



# Impact of Roux-en-Y Gastric Bypass on Bone Metabolism in Chinese Obese Patient

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## Abstract

**Introduction:** Changes in bone metabolism following Roux-en-Y Gastric Bypass (RYGB) in obese patients have yielded inconsistent results. Nevertheless, no data exist on changes in Calcium (Ca) metabolism after RYGB in Chinese obese subjects.

**Objectives:** The aim of this study was to identify the impact of RYGB on vitamin D, Parathyroid Hormone (PTH), Ca and Phosphorus (P) metabolism in Chinese obese patients, and predictors of postoperative change.

**Methods:** The patient undergoing RYGB between January 2015 and October 2018 in our hospital was retrospectively reviewed. Serum PTH, P, Ca, and 25-hydroxyvitamin D (25OHD) levels were collected before and 6 months after RYGB.

**Result:** In total, 165 patients were included in the study. After RYGB, the mean Body Mass Index (BMI) level significantly reduced, the Ca, P and 25OHD levels increased, while the PTH level remained similar. Preoperative PTH level, percentage of Excess Weight Loss (%EWL), and BMI change were independent predictors of postoperative PTH change. Preoperative P and Ca levels could predict postoperative P and Ca change, respectively.

**Conclusion:** A significant increase in serum 25OHD, Ca, and P are expected after RYGB at the short term. And preoperative 25OHD and Ca levels are predictors of postoperative change.

**Keywords:** Roux-en-Y Gastric Bypass (RYGB); Vitamin D; Parathyroid Hormone (PTH); Ca-P Metabolism; Obesity

## Introduction

Obesity has become a serious global public health problem, in China, with around 10% of the population were over 27.5 kg/m<sup>2</sup> [1]. Dietary treatment, medical treatment and physical treatment had a poor effect for morbid obesity patients. Bariatric surgery has been proven to be the most effective way for the morbidly obesity patient to reduce weight, also it could remarkably improve the status of obesity-related diseases, including diabetes, hypertension, and obstructive sleep apnea [2].

Vitamin D, Parathyroid Hormone (PTH), Calcium (Ca) and Phosphorus (P) all participate in calcium metabolism. Obesity was inversely related to serum concentrations of vitamin D and high levels of PTH [3]. A cross-sectional study conducted in China showed a significant inverse association between vitamin D level and waist circumference and waist-to-hip ratio, and concluded that adiposity phenotype were intimately related to low vitamin D levels [4,5].

Roux-en-Y Gastric Bypass (RYGB) was one of the most common surgeries for morbid obesity patient, which was considered by many surgeons as the “global standard” procedure for morbid obesity patient [6]. However, the effect of RYGB surgery on vitamin D, Ca, P and PTH levels have not been fully known yet. In western country, there already have many articles to explain the change of bone metabolism after obesity surgery. But the ethnic differences between Chinese and Westerners, it caused the physiology difference between each other. The aim of this study was to identify the impact of RYGB on vitamin D, PTH, Ca and P metabolism in Chinese obese patients.

## Method

### Study design and patient selection

A retrospective review of a prospectively collected database was conducted in patients undergoing

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RYGB in the department of metabolic and obesity surgery of the First Affiliated Hospital of Jinan University (Guangzhou, China) between January 2015 and October 2018. Inclusion criteria for the study for the study were patients with age 18 to 65 years old, Body Mass Index (BMI)  $\geq 32.5$  kg/m<sup>2</sup> or  $\geq 27.5$  kg/m<sup>2</sup> with uncontrolled Type 2 Diabetes (T2D) or at least one other metabolic disease and preoperative normal parathyroid hormone levels. Exclusion criteria were patients with bariatric surgery history, chronic renal failure, alcohol addiction, hyperparathyroidism, hypoparathyroidism, and any kind of known parathyroid disease. Informed consent was obtained from all the patients included in the study.

Data collected included age, sex, body weight, body height, BMI, Serum PTH, Ca, P, 25OHD levels at baseline and postoperatively at 6 months. Fasting blood samples were obtained from all participants and then analyzed by clinical laboratory of our hospital. Chemiluminescence immunoassay was used to identify the serum hormones; reference values were between 12 and 88 pg/mL for PTH, 2 to 2.80 mmol/L for Ca, 0.96 and 1.62 mmol/L for P, 30 to 100 ng/ml for 25OHD.

The change of serum PTH, Ca, P, 25OHD levels before and after surgery was measured, and predictors of postoperative change were analyzed. Weight loss outcomes were reported as percentage of Excess Weight Loss (%EWL), percentage of Total Weight Loss (%TWL), and change of BMI. %EWL was computed by the formula as followed:  $[\text{Initial weight (kg)} - \text{current weight (kg)}] / [\text{initial weight (kg)} - \text{ideal weight (kg)}] \times 100$ , where ideal weight (kg) =  $25 \times [\text{height(m)}]^2$ . %TWL was determined according to the equation:  $\%TWL = [\text{initial weight (kg)} - \text{current weight (kg)}] / [\text{initial weight (kg)}] \times 100$ . Change in BMI were computed by the formula  $[\text{BMI} = \text{initial BMI (kg/m}^2) - \text{current BMI (kg/m}^2)]$ .

### Surgical intervention

All operations were conducted with laparoscopy by an experienced surgical team. The RYGB procedure included a small gastric pouch around 10 ml to 20 ml, with a biliopancreatic limb with 25 cm long and an alimentary limb with 125 cm to 175 cm long, it's depending on patients' preoperative BMI and/or with T2D. The base length of alimentary limb is 125 cm, but patients with BMI  $\geq 45$  kg/m<sup>2</sup> or T2D would have increase 25 cm long.

### Postoperative management follow-up

After surgery, these patients were suggested to come back for reexamination at 1, 3 and 6 months. However, only the 6-months follow-up data were presented in this study. At every time point, we would give them a systematic investigation, including routine physical examination, the change of weight, obesity-related comorbidities, and fasting blood analyses.

In addition, they were advised to take calcium tablet (Caltrate<sup>®</sup>), which includes 600 mg calcium and 125 IU vitamin D3; and multivitamin supplementations (Centrum<sup>®</sup>), which includes 162 mg calcium and 400 IU vitamin D, 0.4 mg folate, 6 µg vitamin B12, 18 mg iron, 36.3 mg chlorine, 125 mg phosphorus, 40 mg potassium, 100 mg magnesium, 5000 IU vitamin A, 15 mg zinc, 20 mg nicotinamide, 2.5 mg manganese, 1.5 mg vitamin B1, 25 µg chromium, 1.7 mg vitamin B2, 25 µg molybdenum, 2 mg vitamin B6, 25 µg selenium, 60 mg vitamin C, 5 µg nickel, 10 µg tin, 25 µg vitamin K1, 10 µg silicon, 30 µg biotin, 2 mg copper, and 10 µg vanadium. These patients were administrated to take both of the two medications all their life.

**Table 1:** The clinical characteristics of this study.

Variables	All (n=165)
Male/female	104/61
Age (years)	33.70 ± 10.84
Weight (Kg)	124.17 ± 28.915
BMI (kg/m <sup>2</sup> )	43.647 ± 9.828
Hypertension	49 (29.7%)
T2DM	70 (42.4%)
Vitamin D deficiency	161 (97.6%)

BMI: Body Mass Index; T2DM: Type 2 Diabetes

### Statistical analysis

The data was analyzed using the Statistical Product and Service Solution version 19.0 (Spss 19.0, SPSS Inc., Chicagp, IL). Student's t test or Mann-Whitney test for continuous data, and Chi-square test for categorical data. The Pearson or the Spearman coefficients were used for correlation analyses. Univariate and multivariate analyses were used to find the predictors related to postoperative parathyroid level.  $P < 0.05$  was considered as statistically significant.

## Result

### General information

This study enrolled 165 obese patients (104 males and 61 females; average age 33.70 ± 10.84 years; average BMI 43.65 ± 9.83 Kg/m<sup>2</sup>). 49 patients had hypertension, 70 patients had T2D, 161 patients had vitamin D deficiency (Table 1).

As shown in Table 2, the mean BMI level changed from 43.67 to 29.99 kg/m<sup>2</sup> after RYGB ( $P < 0.000$ ). The mean serum Ca level increased from 2.33 ± 0.11 mmol/L to 2.37 ± 0.13 mmol/L ( $P = 0.004$ ). And the mean serum P level increased from 0.205 ± 0.196 mmol/L to 1.30 ± 0.17 mmol/L ( $P = 0.038$ ). The mean serum 25OHD level increased from 15.358 ± 6.463 ng/ml to 20.04 ± 6.22 ng/ml ( $P = 0.005$ ). There was no significant difference regarding serum PTH level before and after surgery ( $P = 0.896$ ).

### Predictors of postoperative variation of serum PTH, P, Ca levels

In our study, univariate and multivariate linear regression analyses were used to explore the predictors of postoperative variation of serum PTH, P, Ca levels at 6 months after RYGB. After adjusting for relevant covariates, preoperative PTH level, %TWL, change in BMI, and change in Ca were independently related with the postoperative PTH decrease; Preoperative PTH and postoperative PTH decrease were independently related with postoperative P increase; preoperative weight, preoperative BMI, hypertension, preoperative Ca, %TWL, postoperative BMI decrease were independently related to postoperative Ca increase (Table 3).

**Table 2:** Variables at Baseline and After RYGB.

Variables	Baseline	6 mo after RYGB (n=64)	P
Weight (kg)	124.170 ± 28.915	84.623 ± 19.046	0.000
BMI (kg/m <sup>2</sup> )	43.647 ± 9.828	29.988 ± 6.067	0.000
PTH (pg/mL)	47.144 ± 20.012	46.435 ± 15.953	0.896
Ca (mmol/L)	2.332 ± 0.110	2.372 ± 0.129	0.004
P (mmol/L)	1.205 ± 0.196	1.298 ± 0.165	0.038
25OHD (ng/ml)	15.358 ± 6.463	20.040 ± 6.220	0.005

BMI: Body Mass Index; T2D: Type 2 Diabetes; PTH: Parathyroid Hormone; P: Phosphorus; Ca: Calcium

**Table 3:** Correlations with variation of serum IPTH, P, Ca levels at 6months after RYGB.

	Change in IPTH				Change in P				Change in Ca			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	r	p	B	p	r	p	b	p	r	p	b	p
Age	0.75	0.678			-0.173	0.292			0.037	0.822		
Sex	-0.064	0.722			-0.096	0.560			-0.127	0.442		
Preoperative weight(kg)	0.129	4.474			0.140	0.396			-0.462	0.003	-0.147	0.447
Preoperative BMI(kg/m <sup>2</sup> )	0.182	0.310			0.011	0.949			-0.666	0.000	-0.173	0.391
Hypertension	-0.182	0.550			0.225	0.169			0.319	0.048	0.113	0.10
T2D	-0.070	0.697			-0.055	0.740			0.373	0.019	0.137	0.612
Preoperative IPTH	0.742	0.000	1.261	0.002	-0.183	0.265			-0.116	0.482		
Preoperative P	-0.330	0.060	0.081	0.591	0.727	0.000	0.773	0.000	0.078	0.636		
Preoperative Ca	-0.281	0.114			-0.007	0.966			0.754	0.000	0.782	0.000
Preoperative 25OHD	-0.005	0.979			-0.119	0.469			0.003	0.987		
% TWL	0.745	0.008	-0.152	0.671	-0.156	0.564			-0.538	0.032	-0.165	-1.107
% EWL	-0.545	0.083	0.160	0.039	0.244	0.362			0.224	0.405		
Change in BMI	0.800	0.003	1.909	0.005	-0.250	0.350			-0.535	0.033	-0.265	0.125
Change in IPTH	1.000	-			-0.395	0.023	-0.046	0.711	-0.169	0.346		
Change in P	-0.395	0.023	0.031	0.872	1.000	-			0.104	0.527		
Change in Ca	-0.169	0.346			0.104	0.527			1.000	-		
Change in 25OHD	-0.245	0.176			0.026	0.879			-0.003	0.985		

Parameters with P value <0.10 were included into multivariate analyses; BMI: Body Mass Index; T2D: Type 2 Diabetes; IPTH: Parathyroid Hormone; P: Phosphorus; Ca: Calcium; %TWL: Percentage of Total Weight Loss; %EWL: Percentage of Excess Weight Loss

## Discussion

Some clinical studies already showed that surgical weight loss in obese patient was related with significantly increase of serum 25OHD, Ca, and P after bariatric surgery, but most of them were sleeve gastrectomy. There was few data to support the relationship between PTH, Ca, P, and 25OHD and weight loss after RYGB, most of previous studies focused on the relationship about the bone density and these four elements [7-9]. In our study, the primary outcome was that serum Ca, P, and 25OHD level significant increased after RYGB in short period. The secondary aim was to explore the predictors of postoperative variation of serum PTH, P, Ca levels.

Our subject showed that there is no significant difference between preoperative serum PTH level and postoperative PTH level. But there is a correlation relationship between %TWL, BMI change, P change and PTH change. Some other studies also showed that vitamin D has a negative correlation with PTH during weight loss process [10,11]. Hewitt et al. found that after 2 years of the RYGB, the levels of serum vitamin D increase, the levels of serum PTH decrease, and caused secondary hyperparathyroidism. Gunther et al. found that vitamin D status was a main key for regulation of PTH levels and PTH was the direct mediator of lipid oxidation, decreased fat mass may lead to increase of vitamin D and decreased PTH level [12]. But some studies showed during weight loss, increased PTH level were seen during 3 months and 6 months following SG [13,14]. Mihmanli et al. showed that there were also significant correlations between PTH, vitamin D and ALP serum values after SG [13]. The change of PTH after bariatric surgery is still unclear, our study showed decreased PTH level after RYGB, and the change have a correlation relationship with weight loss, also increasing of vitamin D may cause the PTH decrease, compare with the other studies, the baseline of the PTH and the change of the PTH and vitamin D are higher, may be RYGB is the

better surgery method for Chinese patient with obesity.

Vitamin D was also an important coordinator of serum Ca and P absorption [15]. Our study indicated that there had a significant difference regarding serum Ca, P, and 25OHD values between pre-operation and 6 months after RYGB. Also Ca change has a negative correlation with weight loss. Ca and P were mainly absorbed by the duodenum and the upper part of the jejunum, and 99% was stored in bone. In SG, there is no need to bypass the duodenum and part of the jejunum, which can explain the maintenance of serum Ca and P levels [14]. But during RYGB process, the duodenum and 125 cm to 175 cm of jejunum need to be bypassed; it could impact the absorption function of serum Ca and P, and cause Ca and P deficiency. During the weight loss process, the adipose tissue will become less, 25OHD will increase, because vitamin D is mainly stored in adipose tissue and it will transfer to 25OHD during weight loss [16]. But we failed to find the relationship between weight loss and serum 25OHD change. When 25OHD increase, it will activate the intestinal mucosa cell and prompt the synthesis of calcium and phosphorus binding protein; it becomes a barrier to prompt the absorption of the Ca and P, therefore increasing the serum level. Sergeev summarized that 25OHD regulates Ca-mediated apoptosis pathway in adiposity, 25OHD-activated apoptosis molecular targets in adiposity were Ca-dependent captain and Ca/calpain-dependent caspase-12. Mature adiposity is susceptible to 25OHD-induced apoptosis apparently, because of their low Ca buffering capacity and/or high permeability of the Ca entry and Ca mobilization pathways [17].

Also our result showed that the P serum change has a negative correlation with serum PTH change. During weight loss, serum Ca level increased, increased Ca will cause the decreasing of PTH serum level in physiology theory, but when P serum level increased, it caused increased PTH serum level, may be increasing of the P

have been created the balance between Ca and PTH. Limited studies have examined the effect of RYGB on the relationship between Ca-P metabolism and PTH, and long term studies are missing [18,19]. Even though this study is not a long-term study, data collection will be continued in our clinical work.

A high prevalence of vitamin D deficiency was reported in China. A multicenter study conducted by Songlin et al. showed that serum 25OHD level lower than 30 ng/ml was found in 2,056 subjects (94%), and the mean age of this group was 18 years old to 39 years old. The main reason for these deficiencies may be serious pressure of work or study and limited amount of indoor activity [20]. Also, vitamin D was mainly stored in adipose tissue. In our study, the mean age of our subject was 33.7 years old and their mean BMI was 43.65 kg/m<sup>2</sup>, it can explain why more than 95% of our subject had vitamin D deficiency. After RYGB, the mean 25OHD level has a significant increase; it may be contributed to two reasons. First is the increased outdoor activity after discharge. We have organized teaching lesson for obese patient, which was mainly about a new arrangement of daily life activity and eating habits. Second is decreased amount of adipose tissue, may relieve more 25OHD into serum.

All of our patients are suggested to take calcium tablet and multivitamin supplementation after surgery, but it does not have any help. Bingsheng et al. showed that even with these administrations, most patients still encountered the nutrition deficiencies after bariatric surgery [19]. The reason of the deficiencies may be caused by the bypass process, the absorption of those supplement are in the duodenum and jejunum, and it could impact the absorption function of supplementation. Even so, we still need to suggest patients to take the supplement after surgery, Muschitz et al. showed two group of patients which were developed into supplementation group and non-supplementation group, the supplementation group have the higher level of the calcium and vitamin than their group, but the level of the calcium and vitamin were still lower than the normal level [21].

This study has some limitation. At first, bariatric surgery is still in the early stage in China, postoperative regular follow-up has not been paid enough attention by some patients, resulting in a high rate of lost to follow-up; therefore, the postoperative sample size was relatively small. In addition, our study was a short-term follow-up study, but long-term follow up will be continued. Third, our result only reveals some clinical phenomenon, further research about the mechanism between small intestine, adipose tissue, absorption of 25OHD and Ca-P metabolism will also be exported in our group.

## Conclusion

A significant increase in serum 25OHD, Ca, and P are expected after RYGB at postoperative short period. And preoperative 25OHD and Ca levels were predictors of postoperative change.

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## References

- Blüher M. Obesity: Global epidemiology and pathogenesis. *Nat Rev Endocrinol.* 2019;15:288-98.
- Fitzpatrick KM, Shi X, Willis D, Niemeier J. Obesity and place: Chronic disease in the 500 largest U.S. cities. *Obes Res Clin Pract.* 2018;12(5):421-5.
- Borges JLC, Miranda ISDM, Sarquis MMS, Borba V, Maeda SS, Lazaretti-Castro M, et al. Obesity, bariatric surgery, and vitamin D. *J Clin Densitom.* 2018;21(2):157-62.
- Zhang Y, Zhang X, Wang F, Zhang W, Wang C, Yu C, et al. The relationship between obesity indices and serum vitamin D levels in China adults from urban settings. *Asia Pac J Clin Nutr.* 2016;25(2):333-9.
- Song Q, Sergeev IN. Calcium and vitamin D in obesity. *Nutr Res Rev.* 2012;25(1):130-141.
- Angrisani L, Santonicola A, Iovino P, Vitiello A, Zundel N, Buchwald H, et al. Bariatric surgery and endoluminal procedures: IFSO worldwide survey 2014. *Obes Surg.* 2017;27(9):2279-89.
- Yu EW. Bone metabolism after bariatric surgery. *J Bone Miner Res.* 2014;29(7):1507-18.
- Santos D, Lopes T, Jesus P, Cruz S, Cordeiro A, Pereira S, et al. Bone metabolism in adolescents and adults undergoing Roux-En-Y gastric bypass: A comparative study. *Obes Surg.* 2019;29(7):2144-50.
- Hage MP, Fuleihan GEH. Bone and mineral metabolism in patients undergoing Roux-en-Y gastric bypass. *Osteoporos Int.* 2014;25(2):423-39.
- Souberbielle JC, Lawson-Body E, Hammadi B, Sarfati E, Kahan A, Cormier C. The use in clinical practice of parathyroid hormone normative values established in vitamin D-sufficient subjects. *J Clin Endocrinol Metab.* 2003;88(8):3501-4.
- Hewitt S, Aasheim ET, Søvik TT, Jahnsen J, Kristinsson J, Eriksen EF, et al. Relationships of serum 25-hydroxyvitamin D, ionized calcium and parathyroid hormone after obesity surgery. *Clin Endocrinol (Oxf).* 2018;88(3):372-9.
- Gunther CW, Legowski PA, Lyle RM, Weaver CM, McCabe LD, McCabe GP, et al. Parathyroid hormone is associated with decreased fat mass in young healthy women. *Int J Obes (Lond).* 2006;30(1):94-9.
- Mihmanli M, Isil RG, Isil CT, Omeroglu S, Sayin P, Oba S, et al. Effects of laparoscopic sleeve gastrectomy on parathyroid hormone, vitamin D, calcium, phosphorus, and albumin levels. *Obes Surg.* 2017;27(12):3149-55.
- Ruiz-Tovar J, Oller I, Priego P, Arroyo A, Calero A, Diez M, et al. Short- and mid-term changes in bone mineral density after laparoscopic sleeve gastrectomy. *Obes Surg.* 2013;23(7):861-6.
- Song Q, Sergeev IN. Calcium and vitamin D in obesity. *Nutr Res Rev.* 2012;25(1):130-41.
- Cordeiro A, Santos A, Bernardes M, Ramalho A, Martins MJ. Vitamin D metabolism in human adipose tissue: Could it explain low vitamin D status in obesity? *Horm Mol Biol Clin Investig.* 2017;33(2).
- Sergeev IN. Vitamin D-Cellular Ca(2+) link to obesity and diabetes. *J Steroid Biochem Mol Biol.* 2016;164:326-30.
- Worm D, Madsbad S, Kristiansen VB, Naver L, Hansen DL. Changes in hematology and calcium metabolism after gastric bypass surgery--a 2-Year follow-up study. *Obes Surg.* 2015;25(9):1647-52.
- Guan B, Yang J, Chen Y, Yang W, Wang C. Nutritional deficiencies in Chinese patients undergoing gastric bypass and sleeve gastrectomy: Prevalence and predictors. *Obes Surg.* 2018;28(9):2727-36.
- Yu S, Fang H, Han J, Cheng X, Xia L, Li S, et al. The high prevalence of hypovitaminosis D in China: A multicenter vitamin D status survey. *Medicine (Baltimore).* 2015;94(8):e585.
- Muschitz C, Kocijan R, Haschka J, Zendeli A, Pirker T, Geiger C, et al. The Impact of Vitamin D, Calcium, protein supplementation, and physical exercise on bone metabolism after bariatric surgery: The BABS Study. *J Bone Miner Res.* 2016;31(3):672-82.