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ORIGINAL CONTRIBUTIONS

Preoperative Thyroid Autoimmune Status and Changes in Thyroid Function and Body Weight After Bariatric Surgery

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Abstract

Background Bariatric surgery has emerged as the most effective therapy for morbid obesity. There is increasing evidence that bariatric surgery could alleviate systemic inflammation and influence thyroid function. The current study aimed to investigate the associations of preoperative thyroid autoimmune status with the changes in body weight and thyroid function after bariatric surgery.

Methods We recruited 101 patients with morbid obesity (44 men and 57 women) who received bariatric surgery at Zhongshan Hospital, Fudan University. Those who had used thyroid hormone replacement or antithyroid drugs were excluded. General linear models were used to compare the changes in body weight and thyroid function in participants with different thyroid autoimmune statuses.

Results After bariatric surgery, serum-free triiodothyronine (FT3) (4.94 ± 0.73 vs 4.33 ± 0.59 pmol/L, $P < 0.001$) and thyroid-stimulating hormone (TSH) (3.13 ± 1.59 vs 2.26 ± 1.26 μIU/mL, $P < 0.001$) were significantly reduced, accompanied by reductions in BMI (42.1 ± 7.6 vs 31.4 ± 6.5 kg/m^2, $P < 0.001$), and estimated basal metabolic rate (2002 ± 398 vs 1700 ± 336 kcal/day, $P = 0.001$) and an improvement in lipid profiles. Serum thyroperoxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) levels also decreased significantly from 79.3 and 177.1 IU/mL to 57.8 and 66.0 IU/mL in participants with positive thyroid antibodies ($P < 0.05$). Further analysis showed that the positive preoperative thyroid autoimmune status was associated with less reduction in serum TSH (0.05 ± 1.59 vs -1.00 ± 1.43 μIU/mL, $P = 0.021$) and BMI (-8.3 ± 3.6 vs -11.0 ± 4.5 kg, $P = 0.049$) after bariatric surgery.

Conclusion Our study highlights a group of patients with morbid obesity, who have positive preoperative thyroid autoimmunity and less reduction in serum TSH levels and body weight after bariatric surgery.

Keywords Bariatric surgery · Morbid obesity · Thyroid autoimmunity · Thyroid function · Retrospective study

Introduction

Obesity has become an epidemic health problem worldwide [1], affecting 11% of male and 15% of female adults [2], and 20% of the patients with obesity suffer from morbid obesity (body mass index (BMI) ≥ 40 kg/m^2 or ≥ 35 kg/m^2 with a comorbidity) in the USA [3]. For the patients with morbid obesity, lifestyle intervention and pharmacotherapy are usually unable to reduce body weight successfully and durably [4], and bariatric surgery is the most effective way to achieve a long-lasting body weight reduction and multiple metabolic benefits [5]. Great variability of weight loss has been noted after bariatric surgery [6]. Since bariatric surgery improves the whole-body metabolic status through a number of physiological mechanisms in addition to restricting calorie intake, such as changes in gut [7] and endocrine [8, 9] hormones, neural signaling [10], the gut microbiota [11], and bile acid secretion

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Hai-Fu Wu, Ming-Feng Xia, Xin Gao, Xin-Xia Chang and Xiao-Peng Zhu contributed equally to this work.

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[12], multiple factors are likely to influence the surgical outcomes but have not been studied yet.

Thyroid hormone is one of the most important hormones in the regulation of body thermogenesis and energy balance. Thyroid dysfunctions (elevation of thyroid-stimulating hormone (TSH) and high conversion of thyroxine (FT4) to triiodothyronine (FT3)) have been found in the obese subjects [13, 14], and reductions in serum TSH and free FT3 levels are accompanied with weight loss after bariatric surgery [15], probably due to changes in the secretion of several adipocytokines (e.g., leptin) [16]. One recent study even found that a high preoperative FT3 level could predict greater weight loss after bariatric surgery [17]. Thyroid autoimmunity is another key factor that determines the association between obesity and thyroid function [18]. Mounting evidence has indicated that bariatric surgery can alleviate systemic and local inflammation in patients with morbid obesity [19]. However, the association between thyroid autoimmunity and weight loss after bariatric surgery is still unknown. In the current study, we retrospectively analyzed the changes in serum thyroid antibodies and thyroid function in 101 Chinese adults after bariatric surgery and compared the changes in thyroid function, thyroid autoimmunity, and body weight after bariatric surgery between the subjects with positive and negative thyroid autoimmune statuses.

Methods

Patients

A total of 101 patients with morbid obesity (44 men and 57 women) who received bariatric surgery (96 vertical sleeve gastrectomies (VSG) and 5 Roux-en-Y gastric bypass surgeries (RYGB)) from June 2014 to June 2017 in Zhongshan Hospital, Fudan University were enrolled for the retrospective analysis. The study was approved by the ethics committee of Zhongshan Hospital, Fudan University and was conducted in accordance with the guidelines of the Declaration of Helsinki. Informed consent was obtained from all patients.

All patients fulfilled the criteria for bariatric surgery according to the guidelines of the Chinese Society for Metabolic and Bariatric Surgery (CSMBS): (1) aged 18 to 60 years and (2) BMI ≥ 32 kg/m^2 or BMI ≥ 27.5 kg/m^2 with one or more comorbidities, such as type 2 diabetes, dyslipidemia, or hypertension. In addition, all patients could not achieve long-term weight loss or control of comorbidities with nonsurgical treatment. Those with past or current use of thyroid hormone replacement or an antithyroid drug were excluded. All bariatric surgeries were performed by the same surgeon (HF Wu).

Study Design

Each patient was hospitalized for preoperative evaluation and postoperative follow-up at 1 month and 3–12 months after surgery. The anthropometric features, basal metabolic rate (BMR), serum lipid profile, systemic inflammation markers, thyroid function, and autoimmunity markers were measured before and at 3–12 months after bariatric surgery.

Anthropometric and Serum Biochemical Measurements

Body height and weight were measured with the participants wearing no shoes or outer clothing. BMI was calculated by dividing the weight in kilograms by the square of the height in meters. Waist circumference (WC) was measured using a soft tape at the midpoint between the lowest rib and the iliac crest in a standing position. Resting blood pressure and heart rate were measured using an oscillometric device (Omron HEM-7136; Omron Corporation, Kyoto, Kansai, Japan). After an overnight fast of at least 12 h, a venous blood sample was collected for biochemical examinations. The total white blood cells (WBCs) and their subtypes (neutrophils, lymphocytes, monocytes, eosinophils, and basophils) were measured using an automated blood cell counter (ADVIA 2120, Siemens Healthcare Diagnostics, Camberley, UK). Serum total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and triglyceride (TG) levels were measured by an oxidase method on a model 7600 automated bioanalyzer (Hitachi, Tokyo, Japan). Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation. Apoprotein A1 (ApoA1), apoprotein B (ApoB), apoprotein E (ApoE), and lipoprotein(a) (Lp(a)) were detected by immunoturbidimetric assays (ApoA1 and ApoB, DiaSys Diagnostic Systems Co. Ltd.; ApoE and Lp(a), Nittobo Boseki Co. Ltd., Tokyo). Serum FT3, free FT4, TSH, thyroglobulin, thyroperoxidase antibodies (TPOAb), and thyroglobulin antibodies (TgAb) were measured using the electrochemical luminescence method with a Modular E170 automatic electrochemiluminescence analyzer (Roche Diagnostics Co. Ltd., Germany). The hs-CRP level was measured by a modified laser nephelometric technique (Behring Diagnostics, GmbH, Rarburg, Germany) and tumor necrosis factor alpha (TNFα), soluble interleukin-2 receptor (IL-2R), and interleukin-6 (IL-6) were measured using a Quantikine Enzyme-Linked Immunosorbent Assay (ELISA) Kit (R&D Systems Inc., Minneapolis, MN, USA) according to the kit instructions.

Measurement of the Basal Metabolic Rate

The BMR was calculated using the Mifflin-St Jeor formula as follows [20].

Table 1 Anthropometric and serum biochemical parameters in obese adults before and after bariatric surgery, categorized by thyroid antibody

	All ($n = 101$)		Negative thyroid antibody ($n = 89$)		Positive thyroid antibody ($n = 12$)	
	Preoperation	Postoperation	Preoperation	Postoperation	Preoperation	Postoperation
Age, year	33.4 ± 11.8	–	32.8 ± 11.7	–	37.6 ± 12.8	–
Gender, M/F	44/57	–	40/49	–	7/5	–
Surgery type (VSG/RYGB)	96/5	–	85/4	–	11/1	–
Follow-up time, months	6 (3–12)	–	6 (3–12)	–	6 (3–12)	–
Weight, kg	121.4 ± 30.0	91.1 ± 23.8^{a}	121.5 ± 27.4	90.2 ± 22.2^{b}	114.1 ± 26.3	95.7 ± 22.0^{c}
BMI, kg/m^2	42.1 ± 7.6	31.4 ± 6.5^{a}	42.3 ± 7.6	31.3 ± 6.6^{b}	40.6 ± 7.7	32.3 ± 6.1^{c}
Waist circumference, cm	125.3 ± 19.5	104.1 ± 17.1^{a}	125.0 ± 20.1	102.7 ± 15.6^{b}	127.4 ± 15.3	107.5 ± 17.1^{c}
Hip circumference, cm	125.9 ± 20.0	113.2 ± 17.4^{a}	125.4 ± 20.8	113.1 ± 18.5^{b}	129.5 ± 13.5	112.1 ± 12.7^{c}
SBP, mmHg	136 ± 15	126 ± 17	137 ± 16	126 ± 18	132 ± 11	124 ± 11
DBP, mmHg	85 ± 12	80 ± 12	85 ± 13	80 ± 12	86 ± 6	79 ± 8
BMR by MSJ equation, kcal/d	2002 ± 398	1700±336^{a}	2015 ± 402	1704 ± 340^{b}	1906 ± 373	1675 ± 323^{c}
TG, mmol/L	1.6 (1.2–2.1)	0.9 (0.8–1.2)^{a}	1.6 (1.1–2.0)	0.9 (0.8–1.2)^{b}	1.6 (1.4–2.7)	1.0 (0.8–1.5)^{c}
TC, mmol/L	4.6 ± 1.0	4.2 ± 0.8^{a}	4.6 ± 0.9	4.2 ± 0.8^{b}	4.6 ± 1.3	4.1 ± 0.7^{c}
HDL cholesterol, mmol/L	1.02 ± 0.24	1.19 ± 0.39^{a}	1.03 ± 0.23	1.20 ± 0.41^{b}	1.03 ± 0.47	1.11 ± 0.23^{c}
LDL cholesterol, mmol/L	2.74 ± 0.84	2.57 ± 0.74^{a}	2.76 ± 0.84	2.57 ± 0.75^{b}	2.57 ± 0.94	2.46 ± 0.63^{c}
ApoA1, g/L	1.30 ± 0.24	1.24 ± 0.25^{a}	1.30 ± 0.24	1.24 ± 0.26^{b}	1.25 ± 0.24	1.25 ± 0.19
ApoB, g/L	0.91 ± 0.24	0.81 ± 0.22^{a}	0.91 ± 0.25	0.82 ± 0.22^{b}	0.89 ± 0.22	0.73 ± 0.18
ApoE, mg/L	45 (37–54)	35 (29–40)^{a}	46 (37-54)	35 (29–40)^{b}	45 (36–58)	35 (28–40)^{c}
Free fatty acid, mmol/L	0.56 ± 0.16	0.51 ± 0.18	0.55 ± 0.16	0.53 ± 0.17	0.59 ± 0.16	0.36 ± 0.17^{c}
FT3, pmol/L	4.94 ± 0.73	4.33 ± 0.59^{a}	4.99 ± 0.74	4.33 ± 0.59^{b}	4.60 ± 0.58	4.26 ± 0.57^{c}
FT4, pmol/L	16.03 ± 2.12	15.98 ± 1.80	15.97 ± 2.14	16.03 ± 1.82	16.19 ± 1.85	15.46 ± 1.57
FT3/FT4 ratio	0.31 ± 0.05	0.27 ± 0.03^{a}	0.32 ± 0.06	0.27 ± 0.03^{b}	0.29 ± 0.04	0.28 ± 0.04
TSH, μIU/mL	3.13 ± 1.59	2.26 ± 1.26^{a}	3.20 ± 1.60	2.20 ± 1.16^{b}	2.68 ± 1.52	2.73 ± 1.80
Thyroglobulin, ng/mL	12.5 (7.7–20.5)	9.5 (5.8–16.5)^{a}	12.8 (8.2–20.5)	9.5 (5.9–17.1)^{b}	6.7 (3.7–19.1) ^{b}	11.0 (2.7–14.2)
TPOAb, IU/mL	10.0 (7.6–13.6)	8.6(7.0–13.0)^{a}	9.5 (7.2–11.9)	8.5 (7.0–12.4)	79.3 (14.5–185.9)^{b}	57.8 (9.0–126.8)^{c}
TgAb, IU/mL	10.7 (10.0–14.0)	10.4 (10.0–12.7)	10.0 (10.0–13.0)	10.1 (10.0–11.9)	177.1 (15.0–341.5)^{b}	66.0 (12.9–212.5)^{c}
WBC, 10^9/L	8.3 ± 2.4	6.8 ± 1.9^{a}	8.4 ± 2.4	6.8 ± 1.7^{b}	7.3 ± 2.3	6.2 ± 2.5^{c}
Neutrophil, 10^9/L	4.9 ± 2.0	3.5 ± 1.3^{a}	5.0 ± 2.0	3.5 ± 1.1^{b}	4.0 ± 1.5	3.0 ± 1.8^{c}
Lymphocyte, 10^9/L	2.7 ± 0.8	2.6 ± 0.8	2.7 ± 0.8	2.6 ± 0.8	2.6 ± 1.0	2.5 ± 1.1
NLR	1.7 (1.4–2.2)	1.3 (1.0–1.7)^{a}	1.7 (1.4–2.2)	1.3 (1.0–1.7)^{b}	1.6 (1.4–1.7)	1.0 (0.8–1.6)^{c}
CRP, mg/L	6.5 (3.7–13.0)	1.5 (0.7–4.2)^{a}	6.6 (3.6–13.2)	1.8 (0.7–4.7)^{b}	5.7 (4.6–11.3)	1.2 (0.8–3.0)^{c}
TNF훼, pg/mL	8.5 (7.3–10.1)	8.4 (6.9–9.8)	8.5 (7.3–10.1)	8.5 (6.8–9.7)	8.0 (7.3–10.1)	7.6 (6.8–8.6)
s-IL-2R, U/mL	341 (268–428)	273 (243–332)^{a}	338 (270–404)	268 (243–323)^{b}	430 (237–505)	329 (196–431)^{c}
IL-6, U/mL	4.1 (2.5–6.1)	2.8 (2.0–4.5)^{a}	3.7 (2.3–5.7)	3.0 (2.0–4.5)	5.8 (4.9–17.5)^{b}	2.6 (2.4–4.5)

VSG, vertical sleeve gastrectomy; *RYGB*, Roux-en-Y gastric bypass surgery; *BMI*, body mass index; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *BMR*, basal metabolic rate; *MSJ equation*, Mifflin St Jeor equation; *TG*, triglycerides; *TC*, total cholesterol; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *ApoA1*, apoprotein A1; *ApoB*, apoprotein B; *ApoE*, apoprotein E; *FT3*, triiodothyronine; *FT4*, thyroxine; *TSH*, thyroid-stimulating hormone; *TgAb*, thyroglobulin antibody; *TPOAb*, thyroperoxidase antibody; *WBC*, white blood cell; *NLR*, neutrophil-to-lymphocyte ratio; *Lp(a)*, lipoprotein(a); *CRP*, C-reactive protein; *TNF훼*, tumor necrosis factor alpha; *s-IL-2R*, soluble interleukin-2 receptor; *IL-6*, interleukin-6

[a] $P < 0.05$ compared with all preoperative participants

[b] $P < 0.05$ compared with preoperative participants with negative thyroid antibody

[c] $P < 0.05$ compared with preoperative participants with positive thyroid antibody

For men: BMR = 10× kg (weight) + 6.25 ×cm (height) −5× years (age) + 5;

For women: BMR = 10× kg (weight) + 6.25× cm (height) − 5 ×years (age) − 161.

The estimated BMR is closely associated with thyroid function according to previous studies [21].

Statistical Analysis

All statistical analyses were performed using SPSS software version 18.0. The data are presented as the mean ± SD, except for skewed variables, which are presented as the median with the interquartile range (25–75%) given in parentheses. A paired *t* test or Wilcoxon test was used for comparisons of continuous data before and after surgery. The normal ranges of serum TPOAb and TgAb are < 34 IU/mL and < 115 IU/mL, respectively. The subjects were further divided into three groups: positive thyroid antibody group ($n = 12$), high normal TPOAb group ($n = 45$), and low normal TPOAb group ($n = 44$). We analyzed the changes in body weight, thyroid function, and BMR before and after surgery using a paired *t* test or Wilcoxon test and compared the changes in the above

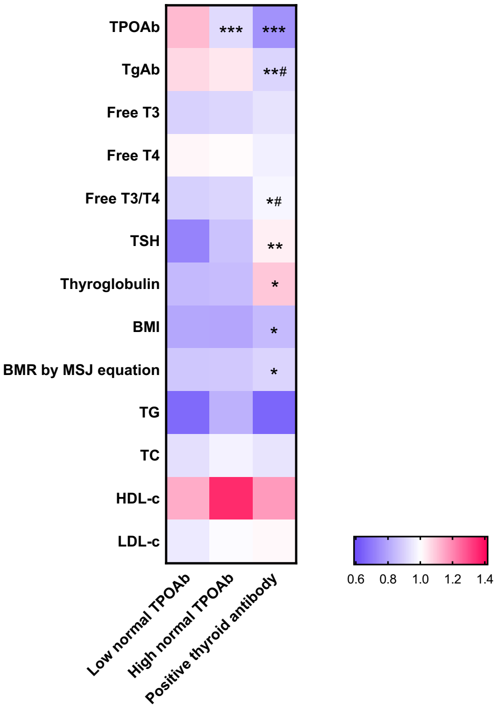

Fig. 1 Heatmap of the fold of change in thyroid function and antibodies, body weight, and lipid profile after bariatric surgery among groups with different thyroid autoimmune status (positive thyroid antibody, high normal TPOAb, and low normal TPOAb). The color code represents the fold change of all variables after bariatric surgery. A darker blue color indicates a greater fold decrease in the variable, and a brighter red color indicates a greater fold increase in the variable after surgery. *$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$, compared to the low normal thyroid antibody group. #$P < 0.05$, compared to the high normal thyroid antibody group

parameters among subjects with different thyroid autoimmune statuses using general linear models. The potential confounders successively adjusted for in multivariable models were age, gender, type of surgery, time after surgery, baseline value of BMI, TSH, and their changes as well as the changes in TPOAb. A value of $P < 0.05$ was considered statistically significant for all analyses.

Results

Baseline Characteristics

A total of 101 patients (44 men and 57 women), with an average age of 33.4 years old and an average BMI of 42.1 kg/m^2, were enrolled in the study. The preoperative and postoperative characteristics of all 101 patients are summarized in Table 1. The median follow-up time after surgery was 6 months. Among all subjects, 4 had a positive serum TgAb status (≥ 115 IU/mL), 5 had a positive serum TPOAb status (≥ 34 IU/mL), and 3 had a positive status for both TgAb and TPOAb.

Changes in Metabolic Parameters, Thyroid Function and Thyroid Autoimmunity after Bariatric Surgery

As shown in Table 1, the BMI decreased rapidly from 42.1 ± 7.6 to 31.4 ± 6.5 kg/m^2, and the WC decreased from 125.3 ± 19.5 to 104.1 ± 17.1 cm at a median of 6 months after surgery. With weight loss after surgery, a significant reduction in BMR from 2002 ± 398 to 1700 ± 336 kcal/day, and an improvement of serum lipid profiles (decrease in serum TG, TC, ApoA1, ApoB, and ApoE levels and increase in serum HDL cholesterol) were observed (all $P < 0.05$).

The serum FT3, TSH, and thyroglobulin levels decreased from 4.94 pmol/L, 3.13 μIU/mL, and 12.5 ng/mL before surgery to 4.33 pmol/L, 2.26 μIU/mL, and 9.5 ng/mL after surgery ($P < 0.001$) (Table 1). No significant change was observed in serum FT4 ($P = 0.783$). The postoperative changes in serum FT3, FT4, and TSH had no significant differences between obese patients undergoing VSG and RYGB (Supplementary Fig. 1). The median serum TPOAb and TgAb concentration was also significantly decreased from 79.3 and 177.1 IU/mL to 57.8 and 66.0 IU/mL in participants with positive thyroid antibodies. Consistent with the changes in thyroid antibodies, serum systemic inflammation markers, such as WBCs, the neutrophil-to-lymphocyte ratio, and CRP, soluble IL-2R and IL-6 levels were significantly decreased after bariatric surgery (all $P < 0.05$) (Table 1).

Comparison Among Subjects with Different Thyroid Autoimmunity Statuses

As shown in Fig. 1, the color code in the heatmap represents the fold change of all metabolic and thyroid parameters after bariatric surgery. Despite a remarkable reduction in serum thyroid antibody levels, participants with positive preoperative thyroid antibodies had significantly lower reductions in body weight, BMR, serum TSH, and FT3/FT4 ratios than those with normal thyroid antibodies after surgery. Participants with high and low normal thyroid antibodies showed no differences in the changes in most metabolic and thyroid parameters, except for a greater reduction in the TPOAb levels in the high normal thyroid antibody group.

Positive Preoperative Thyroid Autoimmunity Predicted Smaller Reductions in Body Weight and Serum TSH

As shown in Table 2, patients with positive thyroid antibodies exhibited smaller reductions in serum TSH levels (0.05 ± 1.59 μIU/mL vs − 1.00 ± 1.43 μIU/mL, $P = 0.021$),

Table 2 Changes in body weight and thyroid function after bariatric surgery according to preoperative thyroid autoimmunity status

	Mean changes (SD)	Additional changes after bariatric surgery		
		Unadjusted	Model 1	Model 2
FT3, pmol/L				
Thyroid antibody (+)	− 0.34 (0.42)	(Reference category)	(Reference category)	(Reference category)
Thyroid antibody (−)	− 0.66 (0.70)	− 0.32 (− 0.73~0.09)	− 0.09 (− 0.39~0.21)	− 0.19 (−0.55~0.18)
FT4, pmol/L				
Thyroid antibody (+)	− 0.73 (1.41)	(Reference category)	(Reference category)	(Reference category)
Thyroid antibody (−)	0.06 (1.85)	0.78 (0.32~1.88)	0.54 (− 0.35~1.43)	0.40 (− 0.68~1.48)
TSH, μIU/mL				
Thyroid antibody (+)	0.05 (1.59)	(Reference category)	(Reference category)	(Reference category)
Thyroid antibody (−)	− 1.00 (1.43)	− 1.05 (− 1.93~− 0.16)*	− 0.72 (− 1.39~− 0.05)*	− 0.99 (− 1.78~− 0.19)*
BMI, kg/m^2				
Thyroid antibody (+)	− 8.3 (3.6)	(Reference category)	(Reference category)	(Reference category)
Thyroid antibody (−)	− 11.0 (4.5)	− 2.7 (− 5.4~− 0.1)*	− 2.2 (− 4.4~− 0.1)*	− 2.0 (− 4.6~0.7)

Model 1: adjusted for age, gender, type of surgery, follow-up time after surgery, and the baseline values of the investigated parameter

Model 2: adjusted for covariates in Model 1, and changes in TPOAb, BMI, and TSH (change in BMI in the models for serum fT3, fT4, and TSH, change in TSH in the model for BMI)

*$P < 0.05$

compared with those with negative thyroid antibodies. After adjustment for age, gender, surgery type, baseline TSH, and changes in TPOAb and BMI, the presence of the positive preoperative thyroid antibodies remained significantly associated with less TSH reduction (~ 0.99 μIU/mL). Moreover, a smaller reduction in BMI was also observed in patients with positive thyroid antibodies than those with negative thyroid antibodies (-8.3 ± 3.6 kg/m^2 vs -11.0 ± 4.5 kg/m^2). However, the association between positive thyroid autoimmunity and less weight reduction after bariatric surgery no longer existed after further adjustment for the changes in serum TSH and TPOAb levels (Table 2).

Discussion

Although several previous studies have found the relationship between changes in thyroid hormones and weight reduction after bariatric surgery [15], the impact of bariatric surgery on thyroid autoimmunity and its association with the changes in body weight and thyroid function have been rarely studied. In our current study, we found that there was an improvement in thyroid autoimmunity after bariatric surgery, and the positive preoperative thyroid autoimmune status was associated with smaller changes in thyroid function and body weight after bariatric surgery in patients with morbid obesity.

Bariatric surgery is currently the most effective treatment for morbid obesity. It has been demonstrated that bariatric surgery is associated with a 24–29% reduction in mortality [22, 23], mainly due to the reduced risks of myocardial infarction and cancer [24, 25]. A substantial percentage of remission of diabetes, hypertension, dyslipidemia, and sleep apnea after bariatric surgery has also been recognized [26]. In addition to providing tremendous metabolic benefits, bariatric surgery is also known to reduce various inflammation markers in patients with obesity, such as CRP [27], IL-6 [28], IL-8, IL-18, and plasminogen activator inhibitor-1 (PAI-1) [29]. Moreover, the changes in inflammation markers might be different among the patients with different health conditions undergoing bariatric surgery, such as the different changes in PAI-1 in patients with and without diabetes [30]. Chronic autoimmune thyroiditis, also called Hashimoto's thyroiditis, is the most prevalent organ-specific autoimmune disease, affects 0.3–3% of the population [31], is closely associated with the inflammatory reaction in the thyroid gland [32] and is regulated by the inflammasome-derived cytokines in obesity [18]. Serum adipocytokine "leptin" levels are also independently associated with thyroid autoimmunity [14]. In our current study, patients with morbid obesity had higher proportion of autoimmune thyroiditis (12%) than the general population, and the serum TPOAb and TgAb levels were decreased after bariatric surgery, a change that was accompanied by alleviation of multiple systemic inflammation markers. Therefore, an improvement in thyroid autoimmunity after bariatric surgery is likely due to its inhibitory effects on multiple inflammatory pathways [19]. In accordance with our study results, one recent pilot study found an improvement in thyroid ultrasound hypoechogenicity related to local chronic inflammation after bariatric surgery-induced weight loss [33].

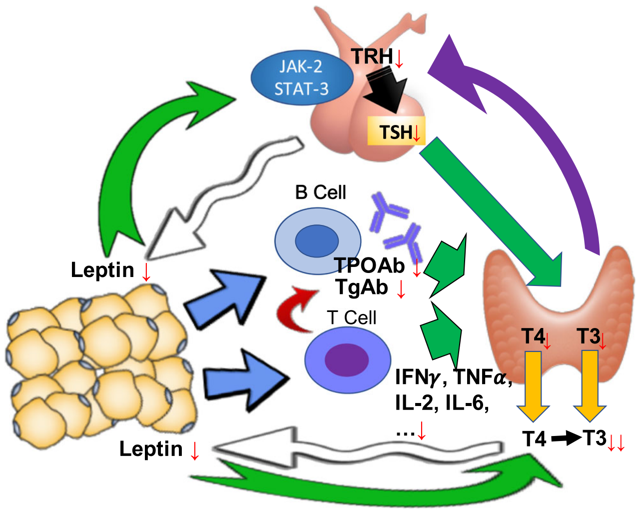

Fig. 2 The two interactions between adipose tissue and the thyroid gland and mechanisms underlying the changes in thyroid function after bariatric surgery. Expanded adipocytes in the condition of obesity release a series of adipokines (e.g., leptin). Green arrows show that leptin regulates thyroid function through two pathways: (1) leptin stimulates the secretion of thyrotropin-releasing hormone (TRH) and TSH via Janus activating kinase 2 (JAK-2) and signal transducer and activator of transcription 3 (STAT-3) factor, and promotes release of serum FT3 and FT4; (2) leptin directly drives the conversion of circulating T4 to T3. Blue arrows indicate that fat accumulation in the adipose tissue can lead to the activation of B and T lymphocytes to release thyroid autoimmune antibodies and a series of cytokines, which cause chronic lymphocytic thyroiditis, also known as "Hashimoto's thyroiditis", and influence the levels of circulating thyroid hormones. White arrows indicate that thyroid function and circulating FT3 and FT4 may regulate individual basal metabolic rate and influence the body weight and fat mass. After the bariatric surgery, the fat mass and the release of leptin from adipocytes are tremendously decreased, which not only reduces the activity of the hypothalamus-pituitary-thyroid axis but also inhibits the peripheral conversion of T4 to T3, thus reducing serum TSH and thyroid hormone concentrations. Bariatric surgery can also inhibit the activity of B and T lymphocytes and reduce the circulating levels of thyroid autoimmune antibodies and various inflammatory cytokines, which may protect the thyroid gland from the inflammatory injuries and forced release of stored thyroid hormones

Many previous studies have investigated the changes in thyroid function after bariatric surgery, but the results are inconsistent [34–37]. Bariatric surgery type, preoperative thyroid function, and postoperative follow-up duration might be associated with the changes in thyroid function after bariatric surgery, but the influence of these factors on the changes in thyroid function varied in different studies [15]. Some studies showed that serum TSH was reduced after RYGB but not laparoscopic adjustable gastric banding (LAGB) [38], while others reported that both VSG and RYGB would influence postoperative thyroid function [39]. In the current study, we found that serum FT3 and TSH were significantly reduced after VSG, and there were no differences in the changes in thyroid function between the obese patients undergoing VSG and RYGB, despite the fact that the changes in thyroid function did not achieve statistical significance in the 5 obese patients undergoing RYGB. Noticeably, we also further found that preoperative thyroid autoimmunity status might influence the changes in TSH after bariatric surgery. Indeed, the positive and negative thyroid autoimmune status might lead to two different types of changes in thyroid function after bariatric surgery: reductions in the serum FT3/FT4 ratio and TSH level in patients with negative thyroid autoimmune status and no changes in the serum FT3/FT4 ratio and TSH level in patients with positive thyroid autoimmune status. This finding is also consistent with previous studies that did not find a relationship between serum TSH and BMI in subjects with the presence of thyroid diseases and a high prevalence of autoimmune thyroiditis at a thyroid clinic [40].

There is a two-way interaction between adipose tissue and the thyroid gland [41]. As is shown in Fig. 2, on the one hand, cytokines (e.g., leptin) from the adipose tissue can act on the central nervous system to activate the hypothalamus-pituitary-thyroid axis and thereby increase TSH and thyroid hormone concentrations [42]. Deiodinase type 1 expression is also upregulated in the condition of obesity, which promotes the conversion of T4 to T3 [43]. On the other hand, chronic autoimmune thyroiditis and its related mild thyroid dysfunction may further contribute to a reduction in the BMR and progressive weight gain in patients with obesity. Our study further indicated that positive preoperative thyroid autoimmune status was related to less weight reduction after bariatric surgery. Multivariable analysis showed that the effect of thyroid autoimmunity on postoperative weight loss was dependent on the changes in thyroid function and autoimmune status after bariatric surgery. Therefore, a pharmacological modulation of thyroid function may help the obese patients with positive thyroid antibodies to achieve better weight reduction after bariatric surgery.

We must acknowledge the limitations of our work. As the first pilot study, only 12 patients with positive preoperative thyroid autoimmune antibodies were enrolled in our analysis due to the limited number of patients with morbid obesity undergoing bariatric surgery and the low percentage of autoimmune thyroiditis in the general population. Therefore, the results still need to be further verified in future larger prospective studies. Moreover, this study was performed on a Chinese cohort mostly undergoing VSG surgery; thus, the results still need to be confirmed in subjects with different ethnicities and bariatric surgery types.

Conclusion

Marked weight loss after bariatric surgery is accompanied by a parallel improvement in thyroid function and autoimmunity status. A positive preoperative thyroid autoimmune status is likely related to a smaller reduction in body weight and change in thyroid function after bariatric surgery.

Furthermore, our study also indicated that the blunted changes in thyroid function might be a potential therapeutic target in patients with positive thyroid autoimmunity submitted to bariatric surgery.

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Compliance with Ethical Standards

Competing Interests All authors state that they have no conflicts of interest.

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

Human Ethical Approval The study was approved by the ethics committee of Zhongshan Hospital, Fudan University and was conducted in accordance with the guidelines of the Declaration of Helsinki.

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