Original Article

Is there a relationship between different types of prior bariatric surgery and post-thyroidectomy hypocalcemia?

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Background: Hypocalcemia is a common complication after total thyroidectomy (TT). A history of bariatric surgery has been identified as a risk factor for this complication. This study aimed to assess the risk of hypocalcemia post TT in patients with a history of obesity procedures: laparoscopic sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGB), and laparoscopic gastric banding (LAGB).

Methods: We compared the risk of hypocalcemia post TT (serum calcium levels <8 mg/dL) between patients with restrictive (LSG and LAGB), malabsorptive (RYGB), and patients without a history of obesity surgery. Hypoparathyroidism was considered permanent if the plasma parathyroid hormone (PTH) levels at 6 months were less than 15 pg/mL (normal range: 15–65 pg/mL) and the patient still required oral calcium (calcium carbonate) and vitamin D supplementation, in addition to the supplements that were taken routinely before thyroidectomy.

Results: From the 13,242 patients who underwent TT from 2006 to 2018, 90 patients (0.7%) had a history of bariatric surgery: 35 LAGB, 29 LSG, and 26 RYGB. The risk of hypocalcemia was higher in RYGB patients (50%, n=13) than in LAGB (17.1%, n=6) or LSG patients (20.6%, n=6) (P=0.003). Furthermore, hypocalcemia risk was similar between patients with a history of restrictive procedures (18.8%, 12/64) and patients with no history of bariatric surgery (17.2%, 2,268/13,152) (P=0.4). Permanent hypoparathyroidism was observed in one and 6 patients from the LAGB and RYGB groups, respectively; however, it was not observed in any patient from the LSG group.

Conclusions: RYGB is a risk factor for hypocalcemia post TT, while restrictive bariatric procedures are not.

Keywords: Bariatric surgery; hypocalcemia; thyroidectomy; gastric bypass; restrictive procedure

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Introduction

Obesity, a global public health problem, is a major risk factor for several conditions including cardiovascular diseases, diabetes, musculoskeletal disorders, and some cancers (1,2).

While bariatric surgery is considered the most effective therapy for morbid obesity (3), it may lead to malnutrition, irrespective of a malabsorptive or restrictive procedure. It is associated with several vitamin and mineral deficiencies, which often do not respond to oral supplements (3-6). For instance, 15–48% of bariatric surgery patients experience low serum calcium levels, while 30–60% have vitamin D deficiency (7,8).

Total thyroidectomy (TT) is commonly performed for either malignant or benign thyroid diseases (9). Hypocalcemia is a relatively frequent complication of TT (15–20%), with a permanent hypoparathyroidism rate of 1–3% (10,11). Certain clinical and biochemical risk factors for postoperative hypocalcemia have been identified. These include female sex, autoimmune and inflammatory thyroid diseases (Hashimoto thyroiditis or Graves' disease), and bilateral central neck dissection for malignancies (11,12). However, the role of bariatric surgery as a risk factor remains debatable (13-20).

Considering the increasing prevalence of obesity in the western world and the rising number of different bariatric procedures, documenting risk factors for hypocalcemia after TT in this cohort is important to prevent and/or treat its complications in them.

Therefore, this study aimed to assess the risk of hypocalcemia following thyroidectomy in patients with a history of various bariatric procedures such as laparoscopic sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGB), or laparoscopic gastric banding (LAGB). We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/gs-21-225).

Methods

All patients with a history of bariatric surgery who underwent TT at our University Hospital from 2006 to 2018 were included in this study. Our department is a high-volume center specialized in endocrine surgery, with 1,500 thyroidectomies per year.

Patients with a history of thyroid, parathyroid, or other cervical surgeries were excluded.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

The study was approved by institutional review board of Assistance Publique-Hôpitaux de Paris (APHP) (IRB number 20200115171338) and informed consent was taken from all the patients.

Data on the demographic, biochemical, and preoperative characteristics [age, sex, serum calcium and vitamin D levels, and body mass index (BMI) at the time of thyroidectomy], along with data on postoperative hypocalcemia, were retrospectively analyzed from the prospectively completed database.

Postoperative hypocalcemia was defined as a serum calcium level of less than 8 mg/dL (normal range: 8.4–10.6 mg/dL) during the postoperative course after TT that was either symptomatic with overt manifestations (such as anxiety, carpopedal spasms, tingling, or numbness of the extremities) or not.

In the event of hypocalcemia, 1.25 g of oral calcium carbonate was administered thrice daily as a calcium supplement; in case of severe symptoms, calcium was administered intravenously. Calcium was supplemented with vitamin D (alfacalcidol: 1 µg/day) if the serum calcium level was less than 7.2 mg/dL. The nadir serum calcium level, defined as the lowest concentration of calcium at any time after thyroidectomy, was recorded.

Hypoparathyroidism was considered permanent if the plasma parathyroid hormone (PTH) levels at 6 months were less than 15 pg/mL (normal range: 15–65 pg/mL) and the patient still required oral calcium (calcium carbonate) and/or vitamin D supplementation, in addition to the supplements that were taken routinely before thyroidectomy. In our clinical practice, we follow a perioperative supplementation protocol for patients undergoing TT; briefly, patients receive 0.25 µg/day of alfacalcidol for 5 days prior to the thyroidectomy.

This protocol was applied to all patients, including bariatric patients, who underwent TT. Postoperatively, at discharge, calcium supplementation was based on the PTH levels (dosed 20 minutes after thyroidectomy).

Our TT technique involved identifying the parathyroid glands (especially the superior glands) for their preservation. If the four parathyroid glands were not observed during the dissection, the resected specimen was examined for the missing glands at the end of the procedure. Patients with compromised parathyroid gland vascularization underwent selective parathyroid auto-transplantation into the ipsilateral sternocleidomastoid muscle.

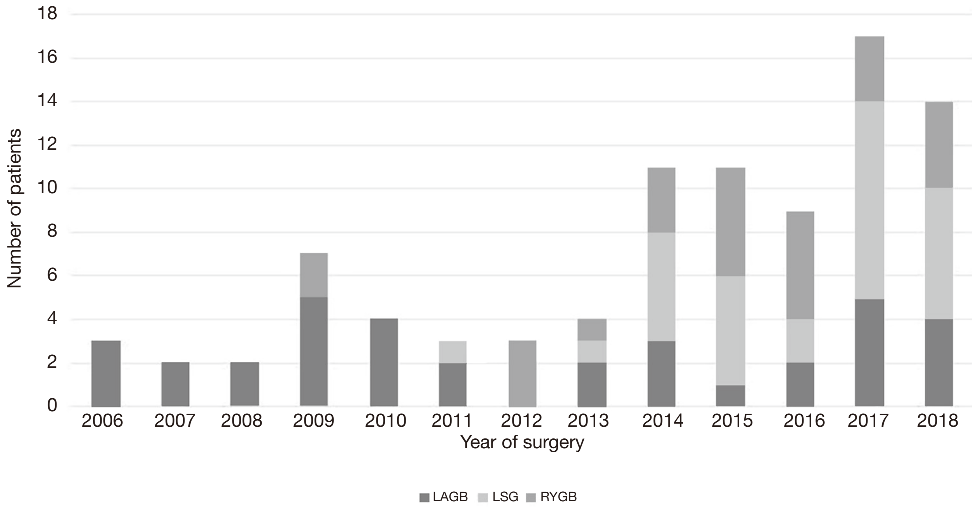

Figure 1 Incidence of patients with a history of bariatric surgery undergoing TT. LAGB, laparoscopic gastric banding; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass; TT, total thyroidectomy.

The follow-up consisted of an outpatient visit 6 weeks after surgery; patients who developed hypocalcemia were seen by their surgeon after 6 and 12 months.

To identify the transient and definitive effects of previous bariatric surgery on postoperative hypocalcemia, we compared patients with a history of restrictive bariatric procedures (LSG and LAGB) with patients having a history of RYGB and patients without a history of obesity surgery.

Statistical analysis

Results are presented as median values (interquartile range) for continuous variables, and numbers (percentages) for categorical variables. The χ^2 test or Fisher's exact test was used for categorical variables, and unpaired *t*-test for continuous variables. A two-sided significance level of 0.05 was used for all statistical tests. Analyses were performed using SAS v. 9.4 (SAS Institute, Cary, NC, USA).

Results

Of the 13,242 patients who underwent TT from 2006 to 2018, 0.7% (n=90) had a history of bariatric surgery and were included in the study; the number of patients with a history of bariatric surgery who underwent TT (mainly LSG and RYGB) steadily increased in the last years of the study period (*Figure 1*). Among these, 38.8% of patients (n=35) underwent LAGB, 32.2% underwent LSG (n=29), and 30% underwent RYGB (n=26). The median interval between bariatric surgery and thyroidectomy was 4 years (range, 2–15 years). The median BMI at the time of TT was 30.9 kg/m^2 (range, 20.2–51.4 kg/m^2). Overall, 92% (n=83) of the patients were women and the median age was 49.2 years (range, 23.1–69.4 years). The three groups presented with no differences in the preoperative clinical and biochemical characteristics (specifically the serum calcium and vitamin D levels) (*Table 1*). There were no differences in the percentage of thyroid surgery for malignancy.

No patient was lost to follow-up. The median follow-up period was 4 years (range, 1–7 years). Twenty-five patients (27.8%) presented with immediate postoperative hypocalcemia. Patients with a history of RYGB were more likely to develop postoperative hypocalcemia (50%; n=13) than patients with a history of LAGB (17.1%; n=6) or LSG (20.6%, n=6) (P=0.003; *Figure 2*).

Calcium, in the form of calcium gluconate, was supplemented intravenously to six patients; one belonged to the LAGB patients, while five belonged to the RYGB patients. Permanent hypoparathyroidism was observed in one patient with a history of LAGB and 5 with a history of RYGB, however, it was not observed in the LSG group. We found no significant differences in the rates of hypocalcemia, both transient and permanent, between patients with a history of restrictive procedures and patients without a history of bariatric surgery [18.8% (12/64) *vs.* 17.2% (2,268/13,152), P=0.4] (*Table 2*).

Table 1 Patients demographic characteristics

Characteristics	No previous bariatric surgery	LAGB	LSG	RYGB	P value
Patient number	13,152	35	29	26	0.8
Sex, male	2,681 (20.4)	4 (11.4)	1 (3.4)	2 (7.7)	0.3
Age, years	52.1 (11.8–90.0)	54 (25.6–63.9)	48.1 (23.1–69.4)	49 (34.9–64.8)	0.8
BMI at time to thyroid surgery, kg/m^2	24.8 (13.3–61.0)	32.7 (20.2–51.4)	31.6 (23.1–44.2)	29.3 (20.4–48.8)	0.01
Reduction of weight loss between bariatric surgery and thyroidectomy, kg	–	10 [5–28]	14 [5–30]	18 [12–55]	0.01
Preoperative biochemical results					
Calcium level, mg/dL	9.3 (8.9–11.2)	9.3 (9.0–10.5)	9.4 (9.0–10.2)	9.6 (8.9–11.4)	0.3
25-hydroxy-vitamin D, ng/mL	31 [21–47]	35 [22–47]	31 [25–40]	29 [21–44]	0.1
Malignant disease	4,317 (32.8)	4 (11.4)	15 (51.7)	9 (34.6)	0.1

Data are presented as n (%) or median (interquartile range). LAGB, laparoscopic gastric banding; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass; BMI, body mass index.

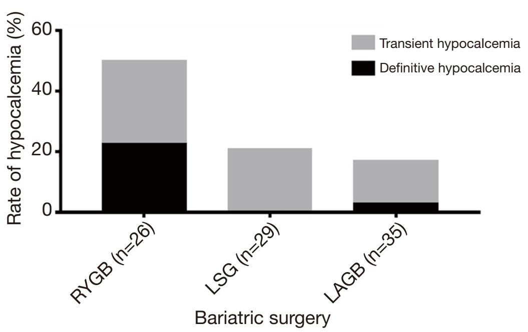

Figure 2 Hypocalcemia rate in patients with a history of bariatric surgery who underwent TT. LAGB, laparoscopic gastric banding; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass; TT, total thyroidectomy.

Discussion

According to the global registry report 2018 (International Federation for the Surgery of Obesity and metabolic disorders), bariatric surgery is on the rise worldwide (21). While different surgical procedures are available, currently, LSG and RYGB are the most commonly performed (21,22).

Many authors believe that LSG has similar mid- and long-term outcomes in terms of weight loss and resolution of obesity-related comorbidities when compared to RYGB (23-25); however, this is debatable (26,27). LSG is based on restriction and hormonal changes that may affect hunger and satiety, and not on malabsorption, thereby causing fewer nutritional or vitamin deficiencies (23).

Our findings show that patients undergoing restrictive procedures such as LSG or LAGB carry the same risk for post-thyroidectomy hypocalcemia as patients without a history of bariatric surgery; however, patients with a history of RYGB show an increased rate of this complication.

One possible explanation could be the malabsorption due to the modified anatomy of RYGB: the duodenum and the proximal jejunum have the highest concentration of calcium transporters, and are thus, the main absorption sites of calcium (28). After gastric bypass surgery, the food no longer passes through these portions of the bowel, resulting in calcium and vitamin D deficiencies (16,18).

Several authors have reported that gastric bypass patients who undergo TT have a higher rate of recalcitrant, symptomatic hypocalcemia and increased postoperative requirements of intravenous calcium, which leads to a prolonged hospital stay (15-19). Different strategies have been evaluated to prevent hypocalcemia in bariatric patients undergoing TT.

Manco *et al.* suggested that candidates for obesity surgery should be screened for thyroid dysfunction; if thyroid surgery is necessary, screening should be performed before the bariatric procedure (29). Controversy remains whether obesity increases intra- and postoperative morbidity. A recent prospective analysis did not reveal higher complication rates, despite a longer duration of the procedure (30). This finding conflicts with previous studies advocating that bariatric surgery should be performed first (31,32). We believe that it is of utmost importance that

Table 2 Hypocalcemia following TT

Variables	No previous bariatric surgery	LAGB	LSG	RYGB	P value
Patient number	13,152	35	29	26	–
Hypocalcemia	2,268 (17.2)	6 (17.1)	6 (20.7)	13 (50.0)	0.003
Transient	–	5	6	7	
Permanent	–	1	0	6	
Postoperative nadir calcium level*, mg/dL	8.8 (7.2–12.4)	8.8 (7.6–10.4)	8.8 (7.6–10.4)	8.4 (7.2–10.4)	0.04

Data are presented as n (%) or median (interquartile range). *, lowest concentration of calcium after thyroidectomy. LAGB, laparoscopic gastric banding; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass; TT, total thyroidectomy.

TT in these patients be performed in high volume centers specialized in endocrine surgery, in order to minimize the risk of complications such as hypoparathyroidism (11,33). Some useful tools during surgery could be considered, for a more meticulous parathyroid identification, such as indocyanine green angiography which assesses intraoperative parathyroid viability and guides autotransplantation (34).

In clinical practice, we may face two situations: (I) a patient candidate to bariatric surgery with a thyroid disease requiring TT and (II) a patient with a history of bariatric surgery who requires TT. Based on our results, we have considered a possible strategy for the management of these situations; however, further studies are mandatory to evaluate its clinical efficacy.

In the first situation, we suggest that TT be performed before RYGB for either malignant or benign thyroid diseases. Therefore, we could select patients unsuitable for RYGB, in case they developed permanent post-TT hypocalcemia. These patients could be rescheduled for restrictive procedures such as LSG; in our study, such patients showed similar results as the general population in terms of hypocalcemia. In obese candidates to a restrictive surgery, the bariatric procedure could be performed first in order to reduce the technical challenges of TT in these.

In the second situation, if thyroidectomy is required in a patient with a history of bariatric surgery, TT can be performed with no additional risk of hypocalcemia, provided that the patient underwent a restrictive procedure. For patients with a history of RYGB, the extent of thyroid surgery should be evaluated carefully, and lobectomy or subtotal thyroidectomy should be preferred when possible. However, this is only a clinical suggestion and is not yet supported by current scientific literature. Further studies are still need, and this suggestion struggles to present as a clinical algorithm. Evidence-based guidelines might be possible one day with the common effort and experience of bariatric and endocrine surgeons, defining metabolic surgery and with big data collecting and sharing systems.

Although patients with a history of bariatric surgery represent a minority of the cases who undergo TT (0.7% in our series), we believe that considering the increasing prevalence of bariatric surgeries worldwide, these patients should receive a greater focus. Hypocalcemia in RYGB patients is a clinical challenge since it might be recalcitrant to oral calcium and/or vitamin D supplementation.

There are some limitations to our study due to its observational and retrospective nature. We lack certain data such as the preoperative PTH levels, nutritional parameters, node dissection, presence of parathyroid in the specimen, and parathyroid auto-transplantation, which could be important in the interpretation of our results. Our results were not adjusted for other risk factors for postoperative hypocalcemia such as thyroid cancer stage nor percentage of Graves's disease. However, to the best of our knowledge, this is the largest series of bariatric patients undergoing TT in literature. Moreover, this cohort of patients represents a homogeneous group who underwent a standardized surgical procedure for thyroid diseases from 2006 to 2018, thereby eliminating the variability in surgical technique and approach. We believe that our findings could be a useful tool for endocrine surgeons performing TT in RYGB patients, as a reminder of a more carefully evaluated surgical indication and/or a more aggressive perioperative supplementation protocol.

Future studies are required to confirm the strength of our preliminary findings and our clinical suggestions. Big data collecting and sharing, such as EUROCRINE and BAETS databases are of the utmost importance in identifying prognostic factors of hypocalcemia in this specific cohort.

Conclusions

In conclusion, RYGB is a risk factor for postoperative hypocalcemia after TT, although restrictive bariatric procedures are not. An accurate preoperative assessment and supplementation of calcium and vitamin D deficiency in RYGB patients undergoing TT is paramount in preventing postoperative hypocalcemia. Further evaluation in prospective studies and big data gathering is necessary.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/gs-21-225

Data Sharing Statement: Available at https://dx.doi.org/10.21037/gs-21-225

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/gs-21-225). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Assistance Publique-Hôpitaux de Paris (APHP) (IRB number 20200115171338) and informed consent was taken from all the patients.

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