Changes in Bone Mineral Content After Surgical Treatment of Morbid Obesity

M.-A. von Mach, R. Stoeckli, S. Bilz, M. Kraenzlin, I. Langer, and U. Keller

Weight loss reduces bone mass and increases the risk of osteoporosis. This study was undertaken to assess changes of bone metabolism following Roux-en-Y gastric bypass (RYGB) and adjustable silicone gastric banding (ASGB) as compared to nonoperated controls of morbidly obese subjects. Fourteen female and 5 male patients with a mean (±SEM) age of 44.3 ± 1.8 years participated in the 24-month prospective study. Nine patients underwent ASGB, 4 patients RYGB operation, and 6 patients were included in the control group. Bone metabolism was assessed by determination of serum parathyroid hormone (PTH), osteocalcin, urinary deoxypyridinoline, and dual energy x-ray absorptiometry (DXA) before, and 6, 12, and 24 months after intervention. The body mass index (BMI) decreased from 41.0 ± 1.1 to 34.0 ± 1.4 kg/m^2 in the ASGB group (P = .001), from 42.7 ± 2.2 to 30.5 ± 2.2 kg/m^2 in the RYGB group (P = .006), and remained unchanged in the control group (from 41.2 ± 1.2 to 41.4 ± 1.4 kg/m^2) after 24 months. Bone mineral content (BMC) showed no significant change in the ASGB 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 loss in BMC was accompanied by significant increases in urinary deoxypyridinoline (P < .05) and in serum osteocalcin (P < .01) after RYGB, suggesting both, increased bone resorption and increased bone formation. The authors were aware of the fact that the study groups were small and conclusions need to be regarded as preliminary. However, the RYGB operation resulted in enhanced weight loss and significant net loss of bone mass in comparison to ASGB and obese control subjects. Patients losing large amounts of body weight should be monitored regularly regarding prevention of osteoporosis.

THE PREVALENCE of obesity has been increasing over the past decades with a disproportional increase in morbid obesity.[1-3] The latter is defined by a body mass index (BMI) of more than 40 kg/m^2, or more than 35 kg/m^2 with significant secondary disease and occurs in 2% to 5% of the population of Europe and in the United States.[4,5] Morbid obesity is accompanied by generally recognized health risks as coronary artery disease, hypertension, diabetes, gallstones, breast cancer, degenerative arthritis, obstructive sleep apnea, and obesity hypoventilation syndrome.[6-8] Since conservative treatments do not result in sustained weight loss,[9,10] surgical treatment based on gastric restriction procedures is increasingly recognized as a treatment of choice for morbidly obese patients.[11,12] Among the currently available surgical procedures Roux-en-Y gastric bypass (RYGB) and adjustable silicone gastric banding (ASGB) are most frequently performed.[13-16] In RYGB, the stomach is divided into an upper small pouch and a large lower segment followed by an anastomosis of a Roux-en-Y intestinal configuration with the proximal gastric pouch, resulting in the intended gastric bypass.[8] In ASGB for partitioning of a small proximal gastric pouch a hollow silicone band is positioned around the upper stomach connected to a tube attached to a reservoir in the upper abdomen on the anterior rectus sheath.[17]

Apart from adequate and prolonged weight loss, typical major adverse effects of bariatric surgery include wound infections, prolonged vomiting, diarrhea, electrolyte loss, dislocation of the silicone band in ASGB, and as described by some investigators a reduction of bone mineral density.[18,19] However, many of these studies were not prospective and did not include corresponding control groups.[11] The present study was designed to investigate prospectively changes of bone metabolism in subjects with morbid obesity who underwent RYGB and ASGB as compared to a nonoperated control group during a period of 2 years.

MATERIALS AND METHODS

Nineteen obese patients with a BMI of greater than 37 kg/m^2 gave their written informed consent to participate. The study was approved by the institutional review board of the University of Basel, Switzerland. Six patients (4 women, 2 men; age 49.0 ± 2.9 years; BMI 41.2 ± 1.2 kg/m^2) who attended a diet consultation served as controls. Fourteen patients opting for a surgical intervention underwent physical and psychological examination and were approved for surgical treatment of obesity. After detailed discussion of the individual situation, 9 patients preferred ASGB (6 women, 3 men; age 41.1 ± 2.2 years; BMI 41.0 ± 1.1 kg/m^2) and 4 patients RYGB operation (all women; age 44.5 ± 4.8 years; BMI 42.7 ± 2.2 kg/m^2), respectively. All patients received daily calcium (1 g) and vitamin D (800 U) supplementation[20]) orally in the morning for the entire study period. Body weight was determined before, 3, 6, 12, and 24 months after the respective intervention. Total body bone mineral content (BMC), bone mineral density (BMD), fat mass, and lean tissue mass (LTM) were measured by dual energy x-ray absorptiometry (DXA) using a Lunar Expert densitometer (Lunar, Madison, WI)[21] before, and 6, 12, and 24 months after the intervention. Additionally, serum parathyroid hormone (PTH), osteocalcin, and urinary deoxypyridinoline were determined before, and 3, 6, 12, and 24 months after the intervention as described previously.[22]

Two-way repeated-measures analysis of variance (ANOVA) was used to assess variables over time and to compare the three groups using SigmaStat software.[23] If an interaction was significant, pairwise

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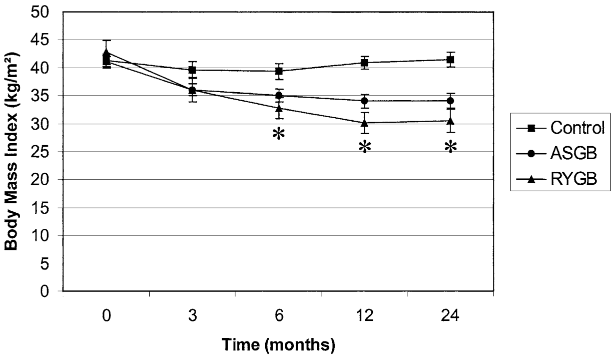

Fig 1. **BMI (kg/m^2) expressed as mean (±SEM) of patients with gastric banding (ASGB, n = 9) or gastric bypass operation (RYGB, n = 4) as compared to a control group (n = 6). *Significant difference of ASGB and RYGB *v* controls ($P < .05$, 2-tailed *t* test).**

comparisons of the different treatment groups were performed using Student's 2-tailed *t*-test or a Mann-Whitney rank sum test. Values were compared before treatment and after 24 months within groups using Student's paired *t*-tests. Data are expressed as means ± SEM.

RESULTS

The BMI decreased from 41.0 to 34.0 kg/m^2 in the ASGB group, decreased from 42.7 to 30.5 kg/m^2 in the RYGB group, and remained almost constant in the control group (from 41.2 to 41.4 kg/m^2) after 24 months (Fig 1). The BMC (Table 1) showed no significant change in the ASGB group (from 3,079 to 3,064 g) and in the control group (from 2,945 to 2,940 g), whereas it decreased from 2,968 to 2,621 g in the RYGB group. BMD (Fig 2) increased in the ASGB group from 1.25 to 1.29 g/m^2, while a decrease from 1.26 to 1.22 g/m^2 was observed in the RYGB group. No significant change was measured in the control group (1.22 to 1.21 g/m^2). The estimated bone area declined from 2,349 to 2,147 cm^2 in the RYGB group, whereas no significant changes were found in the ASGB group (2,454 to 2,368 cm^2) and the control group (2,418 to 2,425 cm^2). Serum PTH showed no significant changes during the observation (ASGB group initially 45.5 ± 5.9 pg/mL and after 24 months 37.5 ± 6.4 pg/mL; RYGB 37.5 ± 7.8 pg/mL and 43.3 ± 13.4 pg/mL; controls 55.1 ± 5.7 pg/mL and 33.3 ± 9.5 pg/mL). For serum osteocalcin and urinary deoxypyridinoline, significant increases could be demonstrated for the RYGB group compared to the other 2 groups (Figs 3 and 4).

DISCUSSION

The present study compared the effect of the two most frequently used surgical techniques for the treatment of morbid obesity on BMC.[24,25] The pronounced weight loss in the RYGB group was accompanied by a significant reduction of BMC as well as of BMD and bone area as compared to the ASGB group, which showed no signs of bone loss despite significant weight loss. As BMD is a calculated variable (BMC divided by bone area) the increase in BMD in the ASGB group was the result of an almost constant BMC in the presence of a slightly decreasing bone area. Therefore, the values of the measured BMC were more reliable than the BMD, as demonstrated previously.[26,27] No significant difference of BMC of the RYGB group was found in comparison to the control group. This could be explained by a slightly lower BMC measured during the investigation in the control group as compared to the ASGB group, resulting in a significant difference compared to the RYGB group. Previous investigators reported on a possible bias of DXA measurements in weight losing subjects that could cause an artificial reduction of BMD.[28] As in the weight-losing ASGB group slightly increased values of BMD could be detected, a simple artifact due to weight loss would be unlikely to explain the reduced values in the RYGB group.

In addition, the significant increases in urinary deoxypyridinoline and in serum osteocalcin in the RYGB group indicated increases in bone resorption and in bone formation, respectively. In the ASGB group a slight nonsignificant increase in the markers of bone metabolism was observed as compared to controls, which might be explained by changes in the bone structure due to reduced biomechanical stress after pronounced weight loss. The biomechanical feedback (mechanostat hypothesis) has been postulated to optimize bone stiffness through a modulation of bone modeling and remodeling.[29] Additionally, in patients losing large amounts of body weight the reduction of fat tissue (>30% in the ASGB and >50% in the RYGB group) has been found to result in reduced leptin levels, which has been demonstrated to increase osteoclast activity by a reduction of osteoprotegrin.[30,31] These findings are supported by epidemiological observations revealing weight loss to be an independent risk factor for osteoporosis.[32] No changes in serum PTH concentrations demonstrated that a secondary hyperparathyroidism, which has been described previously for gastric exclusion surgery, was not induced.[33]

Regarding weight loss, the RYGB procedure revealed slightly better results than ASGB for the study period of 24 months after surgery. Excellent short- and long-term outcomes of RYGB with sustained weight loss and low rates of complications have been reported.[15] ASGB represents a less invasive method and is an effective surgical procedure as compared to conservatively treated control patients.[34,35] However, few long-

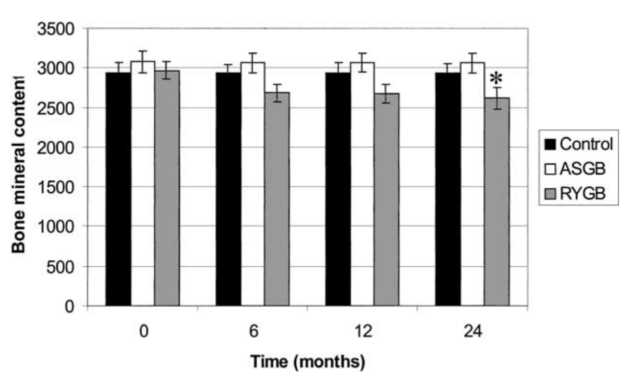

Fig 2. **BMC (mean ± SEM) before, and 6, 12, and 24 months after surgical intervention compared to control subjects with a significant difference after gastric banding (ASGB, n = 9) *v* gastric bypass operation (RYGB, n = 4; *$P = .037$, Mann-Whitney rank sum test).**

Table 1. Changes of Bone Mineral Content and of Fat Mass After Obesity Surgery

	ASGB (n = 9)		RYGB (n = 4)		Control Group (n = 6)	
	Baseline	% Change	Baseline	% Change	Baseline	% Change
Body weight (kg)	117.2 ± 2.5	−16.0 ± 3.2†	113.3 ± 4.9	−28.6 ± 3.6†	113.5 ± 4.9	+0.5 ± 1.2
Total BMC (g)	3,079 ± 140	−0.5 ± 1.8	2,968 ± 111	−11.8 ± 1.7†	2,945 ± 130	−0.2 ± 1.1
Total BMD (g/cm²)	1.25 ± 0.03	+3.0 ± 1.0*	1.26 ± 0.04	−3.5 ± 1.0*	1.22 ± 0.01	−0.4 ± 1.2
Vertebral BMC (g/cm²)	301 ± 15	+0.2 ± 5.1	313 ± 16	−26.3 ± 5.8†	305 ± 17	−5.4 ± 4.3
Vertebral BMD (g/cm²)	1.14 ± 0.05	+4.1 ± 4.5	1.15 ± 0.04	−12.8 ± 3.0*	1.13 ± 0.03	−2.0 ± 2.2
Total bone area (cm²)	2,454 ± 78	−3.5 ± 2.1	2,349 ± 35	−8.6 ± 2.1*	2,418 ± 95	+0.3 ± 0.9
Total fat mass (kg)	63.7 ± 2.2	−33.9 ± 5.3‡	63.6 ± 2.2	−51.0 ± 5.2‡	64.8 ± 4.7	+2.5 ± 3.3
Total LTM (kg)	52.7 ± 2.4	−0.8 ± 1.5	47.2 ± 3.0	−2.0 ± 5.3	47.3 ± 4.3	−3.3 ± 1.9

NOTE. Values are mean ± SEM.
Abbreviations: BMD, bone mineral density; BMC, bone mineral content; LTM, lean tissue mass.
*$P < .05$, †$P < .01$, ‡$P < .001$ (paired *t* test).

term data exist and some investigators reported a progressive loss of efficacy during follow-up,[14] while others found the results acceptable.[32]

Loss of bone mass after RYGB surgery has been discussed controversially in previous studies. While secondary hyperparathyroidism and osteopenia were frequently observed after gastric exclusion and pancreaticobiliary diversion,[33,37] only marginal biochemical evidence of bone loss was found following RYGB.[38]

Although vitamin D deficiency has been well documented following RYGB, hypovitaminosis D was found to be associated with morbid obesity per se and, therefore, may not be caused by surgery.[39] Investigations with moderate energy restriction without bariatric surgery demonstrated an increase in bone resorption in postmenopausal women without vitamin D and calcium supplementation,[40,41] whereas no signs of bone loss were observed in the present ASGB and control group. This might be explained by the daily oral calcium and vitamin D supplementation prescribed to all subjects of the present study. Hence, the continuous reduction in BMD, BMC and bone area after RYGB surgery was associated with an increase in bone resorption, which was only partially compensated by an increase in bone formation despite calcium and vitamin D supplementation.

The authors are aware of the fact that the present study groups were small, and that the changes in bone mass were relatively modest. Therefore, the conclusions need to be regarded as preliminary.

The present findings raise doubt whether weight loss alone accounted for the differences in loss of bone mass and in serum markers between the ASGB and the RYGB groups. The fact that the RYGB group showed only a slightly increased weight loss whereas bone loss was higher compared to the ASGB group suggests that not only reduced biomechanical stress but also additional factors such as diminished absorption of calcium in the duodenum may have played a role.[41]

The present data indicate that bone loss is particularly prevalent in patients after the RYGB procedure, whereas patients with ASGB are expected to maintain their BMC during the first 24 months despite a significant weight loss while receiving calcium and vitamin D supplementation. Nevertheless, patients losing large amounts of body weight should be monitored regarding prevention of osteoporosis.

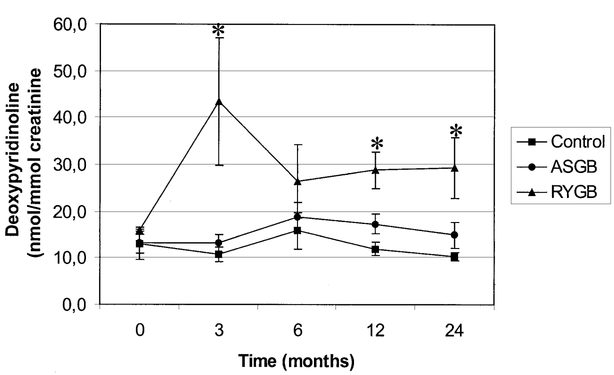

Fig 3. Deoxypyridinoline (nmol/mmol creatinine) given as mean (±SEM) of patients with gastric banding (ASGB, n = 9) or gastric bypass operation (RYGB, n = 4) as compared to a control group (n = 6). *Significant difference of RYGB *v* ASGB and controls (P < .05, 2-tailed *t* test).

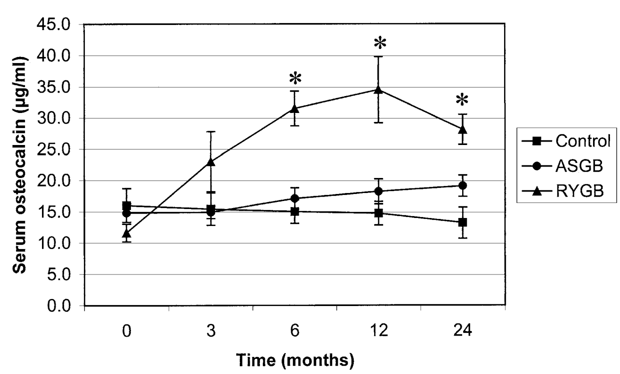

Fig 4. Serum osteocalcin expressed as mean (±SEM) of patients with gastric banding (ASGB, n = 9) or gastric bypass operation (RYGB, n = 4) as compared to a control group (n = 6). *Significant difference of RYGB *v* ASGB and controls (P < .01, 2-tailed *t* test).

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