Clinical outcome of proximal gastrectomy in patients with early gastric cancer in the upper third of the stomach

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***Objective*: To determine whether clinical outcomes after proximal gastrectomy are better than those after total gastrectomy with Roux-en Y reconstruction.**
***Methods*: We studied 10 consecutive patients with early gastric cancer who underwent esophagogastrostomy after proximal gastrectomy (PG group). Nutritional variables in these patients were compared with those in 10 consecutive patients who underwent Roux-en Y reconstruction after total gastrectomy (TG group). Patients were followed up for 5 years after operation.**
***Results*: There was no anastomotic leakage. The total cholesterol level 1 year after operation was higher in the PG group than in the TG group ($p<0.05$). Body mass index was significantly lower than the preoperative value between 1 month and 2 years postoperation in the PG group, whereas the TG group showed decreases between 3 months to 5 years postoperation. The percent decreases in body weight at 3 and 4 years in the PG group were lower than those in the TG group (both $p<0.05$). Postoperative weight loss was thus milder in the PG group than in the TG group.**
***Conclusion*: Esophagogastrostomy after PG may produce better clinical outcomes than Roux-en Y reconstruction after TG in patients with early gastric cancer arising in the upper third of the stomach.**

Key words: Proximal gastrectomy, total gastrectomy, esophagogastrostomy, Roux-en Y reconstruction, gastric cancer

INTRODUCTION

Recent advances in diagnostic techniques have led to the detection of an increasing number of early gastric cancers. Multivariate analysis showed a significant dominance of host- and tumor-related factors over the type of surgical procedure in the prognosis of early gastric cancer patients [1]. A marked and significant shift of gastric adenocarcinoma to the proximal location occurred with a significant stage improvement at presentation [2]. The optimal treatment for these proximal tumors is unknown. The indication for endoscopic mucosal resection (EMR) determined by the Japanese Gastric Cancer Association includes differentiated intramucosal adenocarcinomas less than 20 mm in diameter and without ulcer findings [3]. Endoscopic submucosal dissection (ESD) is a new technique developed to obtain one-piece resection in cases of early gastric cancer [4]. Surgeons who advocate total gastrectomy for patients with proximal gastric cancer have suggested that complete resection results in a tumor-free proximal margin and permits more extended lymph node dissection [5]. However, proximal gastrectomy (PG) and total gastrectomy (TG) have been found to have similar survival and recurrence rates, with the former offering the advantage of the preserved physiologic functions of the gastric remnant in patients with early gastric cancer [6]. A great number of those who survive suffer from postoperative symptoms and a decreased quality of life when the whole stomach is removed [7]. Malnutrition, weight loss, early satiety, dumping, epigastric pain, postprandial fullness, vomiting, and heartburn may occur after TG [8]. Whether clinical outcomes after PG are better than those after TG with Roux-en Y reconstruction remains controversial. We report the clinical outcomes of esophagogastrostomy after PG as compared with Roux-en Y reconstruction after TG.

PATIENTS AND METHODS

Patients

A review of the medical records for gastric adenocarcinomas at Tokai University Tokyo Hospital between 1997 and 2004 identified 305 patients who underwent resection for gastric cancer. We studied 10 consecutive patients who underwent PG for stage 1a gastric cancer [9] arising in the upper third of the stomach. PG was indicated in patients with gastric cancer who were

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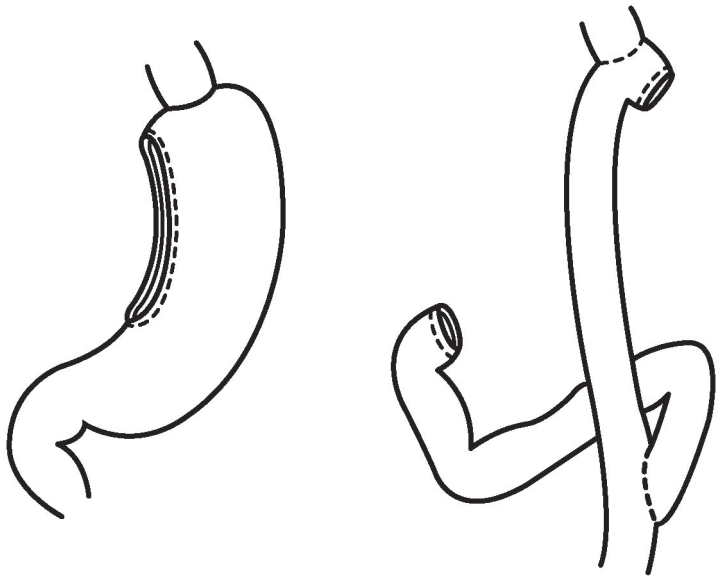

a **b**

Fig. 1 Schematic representation of surgical techniques for esophagogastrostomy after PG (**a**) and Roux-en Y reconstruction after TG (**b**).

scheduled to undergo curative resection of one third or less of the proximal stomach, with preservation of at least the distal two thirds. Neither EMR nor ESD was indicated in these 10 patients, because 5 patients had definite signs of submucosal invasion, 3 adenocarcinomas of the esophago-gastric junction, one endoscopic signs of submucosal invasion, and one ulcer findings. Operation time, intraoperative bleeding volume, starting date of oral intake, white blood cell counts, lymphocyte counts, hemoglobin levels, total protein, serum albumin, total cholesterol, body mass index (weight in kg/height^2 in m) [10] and percent decrease in body weight were examined for 5 years after operation and compared with the preoperative values. As controls, 10 consecutive patients who underwent Roux-en Y reconstruction after TG for stage 1a gastric cancer [9] were studied retrospectively. Neither EMR nor ESD was indicated in these 10 patients, because 5 patients had definite signs of submucosal invasion, 3 poorly differentiated adenocarcinomas, and 2 signet-ring cell carcinomas [9].

The Student's t test and χ^2 test were used for statistical analysis. P values of less than 0.05 were considered to indicate statistical significance.

Surgical procedures

Esophagogastrostomy after PG was performed as described previously [11]. PG was an abdominal-only operation without extraabdominal incision. Splenectomy and distal pancreas resection were not performed. The distal margins were at least 3 cm below the tumor. The esophagus was divided, and a circular stapler was inserted through the distal end of the esophagus into the stomach. End-to-side direct anastomosis was performed between the esophagus and the greater curvature of the upper body of the stomach before PG. To perform PG, a linear stapler was placed and fired across the upper third of the stomach (Fig. 1a). To prevent sliding hernia at the site of esophagogastrostomy, the dorsal anastomosis was sutured to the median arcuate ligament with 2 or 3 interrupted serous-muscular sutures (3-0 silk), according to the Hill's posterior gastropexy. Cardioplasty was performed by the Dor's anterior fundic wrap technique. The serous membrane of the greater curvature of the stomach near the anastomosis was sutured to the anterior wall of the abdominal esophagus with 2 to 3 sutures (3-0 silk). Pyloroplasty was performed manually.

Roux-en Y reconstruction after TG was performed as follows. TG was abdominal-only operation without extraabdominal incision. Splenectomy and distal pancreas resection were not performed. After TG, end-to-side esophagojejunostomy was performed with a circular stapler. The duodenal and jejunal stumps were closed with a lineal stapler. The Roux-en Y anastomosis was made 50 cm distally using the Albert-Lembert techniques (Fig. 1b).

RESULTS

The clinicopathological details of the patients are summarized in Table 1. Histopathologically, the tumor size and invasion did not significantly differ between the PG and TG groups. In PG group, histological types of tumor were 2 papillary adenocarcinomas, and 8 tubular adenocarcinomas. In TG group, those were 5 tubular adenocarcinomas, 3 poorly differentiated adenocarcinomas and 2 signet-ring cell carcinomas [9]. None of the patients had lymph node metastasis. The disease stage was thus stage 1a [9] in both groups. Gender, age, preoperative body weight, and body mass index were similar in the PG and TG groups. Operation time was significantly shorter in the PG group (171.6 ± 44.5 min) than in the TG group (232.3 ± 64.2 min; $p<0.05$). Intraoperative bleeding volume was significantly lower in the PG group (294.5 ± 228.4 ml) than in the TG group (656.9 ± 394.5 ml;

$p<0.05$). The number of postoperative days until starting oral intake was similar in the PG and TG groups (Table 2). There was no anastomotic leakage.

White blood cell counts, lymphocyte counts, hemoglobin, total protein, and serum albumin were essentially stable and did substantially change from the preoperative levels in most patients in the PG and TG groups during the 5 years after operation (Fig. 2a to 2c). The total cholesterol level was significantly higher in the PG group (201.0 ± 48.0 mg/dl) than in the TG group (158.3 ± 19.2 mg/dl; $p<0.05$) 1 year after operation, but did not differ between the groups from the 2 to 5 postoperative year (Fig. 2d). As compared with the preoperative value (23.6 ± 1.8), body mass index in the PG group was significantly decreased from the preoperative value at 1 month (22.2 ± 0.8; $p<0.05$), 3 months (20.3 ± 4.3; $p<0.05$), 6 months (20.9 ± 1.9; $p<0.02$), 1 year (21.3 ± 2.1; $p<0.05$) and 2 years after operation (21.9 ± 1.2; $p<0.05$), but did not differ between the 3 and 5 postoperative year. In the TG group, body mass index was significantly lower than the preoperative value (24.1 ± 2.7) at 3 months (21.6 ± 1.3; $p<0.05$), 6 months (21.0 ± 0.7; $p<0.02$), 1 year (19.9 ± 2.6; $p<0.005$), 2 years (21.3 ± 1.1; $p<0.02$), 3 years (21.1 ± 0.7; $p<0.02$), 4 years (21.2 ± 0.9; $p<0.02$), and 5 years after the operation (21.1 ± 1.1; $p<0.05$) (Fig. 3). As compared with the preoperative value, the percent decrease in body weight in the PG group was 9.0 ± 3.0% at 1 month, 10.8 ± 3.3% at 3 months, 11.2 ± 4.7% at 6 months, 9.0 ± 6.2% at 1 year, 8.5 ± 6.3% at 2 years, 6.7 ± 6.6% at 3 years, 6.3 ± 5.9% at 4 years, and 7.1 ± 7.1% at 5 years after the operation, and that in the TG group was 8.3 ± 3.2% at 1 month, 12.4 ± 5.9% at 3 months, 13.7 ± 5.8% at 6 months, 16.1 ± 9.6% at 1 year, 13.1 ± 6.3% at 2 years, 15.2 ± 6.1% at 3 years, 15.0 ± 7.5% at 4 years, and 14.7 ± 7.6% at 5 years after the operation. The percent decreases in body weight at 3 and 4 years after the operation were significantly lower in the PG group than in the TG group (both $p<0.05$) (Fig. 4).

Table 1 Pathological characteristics of the patients

	PG	TG
Number of patients	10	10
Tumor size (cm)		
Diameter [1)]	2.0±1.0	2.6±1.2
(range)	(1.0 – 4.0)	(0.7 – 4.0)
Depth of tumor invasion		
Mucosa	5	6
Submucosa	5	4
Histological type		
Papillary adenocarcinoma	2	0
Tubular adenocarcinoma	8	5
Poorly differentiated adenocarcinoma	0	3
Signet-ring cell carcinoma [7]	0	2
Lymph node metastasis		
Positive	0	0
Negative	10	10
Stage		
1a	10	10

[1)] Data are means ± standard deviation.

DISCUSSION

Early gastric cancer in the proximal third of the stomach has generally been treated by TG with extended lymph node dissection [12]. Considerable controversy remains regarding the appropriate extent of lymph node dissection in these cancers. The indications for EMR or ESD are determined by the risk of lymph node metastasis and such technical considerations as the size and position of the lesion. The incidence of lymph node involvement ranges from 3 to 5% for gastric cancers limited to the mucosa and 16 to 25% for those limited to the submucosa [13, 14]. Recent studies have shown that early gastric cancer in the proximal

Table 2 Clinical characteristics of the patients [1)]

	PG group	TG group	*P*
Number of patients	10	10	
Sex, male/female	9/1	9/1	NS
Age (years)	67.8±5.9	61.4±8.5	NS
	(59 – 78)	(45 – 76)	
Preoperative body weight (kg)	62.4±7.9	65.4±9.2	NS
	(47.6 – 74.2)	(50.0 – 78.0)	
Preoperative body mass index (kg/m^2)	23.6±1.8	24.1±2.7	NS
	(20 – 25)	(18 – 26)	
Operation time (min)	171.6±44.5	232.3±64.2	$p<0.05$
	(120 – 251)	(135 – 360)	
Intraoperative bleeding volume (ml)	294.5±228.4	656.9±394.5	$p<0.05$
	(36 – 873)	(185 – 1360)	
Postoperative days until starting oral intake	8.0±0.8	7.8±1.0	NS
	(7 – 10)	(7 – 10)	

[1)] Values are means ± standard deviation. Range is shown in parentheses.

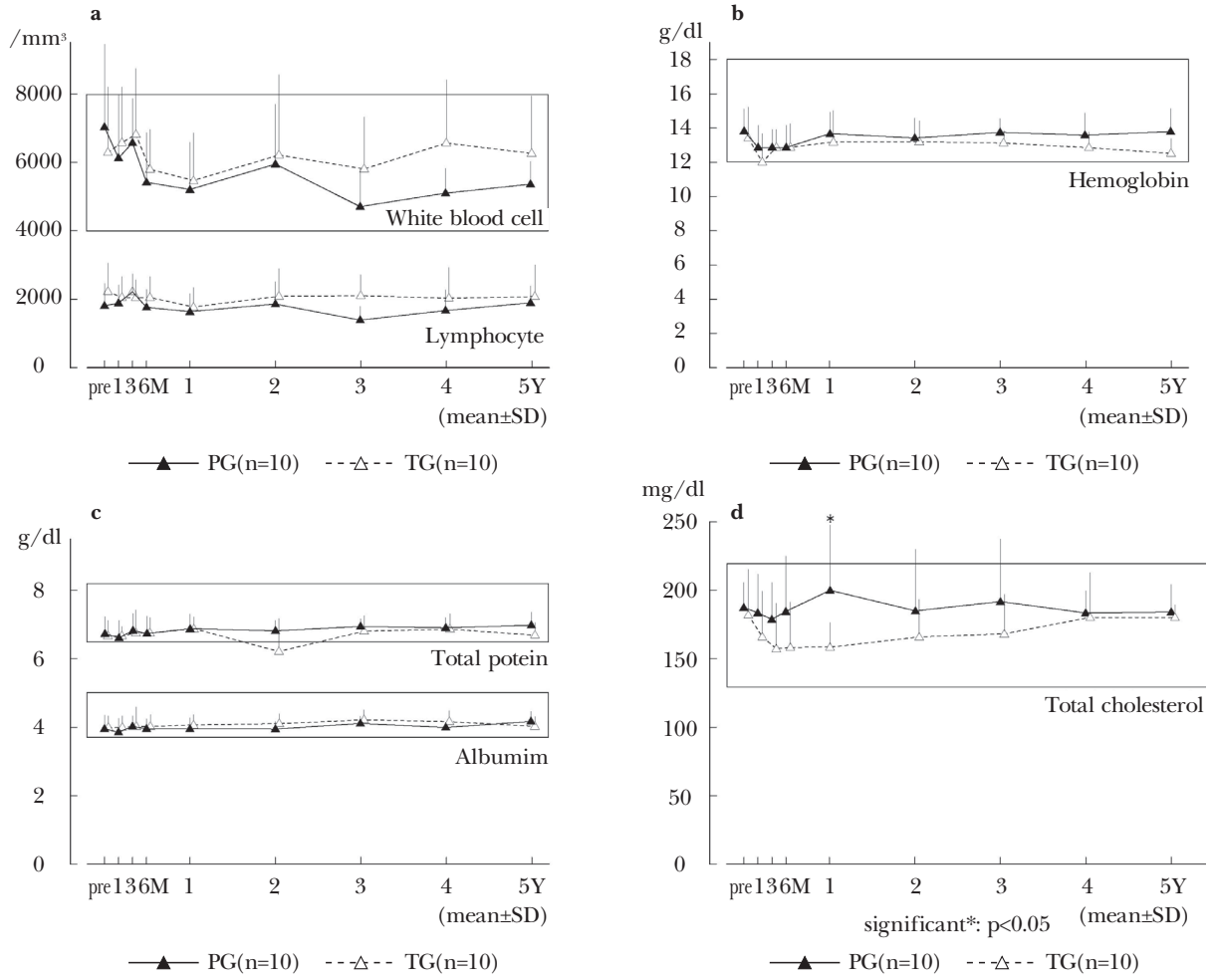

Fig. 2 Hematological and blood chemical parameters before and after surgery.
a White blood cell counts and lymphocyte counts before and after surgery. **b** Hemoglobin levels before and after surgery. **c** Total protein and serum albumin levels before and after surgery. **d** Total cholesterol levels before and after surgery. M, months; Y, years.

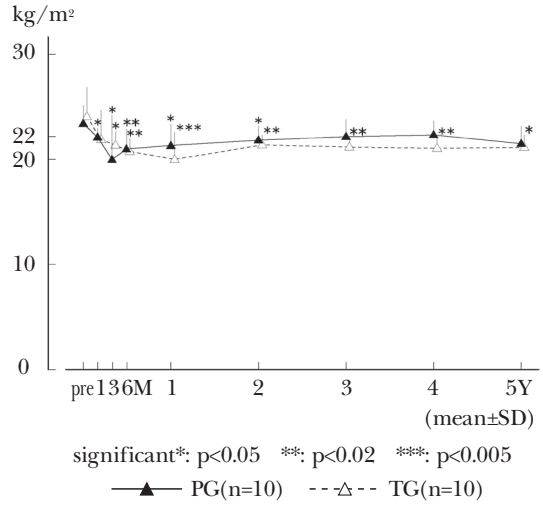

Fig. 3 Body-mass indices (weight in kg/height² in m) before and after surgery.
M, months; Y, years.

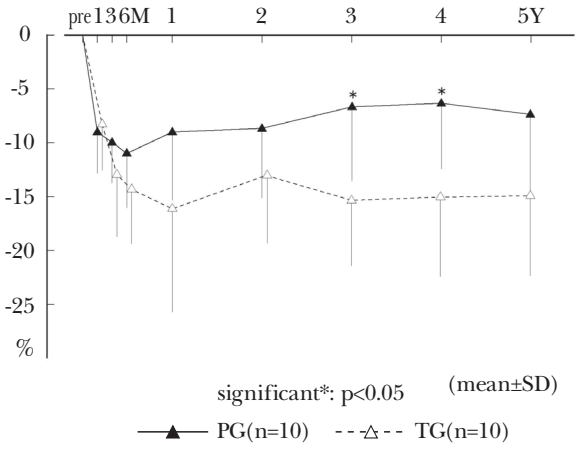

Fig. 4 Percent decreases in body weight after surgery as compared with the preoperative value.
M, months; Y, years.

third of the stomach is free of metastases to the lower perigastric lymph nodes [15, 16]. Overall survival and recurrence rates have been shown to be similar after TG or PG in patients with proximal gastric cancer [6, 17, 18]. Proximal gastrectomy with esophagogastrostomy has a shorter operation time, less blood loss, and a shorter hospital stay after operation than jejunal interposition in patients with gastric cancer [19]. In our study, PG was associated with a significantly shorter operation time and a significantly lower intraoperative bleeding volume than TG. Both PG and TG were safe procedures, with no anastomotic leakage.

Some studies have demonstrated an improved quality of life after distal subtotal gastrectomy as compared with TG in patients with cancer of the lower or middle stomach [20], whereas others have shown that proximal gastric resection results in significantly reduced physical ability and increased psychological disturbances [21]. Heartburn, indicating reflux of duodenal contents into the esophagus, is more common after PG than after TG with Roux-en Y reconstruction in patients with cancer arising in the upper third of the stomach [21]. Reflux esophagitis is associated with many types of reconstruction after PG [22, 23]. Because both PG and TG require esophageal anastomosis, differences in morbidity, such as anastomotic stenosis, should be minimal [18]. Previously we reported that reflux esophagitis and anastomotic stenosis occurred in 40% of the patients having undergone PG [11]. Symptoms due to reflux esophagitis in the PG group responded to conservative treatment with antacids within 2 years after operation. The Hill's posterior gastropexy and the anterior fundic wrap of Dor appeared to have prevented esophagogastric reflux. Anastomotic stenosis required treatment by endoscopic balloon dilatation within 6 months after operation.

White blood cell counts, lymphocyte counts, hemoglobin levels, and blood chemical findings such as total protein and serum albumin were essentially stable. These variables did not substantially differ from the preoperative levels in most patients in the PG and TG groups during the first 5 years after operation. The total cholesterol level 1 year after operation was significantly higher in the PG group than in the TG group ($p<0.05$), but did not significantly differ between the groups from the 2 to 5 postoperative year. Postprandial blood glucose levels were significantly higher in patients with duodenal exclusion than in normal controls, supporting the hypothesis that duodenal exclusion such as Roux-en Y reconstruction disturbs glucose homeostasis more than reconstruction with a preserved duodenal passage [24]. Energy intake is significantly related to increased body mass index after operation. In our study, the body mass indices in the PG group from 1 month to 2 years after operation were significantly lower than the preoperative level (1 and 3 months, $p<0.05$; 6 months, $p<0.02$; 1 and 2 years, $p<0.05$), but did not differ significantly between the 3 and 5 postoperative year. In the TG group, the body mass indices between 3 months to 5 years after operation were significantly lower than the preoperative level (3 month, $p<0.05$; 6 months, $p<0.02$; 1 year, $p<0.005$; 2 to 4 years, $p<0.02$; 5 years, $p<0.05$). Average weight loss after PG was less than that after TG [25]. A recent study reported that mean weight loss 1 year after PG was 11.2% [26]. The percent decrease in body weight after operation in the PG group was the lowest at 6 months (11.2%) and then fluctuated between 6.3% and 9.0%. In the TG group, the percent decrease in body weight was the lowest at 1 year (16.1%), and then fluctuated between 13.1% and 15.2%. The percent decreases in body weight at 3 and 4 years were significantly lower in the PG group than in the TG group (both $p<0.05$). Postoperative weight loss was thus milder in the PG group than in the TG group.

We conclude that esophagogastrostomy after PG may be less invasive, simpler, and produce better outcomes than Roux-en Y reconstruction after TG in patients with early gastric cancer arising in the upper third of the stomach.

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