Effectiveness and safety of laparoscopic Roux-en-Y gastric bypass for the treatment of type 2 diabetes mellitus

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Abstract. Gastric bypass may be conducted to aid in glycemic control in adults with type 2 diabetes mellitus (T2DM). The aim of the present study was to investigate the clinical results of diabetes remission and metabolic syndrome in individuals with T2DM after undergoing a gastric bypass. A total of 85 patients (39 men and 46 women) with T2DM underwent laparoscopic Roux-en-Y gastric bypass (LRYGB). Data regarding patient demographics, body mass index (BMI), co-morbidities and details of diabetes mellitus, including disease duration, remission, β-cell function, blood lipid levels and nutritive status were prospectively collected and analyzed. The mean duration from the onset of T2DM was 7.79±4.84 years (range, 1 month to 22 years). The preoperative mean BMI was 31.60±4.10 (range, 28.53-48.10 kg/m^2), mean percentage of body fat was 36.35±9.12% (range, 18-56%), and the mean HbA1c was 8.32±2.13% (range, 7-15.9%). Five patients (5.9%) developed complications without mortality. T2DM and β-cell function were significantly improved from by month 6 after surgery (P<0.05). Improvements in central obesity, blood pressure (BP; systolic and diastolic) control, blood lipid levels were observed, without malnutrition or severe anemia. Therefore, the present results indicate that laparoscopic RYGBP is a safe and effective procedure for improving glycemic control, obesity, body fat percentage and BP in patients with T2DM and obesity.

Introduction

Diabetes is a chronic progressive disease and the most common endocrine disorder worldwide. According to projections by the World Health Organization, the worldwide prevalence of diabetes will reach a ~334 million individuals worldwide by the 2025 (1). Another study predicted that the prevalence of diabetes in China alone will reach ~100 million individuals by 2030 (2). Furthermore, 25.8% of these patients in China received treatment for diabetes, and 39.7% of those treated had adequate glycemic control. Currently, medical interventions, including diet, exercise, and anti-diabetic medications, are the primary approaches for managing type 2 diabetes mellitus (T2DM). However, there is increasing evidence that surgery may help achieve complete remission, particularly in morbidly obese patients with diabetes (3). The positive effects of bariatric surgery on the remission of T2DM are well established (4-6). A number of conventional and experimental surgical operations have been demonstrated to markedly ameliorate T2DM, among which Roux-en-Y gastric bypass (RYGB) is the most common surgical procedure (7). A number of observational studies have detected improvements in glycemic and metabolic disorders, and diabetic complications have shown to be partially reversible due to weight loss and diabetes control. In addition, patients received beneficial reductions in cardiovascular morbidity and overall mortality.

The purpose of this retrospective study was to analyze the results of laparoscopic Roux-en-Y gastric bypass (LRYGB) treating for diabetes in Chinese people in our department, the outcome of metabolic syndrome is also discussed.

Materials and methods

Patients. The study was conducted with the approval of the ethics committee and institutional review board of the Shanghai Sixth People's Hospital (Shanghai, China). All patients provided written informed consent after being made aware of the current standards of treatment for T2DM and of risks and benefits associated with the procedure. A total of 85 patients (39 men and 46 women) with T2DM underwent LRYGB between February 2011 and May 2013. The mean age was 47.33±12.91 years (range, 24-65 years). The mean duration from the onset of T2DM was 7.79±4.84 years (range, 1 month to 22 years).

Inclusion and exclusion criteria. Inclusion criteria for this study were as follows: Age, 18-65 years; BMI, >28 kg/m^2; and poorly controlled T2DM as indicated by glycosylated hemoglobin (HbA1C) level of ≥7%. Diagnosis of T2DM was based on the criteria of the American Diabetes Association (ADA) (8) and was considered valid if established by an endocrinologist or diabetes specialist. The study exclusion

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criteria were as follows: Patients <18 or >65 years old; those planning a pregnancy within 2 years after entry into the study; and patients with established diagnoses of type 1 diabetes, latent autoimmune diabetes in adults, malignancy, debilitating disease, unresolved psychiatric illness, or substance abuse.

Data collection. Data were collected prospectively and entered into a database. We collected data on patient demographics, fasting blood glucose (FBG), postprandial blood glucose (PBG), blood pressure (BP), C-peptide, insulin levels, HbA1c and blood lipid levels, including profile include cholesterol, triglyceride, high-density and low-density lipoprotein. Blood glucose was measured using the glucose oxidase method. Serum insulin and C-peptide levels were quantified using radioimmunoassays with specific insulin and C-peptide detection kits according to the manufacturer's instructions (Beijing North Institute of Biological Technology, Beijing, China). HbA1c was measured using high-performance liquid chromatography, with a former reference range of 4.0-6.0% (Menarini Group, Florence, Italy). In addition, glycosylated serum protein (GSP) was measured using an ELISA (Hitachi 7100; Hitachi, Ltd., Tokyo, Japan). Lipid profiles were measured using standard commercial methods on a parallel, multichannel analyzer (Hitachi 7600-020; Hitachi, Ltd.). Follow-up visits were scheduled at 6, 12 and 18 months after surgery. In addition, postoperative data regarding patient levels of folic acid, vitamin B12, serum iron, parathyroid hormone (PTH) and 25-hydroxy vitamin D [25(OH)D] were collected as indices of anemic and hypocalcemic status.

Patient outcome criteria. The aims for glycemic and BP control were based on the criteria established by the ADA (8). If patients were not receiving anti-diabetic medications and had normal FPG (<100 mg/dl) and HbA1c (<6%) levels, their condition was considered to be resolved. Patients with an HbA1c of ≤7%, despite no use of anti-diabetic medications, were considered to have achieved glycemic control. If the FPG decreased by >25 mg/dl or the HbA1c reduced by >1%, the patients' condition was considered to have improved. Surgery was considered to have failed if glycemic indices showed no significant improvement, worsened or if a patient required additional anti-diabetic medication.

Surgical technique. The patient was placed in the reverse Trendelenburg position (9), with the surgeon positioned between the patient's legs. General anesthesia supplied by mechanical ventilation (Oxylog 3000 plus; Dräger, Lübeck, Germany). Five ENDOPATH XCEL® trocars (Ethicon; Johnson & Johnson, New Brunswick, NJ, USA) were inserted under direct laparoscopic vision (Stryker 1188 HD autoclavable camera; Stryker Corporation, Kalamazoo, MI, USA). A ~30-ml gastric pouch was created using 2-0 mechanical sutures (Ethicon; Johnson & Johnson), preventing the transection of the left gastric artery. Subsequently, the angle of Treitz was identified, and a 100-cm long jejunal loop (biliopancreatic limb) was ascended anterior to the colon and anastomosed to the gastric pouch with mechanical linear suture (30 mm). A lateral jejuno-jejunal anastomosisadjacent to gastro-jejunal anastomosis was made at 100 cm from the previous nastomosis (alimentary limb), using an EC60A articulating stapler and a 6TB45 articulating linear cutter (Ethicon; Johnson & Johnson).

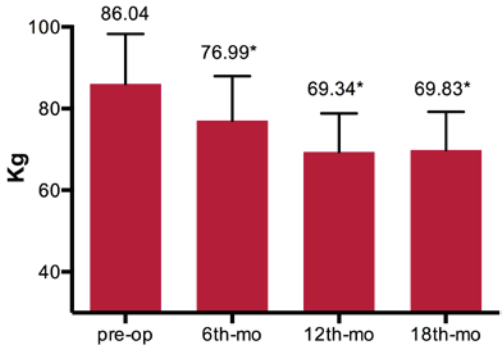

Figure 1. Mean patient body weight at pre-op and at 6, 12 and 18 mo following surgery. *P<0.01 vs. preoperative levels. Pre-op, preoperative; mo, month.

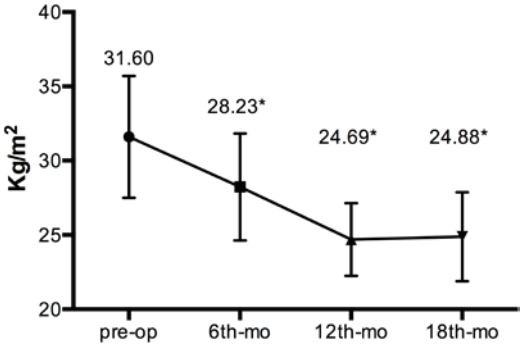

Figure 2. Mean patient body mass index at pre-op and at 6, 12 and 18 mo following surgery. *P<0.01 vs. preoperative levels. Pre-op, preoperative; mo, month.

Statistical analysis. Data extracted for this analysis included preoperative and postoperative body weight, BMI, blood glucose, HbA1c, BP and blood lipid. A weight loss outcome was indicated by a reduction in BMI. Blood lipid included cholesterol, triglycerides, high and low density lipoprotein (HDL and LDL). Comparisons among groups were performed by one-way analysis of variance followed by Tukey's multiple comparison test. Comparisons of means were performed using Student's *t*-test, and contingency tables of categorical variables were analyzed using Fisher's exact test. P<0.05 was considered to indicate a statistically significant difference, and 95% confidence interval (95% CI) was reported as a measure of precision. All statistical analyses were performed using SPSS statistical software, version 20.0 (IBM SPSS, Armonk, NY, USA).

Results

Preoperative patient demographics. The preoperative mean BMI was 31.60±4.10 kg/m^2 (range, 28.53-48.10 kg/m^2) and the mean percentage of body fat was 36.35±9.12% (range, 18-56%). The mean HbA1c was 8.32±2.13% (range, 7-15.9%).

Surgical success and complications. LRYGB was successfully completed in all patients. There were no cases of patient mortality; however, 5 patients (5.9%) developed complications.

Table I. Metabolic syndrome improvement following laparoscopic Roux-en-Y gastric bypass.

Parameter	Pre-operative	6 months	12 months	18 months
Waistline (cm)	104.26±11.51	95.37±9.48[a]	86.22±7.72[a]	86.40±8.00[a]
Hipline (cm)	107.42±9.64	100.80±7.85[a]	95.34±7.16[a]	95.40±6.08[a]
Waist-hip ratio	0.970±0.523	0.946±0.057[a]	0.905±0.051[a]	0.91±0.055[a]
Heartrate (bpm)	78.32±6.39	77.96±10.54	74.92±7.97[b]	71.70±7.43[b]
Cholesterol (mmol/l)	4.94±1.10	4.68±1.08	4.01±0.73[a]	3.97±0.57[a]
Triglycerides (mmol/l)	2.40±2.82	1.51±0.60[b]	1.14±0.47[a]	1.01±0.41[b]
HDL (mmol/l)	1.03±0.23	0.98±0.18	1.15±0.27[b]	1.13±0.27
LDL (mmol/l)	2.88±0.89	2.90±0.89	2.23±0.58[a]	2.20±0.53[a]

[a]P<0.01 and [b]P<0.05 vs. perioperative values. HDL, high density lipoprotein; LDL, low density lipoprotein.

Table II. Result of type 2 diabetes mellitus following laparoscopic Roux-en-Y gastric bypass.

Parameter	Pre-operative	6 months	12 months	18 months
FBG (mmol/l)	8.64±2.95	7.13±2.29[a]	5.78±1.29[a]	5.77±1.13[a]
PBG (mmol/l)	13.55±4.85	8.32±3.18[a]	7.73±3.22[a]	7.70±3.13[a]
HbA1c (%)	8.32±2.13	6.97±1.22[a]	6.10±0.85[a]	6.23±1.16[a]
GSP (%)	20.34±6.65	16.02±3.38[a]	16.41±3.01[a]	16.50±4.23[a]

[a]P<0.01 vs. perioperative values. FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1c, glycosylated hemoglobin; GSP, glycosylated serum protein.

One patient had intra-abdominal infection, another patient had stenosis of gastroenteric stoma, while the other 3 patients had intestinal obstruction which caused by intra-abdominal hernia. All the complications occurred in the first 30 patients, which was within the learning curve (9).

Postoperative follow-up. At the 18-month follow-up, a significant reduction in mean patient body weight was observed in comparison to the mean preoperative weight (P<0.01) (Fig. 1). The mean BMI decreased from 31.60±4.10 kg/m^2 preoperatively to 28.23±3.60, 24.69±2.45 and 24.88±2.99 kg/m^2 at the 6-, 12- and 18-month follow-up examinations, respectively (Fig. 2).

Metabolic syndrome indices. The changes in waistline (cm), hipline (cm) and waist-hip ratio in comparison to the mean preoperative weight were significant (P<0.01), which indicated a marked improvement in central obesity. The blood cholesterol levels were significantly decreased at the 12- and 18-month follow-up examinations (P<0.01) and triglycerides levels were decreased significantly at 6 (P=0.029), 12 (P=0.002) and 18 months (P=0.032) post-operation. HDL levels did not exhibit an evident change following surgery, while the LDL levels were significantly decreased at 12 (P=0.000) and 18 months (P=0.002) following surgery (Table I). The mean BPs (systolic/diastolic pressure, mmHg) decreased from 133.61±16.12/84.61±10.66 mmHg preoperatively to [127.22±15.91 mmHg (P=0.043)/79.67±8.46 mmHg (P=0.010)] at 6-months [124.87±16.12 mmHg (P=0.008)/77.58±8.68 mmHg (P=0.001)] at 12 months and [119.55±11.43 mmHg (P=0.001)/75.55±9.83 mmHg (P=0.004)] at 18 months post-operation (Fig. 3).

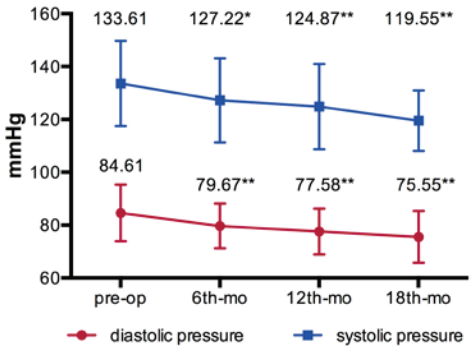

Figure 3. Mean patient systolic and diastolic blood pressure levels at pre-op and at 6, 12 and 18 mo following surgery. *P<0.05 and **P<0.01 vs. preoperative levels. Pre-op, preoperative; mo, month.

T2DM indices. Furthermore, the changes in fasting blood glucose, postprandial blood glucose, HbA1c and GSP in comparison to the mean preoperative levels were significant (P<0.01) (Table II). The fasting insulin levels (Ins 0') and 120 min postprandial insulin levels (Ins 120') were significantly decreased at 6, 12 and 18 months after surgery (P<0.01), while the 30 min postprandial insulin levels (Ins 30') were not significantly reduced (Fig. 4). The fasting C-peptide levels were decreased progressively without significant difference.

Table III. Assessment of nutritive status indices following laparoscopic Roux-en-Y gastric bypass.

Parameter	Pre-operative	6 months	12 months	18 months
Folic acid (ng/l)	8.57±3.07	15.06±16.00[a]	15.11±5.19[a]	14.94±5.40[a]
Vitamin B12 (ng/l)	580.30±293.91	763.72±373.64[a]	490.03±380.27	443.90±342.16
Serum iron (μmol/l)	16.95±5.60	14.27±4.70[a]	15.29±5.88	16.49±5.41
PTH (pg/ml)	37.97±14.63	52.06±18.33[a]	41.30±15.71[a]	46.37±15.14[a]
25(OH)D (ng/ml)	15.48±6.40	13.62±6.48	16.14±6.95	17.02±8.13

[a]P<0.05 vs. perioperative values. PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D.

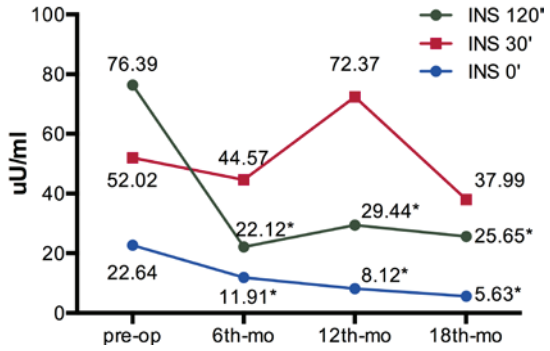

Figure 4. Mean patient insulin levels at pre-op and at 6, 12 and 18 mo following surgery. *P<0.01 vs. preoperative levels. Pre-op, preoperative; mo, month; Ins 0', fasting insulin; Ins 30', 30 min postprandial insulin; Ins 120', 120 min postprandial insulin.

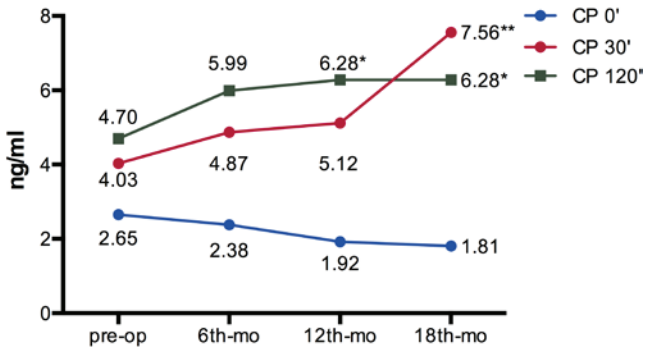

Figure 5. Mean patient C-peptide levels at pre-op and at 6, 12 and 18 mo following surgery. *P<0.05 and **P<0.01 vs. preoperative levels. Pre-op, preoperative; mo, month; CP 0', fasting C-peptide;30 CP 30', 30 min postprandial C-peptide; CP 120', 120 min postprandial C-peptide.

The 30 (CP 30') and 120 min postprandial (CP 120') C-peptide levels were increased at 6 months (P=0.380 for CP 30' and P=0.755 for CP 120'), 12 months (P=0.202 for CP 30' and P=0.036 for CP 120') and 18 months (P=0.001 for CP 30' and P=0.024 for CP 120') after surgery (Fig. 5).

Nutritive status indices. Serum folic acid, vitamin B12 and serum iron levels were detected as indicators of anemia. Furthermore, the levels of PTH and 25(OH)D indicated hypocalcemic status. All patients received follow-up examinations regularly in order to assess their nutritive status, and no malnutrition or severe anemia were observed as a result of the treatments (Table III).

Discussion

Diabetes encompasses a group of chronic progressive metabolic diseases that are characterized by hyperglycemia resulting from defects in insulin secretion or activity (10). Diabetes is grouped into four clinical classes, and T2DM is the most common form of diabetes worldwide.

In the medical management of T2DM, the aim of treatment is to achieve glycemic control in order to reduce complications; which differs from the potential novel end point of euglycemia that metabolic surgery offers (11).

A previous meta-analysis that summarized the diabetic outcomes of 3,188 patients reported a resolution rate of 80.3% using LRYGB, 95.1% after biliopancreatic diversion (BPD), and 56.7% after laparoscopic adjustable gastric banding in morbidly obese individuals (4). Metabolic surgery has been approved as an effective and potentially useful treatment for patients with T2DM and obesity (4,12). Although the precise mechanisms underlying the amelioration of diabetes following surgery are poorly understood, innovative procedures based on the current understanding of mechanisms, such as duodenojejunal bypass and ileal interposition have been investigated (13-16). Furthermore, bariatric surgery has been shown to result in a significant reduction in excess weight, an effective control of comorbidities and a significant reduction in long-term mortality (17-21).

Laparoscopic RYGBP was performed in the present study as the procedure has previously been shown to be a safe and effective, with low mortality rate (0.16-0.40%) (3) and a known morbidity rate (7.4%) (22). Although the exact mechanism remained unclear, prior studies have indicated that weight loss, malabsorptive surgery and change in gut hormone contributed the diabetes control (23,24). We recognize that the extent of excluded intestine is a point still under discussion. A previous study published by our group in 2010 showed the results in glycemic control of patients with T2DM that underwent total or subtotal gastrectomy and Roux-en-Y reconstruction with a 30-50-cm biliopancreatic limb and 70-cm alimentary limb, performed for an indication other than obesity (predominantly cancer), with a remission rate of 65% at two years of follow-up (25).

PTH may be an early detection index for a disorder of calcium-phosphate metabolism in patients with obesity and T2DM following Roux-en-Y gastric bypass (26). Sufficient supplement for relevant trace elements and regular follow-up are crucial postoperatively (27).

Previous studies on bariatric-metabolic surgery have produced novel perspectives for the treatment of T2DM (5,6,12). However, this therapeutic approach requires adjustment to further increase its effectiveness. In addition, the establishment of well-defined recommendations and guidelines for the clinical use and the definition of specific criteria for consideration of T2DM remission and control are required. Therefore, further multicenter studies are required to investigate the benefits of the surgery in different populations, by analyzing the procedures used and investigating the mechanisms involved, in order to propose a model for the development of a safe and effective surgical procedure for T2DM remission in patients with a BMI of <28 kg/m^2.

In conclusion, the results of the present study suggest that LRYGB may be introduced relatively safely on a larger scale in small hospitals; with acceptable complication and mortality rates, good short-term weight loss and a valuable ameliorative effect on T2DM. However, the effects of the learning curve could not be entirely avoided. In order to ensure the surgery outcome, an appropriate surgical team and standardized surgery is necessary, which required adequate experience in order to overcome the learning curve associated with performing surgery.

Acknowledgements

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