Comparison of different gastric bypass procedures in gastric carcinoma patients with type 2 diabetes mellitus

Shao-Wei Xiong, Dong-Yun Zhang, Xian-Ming Liu, Zeng Liu, Fang-Ting Zhang

Shao-Wei Xiong, Xian-Ming Liu, Zeng Liu, Department of General Surgery, Peking University Shenzhen Hospital, Shenzhen 518036, Guangdong Province, China
Dong-Yun Zhang, Department of Chronic Noncommunicable Diseases, Baoan District Chronic Diseases Hospital, Shenzhen 518133, Guangdong Province, China
Fang-Ting Zhang, Central Laboratory, Peking University Shenzhen Hospital, Shenzhen 518036, Guangdong Province, China

Author contributions: Xiong SW designed the research; Xiong SW, Liu XM, and Liu Z performed the research; Xiong SW and Zhang DY analyzed data and wrote the paper; and Zhang FT revised the paper.

Supported by The Basic Research Projects of Shenzhen R&D Funding in Science and Technology, No. JCYJ20130402113802233 and No. JCYJ201005260209A

Correspondence to: Fang-Ting Zhang, Senior Technologist, Central Laboratory, Peking University Shenzhen Hospital, 1120 Lian Hua Road, Shenzhen 518036, Guangdong Province, China. fangtingzhang@126.com

Telephone: +86-755-83923333-3519 Fax: +86-755-83923333
Received: June 12, 2014 Revised: August 1, 2014 Accepted: September 12, 2014 Published online: December 28, 2014

Abstract

AIM: To determine the effect of different Roux-en-Y gastric bypass procedures in gastric carcinoma patients with type 2 diabetes mellitus.

METHODS: A retrospective analysis of the clinical data of 54 patients with gastric cancer and type 2 diabetes mellitus treated in the Department of General Surgery from January 2006 to June 2013 was conducted. The patients underwent gastrectomy using different Roux-en-Y gastric bypass procedures (traditional, n = 26; modified, n = 28). Fasting plasma glucose (FPG), two hour postprandial blood glucose (2 h PBG) and hemoglobin A1C (HbA1c) were analyzed before surgery (0 mo) and 1, 3 and 6 mo after surgery.

RESULTS: FPG and 2 h PBG levels were significantly decreased 1 mo after surgery in the traditional Roux-en-Y gastric bypass group (FPG 7.5 ± 1.3 vs 10.7 ± 1.2, P < 0.05) (2 h PBG 10.2 ± 1.8 vs 13.8 ± 3.2, P < 0.05). FPG and 2 h PBG levels were significantly decreased after surgery in the modified Roux-en-Y gastric bypass group (FPG 6.9 ± 1.2 vs 10.5 ± 1.1, 6.5 ± 1.3 vs 10.5 ± 1.1, 6.4 ± 1.2 vs 10.5 ± 1.1, P < 0.05) (2 h PBG 9.9 ± 2.2 vs 14.1 ± 2.9, 9.2 ± 2.4 vs 14.1 ± 2.9, 8.9 ± 2.6 vs 14.1 ± 2.9, P < 0.05). Compared with the levels before surgery, HbA1c levels were significantly decreased 3 and 6 mo after surgery (7.2 ± 1.1 vs 10.5 ± 1.1, 5.5 ± 1.1 vs 10.5 ± 1.1, P < 0.05). Significant differences between the two groups regarding FPG, 2 h PBG and HbA1c concentration were observed 3 and 6 mo after surgery (FPG 10.1 ± 1.5 vs 6.5 ± 1.3, 10.3 ± 1.4 vs 6.4 ± 1.2, P < 0.05) (2 h PBG 13.1 ± 2.8 vs 9.2 ± 2.4, 13.6 ± 3.1 vs 8.9 ± 2.6, P < 0.05) (HbA1c 10.1 ± 1.4 vs 7.2 ± 1.1, 10.5 ± 1.3 vs 5.5 ± 1.1, P < 0.05).

CONCLUSION: Modified Roux-en-Y gastric bypass can improve glucose metabolism in type 2 diabetic patients with gastric cancer.

Key words: Roux-en-Y gastric bypass; Type 2 diabetes mellitus; Gastric cancer; Fasting plasma glucose; Hemoglobin A1C

Core tip: Type 2 diabetes mellitus (T2DM) is a common chronic disease and is a threat to public health. Modified Roux-en-Y gastric bypass surgery, which results in weight loss and a hypoglycemic effect, has been used in the treatment of patients with T2DM and obesity. However, the therapeutic mechanism involved is unclear. The aim of this study was to evaluate the efficacy of two Roux-en-Y gastric bypass procedures (traditional and modified) on blood glucose control in patients with T2DM and gastric cancer. It is suggested that modified Roux-en-Y gastric bypass may improve glucose metabolism in T2DM patients more effectively than the traditional procedure.
INTRODUCTION

Type 2 diabetes mellitus (T2DM) is the most common form of diabetes \[^{[1]}\]. It is frequently seen in the patients who undergo surgery. Modified gastric bypass surgery, based on traditional Roux-en-Y digestive tract reconstruction was initiated to treat obese patients in the 1990s \[^{[2]}\]. It was later found that this procedure was also effective in patients with T2DM \[^{[3]}\], and the efficiency of this procedure reached 83\% \[^{[4-11]}\], although the therapeutic mechanism involved is still unclear. Traditional Roux-en-Y digestive tract reconstruction is a technique commonly used in gastric cancer surgery, and it is unclear whether it has a hypoglycemic effect in patients with T2DM as there is a lack of research in this field. In this study, we retrospectively analyzed blood glucose control in patients with T2DM and gastric cancer who underwent gastrectomy of stomach neoplasms using either modified or traditional Roux-en-Y gastric bypass surgery.

MATERIALS AND METHODS

**General data**

A retrospective analysis of the clinical data of 54 patients with gastric cancer and T2DM in the Department of General Surgery from January 2006 to June 2013 was conducted. The patients underwent gastrectomy of stomach neoplasms using two Roux-en-Y gastric bypass procedures (traditional, \(n = 26\) or modified, \(n = 28\)). Follow-up data were complete. The patients in this study were diagnosed with T2DM in accordance with the diagnostic criteria of the American Diabetes Association (2003). Specific parameters measured were as follows: symptoms of diabetes mellitus, random blood glucose \(\geq 11.1 \text{ mmol/L} \), fasting plasma glucose \(\geq 7.0 \text{ mmol/L} \) and an oral glucose tolerance test at 2 h \(\geq 11.1 \text{ mmol/L} \). If the patients met one of the above conditions, and a retest the following day conformed to the standards of the diagnosis of diabetes, the patient was then diagnosed with diabetes mellitus. Islet cell antibodies, antibody to insulin, glutamic acid decarboxylase antibody, glycosylated hemoglobin A1c (HbA1c) and C peptide level were examined to define T2DM. All patients were diagnosed with gastric cancer by gastrointestinal biopsy and a pathology report prior to surgery. The gender, age, duration of diabetes and tumor TNM stage of patients in the two surgical groups was comparable (\(P > 0.05\)).

**Statistical analysis**

The measurement data were expressed as the mean \(\pm\) SD. Statistical analyses were performed by the \(T\) test using SPSS 17.0 (SPSS Inc., Chicago, IL, United States). The count data were determined by the \(\chi^2\) test. \(P\)-values of \(< 0.05\) were considered statistically significant.

RESULTS

Compared with the preoperative FPG and 2 h PBG levels, in the traditional surgery group these levels decreased 1 mo after surgery (\(P < 0.05\), however, 3 and 6 mo after surgery these values were gradually restored to preoperative levels. The HbA1c level after 1, 3 and 6 mo was not significantly reduced (\(P > 0.05\)). In the modified surgery group, the FPG and 2 h PBG levels at 1, 3 and 6 mo after surgery and the HbA1c levels at 3 and 6 mo decreased significantly (\(P < 0.05\)). When the FPG, 2 h PBG and HbA1c levels at the same time point were compared between the two groups, the differences were not statistically significant at 1 mo after surgery, however, the differences at 3 and 6 mo after surgery were statistically significant (\(P < 0.05\)) (Table 1, Figure 1).

DISCUSSION

According to statistics, 90\%-95\% of patients with DM have T2DM. At present, DM is the third most common chronic non-communicable disease in humans after...
tumors and cardiovascular disease, and the incidence rate is rising each year. Patients for surgical operation are frequently complicated with T2DM. DM has various etiological factors and complicated mechanisms; therefore, curing DM has become an urgent global medical goal. During the 1990’s, modified Roux-en-Y reconstruction of the digestive tract also known as gastric bypass surgery (GBP) for the treatment of severe obesity resulted in a good outcome. Thus, GBP has now become the standard surgical technique for obesity. Surprisingly, GBP has a good hypoglycemic effect in obese patients with T2DM. Previous research showed that 83%-86% of T2DM patients maintained normal levels of blood glucose following GBP[13,14]. In a follow-up study, Patriti et al[15] showed that this surgical procedure was also efficacious in T2DM patients without obesity. Therefore, GBP surgery for T2DM was widely used in the hope of curing patients with T2DM.

### Table 1  Comparison of fasting plasma glucose, two hour postprandial blood glucose and hemoglobin A1c levels between the two surgical groups

|                | 0 mo     | 1 mo     | 3 mo     | 6 mo     |
|----------------|----------|----------|----------|----------|
| **n**          | FPG mmol/L | 2 h PBG mmol/L | HbA1c%     | FPG mmol/L | 2 h PBG mmol/L | HbA1c%     | FPG mmol/L | 2 h PBG mmol/L | HbA1c%     |
| **Traditional group** | 26       | 10.7±1.2 | 13.8±3.2 | 10.7±1.2 | 7.5±1.3  | 9.8±1.1  | 10.1±1.5 | 13.1±2.8  | 10.1±1.4  |
| **Modified group**  | 28       | 10.5±1.1 | 14.1±2.9 | 10.5±1.1 | 6.9±1.2  | 9.9±2.2  | 10.2±1.3 | 9.2±2.4   | 7.2±1.1   |

Data are shown as mean ± SD. ’P < 0.05 vs the before surgery (0 mo) group; ’P < 0.05 vs the modified group at the same time. HbA1c: Hemoglobin A1c; FPG: Fasting plasma glucose; PBG: Postprandial blood glucose.

![Figure 1](image-url)  
**Figure 1** Comparison of fasting plasma glucose, two hour postprandial blood glucose and hemoglobin A1c levels between the two surgical groups. A: Fasting plasma glucose (FPG) level; B: Two hour postprandial blood glucose (2hPBG) level; C: Hemoglobin A1c (HbA1c) level.
has a hypoglycemic effect requires further investigation.

Traditional Roux-en-Y reconstruction of the digestive tract is a common technique in gastric cancer, and some patients with gastric cancer also have T2DM, therefore, research on the hypoglycemic effect of traditional digestive tract reconstruction is important and may provide a theoretical basis for patients undergoing Roux-en-Y digestive tract reconstruction.

In the present study, we compared the hypoglycemic effect of two types of Roux-en-Y digestive tract reconstruction. We found that in the traditional surgery group, FPG and 2 h PBG levels decreased 1 mo after surgery compared with preoperative levels, however, FPG and 2 h PBG levels were gradually restored to the level before surgery after 3 and 6 mo. The HbA1c level after 1, 3 and 6 mo was not significantly decreased. In the modified surgery group, the FPG, 2 h PBG levels at 1, 3 and 6 mo after surgery and the HbA1c levels at 3 and 6 mo after surgery decreased significantly. A comparison of the FPG, 2 h PBG and HbA1c levels at the same time point between the two groups, showed no statistically significant differences at 1 mo after surgery, however, statistically significant differences at 3 and 6 mo after surgery were observed. This indicated that traditional digestive tract reconstruction had a hypoglycemic effect in the short-term, but did not last, thus this hypoglycemic effect was not ideal. The modified digestive tract reconstruction procedure had a better hypoglycemic effect and lasted longer. Many researchers have investigated this hypoglycemic mechanism. At present, there are many hypotheses related to this mechanism, including gastric inhibitory peptide (GIP) which is the core of the “foregut hypothesis” and glucagon-like peptide-1 (GLP-1) which is the core of the “hindgut hypothesis” which have received significant attention. The “foregut hypothesis” considers that food in the duodenum and proximal jejunum stimulate the production of GIP, thus improving insulin resistance. The “hindgut hypothesis” considers that chyme in the terminal ileum and colon promotes the secretion of GLP-1, and stimulates the secretion of glucose-dependent insulin, which improves the insulin effect and the proliferation of islet B cells.

Following the modified digestive tract reconstruction procedure, food no longer flows through the distal stomach, duodenum and proximal jejunum, and directly enters the distal jejunum then the ileum, thereby reducing the secretion of GIP and stimulating GLP-1, which alters peripheral endocrine factors and the role of islet cells and related target organs. Thus resulting in better regulation of blood glucose.

REFERENCES
1. Rubino F. Is type 2 diabetes an operable intestinal disease? A provocative yet reasonable hypothesis. Diabetes Care 2008; 31 Suppl 2: S290-S296. [PMID: 18227499 DOI: 10.2337/dc08-s271]
2. Wittgrove AC, Clark GW, Tremblay LJ. Laparoscopic Gastric Bypass, Roux-en-Y: Preliminary Report of Five Cases. Obes Surg 1994; 4: 353-357. [PMID: 10742801 DOI: 10.1381/01381-0960892 9476558331]
3. Buchwald H, Estok R, Fahrbach K, Banel D, Jensen MD, Pories WJ, Bantle JP, Sledge I. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 2009; 122: 248-256.e5. [PMID: 19272486 DOI: 10.1016/j.amjmed.2008.09.041]
4. Yip K, Heinberg L, Giegerich V, Schauer PR, Kashyap SR. Equivalent weight loss with marked metabolic benefit observed in a matched cohort with and without type 2 diabetes 12 months following gastric bypass surgery. Obes Surg 2012; 22: 1723-1729. [PMID: 22895804 DOI: 10.1007/s11695-012-0719-8]
5. Mingrone G, Faunzni S, De Gaetano A, Guidone C, Iaconelli A, Lecci E, Nanni G, Pomp A, Castagneto M, Ghirlanda G, Rubino F. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med 2012; 366: 1577-1585. [PMID: 22440317 DOI: 10.1056/NEJMoa1201111]
6. Lee WJ, Hur KY, Lakadawala M, Kasama K, Wong SK, Lee YC. Gastrointestinal metabolic surgery for the treatment of diabetic patients: a multi-institutional international study. J Gastrointest Surg 2012; 16: 45-51; discussion 51-52. [PMID: 22042564 DOI: 10.1007/s11605-011-1740-2]
7. Raj PP, Kumaravel R, Chandramaliteeswaran C, Vaiithiswaran V, Palanivelu C. Laparoscopic duodenoejunal bypass with sleeve gastrectomy: preliminary results of a prospective series from India. Surg Endosc 2012; 26: 688-692. [PMID: 21993937 DOI: 10.1007/s00464-011-2938-0]
8. Reoch J, Mottillo S, Shimony A, Filion KB, Christou NV, Joseph L, Poirier P, Eisenberg MJ. Safety of laparoscopic vs open bariatric surgery: a systematic review and meta-analysis. Arch Surg 2011; 146: 1314-1322. [PMID: 22106325 DOI: 10.1001/archsurg.2011.270]
9. Hirao M, Takiguchi S, Imamura H, Yamamoto K, Kurokawa Y, Fujita J, Kobayashi K, Kimura Y, Mori M, Doki Y. Comparison of Billroth I and Roux-en-Y reconstruction after

COMMENTS
Background
Type 2 diabetes mellitus (T2DM) is one of the most serious diseases that threaten public health. Modified Roux-en-Y gastric bypass surgery, which has better weight loss and hypoglycemic effect, has been applied to the treatment of T2DM patients with obesity. However, the therapeutic mechanism to this function is still unclear due to the lack of research in this field.

Research frontiers
Modified gastric bypass surgery, based on traditional Roux-en-Y digestive tract reconstruction was initiated to treat obese patients in the 1990s. It was later found that this procedure was also effective in patients with T2DM, and the efficiency of this procedure reached 83%, although the therapeutic mechanism involved is still unclear.

Innovations and breakthroughs
The aim of this study was to test the efficacy of traditional and modified Roux-en-Y gastric bypass surgeries on blood glucose control of the patients with type 2 diabetes mellitus and gastric cancer. It is suggested that modified Roux-en-Y gastric bypass may improve glucose metabolism to T2DM patients more effectively than the traditional operation mode may do.

Applications
Modified Roux-en-Y gastric bypass could provide a better hypoglycemic support to type 2 diabetic patients with gastric cancer. This gastric bypass procedure may provide a potential alternative for patients.

Peer review
Authors reported that in this study, patients with gastric cancer and type 2 diabetes mellitus underwent gastrectomy using different Roux-en-Y gastric bypass procedures. The results indicated that modified Roux-en-Y gastric bypass may improve glucose metabolism in T2DM patients more effectively than the traditional procedure. This is very important to know for the clinical setting and educators in the world.
distal gastrectomy for gastric cancer: one-year postoperative effects assessed by a multi-institutional RCT. *Ann Surg Oncol* 2013; 20: 1591-1597 [PMID: 23104705 DOI: 10.1245/s10434-012-2704-9]

10 Sano T, Aiko T. New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points. *Gastric Cancer* 2011; 14: 97-100 [PMID: 21573921 DOI: 10.1007/s10120-011-0040-6]

11 Songun I, Putter H, Kranenbarg EM, Sasaki M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol* 2010; 11: 439-449 [PMID: 20409751 DOI: 10.1016/S1470-2045(10)70070-X]

12 Spanou M, Tziomalos K. Bariatric surgery as a treatment option in patients with type 2 diabetes mellitus. *World J Diabetes* 2013; 4: 14-18 [PMID: 23593531 DOI: 10.4239/wjd.v4.i2.14]

13 Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, Thomas S, Aboud B, Nissen SE, Bhatt DL. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med* 2012; 366: 1567-1576 [PMID: 22449319 DOI: 10.1056/NEJMoa1200225]

14 Lee WJ, Chong K, Ser KH, Lee YC, Chen SC, Chen JC, Tsai MH, Chuang LM. Gastric bypass vs sleeve gastrectomy for type 2 diabetes mellitus: a randomized controlled trial. *Arch Surg* 2011; 146: 143-148 [PMID: 21339423 DOI: 10.1001/archsurg.2010.326]

15 American Diabetes Association. Standards of medical care in diabetes—2013. *Diabetes Care* 2013; 36 Suppl 1: S1-S66

16 An JY, Kim YM, Yun MA, Jeon BH, Noh SH. Improvement of type 2 diabetes mellitus after gastric cancer surgery: short-term outcome analysis after gastrectomy. *World J Gastroenterol* 2013; 19: 9410-9417 [PMID: 24409070 DOI: 10.3748/wjg.v19.i48.9410]

17 Rao RS, Kini S. GIP and bariatric surgery. *Obes Surg* 2011; 21: 244-252 [PMID: 21082290 DOI: 10.1007/s11695-010-0305-x]

18 Bose M, Oliván B, Teixeira J, Pi-Sunyer FX, Laferrière B. Do incretins play a role in the remission of type 2 diabetes after gastric bypass surgery? What are the evidence? *Obes Surg* 2009; 19: 217-229 [PMID: 18820978 DOI: 10.1007/s11695-008-0969-3]

19 Laferrière B, Heslka S, Wang K, Khan Y, McGinty J, Teixeira J, Hart AB, Oliván B. Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. *Diabetes Care* 2007; 30: 1709-1716 [PMID: 17416796 DOI: 10.2337/dc06-1549]

20 Vetter ML, Cardillo S, Rickels MR, Iqbal N. Narrative review: effect of bariatric surgery on type 2 diabetes mellitus. *Ann Intern Med* 2009; 150: 94-103 [PMID: 19153412 DOI: 10.7326/0003-4819-150-2-200901200-00007]

21 Chen MC, Lee YC, Lee WL, Liu HL, Ser KH. Diet behavior and low hemoglobin level after laparoscopic mini-gastric bypass surgery. *Hepatogastroenterology* 2012; 59: 2530-2532 [PMID: 23178620 DOI: 10.5754/hge10757]

22 Abdelmalak B, Ibrahim M, Yared JP, Modic MB, Nasr C. Perioperative glycemic management in insulin pump patients undergoing noncardiac surgery. *Curr Pharm Des* 2012; 18: 620-6214 [PMID: 22762462 DOI: 10.2174/13816121280383271]

23 Aroda VR, Henry RR, Han J, Huang W, DeYoung MB, Darsow T, Hoogwerf BJ. Efficacy of GLP-1 receptor agonists and DPP-4 inhibitors: meta-analysis and systematic review. *Clin Ther* 2012; 34: 1247-1258.e22 [PMID: 22608780 DOI: 10.1016/j.clinthera.2012.04.013]

24 Park YJ, Ao Z, Kieffer TJ, Chen H, Safi Khan N, Thompson DM, Meloche M, Warneck GL, Marzban L. The glucagon-like peptide-1 receptor agonist exenatide restores impaired pro-islet amyloid polypeptide processing in cultured human islets: implications in type 2 diabetes and islet transplantation. *Diabetologia* 2013; 56: 508-519 [PMID: 23262664 DOI: 10.1007/s00125-012-2802-a]

25 Guo N, Sun J, Chen H, Zhang H, Zhang Z, Cai D. Liraglutide prevents diabetes progression in prediabetic OLETF rats. *Endocr J* 2013; 60: 15-28 [PMID: 22986487 DOI: 10.1507/endocrj.EJ10094]

26 Hamilton R, Thai XC, Ameri D, Pai MP. Oral bioavailability of linezolid before and after Roux-en-Y gastric bypass surgery: is dose modification necessary in obese subjects? *J Antimicrob Chemother* 2013; 68: 666-673 [PMID: 23160755 DOI: 10.1093/jac/dkt431]

P- Reviewer: Izawa KP  S- Editor: Gou SX  L- Editor: A
E- Editor: Zhang DN
