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ORIGINAL ARTICLE

Thyroid function tests after sleeve gastrectomy in euthyroid obese patients

Ötiroid obez hastalarda sleeve gastrektomi sonrası tiroid fonksiyon testleri

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ABSTRACT • **Background and Aims:** Obesity is a well-known clinical problem. It has secondary outcomes and complications that cause mortality and morbidity. The aim of this study is to define the alterations in thyroid function tests after sleeve gastrectomy. **Materials and Methods:** A total of 85 patients, 79 females and 6 males, were included in the study. Each patient's body mass indexes, free triiodothyronine (freeT3), free thyroxine (freeT4), and thyroid stimulating hormone levels at preoperative and post-operative 6th and 12th month visits were recorded. Thyroid function tests of the patients grouped as group 0: preoperative, group 1: postoperative 6 months, group 2: postoperative 12-month for each test, respectively. All analyses were performed by means of the chemiluminescence method (Liaison®; DiaSorin S.p.A., Saluggia, Italy). **Results:** Serum freeT3 levels were decreased in all postoperative visits compared to the preoperative period. Median (25% - 75%) values for each visit were as follows: freeT3$_0$: 3.04 pg/mL (3.25 - 2.77), freeT3$_1$: 2.68 pg/mL (2.9 - 2.36), freeT3$_2$: 2.6 pg/mL (2.91 - 2.38). Serum freeT4 levels increased at the post-operative 6th month visit, and then decreased at the post-operative 6th month visit. Median (25% - 75%) values at each visit for were as follows, freeT40: 1.04 ng/dL (1.15 - 0.99), freeT4$_1$: 1.06 ng/dL (1.15 - 0.99), freeT4$_2$: 1.03 ng/dL (1.3 - 0.94). Serum thyroid stimulating hormone levels were decreased at post operative all visits compared to preoperative period. Median (25% - 75%) values at each visit were as follows: thyroid stimulating hormone$_0$: 2.16 µIU/L (2.81 - 1.49), thyroid stimulating hormone$_1$: 1.48 µIU/L (2.46 - : 0.93), thyroid stimulating hormone$_2$: 1.47 µIU/L (2.3 - 0.92). There was no correlation between the decrease in thyroid stimulating hormone levels and the body mass index decrement after sleeve gastrectomy. **Conclusions:** We determined a significant decrease in thyroid stimulating hormone and freeT3 levels, and there was a fluctuating pattern in freeT4 levels after sleeve gastrectomy.

Key words: Obesity, sleeve gastrectomy, thyroid function tests

ÖZET • **Giriş ve Amaç:** Obezite, dünya genelinde bilinen bir klinik problemdir. Mortalite ve morbiditeye yol açan sekonder sonuçları ve komplikasyonları vardır. Bu çalışmanın amacı, sleeve gastrektomi sonrası tiroid fonksiyon testlerindeki değişiklikleri tanımlamaktır. **Gereç ve Yöntem:** Toplamda 85 hasta; 79 kadın ve 6 erkek çalışmaya dahil edilmiştir. Her hastanın, preoperatif ve postoperatif 6. ve 12. ay ziyaretlerinde vücut kitle indeksi, serbest T3, serbest T4, tiroid uyarıcı hormon seviyeleri kaydedilmiştir. Hastaların tiroid fonksiyon testleri, her test için sırasıyla grup 0: preoperatif, grup 1: postoperatif 6. ay, grup 2: postoperatif 12. ay olarak gruplandırılmıştır. Tüm analizler, kemilüminesans yöntemi (Liaison®; DiaSorin S.p.A., Saluggia, İtalya) ile gerçekleştirilmiştir. **Bulgular:** Serum serbest T3 seviyeleri, postoperatif tüm vizitlerde preoperatif döneme göre azalmıştır. Her vizit için medyan (25% - 75%) değerleri aşağıdaki gibidir: serbest T30: 3.04 pg/mL (3.25 - 2.77), serbest T31: 2.68 pg/mL (2.9 - 2.36), serbest T32: 2.6 pg/mL (2.91 - 2.38). Serum serbest T4 seviyeleri, postoperatif 6. ay vizitte artmış, ardından postoperatif 12. ay vizitte azalmıştır. Her vizit için medyan (25% - 75%) değerleri aşağıdaki gibidir: serbest T40: 1.04 ng/dL (1.15 - 0.99), serbest T41: 1.06 ng/dL (1.15 - 0.99), serbest T42: 1.03 ng/dL (1.3 - 0.94). Serum tiroid uyarıcı hormon seviyeleri, postoperatif tüm vizitlerde preoperatif döneme göre azalmıştır. Her vizit için medyan (25% - 75%) değerleri aşağıdaki gibidir: tiroid uyarıcı hormon0: 2.16 µIU/L (2.81 - 1.49), tiroid uyarıcı hormon1: 1.48 µIU/L (2.46 - 0.93), tiroid uyarıcı hormon2: 1.47 µIU/L (2.3 - 0.92). Sleeve gastrektomi sonrası tiroid uyarıcı hormon seviyelerindeki azalma ile vücut kitle indeksi düşüşü arasında bir korelasyon tespit edilmemiştir. **Sonuç:** Sleeve gastrektomi sonrası tiroid uyarıcı hormon ve serbest T3 seviyelerinde önemli bir azalma tespit ettik ve serbest T4 seviyelerinde dalgalı bir patern gözlemlendi.

Anahtar kelimeler: Obezite, sleeve gastrektomi, tiroid fonksiyon testleri

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INTRODUCTION

Obesity has become a major public health problem with increasing prevalence all around the world. It has deleterious effects on many organ systems and metabolism in the body. Current therapeutic options are: Life style changes, reduced calorie intake, pharmacological agents and surgical methods (bariatric surgery) (1).

There are two types of bariatric surgery methods now used in obesity treatment. These methods use either causing shrinkage of the stomach or cause to malabsorbtion (2). The sleeve gastrectomy technique is one of the surgical methods used in the treatment of obesity by reducing the gastric volume. Stomach become tube shaped structure. This method has rare malabsorption complications compared to other bariatric surgery techniques (3).

Sleeve gastrectomy has effects on the endocrine system, entero-endocrine system, nervous system, cardiovascular system, liver functions, renal functions, and psychological status (4-10).

Effects of surgical treatment for obesity on thyroid functions have been the subject of many studies; however, contradictory results have been found in these studies (11-14). Several mechanisms are assumed to explain the relation between thyroid function and weight loss after surgery. Accused mechanisms are as follows: body mass index (BMI) increase cause increament in serum TSH levels (15), decrease in leptin levels may affect thyroxine levels (16), iodothyronine deiodinase type 2 enzyme originated from preadipocytes contribute triiodothyronine levels (17), impaired hypothalamus-pituitary-thyroid axis due to surgery results low circulating thyroid hormone levels (18), and Pontikides et al. suggested, the serum thyroid hormone levels can vary in consequence of alterations in serum levels of adipokines (19).

The purpose of our study is to elucidate the influence of weight reduction on thyroid functions after sleeve gastrectomy (SG) in euthyroid patients.

MATERIALS and METHODS

We retrospectively investigated the files of 298 patients who underwent SG at the Department of General Surgery between 2015 and 2017. Patients' history, physical examination findings, laboratory results, and medication use were investigated from the hospital and the national health database system. Patients who have active thyroid disease or known thyroid disorder, who are taking medicine that can affect thyroid hormone levels, or have inflammatory bowel disease, pituitary insufficiency, thyroid autoantibodies, or are smokers, were excluded from the study. A total of 85 patients, 79 females and 6 males, were included in the study (Figure 1). Each patient's BMI, serum free triiodothyronine (fT3), serum free thyroxine (fT4), and tiroid stimulating hormone (TSH) levels at preoperative and post-operative 6th and 12th month visits were recorded. Median age was 38 (maximum age: 61, minimum age: 18). Thyroid function tests of the patients were grouped as group 0: preoperative, group 1: postoperative 6 months, group 2: postoperative 12 months for each test, respectively. All analyses were performed by means of chemiluminescence methods (Liaison®; DiaSorin S.p.A., Saluggia, Italy). Normal reference ranges for fT3 : 1.71 - 3.71 pg/ml, fT4: 0.7 - 1.48 ng/dl, TSH: 0.35 - 4.94 μIU/L.

The normality of distribution of continuous variables was tested by the Shapiro-Wilk test. The Kruskal-Wallis test (for non-normal data) was used for comparison of three dependent measurements, and the Dunn test was performed as a multiple comparison test. Univariate statistical analysis was performed with SPSS for Windows version 24.0 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). A p-value smaller than 0.05 was considered statistically significant.

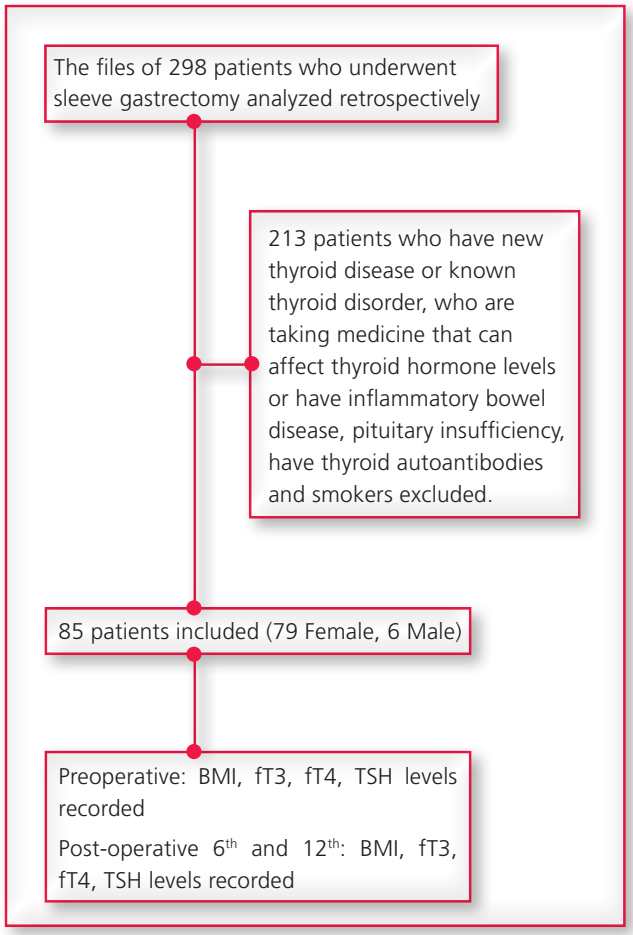

Figure 1 Flow chart of the study

BMI: Body mass index; sfT3: Serum free triiodothyronine; sfT4: Serum free thyroxine; TSH: Thyroid stimulating hormone.

Ethics

This research was approved by Ankara Keçiören Training and Research Hospital Clinical Research Ethics Committee (no: 022019/1851). The study was complied with The World Medical Association Declaration of Helsinki.

RESULTS

A total of 85 patients [6 (7.1%) male; 79 (92.9%) female] were included in the study. Average age was 38 (maxium age: 61, minimum age: 18). Preoperative BMI measurements [mean 45.98 ± 5.77 kg/m^2 (minimum 38.20 - maximum 63.67kg/m^2)] decreased significantly at 12th month after SG [26.1 ± 4.59 kg/m^2 (minimum 18.7 - maximum 47.2 kg/m^2)], ($p < 0.0001$ for whole comparison). Demographic characteristics of patients are shown in Table 1.

Table 1 Demographic characteristics of patients

	Descriptive Statistics	
Variables	**Mean ± SD**	**Min - max**
Age	37.75 ± 10.32	(18 - 61)
BMI	47.66 ± 5.88	(38.20 - 63.67)
	n	**%**
Gender		
Female	79	92.9
Male	6	7.1

BMI: Body mass index, SD: Standart deviation, n: number.

Serum freeT3 (fT3) levels were decreased in all postoperative visits compared to the preoperative period. Median (25% - 75%) values for each visit were as follows: $fT3_0$: 3.04 pg/mL (3.25 - 2.77), $fT3_1$: 2.68 pg/mL (2.9 - 2.36), $fT3_2$: 2.6 pg/mL (2.91 - 2.38) (Figure 2).

Serum free T4 (fT4) levels increased at the post-operative 6_{th} month visit, and then decreased at the post-operative 6th month visit. Median (25% - 75%) values at each visit for were as follows, $fT4_0$:1.04 ng/dL (1.15 - 0.99), $fT4_1$: 1.06 ng/dL (1.15 - 0.99), $fT4_2$: 1.03 ng/dL (1.3 - 0.94) (Figure 3).

Serum TSH levels were decreased at post operative all visits compared to preoperative period. Median (25% - 75%) values at each visit were as follows: TSH_0: 2.16 µIU/L (2.81 - 1.49), TSH_1: 1.48 µIU/L (2.46 - 0.93), TSH_2: 1.47 µIU/L (2.3 - 0.92) (Figure 4).

Thyroid function tests during preoperative, visit 1 (postoperative 6. month) and visit 2 (postoperative 12. month) can be seen in Table 2. The decrease in TSH levels was not correlated with the BMI reduction after sleeve gastrectomy ($p > 0.05$).

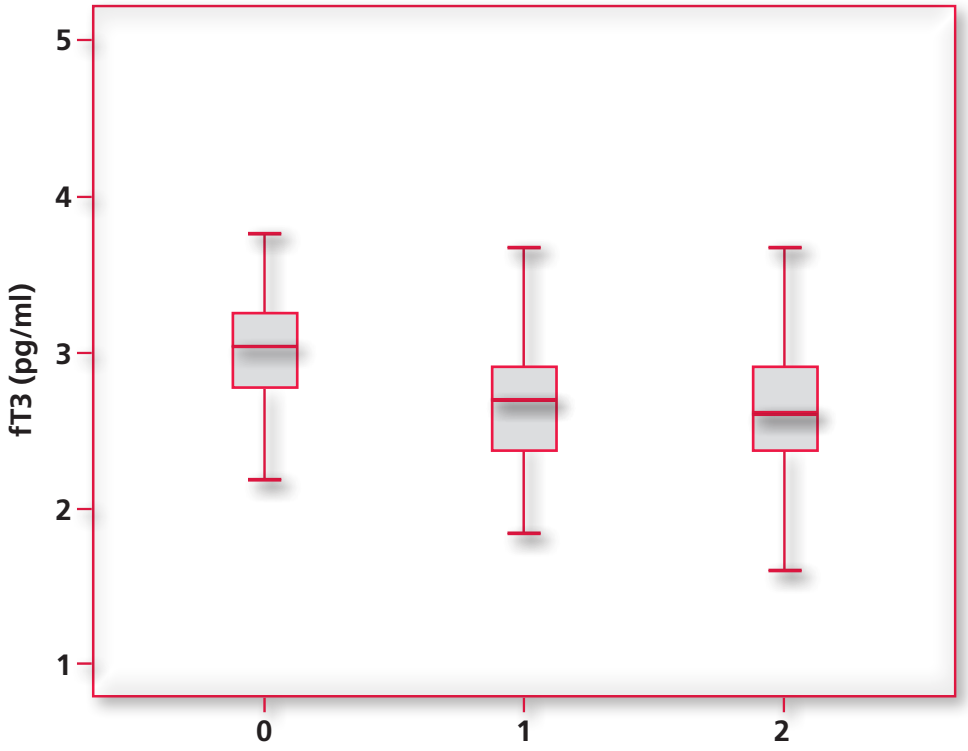

Figure 2 Free T3 levels preoperative and post-operative periods

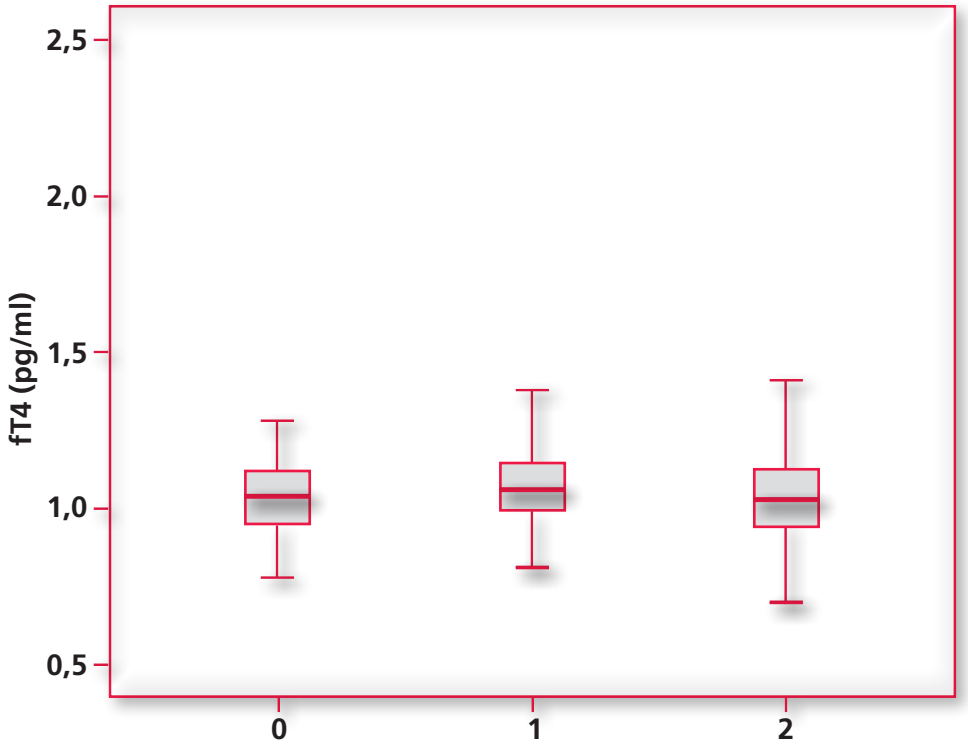

Figure 3 Free T4 levels preoperative and post-operative periods

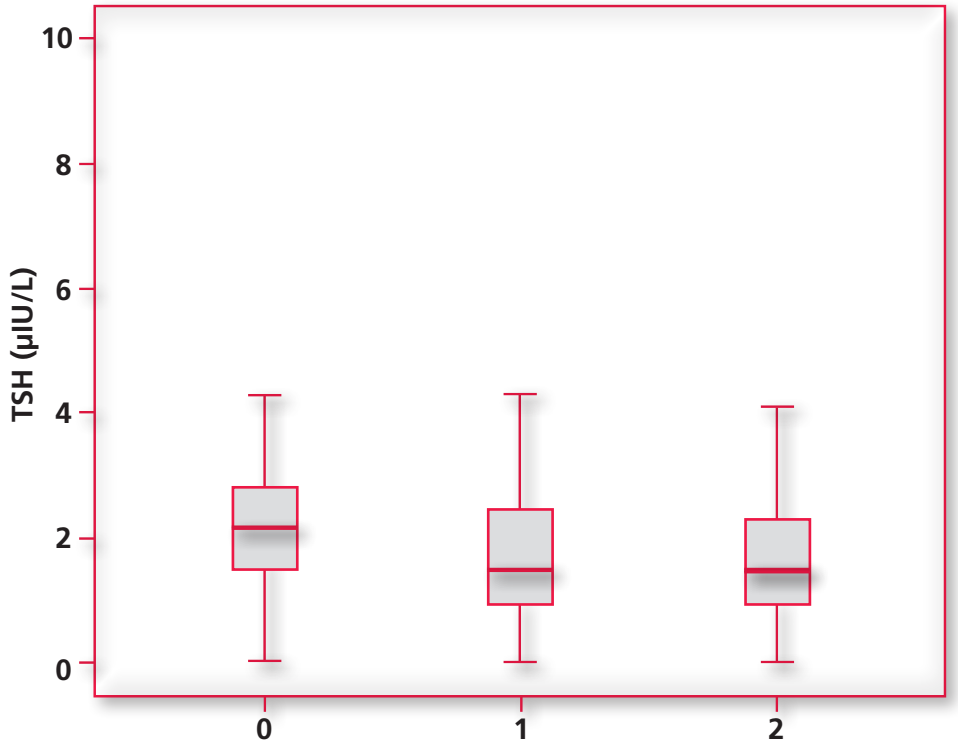

Figure 4 TSH levels preoperative and post-operative periods

Table 2 Thyroid function tests during preoperative, visit 1 (postoperative 6. month) and visit 2 (postoperative 12. month)

	0	1	2	P
Variables (n = 85)	**Median (25% -75%)**	**Median (25% - 75%)**	**Median (25% - 75%)**	
sfT3	3.04 (2.77 - 3.25)	2.68 (2.36 - 2.9)	2.6 (2.38 - 2.91)	**0.001***
sfT4	1.04 (0.95 - 1.12)	1.06 (0.99 - 1.15)	1.03 (0.94 - 1.13)	**0.017***
TSH	2.16 (1.49 - 2.81)	1.48 (0.93 - 2.46)	1.47 (0.92 - 2.3)	**0.001***

*Significant at 0.05 level.
sfT3: Serum free triiodothyronine; sfT4: Serum free thyroxine; TSH: Thyroid stimulating hormone.

DISCUSSION

Sleeve gastrectomy causes improvement of co-morbidities due to being overweight, as well as nutritional, hormonal, and multisystemic changes. There is a close relationship between thyroid hormones and body metabolism. Serum fT3 and serum fT4 affect body metabolism, including lipid metabolism, distribution of adipose cells, and body weight. Changes in the body weight also affect the thyroid functions (20,21).

In our study, we showed that there were significant changes in thyroid function after sleeve gastrectomy. fT3 and TSH levels decreased; conversely, fT4 levels first increased and then decreased significantly after sleeve gastrectomy. Several studies in the literature about the association between sleeve gastrectomy and thyroid function have found controversial results.

After laparoscopic sleeve gastrectomy, Neves et al. found a decrease in TSH and fT3, as in our study, but there was no change in fT4 levels, differing from our study (14). In another study with biliopancreatic diversion (BPD), researchers found a reduction in fT3, but no change in TSH and fT4 was observed (22). In the study of Chikunguwo et al., there was a positive correlation between weight reduction and TSH; however, no relation with fT4 levels was seen after Roux-en-Y gastric bypass and gastric banding operations (23). Mac Cuish et al. found a decrease in TSH levels, and increase in fT4 levels after Roux-en-Y gastric bypass surgery (24). On the other hand, in another study done by Lips et al. did not find a change in fT4 levels after Roux-en-Y gastric bypass (25). A study from China, designed by Jingge Yang, showed significant reductions in TSH, fT3, and fT4 levels after sleeve gastrectomy (26). Two studies from different countries determined similar results after sleeve gastrectomy: TSH decreased but fT4 did not change after surgery (11,27).

There are various uncorroborated mechanisms supposed to explain the changes in thyroid function after sleeve gastrectomy. Some researchers alleged changes in leptin levels (14), but on the contrary, others argued that leptin had no causative effect on thyroid hormone disturbances after surgery (22). Adipokines were also associated with changes in thyroid hormone levels in an article (23). Other accused mechanisms are as follows: BMI increase cause increament in serum TSH levels (15), decrease in leptin levels may affect thyroxine levels (16), iodothyronine deiodinase type 2 enzyme originated from preadipocytes contribute triiodothyronine levels (17), impaired hypothalamus-pituitary-thyroid axis due to surgery results low circulating thyroid hormone levels (18), and Pontikides et al. suggested, the serum thyroid hormone levels can vary in consequence of alterations in serum levels of adipokines (19).

In conclusion; our study found a significant decrease in TSH and fT3 levels, and there was a fluctuating pattern in fT4 levels after sleeve gastrectomy. As with most of the changes after bariatric surgery, it has not been fully elucidated how the alterations in serum thyroid hormones occurred. Molecular based studies may clarify the potential mechanisms behind both thyroid hormone and the other metabolic alterations.

Ethics: *This research was approved by Ankara Keçiören Training and Research Hospital Clinical Research Ethics Committee (no: 022019/1851).*

Conflict of interest: *The authors declared no conflict of interest.*

Disclosure: *The authors have nothing to disclose.*

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