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術前DCF療法が著効した食道原発内分泌細胞癌の1切除例	前田 直見, 白川 靖博, 國府島 健, 大原 利章, 田邊 俊介, 野間 和広, 櫻間 教文, 藤原 俊義	*岡山医学会雑誌*	126(1):39-43 2014	国内

【食道癌・胃癌におけるロボット支援手術の有用性】ロボット支援下噴門側胃切除術後のロボットによる体腔内手縫い食道残胃吻合	西崎 正彦，黒田 新士，岸本 浩行，野間 和広，香川 俊輔，白川 靖博，藤原 俊義	*癌の臨床*	60(3):311-317 2014	国内
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Ⅳ. 研究成果の刊行物・別刷

Impact of reconstruction method on visceral fat change after distal gastrectomy: Results from a randomized controlled trial comparing Billroth I reconstruction and Roux-en-Y reconstruction

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Background. *Visceral fat is one of the causes of metabolic syndrome. Among the various types of bariatric surgery, duodenal–jejunal bypass is one of the most common procedures. However, the effect of duodenal bypass on fat changes is not completely understood. We examined the effect of duodenal bypass on visceral fat changes by comparing Billroth I (BI) and roux-en Y (RY) reconstruction in distal gastrectomy.*

Methods. *This retrospective study used data from 221 patients registered for a prospective randomized trial that compared BI to RY in distal gastrectomy with lymphadenectomy to treat gastric cancer. With a software package, we first quantified the visceral fat area (VFA) on cross-sectional computed tomography scans obtained at the level of the umbilicus before and 1 year after surgery, and then determined the impact of duodenal bypass on visceral fat changes.*

Results. *Clinicopathological background data did not differ between BI and RY. Rates of BMI reduction for BI and RY also did not differ. The VFA reduction rate for RY (47.2 ± 25.5%) was greater than for BI (36.8 ± 34.2%,* $P = .0104$*). Adjuvant chemotherapy (chemotherapy versus no chemotherapy,* $P = .0136$*), type of reconstruction (BI versus RY,* $P < .0001$*), and pathologic stage (p stage I versus p stage II–IV,* $P = .0468$*) correlated significantly with postoperative visceral fat loss. Multivariate logistic regression analysis identified reconstruction (BI versus RY,* $P = .0078$*) as a significant determinant of visceral fat loss.*

Conclusion. *Visceral fat loss after distal gastrectomy was greater for RY than for BI, and duodenal bypass may be associated with reduction of visceral fat. (Surgery 2014;155:424-31.)*

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IT HAS BEEN PROVEN that gastric bypass surgery affects the release of gastrointestinal hormones[1] and induces malabsorption,[2] but there are no conclusive data about the effects of duodenal bypass on visceral fat changes. There are various types of bariatric procedures, including gastric banding, sleeve gastrectomy, roux-en Y bypass, biliopancreatic diversion with duodenal switch, and duodenal-jejunal bypass. However, to the best of our knowledge, no authors have evaluated fat reduction specifically caused by duodenal bypass because the size of the remnant stomach and the length of the jejunal bypass differ among the various procedures.

The selection of the reconstruction method, either Billroth I (BI) or roux-en Y (RY), after distal or subtotal gastrectomy is still controversial. A large, multi-institutional, randomized controlled trial was conducted by the Osaka University Clinical Research Group for Gastroenterological Study (Japan)[3,4] to address this problem. The primary endpoint of this study was to compare body weight loss 1 year after surgery between the BI and RY groups. Secondary endpoints were postoperative complications, nutritional state, and quality of life. This trial gave us an opportunity to prospectively evaluate data about the effects of BI and RY on visceral and subcutaneous fat loss because patients whose remnant stomachs were large enough so that either technique could be performed were assigned randomly intraoperatively to undergo either BI and RY, and the reconstruction methods were prescribed by the protocol.

Visceral fat areas (VFAs) estimated from a single computed tomography (CT) scan at the level of the umbilicus are known to correlate with the total volume of visceral fat.[5,6] On the basis of this knowledge, a practical, standardized technique has been developed to determine the VFA from a single CT scan.[7]

In the present study, we used CT and a software package to quantify the VFA of patients before and 1 year after surgery. We then determined the impact of the type of reconstructive procedure on visceral fat changes in patients with gastric cancer who underwent distal gastrectomy with lymphadenectomy.

METHODS

Patients. Between May 2004 and October 2009, a total of 332 patients with gastric cancer were registered in the original study. After completion of the informed consent process, patients were included in the study if they met the eligibility criteria.[4] After initial laparotomy, the location of the tumor was confirmed to be in the middle or lower third of the stomach and the proportion of residual stomach was regulated as one-third of the original stomach. The operator also checked the length of the residual stomach to confirm that either reconstruction procedure could be performed after distal gastrectomy. The surgeon confirmed the eligibility and exclusion criteria immediately after the initial laparotomy, and patients were then randomized intraoperatively to either the BI group or the RY group. Randomization was performed by the minimization method according to the patient's body mass index (BMI) (<25 or ≥ 25 kg/m^2) and institution.

To evaluate visceral fat changes, we collected CT scans both before and 1 year after surgery. A total of 221 patients, whose CT scans at the umbilicus level both before and 1 year after surgery could be obtained, were retrospectively analyzed in this study. Information about the patients' backgrounds and clinicopathological data were extracted from the data collected by the original study. This study was approved by the institutional review boards of all participating hospitals and was conducted in accordance with the Declaration of Helsinki.

Operative procedure. Patients underwent gastrectomy with systematic lymphadenectomy at 18 high-volume institutions in Osaka, Japan. All 18 institutions were participants in the surgical study group "Osaka University Clinical Research Group for Gastroenterological Study." Overall, more than 50 gastrectomies were performed each year in these 18 hospitals. All operations were performed or supervised by senior surgeons who were members of the Japanese Gastric Cancer Association. During the planning of the study, all participating surgeons reached an agreement concerning the technical details of the reconstructive procedures.

Endotracheal general anesthesia and standard laparotomy or laparoscopic operations were used for all patients in each institution. Gastric tumors located in the lower or middle third of the stomach were treated with distal gastrectomy. Lymphadenectomy approaches were categorized as D1–3, as defined by the Japanese Classification for Standard Dissection.[8] D1 involves dissecting the paragastric nodes, whereas D2 also includes dissection of the nodes along the left gastric, common hepatic, and celiac arteries. D3 includes the nodes dissected in D1 and D2, as well as dissection of the hepatoduodenal and retropancreatic nodes, the nodes along the superior mesenteric vein, and the para-aortic nodes between the level of the celiac axis and the inferior mesenteric artery.

For BI reconstruction, the duodenum and remnant stomach were sutured. For RY reconstruction, the jejunum was divided 20 cm distal to the ligament of Treitz, and the portion of the jejunum closest to the patient's head was closed, followed by the remaining gastric pouch, which was anastomosed to the jejunum. The oral portion of the jejunum was then anastomosed to the mid-jejunum 30 cm distal to the gastrojejunostomy.

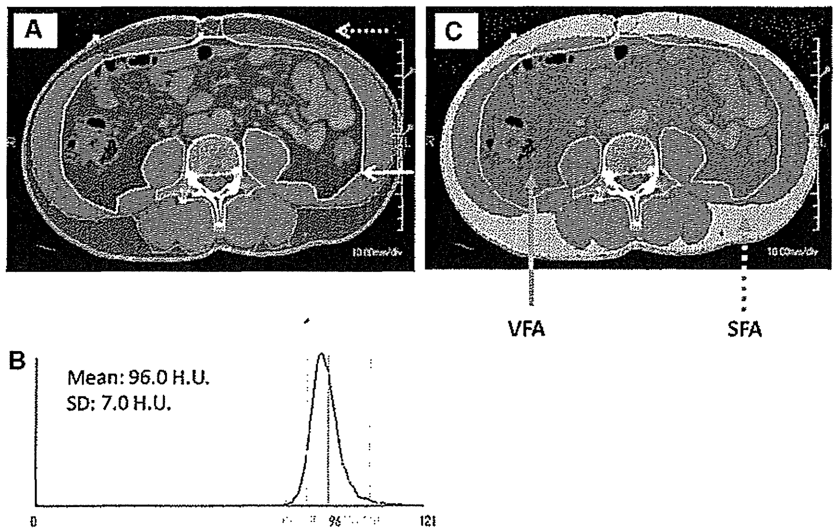

Fig 1. Illustration of method used to determine abdominal fat distribution on a CT scan obtained at the umbilicus level. (*A*) White line (*solid arrow*) outlines the intraperitoneal area. Gray line (*dotted arrow*), drawn with a cursor automatically or manually, outlines the subcutaneous fat layer, in which attenuation is measured. (*B*) Histogram of the CT numbers (in Hounsfield units) in the lesion outlined in (*A*) (mean ± 2 SD). (*C*) Region defined as visceral fat tissue (*solid arrow*). Total fat area was calculated from the region outlining the circumference of the abdominal wall. The VFA was subtracted, and the remainder was regarded as the SFA (*dotted arrow*).

The basic anastomotic procedures, such as sutures made by hand or machine and standard laparotomy or laparoscopic operations, were not prescribed in detail by the protocol.

Of the 118 patients in the RY group, gastrojejunostomy was performed by hand in 8 patients, by circular stapler in 82 patients, and by linear stapler in 28 patients. The Roux-en-Y limb was ascended through the retrocolic route in 71 patients and the antecolic route in 47 patients.

Quantification of VFAs and subcutaneous fat areas (SFAs). The VFA was measured with "FatScan," which was described previously,[7] on one cross-sectional CT scan obtained at the level of the umbilicus. Figure 1 illustrates the method used to determine the fat tissue area on a CT scan. First, the intraperitoneal area was defined by tracing its contour manually on the scan. Thereafter, a region of interest on the subcutaneous fat layer was defined by tracing its contour on each scan either automatically or manually; then, the attenuation range of the CT numbers (in Hounsfield units) for fat tissue was calculated (Fig 1, *A*). A histogram for fat tissue was computed based on the mean attenuation ± 2 SD (Fig 1, *B*). Within the region outlined in Fig 1, *A*, the tissue with attenuation within the mean ± 2 SD was considered to be the VFA. Pixels with attenuation values in the selected attenuation range are depicted. The total fat area was calculated in the region outlining the circumference of the abdominal wall. The VFA (solid arrow) was subtracted, and the remainder was regarded as the SFA (dotted arrow) (Fig. 1, *C*).

Statistical analysis. Differences between groups were examined for statistical significance with the Student *t*-test with Yates' correction, χ^2 test, Fisher's exact probability test, or Wilcoxon rank-sum test. Statistical analysis was performed with JMP version 9.0 (SAS Institute, Cary, NC). Univariate analysis was performed to identify the factors associated with visceral fat loss. The identified variables were subsequently entered into multivariate analysis, and logistic regression analysis was used to identify independent factors that influence visceral fat loss.

RESULTS

Comparison of characteristics of patients who underwent BI or RY. Table I compares the background characteristics of patients who underwent BI or RY. Age, sex, preoperative BMI, preoperative VFA, preoperative SFA, preoperative serum albumin levels, preoperative lymphocyte counts, preoperative prognostic nutritional index values,[9] operative approach, and lymphadenectomy were not significantly different between the two groups. With regard to operative factors, such as operative approach (ie, the proportion of patients who underwent laparoscopy versus

Table I. Patient demographics, tumor characteristics, and operative details

	BI group, n = *103*	*RY group*, n = *118*	P *value*
Age, y*	64.1 ± 9.2	64.1 ± 10.3	.9765
Men/women	65/38	85/33	.1563
Preoperative BMI,* kg/m^2	22.4 ± 3.2	22.7 ± 3.0	.3846
Preoperative total fat area, cm^2*	204.0 ± 73.9	215.6 ± 90.5	.3023
Preoperative VFA, cm^2*	83.9 ± 38.9	92.6 ± 43.6	.1175
Preoperative SFA, cm^2*	120.1 ± 54.8	122.9 ± 62.5	.7243
Preoperative serum albumin, mg/dL	4.12 ± 0.39	4.12 ± 0.51	.9864
Preoperative lymphocyte count	1,846 ± 699	1,924 ± 596	.3966
Preoperative PNI*	50.6 ± 5.7	51.2 ± 6.1	.4862
Operative approach (laparoscopy/ laparotomy)	24/79	28/90	.9404
Lymphadenectomy (D1/D2+D3)	38/57	46/62	.9503
Adjuvant chemotherapy (yes/no)	13/90	16/102	.8368
Recurrence (yes/no)	5/98	4/114	.7372

*Data are mean ± SD. Comparisons between BI and RY groups with the Student *t* test. Other parameters were compared with χ^2 or Fisher exact test.

BI, Billroth I reconstruction; *BMI*, body mass index; *PNI*, prognostic nutritional index; *RY*, roux-en Y reconstruction; *SFA*, subcutaneous fat area; *VFA*, visceral fat area.

Table II. Comparison of postoperative nutritional status of patients in the BI and RY groups

	BI group, n = *103*	*RY group*, n = *118*	P *value*
Postoperative BMI, kg/m^2	20.3 ± 2.8	20.5 ± 2.4	.6106*
Postoperative total fat area, cm^2	139.3 ± 63.2	127.2 ± 61.2	.1497*
Postoperative VFA, cm^2	50.0 ± 27.3	43.9 ± 22.2	.0821*
Postoperative SFA, cm^2	89.7 ± 46.6	83.4 ± 47.8	.3239*
Postoperative serum albumin, mg/dL	4.21 ± 0.34	4.18 ± 0.42	.5789
Postoperative lymphocyte count	1,891 ± 625	1,908 ± 575	.8429
Postoperative PNI*	51.2 ± 5.1	51.3 ± 5.6	.8379
ΔBMI%	8.9 ± 6.6	9.5 ± 7.1	.2634†
Δ Total fat area %	29.6 ± 25.8	37.0 ± 25.4	.0117†
ΔVFA%	36.8 ± 34.2	47.2 ± 25.5	.0032†
ΔSFA%	22.2 ± 28.4	27.3 ± 32.8	.0732†

*Student *t*-test.
†Wilcoxon rank-sum test.
Data are mean ± SD.
BI, Billroth I reconstruction; *BMI*, body mass index; *PNI*, prognostic nutritional index; *Δ Total fat area %*, rate of reduction of total fat area; *ΔBMI%*, rate of reduction of BMI; *ΔSFA%*, rate of reduction of SFA; *ΔVFA%*, rate of reduction of VFA; *RY*, roux-en Y reconstruction; *SFA*, subcutaneous fat area; *VFA*, visceral fat area.

laparotomy) and field of lymphadenectomy, there were no significant differences between the groups. There were also no significant differences between the groups with regard to adjuvant chemotherapy and cancer recurrence. Information about the composition of food consumed after surgery was collected by questionnaire. Most of the patients who underwent BI (90.9%) and RY (86.9%) consumed a normal diet, whereas 9.1% of BI and 13.1% of RY patients consumed a soft or liquid diet (P = .3824). The mean intervals for when the follow-up CT was performed after surgery were 376 ± 111 days for BI and 374 ± 77 days for RY (P= .9980).

Comparison of postoperative nutritional states of patients who underwent BI or RY. Table II lists comparative data for BMI, VFA, and SFA. Postoperative BMI, postoperative SFA, postoperative serum albumin levels, postoperative lymphocyte counts, postoperative prognostic nutritional index values, and the rate of reduction of BMI (ΔBMI %) were not substantially different between the BI and RY groups. The postoperative VFA of the RY group (43.9 ± 22.2 cm^2) was smaller than that of the BI group (50.0 ± 27.3 cm^2), but the difference was not clinically important (P = .0821). The rate of reduction of the VFA (ΔVFA%) in the RY group (47.2 ± 25.5%) was greater than in the BI group (36.8 ± 34.2%; P= .0032). For the muscle reduction rate, there was no difference between the BI (2.5 ± 18.1%) and RY (3.1 ± 16.8%; P = .7970) groups. Figure 2 shows the correlation between preoperative BMI and ΔVFA% according to the reconstruction method used. The ΔVFA% for the RY group was greater in patients with greater BMI than in patients with lesser BMI. In contrast, the ΔVFA% for the BI group was similar between patients with greater and lesser BMI. Patients were divided into two BMI groups according to the median of the preoperative BMI (22.5 kg/m^2). Tables III and IV show postoperative data for the BMI ≥22.5 kg/m^2 and the BMI <22.5 kg/m^2 groups. In the BMI ≥22.5 kg/m^2 group, preoperative BMI, postoperative BMI, and ΔBMI% were not different between the BI and RY groups. The postoperative VFA of the RY group (50.4 ± 21.9 cm^2) was less than that of the BI group (61.9 ± 30.0 cm^2; P = .0218). The ΔVFA% of the RY group (52.1 ± 19.5%) was also greater than that of the BI group (35.4 ± 42.9%;

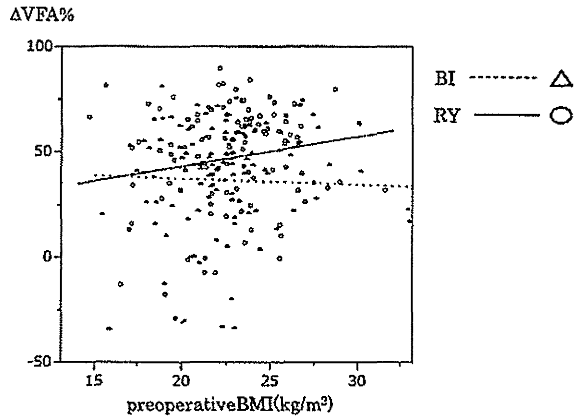

Fig 2. Comparison between BI and RY groups of changes in visceral fat according to preoperative BMI.

Table III. Postoperative BMI and fat areas of the BMI ≥22.5 kg/m² group

High BMI group	*BI group,* n = *47*	*RY group,* n = *62*	P *value*
Preoperative BMI, kg/m²	24.9 ± 2.5	24.9 ± 1.9	.9607*
Postoperative BMI, kg/m²	21.4 ± 2.9	21.3 ± 2.4	.7931*
ΔBMI%	10.2 ± 6.7	12.2 ± 5.6	.1012*
Preoperative VFA, cm²	104.7 ± 40.7	112.3 ± 42.0	.3461*
Postoperative VFA, cm²	61.9 ± 30.0	50.4 ± 21.9	.0218*
ΔVFA%	35.4 ± 42.9	52.1 ± 19.5	.0041†
Preoperative SFA, cm²	143.0 ± 59.2	152.0 ± 63.2	.4510*
Postoperative SFA, cm²	110.2 ± 50.9	104.5 ± 51.7	.5663*
ΔSFA%	20.0 ± 28.6	29.6 ± 21.9	.0930†

*Student *t*-test.
†Wilcoxon rank-sum test.
Data are mean ± SD.
BI, Billroth I reconstruction; *BMI,* body mass index; *ΔBMI%,* rate of reduction of BMI; *ΔSFA%,* rate of reduction of SFA; *ΔVFA%,* rate of reduction of VFA; *RY,* roux-en Y reconstruction; *SFA,* subcutaneous fat area; *VFA,* visceral fat area.

P = .0041). In the BMI <22.5 kg/m² group, there were no significant differences between the BI and RY groups in terms of postoperative BMI, ΔBMI%, postoperative VFA, and ΔVFA%.

Determinants of postoperative visceral fat loss. Before the factors associated with visceral fat loss were analyzed, the study population was divided into a high ΔVFA% group and a low ΔVFA% group by the median ΔVFA% (48.5%). Univariate analysis was used to identify significant factors associated with visceral fat loss. As shown in Table V, among the clinicopathologic factors that we examined, adjuvant chemotherapy (performed versus not performed, P = .0046), type of reconstruction (BI versus RY, P = .0087), and p stage (p stage I versus p stage II–IV, P = .0468) correlated with postoperative visceral fat loss. No deaths occurred during the course of this study. There was no significant difference in morbidity/postoperative complications between the low (10/111; 9.0%) and high (11/110; 10%) VFA groups (P = .8017) when patients were divided by the median of the preoperative VFA value. Multivariate logistic regression analysis that included the above factors identified reconstruction (BI versus RY, P = .0078) and adjuvant chemotherapy (performed versus not performed, P = .0172) as significant predictors of visceral fat loss.

Table IV. Postoperative BMI and fat area of the BMI <22.5 kg/m² group

Low BMI group	*BI group,* n = *56*	*RY group,* n = *56*	P *value*
Preoperative BMI (kg/m²)	20.2 ± 1.8	20.2 ± 2.0	.8691*
Postoperative BMI (kg/m²)	19.4 ± 2.3	19.3 ± 1.8	.7537*
ΔBMI%	7.7 ± 6.2	6.4 ± 7.4	.2949†
Preoperative VFA (cm²)	66.4 ± 27.1	70.9 ± 34.1	.4384*
Postoperative VFA (cm²)	39.4 ± 19.8	36.7 ± 20.4	.4720*
ΔVFA%	38.0 ± 25.2	41.7 ± 30.1	.4729†
Preoperative SFA (cm²)	100.9 ± 42.6	90.7 ± 43.1	.2117*
Postoperative SFA (cm²)	72.4 ± 34.6	60.0 ± 28.9	.0410*
ΔSFA%	24.0 ± 28.2	24.7 ± 41.7	.3594†

*Student *t*-test.
†Wilcoxon rank-sum test.
Data are mean ± SD.
BI, Billroth I reconstruction; *BMI,* body mass index; *ΔBMI%,* rate of reduction of BMI; *ΔSFA%,* rate of reduction of SFA; *ΔVFA%,* rate of reduction of VFA; *RY,* roux-en Y reconstruction; *SFA,* subcutaneous fat area; *VFA,* visceral fat area.

DISCUSSION

Gastrectomy usually leads to body weight loss. The mechanisms of postgastrectomy weight loss include impaired food intake and malabsorption.[10-12] In previous studies authors reported that body weight loss is mainly caused by loss of body fat.[13,14] With respect to anatomical localization, body fat is divided into subcutaneous fat and visceral fat. To our knowledge, there is little information on the changes that take place in visceral and subcutaneous fat after gastrectomy. We found that visceral fat loss after distal gastrectomy was greater in patients who underwent

Table V. Univariate and multivariate analysis of risk factors for visceral fat loss

Factors	*High/low*	*Univariate* P *value*	*Odds ratio*	*95% CI*	*Multivariate* P *value*
Reconstruction		.0087	2.0965	1.2142–3.6573	.0078
RY	69/49				
BI	42/61				
Sex		.6323			
Men	77/73				
Women	34/37				
Lymphadenectomy		.3324			
D2 or D3	64/71				
D1	46/39				
Operative approach		.2182			
Laparotomy	81/88				
Laparoscopy	30/22				
Adjuvant chemotherapy		.0046	4.6106	1.3056–17.9177	.0172
Yes	22/7				
No	89/103				
Recurrence		1.0000			
Yes	5/4				
No	105/106				
Location of tumor		.6364			
M	37/40				
L	74/70				
Age, y		.1582			
≥65	64/53				
<65	47/57				
Pathologic stage		.0468	1.26856	0.4556–3.7129	.6501
II or III	28/16				
I	83/94				
Postoperative complications		.1656			
Yes	10/4				
No	101/106				

BI, Billroth I reconstruction; *L*, lower third of stomach; *M*, middle third of stomach; *RY*, roux-en Y reconstruction.

RY compared with those who underwent BI. In a previous study investigators reported that visceral fat reduction is greater after RY gastric bypass compared to vertical banded gastroplasty.[11] Our results are comparable with other reports in the field of bariatric surgery.

However, in previous reports there were differences, such as the size of the remnant stomach and the length of the jejunal bypass, between the operative procedures. To the best of our knowledge, this was the first study to focus on the specific impact of duodenal bypass on visceral fat loss. Because the jejunal bypass was made as short as possible (the afferent limb was as close as 20 cm) and the size of the remnant stomach was equivalent between the BI and RY groups, variations in malabsorption between the groups were minimized. Thus, we believe that this study was also the first to evaluate prospectively collected data to determine the specific effects of duodenal bypass on visceral and subcutaneous fat loss in a population in which the remnant stomach was of a similar size.

It is assumed that the number of patients with gastric cancer who are obese is increasing because of the high prevalence of obesity among the general population. The number of patients diagnosed with early gastric cancer is increasing as the result of earlier detection of cancer, and the 5-year survival rate for patients with early gastric cancer (most often treated with radical resection) is approximately 95%.[15] Consequently, death by causes other than cancer is the most common cause of death among patients with early gastric cancer. Cerebrovascular disorders, cardiac disease, and respiratory disease are reported to be common causes of death in patients with early gastric cancer.[16] When treating these patients, we should therefore consider the most effective means of reducing the risk of death due to causes other than cancer. In recent years, visceral fat accumulation has been identified as one of the underlying causes of metabolic syndrome. This syndrome is characterized by glucose intolerance, obesity, hypertension, and dyslipidemia. Many studies have demonstrated that body fat distribution is associated with the development of metabolic disorders, and that excessive abdominal fat, especially intra-abdominal visceral fat, is associated with various obesity-related complications and poor prognosis.[17,18] Visceral fat is becoming a target for the treatment of obesity-related complications such as hypertension, dyslipidemia, diabetes mellitus, and cardiovascular disease.[19]

Our study revealed that duodenal bypass in addition to gastrectomy promoted visceral fat loss, especially in obese patients. Previous studies of bariatric surgery have reported that the decrease in absolute BMI in lower BMI groups is less than that of the groups with greater BMI 1 year after RY bypass operation.[20] This finding is consistent with our results. RY reconstruction might be a better choice for obese patients who require distal gastrectomy to treat gastric cancer. Our results also suggest that duodenal bypass is a useful procedure for nonobese patients with metabolic syndrome–associated conditions such as diabetes mellitus, hypertension, and hyperlipidemia, because the reduction in visceral fat was greater after this procedure.

There have been a few reports about the effect on diabetes of rearrangements of gastrointestinal anatomy after surgery for gastric cancer.[21-23] Lanzarini et al[21] reported that gastrectomy with RY reconstruction (60–70 cm limb) in type 2 diabetes patients who underwent operation mainly for gastric cancer correlated with remission of diabetes in 65% and improvement in 30.4% of patients. Another study reported that patients who underwent duodenal bypass had significantly improved diabetes compared with those who did not.[23]

The mechanism by which duodenal bypass reduces visceral fat could not be elucidated in this study. However, previous studies of bariatric operation have reported that visceral fat reduction is greater after RY gastric bypass than after vertical banded gastroplasty.[14] Although the mechanisms of fat reduction or improvement in insulin resistance are not understood completely within the context of bariatric surgery, gut hormones are thought to play a critical role. Among the various gut hormones, gastric inhibitory polypeptide (GIP) is reported to regulate fat metabolism. GIP is released from the duodenal endocrine K cells immediately after the absorption of fat or glucose.[24] Furthermore, fat intake induces hypersecretion of GIP, which increases nutrient uptake and triglyceride accumulation in adipocytes.[25] Korner et al[26] reported lower GIP levels after RY gastric bypass compared to adjustable gastric banding, and concluded that blunted GIP secretion after RY may contribute to the greater weight loss and improved glucose homeostasis compared to adjustable gastric banding. Fat malabsorption may be another factor; clinical tests after RY revealed significantly lower fat absorption than after BI and double-tract reconstruction, in which the passage of food through the duodenum is accommodated.[27]

Our study has several limitations. First, we could not elucidate the mechanism of greater reduction of visceral fat after duodenal bypass, because data about gut hormones were not acquired. In addition, the long-term results are unknown, because we examined CT data only 1 year after surgery. In studies of the long-term results of bariatric surgery, compared with nonsurgical control patients, the use of RY gastric bypass operation in severely obese patients was associated with a greater rate of diabetes remission and a lesser risk of cardiovascular disease and other poor health outcomes after 6 years. On the other hand, there are some reports of recurrence or worsening of diabetes mellitus, especially in nonobese patients, after RY gastric bypass.[28,29] Further investigations will be necessary to provide long-term follow-up data and to understand how duodenal bypass markedly decreases fat.

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TOPIC HIGHLIGHT

WJG 20th Anniversary Special Issues (8): Gastric cancer

Current status of function-preserving surgery for gastric cancer

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Abstract

Recent advances in diagnostic techniques have allowed the diagnosis of gastric cancer (GC) at an early stage. Due to the low incidence of lymph node metastasis and favorable prognosis in early GC, function-preserving surgery which improves postoperative quality of life may be possible. Pylorus-preserving gastrectomy (PPG) is one such function-preserving procedure, which is expected to offer advantages with regards to dumping syndrome, bile reflux gastritis, and the frequency of flatus, although PPG may induce delayed gastric emptying. Proximal gastrectomy (PG) is another function-preserving procedure, which is thought to be advantageous in terms of decreased duodenogastric reflux and good food reservoir function in the remnant stomach, although the incidence of heartburn or gastric fullness associated with this procedure is high. However, these disadvantages may be overcome by the reconstruction method used. The other important problem after PG is remnant GC, which was reported to occur in approximately 5% of patients. Therefore, the reconstruction technique used with PG should facilitate postoperative endoscopic examinations for early detection and treatment of remnant gastric carcinoma. Oncologic safety seems to be assured in both procedures, if the preoperative diagnosis is accurate. Patient selection should be carefully considered. Although many retrospective studies have demonstrated the utility of function-preserving surgery, no consensus on whether to adopt function-preserving surgery as the standard of care has been reached. Further prospective randomized controlled trials are necessary to evaluate survival and postoperative quality of life associated with function-preserving surgery.

Key words: Gastric cancer; Function preserving surgery; Quality of life; Pylorus preserving surgery; Proximal gastrectomy

Core tip: We reviewed the current status of two function-preserving surgeries for gastric cancer (GC), pylorus-preserving surgery and proximal gastrectomy (PG). Although both procedures appear to be oncologically safe for early GC, issues regarding postoperative quality of life remain, especially with PG. The effect of the reconstruction method after PG on postoperative quality of life was analyzed, including the novel double tract reconstruction method, which is expected to overcome disadvantages associated with esophagogastrostomy and jejunal interposition reconstruction. Although some reports showed a benefit with function-preserving surgery, further randomized trials are needed.

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INTRODUCTION

Recent developments in screening programs and endoscopic techniques have allowed the diagnosis of gastric cancer (GC) at an early stage[1]. Early GC (EGC) makes up 50% of the diagnosed cases and the five-year survival rate of EGC treated with surgery is over 90% in Japan[2]. Due to the low incidence of lymph node metastasis and the favorable prognosis of EGC, areas of gastric resection and lymph node dissection areas could be reduced to preserve postoperative gastric function. Although the Japanese GC treatment guidelines advocate resection of at least two-thirds of the stomach with D2 node dissection as the standard treatment for most stages of advanced GC, the guidelines also describe less invasive procedures such as pylorus-preserving gastrectomy (PPG), proximal gastrectomy (PG), and other minimally invasive procedures as investigational treatments (Figure 1)[3].

Here we review PPG and PG as function-preserving procedures for GC.

PPG

PPG was initially used to treat peptic ulcers[4]. Starting in the late 1980s, some surgeons performed PPG in selected patients with EGC to improve postoperative gastric function and maintain patient quality of life[5]. PPG is generally thought to offer several advantages over conventional distal gastrectomy (DG) with Billroth I reconstruction in terms of the incidence of dumping syndrome, bile reflux gastritis, and the frequency of flatus, although the operative duration of PPG is longer than that of DG.

During the procedure, the distal part of the stomach is resected, but a pyloric cuff 2-3 cm wide is preserved[6,7]. The right gastric artery and the infrapyloric artery are preserved to maintain the blood supply to the pyloric cuff. In addition, the hepatic and pyloric branches of the vagal nerves are preserved to maintain pyloric function. The celiac branch of the posterior vagal trunk is sometimes preserved. All regional nodes except the suprapyloric nodes (No. 5) should be dissected as in the standard D2 procedure. However, there are technical challenges associated with completing all of these procedures. Shibata *et al*[8] conducted a questionnaire survey on the PPG procedure in Japanese institutions. According to their report, the vagus nerve was preserved at 73.5% of the institutions, the infrapyloric artery was preserved in 49.4%, and partial dissection of the suprapyloric lymph nodes was performed in 56.2%. These differences in the procedure may affect postoperative gastric function after PPG, leading to postoperative symptoms.

INDICATIONS AND ONCOLOGIC SAFETY OF PPG

Since function-preserving surgeries such as PPG are usually less extensive, patient selection for these procedures should be carefully considered in terms of oncologic safety. In particular, in order to maintain pyloric cuff function with PPG, lymph nodes at the suprapyloric and infrapyloric stations may be incompletely dissected due to preservation of the right gastric artery, the infrapyloric artery, and the hepatic and pyloric branches of the vagus nerves[9-11].

In general, PPG is performed in patients who are preoperatively diagnosed with cT1N0M0 primary GC in the middle third of the stomach when the distal border of the tumor is approximately 4-5 cm away from the pylorus[9-12]. This indication is based on the incidence of lymph node metastasis in patients who have undergone conventional gastrectomy[13-16].

Kim *et al*[17] reported that the incidence of lymph node metastasis at the suprapyloric and infrapyloric stations in EGC located in the middle third of the stomach after PPG and conventional DG was 0.45% (1/220) and 0.45% (1/220), respectively. In addition, Kong *et al*[18] showed that the incidence of lymph node metastasis at the suprapyloric and infrapyloric stations in EGC located ≥ 5 cm from the pylorus was 0.46% (1/219) and 0.90% (2/221), respectively. Both studies also found that the mean number of suprapyloric lymph nodes dissected was significantly lower after PPG than that with conventional DG, but no significant difference was found for infrapyloric lymph nodes. However, incomplete dissection of lymph nodes at the suprapyloric station is considered acceptable because of the low incidence of metastasis. Therefore, patients who are clinically diagnosed with T1N0 disease

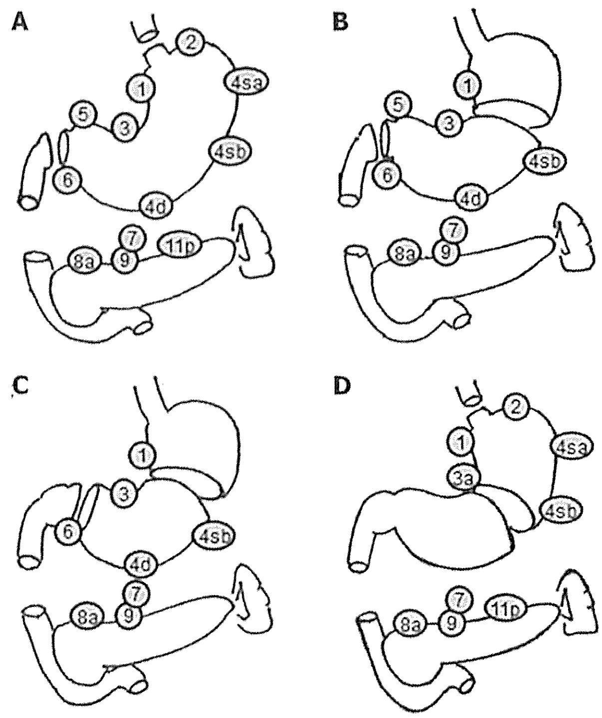

Figure 1 Extent of D1+ lymph node dissection in pylorus-preserving gastrectomy and proximal gastrectomy. A: Total gastrectomy; B: Distal gastrectomy; C: Pylorus-preserving gastrectomy; D: Proximal gastrectomy. The number of lymph node stations is according to the classification of the Japanese Gastric Cancer Association.

Table 1 Postoperative symptomatic outcomes after pylorus-preserving surgery

Ref.	Procedure	No. of patients	Endoscopic findings (%)				Symptom (%)			Change of body weight (%)
			Esophagitis	Food residue	Bile reflux	Gastritis	Reflux	Fullness	Dumping	
Matsuki *et al*[21], 2012	PPG	433	11	19	3	11	6	2		94
Morita *et al*[24], 2013	PPG	408	6	28	12	10	6	9	4	92
Ikeguchi *et al*[25], 2010	PPG	24	35	71			0	4	0	97
	DG-B1	30	26	16			3	10	10	90
Park do *et al*[26], 2008	PPG	22			0	0	32	32		
	DG-B1	17			25	17	46	40		
Nunobe *et al*[27], 2007	PPG	194	6	22	7	12	7	10		93.9
	DG-B1	203	2	13	8	8	6	13		90.2
Tomita *et al*[28], 2003	PPG	10	0	60		10	0	40	0	94.3
	DG-B1	22	23	18		64	68	18	23	91.3
Yamaguchi *et al*[29], 2004	PPG	28		61		28	20	44	12	94.6
	DG-B1	58		33		57	27	36	36	91.3
Nakane *et al*[30], 2000	PPG	25	4	56	4	8	4	35	0	90
	DG-B1	25	8	36	40	68	0	0	4	93

PPG: Pylorus-preserving surgery; DG: Distal gastrectomy; B1: Billroth-I reconstruction.

could be candidates for PPG without suprapyloric lymph node dissection.

The five-year survival rate after PPG with modified D2 lymph node dissection ranges from 95% to 98%[10,11,19-21]. This rate is comparable to the five-year survival rate after gastric resection for EGC, which ranges from 90% to 98%[2,22,23]. In terms of oncologic safety, PPG seems reasonably safe for EGC when the accuracy of preoperative diagnosis can be assured.

POSTOPERATIVE SYMPTOMATIC OUTCOMES AFTER PPG

The advantage of PPG is the prevention of post-gastrectomy symptoms such as dumping syndrome and bile reflux gastritis, as well as reduced frequency of flatus. As shown in Table 1, the ratio of dumping syndrome and bile reflux gastritis was quite low in PPG compared to DG. However, delayed gastric emptying (DGE) after PPG resulting in patient-reported gastric fullness could be a disadvantage of PPG[21,24-30], which make PPG inappropriate in elderly patients and those with hiatus hernia or esophagitis[29,30]. The incidence of gastric stasis after PPG based on endoscopic studies ranges from 19% to 70%, compared to 13% to 36% after DG. Michiura *et al*[31] showed that food intake along with DGE was improved with time. Moreover, the reservoir function of the remnant stomach may promote better body weight (BW) recovery after PPG than after DG with Billroth I reconstruction[21,24,25,27,28].

Preserving the vagal nerve and the infrapyloric artery is thought to prevent gastric stasis[10,32,33], although these techniques have not been evaluated in randomized clinical trials. The length of the pyloric cuff is another important factor with regards to preservation of pyloric function. Nakane *et al*[34] reported that retaining a pyloric cuff of 2.5 cm results in a lower incidence of postoperative stasis compared to retaining a pyloric cuff of 1.5 cm as severe postoperative edema of the pyloric cuff might affect gastric wall motility after PPG. Morita *et al*[24] showed that retaining a pyloric cuff over 3 cm did not affect the incidence of postoperative stasis compared to retaining a pyloric cuff of less than 3 cm. At Japanese institutions, the retained pyloric cuff is usually between 2 and 4 cm[8,35]. Moreover, Hiki *et al*[6] argued that the infrapyloric and right gastric veins should be preserved to maintain blood flow in order to prevent postoperative edema of the pyloric cuff. Complete dissection of both veins could induce severe edema of the pyloric cuff, resulting in long-term postoperative retention of food in the residual stomach.

PG

The incidence of proximal GC has increased in recent years[36]. Total gastrectomy (TG) and PG with lymph node dissection are both performed for EGC located in the upper third of the stomach (U-EGC). In a retrospective study of Japanese institutions, Takiguchi *et al*[37] found that a quarter of the 586 patients with U-EGC underwent PG.

PG is generally thought to offer advantages over conventional TG with Roux-en-Y reconstruction in terms of retention of food in the remnant stomach. On the other hand, heartburn or gastric fullness due to esophageal reflux or gastric stasis is a potential disadvantage. However, these advantages and disadvantages depend on the reconstruction method used.

During the procedure, all regional nodes except the splenic hilar nodes (No. 10), the distal splenic nodes (No. 11d), the suprapyloric nodes (No. 5), and the infrapyloric nodes (No. 6) are dissected, although the dissection of the distal lesser curvature nodes (No. 3) and the right gastroepiploic artery (No. 4d) is incomplete. The hepatic and pyloric branches of the vagal nerve are preserved to

Table 2 Postoperative symptomatic outcomes after proximal gastrectomy

Ref.	Procedure	No. of patients	Endoscopic findings (%)			Symptom (%)			Change of body weight (%)
			Esophagitis	Stenosis	Food residue	Reflux	Fullness	Dumping	
Masuzawa *et al*[41], 2014	PG-EG	49				18	16	0	87
	PG-JI	32				16	0	0	86
	TG-RY	122				12	3	8	85
Nozaki *et al*[42], 2013	PG-JI	102	3		32				88
	TG-RY	49	2						86
Katai *et al*[43], 2010	PG-JI	128	2		9	6		3	88.9
Katai *et al*[44], 2003	PG-JI	45	0			4		9	88.5
Tokunaga *et al*[45], 2008	PG-EG	36	30						
	short-PG-JI	18	9						
	long-PG-JI	22	0						
Ahn *et al*[46], 2013	LAPG-EG	50	32	12					
	LATG-RY	81	4	5					
An *et al*[47], 2008	PG-EG	89	29	38					86.4
	TG-RY	334	2	7					87.4
Yoo *et al*[48], 2004	PG-EG	74	16	35					
	TG-RY	185	1	8					
Tokunaga *et al*[50], 2009	PG-EG	38				8	3		86
	PG-JI	45				9	22		86
Ahn *et al*[52], 2013	LAPG-EG	50		8		32			94
	LAPG-DT	43		5	49	5		12	96.3
Nomura *et al*[53], 2014	PG-JI	10	10			0	30		91.2
	PG-DT	10	10			10	20		87.1

LAPG: Laparoscopy-assisted proximal gastrectomy; LATG: Laparoscopy-assisted total gastrectomy; PG: Proximal gastrectomy; TG: Total gastrectomy; EG: Esophagogastrostomy reconstruction; RY: Roux-en-Y reconstruction; JI: Jejunal interposition reconstruction; DT: Double tract reconstruction.

maintain the function of the remnant stomach and pylorus as in PPG[7].

INDICATIONS AND ONCOLOGIC SAFETY OF PG

In general, to maintain both curability and functional capacity of the remnant stomach, PG is performed in patients who are preoperatively diagnosed with cT1N0M0 primary GC in the upper third of the stomach when at least half of the stomach can be preserved[38].

In patients undergoing PG, the lymph nodes in the lesser curvature (No. 3) and near the right gastroepiploic artery (No. 4d) are incompletely dissected. Thus, the surgical curability of GC may be lower with PG than with TG. However, Ooki *et al*[39] reported that proximal GC confined to the muscularis propria (mp) is not associated with lymph node metastasis at the right gastroepiploic artery (No. 4d), suprapyloric (No. 5), or infrapyloric (No. 6) stations. Sasako *et al*[40] reported that after curative gastrectomy, lymph node metastasis occurs at the suprapyloric and infrapyloric stations in patients with GC located in the upper third of the stomach in approximately 3% and 7% of cases, respectively. Although these percentages seem high, approximately half of the patients had T2 or more advanced GC and the incidence of metastasis may be lower in patients with EGC. Therefore, patients who are clinically diagnosed with T1N0 disease could be candidates for PG without dissection of the right gastroepiploic artery, suprapyloric, and infrapyloric lymph nodes.

The five-year survival rate after PG ranges from 90.5% to 98.5%[41-47]. Some studies have demonstrated that PG confers a survival benefit comparable to that of TG, the standard procedure for GC located in the upper third of the stomach[41,46-48]. Therefore, PG seems oncologically safe for EGC.

POSTOPERATIVE SYMPTOMATIC OUTCOMES AFTER PG

PG is generally thought to offer several advantages over conventional TG with Roux-en-Y reconstruction (Table 2). Ichikawa *et al*[49] reported that reduced food intake volume occurred less often in patients who underwent PG compared to TG. Masuzawa *et al*[41] reported that postoperative nutritional status as analyzed by blood tests such as serum albumin and hemoglobin was better after PG than TG. However, no studies have shown a superior outcome with PG as compared to TG in terms of postoperative BW, with the exception of one study which compared PG with jejunal interposition (JI) for reconstruction and TG at one year after surgery[41,42,47]. Moreover, compared to TG, PG was associated with a much higher rate of complications such as heartburn and anastomotic stenosis, which led An *et al*[47] to conclude that PG is not a better option for U-EGC than TG[46]. However, the reconstruction method was limited to esophagogastrostomy (EG) in these reports which did not demonstrate that PG was better. Therefore, the evaluation of other reconstruction methods is necessary.

Currently, three procedures, TG with Roux-en-Y reconstruction (TG-RY), PG-EG, and PG-JI, are widely