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ORIGINAL SCIENTIFIC REPORT

Functional Advantages of Proximal Gastrectomy with Jejunal Interposition Over Total Gastrectomy with Roux-en-Y Esophagojejunostomy for Early Gastric Cancer

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Abstract

Background The postoperative functional advantages of a proximal gastrectomy over a total gastrectomy remain debatable. The aim of this study was to evaluate the functional outcomes of a proximal gastrectomy with jejunal interposition (PG-JI), compared with those for a total gastrectomy with Roux-en-Y esophagojejunostomy (TG-RY), in patients with early gastric cancer.

Methods Between 2007 and 2012, 65 patients underwent PG-JI and 117 underwent TG-RY for cT1 gastric cancer. Various parameters, including body weight, serum hemoglobin level, and interview-based symptoms, were prospectively evaluated in these patients. In patients who underwent PG-JI, the postoperative endoscopic findings were also assessed.

Results All the surgeries were performed via a laparotomy alone. During a median postoperative follow-up of 42 months (range, 12–78 months), PG-JI offered significant reductions in body weight loss (12.5 ± 5.8 vs. 17.4 ± 6.4 %, $P < 0.001$), serum hemoglobin decline (7.0 ± 5.7 vs. 9.7 ± 5.4 %, $P = 0.002$), and dumping symptoms (11 % [7/65] vs. 30 % [35/117], $P = 0.003$), while being associated with similar incidences of anastomotic stricture (9 % [6/65] vs. 8 % [9/117], $P = 0.781$), small bowel obstruction (0 % [0/65] vs. 2 % [2/117], $P = 0.538$), stasis symptoms (51 % [33/65] vs. 44 % [51/117], $P = 0.358$), and reflux symptoms (34 % [22/65] vs. 23 % [27/117], $P = 0.121$), compared with TG-RY. Four cases of gastric remnant cancer and no cases of endoscopic reflux esophagitis were found after PG-JI.

Conclusions PG-JI has clear functional advantages over TG-RY, although it requires active surveillance for remnant gastric cancer.

Introduction

Gastric cancer is one of the leading causes of cancer death worldwide [1], and surgical resection is the mainstay of its curative treatment. In recent years, the incidence of proximal gastric cancer, including esophagogastric junction cancer, has been increasing [2–4]. In Japan, proximal gastrectomy (PG) is accepted as a modified procedure instead of a standard total gastrectomy (TG) for cT1N0 cancer beyond the endoscopic resection criteria and

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involving the upper third of the stomach [5]. However, the advantages of PG over TG in terms of postoperative quality of life remain debatable [6–8].

In Japan, a Roux-en-Y esophagojejunostomy is almost exclusively used after TG, while various reconstructions, including esophagogastrostomy, jejunal interposition, and the double-tract method, are used after PG [9]. An esophagogastrostomy is the simplest procedure in a PG, but it is associated with an increased risk of postoperative reflux esophagitis and anastomotic stricture [7, 8, 10], which can considerably impair patient quality of life. We have prospectively adopted PG with jejunal interposition (PG-JI) to prevent reflux esophagitis and have reported its technical and oncological feasibility [11, 12].

The aim of this study was to evaluate prospectively the functional outcomes of PG-JI, compared with those of TG with a Roux-en-Y esophagojejunostomy (TG-RY), in patients with early gastric cancer. All the procedures were performed via laparotomy according to the current Japanese standards [5].

Materials and methods

Patients

Between August 2007 and October 2012, a total of 2050 patients with histologically proven gastric cancer underwent a gastrectomy at our institution. Of these, 182 patients who underwent curative PG-JI ($n = 65$) or TG-RY ($n = 117$) for cT1 primary gastric cancer but did not receive adjuvant therapy were enrolled in the study. The remaining 1868 patients who had ≥cT2 tumors, who underwent other types of gastrectomy, who had remnant gastric cancer, who had distant metastasis, who had received adjuvant therapies, or who had concurrent malignant diseases were excluded. In all the cases, the diagnosis of cT1 was made based on conventional endoscopy with or without endoscopic ultrasound. This study was approved by the institutional review board.

The T and N stages were recorded according to the International Union Against Cancer (UICC) TNM Staging System [13]. The tumor location and histologic type were recorded according to the Japanese Classification of Gastric Carcinoma [14]. Papillary adenocarcinoma and well- or moderately differentiated tubular adenocarcinoma were described as differentiated-type carcinoma, while poorly differentiated adenocarcinoma, signet-ring cell carcinoma, and mucinous adenocarcinoma were classified as undifferentiated-type carcinoma. The operative procedures, including the extent of lymphadenectomy, were recorded according to the Japanese gastric cancer treatment guidelines [5]. The postoperative complications were graded according to the Clavien-Dindo classification [15].

Surgery

Our current institutional policy on surgery for cT1 gastric cancer involving the upper third of the stomach is summarized below. PG-JI is indicated for tumors confined to the upper third of the stomach, including esophagogastric junction tumors [11]. More than half of the stomach is preserved in this procedure. TG-RY is indicated for tumors spreading to the middle third of the stomach. Both procedures are performed via laparotomy. A splenectomy is considered if lymph nodes along the greater curvature are involved by metastasis. In principle, a D1+ lymphadenectomy is completed, but in patients with a high operative risk, a D1 lymphadenectomy is also allowed. The hepatic branches of the vagal nerve are preserved, but in patients with a tumor grossly (>10 mm) invading the esophagus, the nerve may be sacrificed to achieve a thorough lymphadenectomy along the esophagus. In PG-JI, pyloroplasty is not performed. Cholecystectomy is added only in patients with gallstones. A 10-cm jejunal interposition in PG-JI and a 40-cm jejunal limb in TG-RY are created through a retrocolic route. The esophagojejunostomy is completed end-to-side using a circular stapler. The jejunogastrostomy and jejunojejunostomy are made using a single-layer serosubmucosal technique with absorbable sutures.

Postoperative follow-up and function evaluation

Postoperative follow-up included clinical and laboratory examinations every 3–6 months for the first year, and every 6–12 months thereafter. Body weight was measured and any changes were recorded. At each examination, the patients were interviewed about the presence/absence of symptoms suggestive of dumping, stasis, and reflux. The presence/absence of dumping was assessed based on the diagnostic criteria established by the Japanese Society of Gastroenterological Surgery [16]. Stasis was considered to be present if the patient complained of persistent symptoms of bloating, nausea, vomiting, belching, hiccups, or epigastric discomfort. Reflux was considered to be present if the patient complained of persistent symptoms of heartburn or regurgitation. After TG-RY, all the patients received an intramuscular injection of vitamin-B12 every 6 months, while none of the patients received an injection after PG-JI. Iron was supplied as appropriate according to the attending doctor's judgment.

Comparisons of the postoperative body weight loss, serum hemoglobin decline, and incidence of iron supplementation between the PG-JI and TG-RY groups were

Table 1 Clinicopathologic features and operative details

	PG-JI ($n = 65$)	TG-RY ($n = 117$)	P value
Sex, no. (%)			0.047
Male	55 (85)	83 (71)	
Female	10 (15)	34 (29)	
Age (years), median (range)	67 (37–77)	67 (30–84)	0.516
Body weight (kg), mean ± SD	64.5 ± 10.5	62.1 ± 12.8	0.201
Body mass index (kg/m^2), mean ± SD	23.7 ± 2.9	23.5 ± 3.4	0.705
Serum hemoglobin (g/dL), mean ± SD	14.3 ± 1.2	13.8 ± 1.4	0.016
Extent of lymphadenectomy, no. (%)			0.554
D1	0 (0)	3 (3)	
D1+	65 (100)	114 (97)	
Preservation of hepatic branches of the vagal nerve, no. (%)			0.099
Yes	60 (92)	115 (98)	
No	5 (8)	2 (2)	
Cholecystectomy, no. (%)			0.177
Yes	3 (5)	13 (11)	
No	62 (95)	104 (89)	
Blood loss (mL), median (range)	240 (40–1075)	255 (12–1846)	0.939
Operation time (min), mean ± SD	261 ± 51	236 ± 68	0.010
Postoperative complication, no. (%)[a]			0.752
None	54 (83)	96 (82)	
Grade I or II	7 (11)	13 (11)	
Grade III	4 (6)	8 (7)	
Postoperative hospital stay (days), median (range)	11 (10–95)	11 (9–72)	0.347
Depth of tumor invasion, no. (%)			0.041
pT1	59 (91)	92 (79)	
≥pT2	6 (9)	25 (21)	
Lymph node metastasis, no. (%)			0.547
pN0	61 (94)	107 (91)	
≥pN1	4 (6)	10 (9)	
Tumor diameter (mm), median (range)	26 (4–85)	44.5 (6–150)	<0.001
Tumor location, no. (%)			<0.001
U or UE	65 (100)	0 (0)	
UM or UME	0 (0)	73 (62)	
MU or MUL	0 (0)	44 (38)	
Esophageal invasion, no. (%)			0.001
Yes	17 (26)	9 (8)	
No	48 (74)	108 (93)	
Length of the esophageal invasion (mm), mean ± SD	8.3 ± 5.7	6.6 ± 7.1	0.551
Histologic type, no. (%)			0.035
Differentiated	48 (74)	64 (55)	
Undifferentiated	15 (23)	49 (42)	
Others	2 (3)	4 (3)	

PG-JI, proximal gastrectomy with jejunal interposition

TG-RY, total gastrectomy with Roux-en-Y esophagojejunostomy

SD standard deviation

[a] According to the Clavien-Dindo classification [15]

Table 2 Postoperative functional outcomes

	PG-JI ($n = 65$)	TG-RY ($n = 117$)	P value
Body weight loss (%), mean ± SD[a]	12.5 ± 5.8	17.4 ± 6.4	<0.001
Decline in serum hemoglobin (%), mean ± SD[a]	7.0 ± 5.7	9.7 ± 5.4	0.002
Iron supplementation, no. (%)[a]			0.426
Yes	4 (6)	13 (11)	
No	61 (94)	104 (89)	
Anastomotic stricture, no. (%)[b]			0.781
Yes	6 (9)	9 (8)	
No	59 (91)	108 (92)	
Small bowel obstruction, no. (%)[b]			0.538
Yes	0 (0)	2 (2)	
No	65 (100)	115 (98)	
Dumping, no. (%)[b]			0.003
Yes	7 (11)	35 (30)	
No	58 (89)	82 (70)	
Stasis, no. (%)[b]			0.358
Yes	33 (51)	51 (44)	
No	32 (49)	66 (56)	
Reflux, no. (%)[b]			0.121
Yes	22 (34)	27 (23)	
No	43 (66)	90 (77)	

PG-JI, proximal gastrectomy with jejunal interposition

TG-RY, total gastrectomy with Roux-en-Y esophagojejunostomy

SD standard deviation

[a] Evaluation at 1 year after the surgery

[b] Evaluation during a median follow-up period of 42 (range, 12–78) months

performed at 1 year after the surgery. The incidences of anastomotic stricture necessitating endoscopic balloon dilation(s), small bowel obstruction necessitating hospitalization, and other symptoms were evaluated over the whole follow-up period. The symptoms were judged as positive if they were present at least once postoperatively. In patients with ≥3-year follow-up, the changes in body weight and serum hemoglobin level from 1 to 3 and 1 to 5 postoperative years were also assessed.

In the PG-JI group, postoperative endoscopy was performed annually. Patients were instructed to fast beginning at 8 p.m. on the day before the examination. The amount of gastric food residue was recorded according to the RGB classification [17]. The presence/absence of bile reflux into the remnant stomach, reflux esophagitis, peptic ulcer, and remnant gastric cancer was also assessed.

Statistical analysis

IBM SPSS Statistics 20.0 (IBM, Corp., Armonk, NY, USA) was used for the statistical analyses. The Chi-square test was applied for the comparisons of nominal variables, and the Student t test or Mann–Whitney U test was used for comparisons of continuous variables. P values of <0.05 were considered to indicate significance.

Results

Clinicopathologic features and operative details

The clinicopathologic features and operative details of the enrolled patients are shown in Table 1.

All the procedures were performed via laparotomy alone, with preservation of the spleen. An R0 resection was achieved in all the cases. The PG-JI group was associated with a higher male predominance (85 % [55/65] vs. 71 % [83/117], $P = 0.047$), a higher baseline serum hemoglobin level (14.3 ± 1.2 vs. 13.8 ± 1.4 g/dL, $P = 0.016$), and a longer operation time (261 ± 51 vs. 236 ± 68 min, $P = 0.010$) than the TG-RY group. The postoperative complications graded as III included two leakages at the

Table 3 Changes in body weight and serum hemoglobin level during periods from 1 to 3 and 1 to 5 postoperative years

	From 1 to 3 years		From 1 to 5 years	
	PG-JI ($n = 36$)	TG-RY ($n = 78$)	PG-JI ($n = 14$)	TG-RY ($n = 30$)
Body weight, no. (%)				
Unchanged (±2 kg)	25 (69)	63 (81)	9 (64)	27 (90)
Increased (>2 kg)	6 (17)	9 (12)	4 (29)	0 (0)
Decreased (>2 kg)	5 (14)	6 (8)	1 (7)	3 (10)
Serum hemoglobin, no. (%)				
Unchanged (±1 g/dL)	25 (69)	67 (86)	9 (64)	18 (60)
Increased (>1 g/dL)	9 (25)	10 (13)	5 (36)	8 (27)
Decreased (>1 g/dL)	2 (6)	1 (1)	0 (0)	4 (13)

PG-JI, proximal gastrectomy with jejunal interposition

TG-RY, total gastrectomy with Roux-en-Y esophagojejunostomy

esophagojejunostomy in the PG-JI group and one leakage at the esophagojejunostomy in the TG-RY group. There were no in-hospital mortalities in either group.

Pathologically, the PG-JI group was associated with fewer ≥pT2 tumors (9 % [6/65] vs. 21 % [25/117], $P = 0.041$) and a smaller tumor diameter (26 [4–85] mm vs. 44.5 [6–150] mm, $P < 0.001$) than the TG-RY group. On the other hand, the PG-JI group had esophagus-invading tumors (26 % [17/65] vs. 8 % [9/117], $P = 0.001$) and a differentiated-type histology (74 % [48/65] vs. 55 % [64/117], $P = 0.035$) more often than the TG-RY group. The mean length of the esophageal invasion was similar between the two groups (8.3 ± 5.7 vs. 6.6 ± 7.1 mm, $P = 0.551$).

Functional outcomes

The postoperative functional outcomes are presented in Table 2. The PG-JI group showed a significant reduction in body weight loss (12.5 ± 5.8 vs. 17.4 ± 6.4 %, $P < 0.001$) and serum hemoglobin decline (7.0 ± 5.7 vs. 9.7 ± 5.4 %, $P = 0.002$), compared with the TG-RY group, while the incidence of iron supplementation was similar between the two groups. During a median follow-up period of 42 months (range, 12–78 months), one patient in each group experienced tumor relapse. The incidences of anastomotic stricture and small bowel obstruction were similar between the two groups. The PG-JI group was associated with less frequent dumping symptoms than the TG-RY group (11 % [7/65] vs. 30 % [35/117], $P = 0.003$), while the incidences of symptoms suggestive of stasis and reflux were similar between the two groups.

Thirty-six patients in the PG-JI group and 78 patients in the TG-RY group had a ≥3-year follow-up. In around 90 % of these patients, the body weight and serum hemoglobin level were unchanged or even increased during the periods of from 1 to 3 and from 1 to 5 postoperative years. The patients in the PG-JI group had a greater probability of experiencing an increase in both their body weight and their serum hemoglobin level within these periods (Table 3).

Endoscopic findings

The endoscopic findings in the PG-JI group are shown in Table 4. In the examinations performed at 1 year after the surgery, more than half of the patients had gastric food residue graded as II or III, but the grades improved over time. Persistent bile reflux was observed in around 10 % of the patients. Reflux esophagitis was not seen. Six cases of peptic ulcer were detected, but all of them were treated successfully with an H2 blocker or proton pump inhibitor. Gastric remnant cancer was found in four patients; three of these patients had early-stage tumors and underwent curative endoscopic resection, while the remaining patient had a rapidly growing tumor with liver metastasis and received palliative chemotherapy.

Discussion

This study showed clear functional advantages of PG-JI over TG-RY in reducing postoperative body weight loss, anemia, and dumping symptoms without increasing the risks of reflux esophagitis, anastomotic stricture, and small bowel obstruction. PG-JI is a relatively time-consuming, complicated procedure, but it is as technically feasible as TG-RY. PG-JI appears to offer a better quality of life to patients with early gastric cancer than TG-RY, at the expense of raising the risk of remnant gastric cancer.

Table 4 Endoscopic findings after a proximal gastrectomy with jejunal interposition

	Time after surgery (years)				
	One ($n = 65$)	Two ($n = 45$)	Three ($n = 34$)	Four ($n = 21$)	Five ($n = 12$)
Food residue, no. (%)[a]					
Grade 0 or I	28 (43)	25 (56)	20 (59)	15 (71)	10 (83)
Grade II or III	37 (57)	20 (44)	14 (41)	6 (29)	2 (17)
Bile reflux, no. (%)					
Yes	6 (9)	4 (9)	3 (9)	2 (10)	1 (8)
No	59 (91)	41 (91)	31 (91)	19 (90)	11 (92)
Reflux esophagitis, no. (%)					
Yes	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
No	65 (100)	45 (100)	34 (100)	21 (100)	12 (100)
Peptic ulcers, no. (%)					
Yes	2 (3)	1 (2)	3 (9)	0 (0)	0 (0)
No	63 (97)	44 (98)	31 (91)	21 (100)	12 (100)
Remnant gastric cancer, no. (%)					
Yes	0 (0)	1 (2)	0 (0)	2 (10)	1 (8)
No	65 (100)	44 (98)	34 (100)	19 (90)	11 (92)

[a] According to the RGB classification [17]

In this study, the body weight and serum hemoglobin level were maintained for from 1 to 3 and from 1 to 5 postoperative years in most patients, suggesting that the functional advantages of PG over TG are long-lasting. These findings are consistent with previous reports: Nozaki et al. [18] showed the superiority of PG-JI to TG-RY, and Ichikawa et al. [19] showed the superiority of PG with esophagogastrostomy to TG-RY for reducing postoperative body weight loss and anemia.

In PG-JI, the preserved stomach can function as a food reservoir and can maintain the absorption of ingested nutrients, including iron and vitamin B12, and the preserved pylorus can regulate gastric emptying and prevent duodenogastric reflux. Furthermore, the interposed jejunum can prevent gastroesophageal reflux. It is conceivable that these mechanisms synergistically contributed to the present study results. In fact, preservation of the pylorus has also been shown to reduce dumping syndrome, frequent flatus, and body weight loss in patients undergoing distal gastrectomy [20].

Gastric food residue observed during endoscopy following PG-JI was found more frequently in the present study than in our previous report [12], which was based on data for patients who had undergone operations between 1993 and 2005. This discrepancy may partly be attributed to the difference in timing of the endoscopic evaluations between the studies. In fact, the amount of food residue decreased over time in the present study. It is speculated that sequential improvement in gastric motility as well as patient adaptation to food habits contributed to this decrease. On the other hand, the incidences of endoscopic bile reflux, reflux esophagitis, and peptic ulcers were consistently low and were comparable to our previous results [12].

Active surveillance for remnant gastric cancer is necessary after PG. Remnant gastric cancer can often be treated successfully by endoscopic resection if detected at an early stage [12, 21]. In the present study, however, we found a surgically unresectable tumor during the periodic follow-up. Stricter endoscopic examinations may be needed for patients undergoing PG, especially during the early postoperative years when gastric food residue is likely to be found.

In this study, all the surgeries were performed via laparotomy alone with almost exclusively D1+ lymphadenectomy, according to the current Japanese standards [5]. In addition, reconstructions of the digestive tract were performed uniformly based on our institutional policy. Our data, supported by such homogeneous open procedures, may be useful as a reference for future evaluations of postoperative functional outcomes of laparoscopic PG and TG, which have been increasingly employed in recent years [22–25].

In this study, the patients who underwent PG-JI were not offered an alternative of undergoing TG-RY, and vice versa. This selection bias is a major limitation of the present study and should be taken into consideration when interpreting the study results. Some of the baseline clinicopathologic features, including the sex, tumor depth, and tumor location, were significantly different between the PG-JI and TG-RY groups. The difference of the tumor depth, however, might bias the study results minimally,

because only one patient in each group experienced tumor relapse during the follow-up. The patients undergoing PG-JI were predominantly male and more often had esophagus-invading tumors. Hereafter, PG is expected to play an increasingly important role in the surgical treatment of esophagogastric junction cancer [3].

Evaluating the quality of life of patients with gastric cancer is an important challenge [26–29]. In the present study, we assessed a limited number of well-known quality of life parameters, including body weight, serum hemoglobin level, and interview-based symptoms suggestive of dumping, stasis, and reflux. Thus, further studies are needed to confirm the superiority of PG-JI to TG-RY. Recently developed Dysfunction After Upper Gastrointestinal Surgery (DAUGS)20 scoring system [30] and Postgastrectomy Syndrome Assessment Scale (PGSAS)-45 [31] are very promising tools to evaluate comprehensively the quality of life of gastrectomized patients. Using PGSAS-45, Takiguchi et al. [32] compared PG and TG-RY and reached conclusions similar to ours. Assessing the comparative effects of various reconstructions after PG on patient quality of life may be a future task.

The volume of the remnant stomach after PG can affect patient quality of life [33]. In the present study, PG was indicated for patients with cancer confined to the upper third of the stomach, and more than half of the stomach was preserved routinely. In this patient population, esophagogastrostomy is the reconstruction method most commonly used in Japan [9]. Jejunal interposition and the double-tract method may be more applicable than esophagogastrostomy when the remnant stomach is smaller (e.g., when the tumor spreads to the middle third of the stomach) [22], though the functional and oncological feasibility of PG used in such a situation has yet to be evaluated. Jejunal interposition and the double-tract method are also considered advantageous to patients with an esophagus-invading tumor necessitating removal of the abdominal esophagus, because these reconstructions do not require a fundoplication [22].

In conclusion, compared with TG-RY, PG-JI with preservation of more than half of the stomach has clear functional advantages and may provide better quality of life for patients with early gastric cancer involving the upper third of the stomach, including esophagogastric junction cancer.

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Compliance with ethical standards

Conflicts of interest None.

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