ORIGINAL ARTICLE

Adiponectin and leptin levels of patients after sleeve gastrectomy, Roux-en-Y gastric bypass, and single anastomosis sleeve ileal bypass surgeries

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Background: Bariatric surgery is an appropriate treatment for obese patients with metabolic syndrome. Adipose tissue is an active endocrine tissue secreting leptin and adiponectin that affect body metabolism. Nowadays, a high incidence of metabolic syndrome with an increased risk of serious diseases has been detected in Shiraz. This study aimed to assess the levels of leptin and adiponectin as well as the adiponectin-to-leptin ratio in three different bariatric surgeries among obese patients in Shiraz. The results will play an important role in physicians' choice of surgery by distinguishing the effects of these three bariatric surgeries. **Materials and Methods:** The serum adiponectin and leptin levels were measured using enzyme-linked immunosorbent assay. Blood glucose, lipid profile, weight, and liver enzyme level were measured before and 7 months after surgery. **Results:** This clinical trial was conducted on 81 obese patients who underwent sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), and single anastomosis sleeve ileal (SASI) bypass surgeries. The results revealed a decrease in fasting blood sugar and triglyceride (TG) levels 7 months after the surgeries. In addition, decrease of body mass index (BMI) was more significantly in the SASI group (12.8 ± 3 4.95) compared to the Roux-en-Y gastric group (8.56 ± 4.61) (P = 0.026). Besides, a more significant improvement in liver function was observed in SG (P < 0.05). Furthermore, the results revealed a significant difference among the three groups regarding the increase in the adiponectin level (P = 0.039). Decrease in the leptin level and increase in the adiponectin level were more significant after the RYGB surgery compared to the SG group (P < 0.05). **Conclusion:** The three bariatric surgeries were effective in increasing the adiponectin level and decreasing the leptin levels. The surgeries also changed the metabolic risk factors including TGs, high-density lipoprotein, fasting blood glucose, and BMI.

Key words: Adiponectin, bypass, gastrectomy, leptin, obesity

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INTRODUCTION

Obesity is caused by high energy intake, low physical activity, and genetic factors. It can result from endocrine disruptions, mental illnesses, consumption of some medications, as well.[1] Obesity is associated with metabolic syndrome and atherosclerosis including insulin-resistant type II diabetes, heart disease, hypertension, and dyslipidemia.[2] Antiobesity medications can be used to reduce appetite or to prevent fat absorption along with a proper diet.[3] If diet, exercise, or medication is not effective, bariatric surgeries are used to induce premature satiety and reduce the ability to absorb nutrients.[4]

Adipose tissue is a dynamic metabolic, biologically active endocrine tissue secreting leptin and adiponectin which affect the body metabolism and are associated with body fat levels.[5] Low concentrations of adiponectin and elevated leptin levels are associated with obesity, insulin resistance, and metabolic syndrome.[6]

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Adiponectin is an adipocin with 274 amino acids. It is also the most abundant and specific protein in adipose tissues that are present in the circulation of trimer, hexamer (low-molecular-weight oligomer), and high-molecular-weight multimer. Adiponectin regulates its homeostasis energy by oxidizing fatty acids to stimulate glucose uptake and gluconeogenesis inhibition, leading to heat generation and weight loss.[7]

Obese people have low expressions of the adiponectin receptors, thereby decreasing their plasma concentrations.[8] Adiponectin is inversely correlated to body weight, abdominal obesity, elevated fasting blood sugar (FBS), high blood pressure, hypertriglyceridemia, and low plasma levels of high-density lipoprotein (HDL). Nonetheless, high levels of adiponectin are associated with anti-atherosclerotic and anti-inflammatory effects by reducing the tumor necrosis factor-alpha.[9] Adiponectin also reduces fatty acid and triglyceride (TG) levels in the liver and muscles which lead to an increase in insulin sensitivity and has anti-diabetic effects.[10] If adiponectin secretion and activity are enhanced through bariatric surgery, it has the potential to treat vascular and metabolic diseases.

Leptin, the obese gene product, is a protein of 167 amino acids with a molecular weight of 16 kDa. Although it is initially made by the adipose tissue, other organs such as the placenta, stomach, and breast glands are capable of its production and secretion. Leptin induces daily satiety and energy consumption through hypothalamus signaling.[11] It is positively correlated to visceral body fat levels (TG), FBS, insulin resistance, metabolic syndrome, cardiovascular disease, and blood pressure.[12] On the other hand, insulin-induced adipocyte glucose metabolism regulates the expression and secretion of leptin and improves insulin sensitivity.[13]

In recent years, studies have been performed to measure lipohormones in obese individuals before and after sleeve gastrectomy (SG).[14] However, to the best of the authors' knowledge, no study has evaluated adiponectin and leptin levels in bariatric surgeries in Iran. Some studies have claimed that the leptin-to-adiponectin ratio is a better marker of metabolic syndrome compared to leptin or adiponectin alone.[15] In general, three or more of the following conditions are diagnosed as metabolic syndrome: high TG level (>150 mg/dl) or history of hypertriglyceridemia therapy, FBS ≥100 mg/dl or type II diabetes mellitus, raised systolic blood pressure (SBP >130 mmHg) or diastolic blood pressure (DBP >85 mmHg) or medical treatment for hypertension, low HDL level (<40 mg/dl in males and <50 mg/dl in females) or history of medical therapy in this area, and waist circumference ≥94 cm in males or ≥80 cm in females.[16] Nowadays, a high incidence of metabolic syndrome with an increased risk of serious diseases has been detected in Shiraz.[17] Therefore, the present study aims to evaluate the adiponectin and leptin levels in obese patients before and 7 months after SG, Roux-en-Y gastric bypass (RYGB), and single anastomosis sleeve ileal (SASI) procedures. The study also aims at analyzing the adiponectin-to-leptin ratio to determine the most effective bariatric surgery in Shiraz. The results will play an important role in physicians' choice of surgery by distinguishing the effects of these three bariatric surgeries.

PATIENTS AND METHODS

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1396.S967 clinical trial code: IRCT20201012049000N2).

This clinical trial was designed to assess the adiponectin and leptin levels among the patients who underwent three different bariatric surgeries in Shiraz. At first, 90 obese patients agreed to take part in the research. However, 9 patients were lost to follow-up. Thus, 81 patients were finally included and underwent SG, SASI bypass, or RYGB surgeries. Surgical methods were explained and appropriate methods were suggested by the physician and the surgery chose by the patient. The *post hoc* calculation by power analysis on the obtained results displayed a power >90% and an error rate of 5%. In other words, this sample size had 90% power to detect real differences among the study groups. Informed consent forms were signed by all patients, and the data were gathered before and 7 months after the surgeries. Blood samples were collected after an overnight fasting (10–14 h) for measuring lipid profile, blood glucose, and leptin and adiponectin levels using standard procedures. Weight and body mass index (BMI) were also measured before and 7 months after the surgeries. The time each patient needed to rest after the surgery to become ready for work was determined, as well. SBP and DBP were measured on the right arm in a sitting position after resting for at least 10 min using an automatic sphygmomanometer (Microlife AG Swiss Corporation, CH-9443 Widnau/Switzerland). The mean of two measurements in the morning was used for the analysis.

Biochemical measurements

All serum samples before and 7 months after the surgeries were prepared in Ghadir laboratory using standard methods and were stored at − 70°C until analysis. FBS was measured by the glucose oxidase method. Plasma total cholesterol, TG, HDL, low-density lipoprotein, and liver enzyme levels Alanine Transaminase (ALT) and Aspartate aminotransferase (AST) were assessed through enzymatic methods. Moreover, leptin and adiponectin levels were determined using enzyme-linked immunosorbent assay (Mediagnost®, Reutlingen, Germany). A quality

control assay was also run to monitor the accuracy of the biochemical tests.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 22 (Chicago, IL, USA). The data were expressed as mean ± standard deviation. Paired samples *t*-test or Wilcoxon signed-rank test was used to compare the parameters in the study groups before and after the surgeries. We used Shapiro–Wilk test for the normality evaluation of data. In addition, one-way ANOVA with Tukey HSD *post hoc* test or Kruskal–Wallis test with pairwise Wilcoxon *post hoc* test was used to compare the three groups. For all statistical tests, the confidence interval was set at 95% and $P < 0.05$ was considered as statistically significant.

RESULTS

Characteristics of the patients

The 81 obese patients were divided into three groups: 14 in the bypass surgery group, 23 in the SASI bypass surgery group, and 44 in the SG group.

The patients' ages ranged from 18 to 62 years (mean: 38.84 ± 9.79 years), which were not significantly different among the study groups ($P = 0.730$). The demographic and laboratory data of the participants are presented in Tables 1 and 2.

The study results revealed a significant decrease in the patients' weight and BMI 7 months after all of the surgeries. The mean weight (Kg) was 124.52 ± 2.59 before all of the surgeries, which decreased to 92.51 ± 2.38 afterward ($P < 0.001$). In addition, the mean BMI was 44.90 ± 0.53 kg/m^2 before all of the surgeries, which decreased to 33.44 ± 0.70 kg/m^2 afterward ($P < 0.001$).

However, no significant difference was observed among the three groups with regard to the rest time required to return to normal daily activities after the surgeries ($P = 0.236$). Although the weight reduction was not significant among the three groups, BMI decreased more significantly in the SASI group than in the RYGB group ($P = 0.026$).

Table 1: Demographic data of the patients in the three groups

Parameters	Mean±SD			P#
	SG (*n*=44)	RYGB (*n*=14)	SASI (*n*=23)	
Age (year)	38.34±10.15	41.08±11.37	38.62±8.25	0.730
Time of rest after surgery (day)	11.80±2.73	25.08±7.59	17.22±3.27	0.236
Weight decrease (kg)	32.07±14.23	25.50±14.17	35.57±15.35	0.176
BMI decrease	11.64±4.75	8.56±4.61	12.83±4.95	0.025

SD=Standard deviation; SASI=Single anastomosis sleeve ileal; BMI=Body mass index; RYGB=Roux-en-Y gastric bypass; SG=Sleeve gastrectomy

Biochemical measurements

The mean FBS (mg/dl) was 112.12 ± 4.30 and 95.64 ± 1.47 before and after all of the surgeries, respectively ($P < 0.001$). The mean TG (mg/dl) was 153.62 ± 7.94 before all of the surgeries, which decreased to 109.05 ± 6.01 afterward ($P < 0.001$). The mean HDL (mg/dl) was 47.52 ± 1.47 before all of the surgeries, which increased to 57.86 ± 1.60 afterward ($P < 0.001$). However, the three groups were not significantly different concerning the amount of decrease in this parameter ($P = 0.075$).

The mean levels of ALT and AST (mg/dl) were, respectively, 37.56 ± 2.59 and 32.39 ± 1.96 before the surgeries and 25.06 ± 1.53 and 26.68 ± 1.26 afterward ($P < 0.001$, $P = 0.003$). The mean level of alkaline phosphatase (IU/L) was 189.67 ± 8.40 before the surgeries, which decreased to 158.91 ± 6.72 after them ($P < 0.001$). The results showed a significant increase in adiponectin levels ($P < 0.001$) as well as a significant decline in leptin levels in the three groups after the surgeries ($P < 0.001$). The means of adiponectin and leptin serum concentrations were 4.33 ± 0.25 µg/mL and 64.86 ± 3.28 ng/mL, respectively, before the surgeries. These measures were, respectively, obtained as 8.31 ± 0.66 µg/mL and 21.33 ± 2.04 ng/mL after the surgeries. Increase in the concentration of adiponectin was significantly different among the three groups ($P = 0.039$). Increase in the adiponectin level was also more significant after the RYGB surgery in comparison to the SG group ($P = 0.04$). Furthermore, the adiponectin-to-leptin ratio increased significantly in all patients ($P < 0.001$) but was not significantly different among the study groups [$P = 0.125$, Table 3].

DISCUSSION

SG is one of the bariatric surgeries, in which a large part of the stomach (about 85%) is removed vertically, leading to weight loss,[18] without any malabsorption or anastomosis between the small intestine and the stomach.[14,18-20]

SASI bypass surgery is a newly introduced bariatric surgery based on mini-gastric bypass operation, in which SG is followed by a side-to-side gastroileal anastomosis.[21] RYGB is yet another bariatric surgery that makes a small pouch from the stomach and connects it directly to the small intestine. RYGB was found to be similar to SG in achieving weight loss, but some studies showed the superiority of RYGB to SG in the 10-year remission of hypertension and dyslipidemia.[22,23] Furthermore, some obese patients presented significant weight regain and intractable reflux after SG, causing it to convert to SASI and RYGB.[22-24]

Table 2: Laboratory data of the patients in the three groups

Groups		SG (*n*=44)		RYGB (*n*=14)		SASI (*n*=23)		*P*#
Parameters	**Time**	**Mean±SD**	***P****	**Mean±SD**	***P****	**Mean±SD**	***P****	
Cholesterol (mg/dL)	Before surgery	187.39±36.72	0.032	148.60±34.51	0.927	184.47±55.91	0.816	0.299
	After surgery	201.34±41.05		149.20±31.62		181.27±35.41		
LDL-C (mg/dL)	Before surgery	120.13±26.05	0.649	91.00±28.29	0.752	123.35±42.26	0.220	0.239
	After surgery	122.24±29.17		89.43±25.49		109.26±34.12		
HDL-C (mg/dL)	Before surgery	47.74±11.58	<0.001	42.60±7.70	0.315	48.60±11.36	0.105	0.075
	After surgery	59.76±11.35		45.40±7.80		57.20±12.57		
TG (mg/dL)	Before surgery	152.53±59.54	<0.001	153.28±79.89	0.010	156.37±63.81	0.001	0.408
	After surgery	115.87±53.27		95.86±44.21		98.62±26.77		
FBS (mg/dL)	Before surgery	110.25±35.58	0.023	118.87±44.37	0.018	113.44±26.74	0.003	0.072
	After surgery	96.30±10.20		91.75±11.03		95.94±15.57		
BUN (mg/dL)	Before surgery	12.60±3.01	0.541	11.00±1.90	0.638	11.73±3.35	0.868	0.805
	After surgery	12.27±4.11		10.67±2.42		11.53±4.84		
Creatinine (mg/dL)	Before surgery	0.87±0.16	0.011	1.03±0.16	0.072	0.86±0.15	0.234	0.050
	After surgery	0.92±0.14		0.94±0.10		0.91±0.13		
Total bilirubin (mg/dL)	Before surgery	0.70±0.27	0.003	0.72±0.31	0.005	0.66±0.30	0.001	0.216
	After surgery	0.91±0.50		1.08±0.38		0.86±0.35		
Direct bilirubin (mg/dL)	Before surgery	0.16±0.07	<0.001	0.19±0.05	0.021	0.19±0.12	<0.001	0.488
	After surgery	0.36±0.19		0.31±0.09		0.32±0.14		
Albumin (g/dL)	Before surgery	4.19±0.33	0.014	4.15±0.21	0.374	4.18±0.29	0.873	0.088
	After surgery	4.40±0.39		3.55±0.78		4.21±0.32		
Protein (g/dL)	Before surgery	7.52±0.58	0.018	7.10±0.40	0.170	7.56±0.65	0.064	0.942
	After surgery	7.27±0.47		6.70±0.25		7.21±0.72		
AST (U/L)	Before surgery	32.20±16.45	0.003	31.14±14.66	0.777	33.37±14.18	0.193	0.510
	After surgery	24.51±7.84		33.43±17.74		29.00±8.86		
ALT (U/L)	Before surgery	38.69±21.82	<0.001	32.00±15.90	0.474	36.87±18.17	0.035	0.493
	After surgery	24.33±11.59		25.00±16.28		26.87±11.60		

*Wilcoxon signed-rank test showed significant differences after the three surgeries; #Kruskal–Wallis test or one-way ANOVA test for the mean difference of each data among the three surgeries. *Post hoc* tests did not show any significant data. SASI=Single anastomosis sleeve ileal; BMI=Body mass index; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; FBS=Fasting blood sugar; BUN=Blood urea nitrogen; AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; SD=Standard deviation; RYGB=Roux-en-Y gastric bypass; TG=Triglyceride; SG=Sleeve gastrectomy

Table 3: Adiponectin and leptin levels and adiponectin: leptin ratio based on different surgeries before and 6 months after the surgeries

Group		SG (*n*=44)		RYGB (*n*=14)		SASI (*n*=23)		*P*#
Parameters	**Time**	**Mean±SD**	***P****	**Mean±SD**	***P****	**Mean±SD**	***P****	
Adiponectin (μg/mL)	Before	4.08±2.09	<0.001	4.82±2.44	0.003	4.51±2.59	<0.001	0.039
	After	7.73±6.16		11.07±7.67		7.70±3.72		
Leptin (ng/mL)	Before	59.99±31.08	<0.001	75.18±25.07	<0.001	67.69±27.41	<0.001	0.054
	After	20.83±16.60		15.77±12.07		25.66±23.31		
Adiponectin: Leptin ratio	Before	121.70±304.53	0.003	72.30±52.49	0.003	78.41±52.22	0.002	0.125
	After	974.30±1550.68		1248.00±1224.85		697.06±869.65		

*Wilcoxon test between before and after surgeries showed differences; #Kruskal–Wallis test with pairwise Wilcoxon *post hoc* test used for the mean difference of each data among the three surgeries, #(p<0.05). SASI=Single anastomosis sleeve ileal; SD=Standard deviation; RYGB=Roux-en-Y gastric bypass; SG=Sleeve gastrectomy

The results revealed a significant decrease in the patients' FBS and TG levels and BMI after the three surgeries. In addition, the HDL concentration increased significantly after SG. In general, obese patients with low HDL levels or liver problems are good candidates for SG. In the present study, most of the patients had the risk factors of metabolic syndrome, and the three bariatric surgeries helped them. According to the results, the decrease in BMI was more significant in the SASI group compared to the RYGB group (P = 0.026).

Adiponectin and leptin are two important adipocytokines modulated by obesity, which can result in insulin resistance, type II diabetes, and metabolic syndrome.[25] The present study findings revealed a significant increase in adiponectin levels (P < 0.001) and a significant decline in leptin levels (P < 0.001) after the surgeries. The decrease in leptin levels was not significant after the surgeries (P = 0.054). Increase in the adiponectin levels was also more significant after the RYGB surgery in comparison to the SG group (P = 0.04). The changes in leptin and

adiponectin levels after the RYGB surgery might be due to the fact that weight loss and other metabolic changes are regulated by intestinal hormones.[26] The present study results indicated no significant difference among the three groups in terms of weight loss. However, another study showed that weight was correlated to enzyme activities and total antioxidant capacity.[27]

The leptin-to-adiponectin ratio can determine the risk of metabolic syndrome more efficiently compared to adiponectin and leptin alone.[28] In the present research, the adiponectin-to-leptin ratio was reported for demonstrate the changes in these two hormones after the surgeries. The results showed no significant difference among the three surgeries in this respect ($P > 0.05$).

CONCLUSION

The results indicated that adiponectin and HDL levels increased and leptin, TG, and FBS levels, BMI, SBP, and DBP (metabolic risk factors) decreased significantly after these three bariatric surgeries. However, no significant difference was observed among the three surgeries with regard to these parameters. Furthermore, the patients' blood pressure was significantly lower and their liver function improved more significantly in the SG group. Besides, BMI decreased more significantly in the SASI group compared to the RYGB group. Moreover, a more significant decrease in the leptin level as well as a more significant increase in the adiponectin level was found after the RYGB surgery in comparison to the SG group. Yet, further investigation is necessary to elucidate the influence of these two adipocytokines on bariatric surgeries.

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Limitations

The data gathering of patients was very hard and the number of volunteers became low ($n = 81$). This short-time, nonclinical trial could not be randomized because the patients could select their procedures according to the surgeon recommendation based on BMI and comorbidities and other clinical factors. The larger sample size and long-time follow-up for patients are recommended for future studies.

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Conflicts of interest

There are no conflicts of interest.

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