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ORIGINAL CONTRIBUTIONS

Laparoscopic Sleeve Gastrectomy with Duodenojejunal Bypass for Type 2 Diabetes Mellitus

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Abstract
Background Laparoscopic sleeve gastrectomy with duodenojejunal bypass (LSG-DJB), which has been positioned as a novel bariatric procedure, is the combination of vertical sleeve gastrectomy and proximal intestinal bypass and is theoretically expected to have strong anti-diabetic effect. Also, preserving the pylorus, a physiological valve, leads to less occurrence of dumping syndrome and anastomotic stenosis which are often problematic after laparoscopic Roux-en-Y gastric bypass (LRYGB), a gold standard. The purpose of this study was to investigate the clinical effects of LSG-DJB on obese patients with type 2 diabetes mellitus (T2DM).
Methods Consecutive 75 obese patients (female 44/male 31) associated with T2DM who underwent LSG-DJB and were followed up for at least 1 year were analyzed. The mean age was 45.5 ± 8.6 years, and the mean preoperative body weight (BW) and body mass index (BMI) were 108.4 ± 21.4 kg and 39.6 ± 7.3 kg/m^2, respectively. The mean hemoglobin A1c (HbA1c) at the first visit was 9.0 ± 1.9 %, and the duration of T2DM from diagnosis was 7.2 ± 6.2 years. Thirty-six out of the 75 patients (48 %) were treated with insulin preoperatively. All patients were evaluated and managed under a strict multidisciplinary team approach. The follow-up rate at 1 year was 89 %.
Results At 1 year, the mean BW and BMI significantly dropped to 74.6 ± 16.9 kg and 27.5 ± 5.7 kg/m^2, respectively. The mean percent of excess weight loss (%EWL) and percent of total body weight loss (%TWL) were 99.4 ± 42.4 and 31.6 ± 8.8 %, respectively. Consequently, 68.7 % of the patients achieved HbA1c less than 6 %, and 82.1 % of them achieved HbA1c less than 6.5 % without diabetes medications. Glycemic control of HbA1c less than 7 % was achieved in 91.0 % of the patients. The percentage of patients who satisfied the American Diabetes Association (ADA)-defined composite endpoints for cardiovascular disease (CVD) risk factor control increased from 0 % (at baseline) to 31 % (at 1 year). A meal tolerance test revealed significant reduction of glucose area under the curve (AUC) and increase of insulin AUC postoperatively.
Conclusions LSG-DJB for obese patients with T2DM has strong anti-diabetic effect in the short-term; however, a larger number of patients with a longer follow-up period are needed for definitive conclusions.

Keywords Sleeve gastrectomy · Duodenojejunal bypass · DJB · Diabetes · T2DM · Japanese · Asian · Laparoscopic

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Introduction

We started laparoscopic sleeve gastrectomy with duodenojejunal bypass (LSG-DJB) in 2007 as an alternative to laparoscopic Roux-en-Y gastric bypass (LRYGB) mainly because the prevalence of gastric cancer is comparatively high and the anatomical difficulty of cancer screening in the remnant stomach by upper GI endoscopy has been considered as a non-negligible problem in Japan [1, 2]. LSG-DJB is a modification of duodenal switch ("short-limb" DS) and has the following features:

1) Pylorus, a physiological valve, is preserved, leading to less occurrence of dumping syndrome and reactive hypoglycemia which are often problematic after LRYGB.

2) Duodenojejunostomy is located at 1–2 cm distal to the pylorus; thus, the anastomotic stoma can be created widely compared to that in LRYGB, which contributes to less occurrence of anastomotic stenosis.
3) Risk of nutritional deficiency after LSG-DJB is expected to be lower than that after DS.
4) Theoretically, the combination of sleeve gastrectomy and DJB (proximal intestinal bypass) is expected to have strong anti-diabetic effect.

Through our years of experience, we noticed that LSG-DJB is as effective as LRYGB in terms of weight loss and actually has strong anti-diabetic effect. Therefore, today, we selectively apply the procedure to obese patients associated with severe diabetes. In this study, we present the clinical effect of LSG-DJB focusing on weight loss, safety, and glucose metabolism.

Methods

This study included the 75 consecutively selected Japanese patients who had type 2 diabetes mellitus (T2DM), who elected to undergo LSG-DJB and presented for at least 1 year of follow-up. The inclusion criteria for laparoscopic bariatric surgery was based on the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Guidelines for Clinical Application of Laparoscopic Bariatric Surgery (medically uncontrolled, with ages between 18–65 years and body mass index (BMI) more than 30 kg/m^2 with obesity-related comorbidities) [3] which was approved by the institutional review board. Each patient was preoperatively screened and evaluated by our multidisciplinary team. Diagnosis of T2DM was based on the American Diabetes Association's (ADA) criteria [4]. Patients with a positive history of T2DM and using diabetic medication before surgery were also classified as having T2DM despite normal values for fasting plasma glucose (FPG) or glycosylated hemoglobin (HbA1c) while on medication. Prior to making a final decision for surgery, every patient underwent a detailed and up-to-date discussion regarding the various available bariatric surgical options, their pros and cons, risks and benefits, the potential postoperative complications, including the possibility of reoperations and likelihood of requiring postoperative nutritional supplementation.

Surgical Techniques

Our operative techniques for LSG-DJB have been described in detail previously [1]. After establishing pneumoperitoneum at 15 mmHg, five laparoscopic ports are placed in the upper abdomen. The short gastric vessels on the greater curvature of the stomach are divided using an ultrasonic energy device from a distance 4 cm proximal to the pylorus up to the gastroesophageal junction. Complete mobilization of the fundus with exposure of the left crus and dissection of the posterior wall of the stomach from the pancreas are routinely obtained. The 36-Fr calibration tube is advanced transorally along the lesser curvature into the pyloric channel. We proceed with dividing the stomach using a 60-mm endoscopic linear stapler (Endo-GIA with tri-staple, Covidien, USA). The staple line is routinely imbricated with a 2-0 non-absorbable suture while keeping the calibration tube in place. Then, the posterior wall of the duodenum is carefully dissected and divided using a 60-mm endoscopic linear stapler (Endo-GIA curved tip with tri-staple, Covidien, USA) 1–2 cm distal to the pylorus. The limb length is 100 cm for the biliopancreatic tract and 150 cm for the alimentary tract. The jejunojejunostomy is performed with a 60-mm linear stapler, and an entry hole is closed by hand-sewing. The mesenteric defect is closed by hand-sewing. The omentum is divided to avoid the tension of anastomosis during an antecolic reconstruction. A duodenojejunal end-to-side anastomosis is created by two layers of hand-sewn running suture (Fig. 1).

Postoperative Management

A clear liquid diet was started on postoperative day 1 (POD1) if no complications were detected by physical examination and/or radiographic testing (Gastrografin swallow). Patients were discharged from the hospital on POD3 after confirming oral liquids were well tolerated. Detailed dietary counseling by a specialist bariatric dietician and written instructions for optimal health management at home were provided, emphasizing dietary sources of protein, B vitamins, iron, and calcium. Liquid food was started by postoperative week 2, semisolid foods by week 4, and solid foods thereafter. Standard follow-up included visits to the outpatient clinic at 1, 3, and 6 months, 1 year, and annually thereafter. Also, patients were encouraged to regularly attend the bariatric surgery patient support group meetings.

Diabetes Remission Classification

Diabetes remission was defined as HbA1c <6.5 % without the use of any diabetes medications [5]. Number/prevalence of the patients who achieved HbA1c <6 % without diabetes medications, those who achieved HbA1c < 7 % regardless of diabetes medications, and those who satisfied the ADA-defined composite endpoints of HbA1c (<7 %), LDL cholesterol (<100 mg/dL), and SBP (<130 mmHg) for cardiovascular disease (CVD) risk factor control were also noted [6].

Meal Tolerance Test

A liquid mixed-meal tolerance test (MTT) at baseline and 6 months postoperatively was routinely conducted. Patients

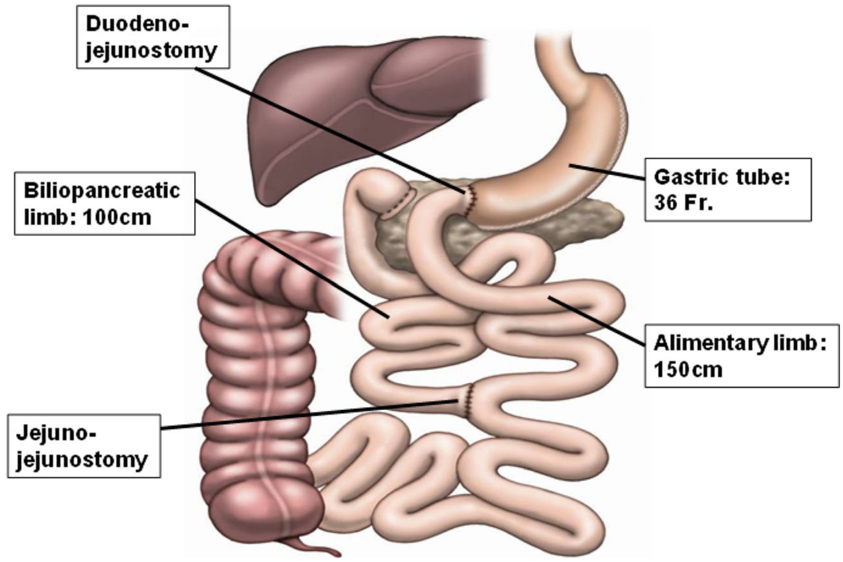


Fig. 1 Scheme of LSG-DJB

were asked to not use diabetic medication 24 h prior to testing. After an overnight fast, patients were given a mixed-meal containing 200 mL and 400 kcal (caloric contribution: 52 % carbohydrate, 34 % fat, and 14 % protein), and blood samples were obtained for glucose and insulin testing at 0, 30, 60, and 120 min after administration. Insulin and glucose area under the curve (AUC) were determined as the sum of the basal area and incremental area from 0 to 120 min. The early insulin secreting response to the mixed-meal was measured by the insulinogenic index. The insulinogenic index was calculated as the ratio of incremental insulin to glucose during the first 30 min of the MTT (Δinsulin to Δglucose = I30 − I0/G30 − G0).

Statistical Analysis

All parametric data was analyzed using Student's *t* test (paired and unpaired) when appropriate. All non-parametric data was analyzed using the Mann-Whitney test. The chi-square test was used to identify any significant difference between proportions and categorical variables. Multiple logistic regression was used to examine the associates of diabetes remission. A two-sided *p* value of 0.05 was considered statistically significant. The statistical analysis was done using the SPSS version 11.0J for Windows.

Results

In this study, the 75 patients (31 men and 44 women) with T2DM underwent LSG-DJB. The mean age was 45.5 ± 8.6 years (range, 20–63 years). The preoperative mean weight and BMI were 108.4 ± 21.4 kg (range, 68.4–167.8 kg) and 39.6 ± 7.3 kg/m^2 (range, 28.1–58.1 kg/m^2), respectively. Twenty-two out of the 75 patients (29 %) had BMIs of less than 35 kg/m^2 after preoperative weight loss induced by a very low caloric diet. The mean duration of T2DM from diagnosis was 7.2 ± 6.2 years (range, 0–24 years). Oral hypoglycemic agents (OHA) were used in 35 patients (47 %) before the operation. Thirteen patients (17 %) required insulin therapy. Twenty-three patients (31 %) were receiving both insulin and OHA. The remaining four patients (5 %) were newly diagnosed as having T2DM through the preoperative check-up. The 1-year follow-up rate was 89 %.

Operative Outcomes

A laparoscopic approach was successfully completed in all patients without conversion. The mean skin-to-skin operative time and blood loss were 229 ± 41 min (range, 149–338 min) and 75 ± 87 mL (range, 0–406 mL), respectively. There was no intraoperative complication. The mean postoperative hospital stay was 3.5 ± 1.0 days (range, 3–8 days). There were four severe complications (Grade III-a or more based on the Clavien-Dindo classification) in four patients during early (within 30 days) postoperative period. All of them were postoperative hemorrhages including one subcutaneous hemorrhage from a trocar site which was controlled by re-opening the wound under local anesthesia, one intraluminal hemorrhage from jejunojejunostomy which required re-laparoscopy, and two intraabdominal hemorrhages which also required re-laparoscopy. There was no leakage in the series. There were seven late complications more than 30 days after surgery in four patients including renal dysfunction in three patients, intractable gastroesophageal reflux disease (GERD) in two patients, repeated hypoglycemia in one patient, and sleeve stenosis in one patient. For the case with sleeve stenosis, laparoscopic seromyotomy was performed as a salvage treatment, however, failed, and laparoscopic revision RYGB was eventually required and successful. There was no mortality.

Weight Loss and Food Intake

At 1 year, the mean weight and BMI declined to 74.6 ± 16.9 kg and 27.5 ± 5.7 kg/m^2, respectively ($p < 0.001$), which accounted for the mean percent total body weight loss (%TWL) and the mean percent excess weight loss (%EWL) of 31.6 ± 8.8 and 99.4 ± 42.4 %, respectively. Dietary intake was assessed by using 24-h dietary recall, including foods, snacks, and beverages eaten over the last 24-h period. Data was collected directly with the patients by one of the authors and analyzed by software (Excel-Eiyoukun version 5.0, Kenpakusha, Japan). Preoperatively, the average food intake per day was 3011 ± 896 kcal/day (range, 1760–5000 kcal/day). At 1 month, the amount of food intake significantly dropped to 638 ± 200 kcal/day (range, 300–1150 kcal/day), gradually increased thereafter, and stabilized after 1.5–2 years (Fig. 2).

Glycemic Control

The mean HbA1c and FPG at the first visit were 9.0 ± 1.9 % and 205 ± 85 mg/dL, respectively. Prior to surgery, intensive medical diabetes treatment was performed and the mean HbA1c and FPG at the time of surgery dropped to 7.8 ± 1.0 % and 147 ± 45 mg/dL, respectively. After surgery, rapid glycemic control was observed, and, at 1 year, the mean HbA1c and FPG were 5.8 ± 0.7 % and 106 ± 24 mg/dL, respectively ($p < 0.001$ for both) (Fig. 3).

To evaluate the glycemic change during the immediate postoperative period, continuous interstitial glucose monitoring (Guardian RT and CGMS Gold, Medtronic MiniMed, Northridge, CA) was performed for selected patients. A typical glycemic change after LSG-DJB is shown in Fig. 4. A 42-year-old male (body weight (BW) 100.5 kg, BMI 32.1 kg/m^2) with long-standing (over 15 years) and medically uncontrolled (HbA1c 8.9 % despite using insulin 34 units/day plus OHA) T2DM underwent LSG-DJB. Continuous glucose monitoring system (CGMS) was performed from 2 days before surgery to POD5. Before surgery, the interstitial glucose reading was more than 200 mg/dL most of the time (70 % at 2 days and 94 % on the day prior to surgery) despite using the above-mentioned medications. On the operation day, bolus administrations of insulin (according to the sliding scale, 32 units in total) were required to maintain glycemic control. On POD1, the required insulin dose significantly fell to 4 units and the interstitial glucose reading was between 70 and 200 mg/dL, 86 % of the time. No diabetic medication was required on or after POD2, and the interstitial glucose reading was below 200 mg/mL 100 % of the time after POD3.

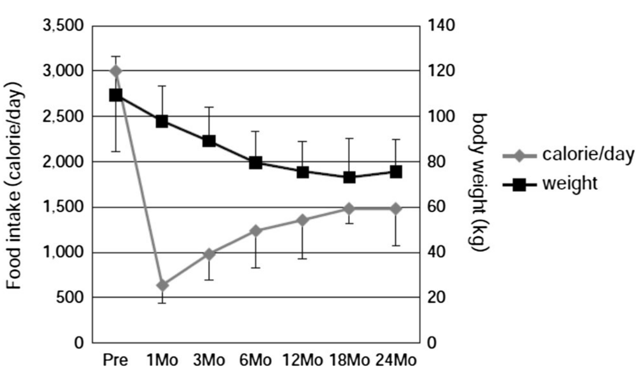


Fig. 2 Change in weight and food intake during the first 2 years after LSG-DJB

Other Metabolic Parameters

At 1 year, metabolic parameters such as fasting C-peptide, fasting insulin, HOMA-IR, systolic blood pressure, diastolic blood pressure, total cholesterol, LDL cholesterol, and triglyceride fell down significantly from the respective baseline. Only HDL cholesterol significantly increased. At baseline, 36 patients out of the 75 patients (48 %) were treated with insulin; however, the number decreased to 1 patient (1 %) at 1 year. Similarly, the number of patients treated with OHA decreased from 57 patients (76 %) to 7 patients (10 %). The number of patients treated with anti-hypertensive drugs and lipid-lowering drugs significantly decreased (Table 1).

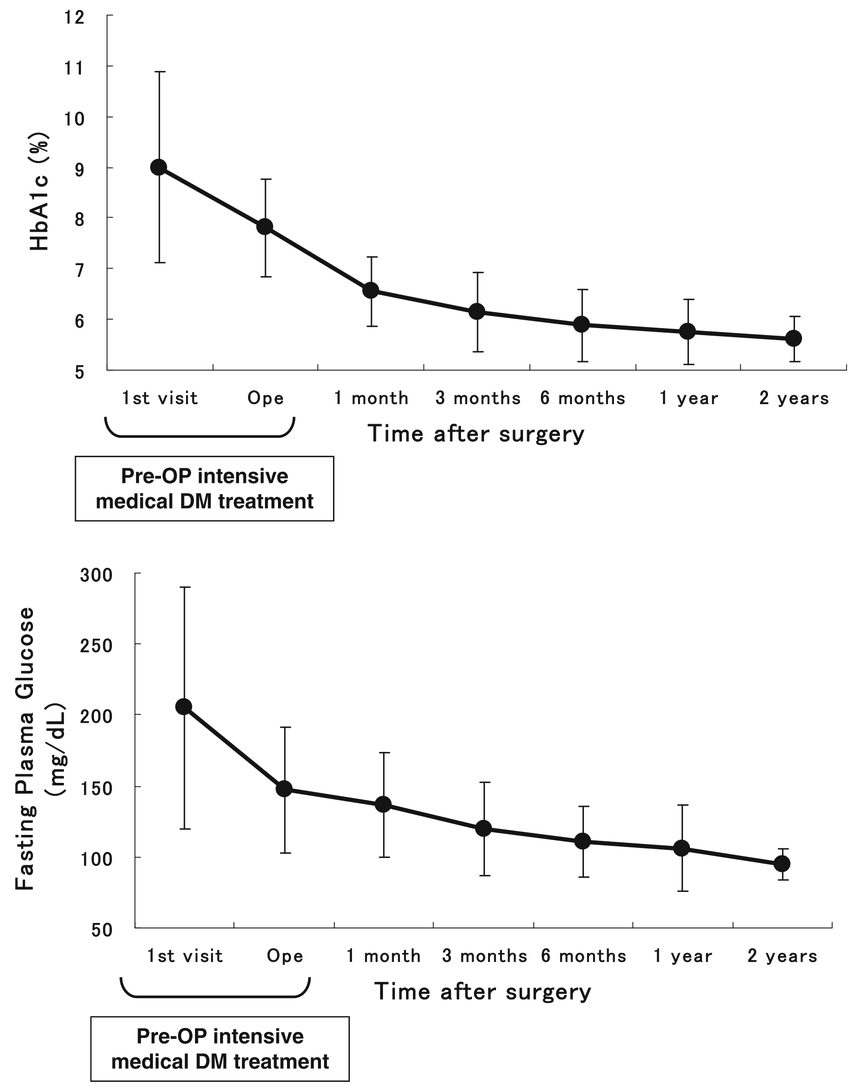
Diabetes Remission

At 1 year, 46 out of the 67 patients (68.7 %) achieved HbA1c less than 6 % without diabetes medications and 82.1 % of them achieved HbA1c less than 6.5 % without diabetes medications. Glycemic control of HbA1c less than 7 % regardless of diabetes medications was achieved in 91.0 % of these patients. The percentage of patients who satisfied the ADA-defined composite endpoints of HbA1c (<7 %), LDL cholesterol (<100 mg/dL), and SBP (<130 mmHg) for CVD risk factor control increased from 0 % (at baseline) to 31.3 % (Table 2). Regarding the severity of the disease (type of treatment), the rates of diabetes remission (HbA1c less than 6.5 % without diabetes medication) in those who were treated with lifestyle modification ($n = 4$), OHA ($n = 35$), insulin ($n = 13$), and OHA plus insulin ($n = 23$) were 100, 90.9, 81.8, and 65 %, respectively.

Comparison Between the Remission and Non-remission Groups

In univariate analysis, the patients who achieved diabetes remission (HbA1c <6.5 % without diabetes medications) at 1 year showed significantly higher preoperative BMI ($p = 0.04$), higher baseline fasting C-peptide value ($p = 0.02$), and shorter duration of diabetes ($p = 0.001$) compared to those who did not. In multiple logistic regression analysis, duration of diabetes was the only significant factor contributing to

Fig. 3 Mean (±SD) HbA1c and FPG for the entire cohort during the 2 years following LSG-DJB



diabetes remission ($p=0.004$, odds ratio 1.173 (1.053–1.306)). Those patients in the remission group showed significantly higher absolute weight loss ($p=0.01$) and lower HOMA-R value ($p=0.01$) than those in the non-remission group at postoperative 1 year (Table 3).

Meal Tolerance Test

The glucose AUC in the overall patients decreased by 23.1 % from 455 ± 85 at baseline to 340 ± 72 mg/dL/h at 6 months after surgery ($p<0.001$). In the remission group, the insulin AUC increased by 48.0 % from 115 ± 62 at baseline to 175 ± 142 ìU/mL/h at 6 months after surgery ($p<0.01$). The postoperative insulinogenic index, a marker of early phase insulin secretion, was significantly higher in the remission group than in the non-remission group ($p<0.01$). The glucose AUC decreased significantly even in patients with long-standing (over 10 years) diabetes; however, both the postoperative insulin AUC and insulinogenic index were significantly lower than those in the short duration group (Table 4).

Discussion

We introduced LSG-DJB as an alternative to LRYGB in 2007 [1, 2] and have applied the procedure to 207 patients so far in April 2015. Through these years of experience, we noticed that LSG-DJB compensates for the shortcomings of LRYGB, a gold standard, and has strong anti-diabetic effect which seems to be at least comparable to LRYGB. In this article, we reported the short-term outcomes of LSG-DJB for obese patients associated with T2DM.

The %TWL and %EWL at 1 year after LSG-DJB were 31.6 and 99.4 %, respectively. Raj et al. reported the preliminary results of a randomized trial comparing LSG-DJB and LRYGB for 57 morbidly obese Indian patients (mean

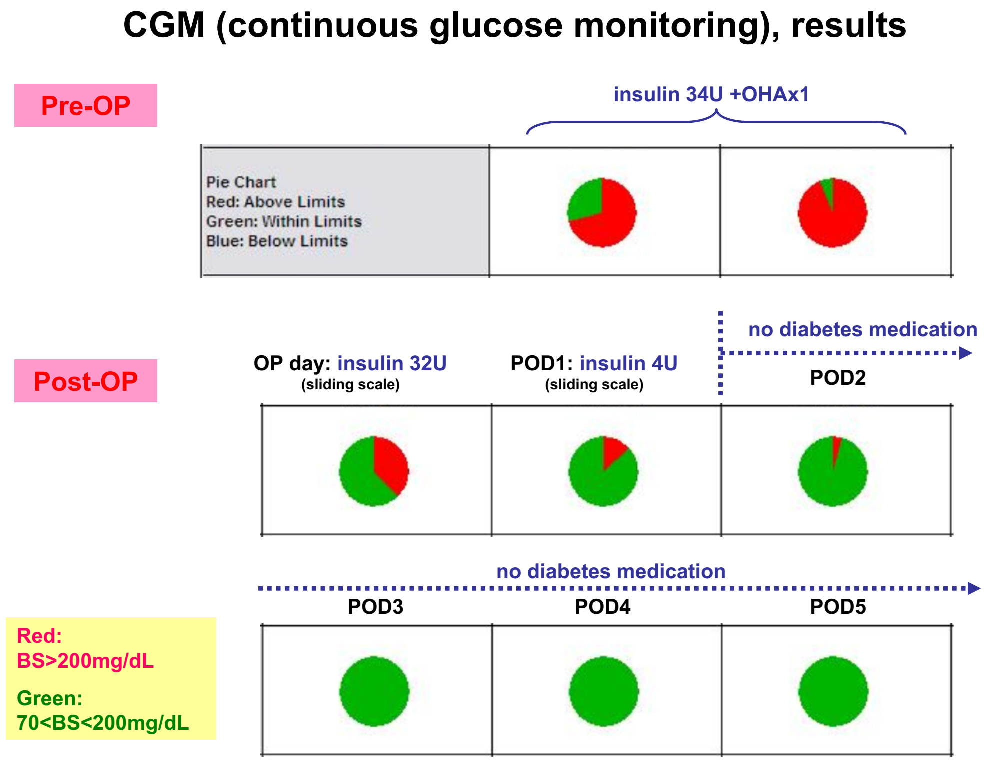


Fig. 4 Results of continuous glucose monitoring in a 42-year-old male with long-standing, medically uncontrolled diabetes

preoperative BMI, 48.28 kg/m^2 in the LSG-DJB group and 49.29 kg/m^2 in the LRYGB group). In their study, the limb lengths were similar in both groups (biliopancreatic limb length of 50 cm and alimentary limb length of 75 cm for <50 kg/m^2 BMI and 150 cm for >50 kg/m^2 BMI), both of which were shorter than those in our technique. The calibration tube (bougie) used in their technique in LSG was 36 Fr. The %EWL in LSG-DJB and LRYGB at 1 year were 81.94 ± 9.51 % and 79.98 ± 4.77 %, respectively (p = 0.326) [7].

Anatomically, in LSG-DJB, the pylorus, a physiological valve, is preserved leading to less occurrence of dumping

Table 1 Change in metabolic parameters

	At baseline (n = 75)	At 1 year (n = 67)	p value
Weight (kg)	108.4 ± 21.4	74.6 ± 16.9	<0.001
BMI (kg/m^2)	39.6 ± 7.3	27.5 ± 5.7	<0.001
HbA1c (%)	9.0 ± 1.9	5.8 ± 0.7	<0.001
Fasting plasma glucose (mg/dL)	205 ± 85	106 ± 24	<0.001
Fasting C-peptide (ng/mL)	3.3 ± 1.7	2.1 ± 0.8	<0.001
Fasting insulin (μU/mL)	28.1 ± 25.3	8.1 ± 8.0	<0.001
HOMA-IR	10.7 ± 13.4	2.2 ± 2.5	<0.001
Patients treated with OHA (number, %)	57 (76 %)	7 (10 %)	<0.05
Patients treated with insulin (number, %)	36 (48 %)	1 (1 %)	<0.05
Systolic blood pressure (mmHg)	141 ± 20	128 ± 21	<0.001
Diastolic blood pressure (mmHg)	83 ± 12	76 ± 15	<0.001
Patients treated with medication for hypertension (number, %)	47 (63 %)	20 (30 %)	<0.05
Total cholesterol (mg/dL)	198 ± 46	183 ± 38	0.01
LDL cholesterol (mg/dL)	125 ± 52	104 ± 30	0.001
HDL cholesterol (mg/dL)	46 ± 10	57 ± 12	<0.001
Triglyceride (mg/dL)	159 ± 134	77 ± 32	<0.001
Patients treated with medication for dyslipidemia (number, %)	42 (56 %)	7 (10 %)	<0.05

Table 2 Change in the number/prevalence of patients who achieved diabetes remission/control

	At baseline ($n = 75$) (number, %)	At 1 year ($n = 67$) (number, %)	p value
HbA1c <6 % without diabetes medications	0/75 (0 %)	46/67 (68.7 %)	<0.001
HbA1c <6.5 % without diabetes medications	2/75 (2.7 %)	55/67 (82.1 %)	<0.001
HbA1c <7 % regardless diabetes medications	9/75 (12 %)	61/67 (91.0 %)	<0.001
Fulfilled ADA composite endpoints	0/75 (0 %)	21/67 (31.3 %)	<0.001

syndrome which is often problematic after RYGB. The reported incidence of dumping syndrome after RYGB varies significantly between 15.7 and 76 % [8–11]. Dumping syndrome is known to debilitate gastric bypass patients and occurring with a higher incidence in diabetics than in non-diabetics [12, 13]. For accurate diagnosis of dumping syndrome, the oral glucose challenge with 75 g of a 50 % glucose solution in water is used as the dumping provocation test. In this analysis, we assessed dumping syndrome simply based on the clinical manifestation. Under the circumstances, there were two patients who were likely to suffer "early" symptoms such as abdominal pain, fatigue, a desire to lie down after meals, facial flushing, palpitations, and perspiration tachycardia. Also, there was one patient who was likely to suffer "late" symptoms such as repeated hypoglycemia. Thus, we considered there were three (4 %) suggestive (not definite) dumpers out of the 75 patients.

Another advantage of LSG-DJB is less occurrence of anastomotic stenosis. In LRYGB, creating a small-diameter gastrojejunal anastomosis is believed to be one of the keys to the long-term success, which occasionally involves an increased incidence of stenosis. The incidence of stenosis developing after gastrojejunostomy has been reported to range from 2.9 to 23 % [14, 15]. In LSG-DJB, the duodenojejunostomy is located 1–2 cm distal to the pylorus; thus, the anastomotic stoma can be created widely compared to that in LRYGB. Actually, we have not experienced any stenosis at the duodenojejunal anastomosis. Marginal ulceration is also a potentially serious complication of LRYGB and the reported incidence ranges from 1 to 16 % [16, 17]. By contrast, the incidence of marginal ulcer after DS is known to be extremely low. Anthone et al. reviewed their prospectively collected data from 701 patients undergoing duodenal switch during the 10-year period and showed that marginal ulcers were not seen [18]. In our experience of LSG-DJB, the incidence of marginal ulcers at the duodenojejunal anastomosis was minimal at 0.48 % (1/207).

Table 3 Univariate analysis comparing the T2DM remission and non-remission groups

	Remission group ($n = 55$)	Non-remission group ($n = 12$)	p value
Preoperative factors			
Gender	F, 33/M, 22	F, 6/M, 6	NS (0.75)
Age	44.7 ± 8.8	49.8 ± 7.4	NS (0.07)
Weight (kg)	110.9 ± 22.6	103.1 ± 19.7	NS (0.39)
BMI (kg/m^2)	40.7 ± 7.6	36.2 ± 7.0	0.04
Excess weight (kg)	42.7 ± 21.1	31.8 ± 19.0	NS (0.08)
Fasting glucose (mg/dL)	207 ± 83	196±76	NS (0.8)
HbA1c (%)	9.0 ± 1.9	8.9±1.7	NS (0.62)
Fasting C-peptide (ng/mL)	3.5 ± 1.7	2.5 ± 1.0	0.02
Fasting insulin (μU/mL)	27 ± 22	23 ± 13	NS (0.88)
HOMA-IR	10.4 ± 14.3	9.8 ± 8.6	NS (0.89)
Duration of diabetes (year)	6.5 ± 5.9	13.0 ± 5.6	0.001
Treated with insulin (number, %)	22 (40 %)	9 (75 %)	NS (0.06)
1-year postoperative factors			
Weight (kg)	74.1 ± 17.7	76.7 ± 12.8	NS (0.3)
BMI (kg/m^2)	27.5 ± 5.9	27.3 ± 4.9	NS (0.96)
Weight loss (kg)	33.0 ± 8.6	25.0 ± 6.2	0.01
% excess weight loss (%)	99.2 ± 43.1	100.0 ± 41.0	NS (0.95)
HbA1c (%)	5.6 ± 0.4	6.9 ± 0.8	<0.001
Fasting C-peptide (ng/mL)	2.1 ± 0.8	2.2 ± 0.6	NS (0.43)
Fasting insulin (μU/mL)	7.0 ± 3.8	12.8 ± 16.3	NS (0.23)
HOMA-IR	1.7 ± 1.1	4.2 ± 5.0	0.01

Table 4 Results of meal tolerance test

	Glucose AUC (mg/dL/hr)			Insulin AUC (μU/mL/hr)			Insulinogenic index		
	Pre	Post		Pre	Post		Pre	Post	
Overall	455 ± 85	340 ± 72		138 ± 169	171 ± 135		0.73 ± 1.16	0.88 ± 0.75	
	*			**					
Remission	458 ± 104	326 ± 56	*	115 ± 62	175 ± 142		0.62 ± 1.00	0.94 ± 0.75	**
Non-remission	488 ± 76	463 ± 83		82 ± 62	111 ± 62		0.35 ± 0.33	0.41 ± 0.20	
	*								
Duration < 10 years	459 ± 89	318 ± 59	**	145 ± 173	205 ± 153	***	0.74 ± 1.22	1.11 ± 0.82	**
10 years ≦ duration	471 ± 132	390 ± 86		90 ± 49	102 ± 53		0.39 ± 0.33	0.50 ± 0.31	
	***								

*$p < 0.001$; **$p < 0.01$; ***$p < 0.05$

It can be said that the patients included in our study were associated with "advanced" diabetes with long-standing disease, with nearly half being treated with insulin preoperatively. Regarding the glycemic impact of LSG-DJB for such advanced pathology, 68.7 % of the patients achieved HbA1c less than 6 % without diabetes medication (the ADA-defined "complete remission") and 82.1 % of them achieved HbA1c less than 6.5 % without diabetes medication ("partial remission"). Among preoperative parameters, BMI, fasting C-peptide, and duration of diabetes were statistically significant contributors to diabetes remission in univariate analysis and only the duration of diabetes was extracted in multiple logistic regression analysis. Multiple systematic reviews indicated that the lower the preoperative BMI is, the lower the expected postoperative diabetes remission rate would be [19, 20]. As is well known, two major pathophysiologies of type 2 diabetes are insulin resistance and impaired insulin secretion. Insulin resistance, mainly caused by the excessive accumulation of body fat, would be easily controlled by bariatric surgery (massive weight loss induced by surgery). In lower BMI patients in general, impaired insulin secretion is relatively of more significance and, consequently, the postoperative diabetes remission rate would become lower. On the other hand, both fasting C-peptide and duration of diabetes reflect the residual pancreatic beta cell function and also have been shown to influence postoperative diabetes remission [21–23]. Diabetes remission rate based on preoperative C-peptide, BMI, and duration of diabetes in our series undergoing LSG-DJB is shown in Table 5. The 1-year remission rate surpassed 90 % in those who fulfilled any one of the following preoperatively: fasting C-peptide more than 3 ng/mL, duration of diabetes shorter than 10 years, and BMI more than 35 kg/m^2.

Regarding the effect on diabetes, there is scarce data comparing LSG-DJB and other procedures. Again, Raj et al. reported in a small randomized controlled trial comparing LRYGB and LSG-DJB that the remission rate of diabetes (defined by achieving HbA1c <7 % without diabetes medication at 1 year) was similar (LSG-DJB 80 %, LRYGB 81 %). Patel and Rubino et al. performed three different types of procedures (intestinal bypass alone (DJB), gastric resection alone (SG), and SG + DJB) in Zucker Diabetic Fatty (ZDF) rats and compared the postoperative weight, food intake (FI), oral glucose tolerance (GT), and stomach hormones. As a result, DJB did not substantially affect weight and FI, whereas

Table 5 Diabetes remission rate after LSG-DJB according to preoperative C-peptide, duration of diabetes, and BMI

	No. of patients	HbA1c <6 % without medication	HbA1c <6.5 % without medication	Others
C-peptide <3 ng/mL	31	16 (52 %)	21 (68 %)	10 (32 %)
3 ≤ C-peptide ≤ 6 ng/mL	32	27 (84 %)	31 (97 %)	1 (3 %)
6 ng/mL < C-peptide	3	3 (100 %)	3 (100 %)	0 (0 %)
DM duration <5 years	28′	25 (89 %)	27 (96 %)	1 (4 %)
5 ≤ DM duration ≤ 10 years	21	15 (71 %)	19 (90 %)	2 (10 %)
10 years < DM duration	18′	7 (39 %)	10 (56 %)	8 (44 %)
BMI <35 kg/m^2	20	7 (35 %)	12 (60 %)	8 (40 %)
35 kg/m^2 ≤ BMI	47	40 (85 %)	44 (94 %)	3 (6 %)

SG significantly reduced weight gain and food consumption. DJB rats showed weight-independent improvement in GT, which improved less after SG. Furthermore, SG significantly suppressed plasma ghrelin and increased insulin, glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic peptide, and peptide YY response to oral glucose, whereas DJB had no effects on postprandial levels of these hormones. The combination procedure (SG + DJB) induced greater weight loss and better GT than SG alone, without reducing food intake further [24].

A case analysis using the CGMS revealed rapid improvement of glucose control immediately after LSG-DJB similar to LRYGB [21]. This indicates the above-mentioned "weight-independent" improvement in GT; however, in our series, the patients who eventually achieved diabetes remission at postoperative 1 year were those who obtained higher (absolute) weight loss. Whether the anti-diabetes mechanism of gastrointestinal bypass is weight-independent or not seems still in debate. Cohen et al. performed LRYGB for 66 mildly obese patients (BMI 30–35 kg/m^2) associated with medically uncontrolled T2DM and reported 88 % of the patients achieved diabetes remission (defined as HbA1c <6.5 % without diabetes medication) at the median follow-up of 5 years under a 100 % follow-up rate. And there were no significant correlations between the amount of weight loss and the magnitude of decrease in either FPG or HbA1c at any time point before 5 years [25]. Mingrone et al. reported in a randomized controlled trial comparing bariatric surgery (gastric bypass or biliopancreatic diversion) and conventional medical therapy for type 2 diabetes that preoperative BMI and weight loss did not predict the improvement in hyperglycemia after these procedures [26]. By contrast, Dixon et al. showed that postoperative weight loss as well as a higher baseline BMI, shorter disease duration, and higher fasting C-peptide had a major influence on glycemic response after gastric bypass [23, 27].

Recently, Lee et al. reported the short-term results of laparoscopic single-anastomosis duodenal-jejunal bypass with sleeve gastrectomy (SADJB-SG) [28]. They used 45-Fr bougie, left antrum 6 cm proximal to the pylorus, and set 150–200-cm biliopancreatic limb according to the initial BMI. The mean %TWL at 1 year was 32.7 % and remission rate of T2DM (80 % of the patients were diabetic and the preoperative HbA1c was 9.2 %) was 60 % (here, remission of T2DM was defined as HbA1c <6 % without diabetes medication), which seem to be similar to our results. The potential advantages of SADJB-SG over LSG-DJB may be to alleviate technical difficulty of RY reconstruction, to shorten the operation time, and to reduce the complication from entero-entero anastomosis. A well-designed randomized controlled trial is needed.

The limitation of our study is that the results are derived from a small number of patients with short-term follow-up. However, in LSG-DJB, weight loss is assumed to be defined by the component of "vertical sleeve", not "proximal intestinal bypass." Considering the long-term (more than 5 years) weight loss outcomes after LSG (both our own [29] and literature data [30]) seem to be durable, the weight loss after LSG-DJB is also expected to be durable. We are currently preparing the long-term results (weight loss and comorbidities changes) after LSG-DJB for publication.

Conclusions

LSG-DJB for obese individuals with T2DM compensates for the shortcomings of LRYGB, a gold standard procedure, and has strong anti-diabetic effect which is at least comparable to LRYGB. The procedure usually takes longer than LRYGB but can be performed safely enough. However, a larger number of patients, longer follow-up, and randomized controlled trials comparing LRYGB and LSG-DJB are needed in order to draw definitive conclusions.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

Ethical Approval All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional and/or Japanese national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in our study.

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