The Effect of Roux-en-Y Reconstruction on Type 2 Diabetes in the Early Postoperative Period

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Abstract. *Aim: The aim of this study was to investigate the effect of Roux-en-Y (RY) reconstruction on type 2 diabetes with gastric cancer in the early postoperative period. Patients and Methods: A total of 44 patients with gastric cancer with type 2 diabetes who underwent total gastrectomy (TG) or distal gastrectomy (DG) with Roux-en-Y reconstruction or DG with Bilroth I were enrolled. All three groups had their fasting glucose and daily insulin dose recorded preoperatively, on day 2 postoperatively (POD2) and at discharge. Results: The TG group showed low fasting glucose and daily insulin dose on POD2 compared to their preoperative state. On discharge, the fasting glucose and daily insulin dose were significantly lower in both TG and DG Roux-en-Y groups than preoperatively. Conclusion: Roux-en-Y reconstruction showed early improvement of type 2 diabetes regardless of any body weight loss. The effect of Roux-en-Y reconstruction in TG on type 2 diabetes was more remarkable than that of DG.*

Diabetes mellitus is the third most common chronic non-communicable disease in the world and in Japan (1). This metabolic disease is characterized by elevated blood glucose and is caused by insulin insufficiency or dysfunction (2). Type 2 diabetes affects the metabolism of other tissues and organs, leading to a series of complications with severe consequences for quality of life (3, 4).

Recently, bariatric surgery has been adapted for morbid obesity or obesity with related co-morbidities such as type 2 diabetes and hyperlipidemia (5). A systematic review and meta-analysis showed an improvement in 76.8% of patients with type 2 diabetes who underwent bariatric surgery (6). In our

previous report, duodenal-jejunal bypass was shown to improve type 2 diabetes and liver steatosis by enhancing glucagon like peptide-1 (GLP1) secretion through increasing serum bile acids and the proliferation of L cells in the ileum (7).

Few studies have reported the improvement of type 2 diabetes in patients with gastric cancer after gastrectomy (8). However, the effect in the early postoperative period remains unclear. The aim of this study was to investigate the effect of Roux-en-Y (RY) reconstruction on type 2 diabetes in the early postoperative period.

Patients and Methods

From January 2012 through December 2015, 44 patients with type 2 diabetes (37 men and seven women; mean age 70 years; age range from 51 to 88 years) were referred to our Institution for treatment of gastric cancer.

Thirty-five patients with gastric cancer with type 2 diabetes who underwent gastrectomy with RY [(total gastrectomy (TG)=20; distal gastrectomy (DG)=15) and nine with Bilroth I (B-I) reconstruction. The patients underwent DG with Bilroth I or RY reconstruction, or TG with RY reconstruction according to the size and location of the tumor. In RY reconstruction, the jejunum was divided at 20 cm distal from the Treitz ligament; the distal limb of the jejunum was anastomosed to the esophagus; and jejuno-jejunostomy was performed at 40 cm distal from the esophago-jejunal anastomosis.

After gastrectomy, the patients were given only water to drink for the first 2 days postoperatively. On day 4 postoperatively they started eating. When recovery proceeded according to plan, they were discharged from our hospital on day 10 to 14 postoperatively.

Statistical analysis. The paired t-test or Bonferroni's test were used for statistical analysis of the three groups in the patient characteristics, fasting glucose, daily insulin dose and changes in body weight. For all tests, a value of $p < 0.05$ was interpreted as significant. Values for continuous variables are expressed as the mean $\pm$ the standard deviation (SD).

Results

Table I shows the characteristics of the patients in the three groups. There was no significant difference in body mass index (BMI), hemoglobin A1c (HbA1c) and the use of anti-

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diabetic agents. However, the proportion of patients who underwent laparoscopic surgery in the B-I group was significantly higher in than the other two groups.

Figure 1 shows the time-dependent change in fasting glucose level after gastrectomy in the three groups. In the TG RY group, the fasting glucose level on day 2 postoperatively (POD2) was significantly lower than that recorded preoperatively ($p<0.05$). The level was reduced by 9%. The TG RY group also showed further decrease of fasting glucose on discharge. Although the fasting glucose level of the DG RY group did not significantly differ preoperatively from that at POD2 ($p=0.23$), at discharge it was significantly lower than preoperatively ($p<0.01$). However, the B-I group did not show this effect (both $p>0.05$).

Figure 2 shows time-dependent change in daily insulin dose after gastrectomy in the three types of reconstruction. On POD2, the daily insulin dose for the TG RY group was significantly lower compared with that recorded preoperatively ($p<0.05$). DG RY and B-I groups did not show this effect. Daily insulin dose on discharge from hospital was significantly lower compared with that recorded preoperatively for all groups ($p<0.05$).

In the three groups, there was no significant difference regarding changes in patient body weight during their stay in hospital ($p>0.05$; Figure 3).

Discussion

This study was designed to investigate the effect of RY reconstruction on type 2 diabetes in the early postoperative period. The fasting glucose and daily insulin dose of the TG RY group on POD-2 were significantly lower than that recorded preoperatively regardless of body weight loss. However, the DG RY and B-I reconstruction led to an early postoperative improvement of type 2 diabetes.

Several studies reported that patients with type 2 diabetes had a high risk of malignant tumors, especially colorectal, liver, pancreatic, breast, endometrial and bladder cancer (9-13). The risk of gastric cancer is also increased in patients with type 2 diabetes (14). Wei *et al.* reported that pre-existing diabetes was associated with poor postoperative prognosis when the diabetes became worse after curative gastrectomy for gastric cancer (15). Insulin was found to enhance the effect of epidermal growth factor on the proliferation of gastric epithelial cells (16). Yoshizawa *et al.* demonstrated that hyperinsulinemia and hyperleptinemia promote gastric carcinogenesis (17). Regarding gastric cancer, patients with uncontrolled type 2 diabetes might have more progressive tumors and worse prognosis. However, patients with cured or improved type 2 diabetes after radical gastrectomy are reported to show better prognosis than patients with worsened or same status of type 2 diabetes (5-year overall survival rate: 62.1% vs. 23.4% respectively) (15).

Table I. Characteristics of patients in the three groups.

Factors	TG (RY) (n=20)	DG (RY) (n=15)	DG (B-I) (n=9)
Age, years	72 (51-88)	68 (58-81)	71 (66-80)
Gender			
Male	18	12	7
Female	2	3	2
BMI (kg/m ²)			
Median (range)	24.7 (18.4-36.5)	24.7 (19-30.3)	23.6 (19.8-25.9)
HbA1c (%)			
Median (range)	7.1 (6.3-8.6)	7.0 (6.2-9.1)	6.6 (6.3-7.5)
Anti-diabetic agent (n)			
None	8	690	450
Oral	11		
Insulin	1		
Approach (n)			
Open	17	7	0
Laparoscopy	3	8	9
Stage (n)			
I	8	8	8
II	4	4	1
III	4	1	0
IV	4	2	0
Complications (n)*			
Yes	1	0	0
No	19	15	9

B-I: Bilroth I reconstruction; BMI: body mass index; DG: distal gastrectomy; RY: Roux-en-Y reconstruction; TG: total gastrectomy; HbA1c: hemoglobin A1c. *Clavien-Dindo grade III or more.

In a previous study, the rates of improvement of type 2 diabetes in patients who underwent DG with B-I or B-II, and TG with RY reconstruction at 1 month postoperatively were 23.0, 52.3, and 82.5%, respectively (18). Our study also showed the effect of TG RY on type2 diabetes was more remarkable than that of DG RY, as can be seen from Figures 1 and 2. However, as no report regarding the early postoperative effect of RY on type 2 diabetes exists as far as we aware, this study is the first report of the effect of RY reconstruction on type 2 diabetes in the early postoperative period.

Several types of bariatric surgery, including sleeve gastrectomy, gastric banding and gastric bypass, are currently performed and these procedures have showed not only body weight loss but also improvement of type 2 diabetes (19). Seki *et al.* reported that a case with sleeve gastrectomy with duodenojejunal bypass had a glucose level below 200 mg/ml 100% of the time after POD3 and no diabetic medication on or after POD2 (20). Sleeve gastrectomy suppressed plasma ghrelin and increased insulin, GLP1 and peptide YY, whereas duodenal jejunal bypass increased ghrelin, insulin, GLP1 and peptide YY (21).

Figure 1. The time-dependent change of fasting glucose level after three types of reconstruction with gastrectomy for patients with gastric cancer. RY: Roux-en-Y reconstruction; TG: total gastrectomy; DG: distal gastrectomy; B-I: Bilroth I reconstruction; POD2: postoperative day 2. Boxes indicate the interquartile range, bars indicate the SD, lines indicate the median, and circles indicate the outlier.

Figure 2. Daily insulin dose during hospital stay after three types of reconstruction with gastrectomy for patients with gastric cancer. RY: Roux-en-Y reconstruction; TG: total gastrectomy; DG: distal gastrectomy; B-I: Bilroth I reconstruction; POD2: postoperative day 2. Boxes indicate the interquartile range, bars indicate the SD, lines indicate the median, and circles indicate the outlier.

Figure 3. Body weight change during hospital stay after three types of reconstruction with gastrectomy for patients with gastric cancer. RY: Roux-en-Y reconstruction; TG: total gastrectomy; DG: distal gastrectomy; B-I: Bilroth I reconstruction; POD2: postoperative day 2. Boxes indicate the interquartile range, bars indicate the SD, lines indicate the median, and circles indicate the outlier.

Ghrelin is well-known to be secreted by the empty (fasting) stomach in order to enhance food intake (22). Endocrine ghrelin cells are located in the fundus and body of the stomach (23). Ghrelin directly interacts with islet β -cells, which leads to suppression of insulin release (24). Regarding the difference between TG RY and DG RY in the improvement of diabetes, a lower level of ghrelin after TG compared with that after DG might lead to higher secretion of insulin.

Bypass surgery improved type 2 diabetes *via* enhanced GLP1, which stimulate insulin secretion (7). Regarding the difference between RY and B-I with DG in the improvement of diabetes, a higher level of GLP1 after RY compared to that after B-I might lead to higher secretion of insulin.

In conclusion, RY reconstruction showed early improvement of type 2 diabetes regardless of body weight loss. The effect of TG RY on diabetes was more remarkable than that of DG RY.

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