Original Article

A Prospective Randomized Control Trial: Two Years Outcome in Diabetes Control after Bariatric Surgery Comparison between Laparoscopic Sleeve Gastrectomy and Laparoscopic Roux-En-Y Gastric Bypass

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Background: Bariatric surgery has been effective in weight loss and comorbidity resolution, especially diabetes. Laparoscopic Roux-En-Y Gastric bypass (LRYGB) is still a standard procedure and thought to play a major role in glucose homeostasis and diabetic control. Laparoscopic sleeve gastrectomy (LSG) is gaining popularity as an optional procedure in morbid obese patient with comparable outcome to gastric bypass. However, there is lack of data in Thailand.

Objective: The primary outcome was to compare the effect on diabetic control after LSG and LRYGB surgery. The secondary outcome was to evaluate the excess weight loss (EWL).

Materials and Methods: The present study was a prospective, randomized clinical trial in morbid obese patient with type 2 diabetes (T2DM). The study examined Thai patients with age between 15 and 60 years, BMI 32.5 to 60, history of T2DM of less than 10 years, and preoperative plasma HbA1c level of more than 7%. Follow-up at six months and two years after surgery to evaluate plasma HbA1c level, percentage of EWL, and remission rate of diabetes after surgery.

Results: One hundred four patients were randomized into 48 patients in LSG group and 56 patients in LRYGB group. There was no difference in baseline BMI and plasma HbA1c level between the two groups. Average EWL at six months were 42.76±3.44% in LSG group and 55.07±10.07% in LRYGB group (p=0.006), and EWL at two years were 58.31±7.78% in LSG group and 70.12±12.12% in LRYGB group (p<0.001). Reduction in mean plasma HbA1c level change (preop to postop) at six months after surgery were 1.87±0.98 in LSG group and 2.72±1.2 in LRYGB group (p=0.619). Reduction in mean HbA1c level change (preop to postop) at two years after surgery were 2.43±1.4 in LSG group and 3.1±1.76 in LRYGB group (p=0.737). Remission rate of T2DM at six months were 58.30% in LSG group and 62.07% in LRYGB group (p=0.481). Remission rate of T2DM at two years were 66.67% in LSG and 70.64% in LRYGB group (p=0.454). Both groups showed a decrease in antihyperglycemic drugs used after surgery but there was no statistically significant difference.

Conclusion: LRYGB is statistically significant more effective than LSG in EWL. However, there is no difference in the effectiveness of diabetic control between the two procedures in both short-term and long-term results.

Keywords: Bariatric surgery, Diabetes control

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Morbid obesity has emerged as a concern in Thailand with an increasing number of patients over the years. The incidence of overweight in Thailand increased from 18.2% in 1991 to 24.1% in 1997, and 28.1% in 2007. From those, the prevalence of morbid obesity is 9.6%[1]. Patients with morbid obesity have not only physical and psycho-social problems but also are at an increased risk for developing many medical problems, including insulin resistance and type 2 diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, stroke, sleep apnea, hyperuricemia and gout, and osteoarthritis[1].

Bariatric surgery is the most successful long-term

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weight loss therapy, and can improve many comorbid diseases, especially in type 2 diabetes (T2DM). Empirical evidence suggests a novel role of bariatric surgical procedures for the treatment of T2DM[2,3]. Laparoscopic Roux-En-Y gastric bypass (LRYGB) surgery is still the gold standard procedure in morbid obesity treatment and proved to effectively decrease diabetes by about 68% to 83%[4-7]. Many recently published reports support the laparoscopic sleeve gastrectomy (LSG). It may provide results comparable to bypass surgery in glycemic control. In addition, LSG seems easier to perform and associates with less complications[8-12]. However, there is lack of data of long-term follow-up and few studies compared the lasting of diabetic remission effect of the operation. Therefore, the present study was conducted to compare the effectiveness of diabetic control at two years after gastric bypass surgery and sleeve gastrectomy among Thai patients.

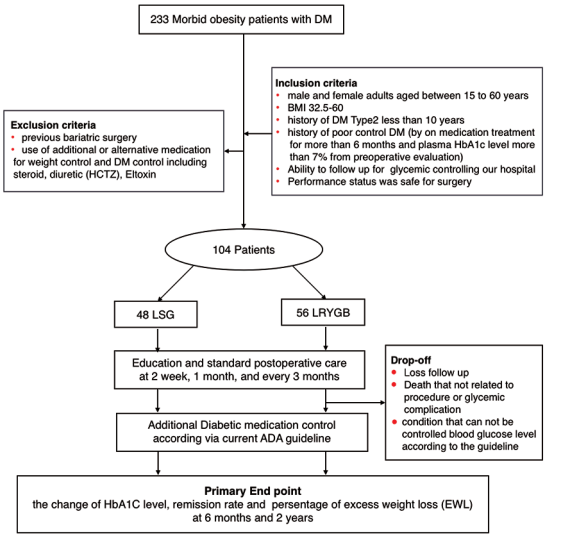

Figure 1. Flow diagram of patients screening and data extraction process.

Materials and Methods

Study design

The present was a prospective randomized, single-blind controlled trial, single center study to compare two types of bariatric operations in morbid obese patients who showed inadequate diabetes control. The study was conducted in the Department of Surgery of the King Chulalongkorn Memorial University Hospital. With an approval by the Institute Human Ethics Committees. The recruitment took place between December 12, 2012 and May 31, 2014. All patients underwent an evaluation including previous medications, co-morbid disease, and sleep test to detect sleep apnea for preoperative evaluation. Blood sampling for glucose, HbA1c, and other laboratory tests at one week before surgery was done. Procedures started in January 2013.

Patients

Patients participating in the present research consisted of male and female adults aged between 15 to 60 years who had 1) body mass index (BMI) between 32.5 and 60, 2) history of T2DM of less than 10 years, 3) history of uncontrolled DM by medication treatment for more than six months and had HbA1c of more than 7 from preoperative evaluation at one week before surgery, 4) ability to follow-up for glycemic control at the authors' hospital, and 5) performance status was safe for surgery, were included in the study after given an informed consent and agreed to participate in the study. Exclusion criteria included 1) previous bariatric surgery and 2) use of additional or alternative medication for weight control and DM control including steroid, diuretic (HCTZ), and Eltoxin.

Randomization

A computerized random number generator in block of four was used for the allocation of all patients into the two procedure groups. Prior to the operation, the type of procedure (LRYGB versus LSG) was transferred in an opaque, sealed envelope and opened by the surgeon just before the operation began. Patient did not know what kind of operation had been performed.

Measurement and data collection

After the operation, all patients were educated about the nutrition, medication, and routine post-operative care. Patients with fasting plasma glucose (FPG) of more than 120 or HbA1c of more than 6% continued antiglycemic control medication according to ADA guideline for DM control[13]. Follow-up was arranged at 2-week, 1-month, and every three months. At six-month and two-year after operation, the evaluation of FPG, HbA1c, and weight loss were performed by physician.

Drop-off patients was defined when 1) loss follow-up more than 30 days after appointment, 2) death that not related to procedure or glycemic complication, 3) condition that cannot control blood glucose level according to the guideline such as pregnancy or complication from antihyperglycemic

Table 1. Baseline demographics data

	LRYGB (56 patients) Mean±SD	LSG (48 patients) Mean±SD	p-value
Age (years)	39.31±8.78	36.93±10.76	0.215
Sex (female/male), n	24/32	21/27	0.934#
BMI (kg/m^2)*	46.12±6.6	47.16±5.35	0.648
FPG	138.15±32.52	145.46±39.22	0.599
HbA1c	8.93±1.52	9.01±1.37	0.872

LRYGB=laparoscopic Roux-En-Y gastric bypass; LSG=laparoscopic sleeve gastrectomy; SD=standard deviation; BMI=body mass index; FPG=fasting plasma glucose

* BMI calculated as weight in kilograms divided by height in meters squared

Values are tested for significant differences between the two groups by Chi-squared test

All continuous values are tested for significant differences between the two groups by the Student's independent t-test

drugs. Drop-off patients were included in the safety analysis (the intent-to-treat population). Stopping policy was applied if any significant adverse effect occurred or the result from interim study found no benefit for glycemic control in both procedures.

Surgical procedures

All operations were performed laparoscopically by the same surgeon and by the same surgical team. The patients were operated under general anesthesia in a reverse Trendelenburg position. A standard laparoscopic technique with four to five ports were used for both procedures. In the bypass procedure, the pouch was created by using linear staple to archive the residual volume of 30 ml. The staple line started from the second branch of right gastric artery and vertically to angle of His. After that, the jejunojejunostomy was done using linear staple to create a 2 cm anastomosis length followed by creating an anticolic antegastric alimentary limb length 150 cm and biliary limb length 15 cm. Finally, the gastrojejunostomy was done using circular staple No.25.

For the sleeve gastrectomy, the procedure was started from mobilized greater curvature of stomach until reach angle of His. The stomach was then incised using linear staple with 4 cm antral sparing and the staple line was continued to create the residual stomach size equally to Bougie 36 Fr.

Data of all patients were collected prospectively following demographic parameter, HbA1c, FPG, excessive weight loss, and remission of DM, which defined by having FPG less than 100, HbA1c less than 6 without any medication used within one year.

Statistical analysis and sample size

Data analyses were performed using the statistical software package, SPSS for Windows V. Continuous values were reported as mean ± standard deviation (SD). Descriptive statistics were used for demographic variables. To test for significant differences between the two treatment groups used the Student's independent t-test and Mann-Whitney U-test. All tests were two-tailed, with p value lower than 0.05 considered statistically significant. Power analysis suggested 42 patients would allow an 80% chance of detecting a clinically significant. Interim analysis was performed at 75% of recruitment or severe adverse effect occurred. The present study protocol included 48 in each arm to include drop-off patients.

Results

Between December 12, 2012 and May 31, 2014, 48 LSG and 56 LRYGB were performed. The mean age was 38.12 years (range 18 to 57 years), mean BMI was 46.7 (range 33.5 to 57.9), mean preoperative HbA1c level was 8.96% (range 7.1% to 12.7%), and mean preoperative FPG was 142.07 mg/dl (89 to 236 mg/dl). There were no statistically significant differences in demographics or values contributing to study outcomes especially baseline BMI and HbA1c between the two groups (as in Table 1).

The safety analysis, all procedures were successfully performed by a laparoscopic technique, with no deaths or major complications in both groups. Minor complication was found in two cases in LRYGB group with wound infection treated by local wound care. The mean postoperative hospital stay was 2.3 day in LSG and 3.2 days in LRYGB. All patients received follow-up at two years.

Average % excess weight loss (EWL) at six months were 42.76% in LSG group and 55.07% in LRYGB group, (p=0.006) and % EWL at two years were 58.32% in LSG group and 70.12% in LRYGB group (p<0.001).

Table 2. Primary and secondary outcome at 6 months and 2 years after surgery

Outcome	LRYGB Mean±SD	LSG Mean±SD	p-value
Excess weight loss (%) at 6 months	55.07±10.07	42.76±3.44	0.006*
Excess weight loss (%) at 2 years	70.12±12.12	58.31±7.78	<0.001*
HbA1c level at 6 months after surgery	5.68±0.43	6.65±0.47	0.467
HbA1c level at 2 years after surgery	5.53±0.88	6.09±0.97	0.589
HbA1c level change (preop to postop) at 6 months	2.72±1.20	1.87±0.98	0.619
HbA1c level change (preop to postop) at 2 years	3.10±1.76	2.43±1.40	0.737
Diabetic remission rate at 6 months (%)	62.07	58.30	0.481#
Diabetic remission rate at 2 years (%)	70.64	66.67	0.454#

LRYGB=laparoscopic Roux-En-Y gastric bypass; LSG=laparoscopic sleeve gastrectomy; SD=standard deviation

* Values are tested by Mann-Whitney U test with p<0.05 is considered statistically significant

Values are tested by Chi-squared test

All continuous values are tested by the Student's independent t-test

Both groups showed a decrease in antihyperglycemic drugs used after surgery. Moreover, mean HbA1c level at six months and two years of both procedures was significantly improved from baseline with p<0.001.

Reduction in mean plasma HbA1c level at six months after surgery from 8.52% to 6.65% in LSG group and from 8.40% to 5.68% in LRYGB group (p=0.619). Reduction in mean HbA1c level at two years after surgery from 8.52% to 6.09% in LSG group and from 8.40% to 5.53% in LRYGB group (p=0.737). Remission rate of T2DM at six months were 58.30% in LSG group and 62.07% in LRYGB group (p=0.481). Remission rate of T2DM at two years were 66.67% in LSG and 70.64% in LRYGB group (p=0.454). There was no death or major complication related to operations or diabetic complication in the present study (Table 2).

Discussion

Bariatric surgery shows effective in weight loss and diabetes control. Many recent studies found that after bariatric surgery, patients have diabetes remission[15], which is the same results as in the present study in Thai patients. However, the present study shows that bypass surgery has comparable result to sleeve gastrectomy in diabetes control, but the result cannot be concluded until a randomized controlled trial (RCT) study is completed.

Recently, some studies found that bypass surgery has comparable effectiveness in weigh loss to sleeve gastrectomy procedure[16,17]. In the present study, although, it still has limitation in the number of patients, the results show that bypass surgery is significantly superior to sleeve gastrectomy procedure in weight loss, which may be due to the different lifestyle and eating behavior. To improve research quality, studies need a larger sample size or multicenter RCT study.

Interestingly, the present study found that although the result of weight loss was significantly

different between both procedures, the effectiveness in diabetes control was not significantly different. This may indicate that remission or reversal of diabetes is independent from weight loss or calorie restriction. Recent studies show that bariatric surgery may have an effect to gut hormone release (Hindgut hypothesis and Foregut hypothesis), which subsequently effect glucose metabolism and insulin resistance[18]. Understanding the mechanism of this pathway may improve the surgery for diabetes control without any weight loss and may be an ideal surgical treatment in poor control DM with low BMI patients[19-21].

From many previous studies, age, duration of T2DM, preoperative FPG, and preoperative A1c are considered as potential predictors of diabetes remission and have been used in several prediction models of diabetes remission after bariatric surgery. Further study should be conducted to identify those factors effect in Thai population[22-24].

By most of meta-analysis studies, LSG achieved diabetic remission rate similar to those of LRYGB within one to two years follow-up. However, recently published trials with three to five years follow-up have reported that LRYGB seem to maintain remission rate more than LSG in some reports[25-28]. Therefore, the

authors could not conclude the long-term result in the present study but may find answer in long-term follow-up. Although the present study only showed short-term result, the controversies about long-term results may be answered by long-term follow-up in future studies.

RYGB is considered a restrictive procedure with a malabsorptive component that promote weight loss and metabolic improvement through additional hormone mediated mechanisms by substantially increasing postprandial gut hormones such as peptide YY (PYY) and glucagon-like peptide 1 (GLP-1). LSG used to be considered as a restrictive technique but recent studies showed that LSG generated significant changes in ghrelin, PP, PYY, GLP-1, amylin, and leptin levels. These metabolic alteration effects may be the key factor that could explain the diabetic control property of LSG independence of weight loss[29,30].

Conclusion

LRYGB is more effective than LSG in EWL with statistical significance. However, there is no difference in the effectiveness of diabetic control between the two procedures in both short-term and long-term results.

What is already known on this topic?

LRYGB surgery is still the gold standard procedure for morbid obesity treatment and proved to effectively decrease diabetes in about 68% to 83% of cases. There are many recently published reports supporting that LSG may provide comparable result to bypass surgery in glycemic control under foregut hypothesis with less complications as compared to LRYGB. However, there is lack of data from randomized controlled trial to show long-term result and there is no report in Thai patients.

What this study adds?

LRYGB is more effective than LSG in EWL with statistical significance. However, there is no difference in the efficacy of diabetic control between the two procedures in both short-term and long-term results.

What are the implications for public health practice?

The present report shows the remission rate and EWL after surgery in Thai patient, which is similar to western or other Asian reports. Although, there are some differences in diet and lifestyle, this may prove that the result of surgery is mainly dependent on the type of procedure. The present study is also the first study that shows the long-term result in Thai patients. LRYGB shows greater weight loss than LSG with the same effect in diabetic control. The present data may help in procedure selection for the patients[21].

Conflicts of interest

The authors declare no conflict of interest.

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