

## Is screening for Cushing's syndrome before bariatric surgery necessary?

### *Bariatrik cerrahi öncesi Cushing sendromu için tarama testi gerekli midir?*

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#### Abstract

**Purpose:** Recent studies have shown a higher prevalence of Cushing's syndrome in obese patients with type 2 diabetes, but its prevalence in overweight and obese populations is not clear. The aim of this study was to evaluate the need for screening tests for Cushing's syndrome in morbidly obese individuals before bariatric surgery.

**Materials and methods:** Between January 2015 and December 2019, 300 patients with Body Mass Index (BMI)  $\geq 35$  kg/m<sup>2</sup> that admitted to our endocrine outpatient clinic for evaluation before bariatric surgery were included in this study. Overnight low dose 1 mg dexamethasone suppression test was applied to all patients. Next day 8 am serum cortisol concentration less than 1.8 µg/dL was defined as normal suppression.

**Results:** Three hundred patients undergoing bariatric surgery were screened for Cushing's syndrome. The mean±standard deviation age of the patients was 39.4±11.7 years and 236 (77.3%) were women. The mean BMI of the patients was 45.9±5.5 kg/m<sup>2</sup> before bariatric surgery. Forty-seven (15.7%) patients in type 2 diabetes mellitus, 28 (9.3%) patients with hypertension and 3 (1%) patients who had achieved euthyroidism after levothyroxine treatment. The mean one year BMI after bariatric surgery was 28±4.6 kg/m<sup>2</sup>. Serum cortisol concentration was <1.8 µg/dL after 1 mg overnight dexamethasone suppression test in all patients.

**Conclusion:** The results of the evaluated data revealed that the routine screening of morbidly obese individuals for Cushing's syndrome before bariatric surgery is not necessary.

**Key words:** Obesity, bariatric surgery, Cushing's syndrome, dexamethasone suppression test.

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#### Özet

**Amaç:** Son çalışmalar diyabeti bulunan obez hastalarda Cushing sendromu prevalansının daha yüksek olduğunu göstermiştir, ancak aşırı kilolu ve obez popülasyonlardaki prevalansı net değildir. Bu çalışmanın amacı, bariatrik cerrahi öncesi morbid obez bireylerde Cushing sendromu için tarama testlerine duyulan ihtiyacı değerlendirmektir.

**Gereç ve yöntem:** Ocak 2015-Aralık 2019 tarihleri arasında bariatrik cerrahi öncesi değerlendirme için endokrin polikliniğimize başvuran Vücut Kitle İndeksi (VKİ)  $\geq 35$  kg/m<sup>2</sup> olan 300 hasta çalışmaya dahil edildi. Tüm hastalara gece 23:00'de düşük doz 1 mg deksametazon supresyon testi uygulandı. Ertesi gün sabah serum kortizol konsantrasyonu 1,8 µg/dL'den az olması normal supresyon olarak tanımlandı.

**Bulgular:** Bariatrik cerrahi geçiren 300 hasta Cushing sendromu açısından tarandı. Hastaların yaşı 39,4±11,7 yıl ve %77,3'ü kadındı. Bariatrik cerrahi öncesi hastaların ortalama VKİ'si 45,9±5,5 kg/m<sup>2</sup> idi. Tip 2 diyabetli 47 (%15,7) hasta, hipertansif olan 28 (%9,3) hasta ve hipotiroidi tedavisi sonrası ötiroidi ile takip edilen 3 (%1) hasta olduğu saptandı. Bariatrik cerrahi sonrası ortalama 1 yıllık VKİ 28±4,6 kg/m<sup>2</sup> idi. Tüm hastalarda 1 gecelik 1 mg deksametazon supresyon testinden sonra serum kortizol konsantrasyonu <1,8 µg/dL idi.

**Sonuç:** Çalışmamızda değerlendirilen verilerin sonuçları, morbid obez bireylerin bariatrik cerrahi öncesi Cushing sendromu için rutin olarak taranmasının gerekli olmadığını göstermiştir.

**Anahtar kelimeler:** Obezite, bariatrik cerrahi, Cushing sendromu, deksametazon supresyon testi.

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## Introduction

Obesity, a multifactorial disease with increasing frequency in the world, is defined as the body fat ratio above normal limits. Since it is impractical to evaluate excess fat mass, body mass index (BMI) can be used for evaluation [1, 2]. Medical and behavioral approaches in the treatment of obesity may be ineffective for many obese individuals. Therefore, bariatric surgical procedures are becoming more and more widespread worldwide due to their efficacy in weight reduction, as well as in the treatment of obese patients with comorbidities such as type 2 diabetes mellitus, hypertension and sleep apnea syndrome [3]. Currently, screening tests (1 mg overnight dexamethasone suppression test, 24-hour urinary excretion cortisol or late-night serum cortisol) are recommended if there are signs suggesting Cushing's syndrome (CS) before bariatric surgery [4]. The aim of this study was to evaluate CS screening results in patients before bariatric surgery.

## Materials and methods

This study was conducted on 300 patients with BMI greater than 35 kg/m<sup>2</sup> admitted to our endocrinology outpatient clinic for evaluation before bariatric surgery between January 2015 and December 2019. Exclusion criteria for this study were as follows;

- (1) patients with creatinine clearance lower than 30 mL/min,
- (2) serious medical conditions that may alter pituitary-adrenal function, exogenous glucocorticoid intake, alcohol dependence, antiepileptic drug use, estrogen use, depression and other psychiatric conditions.

Dorsocervical fat pad, central obesity, abdominal striae, ecchymotic skin lesions, acne and hirsutism, nontraumatic facial plethora and proximal muscle weakness were evaluated in all patients. Weight, height, BMI, systolic and diastolic blood pressure were measured. BMI was calculated by dividing the body weight in kilograms by the square of the height in meters. BMI values of 18.5-24.9 kg/m<sup>2</sup> were considered to be healthy or normal. BMI values, 25-29.9 kg/m<sup>2</sup> were defined as overweight,  $\geq 30$  kg/m<sup>2</sup> as obese and  $\geq 40$  kg/m<sup>2</sup> as morbid obese [1, 2]. The overnight 1 mg dexamethasone test was performed all patients. The next day morning fasting serum cortisol concentration less than 1.8  $\mu$ g/dL at 8 am was defined as normal suppression. Cortisol was measured by electrochemiluminescence immunoassay (ECLIA). Ethical Committee Board approval was obtained from University of Health Sciences, Antalya Training and Research Hospital.

## Statistical analysis

SPSS version 22.0 software (Armonk, NY: IBM Corp) was used for statistical analysis. Results are expressed as mean $\pm$ standard deviation.

## Results

Clinical and demographic data of the patients undergoing bariatric surgery were given in Table 1. All patients were morbidly obese (BMI $\geq 40$  kg/m<sup>2</sup>). Serum cortisol concentration was less than 1.8  $\mu$ g/dL after overnight 1 mg dexamethasone suppression test in all patients. Type 2 diabetes mellitus was present in 47 (15.7%) patients, hypertension in 28 (9.3%) patients, and hypothyroidism in 3 (1%) patients who were treated with levothyroxine sodium.

**Table 1.** Clinical and demographic data of patients undergoing bariatric surgery

		Patients (n=300)
Age (years)		39.4±11.7
Gender	Female (%)	232 (77.3%)
	Male (%)	68 (22.7%)
Pre-bariatric surgery BMI (kg/m <sup>2</sup> )		45.9±5.5
1st year after bariatric surgery BMI (kg/m <sup>2</sup> )		28±4.6
Systolic blood pressure (mmHg)		135.1±7.1
Diastolic blood pressure (mmHg)		87.5±5.3
Diabetes Mellitus		47 (15.7%)
Hypertension		28 (9.3%)
Hypothyroidism		3 (1%)

Values are expressed as means±SD. BMI: body mass index

## Discussion

Obesity is one of the most important public health problems in modern life. In developed and developing countries, it is known that nearly one-third of the adults are overweight and one-third are obese [5]. Based on the data of TURDEP-II study, two out of every three adults in Turkey were overweight or obese [6]. Obesity is an important risk factor that increases the incidence of dyslipidemia, hypertension, type 2 diabetes mellitus, gallbladder diseases, stroke, osteoarthritis, sleep apnea syndrome and some cancers [7-9]. In addition, it increases the risk of morbidity and mortality due to cardiovascular diseases [10]. On the other hand, it is noteworthy that obesity can cause psychosocial and economically important social problems [11]. Indeed, prevention and treatment of obesity are not only a public health problem but also a socioeconomic problem [12]. In this perspective, evaluation of obesity is a multidisciplinary approach to detect and treat obesity-related diseases. The most effective treatment for obesity is bariatric surgery. Bariatric surgery is a cost-effective treatment in morbidly obese people having especially comorbid diseases, including type 2 diabetes mellitus, sleep apnea syndrome, osteoarthritis, hypertension, cancer, hospitalizations, and labor losses [13].

Among various causes of obesity, Cushing's syndrome is one of the rare one. Weight gain and obesity are among the common symptoms and signs of CS. Also, morbid obesity is included in the differential diagnoses of CS. CS screening with one single test, especially

overnight 1 mg dexamethasone test is common in clinical practice. [14, 15]. However, there is a lack of evidence for supporting the widespread screening of obese patients for CS [15]. Baid et al. [16] performed two or three different tests for CS screening in overweight or obese patients. Although they detected at least five clinical features of CS in most patients, they observed no CS and some of their laboratory results were false positive. In addition, Varadhan et al. [17] evaluated the results of bariatric surgery performed in a multidisciplinary bariatric surgery clinic retrospectively and detected no CS in any of the patients and; therefore, they gave up routine CS screening in their clinics. In another study, Sahin et al. [18] reported two cases of CS caused by adrenal glands after CS screening of 354 obese patients. The evaluation of their data revealed that the widespread screening of obese patients for CS suggested only Cushingoid appearance and CS screening in obese patients with hypertension, glucose intolerance or dyslipidemia. On the other hand, Tiryakioglu et al. [19] evaluated 150 simply obese patients for CS and determined a significant proportion of patients (9.33%) with CS. Also, they argued that obese patients should be routinely screened for CS. On the contrary; in our study, cortisol suppression was observed after overnight 1 mg dexamethasone test in all patients, and no secondary test was required. The limitations of our study were retrospective design, and the evaluation of the cases for CS with a single test (overnight 1 mg dexamethasone test). The strengths of the study are the sufficient number of cases and the 1-year follow-up of the cases.

As a result, our study reveals that morbid obesity alone is not an adequate sign for CS screening before bariatric surgery. It can be concluded that routine screening for CS before bariatric surgery in patients with morbid obesity is unnecessary.

**Conflict of interest:** No conflict of interest was declared by the authors.

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## Contributions of authors

M.S.E., M.C. and M.N.K. conceived the study design. M.S.E., M.C. and M.N.K. were involved in data collection. M.S.E., M.C. performed the statistical analysis. M.S.E., M.C. and M.N.K. interpreted data and prepare the manuscript

draft. M.S.E., M.C. and M.N.K. critically reviewed the final version of the manuscript. All authors approved the final version of the manuscript.