
Evaluation of Markers for Calcium Homeostasis in a Population of Obese Adults Undergoing Gastric Bypass Operations

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- BACKGROUND:** Gastric bypass operation has become a very common procedure for treatment of obesity. Changes in calcium absorption can result in changes in total body calcium, parathyroid hormone (PTH), and vitamin D levels. There is little known about the longterm effects of Roux-en-Y gastric bypass on calcium metabolism and bone homeostasis.
- STUDY DESIGN:** Between January 2000 and January 2006, 535 morbidly obese patients underwent standard Roux-en-Y gastric bypass. All patients were given a standard multivitamin, vitamin D, and calcium supplement starting on day 12 after the operation. Metabolic parameters, such as serum calcium levels, vitamin D, and PTH, both pre- and postoperatively, were measured and compared at several intervals.
- RESULTS:** Four hundred forty-four patients were followed for a minimum of 2 years. No statistical significance was found between the pre- and postoperative serum levels of calcium and vitamin D, although vitamin D levels generally increased during the first year after operation. Serum levels of PTH were substantially higher at 18 and 44 weeks after the operation.
- CONCLUSIONS:** Hypocalcemia did not develop in any patients during the postoperative period. Increased PTH levels were observed after gastric bypass operation. This can result in mobilization of calcium from the skeleton and increased renal calcium reabsorption. Total body calcium depletion could occur from bone mobilization, if longterm calcium supplementation is not maintained. Vitamin D supplementation can assist in prevention of bone calcium depletion. (J Am Coll Surg 2007;205:294–297. © 2007 by the American College of Surgeons)
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Obesity is a modern problem in almost all countries of the Western world. In the US, the rate of obese (body mass index [calculated as $\text{kg}/\text{m}^2 \geq 30$] adults has doubled, from 15% to 30%, between the years 1976 and 2000.¹⁻³ It is predicted that, if this trend continues, obesity will soon become the greatest cause of preventable and premature death in this country.⁴ At the same time, the number of patients who seek surgical treatment of obesity is increasing as well. Currently, the majority of patients in the US who undergo operations for morbid obesity will have malabsorptive procedures, such as

Roux-en-Y gastric bypass, biliopancreatic diversion, and the biliopancreatic diversion with duodenal switch. Among the surgical procedures for weight loss, Roux-en-Y gastric bypass, either open or laparoscopic, remains the most commonly performed.

Calcium, vitamin, protein, and iron deficiencies have been shown to occur.⁵ There is limited longterm metabolic followup of patients who have undergone Roux-en-Y gastric bypass operation. This study evaluates objective measures of calcium metabolism and bone homeostasis and in a group of patients who have undergone gastric bypass operations for the treatment of morbid obesity.

Competing Interests Declared: None.

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METHODS

After approval from the Institutional Review Board (no. 046-06) of Beth Israel Medical Center was obtained, a retrospective review of 535 medical records of patients who had undergone gastric bypass operation for treatment of morbid obesity from January 1, 2000 until Jan-

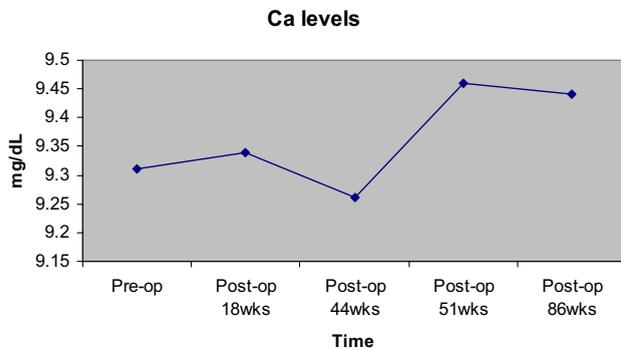


Figure 1. Serum calcium (Ca) levels pre- and postoperatively after gastric bypass operation.

uary 1, 2006 was conducted. Ninety-one patients (17%) were excluded because of followup less than 2 years or because of noncompliance with vitamin supplementation on two consecutive visits. Information gathered included demographic characteristics (age, gender, ethnicity); body mass index; bone mineral density values, if available; past medical history and treatments received; type of gastric bypass performed; degree of weight loss after operation; pre- and postoperative levels of serum vitamin D (25-OH vitamin D); calcium; albumin; blood urea nitrogen; creatinine; and intact parathyroid hormone (PTH). No patient with complete records was excluded from this analysis. Statistical analysis using Student *t*-test was used to compare preoperative and postoperative serum levels of vitamin D and PTH. The level of statistical significance was set at $p \leq 0.05$.

One surgeon (IML), with various assistants, performed all operations using the same operative technique. All patients underwent standard Roux-en-Y gastric bypass operation with the biliopancreatic limb measured to be 150 cm. The alimentary limb was 50 cm

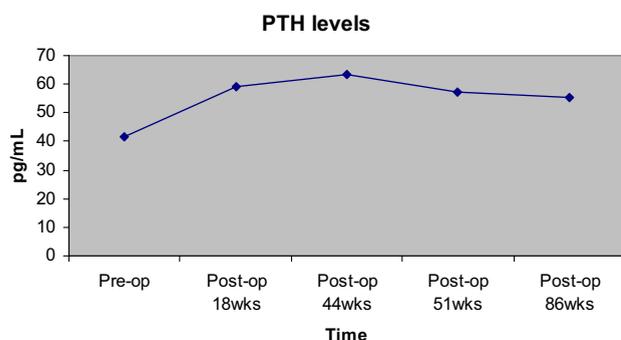


Figure 3. Serum parathyroid levels pre- and postoperatively after gastric bypass operation. PTH, parathyroid hormone.

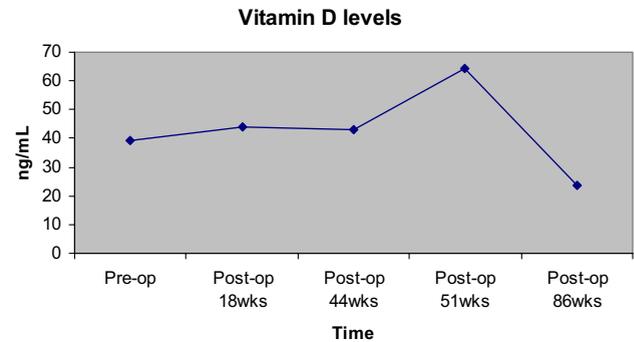


Figure 2. Serum vitamin D levels pre- and postoperatively after gastric bypass operation.

in length. Postoperatively, all patients were given a standard chewable multivitamin (Centrum Chewable, Wyeth Consumer Health Care) and calcium carbonate (1,200 mg) and vitamin D (800 IU total dose) as Caltrate 600 D (Wyeth Consumer Health Care), starting on the 12th day after operation. All patients were followed closely by a team of dietitians, bariatric surgeons, and psychologists, both before and after operation. Compliance with vitamin supplementation was determined by routine questions at the time of their postoperative visits.

Bone density scans obtained pre- and postoperatively were compared.

RESULTS

Of 444 patients analyzed, 91 were men and 353 women, with a mean age of 39.5 years (range 21 to 64 years). Thirty-five percent of female patients were postmenopausal. Average excess weight lost was 42.5%. Blood work was obtained before operation and at 18, 44, 51, and 86 weeks after operation. Laboratory reference levels for low serum 25-OH vitamin D and high PTH levels were < 8 ng/mL and > 55 pg/mL, respectively. Preoperative mean values of serum calcium, vitamin D, and PTH were 9.31 mg/dL, 39.3 pg/mL, and 41.45 pg/mL, respectively. Serial measurements of these parameters are displayed in Figures 1 to 3.

Twenty-five percent of patients had low levels of vitamin D preoperatively. None of these had postoperatively low levels of vitamin D at 18 ($p = 0.807$), 44 ($p = 0.837$), 51 ($p = 0.248$), and 86 weeks ($p = 0.539$). None of the patients had elevated levels of PTH preoperatively. Forty-four percent of patients had elevated intact serum PTH levels ($p = 0.005$) at 18 weeks, 45% ($p = 0.006$) at 44 weeks, 43% ($p = 0.057$) at 51 weeks,

Table 1. Percentage of Patients with Low Vitamin D or High Serum Levels of Parathyroid Hormone Pre- and Postoperatively

| Patients | Preop (%) | Postoperative week | | | | | | | |
|---------------------|-----------|--------------------|---------|----|---------|----|---------|----|---------|
| | | 18 | | 44 | | 51 | | 86 | |
| | | % | p Value | % | p Value | % | p Value | % | p Value |
| With low vitamin D* | 25 | 0 | 0.807 | 0 | 0.837 | 0 | 0.248 | 0 | 0.539 |
| With high PTH† | 0 | 44 | 0.005 | 45 | 0.006 | 43 | 0.057 | 43 | 0.178 |

* < 8 ng/mL.

† > 55 pg/mL.

PTH, parathyroid hormone.

and 43% ($p = 0.178$) at 86 weeks (Table 1) and had to double or even triple their daily calcium and vitamin D supplement, which eventually brought their PTH to normal levels.

There were no measurable changes in postoperative bone density scans when compared with preoperative studies. Changes in serum calcium levels did not vary statistically during the study period.

DISCUSSION

In the absence of effective and safe pharmacologic therapy, the demand for surgical treatment will continue to increase as the percentage of the population with obesity in the US continues to rise. Longterm metabolic consequences of weight-reduction operation are not well-understood or studied. Because of the young age of patients undergoing gastric bypass operations, it is necessary to evaluate calcium homeostasis in these patients to prevent longterm complications, such as osteopenia and osteoporosis.

Low vitamin D levels have been found to exist in the normal population and in patients with morbid obesity. Buffington and colleagues⁶ studied the nutritional and endocrine status of 60 obese people (87 to 184 kg total body weight) and found that 62% had vitamin D levels below normal range, without any substantial correlation with age. This might indicate the importance of measurement and possible oral supplementation of vitamin D preoperatively.

The first observations about endocrine and nutritional problems that develop after malabsorptive operations for weight loss were made as early as about 25 years ago.⁷ Ott and colleagues⁸ reported the first study on metabolic bone disease of patients after Roux-en-Y operations. The authors studied 26 women 10 years after a Roux-en-Y gastric bypass and compared them with patients who had achieved weight loss by dietary restriction. Results showed substantial decreases in vitamin D and calcium levels in the group that underwent opera-

tions compared with the control group, indicating that gastric bypass increases risk of development of metabolic bone disease, especially in postmenopausal women. Other studies have shown similar results.⁹⁻¹⁵

Results of this study showed that no patients experienced serum hypocalcemia during the postoperative period. This might be the result of increased parathyroid activity, demonstrated by elevated PTH levels soon after gastric bypass operation, which results in mobilization calcium from the skeleton and increased renal calcium reabsorption, maintaining normal serum calcium levels. Longterm total body calcium depletion can occur from bone mobilization, if adequate calcium and vitamin D supplementation is not consistently administered after gastric bypass operations. The fact that no patient demonstrated evidence of osteopenia in this study might have been related to aggressive calcium and vitamin D supplementation, or the long time necessary to observe such objective changes.

Severely low levels of vitamin D were not commonly found after gastric bypass operation in patients with preexisting normal serum levels of vitamin D. In a study by Sanchez-Hernandez and colleagues,¹⁶ increased vitamin D levels were found in 42.2% of patients with preexisting deficiency. This can be attributed to defective absorption of fat and fat-soluble vitamins (A, D, E, and K) after gastric bypass operation.¹⁷

This study showed that vitamin D levels did not correlate with calcium or PTH levels. This shows, as reported in previous studies, that vitamin D levels depend largely on sunlight exposure, calcium intestinal absorption, and preoperative levels.¹⁶

High PTH levels were frequently seen after gastric bypass operations, especially during the first year after operation, and the increase reached statistically significant levels ($p < 0.05$). These levels usually return toward baseline if adequate calcium and vitamin D supplementation is maintained. Many patients required additional

supplementation (up to three doses of Caltrate per day) as PTH levels were persistently elevated.

Previous studies have reported both low and high PTH serum levels after gastric bypass operations. We agree with Ybarra and colleagues,¹⁸ that elevated PTH is likely a surrogate for decreased total body calcium resulting from intestinal malabsorption. They reported that 80% of patients who underwent gastric bypass operation presented with both hypovitaminosis D and elevated PTH levels, but Diniz and colleagues¹⁹ report that only 29% of patients had elevated PTH levels.

We currently recommend that, after gastric bypass operations, all patients receive supplementation of calcium and vitamin D starting on 12th day after the operation. This can prevent elevation of PTH to dangerously high levels that could lead to bony calcium mobilization, resulting in osteopenia and osteoporosis. If elevated PTH develops in compliant patients, additional dosing might be required.

Additional study of the effects of gastric bypass operation on calcium, vitamin D, and PTH is necessary. Protocols evaluating postoperative supplementation of calcium and vitamin D for these patients are necessary. We started a prospective study comparing vitamin D replacement therapy with "standard dose" (800 IU daily) versus "high-dose" (2,000 IU daily) for patients with normal vitamin D levels, or 50,000 IU once a week for patients with 25-OH vitamin D levels < 10 ng/mL after gastric bypass operation.

Gastric bypass operation increases the risk of developing low levels of vitamin D and secondary hyperparathyroidism. In addition, supplementation with calcium carbonate and vitamin D, with frequent followup of nutritional status and serum chemistries, is imperative, to intervene before the metabolic consequences of decreased calcium absorption result in osteopenia and osteoporosis. Specific guidelines need to be established about specific dosage of vitamin supplementation of these patients.

Author Contributions

Study conception and design: Avgerinos, Leitman, Martínez, Liao

Acquisition of data: Avgerinos, Leitman

Analysis and interpretation of data: Avgerinos, Leitman, Martínez

Drafting of manuscript: Avgerinos, Leitman

Critical revision: Leitman, Martínez, Liao

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