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Improvement of non-alcoholic fatty liver disease after laparoscopic sleeve gastrectomy in Japanese obese patients

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Abstract

Purpose: The purpose of this study was to evaluate changes in non-alcoholic fatty liver disease (NAFLD) after laparoscopic sleeve gastrectomy (LSG) using computed tomography (CT) images.

Methods: We analyzed data from 57 patients who underwent LSG and had CTs performed before and after surgery. The patients included 34 women and 23 men (with an average age of 43 years); their mean preoperative weight and body mass index were 120 kg and 46 kg/m^2, respectively. Obesity-related health disorders included type 2 diabetes mellitus (T2DM) in 33 patients, hypertension in 33 and dyslipidemia in 32. We diagnosed NAFLD in cases with liver to spleen ratios (L/S ratio) <0.9 on non-contrast CT images. We evaluated changes in body weights, BMIs, comorbidities, metabolic parameters, L/S ratios, and liver volumes after surgery.

Results: The mean interval between CT scans before and after surgery was 26 months. The total weight loss and % excess weight loss were 35 kg and 72%, respectively. The remission rates for T2DM, hypertension, and dyslipidemia were 85%, 76% and 84%, respectively. After LSG, the L/S ratio increased in all the patients, while all except for one had L/S ratio >0.9. We diagnosed 33 out of 57 patients (58%) as having NAFLD before the operation. After the operation, the L/S ratios and liver volumes were not statistically different between the patients with previous NAFLD and those without it.

Conclusion: Laparoscopic sleeve gastrectomy is an effective treatment for obesity-related health disorders including NAFLD in Japanese obese patients.

KEYWORDS
bariatric surgery, laparoscopic sleeve gastrectomy, liver to spleen ratio, liver volume, non-alcoholic fatty liver disease

1 | INTRODUCTION

A high prevalence of overweight and obesity in the last 20 years and increasing incidences have been reported worldwide among children, adolescents, and adults.[1] The World Health Organization estimated 1.9 billion overweight and more than 600 million obese adults existed worldwide in 2014.[2] Obesity is associated with increased risks of type 2 diabetes mellitus (T2DM), hypertension, cardiovascular disease, dyslipidemia, and non-alcoholic fatty liver disease (NAFLD), which form part of the metabolic syndrome.[3] NAFLD is considered a hepatic manifestation of metabolic syndrome, which is characterized by the abnormal accumulation of fats (in the form of triglyceride droplets) in hepatocytes of patients who do not abuse alcohol.[4] NAFLD includes a large spectrum of liver abnormalities, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), and is characterized by inflammatory infiltration of the portal space, fibrosis, cirrhosis, and in some cases, hepatocellular carcinoma. About 30% of adults in developed countries present NAFLD and 10% of them progress to NASH and secondarily develop liver cirrhosis (10% of those).[5]

Since the most common risk factor for developing NAFLD is obesity, clinical management primarily emphasizes weight loss, which can be achieved through diet modification, exercise, and surgical interventions. Bariatric surgery, including laparoscopic sleeve gastrectomy (LSG), has been shown to be more effective for resolution of metabolic diseases than intensive medical treatment alone.[6]

Non-alcoholic fatty liver disease is initially asymptomatic, and the diagnosis usually follows upon the incidental findings of abnormal liver enzyme levels or steatosis on imaging. Noninvasive examinations for NAFLD exist, but histological examination remains the gold standard for diagnosis and staging of the disease. Liver biopsy is an invasive technique and although its complications are rare, they can be life-threatening.[7] Computed tomography (CT) is a useful tool for the evaluation of liver steatosis. When the difference in liver-spleen attenuation is higher than –10 Hounsfield units, the liver is probably steatotic.[8] The liver to spleen ratio (L/S ratio) on the CT is also a non-invasive examination used to detect and even quantify the liver fat content.[9] The measurement correlates with the histological grade in chronic liver disease.[10] However, no reports exist analyzing NAFLD improvements after LSG by using changes in the L/S ratio and liver volumes. We aimed to evaluate the effects of LSG on NAFLD by detecting L/S ratio and liver volume changes after the procedure.

2 | MATERIALS AND METHODS

2.1 | Patients

We conducted a retrospective analysis using a prospective database of Japanese patients (n = 133), who underwent LSG between June 2006 and May 2018 in our institute. We gathered data from 57 patients who had CTs before and after surgery for the study. Of the 57 patients, 34 were women and 23 were men (their average age was 43 years; Table 1); their mean preoperative weight and body mass index (BMI) were 120 kg and 46 kg/m^2, respectively. Obesity-related health disorders in patients included T2DM in 33 patients, hypertension in 33, and dyslipidemia in 32. We followed the ethical principles stated in the guidelines of the World Medical Association's Declaration of Helsinki in this study. This study was approved by the ethics committee of Oita University Faculty of Medicine.

2.2 | Surgical techniques

The surgical techniques for the LSG procedures have been previously published.[11] They involve the insertion of a flexible endoscope (H260 and Q260; Olympus, Tokyo, Japan) into the stomach instead of a bougie, followed by gastric excision of the greater curvature portion with laparoscopic staplers (EndoGIA; Medtronic, Minneapolis, MN, USA) approximately 5 cm proximally from the pyloric ring toward the angle of His. The stump of the stomach is then buttressed by interrupted sutures.

2.3 | Definition of comorbidity improvement

We diagnosed T2DM, hypertension, and dyslipidemia and remissions according to criteria found in the report by Brethauer et al[12] We identified T2DM and hypertension remissions as complete or partial in this study.

2.4 | Evaluation of L/S ratios and liver volumes

We analyzed L/S ratios and liver volumes using a 16-detector row CT scanner (Toshiba, Tokyo, Japan). We used the SYNAPSE VINCENT imaging software (FUJIFILM, Tokyo, Japan) to obtain the volumetric analyses. We measured hepatic and splenic attenuation values on non-contrast CT scans using 20 circular region-of-interest (ROI) cursors in the liver and spleen. In the liver, we located four ROIs at each segment (right anterior, right posterior, left medial and left lateral).[13] We obtained all measurements in regions of uniform parenchymal attenuation, taking care to avoid vessels, artifacts, and other factors that could have spuriously increased or decreased the measurements. The four measurements

TABLE 1 Patient characteristics

Cases	57
Age (y)	43 ± 8
Gender (female/male)	34/23
Body weight (kg)	120 ± 23
Body Mass Index (kg/m^2)	46 ± 9
Comorbidities	
T2DM	33 (58%)
Hypertension	33 (58%)
Dyslipidemia	32 (56%)

in each segment of the liver and spleen were averaged. We calculated the L/S ratio as follows: averaged liver attenuation value/ averaged spleen attenuation value. In this study, we detected NAFLD in patients with an L/S ratio <0.9.[9,14] NAFLD was finally diagnosed after alcohol consumption and viral infection were ruled out according to the previous report.[15]

2.5 | Statistical analysis

We expressed data as mean ± SD for continuous variables and as frequencies or percentages for categorical variables. We used Mann-Whitney U, Fisher's exact, and Wilcoxon tests to determine statistical significances. A P-value < 0.05 was considered statistically significant. We used the JMP software version 13 for Windows (SAS Institute, Cary, NC, USA) to perform all statistical analyses.

3 | RESULTS

The mean interval between CT scans before and after surgery was 26 months. The postoperative total weight loss (TWL), %TWL, and % excess weight loss (%EWL) were 35 kg, 30% and 72%, respectively. Remission rates for T2DM, hypertension, and dyslipidemia were 85%, 76%, and 84%, respectively.

The L/S ratios were increased after the operations in all the patients (0.80 ± 0.30→1.26 ± 0.18, P < 0.001) and the liver volumes were decreased in all the patients (2244 ± 480 mL→1574 ± 318 mL, P < 0.001). In addition, all the patients except for one had L/S ratios >0.9 after LSG (Figure 1). The only patient with a postoperative L/S ratio <0.9 had a preoperative ratio at 0.30. This patient had only 10 kg of TWL and 13% of %TWL; the poor weight reduction might be related to the above-mentioned results.

Thirty-three of 57 patients (58%) were preoperatively diagnosed as having NAFLD, according to the L/S ratio. When comparing the patients without NAFLD to those with NAFLD, we found no statistically significant differences in terms of averaged age, gender, preoperative body weight, and BMI (Table 2). The preoperative rates of T2DM in non-NAFLD and NAFLD groups were 48% and 65%, respectively; additionally, we found no statistically significant differences. The preoperative concurrent rates of hypertension and hyperlipidemia between the non-NAFLD and NAFLD groups were similar, and the preoperative liver enzymes and metabolic parameters between the two groups were not statistically different. Before the operation, the mean L/S ratio was significantly lower (P < 0.001) and the mean liver volume significantly larger (P = 0.007) in the NAFLD group compared to those in the non-NAFLD group.

The postoperative TWL, %TWL, and %EWL were not statistically different between the non-NAFLD and NAFLD groups (Table 3). Furthermore, the remission rates of comorbidities were not statistically different between the groups. Postoperative L/S ratio and liver volume did not differ between the groups (P = 0.70 and P = 0.73, respectively). Therefore, we found significant differences in the liver volume reduction rates between the two groups (P = 0.030).
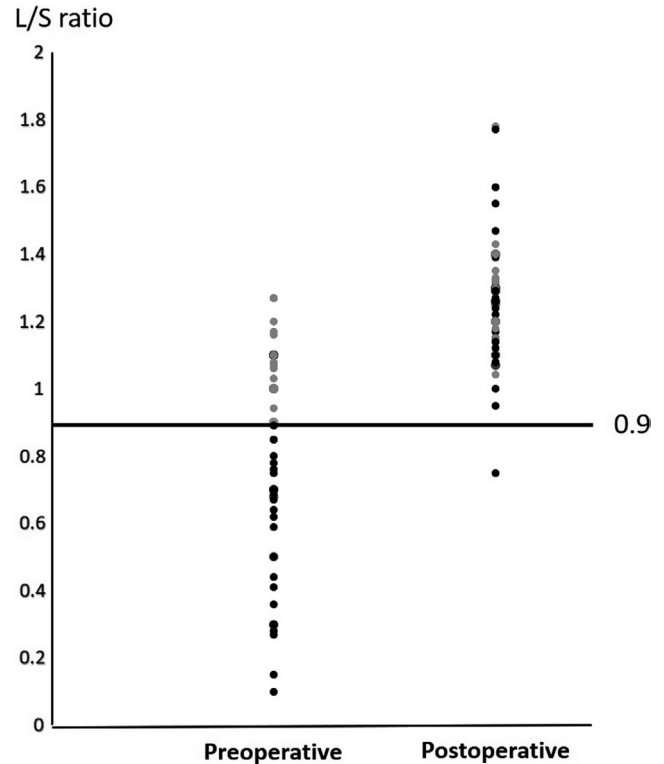

FIGURE 1 Changes in L/S ratio after laparoscopic sleeve gastrectomy. Gray dots indicate patients without non-alcoholic fatty liver disease (NAFLD) and black dots those with NAFLD before the operation

4 | DISCUSSION

In this study, we diagnosed NAFLD using the L/S ratio in 33 of 57 patients (58%). We found no significant differences in terms of age, preoperative body weight or BMI, TWL, %TWL, and %EWL between the patients with and without NAFLD. We also found no significant differences in preoperative rates of comorbidities between the two groups. In addition, the preoperative liver enzymes and metabolic parameters were not significantly different between the two groups. The mean preoperative L/S ratio was lower and liver volume was larger significantly in the NAFLD group than in the non-NAFLD group. On the other hand, the L/S ratio and liver volume data identified were similar in both groups postoperatively (Table 4).

Several studies have reported the efficacy of bariatric surgery for NAFLD. Bower et al[16] demonstrated effects of bariatric surgery on liver and biochemistry in a systematic review and suggested that these procedures significantly improve NAFLD status whenever the disease is in its steatotic, hepatic, or fibrotic stages. A Cochrane review also showed a significant improvement for patients with NAFLD following bariatric surgery, demonstrating that surgical intervention for obesity reduces its associated comorbidities.[17] LSG, one of the most effective and reliable procedures, also demonstrated NAFLD improvement in patients.[6,18]

In patients with NAFLD, the gold-standard diagnosis technique is liver biopsy. However, it is not a universally safe procedure and

TABLE 2 Preoperative characteristics and data in patients with and without non-alcoholic fatty liver disease (NAFLD)

	non-NAFLD (n = 24)	NAFLD (n = 33)	P-value
Age (y)	43 ± 9	44 ± 8	0.65
Gender (female/male)	9/15	14/19	0.59
Body weight (kg)	120 ± 23	119 ± 23	0.89
Body mass index (kg/m^2)	47 ± 9	45 ± 9	0.43
Preoperative liver enzymes and metabolic parameters			
AST (IU/L)	36 ± 34	43 ± 22	0.38
ALT (IU/L)	49 ± 48	55 ± 33	0.58
Fasting blood glucose (mg/dL)	122 ± 40	132 ± 53	0.55
HbA1c (%)	6.5 ± 1.5	6.9 ± 1.4	0.35
Total cholesterol (mg/dL)	202 ± 41	202 ± 39	0.99
HDL-cholesterol (mg/dL)	51 ± 29	46 ± 8	0.38
LDL-cholesterol (mg/dL)	123 ± 38	130 ± 32	0.53
Comorbidities			
T2DM	11 (48%)	22 (65%)	0.20
Hypertension	11 (48%)	22 (65%)	0.20
Dyslipidemia	14 (61%)	18 (53%)	0.55
Preoperative L/S ratio	1.06 ± 0.15	0.61 ± 0.24	<0.001
Preoperative liver volume (mL)	1980 ± 321	2405 ± 494	0.007

TABLE 3 Postoperative data in patients with and without non-alcoholic fatty liver disease (NAFLD)

	non-NAFLD (n = 24)	NAFLD (n = 33)	P-value
Total weight loss (kg)	38 ± 13	34 ± 16	0.31
% total weight loss (%)	32 ± 10	28 ± 11	0.21
% excess weight loss (%)	76 ± 33	70 ± 27	0.51
Postoperative liver enzymes and metabolic parameters			
AST (IU/L)	18 ± 5	19 ± 6	0.54
ALT (IU/L)	14 ± 4	14 ± 6	0.80
Fasting blood glucose (mg/dL)	96 ± 13	92 ± 12	0.47
HbA1c (%)	5.3 ± 0.4	5.5 ± 0.4	0.18
Total cholesterol (mg/dL)	204 ± 29	196 ± 32	0.27
HDL-cholesterol (mg/dL)	61 ± 18	61 ± 12	0.96
LDL-cholesterol (mg/dL)	110 ± 30	113 ± 21	0.69
Remission rates of comorbidities			
T2DM	10/11 (91%)	18/22 (82%)	0.64
Hypertension	7/11 (64%)	18/22 (82%)	0.39
Dyslipidemia	11/14 (79%)	16/18 (89%)	0.63
Postoperative L/S ratio	1.27 ± 0.18	1.25 ± 0.19	0.70
Postoperative liver volume (mL)	1551 ± 202	1589 ± 375	0.73
Reduction rate of liver volume (%)	20 ± 10	32 ± 18	0.03

should not be routinely applied to living donor patients or anti-coagulant users. Noninvasive diagnostic methods using clinical, imaging, and/or biochemical parameters have been explored to avoid the risks associated with liver biopsies.[13,19] The L/S ratio has been used to evaluate steatosis in the liver and its accuracy was shown to be as reliable as that of histological diagnosis.[15] Ricci et al[14] proposed that fatty liver can be diagnosed when the L/S ratio is <0.9; Oliva et al[20] reported that the use of an L/S ratio <1.2 resulted in detection of 100% of fatty liver cases. In addition, Rogier et al[14] reported that the L/S ratio can predict significant steatosis, defined as steatosis in >30% of the liver, and that the cut-off value of 0.9 for the CT L/S ratio provides a sensitivity of 79% and a specificity of 97% to detect severe steatosis. Steatosis can be graded as follows: grade 0 (0%-4% of hepatocytes affected), grade 1 (5%-33% of hepatocytes affected), grade 2 (34%-66% of hepatocytes affected), and grade 3 (>66% of hepatocytes affected).[21] Kan et al[9] showed that the L/S ratio was 1.16 ± 0.20 in grade 0, 0.88 ± 0.28 in grade 1, 0.76 ± 0.20 in grade 2, and 0.40 ± 0.18 in grade 3, in Japanese patients. In this study, NAFLD was defined by an L/S ratio <0.9. All the patients had improvement in L/S ratios after LSG, and all but one patient got over

the NAFLD level. These data clearly demonstrate that the LSG improved the NAFLD in our patients.

A systematic review and meta-analysis showed that bariatric surgery improved NAFLD including NASH.[22] Dixon et al[23] clearly demonstrated that weight reduction after bariatric surgery improved NASH. In addition, a recent study demonstrated that LSG improved NASH.[24] These reports strongly suggest the efficacy of bariatric surgery including LSG on NAFLD and NASH. However, it is difficult to distinguish between NAFLD and NASH using the L/S ratio, as well as to evaluate fibrosis and inflammation.[25] Suzuki et al[26] reported the usefulness of the spleen volume as a marker of early-stage NASH. Hayashi et al[27] demonstrated the usefulness of hepatic volume parameters including the left hepatic lobe to right hepatic lobe volume ratio (L/R ratio) for diagnosing cirrhosis in patients with NAFLD.

Non-alcoholic fatty liver disease was diagnosed in 76.2% of Japanese obese patients that underwent LRYGB using L/S ratio,[28] and it was diagnosed in 82.4% of Japanese patients who underwent bariatric procedures by liver biopsy.[29] These rates of NAFLD were similar,

TABLE 4 Comparison between patients with and without non-alcoholic fatty liver disease (NAFLD)

	Non-NAFLD (n = 23)	NAFLD (n = 34)	P value
Age (y)	43 ± 9	44 ± 8	0.65
Preoperative body weight (kg)	120 ± 23	119 ± 23	0.89
Preoperative BMI (kg/m^2)	47 ± 9	45 ± 9	0.43
Total weight loss (kg)	38 ± 13	34 ± 16	0.31
% Total weight loss (%)	32 ± 10	28 ± 11	0.21
% Excess weight loss (%)	76 ± 33	70 ± 27	0.51
Preoperative co-morbidities			
T2DM	11 (48%)	22 (65%)	0.2
Hypertension	11 (48%)	22 (65%)	0.2
Dyslipidemia	14 (61%)	18 (53%)	0.55
Preoperative liver enzymes and metabolic parameters			
AST (IU/L)	36 ± 34	43 ± 22	0.38
ALT (IU/L)	49 ± 48	55 ± 33	0.58
Fasting blood glucose (mg/dL)	122 ± 40	132 ± 53	0.55
HbA1c (%)	6.5 ± 1.5	6.9 ± 1.4	0.35
Total cholesterol (mg/dL)	202 ± 41	202 ± 39	0.99
HDL-cholesterol (mg/dL)	51 ± 29	46 ± 8	0.38
LDL-cholesterol (mg/dL)	123 ± 38	130 ± 32	0.53
Preoperative L/S ratio	1.06 ± 0.15	0.61 ± 0.24	<0.001
Postoperative L/S ratio	1.27 ± 0.18	1.25 ± 0.19	0.7
Preoperative liver volume (mL)	1980 ± 321	2405 ± 494	0.007
Postoperative liver volume (mL)	1551 ± 202	1589 ± 375	0.73
Reduction rate of liver volume (%)	20 ± 10	32 ± 18	0.03

while the levels of liver enzymes were also similar before the operation. Therefore, these Japanese data demonstrated that the L/S ratio has the same potential to diagnose NAFLD as liver biopsy. In our study, the concurrent rate of NAFLD was 58%, which was clearly lower than those in the previous two reports. Comparing our data with those data, the ALT levels in our patients were lower. In addition, the L/S ratio was obviously higher in this study compared to that in the previous report by Kakizaki et al (0.80 vs 0.63). Therefore, we think the differences in results are probably related to the differing patient populations.

In our study, we analyzed liver volumes before and after LSG. Other studies have identified body weight, body surface area, age, and gender as predictors of total liver volume.[30] Our study also showed that the liver volume in patients with NAFLD was significantly larger than those in patients without NAFLD. In the NAFLD group, the body weight decreased, while the liver volumes almost reached the same levels as those in the non-NAFLD group, and the L/S ratios also reached the same levels as those in the non-NAFLD group. These dramatic changes may indicate that fatty liver disease can be reversible after LSG.

Our study has some limitations that should be noted. This was a retrospective study and included a small number of cases. In addition, we did not include histological data. Therefore, further studies including histological analyses are needed.

In conclusion, LSG is an effective treatment for obesity-related health disorders including NAFLD in Japanese obese patients. LSG may lead to normalization of the L/S ratio and liver volume (reflecting a resolution of NAFLD) after the operation.

CONFLICT OF INTEREST

Authors declare no conflicts of interest for this article.

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