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ORIGINAL ARTICLE

Ghrelin Levels and Hunger Sensation after Laparoscopic Sleeve Gastrectomy Compared with Laparoscopic Greater Curvature Plication in Obese Patients

Amadeus Dobrescu [1], Catalin Copaescu [2], Bogdan Zmeu [2], Ciprian Duta [1], Ovidiu H. Bedreag [3, 4], Laurian Stoica [1], Cristi Tarta [1], Alexandru F. Rogobete [3, 4], Fulger Lazar [1]

[1] *Department of Surgery, "Victor Babeş" University of Medicine and Pharmacy, 2 Eftimie Murgu Square, Timişoara, Romania*
[2] *Center of Excellence in Metabolic and Bariatric Surgery, Ponderas Academic Hospital, Bucuresti, Romania*
[3] *Anesthesiology and Intensive Care Department, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania*
[4] *Faculty of Medicine, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania*

SUMMARY

Background: **The aims of our study were to compare serum acylated ghrelin (the active form of ghrelin) concentrations before and after the surgery of patients undergoing laparoscopic sleeve gastrectomy (LSG) or laparoscopic greater curvature plication (LGCP) and to correlate these levels with excess weight loss and hunger sensations on a short-term basis.**
Methods: **The patients included in the study had either (1) a body mass index (BMI) over 35 kg/m^2 and one comorbidity or (2) a BMI over 40 kg/m^2. Ghrelin levels were measured on the day of the surgery, 1 month after the procedure, and 3 months after the procedure. A questionnaire about hunger sensation was administered to the patients, and changes in the patients' weights were evaluated on the same timeline as the measurement of the ghrelin levels.**
Results: **Eighteen obese patients were included in the study, including 10 patients in the LSG group and 8 patients in the LGCP group. All the procedures were performed laparoscopically. The average level of preoperative ghrelin in the LSG group was 212.21 pg/mL ± 140.57 SD. After 1 month, the average ghrelin level in the LSG group was 74.47 pg/mL ± 29.55 SD (p = 0.01), and it was 41.47 pg/mL ± 15.19 SD (p = 0.002) after 3 months. The average level of preoperative ghrelin in the LGCP group was 318.08 pg/mL ± 161.70 SD. It decreased to 190.58 pg/mL ± 116.75 SD (p = 0.01) after 1 month and to 91.57 pg/mL ± 56.70 SD (p = 0.004) after 3 months. Comparing the two groups, hunger sensation had decreased more in the LSG group (p = 0.03) 3 months after the surgery.**
Conclusions: **Laparoscopic sleeve gastrectomy (LSG) and laparoscopic greater curvature plication (LGCP) produced the same weight loss and diminished hunger sensation in the short term on the selected patients. LSG had an increased effect on ghrelin levels when compared with LGCP at 1 month after the procedure and 3 months after the procedure.**
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Correspondence:
Prof. Ciprian Duta, MD, PhD
Department of Surgery
"Victor Babeş" University of Medicine and Pharmacy
2 Eftimie Murgu Square
300041 Timişoara
Romania
Email: duta.ciprian@umft.ro

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KEY WORDS

ghrelin, metabolic syndrome, bariatric surgery

INTRODUCTION

Ghrelin is a unique peptide with orexigenic, adipogenic, and somatotropic functions. It was discovered in 1999 by Kojima et al. [1]. Ghrelin stimulation causes weight

gain through hyperphagia, adiposity, and anabolic effects [2]. Ghrelin is mainly produced by the oxyntic glands, which are located in the fundus of the stomach and are nowadays referred to as ghrelin cells.

Laparoscopic sleeve gastrectomy (LSG) and laparoscopic greater curvature plication (LGCP) are widely known to be safe and effective procedures for treating obesity. In both procedures the fundus of the stomach is eliminated; this is accomplished by resection in LSG and by plication and subsequent ischemia in LGCP, leading directly to a decrease in ghrelin secretion.

Various studies have evaluated changes in ghrelin levels after bariatric surgery and have obtained conflicting results, thus creating confusion.

Despite the broad use of LSG and LGCP, hormonal changes in ghrelin levels and induced modifications of hunger sensation after these bariatric operations are less well understood.

The aims of our study were to compare serum acylated ghrelin (the active form of ghrelin) concentrations before and after the surgery of patients undergoing LSG or LGCP and to correlate these levels with excess weight loss and hunger sensation in the short term.

MATERIALS AND METHODS

A prospective non-randomized study was carried out in the Second Surgical Department of Timisoara Emergency County Hospital and at the Advanced Metabolic Surgery Center-Bucharest Ponderas Hospital between March and September 2015. Laparoscopic gastric sleeve and laparoscopic greater curvature plication were performed in cases where the patient was motivated to change his or her lifestyle, committing to engage in continuous diet and exercise after the surgical procedure. All the patients underwent a multi-disciplinary evaluation (endocrinological, nutritional, gastroenterological, cardiological, pneumological, and psychiatric assessments).

Before and after the surgery, the patients were required to fill out a questionnaire on subjective hunger sensation, which consisted of a scale of 1 - 10 by which the patient rated his or her sensations.

The inclusion criteria for the bariatric surgery comprised the following: (1) patients with a body mass index (BMI) over 35 kg/m^2 and at least one comorbidity or (2) patients with a BMI over 40 kg/m. The patients had to have a strong will to exercise and to follow a dietary regimen after the surgery.

The exclusion criteria for the patients were as follows: a documented history of alcohol abuse or drug abuse at the time of the preoperative evaluation, previous surgical procedures performed for the treatment of obesity, pregnancy or lactation, diseases that turn the subject into a high-risk surgical candidate, severe cardio-pulmonary disease, liver disease (cirrhosis and portal hypertension), eso-gastrointestinal conditions (Barrett's esophagus, gastrointestinal malignant tumor), and patients with significant psychopathology that could limit their ability to understand the procedure and comply with the medical, surgical, and/or behavioral recommendations.

Ghrelin assay-sampling for ghrelin detection-was done from venous blood in the morning after an overnight, 12-hours fast. The container of the sample was shaken gently by inversion, immediately put on ice, and transported to the laboratory. Harvesting containers (K3 EDTA container + aprotinin) were kept in the refrigerator until the harvest. Aprotinin was used to prevent degradation of the acylated ghrelin by proteases. Within 30 minutes, the harvested plasma was separated by centrifugation in cold temperatures (2 - 8°C) for 10 minutes at 3,500 rpm. The plasma was separated using a plastic pipette, immediately acidified to a pH of 3 - 4 (100 µL of 1 N hydrochloric acid was added to each 1 mL plasma) and then again centrifuged for 5 minutes at 3,500 rpm. The supernatant was transferred to a second tube. The plasma was kept below -20°C in a polypropylene tube until all the samples were collected. All the samples were worked simultaneously using ELISA; a test was performed to detect the acylated form - active ghrelin. The detection limit was 4 pg/mL. Follow-up samples were obtained from the patients who underwent LSG or LGCP, and the ghrelin levels were studied at 3 time points: pre-operation, 1 month after the procedure, and 3 months after the procedure.

The techniques of LSG [3] and LCGP [4] used in this study were the same as described previously by Copăescu.

All the patients gave written, informed consent. The study protocol was created following the guidelines of the Helsinki Declaration 1975 (revised in 2000) and received approval from the local Ethics Committees.

Statistical analysis

Data are presented as mean ± standard deviation of the mean (SD). Paired samples for the means *t*-tests were used when comparing the means of the pre-operative and postoperative values within the same group. Independent samples were used for the *t*-tests when comparing the means across the two groups. A p-value < 0.05 was considered statistically significant. Pearson's correlation coefficients were calculated to determine the association between hunger scores and ghrelin levels.

RESULTS

A total of 18 obese patients was included in the study, including 10 in the LSG group and 8 patients in the LGCP group (Table 1).

All the procedures were performed laparoscopically. The average level of preoperative ghrelin in the LSG group was 212.21 pg/mL ± 140.57 SD. After 1 month, the ghrelin level was 74.47 pg/mL ± 29.55 SD (p = 0.01), and it was 41.47 pg/mL ± 15.19 SD (p = 0.002) after 3 months (Figure 1).

The average level of preoperative ghrelin in the LGCP

Table 1. Demographic characteristics of the patients.

	LSG n = 10	LGCP n = 8	p-value
Gender (male/female)	0/10	1/7	-
Age (years)	34.9 ± 9.7	35.8 ± 8.91	NS
BMI (kg/m^2)	37.33 ± 2.08	36.92 ± 1.43	NS

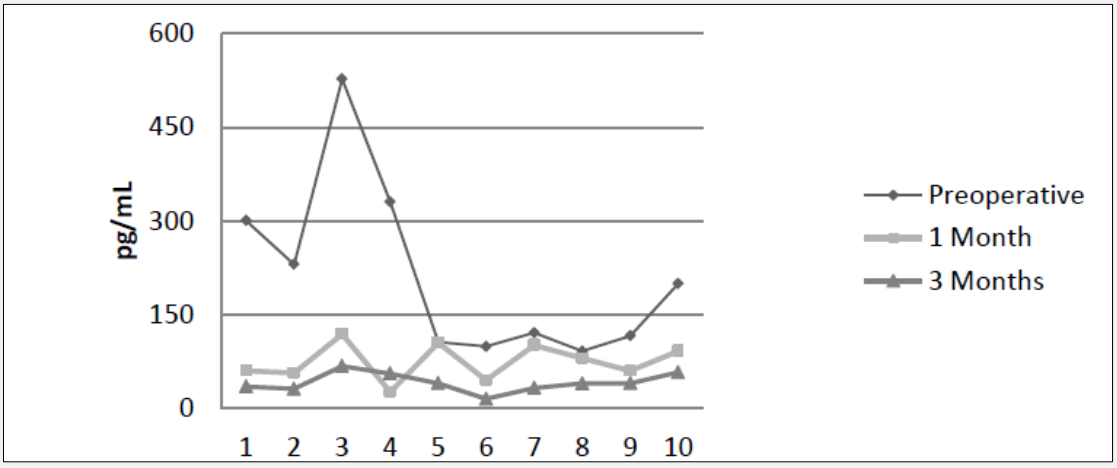

Figure 1. Levels of ghrelin in the LSG group - evolution in every patient.

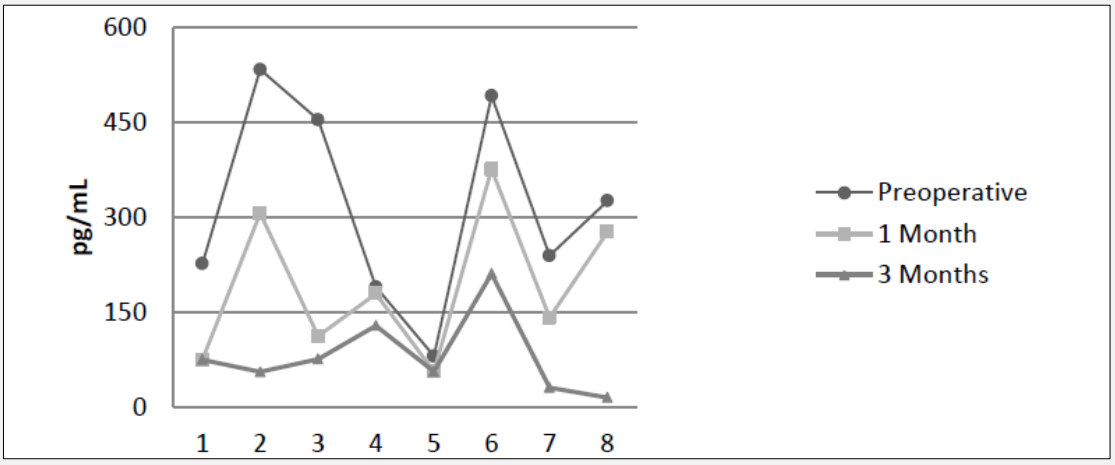

Figure 2. Levels of ghrelin in the LGCP group - evolution in every patient.

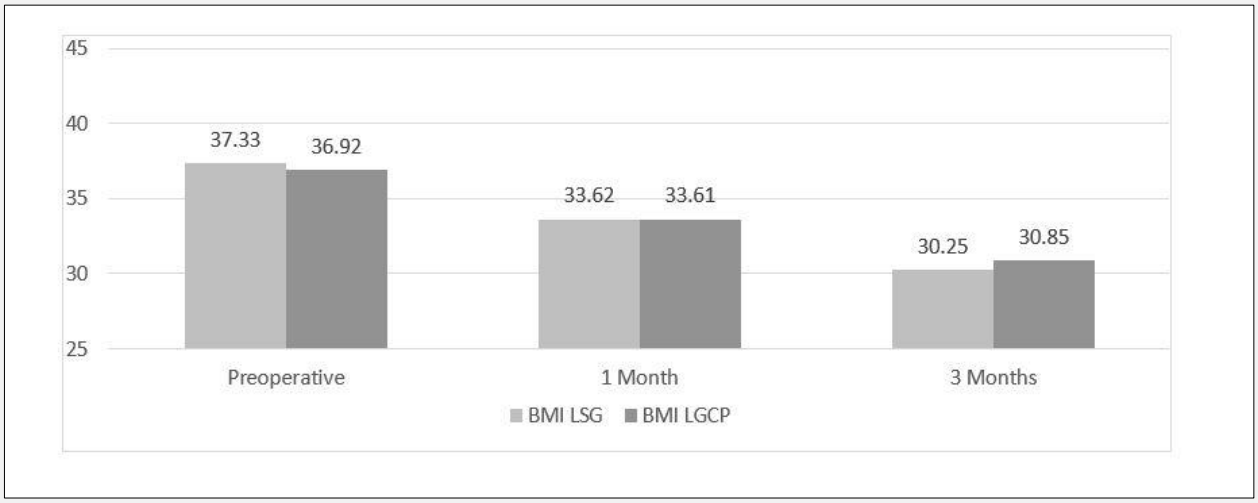

Figure 3. Mean BMI in patients with LSG and LGCP.

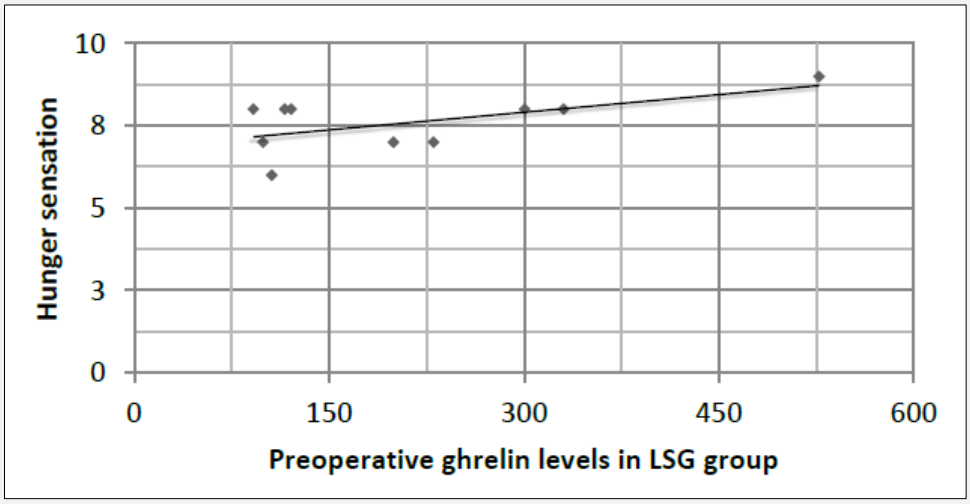

Figure 4. Correlation between the preoperative ghrelin levels and hunger sensation in the LSG group.

group was 318.08 pg/mL ± 161.70 SD. It decreased after 1 month to 190.58 pg/mL ± 116.75 SD (p = 0.01) and after 3 months to 91.57 pg/mL ± 56.70 SD (p = 0.004) (Figure 2).

Comparing the two groups, there were no statistically significant differences regarding preoperative ghrelin levels in the LSG group (212.21 pg/mL ± 140.57 SD) compared with those of the LGCP group (318.08 pg/mL ± 161.70 SD (p = 0.16)). After 1 month, the ghrelin levels decreased more in the LSG group (74.47 ± 29.55) as compared with the LGCP group (190.58 pg/mL ± 116.75 SD), (p = 0.02.). After 3 months, the ghrelin levels were 41.47 pg/mL ± 15.19 SD in the LSG group and 91.57 ± 56.70 SD in the LGCP group, with the differ-

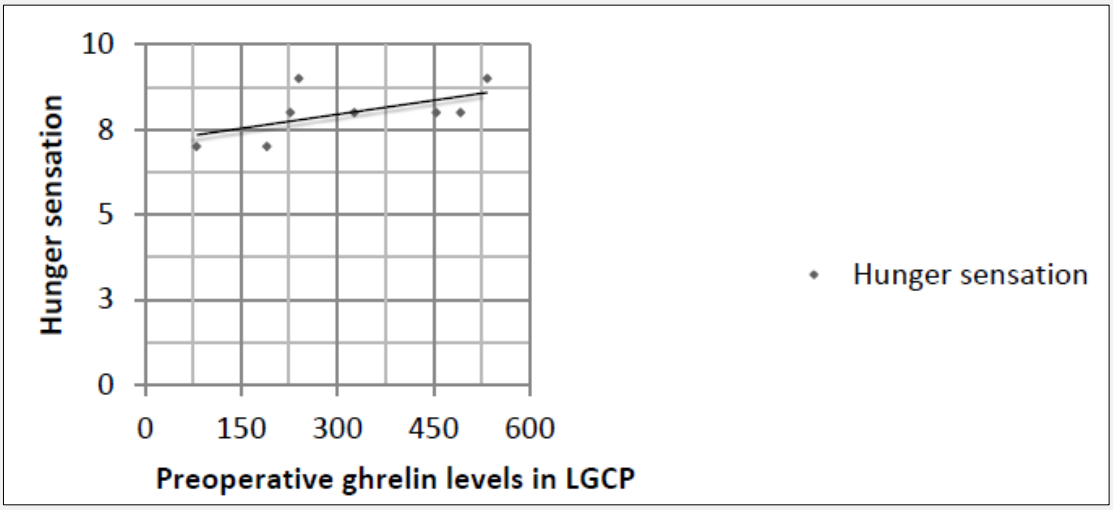

Figure 5. Correlation between the preoperative ghrelin levels and hunger sensation in the LGCP group.

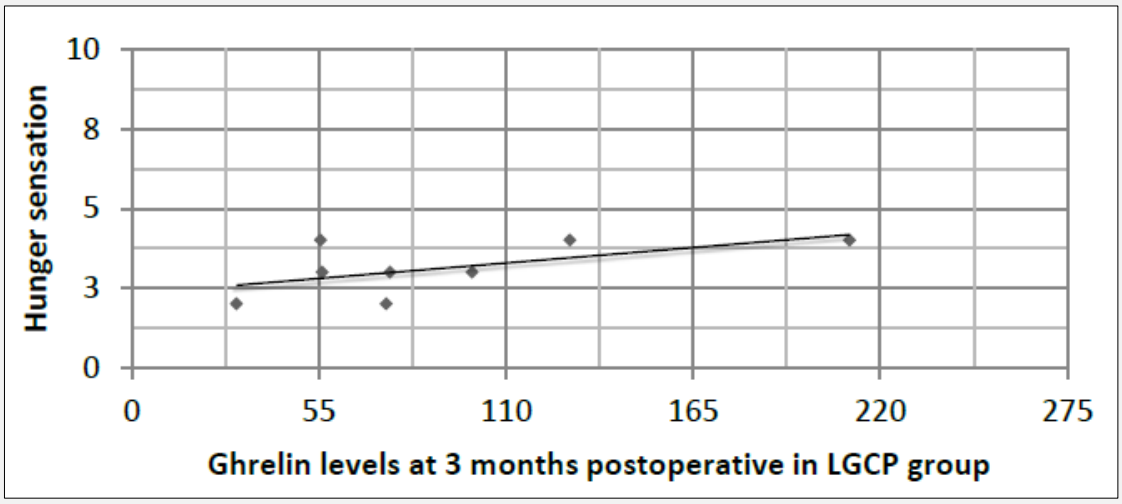

Figure 6. Correlation between the ghrelin levels and hunger sensation in the LGCP group 3 months after the operation.

ence being statistically significant ($p = 0.04$).

The mean BMI in the patients with LSG and those with LGCP before the surgery, 1 month after the surgery, and 3 months after the surgery are presented in Figure 3. In the LSG group, the average preoperative BMI was 37.33 kg/m^2 ± 2.08 SD. After 1 month, the mean BMI decreased to 33.62 kg/m^2 ± 2.13 SD, and at 3 months, it decreased to 30.25 kg/m^2 ± 1.89 SD. In the LGCP group, the mean preoperative BMI was 36.92 kg/m^2 ± 1.43 SD, decreasing to 33.61 kg/m^2 ± 1.14 SD after 1 month and 30.85 kg/m^2 ± 2.34 SD after 3 months. Regarding the correlation between the preoperative ghrelin levels and the subjective sensation of hunger in the LSG group, there was a positive linear relationship

with Pearson's correlation coefficient r = 0.59 (Figure 4).

In the LGCP group, there was a positive linear relationship with respect to the correlation between the preoperative ghrelin levels and the subjective sensation of hunger, with r = 0.58 (Figure 5). In the same group, 3 months after the operation, r = 0.59 (Figure 6).

Comparing the two groups three months after the operation, hunger sensation decreased more in the LSG group (p = 0.03) than in the LGCP group.

No major complications, including leakage, bleeding, or thromboembolism, were observed. However, early episodes of persistent nausea and vomiting and abdominal pain were recorded in both groups.

DISCUSSION

The patients enrolled in this study were young, and there were females in both groups. This was due to the inclusion criteria in the LCGP group requiring the patients to exercise and comply with a diet after the procedure. Before the surgery, there were no differences in the average BMIs and ages across the groups, but there was a difference in the ghrelin level, though it was not statistically significant.

Ghrelin is a hormone that increases food intake. Its level should rise when fasting or losing weight as a compensatory mechanism. Cumming et al. proved this by testing patients who lost weight by diet alone and found that ghrelin levels rose throughout the day in all the subjects, with a maximum rise of 51% before dinner. In the same study, they discovered that after Roux en Y Gastric Bypass (RYGB), the levels of ghrelin dropped by 77% when compared with normal lean subjects and by 72% when compared with obese patients who underwent weight loss with diet and exercise alone [5]. The hypothesis was that the gastric fundus, the main source of ghrelin in the body, would be excluded from the passage of the food, and as a result, the ghrelin-excreting cells would not be stimulated to secrete ghrelin. Others have pointed to the functional integrity of the fundus being directly related to the decreased ghrelin levels [6]. In this study, after LSG, the gastric fundus was removed, and the ghrelin levels of the patients dropped dramatically, even though the subjects were losing weight quickly. This could be one of the mechanisms of this type of weight loss - of rapidly decreased hunger sensation and sustained weight loss over a longer period - when compared with patients submitted to diet alone. There was a significant decrease in hunger sensation three months after LSG, correlating the ghrelin level with a Pearson's r coefficient equal to 0.61. After LSG, the level of ghrelin decreased at a statistically significant pace 1 month after the operation and 3 months after the operation. Some authors have suggested that ghrelin levels should only be tested on subjects with steady weights [7], but the purpose of our study was to determine the short-term changes after the procedure.

LGCP also modifies the functionality and anatomy of the gastric fundus via imbrication of the latter. Brandnova et al. found that ghrelin levels decreased and remained low twelve months after LGCP [8]. Ivan et al. published a study on ghrelin following a simultaneous LGCP and Nissen procedure, leaving the gastric fundus in place, as they used it for preventing hiatal hernia and gastro-esophageal reflux; the levels of ghrelin did not fluctuate after the operation [9]. In our study, ghrelin levels decreased 1 month after LGCP and 3 months after the operation. The same thing happened with hunger sensation, and the ghrelin levels and hunger sensation had a high Pearson's correlation index.

Sista et al. found that the volume of the resected stomach is directly proportional to the post-operative levels of ghrelin and to the speed and intensity of the onset of the beneficial effects of the bariatric surgery [10]. We can only hypothesize that LSG removed a larger volume of the stomach than LGCP, resulting in a lower level of ghrelin 1 month and 3 months after the operation. This was correlated with a higher reduction in hunger sensation following LSG, with a smaller gastric tube leading to early satiety and diminished hunger sensation. Apparently LSG was a better procedure with respect to lowering ghrelin levels and hunger sensation when compared with LGCP. However, comparing EWL and BMI after 1 month and 3 months, there were no statistically significant differences between the two procedures. Nevertheless, this was a premature time to assess the EWL, as the early weight recidivism following LSG usually occurs 1.5 years after surgery and affects about 10% of the subjects of LSG [11-18]. On the other hand, our objective was to determine the ghrelin level and its correlation with the EWL and hunger sensation on a short-term basis before and after the operation. Also, our study included selected patients - active, young, and willing to comply with the post-operative diet and exercise recommendations - and thus, the differences between the two procedures might be minimal due to this selection and short-term evaluation. Others have found that at 1 year, EWL after LGCP was lower than 1 year after LSG [12,13-17].

Our study had a relatively small number of selected patients, but the results were significant when we refer to the higher ability of LSG to lower the ghrelin level after surgery. The decrease of the ghrelin level did not have a proportional effect on hunger sensation. Thus, hunger sensation might have other regulatory hormones besides ghrelin.

CONCLUSION

LSG and LGCP produced the same weight loss and diminished hunger sensation in the short term on the selected patients. LSG had an increased effect on lowering ghrelin levels when compared with the ghrelin levels in the patients in the LGCP group 1 month after the operation and 3 months after the operation.

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Declaration of Interest:
The authors do not have any conflicts of interest.

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