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# Comparison of Short- and Mid-term Efficacy and the Mechanisms of Gastric Bypass Surgeries on Managing Obese and Nonobese Type 2 Diabetes Mellitus: A Prospective Study

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*Background and Aims.* We targeted to investigate the efficacy and the mechanisms of two gastric bypass surgeries, Roux-en-y Gastric Bypass (RYGB) and Billroth II gastrojejunostomy on managing obese patients with T2DM and nonobese T2DM patients, respectively.

*Methods.* Seven nonobese T2DM patients with gastric cancer submitted to Billroth II gastrojejunostomy were compared with nine obese T2DM patients undergoing RYGB about their baseline characteristics, weight loss and glycemic control, 3 months and 2 years after surgery. Meanwhile, β-cell function, glucagon-like peptide 1 (GLP-1), peptide YY (PYY) and gastric inhibitory polypeptide (GIP) levels were also investigated.

*Results.* Significant weight loss and improvement of glycemic control were observed in both groups and in the two follow-up periods. Reduction of body mass index was greater in obese patients with T2DM. The efficacy of Billroth II gastrojejunostomy on controlling blood glucose of nonobese T2DM was similar to that of RYGB on managing obese T2DM. Insulin levels and HOMA-IR were decreased in obese T2DM patients, whereas they remained unchanged in nonobese T2DM patients. Generally, levels of GLP-1 and PYY were increased, whereas GIP levels were decreased in both groups.

*Conclusions.* Glycemic control efficacy of Billroth II gastrojejunostomy on managing nonobese T2DM is similar to that of RYGB on treating obese T2DM in the short- and mid-term. The underlying mechanisms of both surgeries may be related to weight loss and gut hormone modulations. 

*Key Words:* Type 2 diabetes mellitus, Roux-en-Y gastric bypass surgery, Billroth II gastrojejunostomy.

## Introduction

In past decades, bariatric surgery has attracted much attention because of its efficacy in controlling not only obesity but also diabetes (1). The underlying mechanisms are not fully understood. Much evidence suggests gut hormone changes contribute more than the weight loss effect (2–4). Therefore, the use of bariatric surgery to treat nonobese T2DM is of considerable interest. However, studies are limited because bariatric surgery is originally targeted to reduce body weight. It is unclear whether it will lead to underweight in nonobese T2DM.

Billroth II gastrojejunostomy is widely used in patients with gastric cancer or gastric ulcer. It performs a foregut diversion like the procedure of a popular bariatric surgery, gastric bypass procedure (GBP) does, so technically it is a

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similar type of GBP. Therefore, alternatively, nonobese T2DM patients who need to undergo Billroth II could participate in the investigations. In fact, several retrospective studies have reported remission of diabetes in T2DM patients with low BMI who underwent Billroth II gastrojejunostomy or anastomosis gastric bypass due to gastric cancer or gastric ulcer (5−7). However, the underlying mechanisms were not explored in these studies.

In our previous study (8) we prospectively evaluated the short-term glucose metabolism and gut hormone modulations in nonobese T2DM patients with gastric cancer after Billroth II gastrojejunostomy. Results suggest Billroth II gastrojejunostomy to be effective in managing nonobese T2DM in the short term and the mechanisms are attributed to gastric restriction, weight loss and alterations in gut hormones. Therefore, mechanisms responsible for the attenuation of diabetes are expected to be as similar as those found in GBP. In the present study we designed to prospectively investigate the 3-month and 2-year efficacy and the mechanisms of Billroth II on managing nonobese T2DM and to compare the results with RYGB-treated obese patients with T2DM.

## Subjects and Methods

### *Subjects*

Adult T2DM patients (aged 18−65 years) who were scheduled to undergo Billroth II gastrojejunostomy ($n = 7$) or lapascopic RYGB ($n = 9$) in West China Hospital of Sichuan University were recruited. Patients in the RYGB group were obese T2DM with BMI ≥27.5 kg/m$^2$ and with waist circumference ≥90 cm (male) or 85 cm (female), whereas those in Billroth II gastrojejunostomy group were nonobese T2DM with 18.5 kg/m$^2$ ≤BMI <27.5 kg/m$^2$ [referred to the World Health Organization (WHO) published obesity standard for Asian populations (9)] and with gastric cancer. T2DM was diagnosed according to the WHO standard criteria: fasting plasma glucose (FPG) ≥7.0 mmol/L or 2-h plasma glucose (PG) ≥11.1 mmol/L or glucose level determined by oral glucose tolerance test (OGTT) ≥11.1 mmol/L. Diabetes duration was limited as 0.5−10 years in RYGB group and 0−10 years in Billroth II gastrojejunostomy group. In addition, function in β-cell secretion was required. Specifically, the plasma fasting C-peptide should be over 1/2 of normal minimum value. In addition, the 2-h plasma C-peptide in OGTT should be more than two times when compared with that of baseline.

Participation in this study was voluntary and written informed consent was obtained from each participant. The guidelines of the Declaration of Helsinki (2000) of the World Medical Association were followed and the Research Ethics Committee of West China Hospital of Sichuan University approved the study (no. ChiECRCT-2010001).

Exclusion criteria of the obese group included type 1 diabetes mellitus, positive autoantibody to glutamic acid decarboxylase and islet cell autoantibody, severe hepatic and renal impairments, cardiovascular and cerebrovascular diseases, other endocrine system diseases, e.g., Cushing syndrome, respiratory dysfunction such as chronic obstructive pulmonary diseases, chronic consumptive diseases such as cancer, and gastrointestinal diseases, e.g., Crohn's disease. Meanwhile, women who were pregnant or lactating were also excluded. Those patients who were clinically verified as having a metastatic neoplasm or cachexia in the nonobese group were excluded.

### *Preoperative Assessment*

Before surgery, the patients' status was evaluated by a multidisciplinary surgical team. In addition, baseline characteristics, which included age, BMI, duration of T2DM, blood glucose, glycosylated hemoglobin (HbA1c), insulin levels, homeostatic model assessment of insulin resistance (HOMA-IR), early phase insulin secretion index (ΔI30/ΔG30) and use of anti-hyperglycemic medications were examined. Additionally, fasting gut hormones, namely, glucagon-like peptide 1 (GLP-1), peptide YY (PYY) and gastric inhibitory polypeptide (GIP) and their responses to 75g oral glucose were also measured.

### *Surgical Technique*

*Billroth II gastrojejunostomy.* The surgical procedure for Billroth II gastrojejunostomy begun with subtotal gastrectomy regarding the location of carcinoma and left a 20−30% gastric volume in which the fundus could be included. The remnant stomach was then anastomosed to the distal jejunum 30 cm away from the ligament of Treitz.

*RYGB.* The surgical procedure for the RYGB begun with a creation of a 25−50 mL pouch divided from the proximal lesser curvature of the stomach and the fundus was excluded. The pouch was then anastomosed to a Roux limb of jejunum created by the division of the jejunum 75−100 cm distally to the ligament of Treitz. Finally, the proximal jejunal stump was anastomosed to the distal jejunum 100−150 cm from the gastrojejunum anastomosis. The vagal nerves were carefully identified and preserved.

### *Follow-up Criteria*

Three months and also 2 years after surgery, patients returned to the hospital to reexamine the BMI, blood glucose, insulin, C-peptide and gut hormone levels. In order to compare the efficacy of the two surgeries on glycemic control, we evaluated the diabetes remission rate. In specific, complete remission (CR) standards were off diabetes medications, FPG ≤7.0 mmol/L, 2-h PG ≤10.0 mmol/L and HbA1c ≤6.5%. The standards for partial remission (PR)