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ORIGINAL CONTRIBUTIONS

The Effects of Laparoscopic Sleeve Gastrectomy with Duodenojejunal Bypass on Japanese Patients with BMI < 35 kg/m^2 on Type 2 Diabetes Mellitus and the Prediction of Successful Glycemic Control

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Abstract

Background Laparoscopic sleeve gastrectomy with duodenojejunal bypass (LSG-DJB) is a combination of sleeve gastrectomy and proximal intestinal bypass through duodenal exclusion. This technique has shown excellent weight loss and anti-diabetic effects in severely obese patients. In this retrospective study, we examined the clinical effects of LSG-DJB on mildly obese patients (body mass index (BMI) < 35 kg/m^2) with type 2 diabetes mellitus (T2DM) and analyzed factors contributing to the successful postoperative glycemic control.

Methods Seventy-two consecutive Japanese patients with T2DM with a BMI of < 35 kg/m^2 who underwent LSG-DJB in a single institution from September 2007 to March 2015 were included for the study. Weight loss, safety, and the impact on T2DM and metabolic syndrome were examined at 1 year after surgery when weight loss reaches an expected plateau. In addition, pre- and postoperative factors between those who achieved diabetes remission (remitters) and non-remitters were compared.

Results The follow-up rate at 1 year after surgery was 93%. The mean percent total weight loss (%TWL) was 31.6 ± 8.8%, and the mean glycosylated hemoglobin (HbA1c) dropped from 8.9 ± 1.5 to 6.4 ± 1.0%. There were four early- and seven late-severe complications (grade III-A or more based on the Clavien-Dindo classification), which account for the 1-year morbidity rate of 15%. There was no mortality. The complete (HbA1c of < 6% without diabetes medication) and partial (HbA1c of < 6.5% without diabetes medication) remission of T2DM was achieved in 31 and 49% of the patients, respectively. Positive impacts were also observed on hypertension and dyslipidemia. Consequently, the ratio of those who achieved the composite endpoint (HbA1c of < 7%, low-density lipoprotein cholesterol < 100 mg/dL, systolic blood pressure < 130 mmHg) significantly increased from 4.2 to 22% ($p = 0.003$). Duration of T2DM and preoperative use of anti-hypertensive drugs were independent predictors of diabetes remission. Patients with a higher ABCD score were also at a higher rate of success in T2DM remission.

Conclusions LSG-DJB for T2DM patients with a BMI of < 35 kg/m^2 is a feasible and effective surgical method in achieving moderate weight loss and excellent improvement of glycemic control, metabolic syndrome, and cardiovascular risk although the T2DM remission rate was lower compared with severely obese individuals. Proper patient selection for candidates of the procedure is imperative to effectively predict poor responders.

Keywords LSG-DJB · Japanese · Diabetes · Class I obesity · Metabolic surgery

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Introduction

Obesity and type 2 diabetes (T2DM) have spread in the world in epidemic proportions. The relationship of the two diseases is closely knit, and there is difficulty in controlling these through current medical treatments, which include diet, drug therapy, and behavioral modification. There is strong evidence that bariatric surgery can effectively control most of the associated T2DM in severely obese patients with a body mass index (BMI) beyond 35 kg/m^2 [1]. Recently, the role of metabolic surgery, mostly through Roux-en-Y gastric bypass (RYGB), has been explored and was used to treat T2DM in mildly obese patients with a BMI of less than 35 kg/m^2 [2]. Several randomized controlled trials (RCTs) have established the use of metabolic surgery as a viable treatment for T2DM in patients with a range of BMI at 30–35 kg/m^2 [3]. However, several studies have demonstrated that patients with a lower BMI may not benefit from metabolic surgery compared with severely obese patients [4, 5]. Whether the anti-diabetes effects of metabolic surgery are attenuated in lower-BMI patients in nature remains to be a matter of an ongoing debate. However, one certain observation in the real world is that patients seeking surgery primarily to treat diabetes (so-called metabolic/diabetes surgery patients) are generally older, have lower BMI, and have worse diabetes (all of them are known predictors of decreased rates of T2DM remission) as compared with bariatric surgery patients associated with diabetes, whose primary purpose for surgery is a weight reduction [6]. Optimal outcomes for T2DM remission after metabolic surgery will occur if the mechanism is understood and the patients best suited to the surgery are selected and those who will predictably have a poor result are excluded.

Since 2007, our institution has performed laparoscopic sleeve gastrectomy with duodenojejunal bypass (LSG-DJB) as an alternative to LRYGB [7]. This approach was offered due to the concern that gastric cancer is endemic in Japan and there is an inherent difficulty in accessing the entire stomach after LRYGB, making this a non-negligible problem [8]. LSG-DJB is composed of sleeve gastrectomy and duodenal exclusion (proximal intestinal bypass), a modified version of a short duodenal switch. Our experience with this technique on severely obese patients with T2DM has been extensive. We noted in several investigations that the reduction of body weight and improvements in glucose metabolism were comparable with LRYGB, with durability extending up to 5 years [9, 10]. The aim of this retrospective study is to examine the clinical effects of LSG-DJB in mildly obese diabetic patients with a BMI of less than 35 kg/m^2 and to analyze the predictors of successful glycemic control.

Methods

This is a retrospective analysis of a prospectively collected database. From September 2007 to March 2015, 72 consecutively selected diabetic Japanese patients at BMI of < 35 kg/m^2 underwent LSG-DJB, and the patients who presented for at least 1 year of follow-up were included. Approval to proceed with this study was given by the institution's review board, and all patients provided written informed consent. Diagnosis of T2DM was based on the American Diabetes Association's (ADA) criteria [11]. In addition, patients who have a positive history of T2DM and use diabetes medications before surgery were also classified as having T2DM despite normal values for fasting plasma glucose (FPG) or glycosylated hemoglobin (HbA1c) while on medication.

Surgical Procedure

LSG-DJB involves a vertical sleeve gastrectomy sized with a 37.5-Fr bougie and a proximal intestinal bypass (the limb lengths were 100 cm for the biliopancreatic tract and 150 cm for the alimentary tract), as illustrated below (Fig. 1).

Postoperative Management

A clear-liquid diet was started on postoperative day 1 (POD1), if no complications were detected on physical examination and/or radiographic testing. Patients were discharged from the hospital on POD3, when oral liquids were confirmed to be tolerated. Detailed dietary counseling was done by a specialist bariatric surgery dietician, and written instructions for optimal health management at home were provided, emphasizing dietary sources of protein, B vitamins, iron, and calcium. General 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.

Determination of Metabolic Outcomes

Diabetes remission was defined as HbA1c of < 6.5% without the use of any diabetes medication. Number/prevalence of the patients who achieved HbA1c of < 6% without diabetes medication, those who achieved HbA1c of < 7% regardless of diabetes medication, and those who satisfied the ADA-defined composite endpoints of HbA1c (< 7%), low-density lipoprotein cholesterol (LDL-C) (< 100 mg/dL), and systolic blood pressure (BP) (< 130 mmHg) for cardiovascular disease (CVD) risk factor control were also noted [12].

Age, BMI, C-Peptide, and Duration of T2DM Score

The age, BMI, C-peptide, and duration of T2DM (ABCD) diabetes surgery score was proposed by Lee et al. to predict the success of T2DM treatment (diabetes remission) after bariatric surgery. The score system consisted of four variables of independent predictors of T2DM remission: patient age, BMI, C-peptide level, and duration of diabetes. A 4-point score, ranging from 0 (lowest value) to 3 (maximum value), was given to BMI, C-peptide, and duration of diabetes. For age, only a 1-point score was given. The cut-off value for each

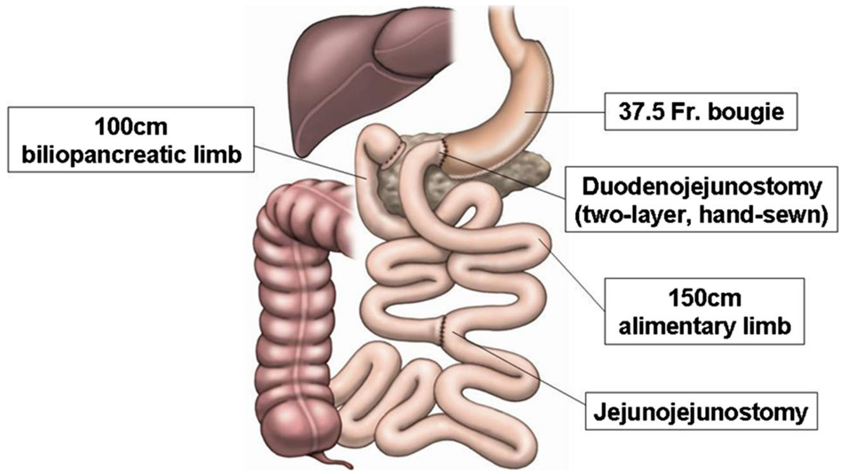


Fig. 1 Scheme of LSG-DJB

point was slightly modified from the original one after further analysis. The modified score cut-off values are defined in Table 1. The points for each variable were added, so that the total ABCD score ranged from 0 to 10 points [13].

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 *U* test. The chi-square test was used to identify any significant difference between proportions and categorical variables. Multiple logistic regression analysis 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

There were 37 men and 35 women with a mean age of 46.8 ± 9.0 years. The preoperative mean body weight and BMI were 88.8 ± 11.5 kg and 31.7 ± 2.0 kg/m^2, respectively. The mean duration of T2DM from diagnosis was 9.6 ± 6.9 years. Oral hypoglycemic agents (OHA) were used in 60 patients (83%) before the operation. Forty-one patients (57%) required insulin. Among them, 31 patients (43%) received both insulin and OHA. Two patients (2.8%) were newly diagnosed as having T2DM through the preoperative check-up.

Operative Outcome

A laparoscopic approach was successfully completed in all patients without conversion. The mean skin-to-skin operative time and blood loss were 215 ± 35 min and 34 ± 54 mL, respectively. There was no intra-operative complication. The mean postoperative hospital stay was 3.3 ± 0.8 days. There were four severe complications (grade III-A or more based on the Clavien-Dindo classification [14]) 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 reopening the wound under local anesthesia, one intra-luminal hemorrhage from jejunojejunostomy which required repeat laparoscopic repair, and two intra-abdominal hemorrhages which also required repair laparoscopically. There were no leakages in this series. There were seven late (postoperative day 31 to postoperative year 1) complications in four patients including renal dysfunction in three patients, intractable gastroesophageal reflux disease (GERD) in two patients, persistent hypoglycemia in one patient, and sleeve stenosis in one patient. For the case with sleeve stenosis, laparoscopic

Table 1 Valuables and scoring system used for computing the ABCD index

Variable	Points on modified ABCD index			
	0	1	2	3
Age	≧ 40	<40		
BMI (kg/m^2)	< 27	27–34.9	35–41.9	≧ 42
C-peptide(ng/m^1)	< 2	2–2.9	3–4.9	≧ 5
Duration of diabetes mellitus (years)	> 8	4–8	1–3.9	< 1

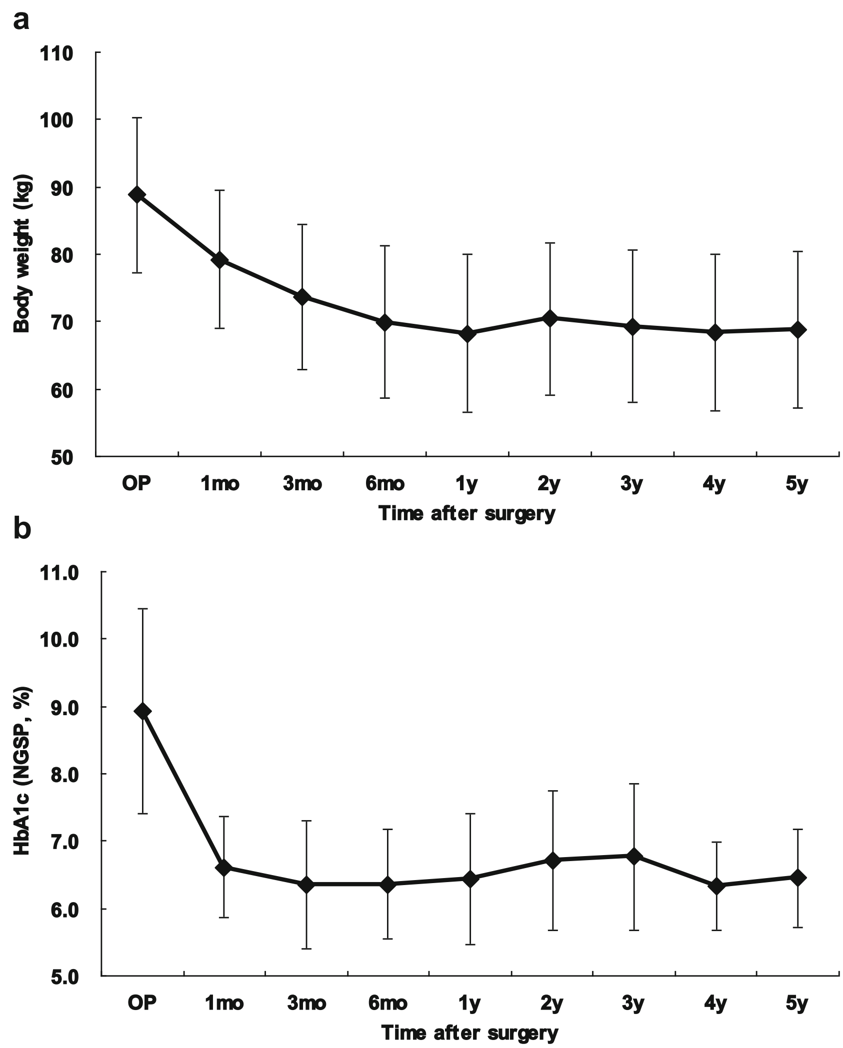
seromyotomy was performed as a salvage treatment, however, failed, and laparoscopic revision RYGB was eventually required and successful. There was no mortality.

Weight Loss

The change in body weight and the follow-up rate at each time point are shown in Fig. 2. After LSG-DJB, rapid weight loss was observed during the initial first year and stabilized thereafter. At 1 year, the mean body weight and BMI declined to 68.3 ± 11.7 kg and 24.4 ± 2.8 kg/m^2, respectively (both for $p < 0.001$), which accounted for the mean percent total body weight loss (%TWL) of 31.6 ± 8.8%. The changes in the other anthropometric parameters are shown in Table 2.

Changes in Metabolic Parameters

The mean HbA1c and FPG at the time of surgery were 8.9 ± 1.5% and 198 ± 65 mg/dL, respectively. After surgery, rapid decrease glycemic parameter was observed (Fig. 2), and, at 1 year, the mean HbA1c and FPG were 6.4 ± 1.0% and 112 ± 31 mg/dL, respectively ($p < 0.001$ for both). Other metabolic parameters such as fasting C-peptide, fasting insulin, systolic BP, diastolic BP, LDL-C, and triglyceride decreased significantly from the baseline. High-density lipoprotein (HDL) cholesterol was noted to have significantly increased. At baseline, 41 patients out of the 72 (57%) were treated with insulin; however, the number decreased to 3 patients (4.6%) at 1 year. Similarly, the number of patients treated with OHA decreased from 60 (83%) to 18 patients (28%). The number of patients



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N	72	71	71	71	67	43	27	13	4
F/U (%)		99	99	99	93	84	75	59	57

Fig. 2 **a** Change in body weight after LSG-DJB (up to 5 years). **b** Change in HbA1c after LSG-DJB (up to 5 years). **c** Follow-up rate at each time point

Table 2 Comparison of clinical data before and after LSG-DJB

Parameter	Pre-OP ($n = 72$)	After 1 year ($n = 65$)	p value
Body weight (kg)	88.8 ± 11.5	68.3 ± 11.7	< 0.001
BMI (kg/m^2)	31.7 ± 2.0	24.4 ± 2.8	< 0.001
Waist circumstance (cm)	108 ± 7	88 ± 9	< 0.001
Hip circumstance (cm)	109 ± 6	96 ± 6	< 0.001
W/H ratio	0.95 ± 0.19	0.92 ± 0.07	NS ($p = 0.270$)
Visceral fat area (cm^2)	162 ± 53	67 ± 51	< 0.001
Subcutaneous fat area (cm^2)	307 ± 82	139 ± 71	< 0.001
V/S ratio	0.57 ± 0.24	0.43 ± 0.26	< 0.001
HbA1c (%)	8.9 ± 1.5	6.4 ± 1.0	< 0.001
Glucose (mg/dL)	198 ± 65	112 ± 31	< 0.001
Insulin	21 ± 16	7.9 ± 8.4	< 0.001
C¯peptide (ng/mL)	3.4 ± 3.7	2.2 ± 0.8	< 0.001
Patients with insulin (number, %)	41/72 = 57	3/65 = 4.6	< 0.001
Patients with oral hypoglycemic agents (number, %)	60/72 = 83	18/65 = 28	< 0.001
Systolic blood pressure (mmHg)	131 ± 19	122 ± 18	< 0.001
Diastolic blood pressure (mmHg)	77 ± 13	70 ± 13	< 0.001
Patients with anti-hypertensive drugs (number, %)	33/72 = 46	11/65 = 17	< 0.001
Total cholesterol (mg/dL)	196 ± 49	188 ± 37	NS ($p = 0.188$)
LDL cholesterol (mg/dL)	122 ± 42	111 ± 34	0.041
HDL cholesterol (mg/dL)	45 ± 11	56 ± 17	< 0.001
Triglyceride (mg/dL)	163 ± 112	100 ± 48	< 0.001
Patients with lipid-lowering drugs (number, %)	42/72 = 58	8/65 = 12	< 0.001
Total protein (g/dL)	7.1 ± 0.5	7.0 ± 0.6	NS ($p = 0.302$)
Albumin (g/dL)	4.2 ± 0.5	4.3 ± 0.3	0.039
Hemoglobin (g/dL)	14.1 ± 1.7	13.2 ± 1.9	< 0.001
Iron (1 g/dL)	94 ± 31	92 ± 38	NS ($p = 0.619$)
AST (U/L)	32.1 ± 22.3	23.5 ± 8.1	0.001
ALT (U/L)	41.7 ± 30.6	25.9 ± 14.7	< 0.001
Urine albumin (mg/gCr)	366 ± 933	232 ± 835	NS ($p = 0.059$)
Positive urine protein (number, %)	31/72 = 43	16/66 = 24	0.030

treated with anti-hypertensive drugs and lipid-lowering drugs have significantly decreased (Table 2).

Glycemic Control

At 1-year postoperative period, 20 out of the 65 patients (31%) achieved the complete remission (HbA1c of less than 6% without diabetes medication) and 49% of them achieved the partial remission (HbA1c of less than 6.5% without diabetes medication) ($p < 0.001$ for both). Glycemic control of HbA1c of less than 7% regardless of diabetes medication was achieved in 71% of these patients ($p < 0.001$). On the other hand, the percent of the patients with poor glycemic control of HbA1c of ≥ 8% significantly decreased from 42% at baseline to 7.7% at 1 year ($p < 0.001$). The percent of those 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 4.2% (at baseline) to 22% ($p = 0.003$) (Table 3).

Comparison Between Remitters and Non-remitters

The change in HbA1c in both the remitters (those who achieved HbA1c of < 6.5% without diabetes medication at 1 year after surgery) and the non-remitters is shown in Fig. 3. In the non-remitters, the HbA1c drop was observed during the initial first month after surgery and leveled off thereafter. Contrary in the remitters, further HbA1c decrease after 1 month was observed.

Through univariate analysis, it was observed that the patients who achieved diabetes remission in 1 year showed significantly lower visceral/subcutaneous (V/S) ratio (less central

Table 3 Change in the number and prevalence of patients who achieved diabetes remission and control

	Pre-OP ($n = 72$)	After 1 year ($n = 65$)	p value (chi-square test)
Alc < 6% without diabetes meds	0/72 = 0%	20/65 = 31%	< 0.001
Alc < 6.5% without meds	1/72 = 1.4%	32/65 = 49%	< 0.001
A1c < 7%	12/72 = 17%	46/65 = 71%	< 0.001
A1c ≧ 8%	30/72 = 42%	5/65 = 7.7%	< 0.001
Composite endpoint (A1c < 7%, sBP < 130, LDL < 100)	3/72 = 4.2%	14/65 = 22%	0.003

obesity, $p = 0.033$), lower HbA1c after intensive medical glycemic control ($p = 0.023$), higher baseline fasting C-peptide value ($p = 0.004$), higher delta C-peptide value ($p = 0.001$), shorter duration of diabetes ($p < 0.001$), lower frequency of insulin use ($p = 0.003$), and lower frequency of anti-hypertensive drugs ($p = 0.026$) compared with those who did not. Using multiple stepwise logistic regression analysis, duration of diabetes ($p = 0.023$; odds ratio, 1.134 (1.018–1.263)) and preoperative use of anti-hypertensive drugs ($p = 0.004$; odds ratio, 1.173 (1.231–16.242)) were the significant factors contributing to diabetes remission. At postoperative 1 year, the remitters showed significantly lower BMI ($p = 0.025$), higher absolute weight loss ($p = 0.013$), higher %TWL ($p = 0.003$), and higher percent excess body weight loss (%EWL, $p = 0.008$) than those in the non-remitters (Table 4).

Prediction of Success

Table 5 shows the number/prevalence of those who achieved complete remission (HbA1c of < 6% without diabetes medication), partial remission (HbA1c of < 6.5% without diabetes medication), and optimal glycemic control (HbA1c of < 7%) of diabetes according to the duration of diabetes. Patients with

Fig. 3 Change in HbA1c in the remitters and the non-remitters

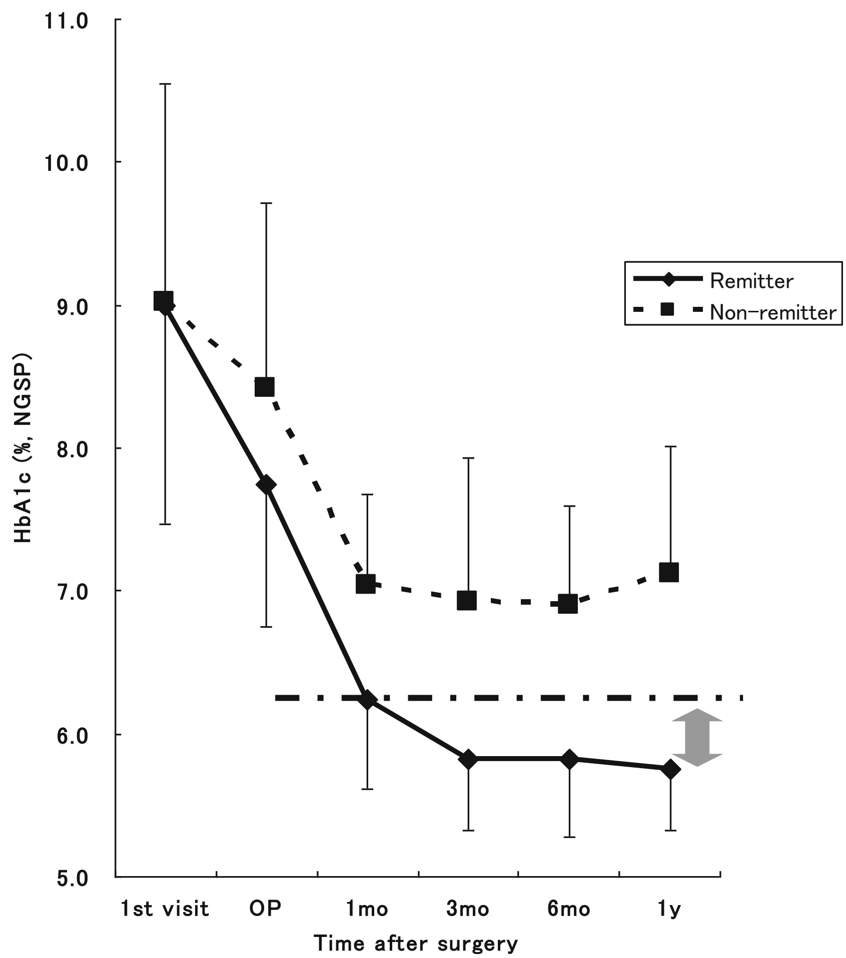

Table 4 Characteristics of the 65 patients, according to whether their diabetes had remission after surgery

Paramater	Remitter ($n = 32$)	Non-remitter ($n = 33$)	p value
Preoperative factor			
Age (years)	45.9 ± 9.0	48.3 ± 9.5	NS ($p = 0.294$)
Sex (female/male)	17/15	14/19	NS ($p = 0.460$)
Body weight (1st visit) (kg)	91.5 ± 11.9	92.2 ± 13.6	NS ($p = 0.824$)
Body weight (pre-OP) (kg)	87.8 ± 11.1	89.1 ± 12.4	NS ($p = 0.671$)
BMI (pre-OP) (kg/m^2)	31.8 ± 2.1	31.5 ± 1.9	NS ($p = 0.484$)
Waist circumstance (cm)	107 ± 8	108 ± 8	NS ($p = 0.684$)
Hip circumstance (cm)	108 ± 6	109 ± 6	NS ($p = 0.678$)
W/H ratio	0.95 ± 0.20	0.95 ± 0.20	NS ($p = 0.953$)
Visceral fat area (cm^2)	157 ± 43	174 ± 62	NS ($p = 0.220$)
Subcutaneous fat area (cm^2)	317 ± 70	289 ± 85	NS ($p = 0.165$)
V/S ratio	0.52 ± 0.17	0.65 ± 0.28	0.033
HbA1c (1st visit) (%)	9.0 ± 1.5	9.0 ± 1.5	NS ($p = 0.943$)
HbA1c (pre-OP) (%)	7.7 ± 1.0	8.4 ± 1.3	0.023
Glucose (1st visit) (mg/dL)	191 ± 68	210 ± 63	NS ($p = 0.247$)
Glucose (pre-OP) (mg/dL)	148 ± 41	168 ± 52	NS ($p = 0.079$)
Insulin	19 ± 10	22 ± 19	NS ($p = 0.397$)
C-peptide (ng/mL)	3.4 ± 1.1	2.7 ± 0.9	0.004
Delta C-peptide (ng/mL)	2.6 ± 0.8	1.8 ± 0.6	0.001
DM duration (years)	7.2 ± 5.2	13.0 ± 7.1	< 0.001
Patients with insulin (number, %)	12/32 = 38	25/33 = 76	0.003
Patients with oral hypoglycemic agents (number, %)	28/32 = 88	29/33 = 88	NS ($p = 1.000$)
Systolic blood pressure (mmHg)	132 ± 17	132 ± 21	NS ($p = 0.949$)
Diastolic blood pressure (mmHg)	79 ± 15	76 ± 12	NS ($p = 0.325$)
Patients with anti-hypertensive drugs (number, %)	11/32 = 34	21/33 = 64	0.026
Total cholesterol (mg/dL)	194 ± 48	196 ± 53	NS ($p = 0.848$)
LDL cholesterol (mg/dL)	118 ± 42	123 ± 43	NS ($p = 0.647$)
HDL cholesterol (mg/dL)	45 ± 12	45 ± 11	NS ($p = 0.836$)
Triglyceride (mg/dL)	186 ± 151	147 ± 61	NS ($p = 0.171$)
Patients with lipid-lowering drugs (number, %)	22/32 = 69	19/33 = 58	NS ($p = 0.443$)
AST (U/L)	34.7 ± 25.3	32.1 ± 20.8	NS ($p = 0.652$)
ALT (U/L)	41.7 ± 29.3	44.5 ± 34.0	NS ($p = 0.718$)
GGT (U/L)	47.3 ± 44.8	48.4 ± 64.7	NS ($p = 0.940$)
Platelet (× 10,000/μL)	24.0 ± 6.0	22.8 ± 5.9	NS ($p = 0.414$)
Urine albumin (mg/gCr)	248 ± 610	516 ± 1178	NS ($p = 0.361$)
Positive urine protein (number, %)	13/32 = 41%	14/33 = 42%	NS ($p = 1.000$)
1-year postoperative factor			
Body weight (kg)	65.5 ± 12.3	71.1 ± 10.8	NS ($p = 0.053$)
BMI (kg/m^2)	23.6 ± 2.9	25.2 ± 2.4	0.025
Absolute weight loss (kg)	22.4 ± 6.7	18.0 ± 7.2	0.013
%TWL (%)	25.8 ± 7.9	20.0 ± 7.3	0.003
%EWL (%)	86.5 ± 30.2	67.5 ± 25.5	0.008

a longer duration of diabetes were at a lower rate of success in T2DM remission. There was no remission in patients with duration of diabetes > 20 years.

Table 6 shows the ABCD score as a predictor of remission after LSG-DJB. Patients with a higher ABCD score were also at a higher rate of success in T2DM remission. There were no complete remissions of T2DM in those receiving LSG-DJB with an ABCD score < 3. On the other hand, nearly 100% of the patients with ABCD score > 3 achieved optimal glycemic control.

Table 5 Number/prevalence of those who achieved complete remission, partial remission, and glycemic control of diabetes

Duration of diabetes (years)	HbA1c < 6% without medication (CR) (%)	HbA1c < 6.5% without medication (PR) (%)	HbA1c < 7% (control) (%)
− 5 (*n* = 20) (number)	12/20 = 60	15/20 = 75	17/20 = 85
6–10 (*n* = 21)	6/21 = 28.6	10/21 = 47.6	13/21 = 61.9
11–20 (*n* = 18)	2/18 = 11.1	7/18 = 38.9	12/18 = 66.7
21– (*n* = 6)	0/6 = 0	0/6 = 0	4/6 = 66.7
Total (*n* = 65)	20/65 = 30.8	32/65 = 49.2	46/65 = 70.8

Discussion

LSG-DJB for T2DM patients with a BMI of < 35 kg/m^2 is effective in achieving modest weight loss and excellent improvement of glycemic control, metabolic syndrome, and cardiovascular risk. To validate the efficacy in this lower BMI range of patients is crucial specifically in East Asian countries, which now includes a fourth of the global diabetes population [15]. Asians are particularly prone to central obesity-induced diabetes and show susceptibility to diabetes at a much lower BMI than Americans of European ancestry [16]. Indeed, the average BMIs of T2DM patients are 32.3 kg/m^2 in the USA, 29.4 kg/m^2 in the UK, and 23.1 kg/m^2 in Japan, while those of general population are 28.5 kg/m^2 in the USA, 24.1 kg/m^2 in the UK, and 22.7 kg/m^2 in Japan [17]. According to a recent cross-sectional analysis of 900,000 individuals in Asian countries investigating the relationship between BMI and diabetes, the percentage of diabetic individuals with a BMI of 35 kg/m^2 or higher was only 0.6% while that with a BMI of 27.5 kg/m^2 or higher was approximately 15.3% [18].

In comparison between the remitters and the non-remitters, several predictive factors were identified. The non-remitters showed to have the higher V/S fat area, which may represent insulin resistance. The HbA1c after preoperative medical glycemic control was higher in the non-remitters than that in the remitters, suggesting those who are refractory to medical diabetes treatment are also refractory to surgical treatment. Fasting C-peptide is an indicator of basal insulin secretion and residual beta cell function whereas delta (stimulated) C-peptide is an indicator of bolus insulin secretion, and both of them appear to be involved in the response after metabolic surgery. Insulin usage is one of the important predictors in the DiaRem score [19]. Duration of diabetes, which most probably reflects the residual beta cell function, was an independent predictor of diabetes remission as is the case with these previous studies [20, 21].

Preoperative body weight did not influence the diabetes remission in this lower BMI cohort; however, those who eventually achieved diabetes remission at 1 year postoperative period were those who obtained a higher absolute weight loss. Whether the anti-diabetes mechanism of gastrointestinal bypass is weight independent or not seems still a matter of 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 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 point in time before 5 years postoperative period [22]. Mingrone et al. reported in a randomized controlled trial comparing bariatric surgery (gastric bypass or biliopancreatic diversion) and conventional medical therapy for T2DM that preoperative BMI and weight

Table 6 T2DM remission rate for each ABCD score

mABCD score	HbAlc < 6% without medication (CR) (%)	HbAlc < 6.5% without medication (PR) (%)	HbAlc < 7% (control) (%)
1 (*n* = 6) (number)	0/6 = 0	1/6 = 16.7	3/6 = 50
2 (*n* = 16)	0/16 = 0	3/16 = 18.8	7/16 = 43.8
3 (*n* = 21)	6/21 = 28.6	12/21 = 57.1	16/21 = 76.2
4 (*n* = 9)	5/9 = 55.6	6/9 = 66.7	9/9 = 100
5 (*n* = 9)	6/9 = 66.7	7/9 = 77.8	7/9 = 77.8
6 (*n* = 2)	1/2 = 50	1/2 = 50	2/2 = 100
7 (*n* = 2)	2/2 = 100	2/2 = 100	2/2 = 100
Total (*n* = 65)	20/65 = 30.8	32/65 = 49.2	46/65 = 70.8

loss did not predict the improvement in hyperglycemia after these procedures [23]. By contrast, Dixon et al. showed that both preoperative BMI and postoperative weight loss had a major influence on glycemic response after gastric bypass [24].

Interestingly, in the non-remitters, the HbA1c drop was observed during the initial 1 month after surgery and leveled off thereafter. Contrary with the remitters, further HbA1c decrease after 1 month was observed. With gastric bypass surgery weight loss, some parameters, such as fasting glucose, fasting insulin, leptin, or adiponectin, improve as a function of weight loss in the first year [25]. Other parameters, such as incretin levels and effect, early-phase insulin release during the oral glucose tolerance test, and the insulinogenic index all improve rapidly 1 month after gastric bypass surgery without further change at 6 and 12 months, in spite of continuous weight loss [26]. This suggests that some changes occur as a result of the surgery, independent of weight loss, whereas other changes are clearly weight loss related. However, the relative role of the change in incretins and of weight loss among the remitters and the non-remitters is difficult to differentiate. Further investigation into this phenomenon is needed.

The ABCD score was invented by Lee et al. to predict the success of T2DM treatment after metabolic surgery and has been well validated in Asian patients [13]. The score has been proven to be useful in differentiating remitters and non-remitters after several types of procedures including gastric bypass and sleeve gastrectomy [27, 28]. Lee et al. also showed that the predictive power of the ABCD score in differentiating the success is superior, especially in Asian patients with relatively lower preoperative BMI, to that of the DiaRem score [29]. So far, there are only few studies validating the usefulness of the ABCD score in LSG-DJB [30]. This study shows that the scoring system is also applicable in LSG-DJB patients with less obesity. In our cohort, none of those who received LSG-DJB with ABCD score of < 3 and/or with duration of diabetes of ≥ 21 years achieved complete remission. However, 50% of them still achieved optimal glycemic control with HbA1c of < 7%. Who would or would not be a good candidate for metabolic surgery? What should be the goals of metabolic surgery? More robust studies analyzing glycemic control, quality of life, and risks, with long follow-ups should answer these questions.

Since LSG-DJB is a modification of duodenal switch ("short-limb DS"), comparison between BPD and LSG-DJB is a matter of interest. Scopinaro et al. performed BPD for 30 diabetic patients with BMI of 25.0–34.9 kg/m^2 and reported the anti-diabetic effect at 1 year. Preoperatively, mean age was 56.4 years, mean weight was 84.8 kg, mean BMI was 30.6 kg/m^2, mean diabetes duration was 11.2 years, and mean HbA1c was 9.3%. Forty percent of them were on insulin therapy. At 1 year postoperatively, the percentages of those who achieved HbA1c of less than 6, 6.5, and 7% without diabetes medication were 47, 63, and 83%, respectively [31]. Therefore, although there are some differences (but quite similar) in background factors between the Scopinaro's patients and ours, the anti-diabetic effect of BPD seems slightly better compared with that of LSG-DJB.

In conclusion, although this is a single-institution study with relatively small number of the patients and follow-up period was not long enough, LSG-DJB for T2DM patients with a BMI < 35 kg/m^2 is safely applicable and effective in achieving moderate weight loss and excellent improvement of glycemic control, metabolic syndrome, and cardiovascular risk. The patients suited to the surgery should be properly selected, and those who will predictably have a poor result should be excluded.

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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.

References

1. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med. 2009;122:248–56.
2. Rao WS, Shan CX, Zhang W, et al. A meta-analysis of short-term outcomes of patients with type 2 diabetes mellitus and BMI ≤ 35 kg/m2 undergoing Roux-en-Y gastric bypass. World J Surg. 2015;39:223–30.
3. Cummings DE, Cohen RV. Bariatric/metabolic surgery to treat type 2 diabetes in patients with a BMI <35 kg/m^2. Diabetes Care. 2016;39:924–33.
4. Malapan K, Goel R, Tai CM, et al. Laparoscopic Roux-en-Y gastric bypass for nonobese type II diabetes mellitus in Asian patients. Surg Obes Relat Dis. 2014;10:834–40.
5. Huang CK, Shabbir A, Lo CH, et al. Laparoscopic Roux-en-Y gastric bypass for the treatment of type II diabetes mellitus in

Chinese patients with body mass index of 25-35. Obes Surg. 2011;21:1344–9.
6. Rubino F, Shukla A, Pomp A, et al. Bariatric, metabolic, and diabetes surgery: what's in a name? Ann Surg. 2014;259:117–22.
7. Kasama K, Tagaya N, Seki Y, et al. Laparoscopic sleeve gastrectomy with duodenojejunal bypass: technique and preliminary results. Obes Surg. 2009;19:1341–5.
8. Tagaya N, Kasama K, Inamine S, et al. Evaluation of the excluded stomach by double-balloon endoscopy after laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2007;17:1165–70.
9. Seki Y, Kasama K, Umezawa A, et al. Laparoscopic sleeve gastrectomy with duodenojejunal bypass for type 2 diabetes mellitus. Obes Surg. 2016;26:2035–44.
10. Seki Y, Kasama K, Haruta H, et al. Five-year-results of laparoscopic sleeve gastrectomy with duodenojejunal bypass for weight loss and type 2 diabetes mellitus. Obes Surg. 2017;27:795–801.
11. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? Diabetes Care. 2009;32:2133–5.
12. American Diabetes Association. Standards of medical care in diabetes—2009. Diabetes Care. 2009;32(Suppl 1):S13–61.
13. Lee WJ, Hur KY, Lakadawala M, et al. Predicting success of metabolic surgery: age, body mass index, C-peptide, and duration score. Surg Obes Relat Dis. 2013;9:379–84.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2): 205–13.
15. International Diabetes Federation. Diabetes Atlas. 7th ed. Brussels, Belgium: International Diabetes Federation; 2015.
16. Moller JB, Pedersen M, Tanaka H, et al. Body composition is the main determinant for the difference in type 2 diabetes pathophysiology between Japanese and Caucasians. Diabetes Care 2014;37: 796–804.
17. Sone H, Yamada N, Akanuma Y, et al. Japan diabetes complication study. J Clin and Exp Med. 2007;220:1275–81.
18. Boffetta P, McLerran D, Chen Y, et al. Body mass index and diabetes in Asia: a cross-sectional pooled analysis of 900,000 individuals in the Asia cohort consortium. PLoS One. 2011;6:e19930.
19. Still CD, Wood GC, Benotti P, et al. Preoperative prediction of type 2 diabetes remission after Roux-en-Y gastric bypass surgery: a retrospective cohort study. Lancet Diabetes Endocrinol. 2014;2: 38–45.
20. Dixon JB, Chuang LM, Chong K, et al. Predicting the glycemic response to gastric bypass surgery in patients with type 2 diabetes. Diabetes Care. 2013;36:20–6.
21. Panunzi S, Carlsson L, De Gaetano A, et al. Determinants of diabetes remission and glycemic control after bariatric surgery. Diabetes Care. 2016;39:166–74.
22. Cohen RV, Pinheiro JC, Schiavon CA, et al. Effects of gastric bypass surgery in patients with type 2 diabetes and only mild obesity. Diabetes Care. 2012;35:1420–8.
23. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;366:1577–85.
24. Dixon JB, Hur KY, Lee WJ, et al. Gastric bypass in type 2 diabetes with BMI < 30: weight and weight loss have a major influence on outcomes. Diabet Med. 2013;30:e127–34.
25. Bose M, Teixeira J, Scherer PE, et al. Weight loss and incretin responsiveness improve glucose control independently after gastric bypass surgery. J Diabetes. 2010;2:47–55.
26. Laferrère B, Heshka S, Wang K, et al. Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. Diabetes Care. 2007;30: 1709–16.
27. Lee WJ, Almulaifi A, Tsou JJ, et al. Laparoscopic sleeve gastrectomy for type 2 diabetes mellitus: predicting the success by ABCD score. Surg Obes Relat Dis. 2015;11:991–6.
28. Lee WJ, Almulaifi A, Chong K, et al. The effect and predictive score of gastric bypass and sleeve gastrectomy on type 2 diabetes mellitus patients with BMI < 30 kg/m^2. Obes Surg. 2015;25:1772–8.
29. Lee WJ, Chong K, Chen SC, et al. Preoperative prediction of type 2 diabetes remission after gastric bypass surgery: a comparison of DiaRem scores and ABCD scores. Obes Surg. 2016;26:2418–24.
30. Haruta H, Kasama K, Seki Y, et al. Long-term outcomes of bariatric and metabolic surgery in Japan: results of a multi-institutional survey. Obes Surg. 2017;27:754–62.
31. Scopinaro N, Adami GF, Papadia FS, et al. Effects of biliopanceratic diversion on type 2 diabetes in patients with BMI 25 to 35. Ann Surg. 2011;253:699–703.