National Osteoporosis Foundation

Fall 2007

OSTEOPOROSIS

CLINICAL UPDATES

Osteoporosis: Clinical Updates is published by the National Osteoporosis Foundation (NOF).

BARIATRIC SURGERY AND OSTEOPOROSIS

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Obesity is a public health issue of major proportions, ranked the number-one threat to American health by the CDC in 2004. Results from the 2003-2004 National Health and Nutrition Examination Survey (NHANES) estimated that 32.2% of U.S. adults were obese (BMI of 30 or higher.)[1] In addition, obesity rates are increasing. According to a RAND survey of weight data, the prevalence of obesity (self-reported BMI over 30) was estimated to have risen 24% between 2000 and 2005. Even worse, the rate of clinically severe, or morbid, obesity (self-reported BMI of 50 or above) was found to have risen three times faster, at a rate of 75% in that time.[2]

Weight loss from diet and exercise alone are not adequate to reduce weight to healthy levels in many people. As a result, there has been a marked increase in bariatric surgery procedures in the U.S. over the past decade. Recent data indicate that the number of bariatric surgeries performed in the U.S. rose from 13,365 in 1998 to an estimated 140,000 procedures in 2004.[3]

Advances in bariatric surgery have addressed many of the more serious issues of malabsorption associated with early techniques. However, the long-term consequences of bariatric surgery on bone metabolism are just now coming into focus.

In this issue of Osteoporosis: Clinical Updates, we will take a look at contemporary bariatric surgical techniques and research on their effects on bone health, both in the short and longer term.

CASE STUDY: 50-YEAR-OLD WOMAN WHO HAD ROUX-EN-Y GASTRIC BYPASS SURGERY

The patient we will discuss is a 50-year-old woman who presents requesting an evaluation for osteopososis and need for further treatment. The patient reports having had weight-control issues beginning in her teens and progressing (with intermittent weight-loss success) to a peak at age 49 of 207 lbs — height 5'2", BMI >42. In August 2006, she underwent Roux-en-Y gastric bypass (RYGB) surgery. Over the year that followed, she lost 100 pounds and is currently at 106 pounds.

The patient's history includes two ankle fractures in her 20s and 30s with minimal trauma (casted). She shows no evidence of height loss. Her BMD spine T-score was measured at -1.9 in December, 2003. She was started on alendronate in early 2004. She experienced a natural menopause at age 46, has received no hormone therapy, and has reported no menopausal symptoms. The patient was diagnosed with hypothyroidism in 2004 and started on thyroxine at 210 µg/day, decreasing to a current dose of 60 µg/day.

Measuring BMD in Bariatric Surgery Patients

Measuring BMD in patients over 250 lbs is complicated by weight limitations of common DXA machines in use, which range from 250 to 350 pounds. New machines that can accommodate people up to 400 pounds have recently been introduced, but are available in few locations.

In addition to machine size/weight limitations, BMD measurement in patients during weight change is further complicated by anomalies in BMD measurements associated with variables such as fat density and distribution and the DXA software used.[12]

One study tested a wide range of DXA machines and found that all showed some degree of inconsistency in measuring total-body BMC and BMD measurements in individuals undergoing weight loss. As a result, the study's authors recommended that total-body BMD measurements during weight change "be treated with suspicion."[3]

Standard central DXA can be used to measure forearm BMD in patients too heavy for full-body scans.

In addition, peripheral BMD measurement can also be used for measuring bone density in patients over 400 pounds. Measurement at the forearm, heel, and finger is commonly performed using peripheral bone density techniques that include:

- pDXA (Peripheral dual-energy x-ray absorptiometry) measures the forearm, heel or finger
- QUS (Quantitative ultrasound) uses sound waves to measure density at the heel, shin bone, and kneecap
- pQCT (Peripheral quantitative computed tomography) measures the forearm

Peripheral DXA measurements at the phalanges and proximal/distal forearm have been shown in studies to correlate 75-90% to BMD measurements at the spine and hip by central DXA.[4] Peripheral QUS appears to be less closely correlated to hip and spine BMD by DXA. All types of peripheral BMD measurement techniques are appropriate for screening and fracture risk predictions, but are not the gold standard for diagnosis and moni-

On alendronate, the patient's spine BMD T-score was -2.2 in January 2007, and -2.8 in June 2007. (This is starting from a baseline spine at -1.9 in 12/03.) The patient has a positive family history for osteoporosis: her mother was diagnosed after suffering multiple rib fractures.

Given the patient's history, what can be done to improve her bone health?

First, the patient should be evaluated for adequate calcium and vitamin D intake. At the outset, the patient reported taking daily multivitamins with calcium and 600 IU vitamin D. Her initial labs were 25-hydroxyvitamin D_3 low at 16, PTH a little high at 72 (normal is 65), and TSH normal (on thyroid replacement therapy). To improve her serum profile, the patient's vitamin D_3 intake is increased to 2000 IU/day. The result is that her 25-hydroxyvitamin D_3 increases to an adequate 31, and her PTH decreases to 54.

How should the patient be followed?

The patient will be followed indefinitely for changes in BMD and serum calcium, PTH, and 25-hydroxyvitamin D_3 levels. She will have repeat BMD measurement periodically as well as biannual or annual serum calcium, 25-hydroxyvitamin D_3, and PTH assessment, with supplementation as needed to maintain healthy levels. In addition, the patient will be monitored for back pain, height loss, or postural changes, which may indicate compression deformities. The patient's response to alendronate therapy will be monitored through periodic measurement of urine NTX or serum CTX (since absorption may be impaired). Problems might crop up in the patient's later years, so she should be monitored for the rest of her life.

BARIATRIC SURGERY: IMPLICATIONS FOR BONE HEALTH AND FRACTURE RISK

Weight loss itself — both surgically induced through gastric bypass or banding procedures and nonsurgical weight loss — has been associated with an increased risk of osteoporosis, perhaps due to reduced serum hormone levels and reduced beneficial mechanical impact of excess weight on bone.

The effects of diet-induced weight loss on bone mass have been documented by multiple studies.[4-8] Data from these studies suggest that diet-induced weight loss is associated with decreased bone mass. Increased fractures as a result of weight loss have been documented, but primarily in middle-aged and older Caucasian women.[9-11] Although similar findings have been reported following bariatric surgery, there is little research addressing the effects of surgically induced weight loss on bone metabolism.

The two most frequently performed types of bariatric surgery are the Roux-en-Y gastric bypass (RYGB) and laparoscopic adjustable gastric banding (LAGB). The LAGB is a restrictive procedure, whereas the RYGB is both a restrictive and malabsorptive procedure. Strictly malabsorptive operations (also called intestinal bypasses) such as duodenal switch, biliopancreatic diversion, isolated intestinal bypass, and gastrectomy are no longer recommended for weight loss because they result in severe nutritional deficiencies and increased morbidity and mortality.

Roux-en-Y Gastric Bypass (RYGB)

The most commonly performed bariatric procedure is Roux-en-Y gastric bypass. The RYGB is called a combined bariatric procedure, because it

restricts both food intake and the calories absorbed by the body.

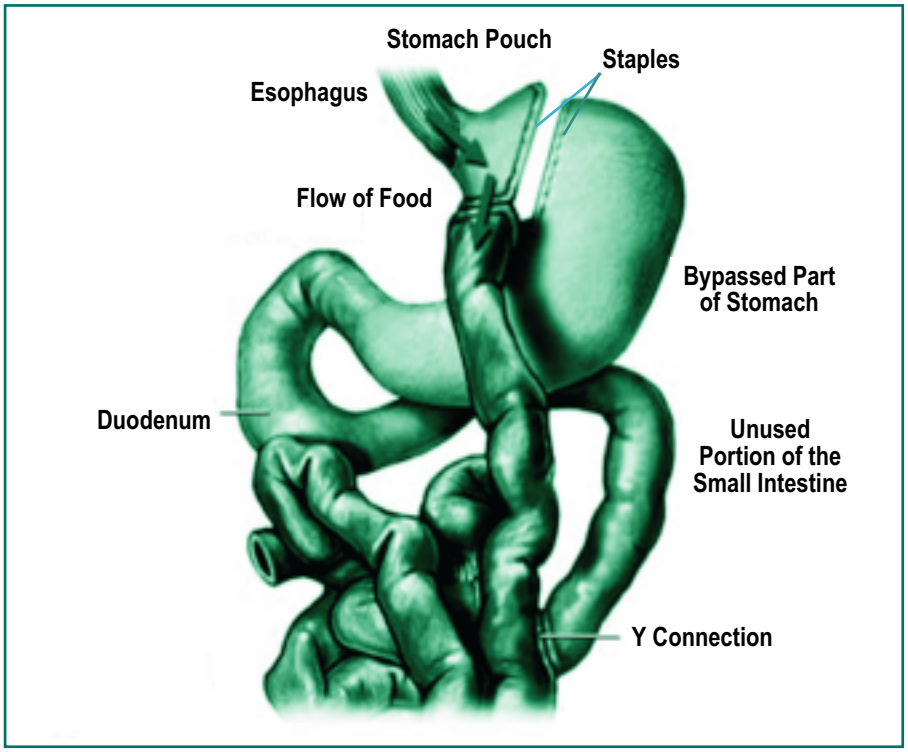
The surgery is performed by creating a small pouch at the opening of the stomach, restricting food intake. Next, a Y-shaped section of the small intestine is attached to the pouch, allowing food to bypass the lower stomach, the duodenum, and the first portion of the jejunum, reducing absorption of calories and nutrients.

Patients who undergo RYGB surgery experience dramatic and sustained weight loss due to decreased food intake as result of dramatically reduced gastric volume. Contemporary data suggests that RYGB yields up to 70% excess body weight loss. This loss is often maintained for 10-14 years postoperatively.[12,13]

However, the metabolic effects of RYGB are similar to Billroth II Subtotal Gastrectomy. These include changes in intestinal hormone secretion. This may be due to rapid transit of nutrients into the intestine. In humans and animal models, RYGB surgery has induced increased secretion of satiety and anorectic GI hormones (Ghrelin and adiponectin, glucagon-like peptide-1 and peptide YY), as well as decreased secretion of insulin and leptin.[14,15] Because RYGB bypasses the duodenum, which is the primary location for the absorption of calcium, calcium malabsorption has long been recognized as a risk for RYGB patients, although research addressing this problem is limited.

RYGB surgery can be performed laparoscopically. The advantages of laparoscopic surgery over traditional abdominal surgery are many, including lower blood loss, faster recovery, and lower risk of hernia.[16]

RYGB: Metabolic Effects. Several prospective studies have investigated the metabolic effects of RYGB. One prospective study of 25 women found that following RYGB calcium absorption declined 24%-36%, with



The Roux-en-Y gastric bypass procedure creates a stomach pouch out of a small portion of the stomach and attaches it directly to the small intestine, bypassing a large part of the stomach and duodenum.

Graphic Source: Google Images: US National Library of Medicine. National Institutes of Health. MedlinePlus. Accessed online 9/2007http://www.nlm.nih.gov/medlineplus/ency/imagepages/19268.htm. Captions added.

toring of treatment in patients with osteoporosis.

References

1. Tothill P. Dual-energy x-ray absorptiometry measurements of total-body bone mineral during weight change. *J Clin Densitom.* 2005 Spring;8(1):31-8.
2. Blake GM, Herd RJ, Patel R, Fogelman I. The effect of weight change on total body dual-energy X-ray absorptiometry: results from a clinical trial. *Osteoporos Int.* 2000;11(10):832-9.
3. Tothill P, Laskey MA, Orphanidou CI, van Wijk M. Anomalies in dual energy X-ray absorptiometry measurements of total-body bone mineral during weight change using Lunar, Hologic and Norland instruments. *Br J Radiol.* 1999 Jul;72(859):661-9.
4. Picard D, Brown JP, Rosenthall L, et. al. Ability of peripheral DXA measurement to diagnose osteoporosis as assessed by central DXA measurement. *J Clin Densitom.* 2004 Spring;7(1):111-8.

References

1 Ogden CL, Carroll MD, Curtin LR, McDowell MA, et. al. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA.* 2006;295 (13):1549-55.

2 Sturm R. Increases in morbid obesity in the USA: 2000-2005. *Public Health.* 2007;121(7):492-6.

3 Maggard MA, Shugarman LR, Suttorp M., et al. Meta-analysis: surgical treatment of obesity. *Ann Intern Med.* 2005;142(7):547-559.

4 Chao D, Espeland MA, Farmer D, Register TC, Lenchik L, Applegate WB, Ettinger BH, Jr. Effect of voluntary weight loss on bone mineral density in older overweight women. *J Am Geriatr Soc.* 2000;48(7):753-759.

5 Gossain VV, Rao DS, Carella MJ, Divine G. Rovner DR. Bone mineral density (BMD) in obesity effect of weight loss. *J Med.* 1999;30(5-6):367-76.

6 Jensen LB, Kollerup G, Quaade F, Sorensen OH. Bone mineral changes in obese women during a moderate weight loss with and without calcium supplementation. *J Bone Miner Res.* 2001;16 (1):141-7.

7 Shapses SA, Von Thun NL, Heymsfield SB, et al. Bone turnover and density in obese premenopausal women during moderate weight loss and calcium supplementation. *J Bone Miner Res.* 2001;16(7):1329-36.

8 Svendsen OL, Hendel HW, Gotfredsen A, Pedersen BH, Andersen T. Are soft tissue composition of bone and non-bone pixels in spinal bone mineral measurements by DXA similar? Impact of weight loss. *Clin Physiol Funct Imaging.* 2002;22(1):72-7.

9 Ensrud KE, Ewing SK, Stone KL, Cauley JA, Bowman PJ, Cummings SR; Study of Osteoporotic Fractures

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Research Group. Intentional and unintentional weight loss increase bone loss and hip fracture risk in older women. J *Am Geriatr Soc.* 2003;51(12):1740-7.
10 Langlois JA, Mussolino ME, Visser M, Looker AC, Harris T, Madans J. Weight loss from maximum body weight among middle-aged and older white women and the risk of hip fracture: the NHANES I epidemiologic follow-up study. *Osteoporos Int.* 2001;12 (9):763-8.
xi Meyer HE, Tverdal A, Selmer R. Weight variability, weight change and the incidence of hip fracture: a prospective study of 39,000 middle-aged Norwegians. *Osteoporos Int.* 1998;8(4):373-8.
12 Brolin RE. Bariatric surgery and long-term control of morbid obesity. *JAMA.* 2002;288(22):2793-6. Review.
13 Pories WJ, Swanson MS, MacDonald KG, Long SB, et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg.* 1995;222(3):339-50; discussion 350-2.
14 Holdstock C, Engstrom BE, Ohrvall M, et.al. Ghrelin and adipose tissue regulatory peptides: effect of gastric bypass surgery in obese humans. *J Clin Endocrinol Metab.* 2003;88(7):3177-83.
15 Strader AD, Vahl TP, Jandacek RJ, Woods SC, D'Alessio DA, Seeley RJ. Weight loss through ileal transposition is accompanied by increased ileal hormone secretion and synthesis in rats. *Am J Physiol Endocrinol Metab.* 2005;288(2):E447-53.
16 Nguyen NT, Goldman C, Rosenquist CJ, Arango A, Cole CJ, Lee SJ, Wolfe BM. Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. *Ann Surg.* 2001;234(3):279-89.
17 Riedt SC, Brolin RE, Sherrell RM, et.al. True fractional calcium absorption is decreased after Roux-en-Y gastric bypass surgery. *Obesity (Silver Spring).* 2006;14(11):1940-8.
18 Diniz MF, Diniz MT, Sanches SR, et.al. Elevated serum parathormone after Roux-en-Y gastric bypass. *Obes Surg.* 2004;14(9):1222-6.
19 El-Kadre LJ, Rocha PR, de Almeida Tinoco AC,Tinoco RC. Calcium metabolism in pre- and postmenopausal morbidly obese women at baseline and after laparoscopic Roux-en-Y gastric bypass. *Obes Surg.* 2004;14(8):1062-6.
20 Coates PS, Fernstrom JD, Fernstrom MH, Schauer PR, Greenspan SL. Gastric bypass surgery for morbid obesity leads to an increase in bone turnover and a decrease in bone mass. *J Clin Endocrinol Metab.* 2004;89(3): 1061-5.
21 Johnson JM, Maher JW, Samuel I, et. al. Effects of gastric bypass procedures on bone mineral density, calcium, parathyroid hormone, and vitamin D. J *Gastrointest Surg.* 2005;9(8):1106-10.
22 Goode LR, Brolin RE, Chowdhury HA, Shapses SA. Bone and gastric bypass surgery: effects of dietary calcium and

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decreased serum estradiol as well.[17] In 110 patients followed in another study, hypocalcemia developed in 1% and elevated PTH was found in 29% of the patients.[18] Another study of 30 premenopausal and 30 postmenopausal women after RYGB surgery, found decreased 25OHD, increased PTH, and increased CTX in both groups.[19] In another study of 25 patients vs 30 controls within 9 months of RYGB procedure, results showed an increase in PTH and a 3-fold increase in NTX.[20]

RYGB: Effects on BMD. Of the bariatric surgeries, the RYGB appears to produce more substantial adverse effects on the skeleton than gastric banding surgery. Postmenopausal women after RYGB bypass have had lower femoral neck and hip BMD. One recent study of 230 subjects collected data on bone mineral density (BMD), calcium, parathyroid hormone, and vitamin D preoperatively and at yearly intervals after gastric bypass procedures. Within 1 year of bypass, total hip BMD had decreased by 4.5%, lumbar spine BMD had decreased by 9.3%, and total forearm BMD had decreased by 0.6 percent. In addition, serum calcium decreased, PTH increased, but 25OHD did not decline. During the second year, BMD at hip and spine did not decline further. Forearm BMD declined an additional 3.6 percent.[21]

A cross-sectional study of 44 patients at least 3 years after bypass vs. 65 controls showed no loss in BMD among premenopausal women following RYGB. The study reported that postmenopausal RYGB women showed evidence of secondary hyperparathyroidism, elevated bone resorption, and patterns of bone loss (reduced femoral neck and higher lumbar spine) similar to other subjects with hyperparathyroidism.[22] No fracture outcomes have been reported to date.

LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING

Vertical banded gastroplasty (VBG) has been in clinical use since 1979 and adjustable gastric banding (AGB) since 1985. Over the years, VBG has been largely replaced by AGB as studies have shown AGB to have more favorable outcomes, in terms of quality of life and lower rates of reintervention and reoperation, with similar weight loss benefits.[23]

Adjustable gastric banding is routinely performed via laparoscopy (LAGB). In a laparoscopic adjustable gastric band procedure (LAGB), a small pouch is created at the top of the stomach through cinching of the stomach by an inflatable band. The pouch holds a very small amount of food, approximately 50 ml. Thus, the new stomach fills quickly and gives the patient a feeling of satiety. In addition, the band slows the flow of food into the digestive tract. The tightness of the band is adjustable through injection of saline via subcutaneous injection port.

The LAGB surgery has been shown to have a faster recovery rate than laproscopic RYGB, is fully reversible, and does not result in the malabsorption syndromes attendant to RYGB and other surgeries that bypass all or portions of the small intestine. However, laparoscopic RYGB has been shown to result in significantly greater weight loss than LAGB, although this difference has been seen to diminish over time.[24]

LAGB Surgery: Metabolic Effects. Prospective studies on post-LAGB patients consistently show normal 25OHD and PTH levels. Several small studies showed no change BMC or BMD in patients after gastric banding.[25,26]Other studies show decreased femoral neck BMD and increased serum CTX (marker of bone resorption).[27,28]

LAGB Surgery: Effects on BMD. We currently have limited knowledge of the short- or long-term skeletal consequences of LAGB surgery. No fracture outcomes have been reported to date. Studies have shown inconsistent effects on BMD, with lesser effects in premenopausal women. However, the predictive power of these studies is limited by many factors, including size, heterogeneity of subject groups, inconsistent lengths of follow-up, differing calcium and vitamin D intakes, and differences in methodology of biochemical and bone density measurements. In addition, effects shown in these studies may reflect intrinsic differences in patient populations.

Compared to RYGB, LAGB surgery has been shown in the limited studies available to have less of an impact on bone. Bone mineral content showed no significant change in the LAGB group (from 3,079 +/- 140 to 3,064 +/- 129 g) and in the control group (from 2,945 +/- 130 to 2,940 +/- 111 g), whereas it decreased from 2,968 +/- 111 to 2,621 +/- 139 g in the RYGB group (P = .005). The effect on BMD appears to be dependent on the magnitude and/or rate of weight loss. No data are available on any bone-preserving interventions.

Recommendations for Patients after Bariatric Surgery

Women and men who have had bariatric surgery should be screened for osteoporosis with bone density testing, and their nutritional status should be evaluated carefully at baseline and regular post-operative intervals. Follow-up should include measurement of 25-hydroxyvitamin D_3 levels and PTH(1-84), especially in those with very low 25OHD (<15 µg/ml).

Patients should be watched carefully for signs of vertebral fracture. To this end, patients should be measured with a stadiometer at baseline and regular post-operative intervals, as well as assessed for vertebral fracture by DXA-based and/or lateral spine radiograph.

Calcium and vitamin D_3 supplementation should be implemented in all bariatric patients. Because vitamin D_3 is a fat-soluable vitamin, it can take more vitamin D_3 to replete morbidly obese patients as well as patients with malabsorption syndromes. Consider slightly higher doses than RDI recommendations: 1500 mg calcium, 2000 IU Vitamin D_3 (cholecalciferol). Ensuring that levels are stable and adequate may require rechecking every three months or so at the initiation of supplementation.

Clinicians need to make sure patients understand how to effectively take calcium and vitamin D_3 supplements. Whereas calcium supplementation needs to be spaced out for absorption (in 500 mg doses), vitamin D_3 does not and can be taken all at once.

Also, consider pharmacologic treatment in patients if BMD is below -1.5 (after calcium and vitamin D_3 have been normalized). It has been hypothesized that because of absorption limitations, patients would have a better response to treatment administered parenterally rather than orally, although no studies have specifically addressed this to date. If severe malabsorption is present, physicians should consider parenteral therapy. In all bariatric patients, regular weight-bearing physical activity should be strongly recommended, to help maintain bone mass, benefit overall health, and aid in achieving and maintaining a healthy weight. Recent data has suggested increased falls in post-operative bariatric surgery patients and perceived distortions in balance.[29] As a result, evaluation of mechanical risks for falls should be addressed and initiation of strategies to prevent skeletal injury emphasized.

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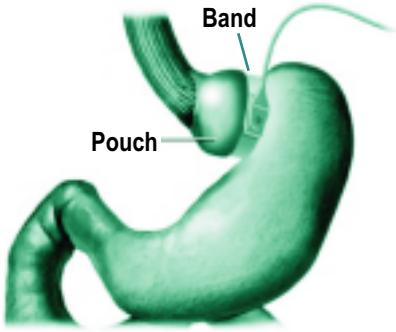

Laparoscopic adjustable gastric banding restricts and decreases food intake and does not interfere with the normal digestive process. The stomach opening can be tightened or loosened over time to adjust the size of the passage.

Graphic Source: US National Library of Medicine. National Institutes of Health. MedlinePlus. Accessed online 9/2007. http://www.nlm.nih.gov/medlineplus/ency/imagepages/19497.htm. Caption added.

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vitamin D. *Obes Res.* 2004;12 (1):40-7.
23 Miller K, Pump A, Hell E. Vertical banded gastroplasty versus adjustable gastric banding: prospective long-term follow-up study. *Surg Obes Relat Dis.* 2007;3(1):84-90.
24 Jan JC, Hong D, Pereira N, Patterson EJ. Laparoscopic adjustable gastric banding versus laparoscopic gastric bypass for morbid obesity: a single-institution comparison study of early results. *J Gastrointest Surg.* 2005;9(1):30-9; discussion 40-1.
25 von Mach MA, Stoeckli R, Bilz S, Kraenzlin M, Langer I, Keller U. Changes in bone mineral content after surgical treatment of morbid obesity. *Metabolism.* 2004;53(7):918-21.
26 Strauss BJ, Marks SJ, Growcott JP, Stroud DB, Lo CS, Dixon JB, O'Brien PE. Body composition changes following laparoscopic gastric banding for morbid obesity. *Acta Diabetol.* 2003;40 Suppl 1:S266-9.
27 Pugnale N, Giusti V, Suter M, et.al.Bone metabolism and risk of secondary hyperparathyroidism 12 months after gastric banding in obese premenopausal women. *Int J Obes Relat Metab Disord.* 2003;27(1):110-6.
28 Giusti V, Gasteyger C, Suter M, et.al. Gastric banding induces negative bone remodelling in the absence of secondary hyperparathyroidism: potential role of serum C telopeptides for follow-up. *Int J Obes (Lond).* 2005;29(12): 1429-35.
29 Berarducci A, Murr MM, Haines K. Risk and incidence of falls and skeletal fragility following Roux-en-Y gastric bypass surgery for morbid obesity. *Osteoporos Int.* 2007;18(S1):201. Abstract.