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ORIGINAL CONTRIBUTIONS

The Impact of Bariatric Surgery on Thyroid Function and Medication Use in Patients with Hypothyroidism

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Abstract
Background Bariatric surgery (BS) is effective in treating obesity and its associated comorbidities. However, there is a paucity of data on the effect of BS on thyroid function in hypothyroid patients, specifically in those treated with thyroid hormone replacement therapy (THR). The aim of this study was to assess the effect of BS on thyroid function and on THR dosage in patients with hypothyroidism.
Methods A retrospective analysis of prospectively collected data of all hypothyroid patients who underwent BS between 2010 and 2014 was performed. Data collected included demographic and anthropometric measurements, as well as changes in thyroid hormone levels and THR dosage up to a year from surgery.
Results During the study period, 93 hypothyroid patients (85 females, 91%), 83 of which treated with replacement thyroid hormone, underwent BS. Laparoscopic sleeve gastrectomy was performed in 77 (82.8%) and Roux-en-Y gastric bypass in 16 patients. Average age and body mass index (BMI) were 46.6 ± 11.2 years and 43.7 ± 6.4 kg/m^2, respectively. Mean BMI and thyroid-stimulating hormone (TSH) significantly deceased after 6 and 12 months following surgery whereas mean free T4 levels remained stable. TSH decrease was directly correlated to baseline TSH but not to BMI reduction. One year after surgery, 11 patients (13.2%) did not require THR, while the rest required a significantly lower average dose ($P < 0.02$).
Conclusions There is a favorable effect of BS on the hypothyroid bariatric population. This includes improvement of thyroid function and reduction of thyroid medication dosages. Further studies are required to evaluate an influence of THR absorption and compare different types of bariatric surgeries.

Keywords Sleeve gastrectomy · Roux-en-Y gastric bypass · Hypothyroidism · Thyroxin

Introduction

Morbid obesity is associated with significant comorbidities, including hypothyroidism [1]. The probability of thyroid replacement medication administration in patients undergoing bariatric surgery is ~20% [1, 2]. The correlation between obesity and hypothyroidism revolves around several putative mechanisms, including adipokines which impact thyroid function, a hypothalamic-pituitary-adipose axis, and the stimulatory effect of leptin on thyroid activity [3–5].

Bariatric surgery is effective in treating obesity-associated comorbidities [6–8]. However, the effect of bariatric surgery on hypothyroid patients is less clear. Weight loss induces a change in thyroid hormone levels, particularly TSH reduction in euthyroid and hypothyroid patients [9, 10]. Moreover, bariatric surgery has an influence on drug absorption and pharmacokinetics. Acidic gastric environment is important for maximal absorption of thyroxine [11].

The aim of this study was to assess the effect of bariatric surgery on thyroid function and dosage of thyroid hormone replacement (THR) in patients with hypothyroidism.

Methods

Retrospective analysis of a prospectively maintained database of all bariatric procedures performed was carried out querying

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all patients with hypothyroidism operated between 2009 and 2014. The diagnosis of hypothyroidism was made by the primary care physicians prior to the patients' referral and was not re-established by the authors. This diagnosis was made by the primary care physicians according to a TSH threshold between 4.5 and10 mIU/L. A minimum of two measurements were obtained before diagnosis was established. None of the patients had history of thyroid resection, ablation, or inflammation. Clinical variables recorded included the following: age, gender, body mass index (BMI) as well as thyroid-stimulating hormone (TSH), free T4 (FT4) levels, and THR dosage at baseline, 6, and 12 months following surgery.

THR therapy was managed by external endocrinologists or family practitioners to maintain a euthyroid state. The correlation between changes in thyroid hormone levels and change in BMI was evaluated at this time point for each individual patient.

Statistical analysis was performed using SPSS, Version 22.0 (Chicago, IL, USA). Continuous variables are described as mean ± standard error and range. Correlations were computed by Spearman rank order correlation. Student's paired sample *t* test was used for comparisons of paired measurements. The linear regression model was used to study the relationship between outcome variables. All tests are two-tailed and considered significant at $P < 0.05$.

Database collection as well as the study were approved by the institutional review board, and all patients signed an approved informed consent form.

Results

Of all bariatric procedures performed during the study period, 93 patients (5.1%) had previously diagnosed hypothyroidism. Patient characteristics are shown in Table 1. Mean age at the time of surgery was 46.6 ± 11.2 years (range 23–69), 85 patients were females (91%). Laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (LRYGB) were performed in 77 (82.8%) and 16 patients, respectively.

All patients were available for follow-up at the specified time points, with data acquired either during scheduled clinic appointments or, when necessary, phone interviews. Mean BMI decreased significantly from 43.7 ± 6.4 kg/m^2 at baseline to 34.4 ± 5.6 kg/m^2 and 29.8 ± 5.7 kg/m^2 after 6 and 12 months, respectively ($P < 0.01$ for both) (Fig. 1a). TSH levels were 3.9 ± 2.8 mU/L at baseline and decreased significantly to 3 ± 2.7 mU/L after 6 months ($P < 0.05$) and remained stable (3 ± 2.6 mU/L) at 12 months following surgery (Fig. 1b). FT4 levels were 13.7 ± 3.1 pmol/L at baseline and increased to 15 ± 4.2 and 14.9 ± 4.9 pmol/L at 6 and 12 months following surgery, respectively.

No correlation was observed between the decrease in TSH and BMI values prior to surgery or with BMI reduction after 6 and12 months (Fig. 2). Changes in TSH levels were significantly correlated with baseline TSH ($P < 0.01$) (Fig. 3).

Eighty-three patients (89%) were treated with THR therapy prior to surgery. The mean weekly LT4 dose prior to treatment was 688.5 + 40.4 mcg and deceased to 628.1 + 45.1 mcg 1 year following surgery ($P = 0.02$). Ten patients (12%) required a lower LT4 dose (by at least 100 mcg) than their initial treatment, and 11 patients (13.2%) discontinued any medical therapy following surgery (Fig. 4). The mean initial LT4 dose in this subgroup of patients was slightly lower compared to the patients who continued therapy (586.4 + 68.2); however, this difference was not statistically significant ($P = 0.16$). Characteristics of the patients with none or decreased LT4 requirement and those in whom it was unchanged did not differ in respect to age, gender, preoperative BMI, or preoperative LT4 dose.

Discussion

We examined the influence of bariatric surgery on thyroid function and thyroid hormone medication use. The prevalence of hypothyroidism in our morbidly obese patients was higher than in the general population, which is consistent with published data [2]. Patients scheduled for bariatric surgery should be screened for thyroid dysfunction and, if replacement therapy is necessary, strictly monitored [12].

There appears to be an improvement in thyroid function following surgery, reaching a statistical significance only at

Table 1 Patient characteristics

	Baseline	6 months after surgery	12 months after surgery
Gender *n* (%)	Female 85 (91%), male 8 (9%)		
Age ± SD (range)	46.6 ± 11.2 (23–69)		
BMI ± SD	43.7 ± 6.4 kg/m^2	34.4 ± 5.6 kg/m^2**	29.8 ± 5.7 kg/m^2**
TSH	3.9 ± 2.8 mU/L	3 ± 2.7 mU/L*	3 ± 2.6 mU/L*
FT4	13.7 ± 3.1 pmol/L	15 ± 4.2 pmol/L	14.9 ± 4.9 pmol/L
Weekly THR dose	688.5 + 40.4 mcg		628.1 + 45.1 mcg*

SD standard deviation, *BMI* body mass index, *TSH* thyroid-stimulating hormone, *FT4* free T4, *THR* thyroid hormone replacement

*$p < 0.05$; **$p < 0.01$

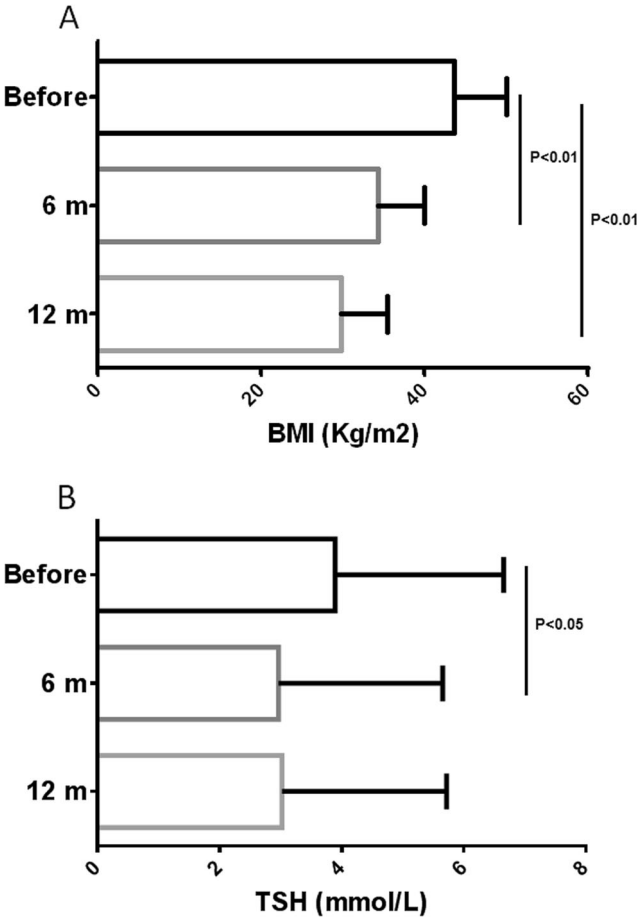

Fig. 1 Body mass index (BMI) (**a**) and thyroid-stimulating hormone (TSH) (**b**) changes 6 and 12 months following surgery

6 months after surgery. This improvement did not correlate with BMI reduction and concurs with similar reports [13]. The baseline TSH was positively correlated with TSH level decrease. The clinical significance of this finding is not clear; however, it emphasizes the positive effect of bariatric surgery in more severely hypothyroid patients.

The mechanism of thyroid dysfunction in morbid obesity is multifactorial. Our findings hint towards an important role of hormonal influence rather than weight loss alone. Ghrelin and leptin have been shown to have strong effect on thyroid function [5, 14, 15]. The change in these hormones' homeostasis following bariatric surgery may constitute a strong causative factor to thyroid function improvement.

We discovered a marked reduction in thyroid replacement therapy usage 1 year following bariatric surgery, including complete drug discontinuation in 13.2% of patients. This was observed at the same time point in which TSH was slightly increased. Thyroid hormone absorption seems to be less influenced by surgery than thyroid function. On the other hand, the reduction in thyroid drug consumption may be responsible for the observed mild deterioration of thyroid function between 6 and 12 months after surgery. It is arguable that, at least in part, the reduction in thyroid hormone replacement might be related to pharmacologic, rather than physiologic causes, mainly drug absorption and pharmacologic "volume of distribution." Thus, the observed improvement noted in our patient cohort does not necessarily reflect thyroid function. Changes in compliance with medications after surgery, when the patients tend to be under tighter medical surveillance, less food-related interference with absorption, or alterations in intestinal absorption of thyroid hormone, might also influence thyroid function tests. Alteration of intracellular conversion of T4 to T3 might also play a part in the generation of active thyroid hormone in tissues, independent of actual thyroid function.

Segal and co-authors reported that thyroid replacement therapy remained relatively constant between baseline and 12 months after surgery [2]. In a retrospective study of patients who underwent LRYGB, 23 of 224 (10.3%) patients were treated for hypothyroidism pre-operatively. Of these, hypothyroidism was improved, and thyroxine requirements were reduced in ten (43.5%) patients [10]. Based on the use of thyroid medication, Fazylov et al. reported that hypothyroidism improved or remained unchanged in most patients, barring those with autoimmune disease [16]. Rubio and co-workers showed that levothyroxine absorption was delayed after Roux-en-Y gastric bypass surgery [17]. There are some limitations of this study: first its retrospective, observational nature, with inherent drawbacks; second, the rather small study cohort limits its

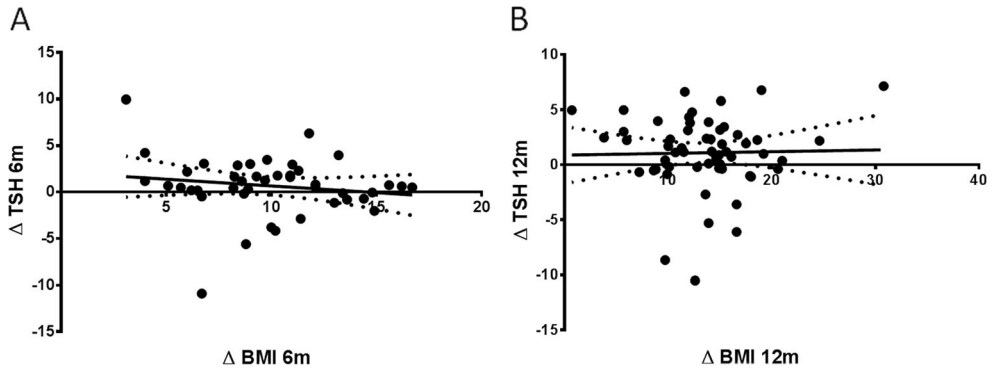

Fig. 2 Correlation between absolute changes in thyroid-stimulating hormone (TSH) levels and body mass index (BMI), 6 (**a**) and 12 (**b**) months following surgery

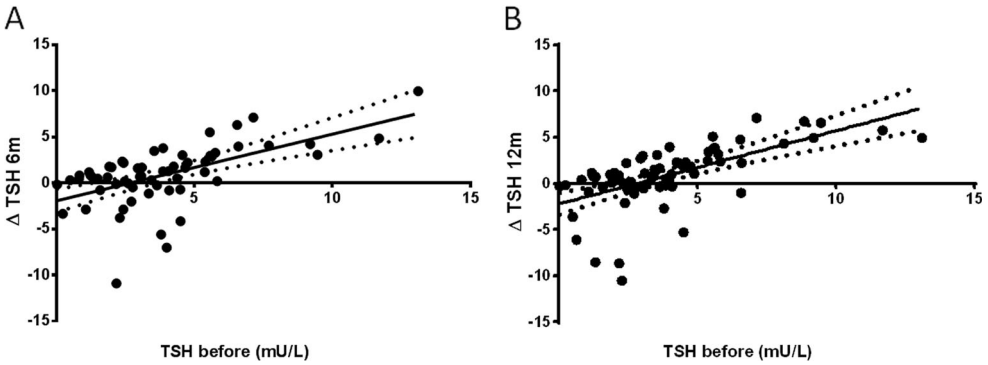

Fig. 3 Correlation between absolute changes in thyroid-stimulating hormone (TSH) levels and baseline TSH, 6 (**a**) and 12 (**b**) months following surgery

power; and third, the acceptance of a preoperative diagnosis of hypothyroidism by the referring physician without careful scrutiny of the severity or cause thereof. Some of the patients could have been treated with small dosages of LT4 or started THR due to small TSH increases without chronic autoimmune thyroiditis. Furthermore, morbid obesity in itself can lead to marginally increased TSH levels without inflammatory autoimmune disease. This subset of patients (not identified in our cohort) may have had marginally increased TSH levels reversed to normal after gastric bypass surgery [13].

To the best of our knowledge, this is the first study in the English literature that shows such a dramatic change in thyroid hormone treatment in a bariatric cohort consisting mainly of LSG patients. This might be of clinical importance since different procedures for morbid obesity influence drug absorption by combination of different mechanisms [18]. Weight loss in itself has a known effect on thyroid hormone levels. A decrease in leptin, which is secreted from adipocytes, has been suggested to have an effect on thyroid axis functioning. However, the lack of direct correlation between the percent of weight loss and TSH levels changes (Fig. 2), which implies that other factors may play a role. One suggested factor is the surgery itself. Previous studies suggested that the type of surgery may lead to different hormonal changes incurring different effects on thyroid function. A recent study by Emami and co-workers has shown that elevated circulating ghrelin levels are associated with TSH levels [14]. Since ghrelin levels were shown to be suppressed following LRYGB and LSG [19], it is plausible that this reduction may have an added effect to weight loss on the reduction in TSH.

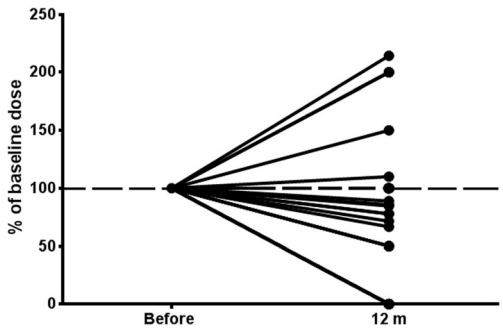

Fig. 4 Percent change in thyroid hormone replacement dose between baseline (100%) and 12 months following bariatric surgery

In summary, a favorable net effect of bariatric surgery on hypothyroid bariatric population was demonstrated, including improvement of thyroid function and reduction of thyroid medication dosages. Further studies are required to evaluate an influence of thyroid replacement therapy absorption and to compare different types of bariatric operations.

Compliance with Ethical Standards

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Conflict of Interest The authors declare that they have no conflict of interest.

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