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Research Article

Semiquantitative Assessment of Bowel Habits and Its Relation with Calcium Metabolism after Gastric Bypass Surgery: A Retrospective Study

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Background. Calcium malabsorption after bariatric surgery may be harmful to skeletal health and demands for optimal skeletal management. *Methods*. 103 Patients were evaluated retrospectively at 12 months after surgery. The evaluation included a questionnaire about stool frequency and consistency and laboratory assessments. *Results*. 103 Patients, 27 males and 76 females, were included in the study. 83 Patients had an alimentary limb of 100 cm and 20 patients one of 150 cm. At 12 months after surgery, 77.7% reported changes of bowel habits, albumin adjusted calcium levels were normal in all but 2 patients, and PTH levels were increased in 35%. Correlations between semiquantified bowel scores (fecal scores) and data from the laboratory demonstrated increasing PTH values along with more frequent and softer/watery stools (RR 30.5, CI 6.2–149.2, $P < .001$). There was a trend for higher PTH levels in patients with an alimentary limb of 150 cm. Normal PTH levels were more frequently found in case of calcium and vitamin D3 use (RR 14.3, CI 3.6–56.5, $P < .001$). *Conclusion*. This study demonstrates interrelationships between semi-quantified fecal scores, PTH levels, and the compliance of taking calcium/vitamin D3 suppletion. However, prospective randomized studies are necessary to show causal relationships.

1. Introduction

Bariatric surgery still remains the most effective treatment for morbid obesity, leading to a reduction of comorbidities in the long term [1]. Roux-en-Y-Gastric Bypass (RYGB) is one of the most frequently performed procedures in the United States and is also widely practiced in Europe [2–4]. Calcium and vitamin D deficiencies, which frequently arise after surgery, may be overlooked because of their slow development. However, they may give rise to secondary hyperparathyroidism (2°HPT) as the body attempts to counter the deficits [5]. Obviously, sufficient dietary calcium and vitamin D are necessary to prevent this condition, which can be difficult to achieve because of the bypassed proximal part of the small intestine. This is the obvious reason for the recommendation of supplying adequate amounts of dietary calcium and vitamin D after surgery [6–8]. Long-lasting 2°HPT for years is believed to be an important contributing factor for increased bone turnover and consequent bone loss. Indeed, epidemiologic data have shown that gastric surgery can lead to a state of 2°HPT with an increased risk of osteoporotic fractures [9–11].

Besides inadequate dietary intake of calcium to compensate for suboptimal calcium absorption, changes of bowel habits after gastrointestinal surgery may also interfere. It is of note that morbidly obese patients frequently have fecal incontinence due to a rise in intra-abdominal pressure with compression and stretch of the pelvic floor and of the muscles and nerves around the anal sphincter complex and in the vicinity of the supporting endopelvic fascia [12]. After bariatric surgery, many patients initially experience less fecal incontinence due to substantial weight loss and associated improvements of intra-abdominal mechanics [13, 14]. For obvious reasons, patients may even have a lowered frequency and hardened consistency of defecation in comparison to the situation prior to the operation. Nevertheless, more frequent

Table 1: Preoperative demographics and laboratory data prior to gastric bypass surgery.

Parameters		
Patient no.	103	
Males/Females	27/76[1]	
Age (yr)	42.3 ± 9.7	
BMI (Kg/m²)	48.6 ± 6.2	
Body weight (Kg)	144.3 ± 21.9	
Alimentary limb		
Patient no. with *100* cm	83	
Patient no. with *150* cm	20	
		Patients with abnormal lab. values
Calcium (mmol/L)[2]	2.31 ± 0.07	2[3]
Vitamin D (nmol/L)	50.4 ± 22.4	
Insufficiency <30 (nmol/L)		18 (17%)
Deficiency <50 (nmol/L)		32 (31%)
PTH (pmol/L)	5.1 ± 1.0	10 (10%)

[1]The number of males versus females was statistically different ($P < .05$). [2]Serum calcium was adjusted for albumin concentrations. [3]1 Patient had a corr. serum calcium of 2.63 and 1 patient of 2.10 mmol/L.

Table 2: Biochemical data categorized according to normal or increased PTH levels at 12 months after gastric bypass surgery.

PTH (pmol/L)	PTH ≤ 6.8	PTH > 6.8	Normal
Patient no.	67	36	
Calcium	2.34 ± 0.08	2.31 ± 0.11	2.10–2.55 mmol/L
Vitamin D	47.5 ± 27.5	40.3 ± 20.3	30–100 nmol/L
Albumin	38.6 ± 3.0	38.6 ± 4.0	35–50 g/L
PTH	4.3 ± 1.4*	9.5 ± 2.8*	1.3–6.8 pmol/L

Lab. results are represented as (mean ± 1SD). *Significant by one-way ANOVA with $P < .0001$.

and looser stools are common in operated patients [15–17]. Studies in laboratory animals elaborating on intestinal calcium absorption have shown that intestinal calcium kinetics depends on intestinal transit time [18]. Similar observations were found after RYGB due to the inability of the small intestine to bind and absorb calcium [19].

To our knowledge, no previous studies were published about interactions between bowel habits after surgery and changes of calcium metabolism. The aim of the present study is to investigate relationships between semiquantified stools scores according to patient reports, compliance for the daily use of extra calcium, and calcium metabolism.

2. Patients and Methods

During a period of 3 years, 423 morbidly obese patients underwent laparoscopic RYGB. Patients were eligible for the study if laboratory data were available at baseline and at 11 to 13 months after surgery. A total of 103 patients, 27 males and 76 females, were eligible, and these were invited to discuss the purpose of the study; all consented to participate. The objectives of the study were (1) to evaluate bowel habit changes after surgery; (2) to evaluate relationships between (1) and laboratory assessments; (3) to evaluate relationships between (1) and (2) with the daily use of a formulation, containing 1 g of elementary calcium and 880 to 1000 IU Vitamin D3. The medical ethical committee of Rijnstate Hospital, Arnhem, The Netherlands approved the study.

All patients were planned for surgery. All patients underwent surgery in a single center for bariatric surgery (Rijnstate Hospital Alysis Zorggroep, The Netherlands). Laparoscopic RYGB was performed by 2 dedicated bariatric surgeons who used standard techniques. According to protocol, patients with a BMI >40 kg/m² received a 45 cm biliopancreatic limb, and a 100 cm alimentary limb, while patients with a BMI >50 kg/m² received a 150 cm alimentary limb. 20 Patients received a 150 cm limb and 83 patients received a 100 cm limb. 22.2% of all males received a 150 cm limb versus 18.8% of all females, meaning no statistical difference in sex distribution. Patients were advised to take daily multivitamins in addition to omeprazol 40 mg (once daily for 6 months) [20] and low molecular heparin SC (fraxiparine 5700 IU once daily for 6 weeks); patients were advised to take a daily calcium/vitamin preparation (CaD 1000/880 sachets, containing calcium citrate and vitamin D3) or, if they refused to take CaD, to try a different formulation containing calcium carbonate and vitamin D3 (Calcichew 500/400 chewing tablets b.i.d.).

After written informed consent, each participant was requested to complete a questionnaire about his/her bowel habits prior to and at 12 months after surgery. Fecal frequency was scored on a five-point scale ranging from less than twice a week (1 point), every two days (2 points), once a day (3 points), twice a day (4 points) to more than twice a day (5 points). In addition, fecal consistency was scored on a five-point scale ranging from watery stools (5 points), watery to solid stools (4 points), normal stools (3 points), firm stools (2 points) to hard stools with concomitant constipation (1 point). Summation of fecal consistency and frequency scores yielded a "fecal score" (FS). Compliance in taking additional calcium and vitamin D3 was arbitrarily defined as daily use with the maximal exception of one day per week. Patients who reported taking the supplement for 5 or less days a week were categorized as noncompliant. For the current analysis, we recorded (1) compliance with regular use of calcium and vitamin D3 containing formulations, (2) the number of patients who requested to switch from liquid formulations (sachets) to chewing tablets, and (3) the number of patients who used laxatives or constipating agents, at least weekly. Calcium, albumin, vitamin D, and PTH at baseline (before surgery) and at 12 months after surgery were used in the final analysis of the study.

Table 3

(a) Changes of bowel habits according to frequency and consistency scores before and after gastric bypass surgery

Time	Baseline frequency	12 mo. frequency	Baseline consistency	12 mo. frequency
Patient no.	*103*	103	*103*	103
Frequency/ Consistency				
<2 per week/ constipated	*9*	6	*12*	8
3 times per week/firm	*23*	19	*26*	14
1 day/normal	*55*	44	*62*	48
2 per day/solid to watery	*13*	19	*2*	27
>2 per day/liquid	*3*	15	*1*	6

Number of patients with frequency and consistency scores ranging from 1 to 5 points.

(b) Fecal scores before and after gastric bypass surgery

Fecal score	Baseline	12 Months
2	7	8
3	4	8
4	12	17
5	29	27
6	39	17
7	8	12
8	4	9
9	0	4
10	0	1

Fecal scores are the summation of stool frequency and consistency ranging from 2 to 10 points and disclosed a significant increase post surgery (γ^2-test: $P < .01$).

2.1. Statistical Analysis. The datasheet was analyzed using SPSS16, statistical software. All data are reported as mean ± 1SD unless otherwise specified; $P < .05$ was considered significant. Results were compared using independent sample *t*-tests, Chi square-tests, relative risk calculation, and one-way ANOVA. Logistic regression was used to differentiate between variables.

3. Results

Demographic data of the included 103 patients, prior to surgery, are listed in Table 1. There were 27 males and 76 females ($P < .05$). All patients were Caucasians. 8 Patients (7.7%) were regular tobacco users, 12 patients were on antidiabetic drugs (11.6%), and 1 patient used prednisone. 6 females were postmenopausal; 1 of them was on hormonal replacement therapy.

2 Patients were diagnosed with a leakage at the gastrojejunostomy and were oversewn successfully, respectively, on the first and third postoperative days. Both patients were discharged within a week after the second operation. Other 2 patients had their gallbladder removed at 6 and 8 months after surgery. There were no other surgical complications.

The excess weight loss (EWL) was >25% for the entire group of 103 patients and exceeded more than half in 83 participants (81%). EWL of the total group at 12 months had decreased by (mean ± 1SD) 63.5 ± 19.5%. The BMI of the whole group decreased from 48.2 ± 6.2 kg/m^2 before surgery to 33.9 ± 5.5 kg/m^2 at 12 months.

Serum calcium concentrations corrected for albumin were normal in 101 patients (98%); vitamin D insufficiency (<50 nmol/L) was demonstrated in 63 patients of whom 32 patients (31%) had vitamin D deficiency (<30 nmol/L). PTH levels were increased (>6.8 pmol/L) in 36 patients (35%), see Table 2.

Notably, none of the patients were regular laxative users, and 79 out of 103 patients (77.7%) reported permanent changes of their bowel habits. Each patient estimated stool frequency and consistency on two 5-point scales ranging from stools less than twice a week to more than twice a day and from watery to hard stools. The summation of each score (frequency plus consistency scores) yielded a fecal score (FS). Memorized stool frequency and consistency data before surgery and at 12 months are listed in Table 3(a) and the distribution of fecal scores (FS) (from 2 to 10 points) in Table 3(b). Each score disclosed a significant change comparing frequency of stools (F), consistency of stools (C), and the fecal score (FS). In general, there was a significant shift towards more frequent and less consistent stools, which overall had resulted in higher fecal scores for (F: $P < .05$, C: $P < .0001$, and FS: $P < .01$).

Laboratory assessments disclosed no significant changes of corrected calcium and vitamin D levels (calcium before surgery 2.31 mmol/L and at 12 months 2.34 mmol/L, vitamin D before surgery 50.4 nmol/L and at 12 months 45.0 nmol/L), while mean PTH levels increased from 5.1 to 6.1 pmol/L ($P = .02$). Before surgery, 10 patients had increased PTH levels, while 4 of them (40%) had also increased PTH levels at 12 months. Before surgery, 32 out of 93 patients had normal PTH levels but developed raised PTH levels at 12 months (34.4%) (NS). PTH levels compared for each domain of stool habits (frequency (F), consistency (C), and fecal score (FS)) per tertile at 12 months, showed no significant changes for F and C. However, PTH levels rose significantly along with tertile FS (RR 30.5, CI 6.2–149.2, $P < .001$), see Table 4.

At 12 months, calcium and vitamin D levels were similar between patients with an alimentary limb of 100 cm ($n = 83$) and 150 cm ($n = 20$) (100 cm: calcium: 2.31 mmol/L, vitamin D 46 nmol/L and 150 cm: calcium: 2.33 mmol/L, vitamin D 42 nmol/L). In addition, there was a trend towards higher PTH levels after inclusion of all patients using two-sided Student *t*-test: 100 cm: PTH: 5.6 pmol/L and 150 cm: PTH 7.9 pmol/L ($P = .001$). PTH levels were not significantly significant after inclusion of compliant calcium/vitamin D3 users (logistic regression) (RR 3.2, CI 0.9–11.8, $P = .08$). At 12 months, there were 36 patients (35%) with increased PTH levels. 24 of these patients had a 100 cm alimentary limb (67%), and 12 patients had a 150 cm alimentary limb (33%).

Table 4: Laboratory results according to fecal scores calculated for each tertile.

Fecal score	Low	Intermediate	High	P-value
Patient numbers (Point range per tertile fecal score)	33 (2–4)	44 (5-6)	26 (7–10)	
Calcium (mmol/L) (Patient numbers with hypocalcemia)	2.35 ± 0.09 (0)	2.32 ± 0.09 (0)	2.34 ± 0.11 (1)	.43
Vitamin D (<30 nmol/L/<50 nmol/L)	41 ± 21.0 (11/22)	51 ± 29.8 (11/25)	39.5 ± 20.4 (10/16)	.12
PTH (≥6.8 pmol/L)	4.9 ± 2.3 (4)	5.8 ± 3.2 (13)	8.0 ± 3.4 (19)	<.001
Patients with an alimentary limb of 150 cm (% of total)	3 (9)	10 (23)	7 (26)	.17*

* P value by χ^2-test, all other comparisons were performed by one-way ANOVA.

According to the definition used in the current study, there were 82 compliant calcium/vitamin D3 users (80%). High PTH levels (PTH >6.8 pmol/L) were found in 21 patients who belonged to this group compliant for suppletion (26%) against 15 patients who belonged to the 21 remaining noncompliant suppletion users (71%) (RR 14.3, CI 3.6–56.5, $P < .001$). In the subgroup of 36 patients with high PTH levels, 21 patients (58%) were compliant suppletion users (PTH: 9.2 ± 2.8 pmol/L) and 15 patients (42%) were not compliant (PTH: 9.9 ± 2.7 pmol/L) (NS).

The reasons for noncompliant suppletion use were being principally against regular use of any prescribed drug, frequently forgetting, and taste aversion against calcium formulations. 69 of the 82 compliant suppletion users (84%) had decided to switch from sachets (liquid formulation) to chewing tablets, while the remaining 13 patients (16%) continued to take sachets. The main reasons for changing from sachets to tablets were nonpalatability reported by 54 patients (78%) and/or the inability to drink large volumes reported by 30 patients (43%). There were 6 reports on dumping-like symptoms with sachets.

4. Discussion

The results of the current study showed significant changes of bowel habits after surgery, which went into the direction of a higher stool frequency, less consistency, and consequent higher fecal scores. There were no correlations with either frequency or consistency and PTH levels, while fecal score and PTH levels were positively correlated. There was also an interaction between compliance for calcium/vitamin D3 suppletion and PTH levels, but it should be emphasized that the current results are nothing but associations, which implicates that prospective intervention studies are needed to clarify how these factors interact. Moreover, it is entirely unclear whether additional calcium and vitamin D supplements are beneficial in suppressing PTH levels and ultimately affect incident osteoporotic fractures in later life. An additional uncertainty is the effect of omeprazol 40 mg (once daily for 6 months) on calcium metabolism after surgery. Indeed, proton pump inhibitor therapy increases the risk to skeletal fracture in the long term, possibly by inhibiting intestinal calcium absorption [21, 22]. Obviously, prospective randomized clinical trials should be long lasting as osteoporotic fractures usually occur much later in life.

Elevation of PTH, even in the presence of unchanged corrected calcium and vitamin D levels, is compatible with 2°HPT [5]. In fact, RYGB serves as a model for 2°HPT exclusively due to inadequate calcium absorption. A study on calcium metabolism of patients who had undergone RYGB and matched controls showed that the patients needed an extra amount of 750 mg calcium per day to maintain similar PTH levels [23]. These calculations were made at 9 months after surgery, meaning that calcium metabolism was still influenced by skeletal calcium effluxes due to high bone turnover [23, 24]. Yet, no calcium balance studies have been published that deal with operated patients with a stable body weight to provide information on the optimal amount of dietary calcium. Notably, too much extra dietary calcium may be harmful because of calcium-related constipation. It has been shown previously that calcium salts bind to free fatty acids and fecal bile acids in the colonic lumen, forming calcium soaps. In other words, calcium suppresses intestinal motility indirectly through binding at the colon level leading to less free fatty acids and to bile acids that are toxic to the colonic mucosa to provoke frequent and watery stools [25].

It is an open question whether increased PTH levels due to chronic calcium malabsorption after RYGB are relevant to future skeletal health. Bone loss after bariatric surgery can be partly ascribed to the direct and secondary effects of rapid weight loss and partly to 2°HPT-related bone loss. Moreover, shortly after bariatric surgery, there will be substantial bone loss, which is obviously driven by the catabolic state of the ongoing weight reduction and not by 2°HPT. Most of this type of rapid bone loss occurs at the hip and ceases with stabilization of body weight. The loss of bone mineral density after surgery occurs mainly at the hip and pelvis, varying between 5 and 10% [23, 24, 26]. However, these analyses were performed around 12 months after surgery, during rapid bone loss. Thus far, there are no data, for example, after a decade available in the literature. Most of the available data come from histological studies of operated patients with a jejunoileal bypass, showing that full-blown osteomalacia was common after this particular procedure [27]. However, jejunoileal bypass surgery is fraught with many long-term complications, among which is vitamin D deficiency, and the operation has therefore been abandoned. Since no histology data are available from obese patients after RouxenY bypass surgery, the jejunoileal bypass bone samples are unique and could help to understand some of the skeletal health issues that should be dealt with. In a comparative histomorphometry study in 21 patients 3–14 years after intestinal bypass surgery for obesity, osteomalacia was found in one-third of all patients. Biopsies of those without osteomalacia disclosed a marked reduction of trabecular thickness, partly as the result of 2°HPT and partly because of insufficient osteoblastic synthesis. This picture differs from that of age-related bone loss and postmenopausal osteoporosis which share loss of density rather than thickness of trabecular plates [28]. Biopsies from 16 middle-aged males after partial gastrectomy with Billroth II anastomosis revealed high bone turnover (leading to bone loss) due to body weight reduction after-surgery and/or 2°HPT [11]. Finally, there is a histological proof for insufficient osteoblastic recruitment and activity, probably due to deficits of unidentified nutrients resulting from the malabsorption caused by bypassing critical parts of the small intestines [28]. In a bone biopsy study among 41 patients after partial or total biliopancreatic bypass, it was found that defective mineralization and a decrease of bone formation rate were present in spite of serum 25-hydroxyvitamin D concentrations being normal [29]. These biopsy data underscore the concept that in one way or another essential nutrients are needed to support bone formation.

This study has several limitations, mainly related to its retrospective and cross-sectional design. However, it underlines the need for more prospective intervention studies in gastric bypass patients, even though this procedure is considered the gold standard, suggesting safety. In the meantime, it remains advisable to consider bone mineral density in the assessments of risk factors prior to surgery, particularly in women.

In conclusion, 12 months after gastric bypass surgery, there was a positive relationship between bowel habits (i.e., the summation of stool frequency and consistency scores) and PTH levels with an interaction for the compliance with calcium/Vitamin D suppletion. This finding is based on fecal score and an arbitrarily chosen definition of compliance. The current study underscores the importance of professional management of bowel habits and tailor-made calcium/vitamin D suppletion. Long-term prospective intervention studies are critical to evaluate efficacy as well as side effects and should be undertaken in the near future.

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