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ORIGINAL ARTICLE

The role of laparoscopic sleeve gastrectomy on inflammatory parameters in morbidly obese patients☆

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KEYWORDS
Morbidly obese patients;
Laparoscopic sleeve gastrectomy;
Zinc;
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Peroxisome proliferator-activated receptor-γ;
Nuclear factor kappa-B

Abstract
Background: Obesity is an excessive increase in body fat mass and triggers chronic inflammation which causes increased fat accumulation in the visceral fat tissue. The aim of this study was to analyze serum zinc (Zn), Zn-alpha 2 glycoprotein (ZAG), peroxisome proliferator-activated receptor-γ (PPAR-γ) and nuclear factor kappa-light-chain-enhancer of activated B cell (NF-κB) levels in morbidly obese patients before and after laparoscopic sleeve gastrectomy (LSG) and determine the association between alteration in body mass index (BMI), the % Excess Weight Loss (% EWL) and the biochemical parameters.
Methods: Thirty healthy individuals as a control group and 30 morbidly obese patients who had undergone LSG were enrolled in this study. Routine anthropometric and laboratory biochemical parameters in venous blood samples of groups at baseline and 1 and 12 months after LSG were recorded.
Results: Significant weight loss was achieved at 1 and 12 months after LSG. At baseline serum ZAG and PPAR-γ levels were lower, while NF-κB levels were higher in morbidly obese patients compared with the control group. Serum ZAG and PPAR-γ levels increased while NF-κB levels decreased 1 month and 12 months after LSG. Decreased %EWL was negatively correlated with changes in NF-κB, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), fasting plasma glucose and insulin at 12 months after LSG in morbidly obese patients. However, %EWL was positively correlated with changes in ZAG.
Conclusions: Obesity was associated with down-regulated serum ZAG and PPAR-γ levels while up-regulated serum NF-κB. Our findings suggest that LSG ameliorates upregulating PPAR-γ expression, thereby inhibiting NF-κB-mediated inflammation by weight loss.
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Introduction

Obesity is an excessive increase in body fat mass. The disease has negative effects on the quality and length of life, and its frequency has increased over the past years due to changing lifestyles and diet [1,2]. Individuals with a body mass index (BMI) (weight/height^2) of over 30 are defined as obese, and a BMI of over 40 is identified as morbidly obese. Obesity is accompanied by type 2 diabetes (T2D), hyperlipidemia, hypertension, coronary artery disease, sleep apnea and many types of cancer; and it increases morbidity and mortality, negatively affecting the quality of life and shortening the life span [1—3]. The prevalence of obesity in Turkey was 16.4% in 1994, but increased to 32% in 2000 [4]. If the rate of obesity continues and increases in this pattern, 50% of the world population will be obese and 85% of the population of United States of America (USA) will be obese or overweight by 2030 [5].

Dieting, exercise, behavioral changes and medical methods have proved ineffective in the treatment of obesity; therefore, the focus is on new surgical techniques and studies that will explain the pathophysiology of obesity on a molecular level [6,7]. Since the 1950s, many methods including restrictive and malabsorptive components emerged for the treatment of obesity, but none of them has yet been embraced as the golden standard. The surgery type is planned based on the metabolic and diet status of the patient and experiences and choices of the surgeon with considering the indications of metabolic surgery [7,8]. Laparoscopic sleeve gastrectomy (LSG), which has been popularly used in recent times, has a restrictive principle due to reduction of the gastric size. LSG is an impressive and well-established surgical technique in patients who have a high BMI value and comorbid diseases [9,10].

Many studies have shown the relation between obesity and concomitant complications with chronic low-grade inflammation. Obesity triggers chronic inflammation which causes increased fat accumulation in the visceral fat tissue, insulin resistance and endothelial dysfunction [11]. Zinc (Zn) is necessary for regular cellular function and metabolism, and it preserves the cells against the damages caused by the free radicals. Furthermore, it has significant status in appetite regulation and insulin secretion through its effect on the leptin system [12,13]. Zn-alpha-2-glycoprotein (ZAG) is an adipokine that affects fat metabolism; weight loss and reduction in muscle and fat tissue occur due to the lipolytic effect of ZAG in cachexia [14,15].

Peroxisome proliferator-activated receptor-γ (PPAR-γ) is a member of transcription factors that belong to the superfamily of nuclear receptors, amply found in white and brown fat tissue. Furthermore, multiple studies have determined that PPAR-γ is the main regulator in adipocyte differentiation (adipogenesis) [16,17]. The nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) takes part in the regulation of apoptosis, cell growth, angiogenesis, and metastasis and cell life. Furthermore, many investigations have demonstrated the importance of NF-κB activity in developing insulin resistance [18,19].

To the best of our knowledge, there is still no study on the association of serum ZAG, PPAR-γ, and NF-κB levels in morbidly obese patients who underwent LSG. Therefore, the current study aimed to assess serum levels of ZAG, PPAR and NF-κB in morbidly obese patients compared to healthy individuals and to follow their variations after up to 12 months after LSG. Baseline levels of all biochemical parameters in morbidly obese patients were also compared with those in age-matched healthy control subjects.

Materials and methods

Subjects

Written informed consent was obtained from all patients and healthy volunteers prior to their participation in the study in accordance with the Helsinki World Medical Association Declaration. The study was accepted by the Cerrahpasa Medical Faculty's Ethical Committee on Human Research, Istanbul University-Cerrahpasa (08/October/2015, 83045809/604.01/02-313597).

The control group ($n = 30$; 16 female and 14 male aged between 46 ± 11) consisted of clinically healthy, volunteer individuals with a normal BMI (WHO recommended international standard: $18.5\,kg/m^2 < BMI < 24.9\,kg/m^2$).

The morbid obesity group ($n = 30$; 20 female and 10 male aged between 44 ± 6) consisted of patients who were diagnosed with morbid obesity with a $BMI > 40\,kg/m^2$ and were referred our clinic for treatment and planned to undergo LSG.

Postoperative month 1 ($n = 30$): The group consisted of patients evaluated 1 month after LSG.

Postoperative month 12 ($n = 30$): The group consisted of patients evaluated 12 months after LSG.

Exclusion criteria included cardiovascular diseases, metabolic diseases (except diabetes mellitus), pregnancy, stomach, chronic kidney or liver disease, smoking, alcohol abuse, or receiving lipid-lowering therapy, vitamins, aspirin, or antioxidants. All of the subjects were free of concomitant vascular disease malignancy and connective tissue diseases.

Surgical LSG procedure

The LSG operation was executed by a surgeon who had extensive experience in bariatric surgery. A sleeve was constituted around a 36F bougie 2—3 cm proximal to the pylorus and extending to the angle of His. The whole staple line was tested for leakage using methylene blue. The gastric specimen was removed through the 12-mm trocar located at the left middle abdomen. A closed suction drain was inserted in all the patients, oral contrast study was performed on the third day of surgery to rule out leak or stricture and the drain was removed 3 days following the surgery. Using this method, reducing the size of the stomach and removing the part of the ghrelin production area causes the patient to eat less and a decrease in appetite, resulting in lower calorie intake.

All patients were assessed preoperatively, then followed up postoperatively at 1 and 12 months, evaluated by the attending surgeon, and completed a questionnaire designed to collect diverse epidemiological data that included age, gender, BMI, past medical history, and treatment. Each clinical measurement was documented during the patients' visits with the assistance of a bariatric nurse. Blood samples were collected from every patient in the morning while in a fasting state, centrifuged, separated within 1 hour of collection, and afterwards stored at $-80\,^{\circ}C$ until analysis.

The excess weight loss percentage (% EWL) was calculated by means of [(Operative Weight—Follow-up Weight)/(Actual Weight—Ideal Weight)] $\times$ 100 [20]. The ideal weight was identified using the standard Devine formula [21]. The ideal body weight for men equaled 50 kg

plus 2.3 kg/1 inches > 5 ft. The ideal body weight for women equaled 45.5 kg plus 2.3 kg/1 inches > 5 ft.

Analysis of biochemical parameters

Serum ZAG, PPAR-γ and NF-κB levels were measured with the use of Enzyme-Linked ImmunoSorbent Assay (ELISA) (YH Bioresearch Laboratory, Shanghai, China) analysis method in serum samples of both groups before and 1 and 12 months following LSG. The analysis was realized in accordance with the kit protocol. Optic density values were measured over 10 minutes using a microplate reader ELX800 (Bio-Tek Instruments, Inc., Vermont, USA). All samples were run in duplicate in the same assay.

Measurement of zinc level

Serum levels of Zn were analyzed with inductively coupled plasma-optical emission spectrophotometer (ICP-OES) (Thermo Scientific iCAP 6000) at the Trace Element Analysis Laboratory at Cerrahpasa Medical Faculty's Biophysics Department. The favorable wavelength for ICP-OES related to Zn was 206.200 nm. Serum samples were diluted by using deionized water in a fresh pretreated tube using an automatic pipette followed with vortexing of the test tubes prior to the analysis. Deionized water was used for a blank all along.

Routine analysis

Biochemical variables were measured at Cerrahpasa Medical Faculty's Central Biochemistry Laboratory. The plasma glucose levels were calculated by using the Olympus AU 800 analyzer with enzymatic methods using commercial kits (Roche Diagnostics, GmbH, Mannheim). Plasma insulin was detected following radioimmunoassay using a commercial kit (DSL-1600, USA) in a clinical biochemistry laboratory. The homeostatic model assessment (HOMA) method was used in estimating the beta-cell function and insulin resistance (HOMA-IR) from basal (fasting) glucose and insulin. HOMA-IR was determined by using the formula [fasting glucose (mmol/L) × fasting insulin (μU/mL)]/22.5.

Statistical analysis

Statistical analysis was realized by using SPSS 21.0 (Statistical Package for Social Science). Biochemical parameters and the levels of Zn, ZAG, and PPAR-γ, NF-κB were determined in different samples, then statistic-descriptive analysis was made for each of the parameters. Significant values from the samples were assessed with the ANOVA tests. One-Way ANOVA parametric test was used for datas that fit to normal range and non-parametric Kruskal Wallis test was used for datas which does not adapt to normal range. All results were described as mean ± standard deviation (M ± SD). $P < 0.05$ was considered as significant.

Results

Baseline characteristics before LSG

In our study, the mean age was 46 ± 10.8 years in the control group (14 males, 16 females) and 43.7 ± 6.8 years in the patient group (10 males, 20 females). There were no statistical differences in terms of age and gender between the groups. The mean weight for the obese patients prior to the surgery was 134.4 ± 21 kg and the mean BMI was 48 ± 5.7 kg/m^2 (Table 1). Prevalence of type 2 diabetes was 63.3% (n:19) in obese patients and there was no diabetic in control group.

Characteristics at the month 1 and 12 after LSG

The mean weight of patients was 125.2 ± 20.3 kg and the BMI was 46.1 ± 7.1 kg/m^2 in the month 1 following the operation, and mean weight was 82.7 ± 6.9 kg in month 12 following the operation. The mean BMI was down to 29.6 ± 2.2 kg/m^2. EWL was 13.4 ± 3.9% in the month 1 and 69.6 ± 8.6% in the month 12. The patients started losing weight in the month 1 following the surgery, and a statistically significant decrease was observed by the month 12 ($P < 0.001$). A statistical comparison of BMI revealed a significant decrease at the end of the month 12 with $P < 0.01$ (Table 2, Fig. 1.A).

The glucose and insulin levels in the patient group were statistically significantly higher ($P < 0.001$) than the values in the control group; a significant decrease was noted in month 12 by $P < 0.001$, compared to the preoperative group (Tables 1 and 2).

A comparison of HOMA-IR values between the control group and the patient group revealed that the values in the patient group were statistically significantly higher (preoperative, $P < 0.001$; postoperative month 1, $P < 0.01$) in comparison with the control group. Follow-up of preoperative obese patients revealed a significant decrease in the month 1 and month 12 following the operation by $P < 0.01$, $P < 0.001$, respectively (Tables 1 and 2, Fig. 1B).

The zinc levels were higher in obese patients when compared with the levels in healthy individuals, but the difference was not statistically significant. A statistically significant decrease was observed in the postoperative month 1 group in comparison with the preoperative group ($P < 0.05$) (Table 2, Fig. 1C).

The ZAG values in the patient group were statistically significantly lower ($P < 0.001$) when compared with the values in the control group; a significant increase was noted in month 1 and month 12 by $P < 0.05$ and $P < 0.001$, respectively, compared with the preoperative group (Tables 1 and 2, Fig. 1D).

A comparison of PPAR-γ values of the patient groups with the control group revealed that the PPAR-γ values of the patient groups were statistically significantly lower than the values of the control group (preoperative, $P < 0.005$; postoperative month 1, $P < 0.05$; postoperative month 12, $P < 0.01$). A significant increase was observed in postoperative month 1 and month 12 by $P < 0.05$, $P < 0.01$, respectively, in comparison to the preoperative patient group (Tables 1 and 2, Fig. 1E).

A comparison of NF-κB values between the control group and patient group showed that the values in the patient groups were statistically significantly higher (preoperative, $p < 0.001$; postoperative month 1, $p < 0.01$) checked against the control group. Follow-up of preoperative obese patients disclosed a significant reduction in postoperative month 1 and month 12 by $p < 0.05$, $p < 0.001$, respectively (Tables 1 and 2, Fig. 1.F).

Correlation analysis

The relationships among the serum zinc, ZAG, PPAR-γ, and NF-κB levels, HOMA-IR, fasting plasma glucose and

Table 1 Clinical measurements, metabolic parameters in controls and morbidly obese patients.

	Controls (*n*:30)	Morbidly Obese Baseline (*n*:30)	*P*
Male/Female	14/16	10/20	NS
Age (year)	46 ± 10.8	43.7 ± 6.8	NS
Body weight (kg)	68 ± 9.9	134.4 ± 21	*P* < 0.001
BMI (kg/m^2)	24 ± 2.2	48 ± 5.8	*P* < 0.001
Type 2 diabetes	%0 (n:0)	%63.3 (n:19)	*P* < 0.001
Zn (μg/dL)	71.4 ± 17.4	78.4 ± 14	NS
ZAG (μg/mL)	70.5 ± 18.9	42.9 ± 9.1	*P* < 0.001
PPAR-γ (ng/mL)	40.2 ± 10.8	33.4 ± 7.3	*P* < 0.05
NF- κB (ng/mL)	1.2 ± 0.9	2.3 ± 0.8	*P* < 0.001
HOMA-IR	2.2 ± 0.5	12.1 ± 5.4	*P* < 0.001
Fasting plasma insulin (μg/mL)	10.6 ± 2.5	28.4 ± 10.3	*P* < 0.001
Fasting plasma glucose (mg/dL)	84.1 ± 6.8	170.5 ± 7.5	*P* < 0.001

BMI: Body mass index, Zn: Zinc, ZAG: Zinc alpha 2-glycoprotein, PPAR-γ: Peroxisome proliferator-activated receptors, NF-κB: Nuclear Factor kappa B, HOMA-IR: Homeostatic model of assessment-insulin resistance, NS: not significant.

Table 2 Metabolic parameters in morbidly obese patients at baseline pre-operative) and at month 1 and 12 after laparoscopic sleeve gastrectomy (post-operative).

	Pre-op (*n* = 30)	Post-op month 1 (*n* = 30)	Post-op month 12 (*n* = 30)
Body weight (kg)	134.4 ± 21.0	125.2 ± 20.3	82.7 ± 6.9 [a]***
BMI (kg/m^2)	48 ± 5.7	46.1 ± 7.1	29.6 ± 2.2 [a]***
Zn (μg/dL)	78.4 ± 14.0	65.4 ± 15.4[a]*	69.5 ± 18.1
ZAG (μg/mL)	42.9 ± 9.1	47.3 ±7.0 [a]*	65.1 ± 13.0 [a]***
PPAR-γ (ng/mL)	33.4 ± 7.3	36.6 ± 6.7 [a]*	40.9 ± 6.9 [a]***
NF- κB (ng/mL)	2.3 ± 0.8	1.8 ± 0.4 [a]*	1.4 ± 0.5 [a]***
HOMA-IR	12.1 ± 5.4	8.2 ± 3.0 [a]**	2.8 ± 0.7 [a]***
Fasting plasma insulin (μg/mL)	28.4 ± 10.3	21.1 ± 6.7[a]**	12.1 ± 3.1[a,b]***
Fasting plasma glucose (mg/dL)	170.5 ± 7.5	157.5 ± 18.4	95.4 ± 13.7[a,b]***
EWL (%)	—	13.4 ± 3.9	69.6 ± 8.6[b]***

BMI: Body mass index, Zn: Zinc, ZAG: Zinc alpha 2-glycoprotein, PPAR-γ: Peroxisome proliferator-activated receptors, NF-κB: Nuclear Factor kappa B, HOMA-IR: Homeostatic model of assessment-insulin resistance, EWL%: Percentage excess weight loss. *P < 0.05; ** P < 0.01; *** P < 0.001.

[a] versus pre-op group

[b] versus post-op 1.month group;

Table 3 *r* values of correlation analysis of the study groups. For body weight and BMI; all groups (control + pre-op + post-op month 1 and 12, *n*: 120), EWL; post-op month 1 and 12 (n: 60) parameters are evaluated.

	Body weight (kg)	BMI (kg/m^2)	EWL (%)
Zn (μg/dL)	*r* = 0.058 *P* = 0.556	*r* = 0.078 *P* = 0.426	*r* = 0.087 *P* = 0.653
ZAG (μg/mL)	*r* = -0.633*P* = 0.000	*r* = -0.677*P* = 0.000	*r* = 0.587 *P* = 0.000
PPAR-γ (ng/mL)	*r* = -0.298*P* = 0.001	*r* = -0.255*P* = 0.005	*r* = 0.344 *P* = 0.054
NF- κB (ng/mL)	*r* = 0.465 *P* = 0.000	*r* = 0.433 *P* = 0.000	*r* = -0.728 *P* = 0.000
HOMA-IR	*r* = 0.708 *P* = 0.000	*r* = 0.692 *P* = 0.000	*r* = -0.799 *P* = 0.000
Fasting plasma insulin (μg/mL)	*r* = 0.672 *P* = 0.000	*r* = 0.659 *P* = 0.000	*r* = —0.699*P* = 0.000
Fasting plasma glucose (mg/dL)	*r* = 0.768 *P* = 0.000	*r* = 0.722 *P* = 0.000	*r* = —0.866*P* = 0.000

Zn: Zinc, ZAG: Zinc alpha 2-glycoprotein, PPAR-γ: Peroxisome proliferator-activated receptors, NF-κB: Nuclear Factor kappa B, HOMA-IR: Homeostatic model of assessment-insulin resistance, BMI: Body mass index, EWL%: Percentage excess weight loss.

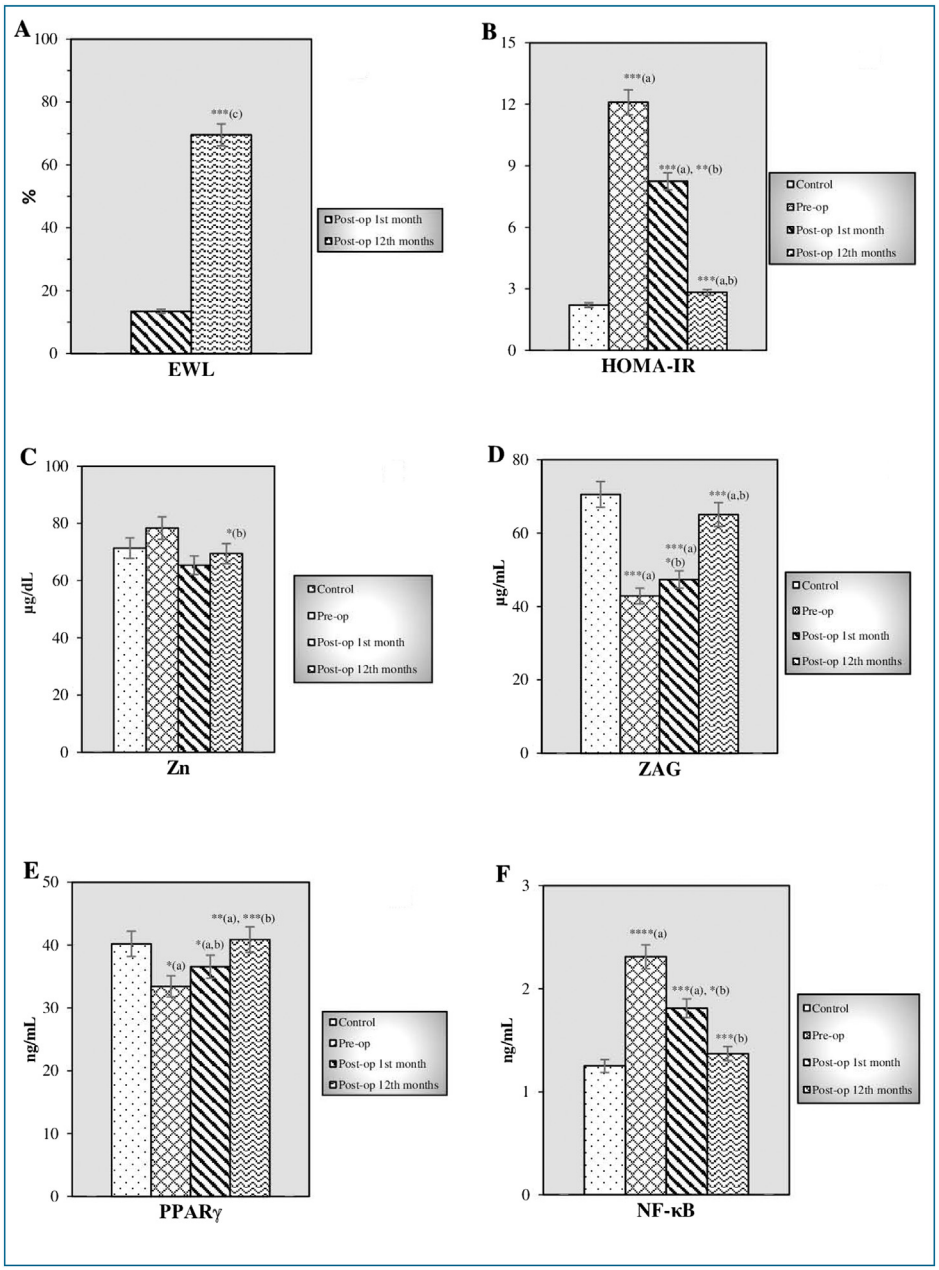

Figure 1. A- EWL%, B- HOMA-IR, C- Zn, D- ZAG, E- PPAR-γ and F- NF-κB levels of the study groups. EWL%: Percentage excess weight loss, HOMA-IR: Homeostatic model of assessment-insulin resistance, Zn: Zinc, ZAG: Zinc alpha 2-glycoprotein, PPAR-γ: Peroxisome proliferator-activated receptors, NF-κB: Nuclear Factor kappa B. a versus control, b versus pre-op, c versus post-op 1st month. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

insulin with body weight, BMI and EWL% in morbidly obese patients are shown in Table 3. There were significant positive correlations between body weight and HOMA-IR, fasting plasma insulin and fasting plasma glucose. There was also a significant negative correlation with ZAG protein and correlation between body weight and the fasting plasma glucose level which had the highest positive value ($r = 0.768$). There was a significant positive correlation between BMI and HOMA-IR, fasting plasma glucose and insulin and negative correlation with ZAG. A significant negative correlation was also observed among EWL% and NF-κB, HOMA-IR, fasting plasma glucose and insulin parameters, whereas the maximum correlation value calculated in the relationship was between EWL% and fasting plasma glucose level ($r = 0.86$). Additionally, there was a significant positive correlation with ZAG protein.

Discussion

Bariatric surgery has been the standard care for obesity and related morbidity over the last decade, the most popular procedure worldwide has become LSG because LSG is a simpler, faster procedure and approaches only one organ in one surgical field without the requirement of advanced end suture skills. In this study, we have demonstrated for the first time that weight loss, increase in ZAG and PPAR-γ, levels and decrease in NF-κB levels were found

in patients who underwent LSG due to morbid obesity. These findings suggest that the LSG technique may regulate fatty acid metabolism, energy balance, insulin sensitivity and glucose levels through weight loss in morbidly obese patients.

In the current study, serum Zn levels in obese patients were higher when compared with the levels in healthy individuals, but the difference was not statistically significant. Zinc levels are significantly reduced 1 month following LSG, with no significant changes until 1 year following surgery. Zn deficiency is not unusual in patients choosing bariatric surgery. A study by Ruz et al. [22] demonstrated that mean plasma Zn, erythrocyte membrane alkaline phosphatase activity, and the size of the rapidly exchangeable Zn pool lowered following RYGBP. Percentage Zn absorption lowered substantially from 32.3% to 13.6% at 6 months after the RYGBP and to 21% at 18 months following surgery. No effect of supplement type was detected. Zinc status is impaired following RYGBP, despite the finding that dietary plus supplemental zinc doubled proposed zinc intakes in healthy people. Zinc absorption capacity is significantly decreased subsequently Roux-en-Y gastric bypass (RYGB), with no major changes until 18 months following surgery. Ferraz et al. [23] proved that at the end a 24-month follow-up, patients who underwent SG, presented serum Zn levels higher than the patients who underwent RYGBP and that the deficit prevalence of the latter micronutrient is significantly higher in the RYGB group. Mahawar et al. [24] proved that a clinically significant zinc deficiency is rare. Reduced protein intake, impaired zinc absorption and deteriorating offsetting mechanisms contribute to zinc deficiency. The mechanisms which are part of it differ according to the type of surgery and time since surgery [22—28]. The information on zinc features the significance of monitoring the mineral in LSG patients. Further studies are required to explore which mechanisms are important in any decrease in the absorption of Zn.

The ZAG values in the patient group were significantly decreased when compared with the control group while a significant increase was noted at 1 month and 12 months in comparison with baseline levels. There were significant positive correlations among body weight and HOMA-IR, fasting plasma insulin and glucose, whereas significant negative correlation with ZAG protein. A significant negative correlation was also observed in the association between EWL% and HOMA-IR, fasting plasma glucose and insulin while there was a significant positive correlation with ZAG protein. The results from our study demonstrated that ZAG is a novel adipokine, regulating energy balance, body weight, and glucose metabolism. ZAG levels may increase in conjunction with weight loss. LSG surgery has been observed to be a significant and effective means for morbidly obese patients to lose weight and also to develop a better metabolic risk profile (increased ZAG levels) over a brief period of time. However, we were not able to find a relationship between Zn, ZAG and PPAR in our study. Morse et al. [29] researched plasma ZAG concentrations in two groups of severely obese individuals who underwent two separate weight loss interventions. There was a significant decrease in ZAG across the groups, but the decrease in ZAG was significant within the RYGB group but not in the very low-calorie diet (VLCD) group. While they cannot relate ZAG to insulin levels, it is possible that the decrease in ZAG following RYGB may result in reduced insulin resistance [29]. Nonetheless, additional clinical studies that include more patients, longer follow-up times and different surgical techniques, are required to support these results.

There are not many reports establishing the relationship between bariatric surgery and PPAR expression [29—32]. Yet, the influence of bariatric surgery on PPAR expression continues to be inconclusive. In the current study, The PPAR-γ values of the patient groups were statistically significantly lower when compared with the values of the control group. A significant rise was determined at 1 month and 12 months following the surgery. There was a significant but weak negative relation between PPAR-γ with body weight, BMI and a significant but weak positive relation with EWL. Costa et al. [31] described that open RYBP lowers PPARγ1—3 mRNA expression in human visceral adipocytes. Kawano et al. [33] presented that PPARγ mRNA expression of retroperitoneal fat in the SG group was significantly greater than in the sham-operated and gastric banding (GB) groups. These results propose that SG develops lipid metabolism when compared with GB, granting that there were no significant discrepancies between the effects of the two procedures on weight loss. Eickhoff et al. [34] described that SG also increased PPAR-γ in adipose tissue in an animal model of adipose T2D. In their obese animal model of T2D, SG significantly developed the health and angiogenesis of adipose tissue while decreasing its insulin resistance, associating PPAR-γ and sprouting angiogenesis markers and endothelial function [34]. Furthermore, PPAR-γ is an essential nuclear receptor that may improve lipid metabolism and increase lipid breakdown and mobilization [35,36]. Therefore, further studies are needed to understand the role of PPAR-γ in related regulations/dysregulations of surgery.

We demonstrated that NF-κB value comparisons between the control group and the patient group affirmed that the values in the patient group were statistically significantly higher in comparison with the control group. Follow-up of preoperative obese patients showed a significant decrease postoperatively at 1 month and 12 months. A significant negative correlation was also observed between EWL% and NF-κB. The role of NF-κB as an aim for the treatment of morbid obesity and the surgical techniques must be widely evaluated as well. Both adipocyte- and macrophage-induced inflammatory changes through NF-κB activation provoke insulin resistance in obesity [37]. PPARγ can suppress the pathway for NF-κB signaling. The pathway activates serine kinases and up-regulates the creation of pro-inflammatory cytokines such as TNF-α and IL-6 [38], as an insulin desensitizing pathway. Weight loss by way of LSG completely modifies levels of PPAR-γ and NF-κB and comprehensively affects insulin sensitivity [39]. Supplementary studies are needed to better perceive the correlation between PPAR-γ and NF-κB and insulin resistance, EWL, body weight and also how these are regulated by LSG. Nonetheless, although the reports propose reduced HOMA-IR and effects of LSG on glucose metabolism, independently from the weight, mechanisms causing such progress are, so far, not quite understood [39].

The current study has several limitations. First, the group sizes were small. We did not follow up the laboratory parameters and clinical consequences of the patient group over longer than one year. There is no control group where weight loss is achieved with medical management (without bariatric surgery). Finally, because of the small number of subjects, we did not compare the groups according to their comorbidities or the drugs being used, such as statins, oral antidiabetics, and renin—angiotensin system (RAS) blockers.

Increased ZAG and PPAR-γ levels and decreased NF-κB levels with decreased weight loss were found in morbidly obese patients who had the LSG operation in our study. LSG improves weight loss through the upregulation of the PPAR-γ expression, and thus limiting NF-κB-mediated inflammation. These findings propose that the LSG technique improves inflammation, energy balance, glucose levels, fatty acid metabolism and insulin sensitivity and levels in morbidly obese patients. However, more clinical studies including more patients, longer follow-up times and different surgical techniques, are required to sustain these results.

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Disclosure of interest

The authors declare that they have no competing interest.

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