World J Surg (2021) 45:3130–3137
https://doi.org/10.1007/s00268-021-06201-5

ORIGINAL SCIENTIFIC REPORT

Laparoscopic Sleeve Gastrectomy has A Positive Impact on Subclinical Hypothyroidism Among Obese Patients: A Prospective Study

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Accepted: 31 May 2021 / Published online: 26 June 2021

Abstract

Background The effect of bariatric surgery on postoperative thyroid function remains incompletely understood. In this study, we aimed to evaluate the changes in thyroid functions after gastric sleeve operation for morbidly obese Egyptian patients.

Methods This was a prospective study that recruited 128 patients who underwent sleeve gastrectomy through the period from December 2016 to April 2020. We measured thyroid-stimulating hormone (TSH), free thyroxin (FT4), and free triiodothyronine. Subclinical hypothyroidism was defined by a TSH level > 4.5 mIU/L but a normal FT4 level. All patients were followed for 12 months after the procedure.

Results Preoperatively, 30 (23.4%) patients had subclinical hypothyroidism. The prevalence of subclinical hypothyroidism decreased significantly to reach 7.8% at the end of follow-up ($p < 0.001$). None of the patients developed de novo hypothyroidism at the end of follow-up. Patients with subclinical hypothyroidism were more likely to be females ($p = 0.037$) and had significantly higher waist circumference ($p < 0.001$), DBP ($p = 0.02$), serum cholesterol ($p < 0.001$), and serum triglyceride ($p < 0.001$). However, patients with subclinical hypothyroidism at the end of follow-up had significantly higher BMI at the end of the sixth month ($p = 0.048$). Similarly, patients with subclinical hypothyroidism at the end of follow-up had significantly higher serum cholesterol ($p = 0.002$), LDL, ($p = 0.038$), and serum triglyceride ($p < 0.001$) at the end of the sixth months of follow-up. A similar trend was noted at the end of the 12th month. The preoperative value of serum TSH correlated significantly with serum cholesterol and triglyceride levels.

Conclusion The positive effect of the LSG procedure on the hypothyroid bariatric population, including enhanced thyroid function, was demonstrated.

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Introduction

Technically, laparoscopic sleeve gastrectomy (LSG) consists of laparoscopic removal of about 75% of the stomach, which results in considerable calorie restriction [1]. This procedure is characterized by the lack of an intestinal bypass that prevents gastrointestinal hernias [2]. In general, females undergo bariatric surgery more frequently than males, according to the literature. Regardless of the weight loss, activation of some hormonal mechanisms such as increased GLP-1 hormone and decreased ghrelin, in addition to increased gastric emptying and intestinal transit, is the main benefit of this surgery [3, 4]. In addition to weight loss, LSG has many well-established metabolic benefits; insulin therapy diabetic patients have consistently experienced a high percentage of complete remission after bariatric operation [5]. Furthermore, bariatric operation changes the distribution of fat from visceral to the subcutaneous portion to support the metabolic change, with substantial loss of fatty tissue [6, 7]. Therefore, bariatric procedures not only manipulate the weight of the obese patients but also cause substantial rehabilitation of their body's damaged glucose and lipid homeostasis. It improves beta-cell sensitivity and hinders resistance to insulin in peripheral tissue [8, 9]

Hypothyroidism is one of the significant comorbidities associated with morbid obesity. In patients undergoing bariatric surgery, the risk of taking thyroid replacement drugs is approximately 20% [10, 11]. The mechanism of thyroid dysfunction in morbid obesity is multifactorial. Serum thyrotropin concentrations in obese are correlated more positively with bodyweight than in healthy individuals. The progression of obesity tends to stimulate the hypothalamic–pituitary–thyroid axis, similar to the changes in primary thyroid disease that may explain the increased TSH in obese populations [12]. Serum TSH was related to weight gain, even in the general population of euthyroid [13]. The thyroid function was reported to be strongly affected by ghrelin and leptin. Thus, following bariatric surgery, any change in the homeostasis of these hormones may contribute significantly to thyroid function improvement [14].

Bariatric procedures induce significant changes in the mechanisms of homeostatic, including glucose and lipid homeostasis, and enhance the hormone regulation system [15]. Thyroid and calcium homeostasis hormones are affected, as well [16]. It was reported that loss of weight causes alteration of thyroid hormone levels, particularly in euthyroid patients and hypothyroid patients [15, 16]. Free triiodothyronine (fT3) was observed to decrease after the surgery, while no changes were observed in the level of free thyroxine (fT4) [17]. Also, drug absorption and pharmacokinetics are impacted by bariatric surgery [18]. For maximum absorption of thyroxine, the acid gastric environment is essential [19]. To date, the impact of bariatric surgery on preoperative subclinical hypothyroidism and whether patients with preoperative hypothyroidism have not been well-studied yet. The effect of bariatric surgery on postoperative thyroid function remains incompletely understood with previous studies showing contradictory results regarding the variation of TSH after bariatric surgery and the relation of TSH variation with postoperative weight loss [20, 21]. Besides, according to the European and Brazilian guidelines, no enough data are available to support the use of hormonal replacement on hypothyroid patients undergoing bariatric surgery [22, 23].

In this study, we aimed to evaluate the changes in thyroid functions after gastric sleeve operation for morbidly obese Egyptian patients.

Materials and methods

Study design and participant

The present report was prepared according to the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) statement [24]. The study's protocol was approved by the local ethics committee of Kasr-Alainy University hospital.

This was a prospective study that recruited 144 patients who underwent sleeve gastrectomy at Kasr-Alainy University hospital. A total of 16 patients were excluded from the final analysis due to a history of L thyroxine therapy ($n = 12$) or lack of follow-up data at the end of the first year of follow-up ($n = 4$). Thus, the study enrolled a total of 128 patients. Written informed consent was obtained prior to the recruitment phase.

Clinical and laboratory parameters

We collected the following data from the records of eligible patients at the preoperative period, six months, and 12 months after the operation: demographic characteristics, anthropometric data (weight, body mass index [BMI], and height), systolic and diastolic blood pressure (SBP and DBP), fasting blood glucose, glycated hemoglobin (HbA1c), lipid profile, thyroid-stimulating hormone (TSH), free thyroxin (FT4), and free triiodothyronine (FT3). Subclinical hypothyroidism was defined by a TSH level > 4.5 mIU/L but a normal FT4 level [1].

Statistical analysis

The results of quantitative variables were described by mean and standard deviation (SD). Qualitative variables were described by frequencies and percentages. Cochran's Q test was used to test the significance of the changes in categorical variables over the follow-up period, while the repeated measures ANOVA was used to assess the changes in the quantitative variables. To evaluate the association between two independent quantitative variables, Spearman correlation coefficients were estimated. The comparison between quantitative and qualitative variables was done by using Student's t test for independent samples or the non-parametric Mann–Whitney U test. The level of significance was determined at the level of less than 0.05.

Results

The changes in patients' characteristics at the end of follow-up

The mean age of the included patients was 36.2 ± 9.7 years old, and 67.2% of the patients were females. The patients had a preoperative weight of 128.6 ± 10.5 kg, a BMI of 47.75 ± 9.46 kg/m2, and a waist circumference of 116.29 ± 4.6 cm. Regarding thyroid variables, the average values of TSH, FT4, and FT3 were 3.37 ± 1.29 mU/L, 1.14 ± 0.55 ng/d, and 2.86 ± 0.35 ng/d, respectively. The serum TSH found decreased significantly to 2.69 ± 1.1 ng/dL and 2.0947 ± 1.2 ng/dL after six and 12 months, respectively ($p < 0.001$). We also found a significant reduction in the serum FT4 after six months (1.04 ± 0.1ug/dL) and 12 months (1.03 ± 0.1ug/dL; $P = 0.015$). Likewise, there was a statistically significant reduction in body weight, BMI, fasting glycemia, total cholesterol, LDL, HDL, triglycerides at the end follow-up (Table 1).

Association between preoperative subclinical hypothyroidism and study's parameters

Preoperatively, 30 (23.4%) patients had subclinical hypothyroidism. The prevalence of subclinical hypothyroidism decreased significantly to reach 7.8% at the end of follow-up ($p < 0.001$; Fig. 1). None of the patients developed de novo hypothyroidism at the end of follow-up. Patients with subclinical hypothyroidism were more likely to be females ($p = 0.037$) and had significantly higher waist circumference ($p < 0.001$), DBP ($p = 0.02$), serum cholesterol ($p < 0.001$), and serum triglyceride ($p < 0.001$; Table 2). However, patients with subclinical hypothyroidism at the end of follow-up had significantly higher BMI at the end of the sixth month ($p = 0.048$). Similarly, patients with subclinical hypothyroidism at the end of follow-up had significantly higher serum cholesterol ($p = 0.002$), LDL, ($p = 0.038$), and serum triglyceride ($p < 0.001$) at the end of the sixth months of follow-up. A similar trend was noted at the end of the 12th month (Table 3).

Correlation analysis

The preoperative value of serum TSH correlated significant with serum cholesterol ($r = 0.37$; $p = 0.001$) and triglyceride levels ($r = 0.37$; $p = 0.001$; Fig. 2). On the other hand, the change in TSH level at the end of follow-up did not correlate significantly with any of the postoperative metabolic parameters ($p > 0.05$).

Discussion

In this study, we aimed to evaluate the changes in thyroid functions after gastric sleeve operation for morbidly obese Egyptian patients. Overall, we observed that the prevalence of subclinical hypothyroidism among obese patients undergoing LSG was 23.4%; the LSG had a positive impact on this prevalence and significantly reduced the prevalence of subclinical hypothyroidism to 7.8% at the end of follow-up. None of the patients developed de novo hypothyroidism at the end of follow-up. Patients with subclinical hypothyroidism were more likely to be females and had significantly higher weight circumference, DBP, serum cholesterol, and serum triglyceride.

Subclinical hypothyroidism significantly increases the risk of cardiovascular diseases, endothelial dysfunction, ventricular dysfunction, and dyslipidemia [25, 26]. The prevalence of subclinical hypothyroidism was higher in our morbidly obese patients (23.4%) than in the general population from Middle East (3–10%) [27, 28], which is consistent with the literature. Thyroid dysfunction should be screened for patients scheduled for bariatric surgery and strictly controlled if replacement therapy is required. A significant association was observed between hypothyroidism and high weight circumference ($p < 0.001$), DBP ($p = 0.02$), serum cholesterol ($p < 0.001$), and serum triglyceride ($p < 0.001$). Razvi et al. [29] showed a significant elevation in the DBP and total cholesterol in the subclinical hypothyroidism patients compared with euthyroid ($p = 0.02$). Atherosclerosis, metabolic syndrome, and heart failure were also reported to be linked to mild dysfunction of the thyroid gland [30].

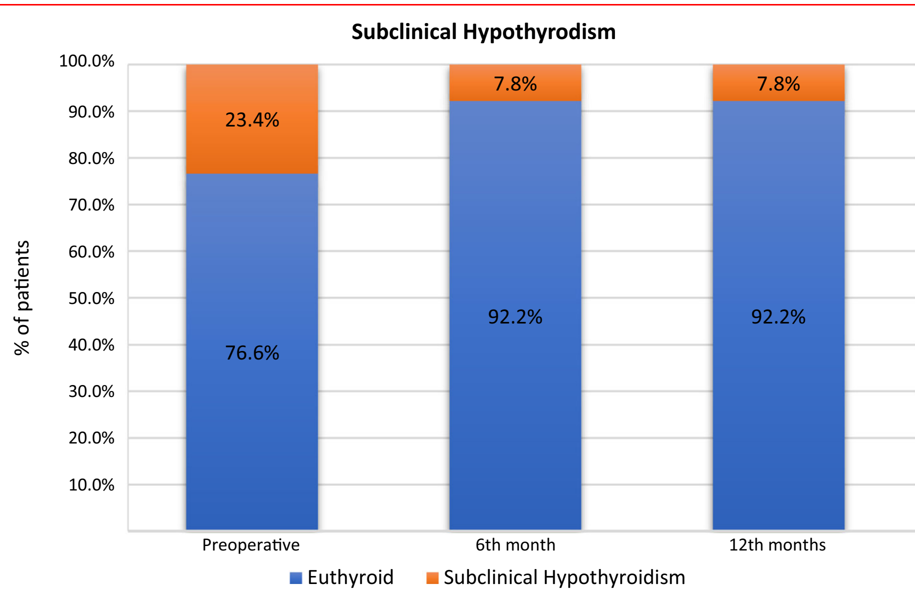
Six months after the procedure, we found a significant reduction in the TSH and fT4 levels ($p < 0.001$). The same was observed 12 months after the procedure. Moreover, the

Table 1 The changes in anthropometric and biochemical parameters

Variables	Patients (n = 128)			p-value
	Baseline	Sixth month	12th months	
Weight (kg), mean ± SD	128.6 ± 10.5	108.48 ± 9.7	94.8 ± 7	< 0.001
BMI (kg/m^2), mean ± SD	47.75 ± 9.46	39.59 ± 3	34.71 ± 2.4	< 0.001
Waist circumference (cm), mean ± SD	116.29 ± 4.6	110.2 ± 3.9	103.5 ± 4.1	< 0.001
SBP (mmHg), mean ± SD	130.42 ± 8.5	127.43 ± 6.1	125.53 ± 5.9	< 0.001
Hypertension, no (%)	20 (15%)	0(0%)	0 (0%)	< 0.001
FBG (mg/dL), mean ± SD	109.42 ± 21	103.2 ± 18.1	99.9 ± 16.5	< 0.001
HbA1c (%), mean ± SD	6.2 ± 0.74	5.76 ± 0.7	5.4 ± 0.47	< 0.001
Diabetes, no. (%)	37 (27.8%)	19 (14.3%)	3 (2.3%)	< 0.001
Prediabetic, no. (%)	37 (27.8%)	22 (16.5%)	3 (2.3%)	< 0.001
Serum cholesterol (mg/dL), mean ± SD	181.13 ± 22.2	165.1 ± 18.3	161.9 ± 17.3	< 0.001
Serum LDL (mg/dL), mean ± SD	113.21 ± 21.6	106.1 ± 17.1	102.7 ± 16.3	< 0.001
Serum HDL (mg/dL), mean ± SD	43.37 ± 5.2	41.3 ± 5.4	42.96 ± 5.1	< 0.001
Serum triglyceride (mg/dL), mean ± SD	145.87 ± 32.8	139.13 ± 25.2	144.4 ± 99.9	< 0.001
Hyperlipidemia, no. (%)	19 (14.3%)	12 (9%)	6 (4.5%)	< 0.001
Serum TSH (ng/dL), mean ± SD	3.37 ± 1.29	2.69 ± 1.1	2.0947 ± 1.2	< 0.001
Serum FT4 (ug/d), mean ± SD	1.14 ± 0.55	1.04 ± 0.1	1.03 ± 0.1	0.015
Serum FT3 (ug/d), mean ± SD	2.86 ± 0.35	2.97 ± 0.35	2.93 ± 0.33	0.003

Repeated measures ANOVA. Cochran's Q test was used in categorical variables

Fig. 1 The changes in the frequency of subclinical hypothyroidism



prevalence of subclinical hypothyroidism decreased significantly to reach 7.8% at the end of follow-up ($p < 0.001$), associated with a significant reduction in body weight, BMI, weight circumference, fasting glycemia, total cholesterol, LDL, HDL, and triglycerides. These findings emphasize the positive effect of bariatric surgery on hypothyroid patients. Besides, weight loss from bariatric operation in euthyroid patients with morbid obesity was reported to be significantly associated with a decrease in TSH [31, 32]. Normalization of TSH after bariatric surgery

Table 2 The difference in preoperative characteristics between patients with euthyroid and patients with subclinical hypothyroidism

Variable	Euthyroid (*n* = 98)	Subclinical hypothyroidism (*n* = 30)	*P*-value
Female, no. (%)	55 (56.1%)	22 (73.3%)	0.037
Age (years), mean ± SD	36.2 ± 9.7	34.2 ± 7.1	0.72
Weight (kg), mean ± SD	127.91 ± 10.1	131.1 ± 11.5	0.15
Height (cm), mean ± SD	164.72 ± 17.7	162.8 ± 9.2	0.57
BMI (kg/m^2), mean ± SD	47.22 ± 10.6	49.5 ± 3.3	0.24
Waist circumference (cm), mean ± SD	115.4 ± 4.1	119.2 ± 5.2	< 0.001
SBP (mmHg), mean ± SD	130.17 ± 7.9	131.23 ± 10.2	0.55
FBG (mg/dL), mean ± SD	111.3 ± 21.3	103.1 ± 18.8	0.06
HbA1c (%), mean ± SD	6.2 ± 0.7	6.3 ± 0.8	0.51
Diabetes, no. (%)	24 (24.5%)	13 (43.3%)	0.05
Prediabetic, no. (%)	29 (38.7%)	8 (26.7%)	0.52
SBP (mmHg), mean ± SD	130.17 ± 7.9	131.2 ± 10.3	0.55
DBP (mmHg), mean ± SD	80.6 ± 6.2	83.6 ± 6.5	0.02
Hypertension, no (%)	14 (14.3%)	6 (20%)	0.45
Serum cholesterol (mg/dL), mean ± SD	175.9 ± 21.3	197.9 ± 18.1	< 0.001
Serum LDL (mg/dL), mean ± SD	111.2 ± 19.5	119.7 ± 26.9	0.061
Hyperlipidemia, no. (%)	7 (7.1%)	12 (40%)	< 0.001
Serum HDL (mg/dL), mean ± SD	43.5 ± 4.2	42.96 ± 5.1	0.94
Serum triglyceride (mg/dL), mean ± SD	139.1 ± 33.5	168.2 ± 16.7	< 0.001
Serum TSH (ng/dL), mean ± SD	2.6 ± 1.1	5.9 ± 2.5	< 0.001
Serum FT4 (ug/d), mean ± SD	1 ± 0.1	1.1 ± 0.13	0.14
Serum FT3 (ug/d), mean ± SD	2.9 ± 0.4	2.9 ± 0.4	0.49

Student's t test for independent samples or the nonparametric Mann–Whitney U test. For categorical Chi-square test

was observed in patients with a clinical diagnosis of hypothyroidism [33, 34]. Previous research provided contradictory results concerning the impact of bariatric surgery on thyroid functions; most [21, 32], but not all [35], studies found that TSH was substantially decreased, but FT4 was not changed, following the procedure due to include specific study population baseline characteristics, the types of operation, and follow-up durations. Zendel et al. conducted a study on 93 hypothyroid patients who underwent bariatric surgery. They demonstrated that mean TSH levels were significantly declined after 6 and 12 months, with no changes in mean FT4 levels [36]. The findings of Neves et al., who found a significant reduction in the TSH levels in patients with high-normal TSH after 12 months of bariatric procedure, indicate that patients with morbid obesity and higher TSH levels tend to normalize thyroid function following metabolic surgery [32]. Zhu and his colleagues showed a significant reduction in TSH levels with no change in T4 levels after LSG in both subclinical hypothyroidism and euthyroid. Moreover, they recorded a 92.8% normalization of TSH among the subclinical hypothyroidism patients 12 months after LSG, which was similar to a 90% remission after LSG described by Ruiz-Tovar et al. [37]. Interestingly, the degree of TSH change at the end of follow-up did not correlate significantly with the degree of weight loss and BMI. In agreement, Zendel et al. and Moulin de Moraes et al. did not report a significant correlation between TSH reduction and weight loss or BMI [36, 38].

While the exact underlying mechanisms associated with the positive impact of bariatric surgery on thyroids function have not fully elucidated yet, many theories have been proposed over recent years. Many authors suggested that the normalization of thyroid hormones following bariatric surgery is closely related to leptin changes after the procedure, and leptin hormone significantly influences the release of THR [39]. According to previous reports, patients exhibited a significant reduction in leptin levels after bariatric surgery, which can be translated into the normalization of TSH levels. The positive impact of LSG on ghrelin levels can provide an additional explanation for thyroid function changes after the surgery [40], and the ghrelin levels were found to be positively correlated with TSH levels [41]. Thus, the combination of weight loss and hormonal changes after the LSG seems to provide potential explanations of the physiologic mechanisms which may be

Table 3 The difference in postoperative characteristics between patients with euthyroid and patients with subclinical hypothyroidism

Variable	Sixth months		*P*-value	12th months		*P*-value
	Euthyroid (*n* = 118)	Subclinical hypothyroidism (*n* = 10)		Euthyroid (*n* = 118)	Subclinical hypothyroidism (*n* = 10)	
Weight (Kg), mean ± SD	108.34 + 9.84	110.2 + 9.1	0.001	94.85 + 7.12	94.3 + 5.1	0.003
BMI (kg/m^2), mean ± SD	39.42 + 3.089	41.63 + 2.99	0.001	34.63 + 2.33	35.7 + 3.31	0.005
FBG (mg/dL), mean ± SD	103.98 + 18.1	93.7 + 16.58	0.001	100.65 + 18.1	90.9 + 15.07	0.001
HbA1c (%), mean ± SD	6.11 ± 0.72	5.34 ± 0.65	0.084	5.9 ± 0.52	5.1 ± 0.39	0.063
Diabetes, no. (%)	16 (13.6%)	3 (30%)	0.169	2(1.7%)	1 (10%)	0.218
Prediabetic, no. (%)	19 (16.1%)	3 (30%)	0.374	2(1.7%)	1 (10%)	0.218
Serum Cholesterol (mg/dL), mean ± SD	163.8 ± 18.33	179.7 ± 11.98	0.001	160.7 ± 17.2	175.8 ± 11.35	0.001
Serum LDL (mg/dL), mean ± SD	105.2 ± 17.0	116.7 ± 14.62	0.001	101.89 ± 16.2	112.8 ± 13.9	0.001
Serum HDL (mg/dL), mean ± SD	41.01 ± 5.4	43.9 ± 3.95	0.001	42.7 ± 5.018	45.5 ± 4.0	0.003
Serum triglyceride (mg/dL), mean ± SD	137.5 ± 25.5	158.2 ± 8.79	0.012	143.6 ± 104.1	153.7 ± 8.76	0.093
Hyperlipidemia, no. (%)	8 (6.8%)	4 (40%)	0.007	5 (4.2%)	1 (10%)	0.392
Serum TSH (ng/dL), mean ± SD	2.5 ± 0.92	4.92 ± .31	0.001	2.46 ± 0.89	4.67 ± .016	0.001
Serum FT4 (ug/d), mean ± SD	1.04 ± 0.1	1.0 ± 0.13	0.001	1.03 ± 0.1	1.02 ± 0.15	0.001
Serum FT3 (ug/d), mean ± SD	2.96 ± 0.35	3.02 ± 0.26	0.001	2.93 ± 0.33	2.97 ± 0.33	0.001

Student's t test for independent samples or the nonparametric Mann–Whitney U test. For categorical Chi-square test

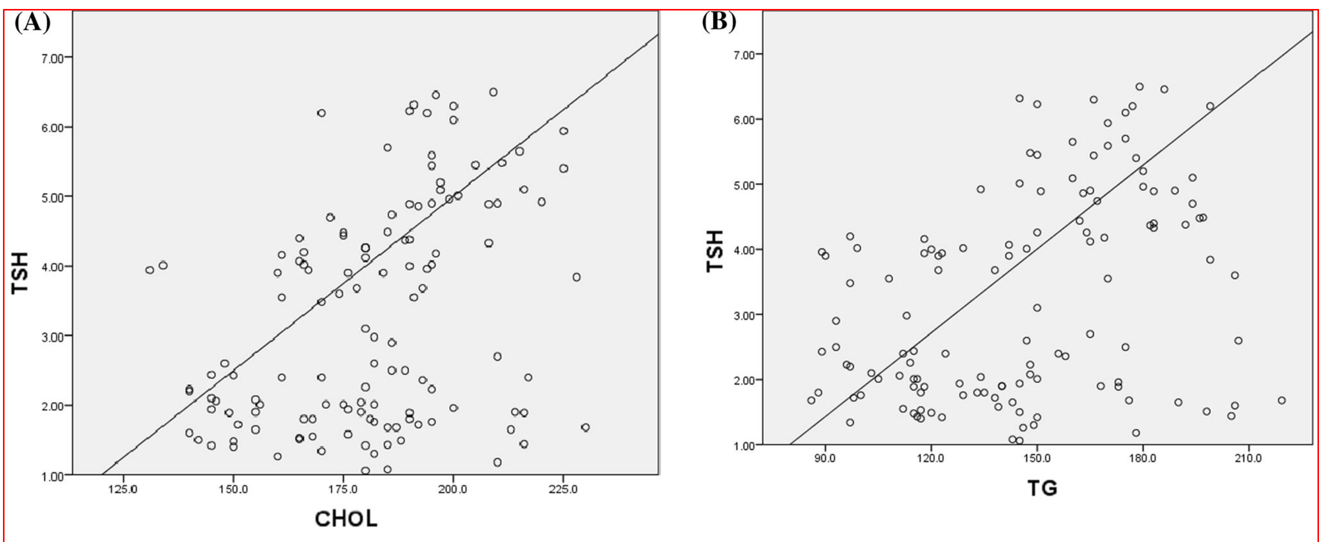


Fig. 2 Correlation between serum TSH and **a** cholesterol and **b** triglyceride

responsible for the observed improvement of thyroid function after LSG.

In conclusion, the positive effect of the LSG procedure on the hypothyroid bariatric population, including enhanced thyroid function, was demonstrated. Further studies are required to evaluate the effect of absorption of thyroid replacement therapy and to compare the various types of bariatric operations.

Funding None. (Authors confirm they did not receive any funding to do this work.)

Declarations

Conflict of interest All authors confirm no financial or personal relationship with a third party whose interests could be positively or negatively influenced by the article's content.

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