Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.4153-19
Intern Med 59: 1133-1139, 2020
http://internmed.jp

【 ORIGINAL ARTICLE 】

A Comparison of the Weight Loss Effect between a Low-carbohydrate Diet and a Calorie-restricted Diet in Combination with Intragastric Balloon Therapy

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Abstract:
Objective Intragastric balloon (IGB) therapy is a low-invasion treatment for obesity. Recently, a low-carbohydrate diet has shown effectiveness for encouraging weight loss, but whether or not a low-carbohydrate diet improves the efficacy of IGB therapy remains unclear. Therefore, we examined the effectiveness of a low-carbohydrate diet compared with a calorie-restricted diet in combination with IGB therapy.
Methods A prospective study was conducted on 51 patients who had undergone IGB therapy from October 2012 to December 2017. Overall, 31 of the 51 patients were included in this study (12-month assessment after IGB placement). These 31 cases consisted of 18 IGB plus low-carbohydrate diet and 13 IGB plus calorie-restricted diet. We compared the two groups with respect to body weight loss as outcomes.
Results At 12 months after IGB placement, the body weight was significantly lower than that observed at baseline in both the IGB plus low-carbohydrate diet group (baseline 101.9±25.8 kg, 12 months 88.2±21.9 kg) ($p<0.0001$) and the IGB plus calorie-restricted diet group (baseline 103.5±17.0 kg, 12 months 89.1±6.2 kg) ($p<0.005$). The percentage of excess weight loss in the IGB plus low-carbohydrate diet group was slightly higher than that in the IGB plus calorie-restricted diet group, but there was no significant difference between the 2 groups at 12 months after IGB placement (IGB plus low-carbohydrate 49.9±60.0%, IGB plus calorie-restricted diet 33.1±27.0%).
Conclusion Our study demonstrated that both a low-carbohydrate diet and a calorie-restricted diet were effective interventions for weight reduction in combination with IGB therapy.

Key words: obesity, intragastric balloon, low-carbohydrate diet, calorie-restricted diet, body weight rebound

(Intern Med 59: 1133-1139, 2020)
(DOI: 10.2169/internalmedicine.4153-19)

Introduction

Obesity is one of the most important public health issues, and its incidence is increasing worldwide (1). There is a clear association between obesity and several chronic diseases, such as type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, cerebrovascular diseases, sleep apnea, osteoarthropathy and some cancers (2, 3). Overweight and obesity are also related to increased mortality rates (4). Evidence suggests that weight loss in obese adults reduces morbidity and mortality (5).

Conventional treatments, such as diet therapy, regular physical activity and behavioral modification, are important and essential for managing obesity. However, those treatments alone are often ineffective (6). Bariatric surgery is the most effective weight loss intervention, resulting in long-term sustained weight loss (7) and long-term resolution of comorbidities (8). Despite these advantages, bariatric surgery is still extremely invasive and costly and is likely to cause a vast number of complications that can be fatal (9).

Intragastric balloon (IGB) therapy is a less invasive and more cost-effective option for the treatment of obesity than surgery (10-16). The presence of an IGB delays gastric

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Received for publication November 10, 2019; Accepted for publication December 9, 2019
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emptying, causing a premature sensation of satiety and resulting in decreased food consumption (10). IGB therapy becomes even more effective in combination with strict diet therapy (11).

In recent years, low-carbohydrate diets have been shown to be effective for weight reduction and have become increasingly popular all over the world (17-22). Since 2008, the American Diabetes Association (ADA) has recognized that a low-carbohydrate diet as well as a calorie-restricted diet are effective interventions for body weight reduction (23). Although a very-low-calorie ketogenic diet was reported to be useful for increasing the efficacy of IGB therapy (11), whether or not a low-carbohydrate diet improves the efficacy of IGB therapy for body weight management remains unclear.

Therefore, we compared the effectiveness of a low-carbohydrate diet with that of a calorie-restricted diet when used in combination with IGB therapy.

Materials and Methods

Study design and subjects

A prospective single-center study was conducted on 51 patients who had undergone IGB therapy between October 2012 and December 2017. We used computer-generated, blocked randomization to allocate participants to either a low-carbohydrate diet or a conventional calorie-restricted diet in combination with IGB therapy. After randomization, 26 participants were assigned to the low-carbohydrate diet group (IGB plus low-carbohydrate diet), and 25 were assigned to the calorie-restricted diet group (IGB plus calorie-restricted diet). The aim of this study was to compare IGB plus a low-carbohydrate diet with IGB plus a calorie-restricted diet with regard to the kinetics of weight loss and metabolic parameters during 12 months of follow-up after IGB placement.

This study was performed in conformity with the Declaration of Helsinki. Written informed consent was obtained from all patients, and the ethics committee of our hospital approved this study.

IGB procedures

The most commonly used IGB worldwide is the Orbera® IGB [Apollo Endosurgery, Austin, USA; formerly Bioenterics® Intragastric Balloon (BIB®)]. The Orbera® IGB was used in all 51 patients of this study. The inclusion criteria were an 1) age between 20 and 75 years old; 2) a body mass index (BMI) ≥27 kg/m^2; 3) the presence of one or more obesity-related diseases [ORDs; impaired glucose tolerance (type 2 diabetes etc.), dyslipidemia, hypertension, hyperuricemia/gout, coronary artery disease, cerebral infarction, nonalcoholic fatty liver disease, menstrual abnormalities/sterility, respiratory disorders, osteoarthropathy and renal disease]; and 3) failure of previous therapeutic lifestyle modification for at least six months. The exclusion criteria were 1) active peptic ulcer; 2) inflammatory bowel disease; 3) cancer; 4) history of gastrectomy; 5) hiatal hernia (>5 cm in diameter); 6) pregnancy; 7) psychological disorders inadequately controlled by drug treatment; 8) chronic therapy with aspirin, anti-inflammatory agents, anticoagulants or steroids.

The IGB placement was performed under intravenous sedation (midazolam) and was placed through the mouth while observing with nasal endoscopy. The balloon was positioned in the gastric fundus under endoscopic guidance, inflated with saline (400-700 mL of 1,000 mL saline mixed with 10 mL of 1% methylene blue) until the balloon distended to fill the gastric fundus. The filling catheter was then removed, and the procedure was completed. All patients remained in the hospital for at least three days to observe them for complications, such as abdominal pain and vomiting. At six months after the IGB placement, the balloon was removed under endoscopic guidance.

Diet interventions

For the low-carbohydrate diet group (IGB plus low-carbohydrate diet), we set the total carbohydrate intake to be <120 g/day, as proposed by Shai et al. (18). The intakes of total calories, protein and fat were not limited. For the calorie-restricted diet group (IGB plus calorie-restricted diet), the target calorie intake was defined based on the Japan Society for the Study of Obesity recommendations as follows: total calorie intake (kcal) ≤ideal body weight [kg; = height(m)×height(m)×22]×2. The target intake of specific macronutrients was as follows: carbohydrate, 50-60%; protein, 15-20%; fat, 20-25% (24). Nutrition education in each group was started at the IGB placement and performed on a one-on-one basis every month after IGB placement by physicians and nutritionists.

Follow-up

Subjects in both groups were asked to attend outpatient guidance sessions and were also reviewed by their physicians every month. The body weight, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured, and the BMI and percentage of excess weight loss [%EWL; (weight loss/(initial weight - weight at BMI 25))×100] were calculated at 1-month intervals. The body weight (BW) rebound was defined when the value of %EWL (6 months) - %EWL (12 months) was more than 10%. Blood and urine samples were collected, and the fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), fasting plasma insulin (FPI), homeostasis model assessment of insulin resistance (HOMA-IR=FPG×FPI/405), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs) and uric acid (UA) were measured at each monthly visit. The visceral fat area (VFA) and subcutaneous fat area (SFA) were measured on computed tomographic images at IGB placement and at 12 months after IGB placement.

During the study period, we did not change the medica-

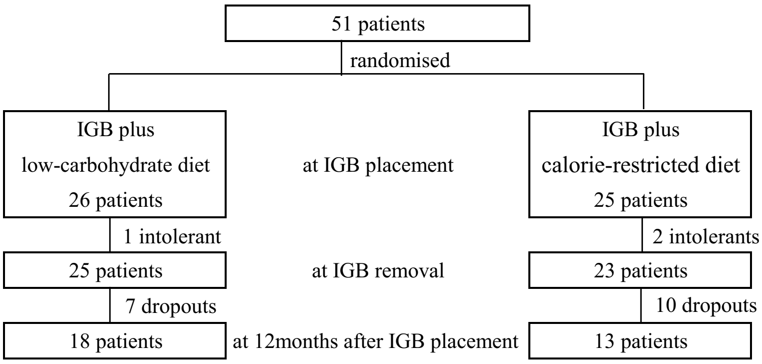

Figure 1. Flow diagram of the patients. IGB: intragastric balloon

tions. The general health of each subject was assessed, and the results of laboratory tests were explained by the physicians, who gave advice to the patients about both diets for 5-10 minutes at every interview. Thereafter, subjects in both groups received 10- to 15-min individual counseling sessions. The study was continued until 12 months after IGB placement (6 months after IGB removal).

Statistical analyses

Results are expressed as the mean±standard deviation. Differences between baseline values and those at 12 months after IGB placement were evaluated by the paired t test for continuous variables. Differences between the two groups were assessed by the unpaired t test for continuous variables and by the chi-square test or Fisher's exact probability test for categorical variables, as the distribution of each variable did not differ significantly between the two groups. In all analyses, $p<0.05$ was considered significant, and analyses were performed with the JMP (Ver. 13; SAS, Cary, USA) software program.

Results

Patients

IGB was placed in 51 patients between October 2012 and December 2017. Twenty-six were allocated to the IGB plus low-carbohydrate diet group, and 25 were allocated to the IGB plus calorie-restricted diet group. Of these 51 patients, 3 did not tolerate the IGB within 2 months after IGB placement (cause of intolerance: anorexia=1, vomiting=2), and 17 stopped attending outpatient guidance sessions within 5 months after IGB removal. Ultimately, 31 of the 51 patients were included in this study (12-month assessment).

The breakdown of these 31 was 18 in the IGB plus low-carbohydrate diet and 13 in the IGB plus calorie-restricted diet (Fig. 1). The general characteristics of the enrolled patients in each group are shown in Table 1. There were no statistically significant differences in any of the parameters between the two groups.

Body weight loss outcomes

At 12 months after IGB placement, the body weight and BMI were significantly lower than those observed at baseline both in the IGB plus low-carbohydrate diet group (baseline 101.9±25.8 kg, 37.6±7.1 kg/m^2, 12 months 88.2±21.9 kg, 32.6±6.3 kg/m^2) ($p<0.0001$ and $p<0.0001$, respectively) and in the IGB plus calorie-restricted diet group (baseline 103.5±17.0 kg, 38.0±6.1 kg/m^2, 12 months 89.1±6.2 kg, 32.9±3.8 kg/m^2) ($p<0.005$ and $p<0.005$, respectively). There were no significant differences in the body weight or BMI outcomes between the two groups (Table 2).

The %EWL in the IGB plus low-carbohydrate diet group was slightly higher than that of the IGB plus calorie-restricted diet group throughout this study (Fig. 2), but the difference between the two groups at 12 months after IGB placement was not significant (IGB plus low-carbohydrate 49.9±60.0%, IGB plus calorie-restricted diet 33.1±27.0%) (Table 2). BW rebound was significantly lower in the IGB plus low-carbohydrate diet (3/18, 16.7%) than in the IGB plus calorie-restricted diet (7/13, 53.8%) ($p<0.05$).

Metabolic parameter outcomes

At 12 months after IGB placement, both groups showed a significant improvement in their HOMA-IR, SBP, DBP and VFA values compared with baseline. However, only the IGB plus low-carbohydrate diet group showed a significant improvement in the HbA1c, TGs, HDL-C, SFA and ORD values compared with baseline at 12 months after IGB placement. There were no significant differences in any of metabolic parameter outcomes between the two groups (Table 2).

Nutrient intake at 12 months after IGB placement

We examined the average daily nutrient intake of the two groups by an interview at 12 months after IGB placement. Results showed that 72.2% (13/18) of those in the IGB plus low-carbohydrate diet group achieved a total carbohydrate intake of <120 g/day, and 61.5% (8/13) of those in the IGB plus calorie-restricted diet achieved a target total calorie intake ≤ideal body weight×25. Although we did not prescribe calorie restriction to the patients assigned to the IGB plus low-carbohydrate diet, the calorie intake at 12 months was

Table 1. Characteristics of the Patients at Baseline.

Characteristics	IGB plus low-carbohydrate diet n=18	IGB plus calorie-restricted diet n=13	p value
Age (years)	45.6±12.8	46.5±13.8	0.8516
Female sex - no. (%)	11 (61.1)	7 (53.8)	0.6977
BH (cm)	163.7±8.0	165.2±8.7	0.6322
BW (kg)	101.9±25.8	103.5±17.0	0.8461
BMI (kg/m^2)	37.6±7.1	38.0±6.1	0.8883
FPG (mg/dL)	107.6±25.3	103.9±11.4	0.6555
HbA1c (%)	6.1±0.7	6.2±0.6	0.7627
HOMA-IR	3.7±2.2	3.7±2.5	0.9848
TGs (mg/dL)	116.7±54.6	128.9±55.1	0.5659
HDL-C (mg/dL)	52.4±11.4	45.3±11.4	0.1110
LDL-C (mg/dL)	128.7±25.9	111.1±40.3	0.1556
UA (mg/dL)	6.3±1.1	6.3±2.4	0.9325
SBP (mmHg)	136.1±15.6	130.9±17.7	0.3996
DBP (mmHg)	85.7±16.0	82.8±9.7	0.5669
VFA (cm^2)	213.0±86.3	249.3±93.6	0.2743
SFA (cm^2)	426.8±189.1	390.1±185.9	0.5949
ORD	2.9±1.9	2.2±1.2	0.3026
IGB volume (mL)	644.4±68.4	653.8±66.0	0.7043

Values are the means±standard deviation.

IGB: intragastric balloon, BH: body height, BW: body weight, BMI: body mass index, FPG: fasting plasma glucose, HbA1c: hemoglobin A1c, HOMA-IR: homeostasis model assessment of insulin resistance, TGs: triglycerides, HDL-C: high-density lipoprotein-cholesterol, LDL-C: low-density lipoprotein-cholesterol, UA: uric acid, SBP: systolic blood pressure, DBP: diastolic blood pressure, VFA: visceral fat area, SFA: subcutaneous fat area, ORDs: obesity-related diseases

Table 2. Efficacy Outcomes.

Variable	IGB plus low-carbohydrate diet			IGB plus calorie-restricted diet			p value†
	Baseline	12 months	p value*	Baseline	12 months	p value*	
BW (kg)	101.9±25.8	88.2±21.9	<0.0001*	103.5±17.0	89.1±6.2	0.0025*	0.8862
BMI (kg/m^2)	37.6±7.1	32.6±6.3	<0.0001*	38.0±6.1	32.9±3.8	0.0022*	0.9130
%EWL (%)	-	49.9±60.0	-	-	33.1±27.0	-	0.3555
BW rebound - no. (%)	-	3 (16.7)	-	-	7 (53.8)	-	0.0290†
FPG (mg/dL)	107.6±25.3	100.5±13.2	0.1738	103.9±11.4	101.5±14.6	0.6113	0.6555
HbA1c (%)	6.1±0.7	5.7±0.6	0.0165*	6.2±0.6	5.9±0.5	0.0992	0.4308
HOMA-IR	3.7±2.2	2.6±1.3	0.0323*	3.7±2.5	2.6±2.2	0.0378*	0.9310
TGs (mg/dL)	116.7±54.6	88.1±41.0	0.0029*	128.9±55.1	109.6±53.2	0.3876	0.2301
HDL-C (mg/dL)	52.4±11.4	58.4±14.5	0.0123*	45.3±11.4	48.8±9.8	0.2041	0.1616
LDL-C (mg/dL)	128.7±25.9	128.6±32.2	0.9837	111.1±40.3	116.1±42.4	0.3402	0.3675
UA (mg/dL)	6.3±1.1	5.9±1.2	0.1801	6.3±2.4	6.0±1.7	0.5944	0.8293
SBP (mmHg)	136.1±15.6	125.7±15.6	0.0103*	130.9±17.7	124.1±17.2	0.0452*	0.7899
DBP (mmHg)	85.7±16.0	75.2±11.6	0.0013*	82.8±9.7	72.1±11.8	0.0032*	0.4642
VFA (cm^2)	213.0±86.3	141.5±64.6	0.0002*	249.3±93.6	174.3±117.3	0.0252*	0.3259
SFA (cm^2)	426.8±189.1	337.7±186.6	0.0094*	390.1±185.9	330.6±191.8	0.2090	0.9187
ORDs	2.9±1.9	2.3±2.1	0.0370*	2.2±1.2	2.0±1.4	0.0821	0.6221

*The results were considered significant at $p<0.05$ for within-group comparisons.

†The results were considered significant at $p<0.05$ for between-group comparisons.

Values are the means±standard deviation.

BW: body weight, BMI: body mass index, %EWL; [weight loss/(initial weight-weight at BMI 25)]×100. The BW rebound was defined when the value of %EWL (6 months)-%EWL (12 months) was more than 10%, FPG: fasting plasma glucose, HbA1c: hemoglobin A1c, HOMA-IR: homeostasis model assessment of insulin resistance, TGs: triglycerides, HDL-C: high-density lipoprotein-cholesterol, LDL-C: low-density lipoprotein–cholesterol, UA: uric acid, SBP: systolic blood pressure, DBP: diastolic blood pressure, VFA: visceral fat area, SFA: subcutaneous fat area, ORDs: obesity-related diseases

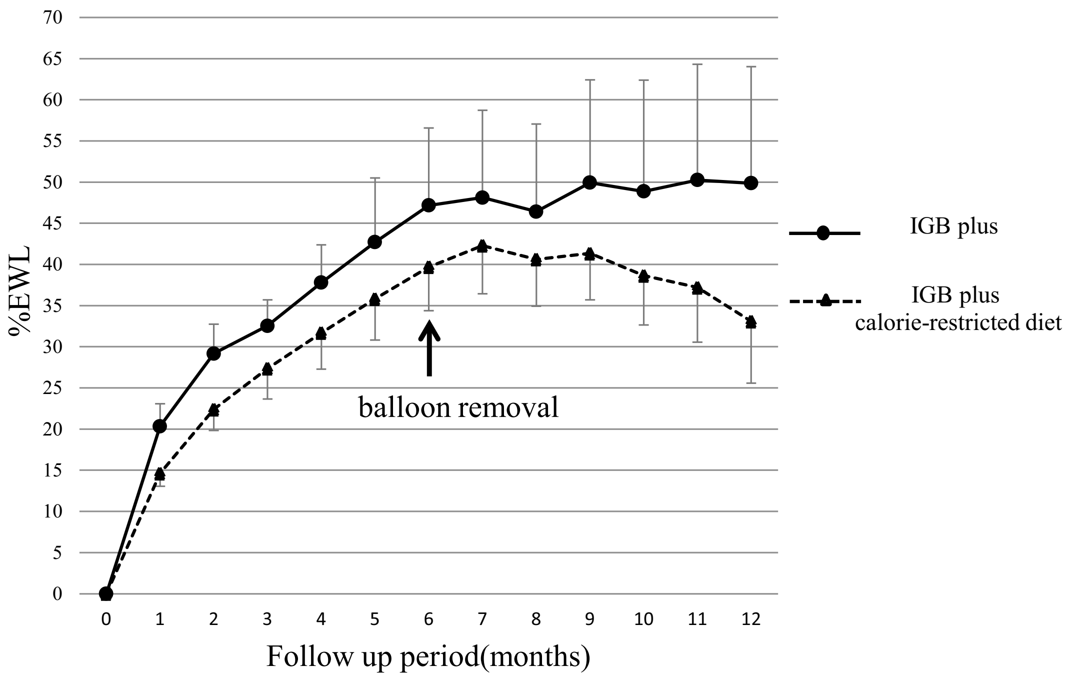

Figure 2. Changes in the %EWL after intragastric balloon (IGB) placement during 12-month intervention. Solid line: IGB plus low-carbohydrate diet, dotted line: calorie-restricted diet. Data points represent the mean±standard error. %EWL: percentage of excess weight loss

Table 3. Nutrition Intake at 12 Months.

	IGB plus low-carbohydrate diet		IGB plus calorie-restricted diet		p value*
	Intake	Energy ratio (%)	Intake	Energy ratio (%)	
Calorie intake (kcal)	1,550.0±146.5	100	1,523.1±178.7	100	0.6486
Calorie intake/IBW	23.2±2.8	-	22.6±3.8	-	0.5615
Carbohydrate (g)	103.9±42.0	26.8±10.4	201.2±35.4	52.9±7.0	<0.0001*
Protein (g)	91.7±25.7	23.6±5.7	66.2±14.2	17.3±2.6	0.0009*
Fat (g)	76.1±11.1	44.3±5.7	49.2±13.1	28.9±6.0	<0.0001*

*The results were considered significant at p<0.05 for between-group comparisons. Values are means±standard deviation. IGB: intragastric balloon, IBW: ideal body weight

similar in both groups (IGB plus low-carbohydrate diet 1,550.0±146.5 kcal, IGB plus calorie-restricted diet 1,523.1±178.7 kcal). The relative nutrient intake of carbohydrates, protein and fat was 26.8±10.4%, 23.6±5.7% and 44.3±5.7% in the IGB plus low-carbohydrate diet group, compared with 52.9±7.0%, 17.3±2.6% and 28.9±6.0%, respectively, in the IGB plus calorie-restricted diet group. The carbohydrate intake was significantly lower in the IGB plus low-carbohydrate diet group than in the IGB plus calorie-restricted diet group ($p<0.0001$). In contrast, the protein and fat intake were significantly lower in the IGB plus calorie-restricted diet group than in the IGB plus low-carbohydrate diet group ($p<0.001$ and $p<0.0001$, respectively) (Table 3).

Discussion

The efficacy of IGB placement for body weight loss was first reported by Nieben et al. in 1982 (25). Since then, various balloons have been tested, but complications have been relatively frequent. In 1999, a new balloon, the BIB®, which has a spherical shape and increased volume of saline (400-700 ml), was introduced (26, 27). Extensive clinical experience with the BIB® has shown a low complication rate, efficacy in weight loss and improvement of comorbidities (13, 14). In Japan, Ohta first reported the efficacy of IGB placement in 2008 (28). However, experience with IGB placement in Japan has been very limited (28-32). In this study, we performed IGB placement therapy in obese Japanese patients and demonstrated the efficacy of IGB placement in achieving weight loss. Three patients did not tolerate the IGB within two months after its placement, but there were no serious complications.

IGB placement is a temporary six-month treatment for obesity, and the maintenance of weight loss after the removal of the balloon is very important. Diet therapy is the most important factor for maintenance. The efficacy of the IGB therapy was linked both to the balloon itself and to a calorie-restricted diet (12-14, 28, 33-35).

A low-carbohydrate diet has become a popular strategy for achieving weight loss and managing weight in recent years. Many reports from all over the world have found that a low-carbohydrate diet is more effective than a calorie-restricted diet for weight loss (17-22). It was recently reported that a low-carbohydrate diet is useful for promoting weight loss in Japan (36). Although a low-calorie diet and very-low-calorie diet are both reportedly useful for increasing the efficacy of IGB therapy (11), whether or not a low-carbohydrate diet improves the efficacy of IGB therapy for weight management remains unclear. Therefore, we compared the effectiveness of a low-carbohydrate diet and a calorie-restricted diet in combination with IGB therapy.

In the present study, at 12 months after IGB placement, the body weight and BMI were significantly lower than those observed at baseline in both groups. There were no significant differences in the body weight or BMI outcomes between the two groups (Table 2). Our study showed that both a low-carbohydrate diet and a calorie-restricted diet are effective interventions for weight management in combination with IGB therapy.

Although we did not prescribe calorie restriction to the patients assigned to the IGB plus low-carbohydrate diet, the calorie intake at 12 months was similar in both groups (Table 3). The patients in IGB plus low-carbohydrate diet may have quickly felt satiated because they ate protein and fat, such as meat or fish, in place of carbohydrates. In addition, it may be difficult to overeat only side dishes, such as meat or fish. Alternatively, this may have been the result of patients in both groups being able to correct their habit of overeating during the period of IGB insertion.

The %EWL in the IGB plus low-carbohydrate diet group was slightly higher than that in the IGB plus calorie-restricted diet group throughout the 12 months of this study, although there were no significant differences (Fig. 2). The BW rebound was significantly lower in the IGB plus low-carbohydrate diet group than in the IGB plus calorie-restricted diet group (Table 2). This may be because a low-carbohydrate diet can be easily understood and maintained because patients need only focus on reducing carbohydrates, compared with a calorie-restricted diet. The patients in the IGB plus low-carbohydrate diet group were able to limit the amount of staple foods consumed (such as rice, bread, noodles and so on) than that of sugary foods (such as cake, ice cream, juice and so on), as carbohydrate-rich foods. Most patients who experienced BW rebound in both groups failed to adhere to the advised nutrient intake. Our study demonstrated that an IGB plus both a calorie-restricted diet as well as a low-carbohydrate diet were effective interventions for reducing and managing weight.

At 12 months after IGB placement, both groups showed a significant improvement in HOMA-IR, SBP, DBP and VFA values compared with baseline. However, only the IGB plus low-carbohydrate diet group showed a significant improvement in the HbA1c, TGs, HDL-C, SFA and ORD values (Table 2). The low-carbohydrate diet may have had a greater effect than the calorie-restricted diet, as there are some reports in which a low-carbohydrate diet showed a significant improvement in the HbA1c, TGs, HDL-C, SFA and ORD values (18-22, 36). Regardless, IGB therapy plus a low-carbohydrate diet was suggested to be effective for improving obesity comorbidities.

Several limitations associated with the present study warrant mention. First, the number of patients we treated was too small to detect significant differences in the between-group comparison, except for BW rebound. Therefore, a large-scale trial is needed in order to indicate the generality of our findings. Second, this study had a short term. A longer trial on a combination diet with IGB therapy will be necessary. Third, we were unable to assess all patients who participated in this study because many of the patients dropped out before the end of the study period. We need to analyze the reasons for dropout and devise efforts to reduce the dropout rate in the future.

In conclusion, our study demonstrated that a low-carbohydrate diet as well as a calorie-restricted diet were both effective interventions for reducing and managing weight when used in combination with IGB therapy. A large-scale study is necessary to confirm the efficacy of a low-carbohydrate diet in combination with IGB therapy.

The authors state that they have no Conflict of Interest (COI).

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