




Therapeutic effect of laparoscopic sleeve gastrectomy on obstructive sleep apnea and relationship of type 2 diabetes in Japanese patients with severe obesity

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Keywords

Laparoscopic sleeve gastrectomy, Obstructive sleep apnea, Type 2 diabetes

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ABSTRACT

Aims/Introduction: Obstructive sleep apnea (OSA) is among the most important obesity-related diseases, and offers the potential for accelerated the early onset and progression of type 2 diabetes. The aim of the present study was to clarify the therapeutic effect of laparoscopic sleeve gastrectomy on OSA in severely obese Japanese patients, and to find correlations between OSA improvements and β -cell function (BCF).

Materials and Methods: Between September 2013 and December 2019, 61 patients who underwent laparoscopic sleeve gastrectomy were enrolled. The apnea–hypopnea index (AHI) was used to diagnose OSA. The tongue area, uvula area and other parameters were measured using cone-beam computed tomography. Regarding BCF parameters, the homeostasis model assessment of β -cell function, insulinogenic, Matsuda and disposition indexes were used to evaluate the improvement in BCF. Improvement of OSA was defined as AHI <15.

Results: The improvement rate of OSA was 51.8% (29/56). The change in AHI was significantly correlated with the excess weight loss percentage ($p = 0.501$), changes in tongue area ($p = 0.350$) and uvula area ($p = 0.341$). Multivariate analysis showed that preoperative AHI and postoperative hemoglobin A1c were independent prognostic factors of OSA non-improvement. The homeostasis model assessment of β -cell function ($P < 0.001$), the insulinogenic index ($P < 0.001$) and the disposition index ($P = 0.019$) of patients with AHI of <15 were significantly higher than those in patients with AHI of ≥ 15 .

Conclusions: Laparoscopic sleeve gastrectomy is a promising procedure for severely obese patients with OSA. BCF recovery was found to be significantly higher in patients with OSA improvement.

INTRODUCTION

Obstructive sleep apnea (OSA) is one of the most important obesity-related diseases. It is characterized by repetitive upper airway collapse during sleep, causing intermittent hypoxemia. This leads to increased respiratory effort and, subsequently, recurrent arousals^{1,2}. Furthermore, severe obesity directly affects

the pathophysiology of the narrowing of the upper airways due to fat deposits in the oropharyngeal muscle and the surrounding tissues, such as the tongue, soft palate, uvula and tonsillar lesion. Approximately 70% of obese patients are reported to suffer from OSA³; therefore, recent studies have clarified the efficacy of metabolic surgery or weight loss procedures for OSA^{3–5}. However, no extant report has evaluated the anatomical changes after metabolic surgery in severely obese patients with OSA.

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Conversely, Itoh established the concept of the “metabolic domino.” Lifestyle changes are the first dominoes to fall, leading to morbid obesity and insulin resistance, followed by postprandial hyperglycemia, hypertension and hyperlipidemia⁶. In this cascade, OSA accelerates the early onset and progression of metabolic syndrome, and eventually leads to type 2 diabetes, ischemic heart disease, cerebrovascular disorders and chronic kidney disease. From this concept, we hypothesized that the severity of the degree of improvement in OSA has a correlation with β -cell function (BCF) in severely obese patients with both OSA and type 2 diabetes.

Regarding surgical treatments for severe obesity in Japan, laparoscopic sleeve gastrectomy (LSG) has been covered by the national health insurance system since 2014. Additionally, we have clarified the weight loss and metabolic effects in severely obese Japanese patients^{7,8}.

The aim of the present study was to clarify the therapeutic effect of LSG on OSA in severely obese Japanese patients using full-night polysomnography (FN-PSG) and airway morphological parameters employing cone-beam computed tomography. Subsequently, the relationships between OSA improvement and BCF recovery were evaluated using various BCF parameters and existing scoring systems for type 2 diabetes remission after LSG.

MATERIALS AND METHODS

Patients

The present study was a single-institution retrospective study involving data collection and analyses. Between September 2013 and December 2019, 61 severely obese Japanese patients underwent LSG at Iwate Medical University Hospital, Iwate, Japan. All patients met the following inclusion criteria for LSG treatment established by Japanese insurance practice: aged between 18 and 65 years, severe obesity with body mass index (BMI) >35 kg/m² and the presence of at least one comorbidity with resistance to medical treatment (hypertension, type 2 diabetes, dyslipidemia and OSA). Regarding surgical procedures, the LSGs involved 70–80% gastric-volume reduction by resecting the stomach alongside a 36-Fr esophagogastroduodenoscopy, beginning 4 cm from the pyloric ring and ending at the angle of His. All patients were continuously evaluated and cared for by a multidisciplinary team from initial visit to postoperative follow-up to improve weight loss and metabolic effects.

The present study was approved by the institutional ethics committee (approval number: H27-47) and was carried out following the ethical principles in the Declaration of Helsinki. We obtained informed consent from each patient before enrollment, and patient anonymity was strictly protected.

Objective OSA evaluation and treatment

Regarding the OSA diagnosis, FN-PSG was routinely carried out, and an apnea–hypopnea index (AHI) of ≥ 5 directly led to OSA. We did not use the STOP-Bang or Epworth Sleepiness Scale as diagnostic tools, because FN-PSG was only determined

as an essential diagnostic modality for introducing continuous positive airway pressure (CPAP) in the Japanese national health insurance system^{9,10}. The severity of OSA was defined as follows: the AHI of mild, moderate and severe OSA was set as 5–15, 15–30 and ≥ 30 , respectively. Subsequently, the CPAP was routinely introduced when the AHI was ≥ 15 (moderate/severe OSA), and the CPAP was continued until the AHI was <15 after LSG. In the present study, enrolled patients with OSA received FN-PSG at baseline, 6 months and 12 months after LSG. The following data were also collected from FN-PSG: rapid eye movement AHI (REM-AHI), non-REM-AHI, minimum arterial oxygen saturation of pulse oximetry and sleep efficiency. In Japanese clinical practice, CPAP for mild OSA has not been covered by the national health insurance system; therefore, OSA improvement was defined as AHI <15 at 12 months after LSG.

Objective evaluation of airway morphological parameters

We used cephalography and cone-beam computed tomography (Kavo op 3D Vision V17; KaVo Dental Systems, Tokyo, Japan) for imaging modalities. Afterward, we measured the tongue area (TA), uvula area (UA), uvula length (UL), posterior airway space and airway diameter at the tip of the epiglottis using a computer workstation (SYNAPSE VINCENT; FUJIFILM, Tokyo, Japan; Figure 1)^{11,12}. We carried out these imaging examinations at the same time as FN-PSG, and expressed cm² for TA and UA, cm for UL, and mm for posterior airway space and airway diameter at the tip of the epiglottis.

Data collection

For all enrolled patients, clinical data, weight loss and metabolic effects were evaluated at baseline, 6 months and 12 months after LSG. The patients flowchart of the present study is shown in Figure 2. Weight loss effects were measured by bodyweight, BMI, excess weight loss percentage (%EWL) and total weight loss percentage (%TWL). The neck circumference was routinely measured simultaneously. The following BCF parameters were measured: fasting blood glucose, immunoreactive insulin (IRI), hemoglobin A1c (HbA1c) and serum C-peptide. To evaluate insulin resistance and the capacity for insulin secretion, the homeostasis model for assessing insulin resistance (HOMA-IR) and the homeostasis model assessment of β -cell function (HOMA- β) were applied. These parameters were measured before the 75-g oral glucose tolerance test (75-g OGTT). Postoperative 75 g OGTT was carried out in the patients with type 2 diabetes, followed by calculations of the insulinogenic, Matsuda¹³ and disposition indexes^{14,15} from the 75-g OGTT results to evaluate the improvement in BCF after LSG. The disposition index is represented as the product between the insulinogenic and Matsuda indexes. The formula of the disposition index is as follows; disposition index = (fasting IRI-IRI at time 30 min)/(fasting glucose – glucose at time 30) \times 10,000/SQRT (fasting glucose \times fasting IRI \times [mean glucose at time 30, 60, 90 and 120 min] \times [mean IRI at time 30, 60, 90 and

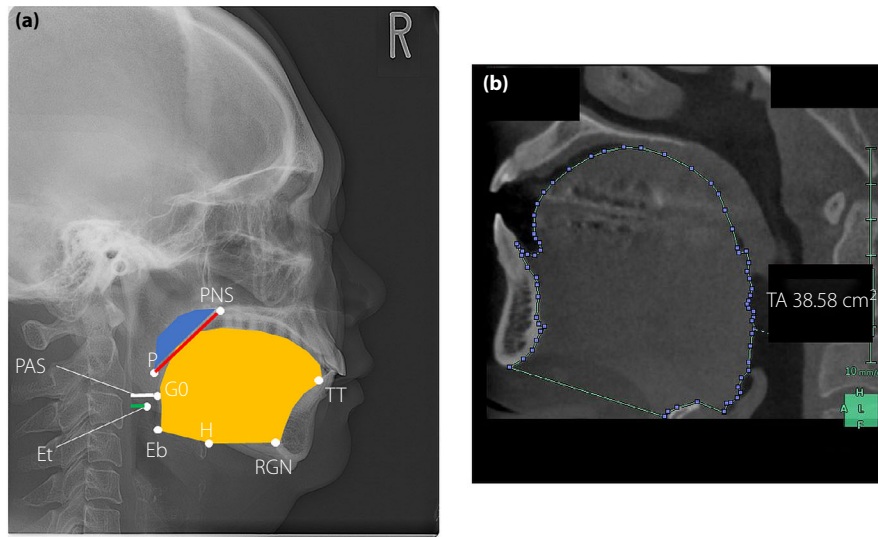


Figure 1 | Definitions and measurement of airway morphological parameters. (a) Tongue area (TA) was defined as the area surrounded by the tongue surface, tongue tip (TT), the most posterior and inferior point on the mandibular symphysis; retrognathion (RGN), the most anterior superior point on the body of the hyoid bone; hyoidale (H) and epiglottis base (Eb; orange area). Uvula area (UA) was also defined as the area surrounded by the most inferior point of the soft palate (P), tip of the posterior nasal spine (PNS) and the outline of the uvula (blue area). UL was the distance between P and PNS (red line). The midpoint of the contour connecting the ramus and body of the mandible was defined as G0, then PAS was also defined as the distance from G0 to the posterior pharyngeal wall (white line). Airway diameter at the tip of the epiglottis was defined as the distance from the tip of the epiglottis (Et) to posterior pharyngeal wall (green line). (b) Airway morphological parameters were measured by a computer work station.

120 min]). We used the individual metabolic surgery (IMS) score proposed by Aminiam *et al.*¹⁶ and the ABCD score proposed by Lee *et al.*¹⁷ to evaluate the preoperative remission of type 2 diabetes. The type 2 diabetes mellitus resolution was evaluated using patient data at 12 months after LSG, and type 2 diabetes remission was defined as no medication required and HbA1c <6.5%.

Additionally, the subcutaneous fat area and visceral fat area (VFA) were measured using a 64-row CT (Aquilion™; Toshiba Medical Systems Corporation, Tokyo, Japan) at the umbilicus-

level single slice. We expressed the subcutaneous fat area and VFA by cm², and these parameters were measured simultaneously.

Statistical analysis

Data are presented as numbers and percentages for categorical variables, and as means ± standard deviations for continuous variables. Statistical analysis was carried out using χ^2 -tests for categorical variables, and Student’s *t*-tests or Mann–Whitney *U*-tests for continuous variables. We used paired *t*-tests or

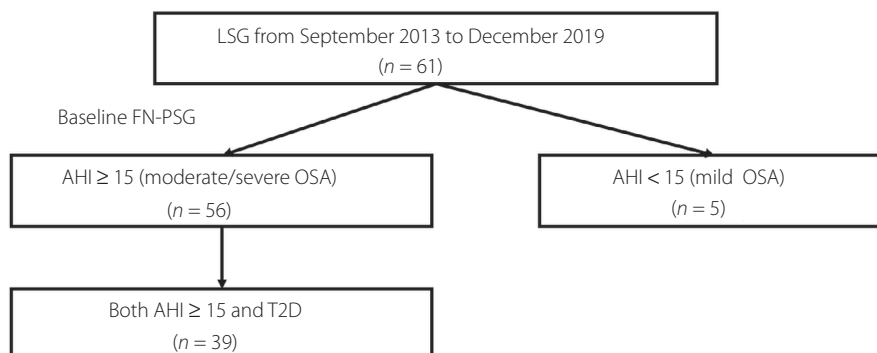


Figure 2 | Patient flowchart of the present study. AHI, apnea hypopnea index; FN-PSG, full-night polysomnography; LSG, laparoscopic sleeve gastrectomy; OSA, obstructive sleep apnea; T2D, type 2 diabetes.

Wilcoxon tests for continuous variables to enable the comparison of all parameters between pre- and postoperative measures. We used Spearman's rank correlation coefficient to investigate the relationships between the weight loss effects and changes in anatomical parameters. Potential factors for decreasing AHI were then analyzed using univariate and multivariate analyses, and a logistic regression model with a stepwise method (forward-backward method). Factors with a *P*-value <0.1 in univariate analysis were subsequently entered into the logistic regression analysis along with the Akaike information criterion. *P*-values <0.05 were considered statistically significant. All statistical analyses were carried out using JMP statistical software, version 15 (SAS Institute, Cary, NC, USA).

RESULTS

Patient characteristics

Of all enrolled patients, 56 had severe/moderate OSA in the present study population, and 41 patients had type 2 diabetes at baseline (Table 1). Patients in the AHI <15 group were significantly younger than those in the AHI ≥15 group (28.6 years vs 46.3 years, *P* = 0.001). In contrast, the VFA of the AHI <15 group was significantly smaller than that of the AHI ≥15 group (182.7 cm² vs 275.4 cm², *P* = 0.017). Factors of FN-PSG were also significantly worse in the AHI ≥15 group, except for sleep efficacy. Regarding the airway morphological parameters, the TA (39.6 cm² vs 29.8 cm², *P* = 0.002) and UA (3.8 cm² vs 2.6 cm², *P* = 0.017) were significantly larger, and the UL (4.4 cm vs 3.7 cm, *P* = 0.016) was significantly longer in the AHI ≥15 group.

Weight loss effects and changes in FN-PSG and airway morphological parameters before and after LSG

Table 2 shows the postoperative changes in all enrolled patients. Regarding the improvement in OSA, the preoperative numbers of moderate and severe OSA were nine and 47, respectively. In contrast, the postoperative numbers of moderate and severe OSA were 14 and 13, respectively. A total of 29 patients could achieve the withdrawal of CPAP, and the OSA improvement rate was 51.8% (29/56).

Correlation analysis between the therapeutic effects of OSA and weight loss or airway morphological parameters

The correlation analysis results are shown in Table 3. The change in AHI was significantly correlated with the %EWL (ρ = 0.501, *P* < 0.001), and changes in VFA (ρ = 0.392, *P* = 0.012), TA (ρ = 0.350, *P* = 0.020) and UA (ρ = 0.341, *P* = 0.037). The change in non-REM-AHI was also correlated with the %TWL (ρ = 0.317, *P* = 0.049), and changes in TA (ρ = 0.402, *P* = 0.013) and UA (ρ = 0.350, *P* = 0.029).

Univariate and multivariate analyses of prognostic factors for OSA improvement after LSG

To enter the stepwise methods, age (odds ratio 0.947, 95% confidence interval: 0.896–1.004; *P* = 0.072) and AHI (odds ratio

0.921, 95% confidence interval 0.880–0.964; *P* < 0.001) were extracted as preoperative parameters. HbA1c (odds ratio 0.385, 95% confidence interval 0.143–1.038; *P* = 0.059), TA (odds ratio 0.876, 95% confidence interval 0.792–0.969; *P* = 0.010), UA (odds ratio 0.218, 95% confidence interval 0.060–0.785; *P* = 0.020) and UL (odds ratio 0.059, 95% confidence interval 0.008–0.432; *P* = 0.005) were extracted as postoperative parameters. Multivariate analysis showed that AHI (odds ratio 0.908, 95% confidence interval 0.857–0.962; *P* = 0.001) and postoperative HbA1c (odds ratio 0.202, 95% confidence interval 0.044–0.934; *P* = 0.041) were independent prognostic factors (Table 4). Furthermore, postoperative HbA1c was higher in patients with non-improvement OSA.

Among the 56 patients with an AHI ≥15 at baseline, 39 had type 2 diabetes. To investigate the specific prognostic factors for OSA improvement in patients with type 2 diabetes, further univariate and multivariate analyses were carried out. To carry out the stepwise methods, male (odds ratio 0.269, 95% confidence interval 0.059–1.221; *P* = 0.089), age (odds ratio 0.932, 95% confidence interval 0.861–1.008; *P* = 0.081), TA (odds ratio 0.864, 95% confidence interval 0.748–0.999; *P* = 0.048), UL (odds ratio 0.883, 95% confidence interval 0.723–1.167; *P* = 0.077) and AHI (odds ratio 0.916, 95% confidence interval 0.864–0.971; *P* = 0.003) were extracted as preoperative parameters. HbA1c (odds ratio 0.360, 95% confidence interval 0.109–1.193; *P* = 0.094), TA (odds ratio 0.902, 95% confidence interval 0.808–1.006; *P* = 0.065), UA (odds ratio 0.207, 95% confidence interval 0.041–1.046; *P* = 0.057) and UL (odds ratio 0.003, 95% confidence interval <0.001–0.268; *P* = 0.010) were extracted as postoperative parameters. Multivariate analysis AHI (odds ratio 0.727, 95% confidence interval 0.534–0.991; *P* = 0.044) was an independent prognostic factor (Table 5). From these results, all populations in the present study showed the same dynamics after LSG.

Improvement in OSA and BCF in type 2 diabetes patients

The BCF parameters had significantly improved 1 year after LSG compared with the initial visit: fasting blood glucose (141.7 ± 55.2 mg/dL vs 99.9 ± 21.3 mg/dL, *P* < 0.001), IRI (18.2 ± 1.8 μU/mL vs 8.5 ± 6.8 μU/mL, *P* < 0.001), HbA1c (8.0 ± 1.8% vs 6.0 ± 0.8%, *P* < 0.001), C-peptide (2.7 ± 1.3 ng/mL vs 1.6 ± 0.8 ng/mL, *P* < 0.001), HOMA-IR (6.5 ± 5.7 vs 2.2 ± 2.0, *P* = 0.002) and HOMA-β (110.0 ± 92.2 vs 98.4 ± 74.8, *P* = 0.589). A total of 26 patients (26/39, 66.7%) could achieve type 2 diabetes remission. For the administration of antidiabetic agents and insulin use, just 13 patients were taking medical treatments 1 year after LSG. The total number of antidiabetic drugs substantially decreased from 92 to 18, with sulfonylurea, thiazolidinedione and α-glucosidase inhibitor completely discontinued (Figure 3). Furthermore, the number of patients using insulin decreased from 12 to four, and the amount of insulin being used also significantly decreased 1 year after LSG (baseline 28.0 ± 18.3 units vs 1 year after LSG 12.0 ± 10.5 units).

Table 1 | Baseline characteristics of enrolled patients

	All patients (n = 61)	AHI \geq 15 (n = 56)	AHI <15 (n = 5)	P-value
Age (years)	44.8 \pm 11.9	46.3 \pm 11.3	28.6 \pm 5.6	0.001*
Male, n (%)	33 (55%)	33 (59%)	0 (0%)	0.149
Bodyweight (kg)	117.3 \pm 21.0	118.3 \pm 21.2	101.8 \pm 13.3	0.086
BMI (kg/m ²)	42.6 \pm 6.4	42.9 \pm 6.6	39.2 \pm 3.3	0.33
Comorbidities (n)	6.7 \pm 1.2	6.7 \pm 1.2	6.2 \pm 1.3	0.343
OSA, n (%)	60 (98.4)	56 (100)	4 (80.0)	0.066
Type 2 diabetes, n (%)	41 (67.2)	39 (69.6)	2 (40.0)	0.32
Medications for type 2 diabetes (n)				0.864
Metformin	23	21	2	
DPP-4 inhibitor	21	19	2	
Sulfonylurea	15	14	1	
SGLT-2 inhibitor	11	10	1	
Thiazolidinedione	7	7	0	
α -Glucosidase inhibitor	7	7	0	
GLP-1 agonist	15	14	1	
Insulin	12	12	0	
FBG (mg/dL)	116.3 \pm 32.7	128.4 \pm 49.9	109.0 \pm 6.2	0.662
IRI (μ U/mL)	20.9 \pm 15.7	20.6 \pm 16.1	23.9 \pm 14.3	0.659
HbA1c (%)	7.2 \pm 1.8	7.2 \pm 1.8	6.9 \pm 1.9	0.646
HOMA-IR (no unit)	6.7 \pm 6.6	6.6 \pm 6.9	6.5 \pm 3.9	0.908
HOMA- β (no unit)	158.6 \pm 119.5	157.6 \pm 121.7	187.7 \pm 115.2	0.847
C-peptide (ng/mL)	2.9 \pm 1.2	2.9 \pm 1.2	2.8 \pm 1.3	0.866
SFA (cm ²)	529.5 \pm 132.2	525.9 \pm 134.2	567.9 \pm 112.6	0.51
VFA (cm ²)	267.4 \pm 86.5	275.4 \pm 84.7	182.7 \pm 60.2	0.017*
Waist (cm)	120.8 \pm 9.0	121.3 \pm 9.1	115.2 \pm 6.2	0.144
AHI (no unit)	51.1 \pm 25.7	55.0 \pm 23.1	7.8 \pm 2.0	<0.001*
ODI (no unit)	51.4 \pm 26.2	55.3 \pm 23.7	8.3 \pm 2.8	<0.001*
REM-AHI (no unit)	55.4 \pm 23.2	59.4 \pm 19.8	12.0 \pm 5.7	<0.001*
Non-REM-AHI (no unit)	49.0 \pm 27.6	52.9 \pm 25.4	6.4 \pm 2.5	<0.001*
Min-SpO ₂ (%)	72.6 \pm 11.7	71.3 \pm 11.4	86.0 \pm 2.6	0.006*
Sleep efficacy (%)	76.8 \pm 14.8	76.8 \pm 15.2	77.8 \pm 9.7	0.884
Neck circumference (cm)	43.3 \pm 3.7	43.6 \pm 3.9	41.3 \pm 0.8	0.346
TA (cm ²)	38.8 \pm 7.0	39.6 \pm 6.7	29.8 \pm 3.5	0.002*
UA (cm ²)	3.7 \pm 1.1	3.8 \pm 1.0	2.6 \pm 0.7	0.017*
UL (cm)	4.4 \pm 0.7	4.4 \pm 0.7	3.7 \pm 0.6	0.016*
PAS (mm)	13.1 \pm 4.0	13.2 \pm 4.0	12.0 \pm 4.3	0.564
AW-Et (mm)	11.4 \pm 4.6	11.5 \pm 4.7	10.9 \pm 4.6	0.805

Values are the mean \pm standard deviation. AHI, apnea hypopnea index; AW-Et, airway diameter at the tip of the epiglottis; BMI, body mass index; DPP-4, dipeptidyl peptidase-4; FBS, fasting blood glucose; GLP-1, glucagon-like peptide-1; HbA1c, hemoglobin A1c; HOMA- β , homeostasis model assessment beta cell function; HOMA-IR, homeostasis model for assessing insulin resistance; IRI, immunoreactive insulin; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; PAS, posterior airway space; REM-AHI, rapid eye movement AHI; Min-SpO₂, minimum arterial oxygen saturation of pulse oximetry; SFA, subcutaneous fat area; SGLT-2, sodium-glucose cotransporter 2; TA, tongue area; UL, uvula length; UV, uvula area; VFA, visceral fat area. *Parameters with $P < 0.05$.

Subsequently, we evaluated the relationships between the AHI and BCF parameters alongside the IMS score (Table 6). The IMS score stratifies type 2 diabetes remission into three criteria¹⁶. In the present study, the remission rate of mild, moderate and severe risks were 74%, 25% and 12%, respectively. If the BCF of the IMS score of the severe/moderate patients with OSA improvement is better than that of the patients without OSA improvement, OSA improvement has a positive effect to improve BCF. There were 32 patients at severe/moderate risk

and seven patients at mild risk, according to the IMS score. Patients with an AHI of <15 and an AHI of \geq 15 were 20 and 12 in IMS score severe/moderate groups, respectively. In this comparison, HOMA- β (119.6 \pm 77.7 vs 58.3 \pm 60.6, $P < 0.001$), the insulinogenic index (1.1 \pm 0.4 vs 0.4 \pm 0.3, $P < 0.001$) and the disposition index (3.4 \pm 2.8 vs 1.9 \pm 1.5, $P = 0.019$) of patients with AHI of <15 were significantly higher than in patients with AHI of \geq 15. Conversely, the Matsuda index was lower in the AHI <15 group (3.5 \pm 1.6 vs

Table 2 | Weight loss effects and changes of full-night polysomnography and airway morphological parameters before and after laparoscopic sleeve gastrectomy

	Initial	6 POM	12 POM	P-value Initial vs 6 POM	P-value Initial vs 12 POM
All patients (n = 61)					
Bodyweight (kg)	117.3 ± 21.0	88.0 ± 14.2	86.4 ± 16.9	<0.001*	<0.001*
BMI (kg/m ²)	42.6 ± 6.4	32.1 ± 4.2	31.4 ± 4.8	<0.001*	<0.001*
%EWL (%)	–	51.4 ± 13.0	55.8 ± 16.3	–	–
%TWL (%)	–	23.7 ± 7.2	26.0 ± 8.6	–	–
SFA (cm ²)	529.5 ± 132.2	344.2 ± 111.5	341.1 ± 137.8	<0.001*	<0.001*
VFA (cm ²)	267.4 ± 86.5	162.4 ± 73.8	141.3 ± 64.7	<0.001*	<0.001*
Waist (cm)	120.8 ± 9.0	103.5 ± 11.0	101.9 ± 12.5	<0.001*	<0.001*
AHI (no unit)	51.1 ± 25.6	25.4 ± 20.7	23.0 ± 20.0	<0.001*	<0.001*
ODI (no unit)	51.4 ± 26.2	23.3 ± 19.3	21.3 ± 18.8	<0.001*	<0.001*
REM-AHI (no unit)	55.4 ± 23.2	29.8 ± 20.6	27.7 ± 20.1	<0.001*	<0.001*
Non-REM-AHI (no unit)	49.0 ± 27.6	23.4 ± 22.5	19.9 ± 19.9	<0.001*	<0.001*
Sleep efficiency (%)	76.8 ± 14.8	79.7 ± 23.1	83.6 ± 10.1	0.482	<0.001*
Min-SpO ₂ (%)	72.6 ± 11.7	79.6 ± 8.5	80.5 ± 8.7	<0.001*	<0.001*
Neck circumference (cm)	43.3 ± 3.7	39.2 ± 3.7	38.6 ± 4.1	<0.001*	<0.001*
TA (cm ²)	38.8 ± 7.0	34.3 ± 6.8	33.3 ± 7.5	<0.001*	<0.001*
UA (cm ²)	3.7 ± 1.1	2.8 ± 0.6	2.7 ± 0.6	<0.001*	<0.001*
UL, cm	4.4 ± 0.7	4.1 ± 0.5	3.9 ± 0.4	<0.001*	<0.001*
PAS (mm)	13.1 ± 4.0	15.0 ± 4.7	14.3 ± 4.8	0.001*	0.027*
AW-Et (mm)	11.4 ± 4.6	12.7 ± 4.4	12.9 ± 4.3	0.155	0.141
AHI ≥15 (n = 56)					
Bodyweight (kg)	118.3 ± 21.2	88.7 ± 14.3	87.0 ± 17.4	<0.001*	<0.001*
BMI (kg/m ²)	42.9 ± 6.6	32.3 ± 4.3	31.6 ± 5.0	<0.001*	<0.001*
%EWL (%)	–	51.6 ± 13.0	56.3 ± 16.4	–	–
%TWL (%)	–	23.8 ± 7.4	26.2 ± 8.7	–	–
SFA (cm ²)	529.9 ± 134.2	344.0 ± 115.4	339.1 ± 142.7	<0.001*	<0.001*
VFA (cm ²)	275.4 ± 84.7	168.3 ± 72.8	144.6 ± 64.5	<0.001*	<0.001*
Waist (cm)	121.3 ± 9.1	104.3 ± 11.0	102.1 ± 12.8	<0.001*	<0.001*
AHI (no unit)	55.0 ± 23.1	27.0 ± 20.6	24.3 ± 19.9	<0.001*	<0.001*
ODI (no unit)	55.3 ± 23.7	24.9 ± 19.1	22.4 ± 18.8	<0.001*	<0.001*
REM-AHI (no unit)	59.4 ± 19.8	32.0 ± 19.8	29.2 ± 19.9	<0.001*	<0.001*
Non-REM-AHI (no unit)	52.9 ± 25.4	25.0 ± 22.6	21.1 ± 20.1	<0.001*	<0.001*
Min-SpO ₂ (%)	71.3 ± 11.4	78.7 ± 8.1	79.9 ± 8.6	<0.001*	<0.001*
Sleep efficiency	76.8 ± 15.2	80.2 ± 21.3	82.9 ± 10.0	0.413	0.003*
Neck circumference (cm)	43.6 ± 3.9	39.6 ± 3.7	38.9 ± 4.1	<0.001*	<0.001*
TA (cm ²)	39.6 ± 6.7	34.7 ± 6.8	33.8 ± 7.6	<0.001*	<0.001*
UA (cm ²)	3.8 ± 1.0	2.8 ± 0.6	2.7 ± 0.7	<0.001*	<0.001*
UL (cm)	4.4 ± 0.7	4.1 ± 0.5	3.9 ± 0.5	<0.001*	<0.001*
PAS (mm)	13.2 ± 4.0	14.9 ± 4.8	14.1 ± 4.8	0.004*	0.034*
AW-Et (mm)	11.5 ± 4.7	12.5 ± 4.5	12.8 ± 4.4	0.250	0.228
AHI <15 (n = 5)					
Bodyweight (kg)	101.8 ± 13.3	78.3 ± 12.2	77.3 ± 12.2	0.002*	0.003*
BMI (kg/m ²)	39.2 ± 3.3	30.1 ± 3.1	29.7 ± 3.0	0.004*	0.006*
%EWL (%)	–	53.3 ± 14.9	55.2 ± 17.0	–	–
%TWL (%)	–	23.1 ± 6.3	24.1 ± 7.7	–	–
SFA (cm ²)	567.9 ± 112.6	347.0 ± 63.1	362.9 ± 65.9	0.003*	0.007*
VFA (cm ²)	182.7 ± 60.2	100.3 ± 56.9	104.6 ± 64.2	<0.001*	0.006*
Waist (cm)	115.2 ± 6.2	95.5 ± 8.8	98.8 ± 8.9	0.007*	0.027*
AHI (no unit)	7.8 ± 2.0	3.7 ± 3.3	4.2 ± 5.3	0.044*	0.304
ODI (no unit)	8.3 ± 2.8	2.0 ± 0.9	4.4 ± 3.9	0.008*	0.106
REM-AHI (no unit)	12.0 ± 5.7	2.7 ± 0.8	5.8 ± 7.2	0.016*	0.258
Non-REM-AHI (no unit)	6.4 ± 2.5	3.8 ± 4.1	3.4 ± 4.2	0.087	0.204

Table 2. (Continued)

	Initial	6 POM	12 POM	P-value Initial vs 6 POM	P-value Initial vs 12 POM
Min-SpO ₂ (%)	86.0 ± 2.6	91.0 ± 13.3	89.7 ± 2.3	0.059	0.163
Sleep efficiency	77.8 ± 9.7	72.6 ± 44.2	93.8 ± 3.9	0.820	0.061
Neck circumference (cm)	41.3 ± 0.8	35.5 ± 0.7	34.5 ± 1.1	0.059	0.069
TA (cm ²)	29.8 ± 3.5	27.8 ± 2.2	26.8 ± 1.5	0.089	0.225
UA (cm ²)	2.6 ± 0.7	2.3 ± 0.3	2.5 ± 0.4	0.154	0.306
UL (cm)	3.7 ± 0.6	4.5 ± 0.7	3.8 ± 0.3	0.068	0.601
PAS (mm)	12.0 ± 4.3	15.9 ± 3.6	15.9 ± 4.0	0.103	0.085
AW-Et (mm)	10.9 ± 4.6	15.2 ± 2.2	15.2 ± 1.0	0.292	0.356

Values are the mean ± standard deviation. 12 POM, 12 postoperative months; 6 POM, 6 postoperative months; AHI, apnea hypopnea index; AW-Et, airway diameter at the tip of the epiglottis; BMI, body mass index; %EWL, percentage excess weight loss; FN-PSG, full-night polysomnography; LSG, laparoscopic sleeve gastrectomy; Min-SpO₂, minimum arterial oxygen saturation of pulse oximetry; ODI, oxygen desaturation index; PAS, posterior airway space; REM-AHI, rapid eye movement AHI; SFA, subcutaneous fat area; TA, tongue area; %TWL, percentage total weight loss; UL, uvula length; UV, uvula area; VFA, visceral fat area. *Parameters with $P < 0.05$.

Table 3 | Correlation analyses between the therapeutic effects of obstructive sleep apnea and weight loss or airway morphological parameters

Variables	Δ AHI		Δ ODI		Δ Non-REM-AHI	
	ρ	P-value	ρ	P-value	ρ	P-value
%EWL	0.501	<0.001*	0.388	0.015*	0.212	0.195
%TWL	0.254	0.119	0.401	0.011*	0.317	0.049*
Δ VFA	0.392	0.012*	0.289	0.074	0.249	0.126
Δ SFA	0.315	0.051	0.403	0.011*	0.158	0.335
Δ TA	0.350	0.020*	0.300	0.063	0.402	0.013*
Δ UA	0.341	0.037*	0.267	0.100	0.350	0.029*
Δ UL	0.280	0.084	0.220	0.179	0.243	0.137
Δ PAS	0.074	0.653	-0.007	0.965	0.107	0.516
Δ AW-Et	0.011	0.946	0.007	0.968	0.082	0.620

AHI, apnea hypopnea index; AW-Et, airway diameter at the tip of the epiglottis; %EWL, percentage excess weight loss; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; PAS, posterior airway space; REM-AHI, rapid eye movement AHI; SFA, subcutaneous fat area; TA, tongue area; %TWL, percentage total weight loss; UL, uvula length; UV, uvula area; VFA, visceral fat area. *Parameters with $P < 0.05$.

5.5 ± 3.4, $P = 0.058$). Figures 4 and 5 show the 75-g OGTT results at baseline and 12 months after LSG of these two groups. Regarding glucose levels, the curves of both groups were similar at baseline. A total of 12 months after LSG, there were significant decreases in every glucose measuring point in IMS moderate/severe patients in the AHI <15 group: at 0 min (94.0 ± 16.1 mg/dL vs 110.5 ± 23.5 mg/dL, $P = 0.039$), 30 min (196.1 ± 36.5 mg/dL vs 231.6 ± 34.7 mg/dL, $P = 0.011$), 60 min (206.6 ± 43.6 mg/dL vs 267.3 ± 52.4 mg/dL, $P = 0.002$), 90 min (183.2 ± 59.6 mg/dL vs 238.1 ± 66.1 mg/dL, $P = 0.026$) and 120 min (125.8 ± 57.4 mg/dL vs 190.8 ± 71.6 mg/dL, $P = 0.012$) (Figure 4). Peak glucose levels moved from 90 to 60 min before and after LSG. In contrast,

IRI levels at 0 min (20.9 ± 11.8 μU/mL vs 12.1 ± 7.1 μU/mL, $P = 0.025$) and 90 min (114.9 ± 68.6 μU/mL vs 76.3 ± 51.0 μU/mL, $P = 0.014$) were significantly higher in IMS moderate/severe patients in the AHI <15 group at baseline (Figure 5). A total of 12 months after LSG, IRI levels at 30 min (120.4 ± 69.5 μU/mL vs 58.3 ± 43.7 μU/mL, $P = 0.006$) were also significantly higher in IMS moderate/severe patients in the AHI <15 group, and peak IRI levels also moved from 120 to 30 min before and after LSG (Figure 5).

The relationships between the AHI and BCF parameters alongside the ABCD score are shown in Table 7. According to the original report by Lee *et al.*¹⁷, the type 2 diabetes remission rate decreases to <50% in patients with ABCD scores <5 points. Our previous study also showed that the type 2 diabetes remission rate clearly decreased <50% in patients with ABCD score <5 points.⁷ Therefore, the cut-off was set at 5 points. If the BCF of the ABCD score was <5 points, the condition of patients with OSA improvement is better than that of patients without OSA improvement. Therefore, OSA improvement has a positive effect on BCF improvement. There were 15 patients with <5 points and 24 patients with ≥5 points according to the ABCD score. The numbers of patients with AHI of ≥15 and AHI of <15 were nine and six in the ABCD score <5 points groups, respectively. There were 15 patients with <5 points and 24 patients with ≥5 points according to the ABCD score. The numbers of patients with AHI of ≥15 and AHI of <15 were nine and six in the ABCD score <5 points groups, respectively. In this comparison, HbA1c was higher in the AHI ≥15 group (6.5 ± 0.8% vs 5.8 ± 0.6%, $P = 0.141$). However, there were no significant differences in BCF and insulin resistance.

DISCUSSION

To the best of our knowledge, this is the first study to clarify the improvement of OSA after LSG by evaluating the various

Table 4 | Univariate and multivariate analyses of prognostic factors for obstructive sleep apnea after laparoscopic sleeve gastrectomy

Univariate analysis				
Parameters	Improvement AHI <15 (<i>n</i> = 23)	Non-improvement AHI ≥15 (<i>n</i> = 33)	Odds ratio (95% confidence interval)	<i>P</i> -value
Preoperative parameters				
Male, <i>n</i> (%)	11 (48%)	22 (67%)	0.500 (0.148–1.693)	0.265
Age (years)	43.2 ± 11.7	49.5 ± 10.4	0.947 (0.896–1.004)	0.072*
Bodyweight (kg)	115.8 ± 22.6	120.3 ± 22.2	0.990 (0.963–1.019)	0.506
BMI (kg/m ²)	41.9 ± 5.9	44.0 ± 7.8	0.975 (0.891–1.067)	0.591
HbA1c (%)	6.9 ± 1.8	7.4 ± 1.6	0.850 (0.580–1.245)	0.404
VFA (cm ²)	270.3 ± 93.8	280.8 ± 81.5	0.998 (0.991–1.006)	0.659
Neck circumference (cm)	43.1 ± 4.1	44.2 ± 5.2	0.937 (0.734–1.196)	0.602
TA (cm ²)	38.5 ± 4.7	40.6 ± 7.7	0.946 (0.859–1.042)	0.266
UA (cm ²)	3.6 ± 0.9	3.9 ± 1.0	0.747 (0.401–1.394)	0.360
UL (cm)	4.3 ± 0.6	4.5 ± 0.6	0.541 (0.194–1.511)	0.241
PAS (mm)	13.2 ± 3.5	13.3 ± 4.5	0.990 (0.851–1.154)	0.904
AW-Et (mm)	11.4 ± 3.8	11.8 ± 4.9	1.015 (0.882–1.167)	0.837
AHI (no unit)	39.9 ± 15.1	69.9 ± 19.7	0.921 (0.880–0.964)	<0.001
Postoperative parameters (1 year after LSG)				
Bodyweight (kg)	84.8 ± 17.3	88.8 ± 15.2	0.975 (0.936–1.014)	0.211
BMI (kg/m ²)	30.5 ± 4.7	32.4 ± 5.1	0.922 (0.809–1.051)	0.224
%TWL (%)	27.6 ± 7.5	24.6 ± 8.5	1.046 (0.969–1.129)	0.247
%EWL (%)	58.6 ± 16.5	53.1 ± 15.4	1.030 (0.991–1.073)	0.133
HbA1c (%)	5.4 ± 0.5	5.9 ± 0.8	0.385 (0.143–1.038)	0.059*
VFA (cm ²)	138.1 ± 64.8	151.0 ± 59.4	0.996 (0.986–1.006)	0.432
Neck circumference (cm)	38.3 ± 3.3	39.7 ± 4.6	0.908 (0.733–1.124)	0.375
TA (cm ²)	30.0 ± 5.5	36.4 ± 7.9	0.876 (0.792–0.969)	0.010**
UA (cm ²)	2.4 ± 0.4	2.9 ± 0.7	0.2176 (0.060–0.785)	0.020**
UL (cm)	3.7 ± 0.3	4.1 ± 0.5	0.059 (0.008–0.432)	0.005**
PAS (mm)	14.0 ± 3.5	14.2 ± 5.7	0.984 (0.866–1.118)	0.808
AW-Et (mm)	12.9 ± 3.5	12.8 ± 5.1	1.003 (0.873–1.153)	0.962
Multivariate analysis				
Parameters	Odds ratio	95% Confidence interval	<i>P</i> -value	
AHI	0.908	0.857–0.962	0.001***	
HbA1c (postoperative)	0.202	0.044–0.934	0.041***	

AHI, apnea hypopnea index; AW-Et, airway diameter at the tip of the epiglottis; BMI, body mass index; HbA1c, hemoglobin A1c; LSG, laparoscopic sleeve gastrectomy; OSA, obstructive sleep apnea; PAS, posterior airway space; TA, tongue area; UL, uvula length; UV, uvula area; VFA, visceral fat area. *Parameters with *P* < 0.1 in univariate analysis. **Parameters with *P* < 0.05 in univariate analysis. ***Parameters with *P* < 0.05 in multivariate analysis.

airway morphological parameters. We also clarified the relationships between the FN-PSG parameters and weight loss and airway morphological parameters. In addition, we showed that BCF significantly improved depending on the degree of OSA in type 2 diabetes patients with moderate/severe IMS.

There are some influencing factors of inducing and progressing OSA, such as micrognathia, nasal septum deviation, tonsil swelling, adenoid hypertrophy and severe obesity^{18–21}. Among them, severe obesity is known to be the most influential factor of OSA, because respiratory mechanical impairment leads to upper airway collapse during sleep²². In the present study, the remission rate of OSA was 51.8%.

However, previous studies have reported that improvement of moderate/severe OSA was observed in 72.2–88.5% of patients undergoing LSG^{3,5,23}. The reason for this discrepancy is that the prevalence of micrognathia is higher among Japanese people than among other ethnic groups, and the skeletal component of the oral cavity is also smaller²⁴. Therefore, tongue volume can be relatively larger²⁴. Wang *et al.*²⁵ showed that weight loss was significantly associated with reductions in tongue fat (*P* < 0.0001), and pterygoid and total lateral wall volumes (*P* < 0.002)²⁵. Additionally, reductions in tongue fat were strongly correlated with reductions in the AHI ($\rho = 0.62$, *P* < 0.0001).

Table 5 | Univariate and multivariate analyses of prognostic factors for obstructive sleep apnea in patients with type 2 diabetes

Univariate analysis				
Parameters	Improvement AHI <15 (n = 16)	Non-improvement AHI ≥15 (n = 23)	Odds ratio (95% confidence interval)	P-value
Preoperative parameters				
Male, n (%)	4 (33%)	13 (65%)	0.269 (0.059–1.221)	0.089*
Age (years)	45.6 ± 12.2	52.5 ± 8.7	0.932 (0.861–1.008)	0.081*
Bodyweight (kg)	110.1 ± 23.0	116.9 ± 18.4	0.984 (0.948–1.022)	0.417
HbA1c (%)	7.6 ± 1.9	6.1 ± 0.8	0.930 (0.598–1.447)	0.749
Neck circumference (cm)	41.5 ± 3.6	42.4 ± 7.3	0.609 (0.326–1.140)	0.122
TA (cm ²)	31.0 ± 5.3	42.4 ± 7.3	0.864 (0.748–0.999)	0.048**
UA (cm ²)	3.5 ± 1.0	4.0 ± 0.9	0.554 (0.239–1.286)	0.169
UL (cm)	4.3 ± 0.6	4.6 ± 0.5	0.242 (0.050–1.167)	0.077*
PAS (mm)	12.6 ± 3.6	15.1 ± 5.4	0.883 (0.723–1.079)	0.225
AW-Et (mm)	11.7 ± 2.7	13.6 ± 4.5	0.927 (0.769–1.117)	0.428
AHI (no unit)	34.7 ± 11.9	66.4 ± 21.4	0.916 (0.864–0.971)	0.003**
Postoperative parameters (1 year after LSG)				
Bodyweight (kg)	80.8 ± 16.8	88.5 ± 15.0	0.966 (0.918–1.017)	0.189
%TWL (%)	26.9 ± 5.7	24.0 ± 7.4	1.064 (0.957–1.184)	0.249
HbA1c (%)	5.6 ± 0.5	6.1 ± 0.8	0.360 (0.109–1.193)	0.094*
Neck circumference (cm)	37.5 ± 3.6	39.8 ± 4.4	0.853 (0.650–1.119)	0.251
TA (cm ²)	30.9 ± 5.3	36.2 ± 8.3	0.902 (0.808–1.006)	0.065*
UA (cm ²)	2.4 ± 0.5	2.9 ± 0.7	0.207 (0.041–1.046)	0.057*
UL (cm)	3.7 ± 0.3	4.1 ± 0.4	0.003 (0.0005–0.268)	0.010**
PAS (mm)	14.1 ± 4.1	15.1 ± 5.5	0.956 (0.819–1.115)	0.569
AW-Et (mm)	13.3 ± 3.8	13.6 ± 4.5	0.983 (0.824–1.173)	0.854
Multivariate analysis				
Parameters	Odds ratio	95% Confidence interval	P-value	
AHI	0.727	0.534–0.991	0.044***	

AHI, apnea hypopnea index; AW-Et, airway diameter at the tip of the epiglottis; BMI, body mass index; HbA1c, hemoglobin A1c; LSG, laparoscopic sleeve gastrectomy; OSA, obstructive sleep apnea; PAS, posterior airway space; TA, tongue area; UL, uvula length; UA, uvula area; VFA, visceral fat area. *Parameters with $P < 0.1$ in univariate analysis. **Parameters with $P < 0.05$ in univariate analysis. ***Parameters with $P < 0.05$ in multivariate analysis.

In the present study, the airway morphological parameters significantly improved with the weight loss effect. As a result, changes in TA and UA were correlated with AHI improvement. We showed that changes in AHI and non-REM-AHI were correlated with both weight loss effects (%EWL or %TWL) and changes in airway morphological parameters, such as TA and UA. Based on these results, the tongue and the uvula are estimated as fat storing organs, such as visceral fat; therefore, the tongue and the uvula can benefit from LSG. Furthermore, some studies have also shown that neck circumference is associated with OSA remission after a bariatric procedure. The present study also showed that neck circumference significantly decreased after LSG^{3,26}; however, it was not correlated with the improvement in the FN-PSG parameters²⁷. Contrary to our expectations, posterior airway space and airway diameter at the tip of the epiglottis did not significantly improve after LSG, despite a sufficient weight loss effect,

because the oropharyngeal airway and hyoid positions might vary according to the mandible position²⁸, and the anterior–posterior space of these parameters was dependent on the location of the posterior tongue and epiglottis^{3,29}.

We first found that a decrease in AHI 1 year after LSG had a significant metabolic effect on BCF. Multivariate analyses showed that HbA1c at 1 year after LSG was the correlated factor of OSA improvement. Some studies clarified that diabetic retinopathy (odds ratio 2.875, 95% confident interval 1.224–6.752; $P = 0.0015$) and glycemic control impairment (β 0.063, 95% confident interval 0.025–0.101; $P = 0.001$) are strongly correlated with REM-AHI^{30,31}. Therefore, chronic intermittent hypoxia as a result of OSA causes altered ventilatory control and oxidative stress in developing type 2 diabetes, and chronic hyperglycemia also contributes to an accelerated increase in oxidative stress^{32,33}. These phenomena show that the changes in HbA1c levels are brought about by OSA improvement.

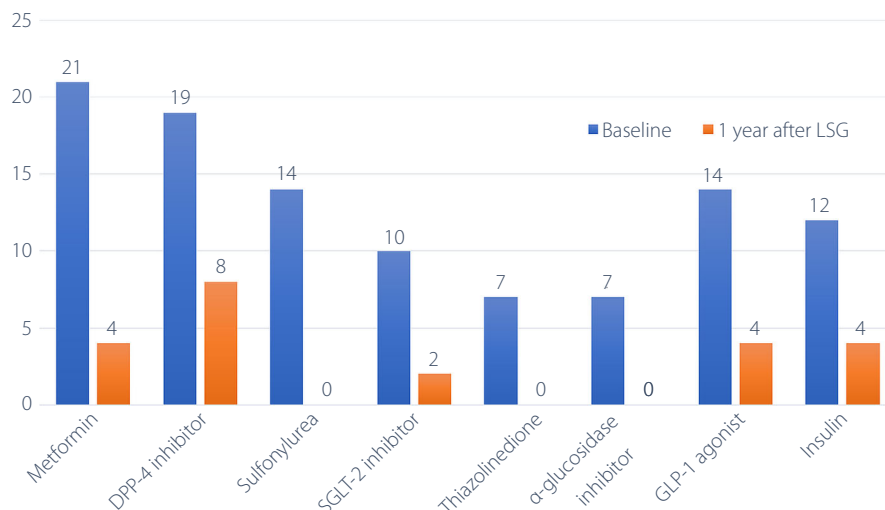


Figure 3 | Changes of medical treatment for type 2 diabetes in patients with moderate/severe obstructive sleep apnea. DPP-4 inhibitor, dipeptidyl peptidase-4 inhibitor; GLP-1 agonist, glucagon-like peptide-1 receptor agonist; LSG, laparoscopic sleeve gastrectomy; SGLT-2 inhibitor, sodium–glucose cotransporter 2 inhibitor.

Table 6 | Relationships between apnea hypopnea index and β -cell function parameters along with the individual metabolic surgery score

	AHI ≥ 15 IMS score	AHI < 15	P-value
IMS score severe/moderate, <i>n</i> (type 2 diabetes remission)	20 (11)	12 (8)	0.71
HbA1c (%)	6.2 \pm 0.8	6.0 \pm 0.7	0.652
IRI (μ U/mL)	7.7 \pm 7.0	10.3 \pm 7.9	0.343
HOMA-IR (no unit)	2.1 \pm 1.9	2.4 \pm 2.8	0.616
HOMA- β (no unit)	58.3 \pm 60.6	119.6 \pm 77.7	<0.001*
Insulinogenic index (no unit)	0.4 \pm 0.3	1.1 \pm 0.4	<0.001*
Matsuda index (no unit)	5.5 \pm 3.4	3.5 \pm 1.6	0.058
Disposition index (no unit)	1.9 \pm 1.5	3.4 \pm 2.8	0.019*
IMS score mild, <i>n</i> (type 2 diabetes remission)	3 (3)	4 (4)	1

AHI, apnea hypopnea index; BCF, β -cell function; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model for assessing insulin resistance; HOMA- β , homeostasis model assessment beta cell function; IMS, individual metabolic surgery; IRI, immunoreactive insulin. *Parameters with $P < 0.05$.

However, when contemplating the prediction of OSA improvement without FN-PSG data, we can presume that patients with high levels of HbA1c after LSG might not achieve OSA improvement regardless of weight loss effects.

Subsequently, the hypoxia-inducible factor-1 α and nuclear factor- κ B pathway are stimulated and cause type 2 diabetes, along with the activation of I κ B kinase β as a result of overnutrition^{34–36}. In contrast, hypoxia might cause a stress-related increase in hypothalamic–pituitary–adrenal axis activity and secretion of higher circulating cortisol concentration³⁷. Cortisol interferes with glucose metabolism, increases insulin

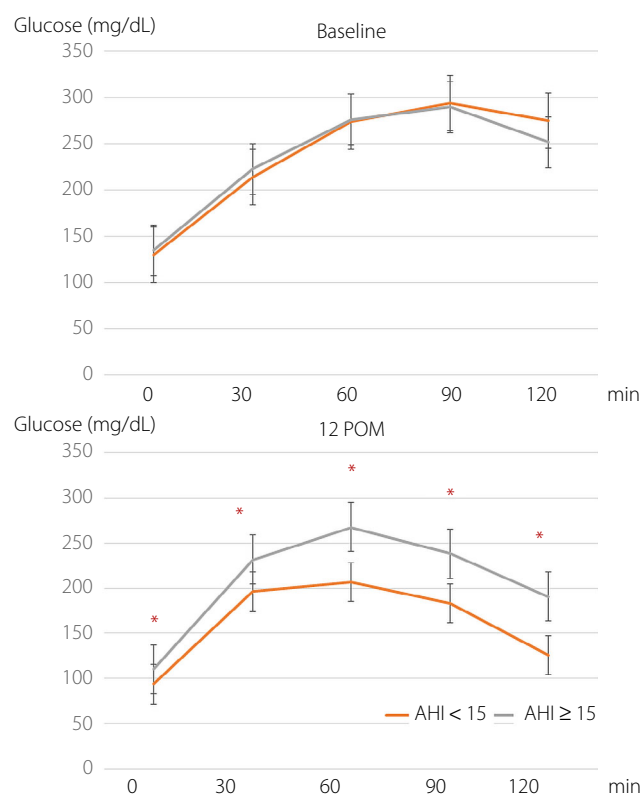


Figure 4 | Changes of glucose levels during the 75-g oral glucose tolerance test (75-g OGTT). *Parameters with $P < 0.05$. AHI, apnea hypopnea index; POM, postoperative months.

resistance and increases lipotoxicity³⁸. In addition, intermittent hypopnea can also increase sympathetic activity, and cause nocturnal endothelin release and vascular cell dysfunction³⁹. From

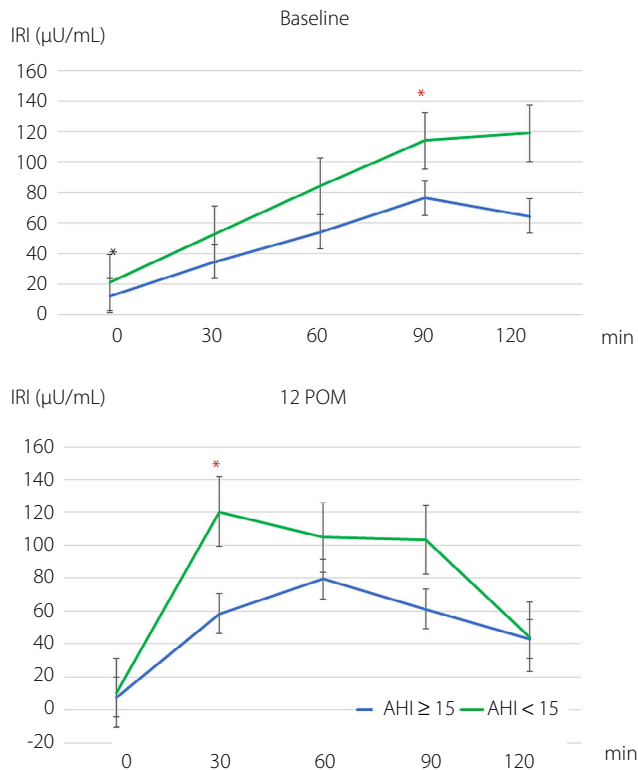


Figure 5 | Changes of immunoreactive insulin (IRI) levels during 75-g oral glucose tolerance test (75-g OGTT). *Parameters with $P < 0.05$. AHI, apnea hypopnea index; POM, postoperative months.

these results, hypertension and arterial sclerosis are accelerated, causing ischemic heart disease, cerebrovascular disorders and chronic kidney disease⁴⁰. Although this vicious cycle might progress the “metabolic domino” in severely obese patients, the present study clarified that this domino can be stopped by bariatric procedures, including LSG.

Metabolic surgeries undoubtedly have both weight loss and metabolic effects on severely obese patients with metabolic

syndrome and OSA. In other words, metabolic surgeries unitarily improve obesity and metabolic syndrome by weight loss and secondary metabolic effects. However, there was no clear correlation between initial BMI and OSA severity in severely obese Japanese patients who underwent LSG according to previous Japanese nationwide retrospective analyses⁴¹. The present study has also clarified that improvements in BCF and OSA could not be stratified along with the ABCD score, which could mean that initial BMI does not affect the relationships of those, such as multivariate analyses. Furthermore, the IMS score, which does not include the bodyweight factor, stratified the degree of BCF improvement as higher in the AHI <15 groups, even if among severe/moderate-risk patients. Therefore, improvement of intermittent hypoxia contributes to the BCF function recovery over and above the usual weight loss and metabolic effects after LSG.

Metabolic dominos are usually described as four rows of dominos, with the first row constituting obesity; the second row constituting metabolic syndromes, such as type 2 diabetes, hypertension and dyslipidemia; the third row constituting important organ diseases, such as myocardial infarction, brain stroke, peripheral arterial disease and chronic kidney disease; and finally, the fourth row constituting the critical complications⁶. We postulate that OSA is situated between the first and second rows of the metabolic domino, because LSG does not only bring about strong weight loss effects, but also BCF recovery. The relationships between hypertension or/and dyslipidemia and OSA in severely obese patients should be elucidated to clarify this hypothesis.

In interpreting the results of the present study, some limitations must be considered. First, the number of participants was relatively small, and the study was single-institution and retrospective in nature. Second, the follow-up period was short. Long-term studies that include many patients are required to make a definite conclusion on this issue. Third, we did not carry out postoperative 75-g OGTT in patients without type 2 diabetes due to medical care costs. Therefore, we were unable

Table 7 | Relationships between apnea hypopnea index and β -cell function parameters along with the ABCD score

	AHI ≥ 15	AHI <15	P-value
ABCD score	≥ 15	<15	
ABCD score 0–4 points, <i>n</i> (type 2 diabetes remission)	9 (4)	6 (3)	0.597
HbA1c (%)	6.5 \pm 0.8	5.8 \pm 0.6	0.141
IRI (μ U/mL)	7.2 \pm 5.4	4.7 \pm 2.0	0.35
HOMA-IR (no unit)	2.1 \pm 1.6	1.1 \pm 0.5	0.229
HOMA- β (no unit)	65.4 \pm 48.1	57.0 \pm 30.4	0.842
Insulinogenic index (no unit)	0.5 \pm 0.4	0.7 \pm 0.7	0.44
Matsuda index (no unit)	5.7 \pm 4.0	4.9 \pm 1.9	0.651
Disposition index (no unit)	2.4 \pm 2.2	4.4 \pm 5.9	0.364
ABCD score 5–10 points, <i>n</i> (type 2 diabetes remission)	14 (10)	10 (9)	0.308

AHI, apnea hypopnea index; BCF, β -cell function; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model for assessing insulin resistance; HOMA- β , homeostasis model assessment beta cell function; IRI, immunoreactive insulin.

to analyze the postoperative insulinogenic, Matsuda and disposition indexes of all patients. Further studies are warranted to investigate the role of these parameters brought about by 75-g OGTT.

Overall, LSG was a promising procedure for severely obese patients with OSA, and the decrease in AHI was closely correlated with the %EWL and changes in TA and UA. Additionally, the upper airway was dilated owing to the weight loss effect by evaluating the airway morphological parameters. Furthermore, BCF recovery was significantly higher in patients with OSA improvement at 1 year after LSG.

DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: The research protocol was approved by the institutional ethics committee (approval number: H27-47).

Informed consent: We obtained informed consent from each patient before enrollment.

Registry and the registration no. of the study/trial: This study was a retrospective data-collection study; therefore, this study was not registered with any national registry.

Animal studies: N/A.

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