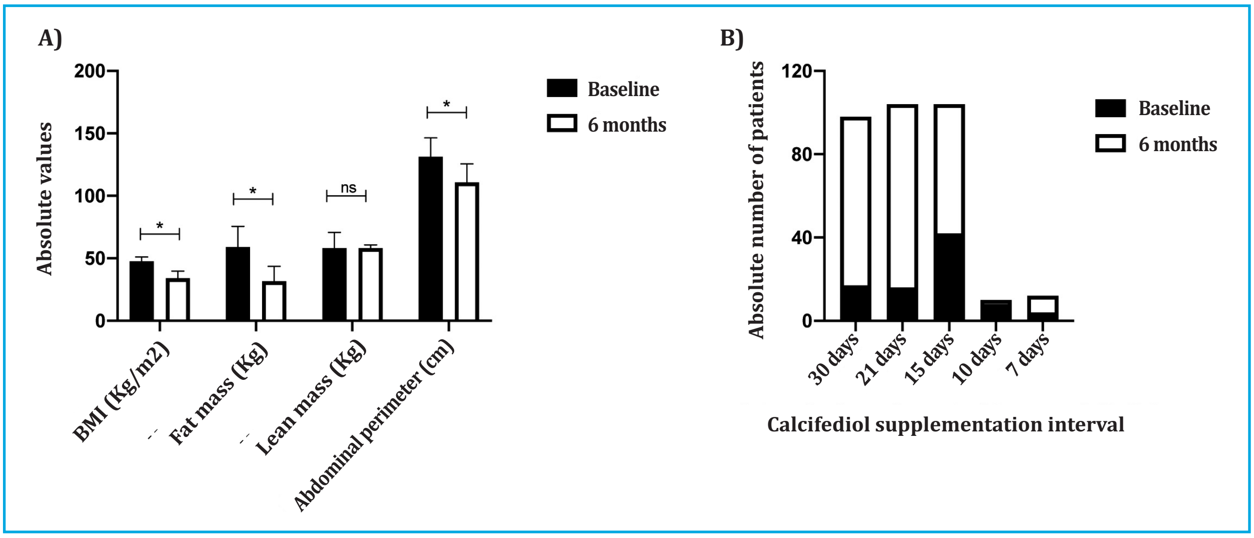
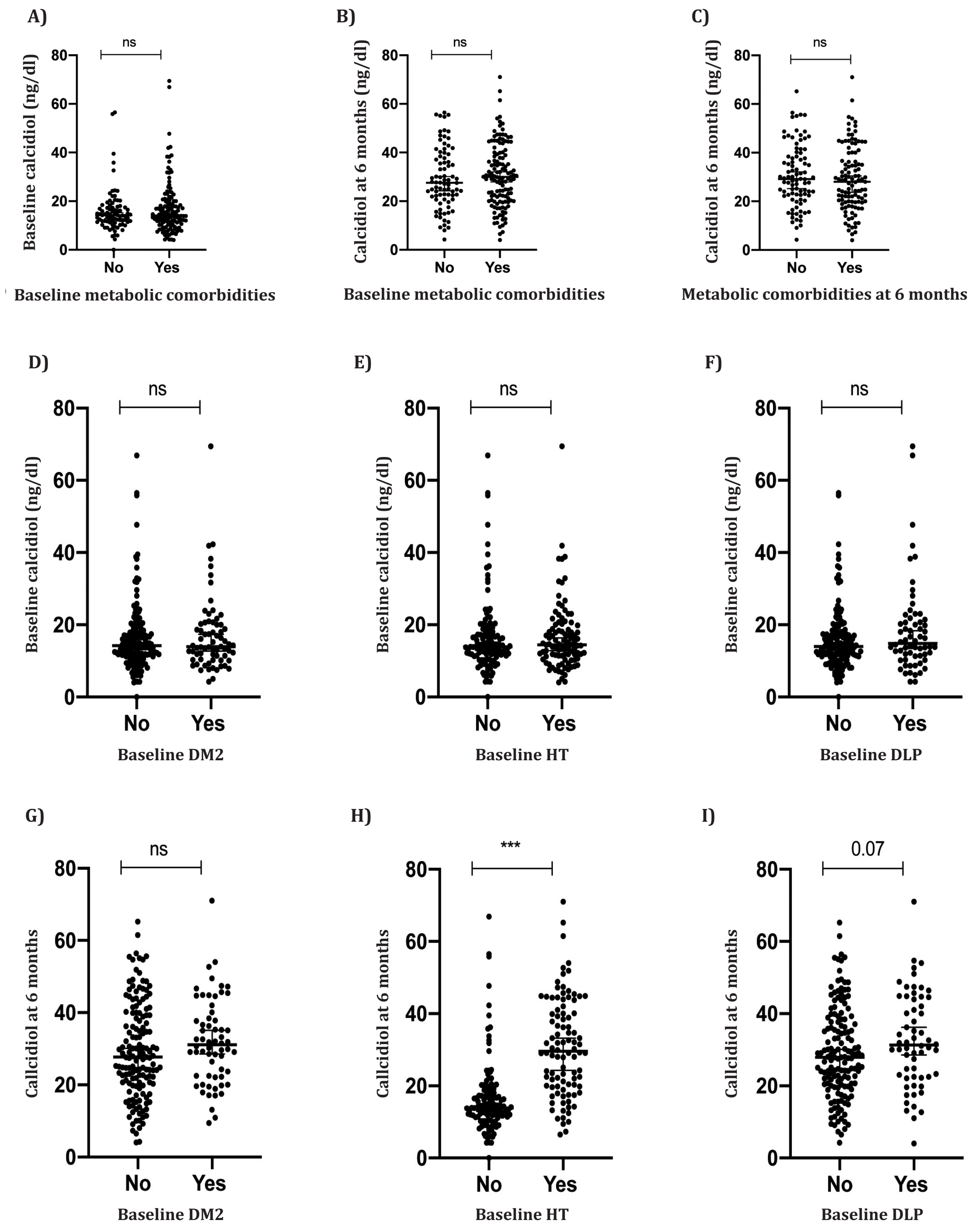


Figure 2. Association between metabolic comorbidities and serum levels of 25-OH vitamin D (calcidiol). A) metabolic comorbidities and basal calcidiol; B) metabolic and calcidiol comorbidities at 6 months; C) metabolic and calcidiol comorbidities 6 months after BS; D) presence of baseline DM2 and basal calcidiol levels; E) presence of baseline HTN and basal calcidiol levels; F) presence of baseline DLP and basal calcidiol levels; G) presence of baseline DM2 and calcidiol levels at 6 months; H) presence of baseline HTN and calcidiol levels at 6 months; I) presence of baseline DLP and calcidiol levels at 6 months

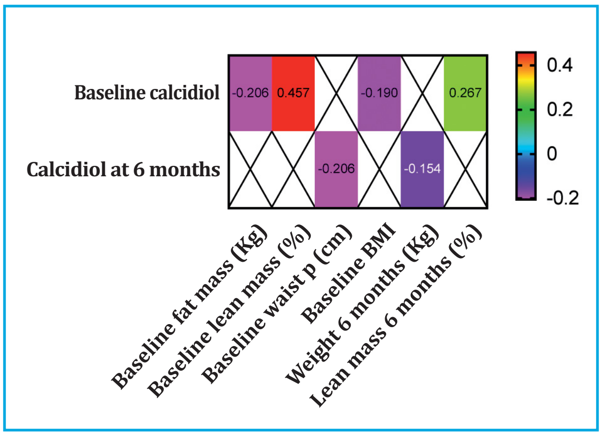


also hypotheses about the "sequestration" of 25-OH-vitamin D by adipose tissue, accompanied by less hepatic activation due to a decrease in 25-hydroxylase activity[35,36]. The specific mechanisms, however, are not known and are still under study. In our cohort, serum 25-OH-vitamin D levels were negatively correlated only at baseline with fat mass, and in contrast, they were positively correlated with lean mass both before and 6 months after surgery.

Among the strengths of this study is the number of patients included, as well as the availability of bioimpedance measurement in all of them, the technique for determining 25-OH-vitamin D and the fact that it is a prospective study at 6 months. However, as limitations we should point out the evolution time, which is limited to 6 months and that, at the time of the analysis, only 260 of the initially included patients had been evaluated. If the follow-up of these patients is continued, a longer-term evolution of the comorbidities and the behavior/adherence of the supplementation may provide additional information and with greater specificity. Finally, in this study, associations are observed that do not demonstrate a direct causal relationship.

To sum up, in our cohort, no relationship was observed between serum levels of 25-OH-vitamin D, the presence or evolution of metabolic comorbidities, but with the body composition of the individuals evaluated.

Figure 3. Correlations between anthropometric parameters and serum levels of 25-OH vitamin D (calcidiol) at baseline and at 6 months after BS. Only statistically significant correlations are represented (p<0.05)



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