Research Article

Laparoscopic Sleeve Gastrectomy Significantly Increases Serum Lipoprotein Lipase Level in Obese Patients

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Keywords

Laparoscopic sleeve gastrectomy · Lipoprotein lipase · Nonsurgical treatment · Obesity · Preheparin serum

Abstract

Objectives: Obesity is one of the causes of metabolic disorders. Laparoscopic sleeve gastrectomy (LSG) confers beneficial effects not only on body weight (BW) but also on metabolic disorders. The lipoprotein lipase (LPL) level in preheparin serum is associated with visceral adipose tissue and reflects insulin resistance. However, the change in serum preheparin LPL levels after LSG remains unclear. This study aimed to examine the effect of LSG on preheparin LPL level in obese patients compared with nonsurgical treatment. **Methods:** We retrospectively reviewed a total of 100 obese patients who were treated for obesity and had preheparin LPL levels measured before and 12 months after LSG or after 12 months of nonsurgical treatment. Fifty-six patients received LSG (LSG group), and 44 patients had no surgical treatment (nonsurgical group). We compared clinical parameters such as body mass index (BMI), hemoglobin A_{1c} (HbA_{1c}), and preheparin LPL level before and 12 months after treatment. **Results:** BMI and HbA_{1c} decreased significantly in both groups, but decreases in both parameters were greater in the LSG group than in the nonsurgical group. Estimated glomerular filtration was significantly improved only in the LSG group. Preheparin LPL level increased sig-

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nificantly only in the LSG group (from 45.8 ± 21.6 to 75.0 ± 34.9 ng/mL, $p < 0.001$). Multiple regression identified LSG and decreased BMI as independent predictors of preheparin LPL level increase. **Conclusions:** These results suggest that LSG independently increases preheparin LPL level beyond BW reduction in obese patients.

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Introduction

Obesity leads not only to metabolic disorders such as diabetes and lipid disorders but also to hypertension. These metabolic disorders and hypertension increase the risk of cardiovascular disease. Furthermore, a higher body mass index (BMI) and an increase in BMI over the life span are associated with a higher risk of cancer [1]. As a result, obesity increases mortality and is therefore a serious problem globally. However, lifestyle modifications alone for the treatment of obesity have limited success, achieving only 5–10% of total body weight (BW) loss at 1 year and showing high rates of rebound weight gain [2–4]. Indeed, patients regain >30% of the lost weight within the first year and almost return to the pretreatment weight by the second year [5, 6]. Thus, obesity is difficult to treat.

Bariatric surgery has been demonstrated to be the single most effective weight loss therapy available [7]. The Swedish Obese Subjects Study showed an overall reduction in mortality after bariatric surgery with an adjusted odds ratio of 0.71 compared with the control group [8]. In that study, the average weight change in the control group was less than a few percentage points over the study period, whereas the average total weight loss 10 years after gastric bypass surgery was 25%. Laparoscopic sleeve gastrectomy (LSG) is one of the bariatric surgical procedures, and this modality reduces excess weight by 69.7% 1 year after operation [9]. LSG has been shown to effectively improve diabetes, hypertension, and dyslipidemia, with remission rates of 67–91% after LSG [10]. Thus, bariatric surgery including LSG has amazing therapeutic effects not only for obesity but also for obesity-related diseases.

Lipoprotein lipase (LPL) is well known as a triglyceride (TG) hydrolase. LPL activity and its level in serum are generally measured after heparin injection [11, 12]. However, a sensitive immunoassay system using a specific monoclonal antibody against LPL is capable of detecting LPL in serum before heparin injection [13, 14]. Although the LPL in preheparin serum (preheparin LPL) has no activity, preheparin LPL level correlates negatively with BMI and intra-abdominal visceral fat area evaluated by computed tomography [15]. Furthermore, preheparin LPL level reflects the severity of the metabolic syndrome and is increased by some medications for metabolic syndrome-related diseases [16–19]. These studies indicate that preheparin LPL level is a good marker of obesity and the metabolic syndrome, but changes in preheparin LPL level after bariatric surgery have not been evaluated.

In the present study, we investigated changes in preheparin LPL level and the relationship between preheparin LPL level and other clinical parameters after LSG or nonsurgical treatment.

Materials and Methods

Study Subjects

In the present study, we retrospectively reviewed the clinical data recorded at the Toho University Sakura Medical Center between July 2010 and February 2016 to identify patients treated for obesity ($\text{BMI} \geq 32 \text{ kg/m}^2$) who had preheparin LPL levels measured before and

Table 1. Comparisons of baseline characteristics in both study groups

	LSG group	Nonsurgical group	p value
Subjects (male/female), n	56 (25/31)	44 (24/20)	0.326 ^a
Age, years	42.0±9.3	43.0±13.6	0.683 ^b
Body weight, kg	108.1±21.9	103.7±27.3	0.369 ^b
BMI, kg/m ²	40.4±6.4	37.7±8.2	0.055 ^c
Serum albumin, mg/dL	4.4±0.3	4.5±0.3	0.340 ^b
AST, IU/L	35.0±19.9	39.1±24.1	0.649 ^c
ALT, IU/L	44.1±27.6	55.9±45.7	0.483 ^c
BUN, mg/dL	13.4±4.8	13.7±5.1	0.724 ^c
Serum creatinine, mg/dL	0.7±0.2	0.8±0.3	0.196 ^c
eGFR, mL/min/1.73 m ²	87.3±23.6	84.1±28.2	0.427 ^c
TC, mg/dL	189.1±30.1	206.5±41.6	0.013 ^c
TG, mg/dL	143.5 (109–197.5)	109.5 (78–160.5)	0.051 ^c
HDL cholesterol, mg/dL	43.7±13.0	42.4±8.2	0.944 ^c
LDL cholesterol, mg/dL	123.3±24.6	135.1±35.9	0.117 ^c
Fasting blood glucose, mg/dL	121.5±44.4	153.0±57.7	<0.001 ^c
HbA _{1c} , %	6.8±1.8	8.1±2.2	<0.001 ^c
Diabetics, %	62.5	75.0	0.184 ^a
Medications, %			
Biguanide	21.4	25.0	0.674 ^a
Thiazolidinediones	12.5	9.1	0.589 ^a
Insulin	1.8	11.4	0.045 ^a
Sulfonyl urea	16.1	22.7	0.400 ^a
DPP-4 inhibitor	25.0	13.6	0.159 ^a
GLP-1 analog	7.1	2.3	0.267 ^a
SGLT-2 inhibitor	1.8	0	0.373 ^a
α-Glucosidase inhibitor	5.4	18.1	0.042 ^a
ARB	39.3	29.5	0.311 ^a
Statin	17.9	22.7	0.546 ^a
Fibrate	10.7	2.3	0.101 ^a

Data are presented as means ± SD. Triglycerides are presented as medians (interquartile ranges). LSG, laparoscopic sleeve gastrectomy; BMI, body mass index; AST, aspartate transaminase; ALT, alanine transaminase; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA_{1c}, glycosylated hemoglobin; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT-2, sodium-glucose cotransporter-2; ARB, angiotensin receptor blocker. ^a χ^2 test, ^b ANOVA, ^c Wilcoxon test.

12 months after treatment. A total of 136 patients were identified, 56 of whom received LSG, 44 did not receive surgical treatment, 9 underwent sleeve gastric bypass, and 7 underwent gastric bypass. Patients who underwent sleeve gastric bypass or gastric bypass were excluded, because the objective was to study LSG specifically as a surgical treatment. Eventually, 56 patients who underwent LSG (LSG group) and 44 patients who received no surgical treatment (nonsurgical group) were included. Subjects in the nonsurgical group were prescribed a diet of 20–25 kcal/kg of ideal BW per day and antihyperglycemic agents aiming to maintain HbA_{1c} at <7%. Table 1 shows the clinical characteristics of the subjects at baseline (before operation, i.e., not at their first visit in the LSG group).

We compared the following parameters before and 12 months after LSG or after 12 months of nonsurgical treatment (hereinafter referred to as “after 12 months” for both treatments): BW, BMI, serum albumin, aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen, serum creatinine, estimated glomerular filtration rate (eGFR), total cholesterol (TC) level, TG level, high-density lipoprotein cholesterol (HDL-C) level, low-

density lipoprotein cholesterol (LDL-C) level, fasting blood glucose (FBG), glycosylated hemoglobin (HbA_{1c}), and preheparin LPL level.

Measurement of BW and Blood Sampling

BW was measured, and a blood sample was collected in the morning after 12 h of fasting. Serum was separated within 1 h, and the sample was used for measurements of HbA_{1c}, albumin, AST, ALT, blood urea nitrogen, creatinine, eGFR, lipids, and preheparin LPL level.

Measurement of HbA_{1c} and Plasma Lipid Concentrations

To measure HbA_{1c}, blood was collected in tubes containing ethylenediaminetetraacetic acid. The stable and unstable fractions of HbA_{1c} were measured by high-performance liquid chromatography using Hi-Auto A1c (Kyoto Daiichi Kagaku, Kyoto, Japan). Data for the stable form were used in the present analysis. HbA_{1c} was expressed as that of the National Glycohemoglobin Standardization Program.

Plasma TC and TG levels were measured enzymatically using kits from Nippon Shoji Co., Ltd. (Osaka, Japan) and a HITACHI 7150 analyzer (Hitachi, Ltd., Tokyo, Japan). Serum HDL-C was measured by a selective inhibition assay (Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan). Serum LDL-C level was calculated using the Friedewald formula.

Measurement of Preheparin LPL Level

Serum preheparin LPL level was measured by a sandwich enzyme-linked immunosorbent assay using a specific monoclonal antibody against LPL (Daiichi Pure Chemicals, Japan), as described by Kobayashi et al. [13]. The linearity and coefficient of variation for this assay have been described in our previous report [18].

Statistical Analysis

Data are expressed as means ± SD. Normal distribution was tested using the Shapiro-Wilk test. Statistical analysis was performed using Student's *t* test and analysis of variance for data showing normal distribution. If the data did not show normal distribution, we analyzed the data using the Wilcoxon test. Simple linear regression analysis and multiple regression analysis were performed using JMP computer software version 9.0 (SAS, Cary, NC, USA). *p* values <0.05 were considered significant.

Results

Baseline Characteristics of the LSG Group and the Nonsurgical Group

Table 1 shows the baseline characteristics of the LSG group and the nonsurgical group. The mean age was not significantly different between both groups. The mean BMI was slightly higher in the LSG group than in the nonsurgical group, but the difference was not significant. TC was significantly higher in the nonsurgical group. FBG and HbA_{1c} were also significantly higher in the nonsurgical group, while the rate of diabetes was not significantly different between both groups. Other baseline parameters were not significantly different. The frequencies of insulin and α-glucosidase inhibitor administration were significantly higher in the nonsurgical group than in the LSG group (Table 1).

Changes in Clinical Parameters and Medications after 12 Months

After 12 months of treatment, BW, BMI, AST, ALT, LDL-C, and HbA_{1c} were significantly decreased, and HDL-C was significantly increased in both groups. On the other hand, serum albumin, serum creatinine, eGFR, TG, and FBG were only significantly improved in the LSG

Table 2. Changes in clinical parameters and use of medications after 12 months in both groups

	Change from baseline		p value
	LSG group	nonsurgical group	
ΔBody weight, kg	-23.6±12.1 ^{††a}	-4.5±8.5 ^{†a}	<0.001 ^a
ΔBMI, kg/m ²	-8.9±4.3 ^{††a}	-1.7±3.2 ^{†a}	<0.001 ^a
ΔSerum albumin, mg/mL	+0.19±0.32 ^{††a}	+0.02±0.28	0.020 ^a
ΔAST, IU/L	-14.9±22.4 ^{††a}	-8.4±26.2 ^{*a}	0.038 ^a
ΔALT, IU/L	-20.8±53.6 ^{††a}	-15.8±46.6 ^{*a}	0.010 ^a
ΔBUN, mg/dL	+0.8±3.7	+1.0±4.4	0.954 ^a
ΔSerum creatinine, mg/dL	-0.05±0.11 ^{†a}	+0.06±0.15 ^{*a}	<0.001 ^a
ΔeGFR, mL/min/1.73 m ²	+6.9±16.5 ^{***a}	-4.8±10.4 ^{*a}	<0.001 ^a
ΔTC, mg/dL	+6.8±39.3	-7.6±36.1 ^{*a}	0.019 ^a
ΔTG, mg/dL	-54.3±79.7 ^{††a}	-0.1±96.7	0.001 ^a
ΔHDL cholesterol, mg/dL	+17.6±13.4 ^{††c}	+2.4±7.5 ^{*a}	<0.001 ^b
ΔLDL cholesterol, mg/dL	-7.9±31.6 ^{*a}	-9.5±31.9 ^{**a}	0.970 ^a
ΔFasting blood glucose, mg/dL	-21.0±43.7 ^{††a}	+3.5±74.1	0.179 ^a
ΔHbA _{1c} , %	-1.1±1.5 ^{††a}	-0.5±1.9 ^{*a}	0.022 ^a
Medications, %			
Biguanide	10.7	38.6	0.001 ^d
Thiazolidinediones	1.8	6.8	0.202 ^d
Insulin	0	11.4	0.010 ^d
Sulfonyl urea	0	29.5	<0.001 ^d
DPP-4 inhibitor	7.1	22.7	0.026 ^d
GLP-1 analog	8.9	4.5	0.394 ^d
SGLT-2 inhibitor	3.6	9.1	0.249 ^d
α-Glucosidase inhibitor	0	11.4	0.010 ^d
ARB	25.0	27.3	0.797 ^d
Statin	12.5	29.5	0.034 ^d
Fibrate	1.8	6.8	0.202 ^d

Data are presented as means ± SD. Δ denotes the difference between the value at baseline and the value after 12 months. Abbreviations are as in Table 1. * $p < 0.05$, ** $p < 0.01$, † $p < 0.0005$, †† $p < 0.0001$, vs. month 0 in each group. ^a Wilcoxon test, ^b ANOVA, ^c paired t test, ^d χ^2 test.

group. Especially serum creatinine and eGFR had significantly deteriorated in the nonsurgical group. However, TC was only significantly improved in the nonsurgical group. Comparing the changes in clinical parameters after 12 months between both groups, BW, BMI, serum albumin, AST, ALT, serum creatinine, and eGFR were significantly better in the LSG group than in the nonsurgical group. TC was significantly lower in the nonsurgical group than the LSG group, but HDL-C was significantly higher in the LSG group than in the nonsurgical group. The decrease in HbA_{1c} was significantly different between both groups; LSG significantly reduced HbA_{1c} compared with nonsurgical treatment (Table 2). After 12 months of treatment, the frequencies of biguanide, insulin, sulfonyl urea, dipeptidyl peptidase-4 inhibitor, α-glucosidase inhibitor, and statin administration were significantly higher in the nonsurgical group than in the LSG group (Table 2). The frequencies of biguanide, sulfonyl urea, dipeptidyl peptidase-4 inhibitor, and statin administration were not significantly different between the LSG group and the nonsurgical group before treatment but became significantly lower in the LSG group than in the nonsurgical group after 12 months (Tables 1, 2).

Preheparin LPL Level Changes in the LSG Group and the Nonsurgical Group

At baseline, preheparin LPL levels were not significantly different between both groups (45.8 ± 21.6 ng/mL in the LSG group vs. 41.2 ± 15.9 ng/mL in the nonsurgical group, $p =$

Fig. 1. (A) Changes in preheparin LPL level before and 12 months after LSG. * $p < 0.001$ vs. month 0, paired t test. (B) Changes in preheparin LPL level before and after 12 months of nonsurgical obesity treatment. (C) Changes in preheparin LPL level 12 months after LSG or after 12 months of nonsurgical obesity treatment. Δ indicates the difference between the value at baseline and the value after 12 months. * $p < 0.001$, vs. nonsurgical group, unpaired t test. (A–C) Data are presented as means $\pm$ SD. Abbreviations are as in Table 1.

0.466). In the LSG group, preheparin LPL level significantly increased from 45.8 ± 21.6 ng/mL at baseline to 75.0 ± 34.9 ng/mL ($p < 0.001$) 12 months after treatment (Fig. 1A). There was no significant change in the preheparin LPL level after 12 months of nonsurgical treatment (Fig. 1B). The changes in preheparin LPLs level during this study are shown in Figure 1C. After 12 months, the preheparin LPL level was significantly more increased in the LSG group than in the nonsurgical group ($+29.2 \pm 23.5$ ng/mL in the LSG group vs. $+3.8 \pm 16.5$ ng/mL in the nonsurgical group, $p < 0.001$) (Fig. 1C).

Correlation between Changes in the Preheparin LPL Level and in Each Clinical Parameter after 12 Months

Table 3 shows the correlation between changes in preheparin LPL level and in various clinical parameters after 12 months. BW and BMI changes showed a significant negative correlation with preheparin LPL level change, and HDL-C change showed a significant positive correlation with preheparin LPL level change (BW: $r = -0.4684$, BMI: $r = -0.4747$, and HDL-C: $r = 0.4776$) (Table 3). A significant negative correlation was also observed between LSG or nonsurgical treatment (LSG; 0, nonsurgical; 1) and preheparin LPL level changes ($r = -0.5241$, $p < 0.001$). This result implied that LSG increased the preheparin LPL level (Table 3). Changes in serum creatinine, eGFR, and TC also correlated significantly with preheparin LPL level changes, and correlation coefficients were almost 0.3 (serum creatinine: $r = -0.2988$, eGFR:

Table 3. Correlation between changes in preheparin LPL level and changes in various clinical parameters after 12 months in both groups

	<i>r</i>	<i>p</i> value
ΔBody weight	−0.4684	<0.001
ΔBMI	−0.4747	<0.001
ΔSerum albumin	0.2067	0.039
ΔAST	−0.1637	0.104
ΔALT	−0.0775	0.443
ΔBUN	0.0648	0.526
ΔSerum creatinine	−0.2988	0.003
ΔeGFR	0.2967	0.003
ΔTC	0.2796	0.005
ΔTG	−0.2485	0.013
ΔHDL cholesterol	0.4776	<0.001
ΔLDL cholesterol	0.0729	0.471
ΔFasting blood glucose	−0.0858	0.396
ΔHbA _{1c}	−0.2035	0.042
LSG (0) or nonsurgical (1)	−0.5241	<0.001

Δ denotes the difference between the value at baseline and the value after 12 months. Abbreviations are as in Table 1.

Table 4. Correlation of Δpreheparin LPL level (<15: 0, ≥15: 1) with other variables analyzed by multiple regression in both groups

	β coefficient	SE	<i>p</i> value
Age (<40: 0, ≥40: 1)	−0.0701	0.1002	0.480
Gender (male: 0, female: 1)	−0.1185	0.0898	0.191
ΔBMI (≤−4.8: 0, >−4.8: 1)	−0.2744	0.1287	0.036
ΔSerum albumin (<0.1: 0, ≥0.1: 1)	−0.0499	0.0925	0.590
ΔeGFR (<1.9: 0, ≥1.9: 1)	0.0022	0.0961	0.982
ΔHDL cholesterol (<10: 0, ≥10: 1)	0.0626	0.1104	0.573
ΔHbA _{1c} (<0.5: 0, ≥0.5: 1)	−0.0110	0.0993	0.912
Diabetes (no: 0, yes: 1)	−0.0195	0.1162	0.858
LSG (0) or nonsurgical (1)	−0.2982	0.1309	0.024

SE; standard error. Other abbreviations are as in Table 1. Δ denotes the difference between the value at baseline and the value after 12 months. Model: $r^2 = 0.3263$, $p < 0.0001$.

$r = 0.2967$, and TC: $r = 0.2796$) (Table 3). TG level changes showed a significant negative correlation with preheparin LPL level changes (correlation coefficient: -0.2485) (Table 3).

Correlation of Preheparin LPL Level Changes with Changes in Other Variables Analyzed by Multiple Regression

We examined the effects of clinical parameter changes on preheparin LPL level changes in all subjects. Table 4 summarizes the results of multiple regression analysis for the correlation between preheparin LPL level changes and changes in other clinical variables. Age and changes in preheparin LPL level, BMI, serum albumin, eGFR, HDL-C, and HbA_{1c} were divided based on the 50th percentile of each parameter. LSG was the major independent predictor that increased preheparin LPL level (β coefficient = -0.2982 , $p = 0.024$). A decrease in BMI was also an independent predictor of preheparin LPL level increase. Other variables were not selected as independent predictors (Table 4).

Discussion

In the present study, both LSG and nonsurgical treatment significantly improved BW, BMI, AST, ALT, HDL-C, LDL-C, and HbA_{1c} after 12 months. Serum creatinine, eGFR, TG, and FBG were only significantly improved in the LSG group. Compared with nonsurgical treatment, LSG was superior in improving BW, BMI, AST, ALT, serum creatinine, eGFR, TG, HDL-C, and HbA_{1c}. Preheparin LPL level increased significantly only in the LSG group, and the change in preheparin LPL level was significantly different between both groups. In univariate analysis, preheparin LPL level changes correlated strongly with changes in BW, BMI, and HDL-C. A strong correlation was also observed between LSG and preheparin LPL level change. Multiple regression analysis showed that LSG and decreased BMI were independent predictors of increased preheparin LPL level.

Our study showed that both LSG and nonsurgical treatment significantly reduced weight and HbA_{1c}. However, LSG was superior to nonsurgical treatment in both effects. A previous study showed that LSG was superior to intensive medical treatment in weight reduction, but the decrease in HbA_{1c} was not significantly different between LSG and intensive medical treatment [20]. In the present study, HbA_{1c} at baseline was significantly higher in the nonsurgical group than in the LSG group. Although the rate of diabetes was not significantly different between both groups, diabetes may have been more severe in the nonsurgical group than in the LSG group. Therefore, the magnitude of decrease in HbA_{1c} was possibly smaller in the nonsurgical group than in the LSG group. Other studies showed that LSG significantly reduced HbA_{1c} when HbA_{1c} was high, slightly high, or within normal range [21, 22]. A previous report showed increases in glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) after LSG [23]. In our opinion, this may be one reason why LSG reduced BW and HbA_{1c} significantly more than nonsurgical treatment.

LSG significantly improved serum creatinine and eGFR in this study. Obesity is a cause of chronic kidney disease (CKD) [24] and is known to cause hypertension and diabetes, which are risk factors of CKD. However, other mechanisms exist in obesity-related glomerulopathy (ORG). In ORG, glomerulomegaly may or may not be accompanied by focal and segmental glomerulosclerosis lesions [25]. Increased tumor necrosis factor- α (TNF- α) and monocyte chemoattractant protein-1 (MCP-1) as well as ectopic lipid accumulation in the kidney were regarded as important mechanisms of ORG [26, 27]. Bariatric surgery increased eGFR in obese patients with CKD [28]. In a previous study, although improvement of eGFR was greater by Roux-en-Y gastric bypass than LSG, eGFR increased from 48.5 to >60 mL/min/1.73 m² 1 year after LSG [28]. Our study also showed significant improvement of eGFR 1 year after LSG.

Preheparin LPL level increased significantly 1 year after LSG. Preheparin LPL level showed a significant negative correlation with BMI and visceral fat area in a previous report [15]. LSG may increase preheparin LPL level via a reduction in visceral adipose tissue, because LSG significantly reduced visceral adipose tissue in Japanese patients with severe obesity [29]. Furthermore, preheparin LPL level was related to insulin resistance. Indeed, preheparin LPL level correlated significantly with the homeostasis model assessment of insulin resistance (HOMA-IR) and plasma adiponectin [16, 30]. Metformin and pioglitazone, which are insulin sensitizers, increased preheparin LPL level in type 2 diabetes patients [18, 19]. LSG improved insulin resistance, because HOMA-IR decreased significantly and adiponectin increased significantly after LSG [20]. We speculate that LSG improved insulin resistance through visceral adipose tissue reduction and consequently increased preheparin LPL level because of enhanced insulin action. In our previous reports, preheparin LPL level was increased 19.1% by treatment with metformin for 3 months and 25.9% by pioglitazone for 6 months [18, 19]. In this study, preheparin LPL levels were 57.7 ± 28.2 ng/mL after 3 months

and 63.4 ± 26.3 ng/mL 6 months following LSG (data not shown in the Results section), and the rates of preheparin LPL level increases were 26.0 and 38.4%, respectively. Hence, the effect of preheparin LPL level increase by LSG was stronger than that by the 2 above-mentioned insulin sensitizers.

The multiple regression model showed that LSG and decreased BMI were independent predictors of increased preheparin LPL level in this study. Despite the fact that nonsurgical treatment also significantly reduced BW and BMI in this study, LSG itself was selected as an independent predictor of preheparin LPL level increases. Furthermore, the frequencies of using metformin and statin, which were known to increase preheparin LPL level [18, 31], became significantly lower in the LSG group than the nonsurgical group after 12 months, although the preheparin LPL level increased only significantly in the LSG group. Several reports have described that bariatric surgery (or metabolic surgery) improved obesity-related metabolic disorders, especially diabetes, beyond simple weight loss [32–34]. Some studies have suggested mechanisms involved in the beneficial effects of bariatric surgery on obesity-related metabolic disorders beyond simple weight loss. LSG, but not a low-calorie diet, reversed the gut microbiota profile in obese patients toward a composition similar to that found in normal individuals [35]. Gut microbiota played a key role in modulating bile acids, including their biosynthesis and biotransformation [36]. Serum bile acid levels increased significantly after Roux-en-Y gastric bypass surgery [37]. Furthermore, serum bile acid level correlated negatively with postprandial blood glucose and positively with peak GLP-1 levels [37]. These reports thus indicate that serum bile acid levels were increased by bariatric surgery through normalizing of the gut microbiota profile and possibly associated with improved glucose and lipid metabolism, including insulin resistance after metabolic surgery. In addition, vertical sleeve gastrectomy, but not a hypocaloric diet, increased circulating serum bile acid level in obese patients with diabetes [38]. These findings may support the notion that LSG increased preheparin LPL level independent of the decrease in BMI. Although reductions in BW and BMI were significantly different between the LSG group and the nonsurgical group, LSG may increase preheparin LPL level beyond simple weight loss via changing gut microbiota and increasing serum bile acid levels. We therefore hypothesized that LSG per se is an independent predictor of preheparin LPL level increase independent of BMI decrease.

LSG significantly improved renal function and increased preheparin LPL level in this study. Angiotensin II played an important role in both ORG and LPL. Angiotensin II was also considered an important mechanism in ORG, similar to TNF- α and MCP-1 [26, 27]. Plasma angiotensin II was associated with BW and visceral fat area and decreased during weight reduction in obese subjects with type 2 diabetes [39]. Angiotensin II suppressed LPL production in 3T3-L1 cells, and valsartan, an angiotensin II receptor antagonist, increased preheparin LPL level in type 2 diabetes with hypertension [17, 40]. Although eGFR was not identified as an independent predictor of preheparin LPL level increase, it is possible that LSG may reduce plasma angiotensin II through marked BW reduction and consequently improve eGFR and increase preheparin LPL level.

There are some limitations in this study. First, some clinical parameters at baseline were significantly different; in particular, FBG and HbA_{1c} were significantly higher in the nonsurgical group than in the LSG group. However, the correlation coefficient between HbA_{1c} and preheparin LPL level was -0.0999 ($p = 0.3226$) in all subjects (LSG and nonsurgical combined) at baseline, and there was no significant correlation between both parameters. Thus, we considered that the difference in HbA_{1c} at baseline did not influence preheparin LPL level in this study. Second, we hypothesized that LSG increased preheparin LPL level through reducing visceral adipose tissue, but we did not measure visceral adipose tissue in this study. Further study is needed. Lastly, this study was retrospective. A prospective study is desirable to verify

the present findings. Although there were some limitations in this study, we were able to show that LSG significantly increased preheparin LPL level after 12 months of treatment.

In conclusion, LSG significantly improved BW, BMI, AST, ALT, serum creatinine, eGFR, TG, HDL-C, and HbA_{1c} compared with nonsurgical treatment. Preheparin LPL level increased significantly only in the LSG group. The change in preheparin LPL level correlated significantly with changes in BW, BMI, HDL-C, and LSG in all subjects. A multiple regression model showed that LSG and BMI decrease were independent predictors of preheparin LPL level increase. These results suggest that preheparin LPL level increases through BW reduction and LSG in obese patients.

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Statement of Ethics

The protocol of the study was prepared in accordance with Declaration of Helsinki and was approved by the Ethics Committee of Toho University Sakura Medical Center (S18061).

Disclosure Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

T.Y., A.S., S.N., S.T., R.O., Y.W., Y.S., and T.O., contributed to collection and/or assembly of data. M.O. contributed to the research concept and design, collection and/or assembly of data, data analysis, and writing of the article. T.M. contributed to data analysis and interpretation. I.T. contributed to data interpretation and critical revision of the manuscript. All authors approved the version to be published.

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