

Effects of Obesity Surgery on Type 2 Diabetes Mellitus Asian Patients

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Abstract

Background Obesity is a major risk factor for the development of type 2 diabetes mellitus (T2DM). Surgery is the most effective treatment for morbid obesity, and has been shown to lead to dramatic improvement in T2DM. However, data concerning obese Asian patients have not been reported, and the mechanism of improving T2DM after bariatric surgery in this population remains speculative.

Methods From April 1997 to March 2006, 1,375 patients undergoing obesity surgery were recruited for our study. The effects of weight loss surgery on type 2 diabetes mellitus (T2DM). Laparoscopic vertical banded gastric partition (LVBG) was performed in 552 patients (40.1%), and laparoscopic gastric bypass in 660 patients (48.0%), and laparoscopic adjustable gastric banding (LAGB) in 140 patients (10.2%). Another 23 patients (1.7%) received revision surgery. We evaluated the clinical data and effect of obesity surgery on T2DM, impaired fasting

glucose (IFG) and compared the changes with those with normal fasting glucose.

Results Among all the patients, 166 (12.1%) had impaired fasting glucose (IFG) and 247 (18.0%) had T2DM. Patients with IFG or DM were significantly older, more central obese, and they had higher insulin resistance and a higher HbA1C level than those with normal fasting glucose. The mean total weight loss for the population was 28.6%, 29.1%, 28.5%, 23.8%, and 24.4% (at 1, 2, 3, 5, and 7 years after surgery). There was no increase of surgical risk in T2DM or IFG patients. One year after operation, fasting plasma glucose returned to normal in 78.5% of T2DM patients and 94.7% of IFG patients. The HbA1C level returned to under 7.0 in 81.5% of T2DM and in 100% of IFG patients. Laparoscopic gastric bypass patients had a greater weight loss and a higher rate of glucose normalization (93.1%) than the LVBG patients (85.3%) and LAGB patients (73.9%), but no difference in HbA1C normalization.

Conclusions Obesity surgery resulted in significant and sustained weight loss with a cure rate of T2DM up to 80% in morbidly obese Asian patients. Gastric bypass surgery had a better result in T2DM cure rate than LVBG and LAGB because of better weight reduction.

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Introduction

Type 2 diabetes mellitus (T2DM) is an epidemic health problem worldwide, affecting more than 150 million people, and that number is expected to double by the year 2025 [1]. More than 90% of those patients have T2DM, versus 10% with early-onset DM [2]. Tight control of hyperglycemia is the cornerstone for the treatment and reduction of the complications of T2DM [3]. However, current

therapies, including diet, exercise, behavior modification, oral drugs, and insulin, rarely return patients to euglycemia [4, 5].

There is strong evidence that bariatric surgeries can cure most of the associated T2DM in morbidly obese patients [6–9]. However, data concerning the effect of weight-reduction surgery on severely obese Asian T2DM patients is lacking. Also the mechanism of different types of surgery for glycemic control remains unknown.

The aim of the present study was to explore, in a substantial number of morbidly obese Asian patients, the effect of different types of obesity surgery on T2DM and related comorbidities. We specifically evaluated the clinical character of the patients before operation and the postoperative outcomes, including surgical complications and weight loss, as well as changes in fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1C), and other comorbidities.

Materials and methods

A comprehensive, multidisciplinary, bariatric management program was in place for the preoperative preparation and postoperative management of patients. The program included support groups and ancillary personnel to provide nutritional, exercise, and psychological care. Nurse specialists for medical and psychiatric management were part of the team. Inclusion/exclusion criteria followed the Asia-Pacific Bariatric Guidelines: age ≥ 18 years, body mass index (BMI) $>32 \text{ kg/m}^2$ with diabetes or other important comorbidities, no alcohol abuse, and no concurrent psychiatric illness [3]. Written informed consent was obtained from each individual, and the study was reviewed and approved by the institutional Review Board.

Diagnosis and classification of T2DM was based on criteria for IFG, and T2DM. Patients who had IFG or T2DM were significant criteria established by the American Diabetes Association [14]. The categories of FPG include (1) normal, defined as FPG $<110 \text{ mg/dl}$; (2) impaired fasting glucose (IFG), defined as FPG $>110 \text{ mg/dl}$ and $<126 \text{ mg/dl}$; and (3) clinical diabetes, defined as FPG $\geq 126 \text{ mg/dl}$. Impaired fasting glucose is the term used to refer to a metabolic stage intermediate between normal glucose homeostasis and diabetes, now referred to as pre-diabetes.

The study group consisted of 1,375 patients who had undergone obesity surgery between April 1997 and March 2006 at our department and who had follow-up for at least one year. Three major types of obesity surgeries were used during the study period. The first operation was laparoscopic vertical banded gastric partition (LVBG), which was performed in 552 patients (40.1%) [5]. We stopped performing this procedure after 2002 because of the long-term

Operative outcomes

There were 22 early major complications (1.6%) that resulted in the deaths of 3 patients (0.2%). Minor early

Table 1 Patient characteristics of study population by level of fasting plasma glucose

	Normal F	Impaired NON-MS	T2DM	p Value
Number	962	166	247	
Age, years	30.0± 8.4	34.1± 9.8	34.0± 9.5	0.000*
Sex (% men)	695/267	109/57	159/88	0.023*
BMI, kg/m ²	41.5± 6.6	42.1± 6.7	42.3± 6.8	0.0197
Waist, cm	118.2± 15.9	121.5± 16.5	122.8± 17.5	0.000*
SBP, mmHg	133.4± 16.7	136.5± 17.8	135.7± 15.4	0.008*
DBP, mmHg	84.1± 12.7	86.2± 14.9	85.4± 11.9	0.077
Glucose, mg/dl	92.2± 9.3	115.8± 4.5	190.3± 71.6	0.000*
T-cholesterol, mg/dl	196.6± 37.0	196.0± 36.5	205.4± 39.7	0.003*
HDL-C, mmol/dl	45.6± 12.6	42.3± 14.0	42.1± 17.5	0.018*
Triglyceride, mg/dl	168.9± 115.9	209.0± 132.3	293.7± 154.7	0.000*
Uric acid, mg/dl	7.5± 1.8	7.5± 1.9	7.4± 2.0	0.621
AST, IU/l	30.6± 21.4	38.9± 31.3	45.4± 34.3	0.000*
ALT, IU/l	44.4± 38.3	53.1± 52.1	61.3± 46.2	0.000*
GGT, IU/l	41.5± 28.7	56.2± 39.4	61.5± 52.6	0.000*
A1bumin, gm/dl	4.5± 0.4	4.4± 0.3	4.4± 0.4	0.025*
ALP, IU/l	107.6± 52.3	118.3± 56.3	128.0± 66.8	0.000*
Insulin, μU/ml	21.2± 20.7	33.4± 37.6	45.5± 66.6	0.000*
C-peptide, ng/dl	3.8± 1.9	5.3± 2.8	4.2± 2.5	0.000*
HbA1C, %	5.6± 2.4	6.3± 1.0	7.8± 2.1	0.000*
Metabolic syndrome	15.28%	39.76%	46.56%	0.000*

* p < 0.05

BMI body mass index; SBP systolic blood pressure; DBP diastolic blood pressure; HDL high density lipoprotein cholesterol; WBC white blood cell; ALT alanine aminotransferase; AST aspartate aminotransferase; GGT gamma-glutamyl transferase; ALP alkaline phosphatase

complications occurred in 66 (4.8%) patients. The perioperative weight loss decreased from 113.5 kg to 80.8 kg, for a mean weight loss of 28.6% (32.7 kg) or 62% of excess body weight. The mean total weight loss for the population was 28.6%, 29.1%, 28.5%, 23.8%, and 24.4% at 1, 2, 3, 5, and 7 years. The preoperative mean BMI was 41.7 kg/m² and decreased to 29.8, 30.1, 32.1, and 32.8 kg/m² at 1, 2, 3, 5, and 7 years. The gastric bypass group had more rapid and greater weight loss than the LVBG and LAGB groups (Fig. 1). Generally, the weight loss after LAGB is gradual but exceeds the weight loss achieved after LVBG and LAGB groups (Fig. 1). The changes in weight among the patients followed for 7 years are shown in Fig. One year after operation, 3 years. Patients who underwent LVBG started to regain weight and approached the levels obtained with gastric bypass after 7 years.

Weight loss and co-morbidity assessment

The changes in weight among the patients followed for 7 years are shown in Fig. One year after operation, 3 years. Patients who underwent LVBG started to regain weight and approached the levels obtained with gastric bypass after 7 years.

Table 2 Perioperative outcomes among patients with different types of surgeries

	LVBG (n = 552)	LGB (n = 660)	LAGB (n = 140)	p Value
Operative time, min	124.2± 40.8	115.9± 42.6	85.5± 30.3	0.000*
Morbidity (major)	4 (0.74%)	18 (2.48%)	0 (0%)	0.012*
Mortality	1 (0.18%)	2 (0.30%)	0 (0%)	0.797
Flatus passage, days	1± 0.7	1.8± 0.8	1.2± 0.5	0.000*
Mean length stay, days	3± 2.3	6.2± 5.3	3.2± 1.7	0.000*

Table 3 Perioperative outcomes among patients with different level of fasting plasma glucose (FPG)

	Normal FPG (n = 962)	Impaired FPG (n = 166)	DMII (n = 247)	p Value
Operative time, min	113.4 ± 41.2	124.2 ± 47.2	123.2 ± 44.5	0.000*
Surgery (% bypass)	468 (48.6%)	73 (44.0%)	104 (42.1%)	0.133
Estimated blood loss, ml	33.4 ± 40.6	39.4 ± 63.6	40.1 ± 58.9	0.083
Morbidity (major)	15 (1.6%)	1 (0.6%)	6 (2.4%)	0.343
Mortality	2	1	0	0.055
Mean length stay, days	4.9 ± 4.4	4.7 ± 2.1	5.3 ± 5.1	0.289

* p < 0.05

body weight 2 years after operation, and this procedure was abandoned in our center after 2002. The weight group and 6.3 for the IFG group. The HbA1C of T2DM reducing curves were similar between the T2DM, IFG, and normal groups, although slightly less in T2DM group stabilized within 3 months postoperation. The HbA1C (Fig. 2). Table 4 shows the quantity of change of various level returned to normal in 81.5% of T2DM patients and clinical variables one year after obesity surgery. At one year, the reduction in BMI was slightly lower in T2DM

patients, yet they had dramatic decreases in FPG. FPG ratio was 93.1% for gastric bypass, 85.3% for LVBG, (100.2 mg/dl) and insulin level (54.4 U/ml) compared to the other groups (Table 4). The T2DM patients also had a significantly higher improvement in triglyceride, uric acid, ALT, AST, ALP, and C-peptide levels than the other two groups. For different procedures, the overall normalization of FPG ratio was 93.1% for gastric bypass, 85.3% for LVBG, and 73.9% for LAGB. This discrepancy is compatible with the efficacy of weight reduction associated with different procedures. There was no significant difference in HbA1C reduction between the gastric bypass procedure and restrictive type procedures.

Impact on diabetes

Discussion

The T2DM group had a sharper reduction in FPG and HbA1C immediately after operation than the normal group (Fig. 3). Fasting plasma glucose returned to normal in 78.5% of T2DM patients and 94.7% of IFG patients. Obesity and T2DM are the two most common chronic, debilitating diseases of the Western world. In the United States about 30% of the adult population is obese, and

Fig. 1 Weight changes among patients over a 7-year period

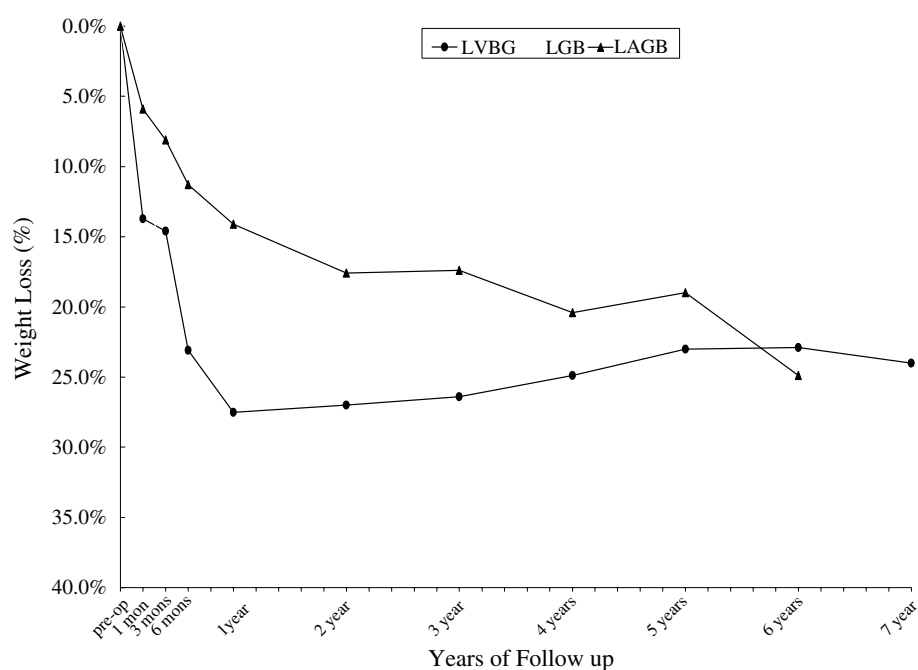


Fig. 2 Weight changes among type 2 diabetes mellitus (T2DM) patients, impaired fasting glucose (IFG) patients, and normal glucose patients

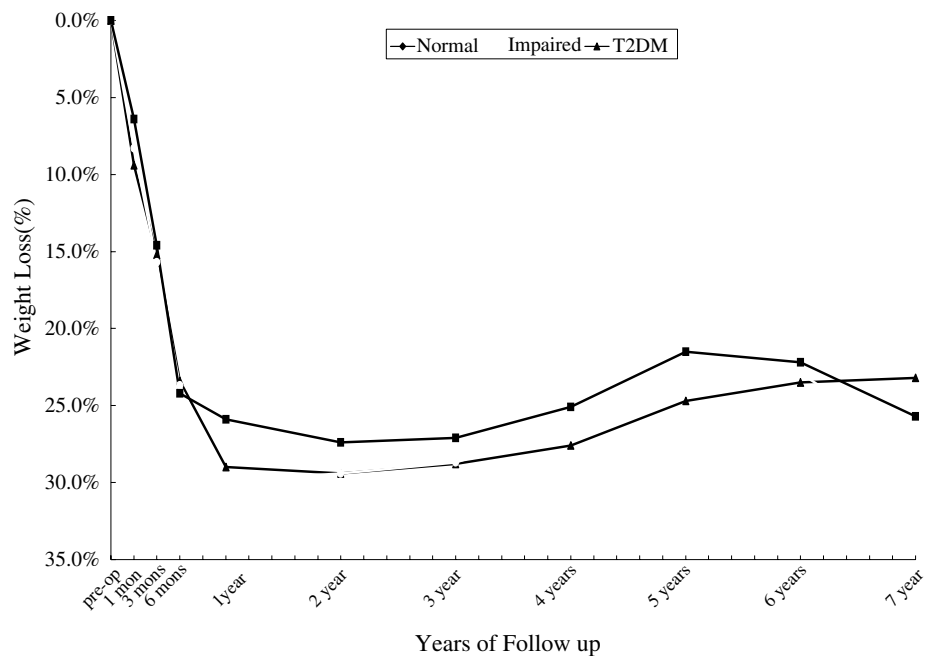


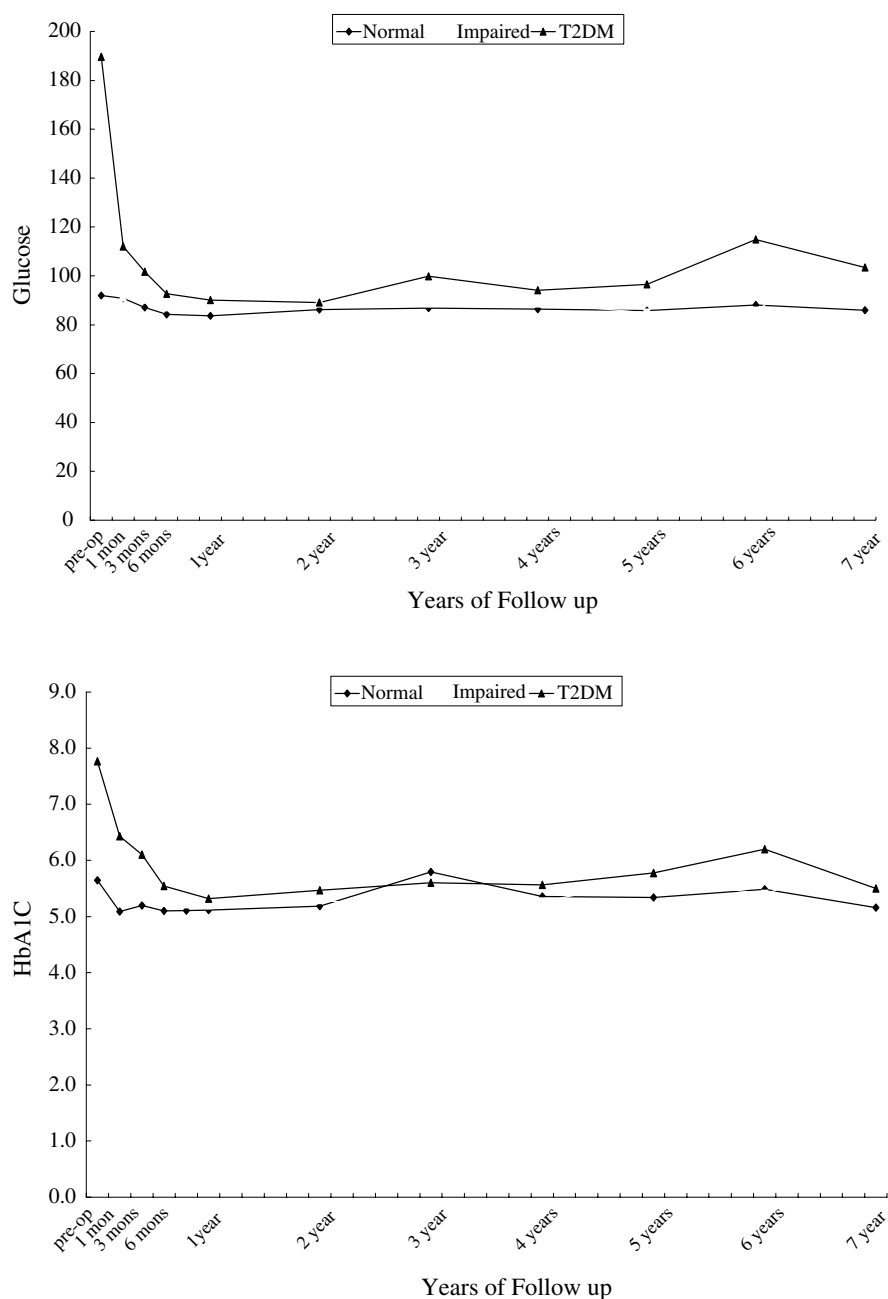
Table 4 Changes in laboratory data one year after obesity surgery

	Normal F	Impaired	T2DM	p value
BMI, kg/m ²	12.2 ± 5.1 (29.4%)	12.8 ± 5.6 (30.4%)	11.3 ± 5.0 (26.7%)	0.041*
SBP, mmHg	6.3 ± 22.9 (4.7%)	12.9 ± 23.5 (9.5%)	7.6 ± 20.8 (5.6%)	0.199
DBP, mmHg	8.3 ± 15.8 (9.9%)	12.9 ± 16.7 (15.0%)	9.0 ± 18.8 (10.5%)	0.221
Glucose, mg/dl	8.3 ± 12.8 (9.0%)	27.8 ± 10.9 (24.0%)	100.2 ± 76.9 (52.7%)	0.000*
T- CHO (mmol/L)	34.8 ± 35.5 (17.7%)	33.2 ± 30.2 (16.9%)	33.1 ± 40.2 (16.1%)	0.913
HDL-C, mmol/dl	5.8 ± 14.3 (12.7%)	5.9 ± 20.5 (13.9%)	0.9 ± 27.3 (2.1%)	0.018
Triglyceride (mg/dl)	85.2 ± 116.6 (50.4%)	145.6 ± 158.9 (69.7%)	184.6 ± 261.6 (62.9%)	0.000*
Uric acid, mg/dl	1.9 ± 1.6 (25.3%)	1.6 ± 1.3 (21.3%)	1.1 ± 2.0 (14.9%)	0.001*
GOT, IU/l	8.3 ± 23.2 (27.1%)	14.1 ± 26.6 (36.2%)	19.0 ± 31.9 (41.9%)	0.004*
GPT, IU/l	21.2 ± 42.0 (47.7%)	23.0 ± 33.8 (43.3%)	38.1 ± 48.0 (62.2%)	0.010*
GGT, IU/l	19.5 ± 18.4 (47.0%)	19.0 ± 13.2 (33.8%)	17.4 ± 14.1 (28.3%)	0.940
A1bumin, g/dl	0.15 ± 0.41 (3.3%)	0.07 ± 0.33 (1.6%)	0.03 ± 0.45 (0.7%)	0.096
ALP, IU/l	39.4 ± 54.1 (36.6%)	31.3 ± 62.3 (26.5%)	77.0 ± 67.7 (60.2%)	0.016*
Insulin, μU/ml	17.2 ± 23.0 (18.4%)	21.1 ± 22.4 (63.2%)	54.4 ± 92.3 (119.6%)	0.000*
C-peptide, ng/dl	2.0 ± 2.2 (52.6%)	3.2 ± 3.4 (60.4%)	4.0 ± 4.9 (95.2%)	0.001*
HbA1C, %	0.8 ± 4.0 (13.8%)	0.8 ± 0.8 (12.5%)	2.2 ± 1.9 (27.8%)	0.125
Metabolic syndrome	2.9%	2.3%	4.7%	0.720

* p < 0.05

8% have T2DM (mostly obesity related) [10]. However, Asians are more prone to central obesity [20]. A study in it was found that although Americans had the highest rates of obesity, they had the lowest levels of diabetes. In the present study, 30.0% was estimated that India has 31.7 million diabetes patients and China has 20.8 million diabetes patients, mean BMI around 42, higher than the incidence of 21% higher numbers than the 17.7 million patients reported in the United States [1]. Numerous studies have demonstrated high levels of metabolic risk factors at relatively young ages and treatment of T2DM in Asia, as well as in Western countries.

Fig. 3 Change in fasting plasma glucose level and HbA1C after surgery in T2DM, IFG, and normal groups



Obesity is the most important risk factor for the development of T2DM in obese patients. Elucidation of the development of T2DM. The relative risk of diabetes in the obese underlying genetic mechanism may help in overcoming population is ten times that of the normal BMI population this disease and developing new treatment modalities. [23]. However, in contrast to the previous study from the Although understanding the relationship between obesity and general population, the development of IFG and T2DM in obesity and T2DM is well accepted, there is no medical cure for severely obese patients is not related to BMI, as shown in T2DM [24, 25]. Despite various treatments, the natural course of the disease is characterized by progression to microvascular complications leading to neuropathy, nephropathy, retinopathy, and cardiovascular disease [25]. Although female patients had a greater tendency to develop T2DM than male patients, and although age also played a significant role, the combination of central obesity and insulin resistance is likely the most significant factor [26]. At present, even with best medical management of the development of T2DM. It is speculated, therefore, that genetic factors may play a crucial role in the tight glycemic control [27, 28]. Bariatric surgery,

however, has been shown to provide good weight loss and more than three times the risk of major complications as significant resolution of obesity-related T2DM [9, 29]. In laparoscopic mini-gastric bypass [8]. Two surveys in the the Swedish Obese Subjects (SOS) study, 2,016 subjects in the United States also disclosed high morbidity and mortality were surgically treated with 2.2% major complication rate after gastric bypass [33, 34]. A recent study also cautioned and 0.2% mortality. The weight loss was 23.4% and 16.3% that there is a significant risk associated with gastric bypass at 2 and 10 years, respectively, in comparison with a 1.6% surgery in low BMI patients [35].

increase at 10 years in a control group. The surgically Although bariatric surgery has been shown to provide induced weight loss resulted in resolution of diabetes good weight loss and significant resolution of T2DM, the mellitus in 87.5% and 70.8% of the patients at postoperative exact mechanism for the dramatic effect of obesity surgery tive 2 and 10 years separately [9]. In this study of 1,375 on T2DM remains unknown [9-12]. Hypotheses include bariatric surgical patients, we also demonstrated that weight reduction, decreased caloric intake, and bypass of obesity surgery resulted in significant weight loss (24.4%) the hormonally active foregut. Several reports support the and resolution of T2DM in 86.6% of the patients during a concept that the superior effect of gastric bypass over 7-year period. This study had a better weight loss, with restrictive procedures is a direct effect of bypassing the 29.1% at 2 years, than the 23.4% in SOS study, probably hormonally active foregut. Rubino et al. also support the because more gastric bypass surgeries were performed at foregut in a human study and an animal experiment [2, 36]. adjustable banding was used instead of a fixed banding Our study did not reveal the effect from duodenal jejunal which was used in the SOS study. However, the efficacy of exclusion suggested by these other studies, but it did corroborate the findings of a study on insulin resistance by obesity surgery to cure T2DM is similar between Asian and Caucasian populations. Our results are consistent with Ballantyne et al. [37]. While the gastric bypass group had a recent studies demonstrating a significant and sustained dramatic improvement of glucose and HbA1C levels at the improvement in T2DM after obesity surgery [9, 29].

Our study has also shown that bariatric surgery performed the gastric banding group had the same effect accompanied in patients with diabetes mellitus is as safe as with decreased caloric intake. After longer follow-up, the nondiabetic patients, although with longer operative times gastric banding group had improvement of glucose and probably because of central obesity [29]. Nevertheless, HbA1C similar to that observed in the bypass group, and central obesity or diabetes mellitus should not be a risk factor for bariatric surgery. Bariatric surgery procedures bypass surgery led to a more rapid and higher decrease in are evolving and have made a lot of progress over the past 50 years [30]. We performed LVBG for the treatment of very good therapeutic effect on FPG and HbA1C. Although morbid obesity beginning in 1998 [5]. The procedure is a safe and effective, and a long-term weight reduction up to 20% can be achieved, although some late weight regain from iron and calcium deficiency at long-term follow-up. and troublesome gastrointestinal symptoms have been reported [6, 31]. The LAGB procedure has replaced advantages of using gastric bypass for the treatment of T2DM LVBG as the choice of pure restrictive procedure because of its simplicity and adjustability [9, 20]. Our study confirmed that LAGB is the safest bariatric procedure and can be performed with a very low complication rate in multiple cardiovascular and metabolic co-morbidities. Our expert hands. The weight loss is gradual but ultimately exceeds that with LVBG, approaching the weight loss abnormalities in the obese Taiwanese patients referred for associated with gastric bypass after 3 years. Gastric bypass weight-reduction surgery [39]. However, significant is also commonly performed. Although it is more effective weight reduction 1 year after operation markedly in producing weight reduction than LAGB, it is the most improved all aspects of the metabolic syndrome and technically demanding surgery when performed laparoscopically [30, 32]. Significant morbidity and mortality— difference in the resolution rate between gastric bypass up to 10% and 2%, respectively—have been reported [40]. There was also no significant difference in the resolution rate between gastric bypass and restrictive-type surgery. Long-term survival benefit of Although we performed a simplified gastric bypass (laparoscopic mini-gastric bypass) on the patients in this study [41]. Considering the efficacy of bariatric surgery in the major complication rate is still significantly higher than the resolution of associated metabolic complications and that of laparoscopic gastric banding (2.6% versus 0%). In the long-term survival benefit, a freer usage of bariatric previous study, we found that laparoscopic Roux-en-Y surgery and transition to metabolic surgery is expected gastric bypass is even more technically difficult and carried [35, 42].

In summary, our study demonstrates significant improvement in T2DM and IPG of morbidly obese patients after bariatric surgery. At present, bariatric surgery is the most effective weight-loss treatment; it results in significant weight loss that is maintained for many years. Patients with IPG had a better result than those with T2DM. These significant benefits of surgery appear to justify the earlier and freer use of obesity surgery in patients with IPG or those in whom diabetes has recently become clinically evident.

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