

**ORIGINAL ARTICLE**

# Background characteristics and postoperative outcomes of insufficient weight loss after laparoscopic sleeve gastrectomy in Japanese patients

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**Funding information**

Ministry of Health, Labour and Welfare of Japan, Grant/Award Number: H28-nanj-ippan-014

**Abstract**

**Aim:** Laparoscopic sleeve gastrectomy (LSG) is becoming popular in Japan, but insufficient weight loss is often observed in patients after LSG. We investigated the effect of LSG on obesity-related comorbidities and identified the background characteristics of Japanese patients with insufficient weight loss after LSG.

**Methods:** In this multi-institutional retrospective study at 10 certified bariatric institutions, 322 Japanese patients who underwent LSG with a follow-up period of more than 2 years were analyzed. Anthropometry, obesity-related comorbidities and psychosocial background data were collected. Weight loss was expressed as 2-year percent total weight loss (%TWL).

**Results:** Mean age, body weight, body mass index (BMI) and glycated hemoglobin were 46.9 years, 119.2 kg, 43.7 kg/m<sup>2</sup> and 7.1%, respectively. Prevalence of mental disorders was 26.3%. Mean BMI declined to 30.3 kg/m<sup>2</sup> at 2 years and %TWL was 29.9%. Improvements in the markers and prevalence of obesity-related comorbidities were observed. Remission rates of diabetes, dyslipidemia and hypertension were 75.6%, 59.7% and 41.8%, respectively. %TWL at the respective cut-off level of diabetes remission was 20.8%. Lower remission rates of diabetes in patients with %TWL <20%, and less calorie restriction and higher prevalence of mental disorders (46.9%) in patients with %TWL <15% were observed. Frequencies of %TWL <15% and <20% were 6.5% and 18.5%, respectively.

**Conclusion:** %TWL 20% was a candidate cut-off point of insufficient weight loss for diabetes remission after LSG, and mental disorders might be relevant to intractable obesity in Japanese patients.

**KEYWORDS**

diabetes remission, insufficient weight loss, Japanese, mental disorder, sleeve gastrectomy

**1 | INTRODUCTION**

Obesity is a chronic health problem and has reached worldwide epidemic proportions.<sup>1</sup> Obesity is associated with an increased risk of obesity-related comorbidities such as type 2 diabetes (T2DM), dyslipidemia, hypertension and sleep apnea syndrome (SAS). In Japanese patients, T2DM tends to become severe at a relatively lower BMI.<sup>2-5</sup> Hence, obesity is also a critical health problem in Japan. Treatment of obesity aims to restore the imbalance between energy intake and energy expenditure. However, conventional approaches such as lifestyle modification, dietary control, increasing physical activity and pharmacotherapy are usually insufficient to achieve satisfactory weight loss.

Bariatric surgery has become a popular treatment option for obesity. Laparoscopic Roux-en-Y gastric bypass was the most widely used bariatric procedure and, recently, laparoscopic sleeve gastrectomy (LSG) as a single-stage procedure is becoming more popular worldwide.<sup>6</sup> In Japan, LSG is the only bariatric procedure which is covered by the national health insurance and is therefore the main procedure used. A Japanese multi-institutional survey reported that % total weight loss (%TWL) was 29% at 1 year and complete or partial diabetes remission rate was 85% after LSG.<sup>7</sup> The results are comparable

to similar surveys in American and European countries. In contrast, insufficient weight loss is often observed in patients after undergoing LSG, but background characteristics of these patients and the effect of LSG on obesity-related comorbidities have not been fully investigated in Japan. The cause of obesity is multifactorial, including genetic, social, economic, educational, environmental and psychological factors. Therefore, there is a possibility that these preoperative factors predict success or failure of postoperative weight loss. The number of patients who undergo bariatric surgery in Japan is still quite low compared with American, European and other Asian countries. We established a retrospective study group "Japanese Survey of Morbid and Treatment-Resistant Obesity" (J-SMART). The aim of the present study was to investigate the effects of LSG on obesity-related comorbidities and to identify the background characteristics of Japanese obese patients with insufficient weight loss after LSG.

**2 | SUBJECTS AND METHODS**

Japanese Survey of Morbid and Treatment-Resistant Obesity was supported by a grant for research on intractable diseases from the Ministry

of Health, Labour and Welfare of Japan. This was a multicenter and retrospective database analysis. In this study, a total of 369 Japanese patients who underwent LSG at 10 bariatric institutions certified by Japanese Society for Treatment of Obesity between January 2011 and December 2014 with a follow-up period of more than 2 years were enrolled. Patients whose BMI was 30–34.9 kg/m<sup>2</sup> with at least one obesity-related comorbidity or more than 35 kg/m<sup>2</sup> at the first visit were included. Of these, 47 patients were excluded due to lack of clinical data at 2 years after LSG. Data from the remaining 322 patients were analyzed. Our surgical method for LSG generally follows the global standard techniques.<sup>8</sup> Average bougie size was 36.7 ± 3.2 Fr and the gastric resection started from 4–5 cm proximal to the pylorus.

The following preoperative data were collected from patient records: age, anthropometric measurements, visceral fat area (VFA), subcutaneous fat area (SFA), blood pressure, glycated hemoglobin (HbA1c), fasting blood glucose (FBG), fasting serum C-peptide, lipid markers, liver and renal functions, history of insulin administration, number of medications, history of cerebral infarction, ischemic heart disease, peripheral arterial disease, diabetic retinopathy, heart failure, menstrual disorder, joint disorders, SAS, arrhythmia and apnea-hypopnea index (AHI) in patients with SAS. Joint disorders were defined as presence of osteoarthritis in knee, hip and/or hand joint disorders diagnosed by orthopedic surgeons. AHI ≥5 was diagnosed as SAS in patients with sleep-related symptoms of obstructive sleep apnea. VFA was determined using computed tomography (CT). The CT scan was carried out at the umbilical level with the subject resting in the supine position. SFA was calculated by subtracting VFA from total fat area. Information on nutrition, physical activity, mental disorders, intelligence, economic status, family background, education and childhood-onset obesity were also collected. Routine exercise was defined as exercise for 30 minutes at least twice a week. Mental disorders, mental retardation, developmental disorders, and binge eating were diagnosed by skilled psychiatrists in doubtful cases, according to Diagnostic and Statistical Manual of Mental Disorders 4th or 5th edition or International Statistical Classification of Diseases and Related Health Problems 10th Revision criteria. Contraindications to bariatric surgery were persistent alcohol and drug dependence, uncontrolled severe psychiatric illness such as depression, bipolar disorder, schizophrenia or binge-eating disorder.<sup>9</sup> The prevalence of mental disorders was the sum of mental retardation, developmental disorders, binge eating and/or other mental disorders. The Wechsler Adult Intelligence Scale (WAIS) III was carried out as the intelligence test within general practice. WAIS III was administered and scored by trained psychiatrist or psychologist. WAIS III was used not to eliminate patients, but to estimate their postsurgical outcomes such as lifestyle changes. Childhood-onset obesity was defined as onset before 6 years of age and BMI above 95th percentile. Anthropometric measurements, VFA, SFA, blood pressure, and blood samples were also collected at 1, 2, 3, 4 and 5 years after LSG. Calorie intake and dietary composition were assessed by standardized interview by trained dieticians using a computerized database, based on the analysis of the semiquantitative food record of 3 consecutive days for each 2-week period. Physicians also retrieved these nutritional data. All participants were prescribed daily

supplements of multivitamins and multiminerals. Participants were encouraged to regularly attend the bariatric surgery patient support group meetings.

Outcome of weight loss after LSG was evaluated as 2-year %TWL. Patients were divided into five groups according to %TWL (≤14.9%, 15.0%–19.9%, 20.0%–24.9%, 25.0%–29.9% and ≥30.0%). Remission of diabetes, dyslipidemia and hypertension was also evaluated at 2 years after LSG. Complete diabetes remission (CR) was defined as HbA1c <6.0% without using any diabetes medication.<sup>10</sup> Dyslipidemia remission was defined as total cholesterol (TC) level <220 mg/dL, triglyceride (TG) level <150 mg/dL and high-density lipoprotein cholesterol (HDL-C) level ≥40 mg/dL without using any medical treatment for dyslipidemia, based on the criteria of Japan Atherosclerosis Society Guidelines.<sup>11</sup> Hypertension remission was defined as systolic blood pressure (SBP) <130 mm Hg, diastolic blood pressure (DBP) <85 mm Hg and no medication for hypertension required, based on the normal range of the Japanese Society of Hypertension Guidelines for the Management of Hypertension.<sup>12</sup>

Results were expressed as mean ± SD (SPSS 15.0; SPSS Inc., Chicago, IL, USA) in all statistical analyses. All parametric data were analyzed using Student's *t* test (paired and unpaired where appropriate). All non-parametric data were analyzed using the Mann-Whitney *U* test. Fisher's exact test was used to identify any significant difference between proportions and categorical variables. Comparisons of 2-year metabolic remission rates among %TWL groups were conducted using simple linear regression, one-way ANOVA and Tukey post-hoc test. Sensitivity and specificity with respect to diabetes remission were analyzed using a conventional receiver-operating-characteristic (ROC) curve. A two-sided *P* value of .05 was considered statistically significant. If a case had missing data for any of the variables, we simply excluded that case from the analysis.

### 3 | RESULTS

The 322 patients analyzed in the present study comprised 144 men and 178 women with a mean age of 46.9 years. At the first visit, mean body weight, BMI and HbA1c were 119.2 kg, 43.7 kg/m<sup>2</sup> and 7.1%, respectively (Table 1). The follow-up rates, which were expressed as the ratio of expected number to actual number, during the study period at 1, 2, 3, 4 and 5 years after LSG were 87.3%, 87.3%, 81.3%, 77.3% and 73.5%, respectively. There was no intraoperative and postoperative mortality. Prevalence of T2DM, dyslipidemia and hypertension before surgery was 63.2%, 77.1% and 77.1%, respectively (data not shown).

#### 3.1 | Weight loss

Changes in body weight and BMI at various time points are shown in Table 1. After LSG, rapid weight loss was observed during the initial first year and the weight stabilized thereafter. Following surgery, mean body weight (BMI) declined to 82.2 kg (30.2 kg/m<sup>2</sup>) at 1 year and 82.6 kg (30.3 kg/m<sup>2</sup>) at 2 years. The %TWL achieved was 30.5% at

**TABLE 1** Changes in various parameters after LSG

	1st visit (n = 322)	Pre-op (n = 322)	1-y post-op (n = 322)	2-y post-op (n = 322)	3-y post-op (n = 195)	4-y post-op (n = 109)	5-y post-op (n = 50)
Body weight (kg)	119.2 ± 29.3	110.9 ± 25.3***	82.2 ± 20.9***	82.6 ± 21.3***	83.5 ± 19.5***	82.2 ± 17.8***	85.2 ± 19.3***
BMI (kg/m <sup>2</sup> )	43.7 ± 8.8	40.7 ± 7.4***	30.2 ± 6.5***	30.3 ± 6.6***	30.3 ± 6.4***	30.1 ± 6.5***	31.2 ± 6.6***
Visceral fat area (cm <sup>2</sup> )	247.6 ± 91.9	197.2 ± 82.5**	85.4 ± 58.2***	119.1 ± 76.0***	130.2 ± 58.8***	158.5 ± 68.1***	161.5 ± 100.1***
Subcutaneous fat area (cm <sup>2</sup> )	512.5 ± 150.8	503.1 ± 179.6	297.5 ± 145.5***	353.2 ± 162.4***	348.8 ± 151.4***	369.8 ± 169.5***	455.5 ± 123.8*
Systolic blood pressure (mm Hg)	140.0 ± 19.5	126.7 ± 16.6**	125.1 ± 18.5***	127.0 ± 18.8***	125.5 ± 18.8***	129.3 ± 20.1*	128.1 ± 18.5*
Diastolic blood pressure (mm Hg)	87.1 ± 15.2	74.8 ± 13.6**	73.6 ± 15.0***	76.2 ± 14.5***	74.9 ± 14.3***	78.9 ± 13.6**	77.3 ± 14.5*
% Patients using antihypertensive drugs	63.0	58.9	29.3***	30.2***	30.5***	30.6***	28.9**
HbA1c (%)	7.1 ± 1.8	6.5 ± 1.4***	5.9 ± 0.7***	5.7 ± 0.7***	5.6 ± 0.6***	5.7 ± 0.7***	5.8 ± 0.8***
FBG (mg/dL)	127.7 ± 49.8	110.8 ± 30.6***	96.5 ± 19.9***	97.8 ± 20.1***	96.3 ± 16.0***	97.6 ± 16.3***	103.5 ± 25.0***
% Patients using antidiabetic drugs	58.6	50.7	7.3***	9.6***	6.9***	7.3***	8.7***
% Patients using insulin	12.3	16.3	1.8***	1.0***	1.7***	3.1***	4.4**
TC (mg/dL)	199.6 ± 42.5	189.8 ± 36.2***	195.7 ± 35.5*	199.3 ± 36.5	199.6 ± 34.6	199.9 ± 36.8	206.7 ± 29.0
TG (mg/dL)	183.5 ± 137.1	136.1 ± 73.1***	88.1 ± 58.1***	96.7 ± 59.0***	88.4 ± 49.7***	94.3 ± 68.7**	132.7 ± 63.2*
HDL-C (mg/dL)	46.4 ± 9.9	44.5 ± 10.5***	61.5 ± 14.5***	64.0 ± 16.7***	64.3 ± 14.9***	63.7 ± 15.4***	61.5 ± 12.6***
% Patients using lipid-lowering drugs	39.1	42.2	11.5***	13.3***	10.6***	11.4***	7.3***
AST (IU/L)	38.4 ± 25.0	34.7 ± 20.8***	21.3 ± 38.8***	20.1 ± 10.6***	20.1 ± 14.8***	21.1 ± 13.0***	19.7 ± 5.1***
ALT (IU/L)	52.9 ± 35.8	47.4 ± 39.0***	20.9 ± 44.7***	17.5 ± 10.7***	17.0 ± 12.3***	17.0 ± 8.7***	17.1 ± 9.6***
γGTP (IU/L)	57.4 ± 41.5	48.0 ± 55.7***	24.7 ± 34.9***	24.7 ± 24.9***	27.1 ± 39.4***	27.1 ± 28.8***	30.7 ± 36.7***
Cr (mg/dL)	0.8 ± 0.7	0.7 ± 0.6	0.7 ± 0.7*	0.7 ± 0.5	0.8 ± 1.0	0.7 ± 0.2	0.7 ± 0.2
Urine alb (mg/gCr)	86.6 ± 262.3	33.9 ± 69.2	24.7 ± 63.8*	30.9 ± 74.9*	16.9 ± 34.2	30.5 ± 81.6	21.6 ± 42.8
Uric acid (mg/dL)	6.3 ± 1.6	6.8 ± 1.6	5.7 ± 1.5***	5.6 ± 1.5***	5.6 ± 1.5***	5.7 ± 1.5***	6.0 ± 1.7***
Daily Calorie intake (kcal/day)	2997.5 ± 1361.4	2371.7 ± 1147.5*	1230.8 ± 359.9***	1395.8 ± 407.9***	1488.2 ± 473.8**	1570.7 ± 344.1**	1493.6 ± 258.9*
Heart failure (%)	1.3	1.0	0.0	0.0	0.0	0.0	0.0
Menstrual disorder (female)(%)	21.3	22.9	13.1***	7.0**	3.2*	-	-
Joint disorders (%)	45.4	28.4	24.1*	19.6**	21.7*	18.0*	28.6
Sleep apnea syndrome (%)	62.8	79.2	35.3***	31.0***	35.2***	34.4***	38.9***

Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; Cr, Creatinine; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LSG, laparoscopic sleeve gastrectomy; TC, total cholesterol; TG, triglyceride; γGTP, glutamyltranspeptidase. \*P < 0.05\*\* P < 0.01\*\*\* P < 0.001 (vs 1st visit). -, the prevalence is less than 10 cases.

1 year and 29.9% at 2 years. Figure 1 shows a histogram of %TWL at 2 years after LSG. Frequencies of %TWL <15% and <20% at 2 years, which were indicators of insufficient weight loss, were 6.5% and 18.5%, respectively (data not shown). Changes in VFA and SFA are shown in Table 1, and both decreased significantly in all postoperative periods compared to the first visit.

### 3.2 | Changes in metabolic parameters and relationship with %TWL

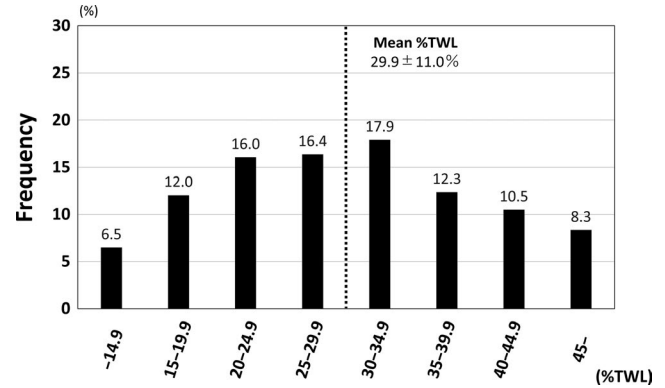
After LSG, mean HbA1c and FBG decreased rapidly to 5.9% and 96.5 mg/dL, respectively, at 1 year, and to 5.7% and 97.8 mg/dL at 2 years (Table 1). Other metabolic parameters such as TC, TG, SBP and DBP also decreased significantly compared to the first visit. HDL-C increased significantly in all postoperative periods ( $P < .0001$ ). Frequency of patients using antidiabetic drugs (including insulin) decreased from 58.6% at the first visit to 7.3% at 1 year and 9.6% at 2 years after LSG. The frequency of insulin use decreased from 12.3% to 1.8% at 1 year and to 1.0% at 2 years. Similarly, frequency of patients using lipid-lowering drugs and antihypertensive drugs decreased significantly. At 2 years after LSG, 177 of 234 patients (75.6%) achieved diabetes CR. Remission rates of dyslipidemia and hypertension were 59.7% and 41.8%, respectively.

Metabolic parameters at the first visit in patients stratified by %TWL are shown in Table 2. One-way ANOVA detected no statistically significant differences in all of the metabolic parameters studied among the %TWL groups. Simple linear regression analysis showed that %TWL correlated positively with preoperative body weight ( $r = .281, P < .0001$ ), BMI ( $r = .313, P < .0001$ ) and VFA ( $r = .281, P < .0001$ ) (data not shown).

Figure 2A compares the 2-year metabolic remission rates among %TWL groups. Diabetes CR rate was above 80% when %TWL was  $\geq 20\%$ , but decreased to below 60% when %TWL was <20%. Diabetes CR rates in %TWL  $\leq 14.9\%$  and 15.0%–19.9% groups were significantly lower compared to other groups. ROC curve of %TWL at the optimal cut-off level of diabetes CR is shown in Figure 2B. At the cut-off level (20.8%), sensitivity was 86.2% and specificity was 52.7%. Remission rate of dyslipidemia also decreased in low %TWL groups. Remission rate in %TWL  $\leq 14.9\%$  group was 17.7% and was significantly lower than that in %TWL  $\geq 30.0\%$  group (77.3%). The remission rate of hypertension was lower than the other metabolic remissions and did not differ significantly among %TWL groups.

### 3.3 | Other obesity-related comorbidities

Changes in markers of liver and renal functions, and uric acid from the first visit to various postoperative periods are shown in Table 1. Liver function markers and serum uric acid decreased significantly in all postoperative periods, and renal markers decreased significantly at 1 year after LSG. Prevalence of heart failure, menstrual disorder in females, joint disorders and SAS at first visit was 1.3%, 21.3%, 45.4% and 62.8%, respectively (Table 1). After LSG, the prevalence of menstrual disorder, joint disorders and SAS decreased significantly. The prevalence of other obesity-related comorbidities at first visit in patients stratified by %TWL is shown in Table 3. There were no significant



**FIGURE 1** Histogram of percent total weight loss (%TWL) at 2 y after laparoscopic sleeve gastrectomy. Patients were divided into eight groups according to %TWL (every 5% of TWL). Black dotted line indicates mean %TWL ( $29.9 \pm 11.0\%$ )

differences among the %TWL groups. Simple linear regression analysis showed that %TWL correlated positively with AHI in patients with SAS ( $r = .228$  and  $P = .0016$ , data not shown), but did not correlate with other obesity-related comorbidities (data not shown).

### 3.4 | Psychosocial background, eating behavior and physical activity

Parameters for psychosocial background, eating behavior and physical activity at first visit in patients stratified by %TWL are shown in Table 3. Mean prevalence of mental disorders was 26.3%, of which mental retardation/developmental disorders and binge eating were 4.5% and 20.8%, respectively. Frequency of childhood-onset obesity was 38.5%. Mean daily calorie intake was 2997.5 kcal/d at first visit, and decreased significantly in all postoperative periods (Table 1). There were no significant differences among the %TWL groups for all of the parameters of psychosocial background, smoking, alcohol, daily calorie intake and ratio of protein, fat and carbohydrate intake (Table 3).

Figure 3A shows the prevalence of mental disorders stratified by %TWL. To investigate the characteristics of patients not only with insufficient weight loss, but also those with excessive weight loss after LSG, the patients were divided into eight groups according to %TWL ( $\leq 14.9\%$ , 15.0%–19.9%, 20.0%–24.9%, 25.0%–29.9%, 30.0%–34.9%, 35.0%–39.9%, 40.0%–44.9% and  $\geq 45.0\%$ ). Relationship between frequencies of mental disorders and %TWL was a U-shaped curve, and the trend was significant (Figure 3A). In patients with %TWL <15%, the frequency was 46.9% and significantly higher than in those with %TWL  $\geq 15\%$  (Figure 3B). Similarly, the prevalence of mental retardation and developmental disorders in patients with %TWL <15% tended to be higher than in those with %TWL  $\geq 15\%$  ( $P = .0817$ ) (data not shown). Furthermore, the prevalence of mental disorders in patients with %TWL  $\geq 45\%$  was also significantly higher than in those with %TWL <45% (Figure 3C).

### 3.5 | Characteristics of patients with %TWL <15%

As mentioned above, patients with %TWL <15% had a high prevalence of mental disorders. Therefore, to clarify the characteristics

**TABLE 2** Metabolic parameters prior to LSG according to 2-y %TWL in 322 Japanese patients

%TWL group	Total	-14.9 (n = 20)	15.0-19.9 (n = 39)	20.0-24.9 (n = 52)	25.0-29.9 (n = 53)	30.0- (n = 158)
Gender (male/female)	144/178	9/11	14/25	23/29	31/22	67/91
Age (y)	47.5 ± 10.8	47.1 ± 11.2	52.4 ± 12.4	49.7 ± 10.0	47.9 ± 11.6	45.4 ± 9.8
Height (cm)	164.7 ± 9.4	161.8 ± 13.5	162.5 ± 8.0	165.1 ± 8.8	166.5 ± 9.8	164.9 ± 9.1
Body weight (kg)	119.2 ± 29.3	115.5 ± 35.9	101.6 ± 20.8	115.8 ± 25.3	120.4 ± 26.8	124.8 ± 30.7
BMI (kg/m <sup>2</sup> )	43.7 ± 8.8	43.6 ± 10.5	38.3 ± 6.5	42.3 ± 7.8	43.3 ± 8.0	45.6 ± 9.1
Visceral fat area (cm <sup>2</sup> )	247.6 ± 91.9	191.7 ± 84.8	206.3 ± 90.1	227.3 ± 76.6	283.1 ± 81.5	264.0 ± 96.8
Subcutaneous fat area (cm <sup>2</sup> )	512.5 ± 150.8	669.4 ± 43.6	421.9 ± 127.9	568.9 ± 190.1	516.9 ± 82.2	509.9 ± 156.3
VFA/SFA ratio	0.5 ± 0.2	0.3 ± 0.1	0.5 ± 0.2	0.4 ± 0.2	0.6 ± 0.2	0.6 ± 0.3
Systolic blood pressure (mm Hg)	140 ± 20	148 ± 34	134 ± 19	144 ± 14	142 ± 20	139 ± 20
Diastolic blood pressure (mm Hg)	87 ± 15	90 ± 16	80 ± 11	89 ± 10	86 ± 10	89 ± 19
% Patients using antihypertensive drugs	63.0	68.5	72.0	71.7	71.0	57.8
HbA1c (%)	7.1 ± 1.8	6.8 ± 1.5	8.4 ± 2.6	7.5 ± 1.7	6.8 ± 1.4	6.9 ± 1.7
FBG (mg/dL)	127.7 ± 49.8	125.4 ± 29.8	136.1 ± 50.4	140.0 ± 63.9	119.5 ± 33.0	125.5 ± 51.3
Serum CPR (ng/mL)	3.6 ± 1.6	3.2 ± 1.1	3.4 ± 1.4	3.4 ± 1.3	3.6 ± 1.8	3.7 ± 1.6
% Patients using antidiabetic drugs	58.6	73.3	78.4	50.0	51.4	54.0
% Patients using insulin	12.3	17.4	18.8	12.8	10.0	10.6
TC (mg/dL)	199.6 ± 42.5	190.9 ± 46.5	199.2 ± 38.1	211.4 ± 46.1	191.1 ± 35.3	202.2 ± 44.5
TG (mg/dL)	183.5 ± 137.1	186.7 ± 115.5	174.5 ± 78.8	182.4 ± 104.2	189.1 ± 119.7	183.0 ± 165.4
HDL-C (mg/dL)	46.4 ± 9.9	42.5 ± 7.6	48.0 ± 11.8	45.5 ± 6.8	46.8 ± 9.3	47.3 ± 10.5
% Patients using lipid-lowering drugs	39.1	48.8	42.9	45.5	48.4	29.3
AST (IU/L)	38.4 ± 25.0	34.8 ± 18.0	36.7 ± 12.5	50.3 ± 38.5	31.9 ± 19.6	38.4 ± 24.7
ALT (IU/L)	52.9 ± 35.8	44.8 ± 25.7	49.6 ± 22.0	69.2 ± 50.2	43.4 ± 30.1	53.8 ± 36.1
γGTP (IU/L)	57.4 ± 41.5	51.2 ± 35.8	59.8 ± 34.2	71.8 ± 47.0	49.6 ± 37.0	59.2 ± 43.5
Cr (mg/dL)	0.8 ± 0.7	0.7 ± 0.2	0.8 ± 0.4	1.1 ± 1.9	0.7 ± 0.2	0.7 ± 0.2
Uric acid (mg/dL)	6.3 ± 1.6	5.7 ± 1.5	6.8 ± 1.7	6.5 ± 1.6	6.2 ± 1.6	6.2 ± 1.6

Note: One-way ANOVA detected no statistically significant differences in all metabolic parameters studied among the %TWL groups.

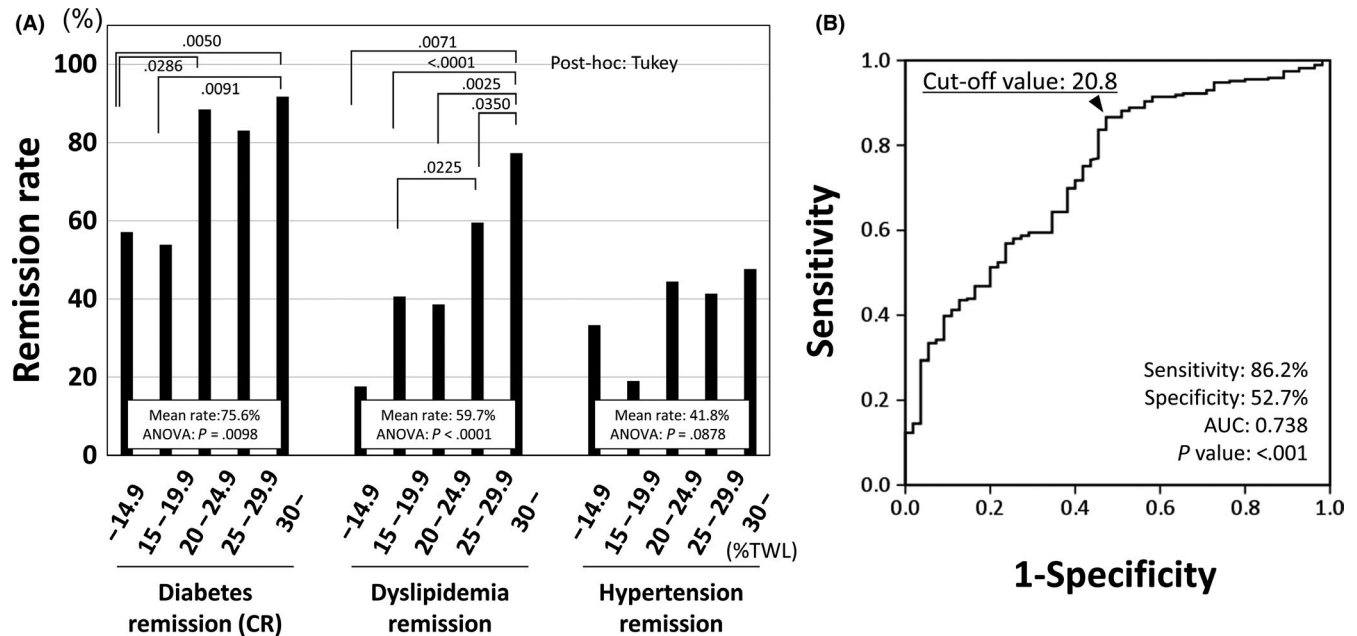
Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; CPR, C-peptide response; Cr, creatinine; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LSG, laparoscopic sleeve gastrectomy; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglyceride; %TWL, percent total weight loss; VFA, visceral fat area; γGTP, gamma-glutamyl transpeptidase.

of patients with %TWL <15%, further investigation was carried out (Figure 4). Patients with %TWL <15% not only had a smaller decrease in body weight compared to patients with %TWL ≥15%, they also showed significant weight regain from 1 year to 2 years after LSG ( $P = .0002$ ). Patients with %TWL <15% had significantly higher daily calorie intake at 2 years after LSG than those with %TWL ≥15% ( $P < .0001$ ) and showed a significant increase in calorie intake from 1 year to 2 years after surgery ( $P = .0486$ ).

## 4 | DISCUSSION

This is the first nationwide survey at 10 certified bariatric institutions to clarify the relationship between insufficient weight loss

after LSG, metabolic remission and psychosocial background in Japanese patients. In a Japanese survey (published in Japanese), 100-200 patients per year underwent LSG between 2011 and 2014, and there were 10 institutions that carried out more than 10 bariatric/metabolic surgery cases in 2015. Therefore, the sample size in the present study could correspond to that nationwide. LSG has been established as a safe and effective procedure worldwide.<sup>13-15</sup> Seki et al<sup>16</sup> reported that LSG is safe, effective, and acceptably durable for up to 5 years in morbidly obese Japanese patients. Our study found mean %TWL of 29.9% and diabetes CR of 75.6% at 2 years after surgery, together with high remission rates of other metabolic diseases. These findings are consistent with the results of a previous Japanese multi-institutional survey.<sup>7</sup>



**FIGURE 2** Comparison of 2-y metabolic remission rates among percent total weight loss (%TWL) groups. (A) Patients were stratified by %TWL into five groups ( $\leq 14.9$ , 15.0-19.9, 20.0-24.9, 25.0-29.9 and  $\geq 30.0$ ). Diabetes complete remission rate was 57.1% in the  $\leq 14.9\%$  group, 53.9% in the 15.0-19.9 group and more than 80% in %TWL  $\geq 20\%$  groups. Remission rate of dyslipidemia in %TWL  $\leq 14.9\%$  group was 17.7%. The remission rate of hypertension was lower than the other metabolic remissions. (B) Receiver operating characteristic curve of %TWL at optimal cut-off level of diabetes complete remission. At the cut-off level (20.8%), sensitivity was 86.2% and specificity was 52.7%

As a definition of weight loss failure after bariatric surgery, Reinhold's classification<sup>17</sup> of BMI  $>35$  or % excess weight loss (EWL)  $<50\%$  is widely used and, using this definition, the rate of weight loss failure was reported to be 20.4%.<sup>18</sup> However, the definition of weight loss failure using %TWL has not been established. van de Laar et al<sup>19</sup> reported that  $\geq 25\%$  TWL was a useful criterion with sensitivity and specificity of 90%, but that  $\geq 15\%$  and  $\geq 20\%$  TWL were inadequate criteria with specificity  $<30\%$  for weight loss success with reference to the baseline BMI-independent weight loss percentile chart based on retrospective data after bariatric surgery. In the present study, diabetes remission rates were considerably lower in patients with %TWL  $<20\%$  compared with higher %TWL. The ROC curve of %TWL at the optimal cut-off level of diabetes CR was 20.8%. There is a possibility that %TWL 20% is a candidate cut-off point of insufficient weight loss for diabetes remission after LSG. Furthermore, a lower remission rate of dyslipidemia was shown in patients with %TWL  $<15\%$ .

This is the first report that comprehensively investigated obesity-related comorbidities other than metabolic disorders in bariatric patients in Japan. In the systematic review conducted by Buchwald et al,<sup>13</sup> the prevalence of SAS, coronary artery disease, congestive heart failure and degenerative joint disease was 19.6, 7.0, 2.3 and 50.3%, respectively, in patients undergoing bariatric surgery. Jamal et al<sup>20</sup> reported that 5.5% of patients undergoing bariatric surgery had a history of polycystic ovary syndrome, whereas Musella et al<sup>21</sup> reported that 45.8% of patients were identified as having obesity-related infertility. The prevalence of heart failure and joint disorders in our study was similar to these previous reports, whereas the

prevalence of SAS was higher in our Japanese study. There are few reports on the beneficial effects of LSG on other obesity-related comorbidities. Previous reports showed that other bariatric surgery procedures such as laparoscopic Roux-en-Y gastric bypass improved cardiovascular risk factors, sleep apnea and joint pain,<sup>13,22,23</sup> which is supported by the findings in our study. Sarkhosh et al<sup>24</sup> found that all the bariatric procedures achieved profound effects on SAS, and 85.7% of patients reported subjective improvement of SAS. However, the relationship between %TWL and improvement in heart failure, menstrual disorder, joint disorders and SAS was not detected in the present study as a result of a lack of available data. Further prospective investigation is required to elucidate how much weight obese patients need to lose to improve their comorbidities.

The present study is also the first nationwide survey in Japan to investigate the psychosocial background of morbidly obese patients. Previous studies have shown that 20.9%-37.8% of bariatric surgery candidates had at least one mental disorder at the time of preoperative evaluation.<sup>25-27</sup> The reported prevalence of eating disorders at the time of preoperative evaluation ranged from 7.1% to 16.3%.<sup>25-27</sup> In this Japanese survey, the prevalence of mental disorders was 26.3% and that of binge eating was 20.8%. A meta-analysis by Dawes et al<sup>28</sup> concluded that there was conflicting evidence regarding the association between preoperative mental health conditions and postoperative weight loss. In our study, the prevalence of mental disorders was quite high in patients with %TWL  $<15\%$ . Our findings might affirm that there is a relationship between mental disorders and insufficient weight loss after bariatric surgery. Also, interestingly, the prevalence of mental disorders

**TABLE 3** Other obesity-related comorbidities, psychosocial background, eating behavior and physical activity among %TWL groups

%TWL group	Total	≤14.9 (n = 20)	15.0-19.9 (n = 39)	20.0-24.9 (n = 52)	25.0-29.9 (n = 53)	≥30.0 (n = 158)
History of cerebral infarction (%)	1.3	0.0	0.0	0.0	1.9	1.9
Ischemic heart disease (%)	2.1	0.0	5.1	2.0	3.8	1.3
Peripheral arterial disease (%)	0.7	0.0	0.0	0.0	1.9	0.7
Diabetic retinopathy (%)	3.2	10.5	5.4	4.0	2.0	2.0
Heart failure (%)	1.3	0.0	0.0	0.0	1.9	1.9
Menstrual disorder (female, %)	21.3	16.7	15.0	17.7	13.3	26.8
Joint disorders (%)	45.4	63.2	48.7	47.1	30.2	47.1
Sleep apnea syndrome (%)	62.8	36.4	67.7	71.0	67.9	60.9
AHI in SAS patients (per h)	45.5 ± 33.6	38.4 ± 42.6	37.9 ± 18.8	28.3 ± 21.4	53.5 ± 33.6	50.8 ± 36.0
Arrhythmia (%)	3.7	5.3	5.3	3.9	3.8	3.2
Gait abnormality (%)	3.2	4.8	0.0	2.0	1.9	4.5
Mental disorders (%)	26.3	46.9	24.3	19.6	15.7	28.0
Mental retardation and developmental disorders (%)	4.5	18.2	5.9	0.0	0.0	5.4
Binge eating (%)	20.8	8.3	29.4	29.2	19.2	18.5
Full IQ (WAIS-III)	96.6 ± 17.3	96.5 ± 18.5	98.8 ± 23.2	102.3 ± 19.5	98.0 ± 8.8	94.8 ± 18.6
Verbal IQ (WAIS-III)	97.8 ± 16.2	99.8 ± 17.3	95.3 ± 23.3	102.0 ± 23.6	97.2 ± 6.5	97.0 ± 16.4
Performance IQ (WAIS-III)	96.4 ± 17.7	94.4 ± 17.3	103.5 ± 19.6	102.0 ± 13.0	98.0 ± 11.5	94.2 ± 20.4
Economic independence (%)	68.5	63.2	71.4	66.7	85.1	63.6
Household on welfare (%)	1.3	5.3	0.0	0.0	0.0	2.0
History of divorce (%)	10.9	22.2	11.4	8.2	4.3	12.4
Living with family (%)	85.2	63.2	87.2	86.3	84.6	87.5
Marriage (%)	52.7	26.3	53.9	63.5	56.6	51.0
Living with one's parent(s) (%)	24.3	29.4	27.1	25.0	30.9	20.8
Maternal obesity (%)	30.3	14.3	38.5	29.4	28.6	31.7
Parental obesity (%)	18.9	14.3	25.0	20.0	10.0	21.1
Educational background (Other/University/Graduate school)	87/56/3	5/4/0	17/10/0	12/5/0	41/25/2	12/12/1
Childhood-onset obesity (%)	38.5	44.4	46.0	29.0	40.9	38.8
Smoking (Current/Quit/No)	25/50/99	2/4/6	2/12/17	2/9/10	14/24/48	5/1/18
Alcohol (No/Social/Regular)	119/89/26	8/8/0	19/15/4	16/7/3	59/44/15	17/15/4
Daily calorie intake (kcal/d)	2997.5 ± 1361.4	3363.2 ± 1585.9	2620.0 ± 766.8	2465.1 ± 812.7	2998.6 ± 952.5	3020.0 ± 1303.4
Ratio of protein intake (%)	17.2 ± 9.0	16.5 ± 8.3	18.1 ± 5.2	22.5 ± 16.9	14.9 ± 3.0	17.2 ± 9.3
Ratio of fat intake (%)	25.5 ± 9.1	32.3 ± 8.8	24.3 ± 7.8	23.2 ± 4.1	27.0 ± 9.2	24.2 ± 9.9
Ratio of carbohydrate intake (%)	55.9 ± 12.0	51.1 ± 11.9	57.6 ± 7.9	54.8 ± 15.4	55.5 ± 10.8	57.6 ± 12.3
Routine exercise (%)	8.8	8.3	9.5	4.4	6.7	10.8

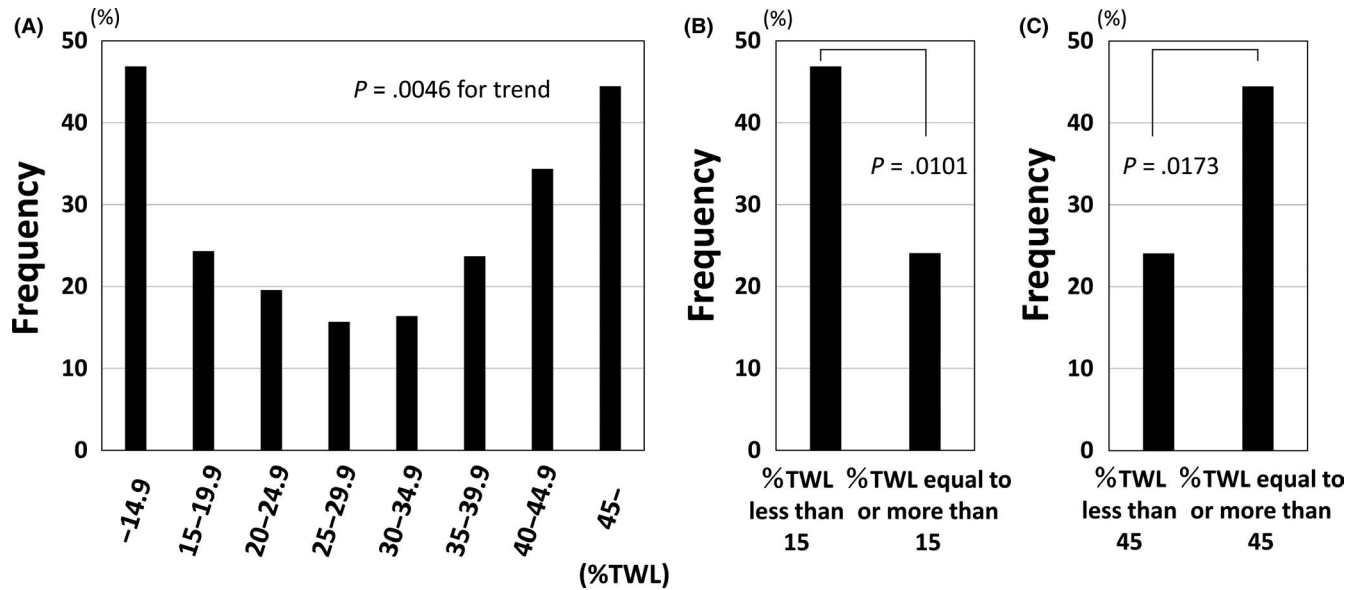
Note: One-way ANOVA detected no statistically significant differences in these parameters among the %TWL groups. Abbreviations: AHI, apnea hypopnea index; SAS, sleep apnea syndrome; %TWL, percent total weight loss.

in patients with %TWL ≥45% was also significantly high. Further investigation is needed to clarify the characteristics of patients with excessive weight loss and the types of mental disorders in patients with both insufficient and excessive weight loss.

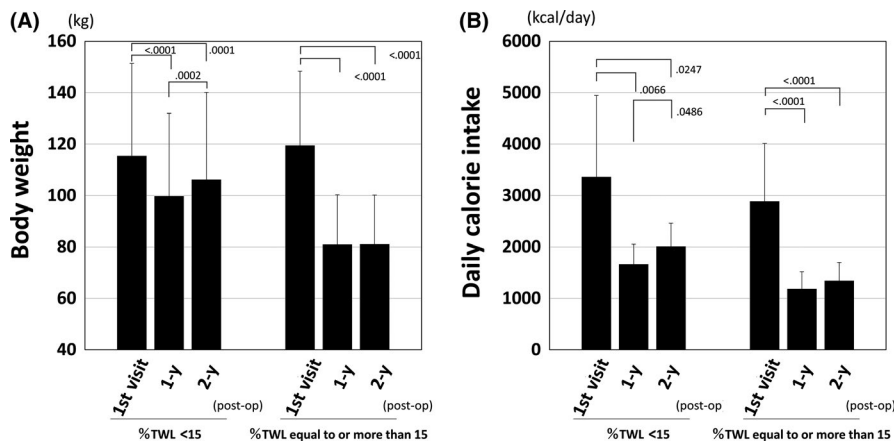
There are several limitations in the present study. We carried out multivariate analysis to identify risk factors that caused insufficient weight loss after LSG; however, there was no independent factor identified (data not

shown). The design was retrospective and observational. Lack of available data in some subjects could restrict the scope of our analysis. Also, the size of the sample analyzed could be a significant obstacle in identifying a trend and a significant relationship. The outcomes might also be influenced among institutions by various surgical techniques and surgeon's preference. Moreover, the small sample size is a critical problem, but this could not be avoided as a result of the current situation in Japan.





**FIGURE 3** Prevalence of mental disorders stratified by percent total weight loss (%TWL). (A) Patients were divided into eight groups according to %TWL (every 5% of TWL). Relationship between frequency of mental disorders and %TWL was a U-shaped curve, and the trend was significant using Fisher's exact test ( $P = .0046$ ). (B) In patients with  $\%TWL < 15\%$ , the frequency was 46.9% and significantly higher than in those with  $\%TWL \geq 15\%$  ( $P = .0101$ ). (C) Frequency in patients with  $\%TWL \geq 45\%$  was also significantly higher than in those with  $\%TWL < 45\%$



**FIGURE 4** Changes in (A) body weight and (B) daily calorie intake in patients with percent total weight loss (%TWL)  $< 15\%$  compared with  $\%TWL \geq 15\%$ . In patients with  $\%TWL < 15\%$ , significant weight regain was observed from 1 y after laparoscopic sleeve gastrectomy (LSG) (mean body weight was 99.8 kg at 1 y and 106.2 kg at 2 y,  $P = .0002$ ). In patients with  $\%TWL < 15\%$ , daily calorie intake at 2 y after LSG was significantly higher compared to  $\%TWL \geq 15\%$  (2012.4 vs 1339.2 kcal/d,  $P < .0001$ ), and a significant ( $P = .0486$ ) increase in daily calorie intake from 1 y (1666.8 kcal/d) to 2 y after LSG (2012.4 kcal/d) was observed

## 5 | CONCLUSIONS

This is the first nationwide survey in Japan to clarify the relationship between insufficient weight loss after LSG, metabolic remission and psychosocial background. Our study showed that mean %TWL was 29.9%, and that weight loss resulted in significant improvement in obesity-related comorbidities. %TWL 20% might be an optimal cut-off point for diabetes remission in Japanese obese patients. Furthermore, patients with  $\%TWL < 15\%$  might have increased appetite and mental disorders. Patients with insufficient

weight loss may have treatment resistance that involves certain physical and psychological factors. Further investigation in collaboration with pediatricians and psychiatrists is required to clarify the mechanism of insufficient weight loss.

## DISCLOSURE

Funding: J-SMART was supported by a grant for research on intractable diseases from Ministry of Health, Labour and Welfare of Japan (H28-nanji-ippan-014).

**Conflicts of Interest:** Authors declare no conflicts of interest for this article.

**Ethical Approval:** All procedures and data collection were in accordance with the ethical standards of the institutional and Japanese national research committees or the ethical standards of the Helsinki Declaration of 1975. LSG was done per usual clinical practice. Informed consent to undergo the procedure was obtained from all individual participants included in this study. All clinical data were anonymized to protect privacy.

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**How to cite this article:** Saiki A, Yamaguchi T, Tanaka S, et al. Japanese Survey of Morbid and Treatment-Resistant Obesity Group (J-SMART Group). Background characteristics and postoperative outcomes of insufficient weight loss after laparoscopic sleeve gastrectomy in Japanese patients. *Ann Gastroenterol Surg*. 2019;3:638–647. <https://doi.org/10.1002/ags3.12285>