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Can serum basal cortisol values predict successful operations for bariatric surgery patients?

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Abstract. – OBJECTIVE: Obesity is a chronic metabolic disease declared as the 21st century pandemic by the World Health Organization. Obesity has become an alarming situation for society, and it has to be treated. If the appropriate criteria are met by patients, bariatric surgery is an effective treatment method that provides weight loss in a short time. There are no definitive criteria regarding which groups of patients and characteristics may benefit most from bariatric surgery. In this study, we evaluate whether serum basal cortisol levels can predict successful outcomes of bariatric surgery and whether there is any difference in outcome between diabetic and non-diabetic patients.

PATIENTS AND METHODS: This observational study included 244 obese patients who had undergone laparoscopic sleeve gastrectomy (LSG). Preoperative and postoperative 6-month weight, body mass index (BMI), serum basal cortisol, fasting plasma glucose, 1-mg dexamethasone suppression test (DST) results, and Type 2 Diabetes Mellitus (T2D) history were recorded. We analyzed the patients first by dividing them into two groups as excessive weight loss (%EWL) ≥50% and %EWL< 50%, and then into two groups as diabetic and nondiabetic patients.

RESULTS: The mean age of patients with %EWL≥ 50% was found to be statistically significantly lower than that of patients with %EWL< 50% [39 (19-60) *vs.* 47 (36-61) years; *p*=0.046]. While there was no significant difference in basal cortisol values (*p*=0.513), DST results were statistically significantly lower in patients with %EWL≥ 50% than patients with %EWL< 50% [0.6 (0.1-2.1) *vs*. 0.8 (0.7-1.1); *p*=0.040].

CONCLUSIONS: In obese patients undergoing LSG, serum basal cortisol level may not predict the success of operation. However, the result of 1 mg DST may predict the operation success.

Key Words:
Laparoscopic sleeve gastrectomy, Serum basal cortisol, Operation success.

Introduction

Obesity is a global epidemic, estimated adult obesity rate to be 20% in 2030[1]. Obesity is a chronic progressive metabolic disease characterized by comorbidities such as hypertension, Type 2 Diabetes Mellitus (T2D), stroke, cancer and associated with early mortality[2]. Studies show that bariatric surgery (BS) is associated with a reduction in long-term all-cause mortality[3]. BS is recommended for patients who do not experience weight loss despite regular physical activity and diet. The most preferred method among bariatric surgical procedures is laparoscopic sleeve gastrectomy (LSG)[4,5].

It is thought that patients with obesity may have a hyperactive hypothalamic-pituitary-adrenal (HPA) axis that leads to functional hypercortisolism. This is because cortisol release increases in response to both chronic stress and food intake. In previous studies, it was shown that the rate of operation success for obese patients with irregularities in the HPA axis is lower than that for patients without such irregularities[6].

Patients with T2D have also been shown to have higher levels of saliva cortisol in the evening than non-diabetics patients. Higher basal cortisol values in patients with T2D have been associated with increased obesity and cardiac complications. Studies on serum cortisol levels in obese patients have reported both positive and negative associations. For example, the urine cortisol/creatine ratio was found to be high in obese individuals, while hair cortisol has been associated with BMI and fat mass in obese children[7].

In the present study we investigate whether serum basal cortisol values can predict the success of the operation in patients undergoing LSG and whether serum cortisol levels have any difference

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in outcome between diabetic and non-diabetic patients.

Patients and Methods

In this retrospective study, we included 244 patients who had undergone LSG. Patients were included if they were 18-65 years old and had undergone LSG according to the following criteria: BMI≥ 40 kg/m^2 or BMI> 35 kg/m^2 with one or more additional comorbidity and approved for surgery due to an inability to lose weight with diet and physical activity[8]. We recorded the preoperative and postoperative 6-month fasting plasma glucose (FPG), serum basal cortisol, 1-mg dexamethasone suppression test (DST) result, weight, height, BMI, and history of T2D for all patients. Blood samples for serum cortisol measurements were taken on between 08:00 and 09:00 a.m. after an overnight fast. Serum cortisol level were measured using an electrochemiluminescence immunoassay with Access cortisol kit (Beckman Coulter, Hormone Analyzer, Brea, CA, USA). The presence of Cushing syndrome was excluded with the 1-mg DST in the preoperative period and the suppressed cortisol value was noted. Serum cortisol was measured at 08.00-09.00 a.m. after the administration of 1 mg dexamethasone at 23.00 p.m. on the previous day (1-mg DST, normal values <1.8 μg/dL, 50 nmol/L). All included patients were euthyroid individuals. Patients with using steroid, renal dysfunction, liver dysfunction, solid and hematological malignancy, pituitary disease, pregnant and breastfeeding women were excluded from the study. BMI was calculated by dividing the weight in kilograms by height in meters squared (kg/m²). The percentage of excess weight loss (%EWL) was calculated according to the following formula: [(preoperative weight - postoperative weight)]/[(preoperative weight - ideal weight)] × 100[9]. The weight corresponding to BMI = 25 kg/m^2 was considered the ideal body weight. Failed weight loss after LSG was defined as %EWL< 50% according to relevant guidelines[10].

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and/or median (min-max), and categorical data were expressed as numbers and percentages. Normality analyses were performed with the Kolmogorov-Smirnov test. The Wilcoxon signed-ranks test was used in dependent group analyses of continuous variables that did not comply with normal distribution, and the Mann-Whitney U test was used in independent group analyses. The linear relationship between variables was determined with partial correlation analysis controlled for T2D. Analyses were performed with IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA). The statistical significance level was accepted as $p<0.05$.

Results

The mean age of the 244 patients evaluated within the scope of this study was 38.73±10.29 (range: 19-61) years, 79.1% were female, 20.9% were male, and 24.6% were diagnosed with T2D. The mean height of the patients was 164.59±9.30 cm, mean preoperative weight was 125.17±19.93 kg, and mean preoperative BMI was 46.14±5.82 kg/m^2, while the 6-month postoperative mean weight was 72.91±12.51 kg and 6-month mean BMI was 26.99±4.59 kg/m^2 ($p<0.001$ and $p<0.001$ for both). While the mean %EWL of the patients was 92.67±19.34%, the difference between mean preoperative and mean 6-month postoperative weight was 52.26±15.03 kg. The mean FPG value was 107.77±37.88 mg/dL, the mean basal cortisol value was 10.39±3.38 μg/dl, and the mean DST result was 0.69±0.26 μg/dl (Table I).

The median age of patients with %EWL≥ 50% [39 (19-60) years] was found to be statistically significantly lower than that of patients with %EWL< 50% [47 (36-61) years] ($p=0.046$). 6-month postoperative weight and BMI values were found to be statistically significantly lower in the patient group with %EWL≥ 50% [70 (45-115) kg and 25.9 (17.9-42.5) kg/m^2, respectively] compared to patients with %EWL< 50% [101 (70-122) kg and 38.5 (34.7-47.3) kg/m^2, respectively] ($p<0.001$ and $p<0.001$ for both). The difference between preoperative and 6-month postoperative weights was statistically significantly higher in the group with %EWL≥ 50% compared to patients with %EWL< 50% [52 (21-122) *vs.* 25.5 (13-48) kg; $p<0.001$]. While there were no significant differences in FPG or basal cortisol values ($p=0.986$ and $p=0.513$, respectively), DST result was statistically significantly lower in the patient group with %EWL≥ 50% than in patients with %EWL< 50% [0.6 (0.1-2.1) *vs.* 0.8 (0.7-1.1); $p=0.040$] (Table II).

There were no significant correlations between basal cortisol values and age, height, weight,

Table I. Age, height, weight, BMI, FPG, basal cortisol, and DST result of the patients.

	Mean±SD	
Age, years	38.73±10.29	
Height, cm	164.59±9.30	
Preoperative weight, kg	125.17±19.93	***p*<0.001***
Postoperative weight at 6 months, kg	72.91±12.51	
Preoperative BMI, kg/m^2	46.14±5.82	***p*<0.001***
Postoperative BMI at 6 months, kg/m^2	26.99±4.59	
%EWL	92.67±19.34	
Weight difference, kg	52.26±15.03	
FPG, mg/dL	107.77±37.88	
Basal cortisol, µg/dl	10.39±3.38	
DST result, µg/dl	0.69±0.26	

*Wilcoxon signed-ranks test.

BMI, weight difference, %EWL, FPG, or DST result (Table III).

The mean age of patients with T2D was found to be statistically significantly higher than that of patients without T2D [46 (25-61) *vs.* 37.5 (19-60) years; $p< 0.001$]. It was determined that the preoperative weight, height, and BMI values of the patients did not make a significant difference according to the presence of diabetes ($p> 0.05$). However, the 6-month postoperative weight and BMI values were statistically significantly higher in the group of patients with T2D [72 (58-122) kg and 28.2 (20.8-41.1) kg/m^2, respectively] compared to patients without T2D [69.5 (45-121) kg and 25.5 (17.9-47.3 kg/m^2, respectively] (p=0.026 and p=0.001, respectively). FPG and DST result were statistically significantly higher for diabetics [128 (70-314) and 0.8 (0.3-2.1), respectively] compared to patients without T2D [94 (68-150) and 0.6 (0.1-1.5), respectively] ($p< 0.001$ for both). However, there was no significant difference in basal cortisol values (p=0.670) (Table IV).

Discussion

In our study, the mean age of patients with %EWL≥ 50% was significantly lower, thus supporting the importance of younger age for operation success. When the literature is examined, various studies are seen regarding the criteria that should be considered while investigating the factors that predict the success of the operation for bariatric surgery patients. However, no consensus has been reached about evidence-based criteria. The most used criteria are %EWL[11]. We also used

Table II. Comparison of age, height, preoperative and 6-month postoperative weight and BMI, weight difference, FPG, and basal cortisol, DST result of the patients according to % EWL.

	%EWL< 50% [median (min-max)] (n=8)	**%EWL≥ 50% [median (min-max)] (n=236)**	***P***
Age, years	47 (36-61)	39 (19-60)	**0.046***
Height, cm	158.5 (142-175)	163.5 (145-193)	0.120*
Preoperative weight, kg	131.5 (83-163)	122 (87-204)	0.485*
Preoperative BMI, kg/m^2	48 (41.1-66.6)	44.3 (36.8-70.8)	0.109*
Postoperative weight at 6 months, kg	101 (70-122)	70 (45-115)	**<0.001***
Postoperative BMI at 6 months, kg/m^2	38.5 (34.7-47.3)	25.9 (17.9-42.5)	**<0.001***
Weight difference, kg	25.5 (13-48)	52 (21-122)	**<0.001***
FPG, mg/dL	96 (76-138)	96.5 (68-314)	0.986*
Basal cortisol, µg/dl	10.1 (4.5-12.1)	10.2 (3.7-21.8)	0.513*
DST result, µg/dl	0.8 (0.7-1.1)	0.6 (0.1-2.1)	**0.040***

* Mann-Whitney U test.

Table III. Correlations between basal cortisol values and age, height, preoperative and 6-month postoperative weight, BMI, weight difference, %EWL, FPG, and DST result.

	Basal cortisol, µg/dl (correlation coefficient)	p
Age, years	-0.028	0.669
Height, cm	0.084	0.193
Preoperative weight, kg	0.096	0.137
Preoperative BMI, kg/m^2	0.060	0.349
Postoperative weight at 6 months, kg	-0.005	0.944
Postoperative BMI at 6 months, kg/m^2	-0.058	0.372
Weight difference, kg	0.132	0.040
%EWL	0.086	0.182
FPG, mg/dL	0.066	0.305
DST result, µg/dl	0.195	0.002

*Partial correlation analysis, controlled for T2D.

Table IV. Comparison of age, height, preoperative and 6-month postoperative weight and BMI, weight difference, %EWL, FPG, and DST result in patients with and without T2D.

	Non-T2D [median (min-max)] (n=8)	T2D [median (min-max)] (n=236)	p
Age, years	37.5 (19-60)	46 (25-61)	**<0.001***
Height, cm	164 (142-193)	162 (145-185)	0.126*
Preoperative weight, kg	123 (83-204)	122 (87-200)	0.939*
Preoperative BMI, kg/m^2	44 (38.2-70.7)	47.2 (36.8-61.7)	0.194*
Postoperative weight at 6 months, kg	69.5 (45-121)	72 (58-122)	**0.026***
Postoperative BMI at 6 months, kg/m^2	25.5 (17.9-47.3)	28.2 (20.8-41.1)	**0.001***
Weight difference, kg	52 (13-122)	49 (21-91)	0.059*
FPG, mg/dL	94 (68-150)	128 (70-314)	**<0.001***
Basal cortisol, µg/dl	10 (3.7-20)	10.5 (5.5-21.8)	0.670*
DST result, µg/dl	0.6 (0.1-1.5)	0.8 (0.3-2.1)	**<0.001***
%EWL	96.2 (39.9-140.7)	86.1 (33.6-132.7)	**<0.001***

* Mann-Whitney U test.

%EWL in our study. In their study, Nickel et al[12] showed that relationship between higher BMI with lower %EWL, and also the importance of younger age for optimal treatment. Eusebio et al[13] reported an association of unsuccessful postoperative weight loss with advanced age, again supporting the importance of younger age for successful operations. Obanda et al[14] concluded that approximately 20% of patients undergoing bariatric surgery would lose no more than 50% of excess weight in the first 12 months, which may be a population-specific finding differing from those of other authors. In another study, preoperative BMI was found to be the only factor that could predict the success of the operation after 1 year in obese patients who underwent laparoscopic gastric bypass surgery, and its predictiveness was strong[15]. The preoperative BMI values of patients with %EWL≥ 50% being lower in our study compared to other studies may be due to the fact that the number of patients with %EWL< 50% was rather low.

In the present study, we did not detect a difference in serum basal cortisol values between in patients with %EWL≥ 50% and %EWL< 50%. However, it was interesting that the results of the DST reflected more suppression among patients with %EWL≥ 50%. However, there is no study in the literature on the suppression of cortisol values in 1-mg dexamethasone tests and its ability to predict a successful surgery.

There is a stress factor caused by being obese and accompanying overeating behaviors due to stress in patients with obesity. The positive relationships between basal cortisol level and food intake, disruption in the HPA axis, and cortisol reactivity have been considered as possible mechanisms of cortisol reactivity in patient with obesity[16]. In a study of elderly patients with obesity, cortisol-induced obesity was not detected and an inverse relationship between cortisol levels and body weight was found[17]. Considering the hypothesis of the correlation of basal cortisol elevation, high-calorie diet, and higher preoperative weight, in our correlation analysis for basal cortisol levels, we did not find any correlations with preoperative weight, weight difference, or %EWL. We think that basal cortisol levels in obese individuals are not indicators of cortisol diurnal rhythm or cortisol release.

In a cohort study of 1030 non-diabetic patients with morbid obesity, it was determined that patients with higher levels of cortisol excretion had better metabolic profiles. This finding was attributed to excessive activity of the HPA axis. When grouped according to cortisol excretion, however, there was no significant difference in morning cortisol, with patients with the highest excretion levels having higher BMI values[18]. Joseph et al[19] associated increased BMI with more profiles of vestigial diurnal cortisol. In a recent study examining the relationship between leptin and cortisol, a negative relationship was found for BMI, waist circumference, and cortisol level, which was explained by the hypothesis that the hormone leptin, which is produced in subcutaneous fat tissue, would suppress cortisol production in the hypothalamus and adrenal glands[20]. Schorr et al[21] showed that cortisol levels were lowest in overweight and obese women, increasing with more pronounced obesity, and they concluded that hypercortisolemia may contribute to increased levels of fat by activating the HPA axis in the event of excess weight.

In our study, while there was no significant difference between the preoperative BMI values of with and without T2D patients, we found that the BMI values of non-diabetic patients were significantly lower in the 6th postoperative month and their DST results were also significantly lower. There are also studies in which T2D was associated with neuroendocrine dysfunction and cortisol levels were evaluated[22]. Different results have been obtained in various studies on cortisol levels in obese patients with T2D in the literature. Among the previous studies on cortisol levels in diabetic individuals, the Multi-Ethnic Study of Atherosclerosis (MESA) reported that a significant increase in FPG was associated with an increase in the slope of wake-up cortisol and a flattening of the slope of cortisol at 6 years of follow-up in diabetic individuals[23]. Abraham et al[24] conducted a study with 369 overweight and obese patients for whom a diagnosis of Cushing syndrome had been ruled out, and they showed that salivary cortisol tended to increase at night as BMI increased, while 24-hour urine cortisol and DST result were not associated with BMI or weight. In a cross-sectional study, it was found that the cortisol daily rhythm was maintained in patients with T2D, but the cortisol awakening response was blunted and hippocampal volume decreased[25]. In a cohort study, Hackett et al[26] found elevated evening cortisol levels and a flattened slope of cortisol levels throughout the day in patients with T2D. Unlike the previously mentioned study, no relationship was found between morning cortisol or cortisol awakening response and T2D. In a study of African Americans, high morning serum cortisol was associated with high FPG and low beta cell function in non-diabetic patients, while it was associated with high FPG and HbA1c in diabetic patients[27].

Limitations

We only included a specific group of obese patients who had undergone LSG. The study can be planned to compare the same parameters in patients who have been operated with other bariatric surgery procedures. Another limitation is that ACTH level could not be evaluated because it could not be reached in the records.

Conclusions

Although there are many studies in the literature evaluating factors that may predict weight loss after bariatric surgery for obese patients, our study is the first to evaluate the predictiveness of serum basal cortisol levels. We conclude that serum cortisol level does not predict the success of LSG operations, but we believe that comprehensive research is needed regarding both cortisol diurnal rhythm and other non-pituitary hypothalamus factors affecting cortisol release and changes in those factors in the postoperative period. In addition, more comprehensive studies are needed to determine the predictive role of degree of cor-

tisol suppression as a result of the 1-mg DST for successful operations.

Conflicts of Interest
The authors declare no conflicts of interest.

Ethical Approval
This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethics Committee approval was obtained from Kecioren Training and Research Hospital (Ethics Committee Approval No: E-53610172).

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Authors' Contributions
Conception and design: Keskin M, Koca AO; Acquisition of data: Öztürk D, Bulus H; Analysis and interpretation of data: Keskin M, Koca AO; Drafting the article: Bulus H; Supervision: Öztürk D; Validation and final approval: All authors.

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