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ORIGINAL CONTRIBUTIONS

Short- and Mid-term Changes in Bone Mineral Density After Laparoscopic Sleeve Gastrectomy

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Abstract

Background Bariatric surgery is the most effective treatment for achieving a significant weight loss. Morbidities present a significant reduction after bariatric surgery, but it may also result in several health complications, related to nutritional deficiencies, including bone metabolism. Several studies have reported a decrease in bone mineral density (BMD), but most of them referring to malabsorptive procedures. Restrictive procedures do not imply changes in gastrointestinal anatomy, so that one may expect fewer metabolic disturbances.

Methods We performed a retrospective observational study of all morbidly obese patients undergoing LSG between 2008 and 2011 at our institution. Bone densitometry was performed before surgery and 1 and 2 years after the intervention. Body size measurements, analytical variables and densitometric values in the lumbar spine (BMD, *t* score and *z* score) were investigated.

Results Forty-two patients were included, 39females and 3males. Mean BMI was 51.21 kg/m^2. Mean excessive BMI loss was 79.9 % after 1 year and 80.6 % after 2 years. Mean BMD values for spine increased progressively, reaching statistical significance at 1 and at 2 years. Percentage of BMD increase was 5.7 % at 1 year and 7.9 % at 2 years. An inverse correlation was observed between BMD increase and parathyroid hormone (PTH) decrease and a direct correlation between BMD and vitamin D increase.

Conclusion Bone mineral density showed a progressive increase during the first and second year after sleeve gastrectomy. BMD changes are not associated with weight loss, but showed a direct correlation with vitamin D and an inverse correlation with PTH levels.

Keywords Body mass density · Densitometry · Laparoscopic sleeve gastrectomy · Vitamin D · PTH

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Introduction

Obesity has shown a progressive increase over the last years in developed countries, reaching a prevalence of about 30 % in USA and 17.1 % in Spain in 2009 [1–3]. In an important rate of obese patients, modifications of lifestyle and pharmacotherapy fail to reach a significant weight loss. Actually, bariatric surgery is the most effective treatment for achieving a significant weight loss, improving quality of life and morbidity and mortality among obese subjects [4]. The prevalence of weight-related morbid conditions presents a significant reduction after bariatric surgery [5], but it may also result in several health complications, related to nutritional deficiencies, including bone metabolism [6]. Several studies have reported a decrease in bone mineral density (BMD), but most of them referring to malabsorptive procedures, such as Roux-en-Y gastric bypass (RYGBP) [7–9] and biliopancreatic diversion [10, 11]. Duodenum is the main place of calcium absorption and in malabsorptive procedures it is bypassed, justifying at least partly the calcium deficiencies [12]. Moreover, absorption of vitamin D from the diet also takes place in duodenum and jejunum, both segments bypassed in malabsorptive procedures. Therefore, levels of parathyroid hormone (PTH) increase after these techniques [13].

Restrictive procedures, such as laparoscopic sleeve gastrectomy (LSG), do not imply bypassing segments of small bowel where micronutrient absorption takes place, so that one may expect fewer metabolic disturbances [5]. Little is

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known about BMD status after LSG. The aim of this study was to analyze changes in BMD at 1 and 2 years and correlate them with weight loss and nutritional components.

Patients and Methods

We performed a retrospective observational study of all morbidly obese patients undergoing LSG between May 2008 and December 2011 at our institution.

The selection for surgical treatment was made in accordance with the IFSO guidelines, i.e., in individuals with BMI >40 kg/m^2 or of BMI >35 kg/m^2 with comorbidities. The study was approved by the Local Ethics Committee.

A total of 42 patients were included in the study, 39 females (92.8 %) and 3 males (7.2 %), with a mean age of 43.6+10.1 years, ranging from 20 to 62 years. Mean BMI was 51.2+6.7 kg/m^2. All the patients presented dietary habits of “big eaters” and a sedentary lifestyle. As comorbidities, the patients presented diabetes mellitus in 39 % of the cases, dyslipidemia in 50 %, hypertension 33 %, osteoarthritis in 19 % and obstructive sleep apnea hypopnea syndrome in 17 %. All the cases with diabetes mellitus were under treatment with metformin, and in six patients insulin was also necessary for a better control of glycemia. Dyslipidemia was treated with statins and hypertension with angiotensin II-converting enzyme inhibitors and hydrochlorotiazide in refractory cases. Obstructive sleep apnea hypopnea syndrome was managed with CPAP in all the cases. No patients were under treatment with biphosphonates or hormone replacement therapy.

Preoperative Evaluation

Potential surgical candidates for LSG as bariatric procedure were evaluated by all the members of the Obesity Unit at our institution. Preoperative assessment included abdominal ultrasound, bone densitometry, functional respiratory tests, upper gastrointestinal endoscopy and blood analysis including nutritional parameters. A preoperative 1,200 kcal diet was established by the dietician, expecting a weight loss of at least a 5 % of the patient’s overweight; if this condition was not met, the patient was considered not suitable to undergo a LSG and was sent to the referral hospital to undergo a Roux-en-Y gastric bypass. In the same way, patients with contraindications for undergoing LSG (gastroesophageal reflux) were also sent to the referral hospital.

Surgical Technique

A 50-French bougie was used to calibrate the sleeve. Longitudinal resection was performed from 3–4 cm orally to the pylorus up to the angle of His.

Follow-up

All the patients were followed up by the surgeon and the endocrinologist 1, 3, 6, 12, 18, and 24 months after surgery, and later on yearly. Median follow-up of the patients was 33 months (range 12–54 months), including results from follow-up longer than 2 years when available. Data of all the patients (42) were available at 12 months follow-up, data of 30 patients (71.4 %) were available at 24 months follow-up.

During the follow-up, routine blood analysis were performed in the 3rd, 6th, 12th, 18th, and 24th postoperative months, including measurements of calcium, vitamin D, PTH, liver enzymes, glucose parameters, creatinine, thyroid-stimulating hormone (TSH) and proteins.

After surgery, vitamin D supplements were not prescribed. Patients were encouraged to play sports or to do outdoor activities in all seasons.

Bone Densitometry

Bose densitometry was performed using a LUNAR iDXA (GE Healthcare, USA). Densitometer performed a dual-energy X-ray absorptiometry. The programs OneScan^{TM}, Composer^{TM} and Connectivity^{TM} , belonging to the Prodigy^{TM} system were used for the computer processing. Lumbar spine (L1–L4) BMD was measured.

t score is defined as the number of standard deviations above or below the mean for a healthy 30-year-old adult of the same sex and ethnicity as the patient. *z* score is defined as the number of standard deviations above or below the mean for the patient’s age, sex, and ethnicity.

Biochemical Parameters

25-OH-D3 (vitamin D) was measured with isotope- dilution liquid chromatography–tandem mass spectrometry (Sigma-Aldrich, TM). Intact PTH was determined by Elecsys 2010 analyzer (Roche Diagnostics GmbH).

Variables

Body size measurements (body weight, BMI, weight loss, percent of excess weight loss), blood tests variables (calcium, vitamin D (25-OH-D3), intact PTH, liver enzymes, creatinine, TSH, and total proteins) and densitometric values (BMD, *t* score and *z* score) were investigated.

Statistical Analysis

All statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL). Results are expressed as mean+standard deviation or number and percentages. Paired

Student's *t* tests and ANOVA with repeated measures were used to compare baseline data and at follow-up. Correlation between quantitative variables was performed using Pearson test or Spearman application when at least one of the variables did follow a Gaussian distribution. A *p* value<0.05 was considered statistically significant.

All quantitative variables, except PTH, followed a Gaussian distribution. Therefore, all the analyses with variable PTH were performed with nonparametric tests.

Results

Baseline and 1-year postoperative data are obtained from 42 patients, while 2 years postoperative data were available only from 30 patients. Mean excessive BMI loss was 79.9 % after 1 year and 80.6 % after 2 years. The periodical BMI loss is summarized in Table 1.

Bone Mineral Changes

Mean BMD values, *t* score and *z* score for spine increased progressively, reaching statistical significance at 1 and at 2 years. Mean values obtained in the second year examination showed a significant increase in all the body mineral parameters, when compared with the baseline values and with those obtained in the examination performed the first postoperative year. Percentage of BMD increase was 5.7+0.5 % at 1 year and 7.9+1.4 % at 2 years. Densitometric data are presented in Table 2 and Fig. 1.

Changes in the Calcium Metabolism and Nutritional Status

Prevalence of Preoperative Deficiencies

Before surgery, 95 % of the patients presented vitamin D deficiency (normal range 30–100 ng/ml), 43 % had elevated PTH (normal range 11.7–63.3 pg/ml) and 3 % hypoalbuminemia (normal range 3.5–5 g/dl), 3 % folic acid deficiency. Calcium, phosphate, creatinine, TSH, alkaline phosphatase, and liver enzymes (AST and ALT) were within normal range.

Table 1 Evolution of weight loss during the follow-up

	Preoperative (42 patients)	1 year post (42 patients)	2 years post (30 patients)
Weight (kg)	117+19.6	71.7+9.7	69.2+9.5
BMI (kg/m^2)	51.2+6.7	27.7+2.1	27+2.1
Excesso of weight (kg)	57.7+15.1	11.9+7.7	9.4+7.9
Weight loss (kg)	–	45.5+6.6	43.6+6.8
Percentage of excess weight loss (%)	–	79.9+10.2	80.6+9.9

Prevalence of Postoperative Deficiencies

One year after surgery, only one patient (2.4 %) presented vitamin D deficiency and had elevated PTH. The rest of investigated values were within normal range. The second year after surgery, the results remain similar. Changes in analytical values are described in Table 3.

Vitamin D showed a significant increase, when comparing pre and postoperative values (increase of 25.9 ng/dl, CI 95 % (22.9–28.9); $p<0.001$ at 1 year follow-up, and increase of 33.2 ng/dl, CI 95 % (28.2–38.2); $p<0.001$ at 2 years follow-up). Seasonal changes in vitamin D levels could not be established, because of their progressive increase in the postoperative course.

In the same way, PTH values presented a significant decrease when comparing pre and postoperative levels (decrease of 31.1 pg/ml, CI 95 % (18.5–43.7); $p=0.03$ at 1 year follow-up, and decrease of 32.2 pg/ml, CI 95 % (19.1–45.3); $p<0.001$ at 2 years follow-up) (Fig. 2).

Correlation of Densitometric Values with Weight Loss

A significant correlation could not be observed between weight loss and BMD, *t* score and *z* score.

Correlation between Densitometric and Blood Tests Parameters

An inverse correlation was observed between BMD increase and PTH decrease 1 year after surgery (Pearson −0.899; $p=0.003$) and 2 years after surgery (Pearson −0.917; $p=0.02$). A direct correlation could also be established between BMD and vitamin D increases at 1 year (Pearson 0.763; $p=0.021$) and 2 years postoperatively (Pearson 0.698; $p=0.048$).

t score and *z* score values did not show any significant correlation with vitamin D or PTH.

Discussion

Up to our knowledge, this is the third study reporting changes in BMD in patients after LSG and the one with bigger sample size. Moreover, we simultaneously compare BMD, nutritional components and markers of bone metabolism. The two previously mentioned reports were a small study also conducted in

Table 2 Densitometric variables at baseline and after 1 and 2 years

	Baseline (42 patients) Mean	After 1 year (42 patients) Mean	After 2 years (30 patients)			
			p value vs baseline examination	Mean	*p* value vs baseline examination	*p* value vs examination after 1 year
BMD (g/cm^2)	1.18+0.09	1.24+0.08	0.003	1.27+0.09	0.001	0.012
t score	1.1+0.6	1.2+0.6	0.008	1.2+0.7	0.006	0.026
z score	1.2+1	1.2+0.9	0.02	1.3+1	0.012	0.032

BMD bone mineral density

Spain, including 15 women, and a Czech report including 29 patients. The Spanish series analyzed 15 women, comparing the results of 8 patients who underwent LSG versus 7 undergoing RYGBP. They observe a significant BMD decrease in both groups, without differences between them [14]. The Czech study included 29 patients, all of them undergoing LSG. They also report a decline in BMD parallel to body weight reduction. In contrast to these studies, our patients showed a significant increase in BMD. One of the main differences between our series and the other two studies is that BMD measurement was done in the lumbar spine (L1–L4) in our series, while the measurement was performed in spine and proximal femur. Both reports describe a more pronounced decrease in BMD in femur than in spine, revealing that femur seems to be a more sensible location for BMD changes. Several studies analyzing BMD changes after RYGBP confirm that average decrease of BMD is significantly higher in lumbar spine determinations than in proximal femur [7, 15]. Fleischer et al. [16] even reported a decrease of 9.2 % in the femoral neck, but did not observe any changes in lumbar spine. A potential explanation for why densitometers detect different BMD in the lumbar spine and in proximal femur is that they are unable to accurately measure changes in adipose tissue density and distribution following bariatric surgery [17]. Though the lack of BMD measurements in proximal femur in our patients is a limitation of our study, we are the first ones describing an increase in BMD in the lumbar spine in up to a 7.9 % 2 years after surgery. As this is a retrospective study, BMD data were obtained from lumbar densitometry, thus this is the analysis that is routinely performed at our institution.

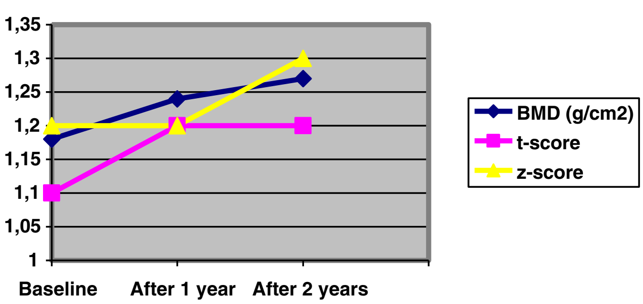


Fig. 1 Changes in densitometric parameters

Most studies have reported an association between weight loss and decrease in BMD, showing a more pronounced BMD reduction in those patients with greater weight loss [8, 14, 16]. However, some authors have reported that this association is valid with proximal femur measurements, but not for those values obtain from lumbar spine [18]. We confirm this affirmation, as we could not demonstrate this association in our series, but the measurements were performed in lumbar spine.

To adequately evaluate bone metabolism after surgery, it is essential to analyze serum vitamin D, PTH, calcium, and phosphate levels. These parameters are crucial for BMD maintenance in periods of weight loss and catabolic state. Some morbidly obese patients present preoperative nutrient deficiencies, secondary to their alimentary disorders. However, it has been widely described that the prevalence of abnormalities 1 year after surgery is usually higher [19–21], mostly associated with a decrease in food intake and with the anatomical changes in the gastrointestinal tract, presenting malabsorptive procedures the highest risk [21, 22]. Therefore, given the reduction of calcium absorption, the organism starts bone resorption to maintain serum calcium within normal range. This bone resorption is mediated by PTH, thus PTH levels increase in the postoperative course [7]. Notwithstanding, 95 % of our patients presented preoperative deficiencies of vitamin D and 43 % elevated levels of PTH. After surgery, vitamin D and PTH levels normalize in all the cases but one. Vitamin D deficiency in morbidly obese patients ranges from 33 to 80 % [19, 23–25], while secondary hyperparathyroidism appears in around 48 % of cases preoperatively [25, 26]. Malnutrition secondary to food restrictions may justify this, but a lower sunlight exposure can also be involved. The latter is secondary to little or complete absence of physical activity; psychological lability leads these patients to a tendency of living indoors [19]. Moreover, adipose tissue is a pool of vitamin D. It is taken up from the intestinal absorption or the cutaneous synthesis and released at times when production is reduced, as occurs in winter [27, 28]. We have demonstrated a direct

Table 3 Changes in analytical values

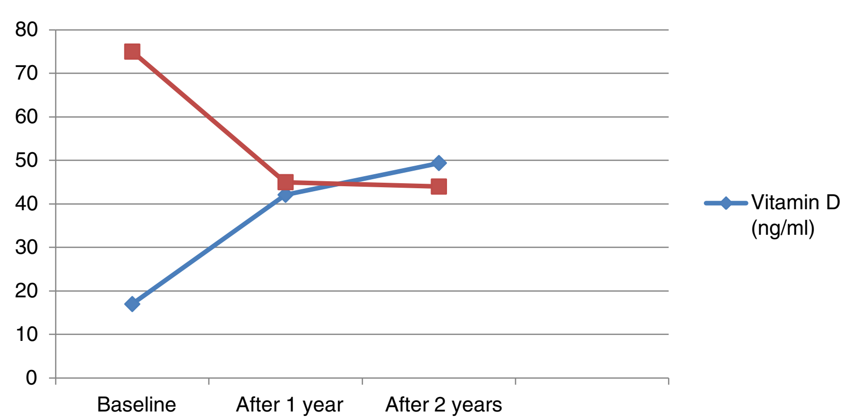
	Baseline (42 patients)	After 1 year (42 patients)	After 2 years (30 patients)	*p*	Normal range
Calcium (mg/dl)	9.4+0.4	9.5+0.5	9.6+0.4	NS	8.4–10.2
Vitamin D (ng/ml)	17.4+8	42.1+10.2	49.4+14.4	<0.001	30–100
PTH (pg/ml)	75.3+20.8	45.7+10.5	44.6+10.6	0.003	11.7–63.3
Phosphate (mg/dl)	3.5+0.5	3.6+0.5	3.5+0.5	NS	2.5–4.5
Total proteins (g/dl)	7.2+0.2	7+0.2	6.9+0.2	NS	6.3–8.2
Albumin (g/dl)	3.9+0.3	4.1+0.3	4.1+0.4	NS	3.5–5
Alkaline phosphatase (U/L)	80.6+19.9	82.1+16.7	72.8+16	NS	38–126
AST (U/L)	26.2+9.2	21.2+6.1	18.5+5.6	NS	14–36
ALT (U/L)	35.2+13.9	20.4+7.9	19.1+8.4	NS	9–52
Creatinine (mg/dl)	0.8+0.2	0.8+0.1	0.8+0.1	NS	0.52–1.04
TSH (pg/ml)	2.1+1.2	1.9+1.1	2.6+1.1	NS	0.47–4.68

NS not significant

correlation between BMD and vitamin D increase and an inverse correlation between BMD increase and PTH decrease. Probably, the preoperatively low vitamin D levels led to a secondary hyperparathyroidism that started bone resorption. With the weight loss, the vitamin D sequestrated in the adipose tissue is freed and enters bloodstream, increasing their serum levels. At this moment, vitamin D increases the intestinal absorption of calcium, stopping bone resorption as source of calcium. Moreover, with enough serum calcium and vitamin D availability, calcium can be targeted to the bone to restore the original BMD. In our results, we have observed that a significant increase in vitamin D and decrease in PTH levels appeared after 1 year and these levels are maintained after 2 years. However, BMD showed a significant but mild increase after 1 year, but a higher increase after 2 years. This probably reflects that during the first postoperative year, the main goal of the organism is to normalize serum vitamin D values. Once they reach the normal range the goal is to restore BMD before bone resorption.

A seasonal variation in serum vitamin D has been widely described, especially at higher latitudes, with maximum levels in summer months and correlating with the number of hours spent outside [29]. In our study, we could not determine this seasonal variation, because after surgery vitamin D levels showed a progressive increase, so that any possible seasonal change has been masked. Anyway, as this study has been conducted in Spain, a region with high sunlight exposure, and the patients were stimulated to perform outdoor activities, seasonal changes would not have been as relevant as in other latitudes. Based on this hypothesis, we have also justified in our previous report [23] the postoperative increase of vitamin D levels, in contrast to other studies, conducted in Northern Europe or North America, regions with lower sunlight exposure, that reported a reduction [19]. Moreover, this could be also an explanation why we report an increase of postoperative BMD, while the Czech study described a reduction [18]. Notwithstanding, the other previous study performed on patients undergoing LSG, was also performed in Spain, but this study described only eight patients [14]. Anyway, our sample size of 42 patients is also relatively small, also limiting the reliability of the findings. So, future studies with a higher number of patients should be conducted to confirm our results.

Fig. 2 Changes in vitamin D and PTH values



Conclusion

Bone mineral density measure in the lumbar spine showed a progressive increase during the first and second year after sleeve gastrectomy. BMD changes are not associated with weight loss, but showed a direct correlation with vitamin D and an inverse correlation with PTH levels.

References

1. Rockholm B, Baker JL, Sorensen TI. The leveling off of the obesity epidemic since the year 1999—a review of evidence and perspectives. Obes Rev. 2010;11:835–46.
2. Flegal KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. 2010;11:835–46.
3. Encuesta Europea de Salud en España 2009. Instituto Nacional de Estadística. INEbase. http://www.ine.es/jaxi/menu.do?type=pcaxis&path=/t15/p420&file=inebase&L=0
4. Colquitt JL, Picot J, Loveman E, et al. Surgery for obesity. Cochrane Database Syst Rev 2009;CD 003641.
5. Ruiz-Tovar J, Oller I, Tomas A, et al. Midterm impacto f sleeve gastrectomy, calibrated with a 50-Fr bougie, on weight loss, glucose hemostasis, lípido profiles and comorbidities in morbidly obese patients. Am Surg. 2012;78:969–74.
6. Wucher H, Ciangura C, Poitou C, et al. Effects of weight loss on bone status after bariatric surgery: association between adipokines and bone markers. Obes Surg. 2008;18:58–65.
7. Schaan Casagrande D, Repetto G, Cora Mottin C, et al. Changes in bone mineral density in women following 1-year gastric bypass surgery. Obes Surg. 2012;22:1287–92.
8. Vilarrasa N, San Jose P, Garcia I, et al. Evaluation of bone mineral density loss in morbidly obese women after gastric bypass: 3-year follow-up. Obes Surg. 2011;21:465–72.
9. Mahdy T, Atia S, Farid M, et al. Effect of Roux-en-Y gastric bypass on bone metabolism in patients with morbid obesity: Mansoura experiences. Obes Surg. 2008;18:1526–31.
10. Balsa JA, Botella-Carretero JI, Peromingo R, et al. Chronic increase of bone turnover markers after biliopancreatic diversion is related to secondary hyperparathyroidism and weight loss. Relation with bone mineral density. Obes Surg. 2010;20:468–73.
11. Tsiftsis DD, Mylonas P, Mead N, et al. Bone mass decreases in morbidly obese women after long limb-biliopancreatic diversion and marked weight loss without secondary hyperparathyroidism. A physiological adaptation to weight loss? Obes Surg. 2009;19:1497–503.
12. Bronner F. Recent developments in intestinal calcium absorption. Nutr Rev. 2009;67:109–13.
13. Christakos S. Recent advances in our understanding of 1,25-dihydroxyvitamin D(3) regulation of intestinal calcium absorption. Arch Biochem Biophys. 2012;523:73–6.
14. Nogués X, Goday A, Peña MJ, et al. Pérdida de masa ósea tras gastrectomía tubular: Estudio prospectivo comparativo con el bypass gástrico. Cir Esp. 2010;88:103–9.
15. Vilarrasa N, Gómez JM, Elio I, et al. Evaluation of bone disease in morbidly obese women after gastric bypass and risk factors implicated in bone loss. Obes Surg. 2009;19:860–6.
16. Fleischer J, et al. The decline in hip bone density after gastric bypass surgery is associated with extent of weight loss. J Clin Endocrinol Metab. 2008;93:3735–40.
17. Tothill P. Dual-energy X-ray absorptiometry measurements of total body bone mineral during weight change. J Clin Densitom. 2005;8:31–8.
18. Pluskiewicz W, Buzga M, Holeczy P, et al. Bone mineral changes in spine and proximal femur in individual obese women after laparoscopic sleeve gastrectomy: a short-term study. Obes Surg. 2012;22:1068–76.
19. Gehrer S, Kern B, Peters T, et al. Fewer nutrient deficiencies after laparoscopic sleeve gastrectomy than after laparoscopic Roux-Y-Gastric bypass—a prospective study. Obes Surg. 2010;20:447–53.
20. Malinowski SS. Nutritional and metabolic complications of bariatric surgery. Am J Med Sci. 2006;331:219–25.
21. Toh SY, Zarshenas N, Jorgensen J. Prevalence of nutrient deficiencies in bariatric patients. Nutrition. 2009;25:1150–6.
22. Davies DJ, Baxter JM, Baxter JN. Nutritional deficiencies after bariatric surgery. Obes Surg. 2007;17:1150–8.
23. Ruiz-Tovar J, Oller I, Tomás A, et al. Mid-term effects of sleeve gastrectomy on calcium metabolism parameters, vitamin D and Parathormone (PTH) in morbid obese women. Obes Surg. 2012;22:797–801.
24. Ybarra J, Sánchez-Hernández J, Gich I, et al. Unchanged hypovitaminosis D and secondary hyperparathyroidism in morbid obesity after bariatric surgery. Obes Surg. 2005;15:330–5.
25. Carlin AM, Rao DS, Yager KM, et al. Effect of gastric bypass surgery on vitamin D nutritional status. Surg Obes Relat Dis. 2006;2:638–42.
26. Carlin AM, Rao DS, Meslemani AM, et al. Prevalence of vitamin D depletion among morbidly obese patients seeking gastric bypass surgery. Surg Obes Relat Dis. 2006;2:98–103.
27. Tsiaras WG, Weinstock MA. Factors influencing vitamin D status. Acta Derm Venereol. 2011;91:115–24.
28. Blum M, Dolnikowski G, Seyoum E, et al. Vitamin D(3) in fat tissue. Endocrine. 2008;33:90–4.
29. Bird ML, Hill KD, Robertson IK, et al. Serum [25(OH)D] status, ankle strength and activity show seasonal variation in older adults: relevance for winter falls in higher latitudes. Age Ageing 2012; PMID: 22585931.