



Pathophysiological Studies on the Relationship between Postgastrectomy Syndrome and Gastric Emptying Function at 5 Years after Pylorus-preserving Distal Gastrectomy for Early Gastric Cancer

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Abstract. Pylorus-preserving distal gastrectomy (PPG) has frequently been performed on patients with early gastric cancer in Japan to prevent the postgastrectomy syndrome seen after conventional distal gastrectomy (CDG). The long-term postoperative quality of life (QOL) and gastric emptying function in patients after PPG has not been assessed in detail. To clarify the usefulness of PPG for treating early gastric cancer we investigated the relation between postgastrectomy syndrome and gastric emptying function 5 years after PPG and then compared the results with those 5 years after CDG. Altogether, 32 patients who underwent curative gastrectomy at our clinic for early gastric cancer (submucosal cancer without lymph node metastasis) were studied. Ten subjects who underwent PPG with D2 lymphadenectomy without preserving the hepatic and pyloric branches of the vagal nerve [group A: eight men, two women; age 33–70 years (mean 60.7 years)] were interviewed and asked about appetite, weight loss, epigastric fullness, reflux esophagitis, and early dumping syndrome. They were compared with patients after CDG [group B: 36–72 years (mean 63.6 years)]. Esophagogastric endoscopy, abdominal ultrasonography, and gastric emptying function were also studied. The gastric emptying time of a semisolid diet was measured with a radioisotope method using ^{99m}Tc-labeled rice gruel; the gastric emptying time of a liquid diet was measured with the acetaminophen method using orange juice. The control subjects (group C) consisted of 18 healthy volunteers (10 men, 8 women) without gastrointestinal symptoms aged 38 to 68 years (mean 60.8 years). The following results were obtained: PPG (group A) alleviated postoperative gastrointestinal symptoms such as appetite loss, reflux esophagitis, early dumping syndrome, lost body weight, endoscopic reflux esophagitis, endoscopic gastritis in the remnant stomach, and postgastrectomy cholecystolithiasis better than did CDG (group B). The only weak point with the PPG procedure was that it produced a feeling of epigastric fullness. The pattern of the gastric emptying curve for the semisolid diet was almost the same among groups A, B, and C, although delayed gastric emptying was clearly more frequent in group A than in group B or C ($p < 0.05$). Gastric emptying with the liquid diet in group B was significantly faster than that in groups A and C ($p < 0.01$). Gastric emptying in groups A and C was similar. These results showed that PPG improved the postoperative QOL, but the delayed emptying of semisolid diet after PPG led to a feeling of epigastric fullness after meals due to retention of contents in the residual stomach. Epigastric fullness after meals continued in many patients after PPG. Thus the only disadvantage of the PPG procedure is the sensation of epigastric

fullness and gastric stasis due to delayed gastric emptying of a semisolid diet.

Conventional distal gastrectomy (CDG) with D2 lymph node dissection has generally been performed for early gastric cancer in Japan. However, postgastrectomy syndrome such as malnutrition due to loss of appetite, weight loss, dumping syndrome, alkaline reflux esophagitis, alkaline gastritis of the remnant stomach, and gallbladder dysfunction are distressing sequelae in patients who have undergone CDG [1, 2]. Recently, the number of small early gastric cancers detected has increased, which has led to the frequent application of various limited operations including radical gastrectomy with endoscopic mucosal resection, local resection, segmental resection, and pylorus-preserving distal gastrectomy (PPG) to prevent postgastrectomy syndrome [3]. PPG is now frequently performed in Japan.

Pylorus-preserving distal gastrectomy was first developed by Maki et al. [4] in 1967 to treat gastric ulcers. Kodama et al. [1] first reported the indications of PPG for early gastric cancer in 1991 based on clinicopathologic analyses. PPG has been reported by several investigators to be beneficial in terms of the postoperative quality of life (QOL); it is also associated with a significantly lower incidence of early dumping syndrome, bile regurgitation in the remnant stomach (alkaline gastritis) and esophagus (alkaline reflux esophagitis), postoperative cholecystolithiasis, and a significant decrease in postoperative malnutrition due to loss of appetite and postoperative body weight loss [5–10]. That is, as foods and regurgitation of intestinal contents are maintained by the preserved pyloric ring with this technique, early dumping syndrome, alkaline gastritis, and alkaline reflux esophagitis (most common disorders occurring after CDG) are not present after PPG. Consequently, the PPG technique has been considered reasonable reduction surgery [1]. Moreover, it has been reported that the results of the gastric emptying function test for solid diet showed no acute emptying of ingested food; and the emptying function of the residual stomach showed a slow emptying pattern compared with that in normal subjects and patients who had undergone CDG [1, 6].

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With the accumulation of experience with PPG, however, disadvantages have emerged. Even PPG patients for whom more than 1 year had passed since surgery frequently had a feeling of epigastric fullness after meals and long-term retention of foods in the residual stomach. This postoperative epigastric fullness due to the retention of foods after PPG has not been assessed in detail.

It has been recognized that control of emptying is different for the proximal and distal parts: The former empties liquid diet, and the latter empties semisolid or solid diet (or both) [11, 12]. Well known emptying function tests include the radioisotope method when emptying of semisolid diet or solid diet is examined and the acetaminophen method when emptying of liquid diet is examined [13]. The radioisotope and acetaminophen methods are the most frequently used physiologic and quantitative tests; they are noninvasive and cause patients no pain. Quality of life and gastric emptying function after PPG over a period of 5 years or more have not been reported to date. We therefore studied the postoperative QOL and emptying function of the residual stomach during the fifth year after operation in patients who underwent PPG for early gastric cancer and compared them with those of patients after CDG. For the gastric emptying of solid food (a semisolid diet of rice gruel) a radioisotope method using ^{99m}Tc tin colloid (short half-life of about 6 hours; a small radiation dose of 40 MBq, equivalent to the dose used to obtain one plain abdominal radiogram) was used. The acetaminophen method was used with orange juice to examine the emptying of a liquid diet. The patients were also interviewed concerning postgastrectomy syndrome, esophagogastric endoscopy, and abdominal ultrasonography.

Patients and Methods

Patients

A total 32 patients with early gastric cancer who underwent gastrectomy at the First Department of Surgery, Nihon University School of Medicine, between January 1993 and December 1996 were included in this study. The present studies were performed in 10 patients who underwent PPG (group A: D2 lymph node dissection without preserving the hepatic and pyloric branches of the vagal nerve) and 22 patients who underwent conventional distal gastrectomy (CDG) (group B: D2 lymph node dissection without preserving the hepatic and pyloric branches of the vagal nerve) to treat early gastric cancer (histologically all were submucosal cancer without lymph node metastasis).

Patients in group A consisted of eight men and two women aged 33 to 70 years (mean 60.7 years). Patients in group B consisted of 14 men and 8 women aged 34 to 70 years (mean 64.7 years). The controls (group C) were 18 healthy volunteers (10 men, 8 women) without gastrointestinal symptoms aged 38 to 68 years (mean 60.8 years).

There were no complications after the surgery, and none of the patients underwent chemotherapy.

The patients (groups A and B) were interviewed concerning their postgastrectomy symptoms, esophagogastric endoscopy, abdominal ultrasonography, and the examinations to determine gastric emptying function 5 years after the surgery. Results in group A were compared with those in group B.

During the PPG procedure, the hepatic and pyloric branches of the vagal nerves were cut with suprapyloric lymph node dissection, and the distal two-thirds of the stomach was resected while retain-

Table 1. Diagnostic criteria for dumping syndrome (Japan Society of Gastrointestinal Surgery).

Systemic symptoms	
Do you have cold sweat?	
Is your heart pounding?	
Do you have dizziness?	
Do you have numbness and/or syncope?	
Do you become red in the face?	
Do you become pale in the face?	
Does your body become hot?	
Do you feel general malaise and become weakened?	
Do you find it impossible to resist sleepiness?	
Do you have headache or dull headache?	
Do you feel chest pressure?	
Abdominal symptoms	
Is your stomach growling?	
Do you have abdominal pain (except when drinking milk)?	
Do you have diarrhea (except when drinking milk)?	
Do you have nausea?	
Do you vomit?	
Do you have abdominal distension?	
Do you have abdominal discomfort?	

Early dumping syndrome: patients with one or more systemic symptoms. Pseudo-dumping syndrome: patients with any of the abdominal symptoms.

ing a 1.5-cm pyloric cuff. In accordance with the Japanese classification of gastric carcinoma issued by the Japanese Research Society for Gastric Cancer [10], group 2 lymph nodes (including suprapyloric lymph nodes and lymph nodes along the left gastric artery) were dissected. The reconstruction was performed using a method similar to the Billroth I procedure with gastrogastrostomy using two layers of sutures. For the CDG procedure, D2 lymph node dissection was also performed with denervation of the hepatic and pyloric branches of the vagal nerve. The size of the remnant stomach in the two patient groups was almost the same, with one-third of the stomach being retained. Patients in groups A and B were interviewed about postgastrectomy syndrome, esophagogastric endoscopy, abdominal ultrasonography, and measurements of the gastric emptying function 5 years after surgery. Gastric emptying function was measured again in the two groups 1 month after stopping the associated medications.

Methods

Interview. Prior to assessing the gastric emptying function for the semisolid diet, subjects were interviewed directly by an investigator (R.T.) to obtain information on their appetite, body weight loss compared to that at their normal state, early dumping symptoms (based on the diagnostic criteria for dumping syndrome established by the Japanese Society of Gastroenterological Surgery) (Table 1), symptoms of reflux esophagitis (heartburn, chest pain, dyspepsia, feeling of regurgitation, dysphagia, difficult swallowing), and epigastric fullness.

Esophagogastric Endoscopy. Patients with or without reflux esophagitis, gastritis, and gastric stasis were subjected to esophagogastric endoscopy.

Abdominal Ultrasonography. Patients with or without cholecystolithiasis were subjected to abdominal ultrasonography.

Gastric Emptying Function. SEMISOLID DIET (RADIOISOTOPE METHOD).

After ^{99m}Tc tin colloid was added to the diet (a semisolid diet of 200 g of rice gruel with a raw egg) and mixed well, the entire amount of the preparation was ingested by subjects within 5 minutes in a sitting position. Measurements were performed with a scintillation camera (Hitachi HARP I; Hitachi, Tokyo, Japan). Scanning (imaging) was performed from the abdominal (front) side in the supine position for 1 minute. The scanning time was from 0 (immediately after completion of diet intake) to 120 minutes. The data were fed into the computer to count radioactivity in the region of interest (ROI) of the stomach. After adjusting for the half-life of ^{99m}Tc , residual rates (percent) of radioactivity in the stomach at 15, 30, 45, 60, 75, 90, 105, and 120 minutes after ingesting the diet were calculated, considering the residual rate at time 0 as 100. A gastric emptying curve was then drawn. The time to a 50% residual rate was defined as the time until the radioactivity fell to 50% of its initial value as determined from the gastric emptying curve. A regression line was prepared based on the gastric emptying curve, and the emptying rate was defined as the absolute value of the slope (percent per minute).

LIQUID DIET (ACETAMINOPHEN METHOD). After 1 g of acetaminophen (Yamanouchi, Tokyo, Japan) was dissolved in 250 ml of orange juice and mixed well, the orange juice was promptly drunk by subjects in a sitting position. Subjects assumed the same supine position for blood collection as for the radioisotope method. This was considered time 0, and blood was collected at 15, 30, 45, 60, 75, 90, and 120 minutes. The blood concentration of acetaminophen was determined with a whole-blood concentration determination system (TDX; Abbott, Abbott Park, IL, USA) based on the principle of the immunofluorescence polarization assay. A gastric emptying curve was drawn plotting the blood acetaminophen concentration by time, and the time of the peak blood concentration of acetaminophen was determined.

Subjects discontinued any drugs that might affect gastrointestinal movement beginning on the morning of the day before the examination, and they did not ingest any food or drink beginning on the afternoon of the day before the examination. The examination was performed starting at 9:00 a.m. of the following day. The gastric emptying function test for the semisolid diet was followed by the test for the liquid diet, with an interval of 1 week.

Statistical significance was determined using repeated measure analysis of variance (ANOVA), with post hoc analysis using Fisher's protected least significant difference (PLSD) comparisons (Stat View 4.0, Macintosh). Results are expressed as the mean \pm standard deviation (SD). For statistical analysis of the interviews, the chi-square test was used. For statistical analysis of the current percent body weight based on the preillness weight, Student's *t*-test was used. A *p* value of less than 0.05 was regarded as significant.

Results

Direct Interview

Appetite. "No change from normal" was reported significantly more often for group A patients ($n = 10$; 100%) than for group B patients ($n = 8$; 36.4%). "Decreased appetite compared to normal" was found more frequently in group B (14 patients; 63.4%) than in group A (0 patients) ($p = 0.0007$) (Table 2).

Table 2. Clinical symptoms 5 years after operation.

Symptom	Group A ($n = 10$)	Group B ($n = 22$)	<i>p</i>
Appetite			
No change vs. normal status	100% (10/10)	36.4% (8/22)	0.0007
Decreased vs. normal status	0% (0/10)	63.4% (14/22)	
Gastric fullness			
Negative	60.0% (6/10)	81.9% (18/22)	0.0180
Positive	40.0% (4/10)	18.1% (4/22)	
Symptoms (esophagitis: heartburn, chest pain, dyspepsia, regurgitation, dysphagia)			
Negative	100% (10/10)	31.8% (7/22)	0.0435
Positive	0% (0/10)	68.2% (15/22)	
Early dumping syndrome (systemic symptoms)			
Negative	100% (10/10)	77.3% (17/22)	0.1007
Positive	0% (0/10)	22.7% (5/22)	
Percent of preillness weight	94.3–2.8%	91.3–4.9%	0.0837

Group A: patients with pylorus-preserving distal gastrectomy.
Group B: patients with conventional distal gastrectomy.

Epigastric Fullness. Epigastric fullness occurred, but it was less frequent in group B (4 patients, 18.1%), than in group A (6 patients, 60.0%) ($p = 0.0180$) (Table 2).

Reflux Esophagitis. Symptoms of reflux esophagitis (heartburn, chest pain, dyspepsia, regurgitation, dysphagia) were noted in none of the patients in group A and in 15 patients (68.2%) in group B, indicating a significant difference between the two groups ($p = 0.0435$) (Table 2).

Early Dumping Syndrome. Early dumping symptoms (which are systemic and are defined by the diagnostic criteria for dumping syndrome established by the Japanese Society of Gastrointestinal Surgery) (Table 2), were not seen in any of the patients in group A and in 5 patients (22.7%) in group B. There were no significant differences between groups A and B ($p = 0.1007$) (Table 2). Early vasomotor dumping symptoms (within 30 minutes after food intake) including palpitations, dizziness, weakness, flushing, and diaphoresis were seen in group B.

Body Weight Recovery. Recovery of body weight (current body weight/preillness weight) in group A (94.3% \pm 2.8%) was better than that in group B (91.3% \pm 4.9%) ($p = 0.0837$) (Table 2).

These results suggest that PPG (group A) maintained or alleviated postoperative gastrointestinal symptoms such as appetite loss, reflux esophagitis, and early dumping syndrome and facilitated recovery of lost body weight better than CDG (group B). The only weak point of the PPG procedure was the sensation of epigastric fullness, potentially persisting for 5 years or more after PPG.

Endoscopic Findings

Reflux Esophagitis. Endoscopic reflux esophagitis (Savary-Miller, stage I) was noted in five patients (22.7%) in group B and no patients in group A. There was no significant difference between groups A and B ($p = 0.1007$) (Table 3).

Table 3. Endoscopic and abdominal sonographic findings 5 years after operation.

Findings	Group A (n = 10)	Group B (n = 22)	p
Endoscopy of lower esophagus and remnant stomach			
Reflux esophagitis			
Negative	100% (10/10)	77.3% (17/22)	0.1007
Positive	0% (0/10)	22.7% (5/22)	
Gastritis			
Negative	90.0% (9/10)	36.4% (8/22)	0.0048
Positive	10.0% (1/10)	63.6% (14/22)	
Gastric stasis			
Negative	40.0% (4/10)	81.9% (6/22)	0.0180
Positive	60.0% (6/10)	18.1% (16/22)	
Abdominal sonography of the gallbladder			
Gallstones			
Negative	100% (10/10)	81.9% (17/22)	0.1494
Positive	0% (0/10)	18.1% (5/22)	

Gastritis in the Remnant Stomach. Endoscopic gastritis was noted in 14 patients (63.6%) in group B and 1 patient (10.0%) in group A. There was a significant difference between groups A and B ($p = 0.0048$) (Table 3).

Gastric Stasis in the Remnant Stomach. Gastric stasis was noted in four patients (40.0%) in group A and six patients (18.1%) in group B. There was a significant difference between groups A and B ($p = 0.0180$) (Table 3).

These results suggest that PPD (group A) maintained or alleviated postoperative reflux esophagitis and gastritis in the remnant stomach. However, epigastric fullness and gastric stasis in the remnant stomach were more prevalent in group A than in group B.

Abdominal Sonographic Findings in the Gallbladder

Postoperative cholecystolithiasis was noted in five patients (18.1%) in group B and no patients in group A. There was no significant difference between groups A and B ($p = 0.1494$) (Table 3). Postoperative cholecystolithiasis was not detected in group A.

Gastric Emptying Function

Semisolid Diet (Radioisotope Method). Figure 1 shows the gastric emptying curves for the semisolid diet in groups A, B, and C; they are based on residual rates of radioactivity determined at 15-minute intervals for 120 minutes by the radioactivity method. The gastric emptying curves for groups A and B were similar to that for group C. In addition, gastric emptying was slower in groups A and B than in group C, and it was slower in group A than in group B. In group C, the residual rates at 45, 60, 75, 90, 105, and 120 minutes were significantly decreased compared with those for group A ($p = 0.0027$, $p = 0.0183$, $p = 0.0017$, $p = 0.0002$, $p < 0.0001$, and $p < 0.0001$, respectively). In group C, the residual rates at 30, 45, 60, 75, 90, 105, and 120 minutes were significantly decreased compared with those for group B ($p = 0.0384$, $p = 0.0004$, $p = 0.0041$, $p = 0.0051$, $p = 0.0002$, $p < 0.0001$, and $p < 0.0001$, respectively). There were no significant differences between groups A and B in terms of

the residual rates at 15, 30, 45, 60, 75, 90, 105, and 120 minutes ($p = 0.4658$, $p = 0.7340$, $p = 0.9245$, $p = 0.9876$, $p = 0.3247$, $p = 0.4557$, $p = 0.1487$, and $p = 0.2126$, respectively).

The times to 50% residual rate for groups A and B were significantly delayed compared with that for group C ($p = 0.0006$, $p = 0.0056$, respectively). The time to 50% residual rate for group A was slower than that for group B, but there was no significant difference between groups A and B ($p = 0.1763$) (Table 4).

Figure 2 shows the regression lines for groups A (Fig. 2a), B (Fig. 2b), and C (Fig. 2c). The gastric emptying curves in all groups were linear. There was an inverse correlation between the residual activity rate (percent) in the stomach and time (group A: $r = -0.55$, $p < 0.0001$; group B: $r = -0.62$, $p < 0.0001$; group C: $r = -0.97$, $p < 0.0001$).

The gastric emptying rate in group A was significantly slower than that in group C ($p = 0.0001$), as it was in group B ($p = 0.0238$). There was no significant difference between groups A and B ($p = 0.0593$) (Table 4).

The pattern of the gastric emptying curve was almost the same among groups A, B, and C, although delayed gastric emptying for semisolid was more pronounced in group A than in groups B and C.

Liquid Diet (Acetaminophen Method). Figure 3 shows the gastric emptying curves for the liquid diet in groups A, B, and C. These curves were drawn based on the blood concentration of acetaminophen determined at 15-minute intervals for 90 and 120 minutes. The concentration in group B was generally higher than that in groups A and C. The blood acetaminophen concentration curve for group A showed a pattern similar to that for group C.

The gastric emptying time for group B was faster than that for groups A and C, whereas the gastric emptying for group A was similar to that for group C. In group A, the blood concentrations at 15, 30, 45, 60, 75, 90, and 120 minutes were significantly lower than those in group B ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p = 0.0002$, and $p = 0.0003$, respectively). In group B, the blood concentrations at 15, 30, 45, 60, 75, 90, and 120 minutes were significantly lower than those in group C ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, and $p = 0.0026$, respectively). There were no significant differences between group A and C in terms of the residual rates at 15, 30, 45, 60, 75, 90, and 120 minutes ($p = 0.469$, $p = 0.3982$, $p = 0.0968$, $p = 0.3116$, $p = 0.3499$, $p = 0.2915$, and $p = 0.2174$, respectively).

The time to the peak concentration of acetaminophen in group B was faster than that in groups A and C. In addition, there were significant differences between groups A and C and between groups B and C ($p < 0.0001$, $p < 0.0001$, respectively). There was no significant difference between groups A and B ($p = 0.1763$) (Table 3).

Gastric emptying of the liquid diet in patients after CDG was significantly accelerated compared with the emptying in PPG and control subjects. The emptying curves in patients with PPG showed almost the same pattern as those in the control subjects.

Discussion

The PPG procedure with vagal nerve-preserving D2 lymphadenectomy can be performed safely with a low incidence of major complications and a better postoperative outcome than the CDG procedure [8]. Generally, postoperative appetite loss and body weight loss of the patients after CDG are significantly greater than those of

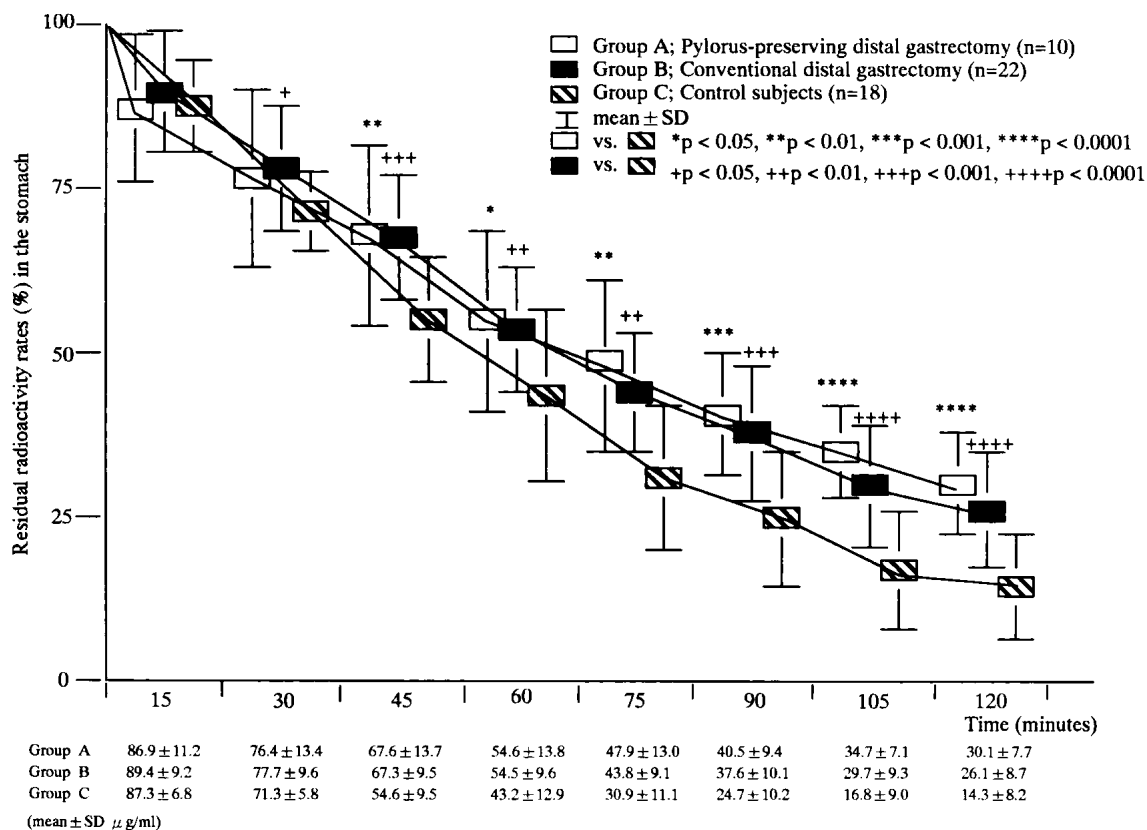


Fig. 1. Gastric emptying curves for semisolid diet in groups A, B, and C. The pattern of the emptying curve was almost the same among groups A, B, and C. Delayed gastric emptying of the semisolid diet was clearly seen in groups A and B compared with that in group C.

Table 4. Parameters of gastric emptying function.

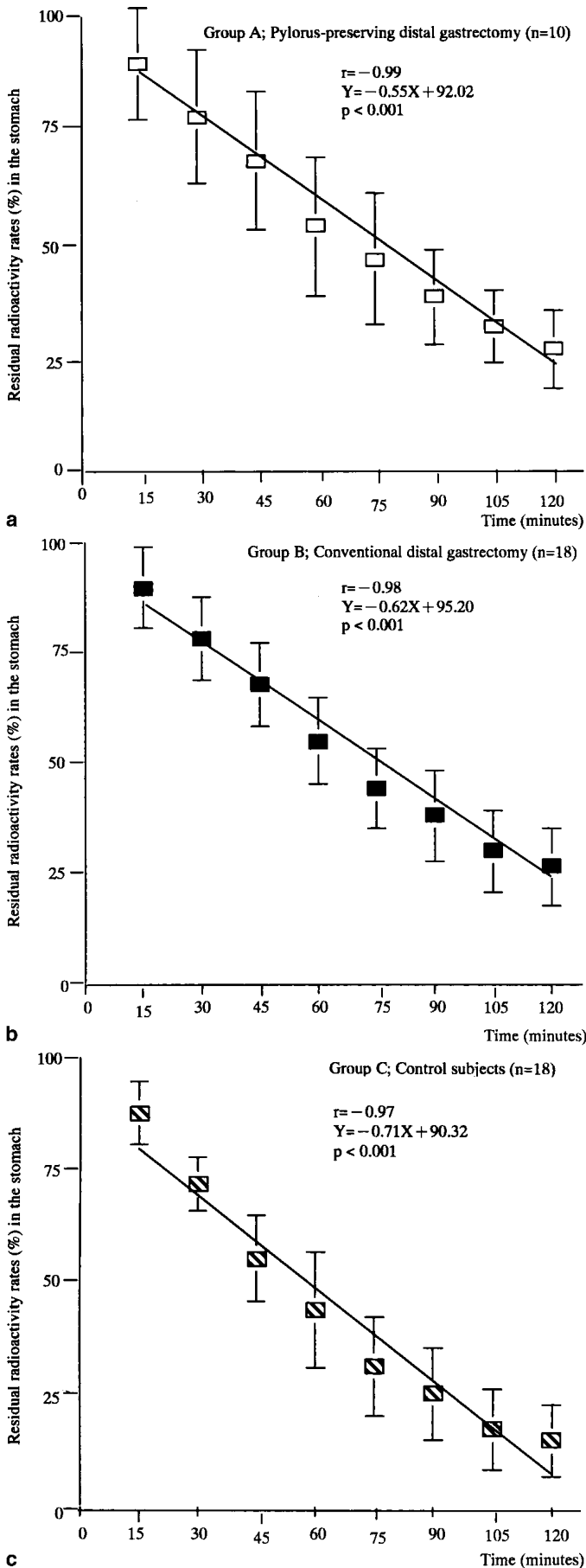
Parameter	Result	p
Time to 50% residual rate in the stomach (minutes)		
Group A	69.5 ± 12.7	0.1763
Group B	63.1 ± 9.8	
Group C	51.9 ± 14.2	
		0.0006
Gastric emptying rate (%/min)		
Group A	0.55 ± 0.09	0.0593
Group B	0.62 ± 0.13	
Group C	0.71 ± 0.09	
		0.0238
Time of the peak blood concentration of acetaminophen (minutes)		
Group A	48.0 ± 9.5	< 0.0001
Group B	19.7 ± 7.1	
Group C	48.3 ± 6.4	
		0.1763

Group A: pylorus-preserving distal gastrectomy (n = 10).
 Group B: conventional distal gastrectomy (n = 22).
 Group C: normal subjects (n = 18)

patients after PPG. Moreover, patients who undergo PPG have fewer postgastrectomy syndromes (e.g., malnutrition due to appetite loss, dumping syndrome, alkaline reflux esophagitis, alkaline gastritis in the remnant stomach, postoperative cholecystolithiasis) than those who undergo CDG [1, 5–10]. Patients after PPG also have less endoscopic reflux esophagitis, endoscopic gastritis in the remnant stomach, and postoperative cholecystolithiasis than those after CDG [1, 14]. Many reports have suggested that the reasons for these symptoms after CDG are the loss of the pyloric sphincter and denervation of the vagal nerve. A high incidence of epigastric fullness after meals and retention of food in the residual stomach after

PPG have also been reported [1, 6], and many have noted that epigastric fullness due to gastric stasis in the remnant stomach can be found up to 1 year after PPG with preserved hepatic and pyloric branches of the vagal nerve. So far, it has been generally believed that the hepatic and pyloric branches of the vagal nerve are necessary for pyloric sphincter and gallbladder functions in patients after PPG [1, 5–10, 14]. Kodama et al. [1] demonstrated that the most frequent complication was remnant gastric stasis. Following PPG with preservation of the pyloric branch of the vagal nerve D2 lymphadenectomy 17% patients demonstrated mild stasis and 6% severe stasis, whereas 17% and 10% CDG patients, respectively, had these problems. It was thought that gastric stasis in PPG patients was due to damage to the vagal nerve and blood supply as a result of skeletonization of the subpyloric region achieved with subpyloric lymph node dissection.

Some [15–18] have concluded that preservation of the hepatic and pyloric branches of the vagal nerve is not necessary for gastropyloroduodenal motility and gallbladder function in patients after PPG. Nakabayashi et al. [18] suggested that gastric stasis during the early postoperative period in patients after PPG without preservation of the pyloric branch of the vagal nerve is due to tonic and phasic contractions of the pylorus. Nakane et al. [19] pointed out that epigastric fullness and a high incidence of food residue in the remnant stomach after meals was more common after PPG with transection 1.5 cm proximal to the pyloric ring than after PPG with transection 2.5 cm proximal to the pyloric ring and that it resulted in poor food intake and poor recovery of body weight. They further demonstrated that PPG with transection 2.5 cm proximal to the



pyloric ring was superior to PPG with transection at 1.5 cm in terms of postprandial symptoms, food intake, recovery of body weight, and gastric emptying. They therefore concluded that the length of the retained antrum plays an important role in the motility of the pyloric ring following PPG.

In the present study, the PPG procedure without preserving the hepatic and pyloric branches of the vagal nerve alleviated postoperative gastrointestinal symptoms such as appetite loss, body weight loss, early dumping syndrome, reflux esophagitis, endoscopic reflux esophagitis, endoscopic gastritis in the remnant stomach, and postgastrectomy cholecystolithiasis better than did CDG. The only weak point of the PPG procedure was the sensation of epigastric fullness due to gastric stasis of food in the remnant stomach. Epigastric fullness and gastric stasis have lasted 5 years or more. With our PPG technique the hepatic and pyloric branches of the vagal nerve were not preserved as well as with CDG. Our results of the postgastrectomy syndrome were the same as those of previous reports concerning PPG with preservation of the hepatic and pyloric branches of the vagal nerve.

It has also been reported that patients after CDG without preservation of the hepatic and pyloric branches of the vagal nerve are at increased risk of developing cholecystolithiasis, the incidence being reported at 10% to 40% [1]. On the other hand, the remainder of patients after CDG (60-90%) do not have postoperative cholecystolithiasis. Therefore we think that the vagal nerve does not play an important role in stone formation. Nabae et al. [20] suggested that preservation of pyloroduodenal myoneural continuity during PPG would help maintain a normal sphincter of Oddi and gallbladder motility. Nakabayashi et al. [18] reported that preservation of the pyloric sphincter helped to maintain gallbladder function.

It is clear that the roles of the hepatic and pyloric branches of the vagal nerve during PPG are not completely understood. Therefore the postoperative pathophysiology of the gastric emptying function in patients after PPG has not been assessed in detail.

In our PPG patients, the only weak point of the PPG procedure was epigastric fullness and gastric stasis in the remnant stomach. To clarify the reasons for this persistent epigastric fullness, we investigated the gastric emptying function 5 years after PPG and compared the results with those of patients 5 years after CDG.

The radioisotope method has been used to assess gastric emptying functioning with both a solid diet and a liquid diet. This method has advantages in terms of reproducibility and quantitative determination [11]. ^{99m}Tc tin colloid or ^{99m}Tc-DTPA was used as the nuclide for the solid diet assay and ¹¹¹In-DTPA for the liquid diet assay [21], although as ¹¹¹In-DTPA is expensive it is difficult to justify its use. The acetaminophen method can be safely performed at a reasonable cost, so it is widely used to determine the emptying time for liquid diets instead of the radioisotope method. It is preferable to use a diet that resembles meals usually ingested to assess the objective physiologic emptying function; accordingly, it is said that a solid diet is the best choice for this purpose.

Fig. 2. a. Regression line for group A. Gastric emptying curve was linear. There was a correlation between the residual activity rate (%) in the stomach and time, in inverse proportion ($p < 0.0001$, $r = -0.55$). b. Regression line for group B. Gastric emptying curve was linear. There was a correlation between the residual activity rate (%) in the stomach and time, in inverse proportion ($p < 0.0001$, $r = -0.62$). c. Regression line for group C. Gastric emptying curve was linear. There was a correlation between the residual activity rate (%) in the stomach and time, in inverse proportion ($p < 0.0001$, $r = -0.97$).

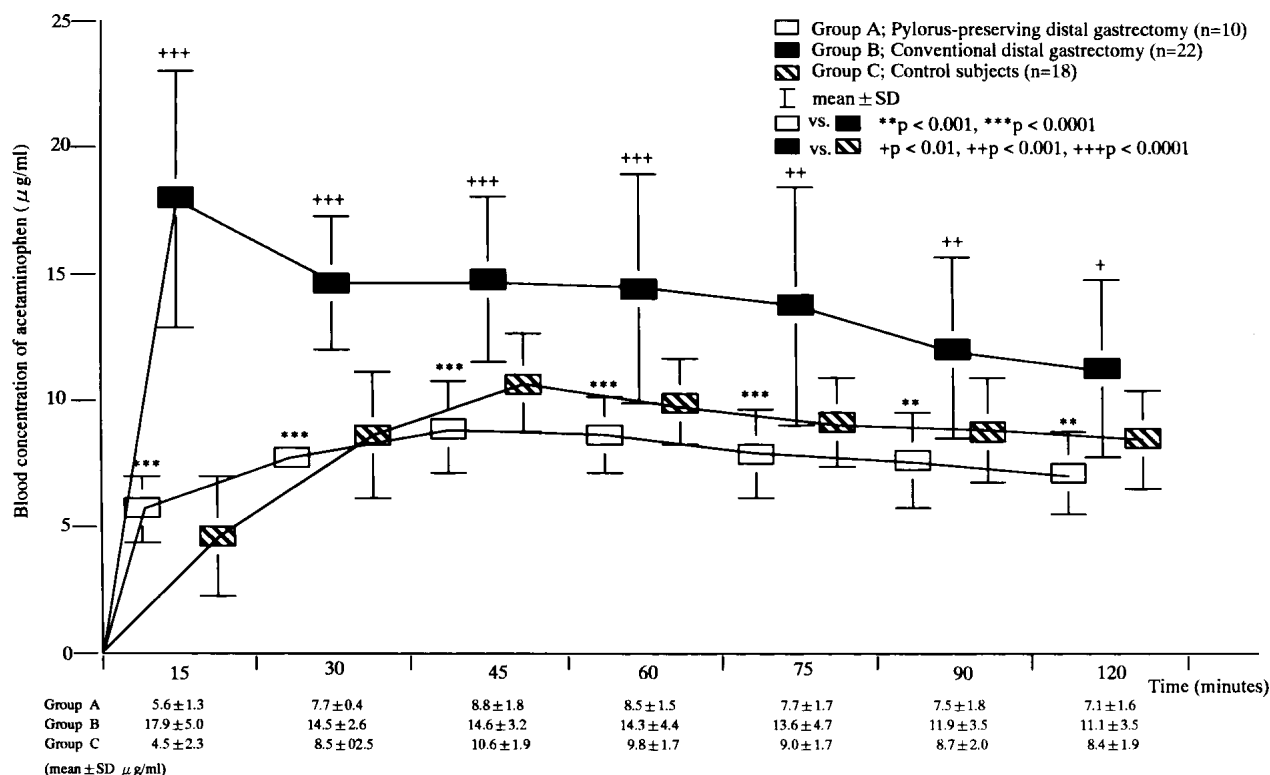


Fig. 3. Blood acetaminophen concentration curves for groups A, B, and C. Emptying of liquid diet in group B was significantly accelerated compared with that in groups A and C. The emptying curves for group A showed almost the same pattern as that for group C.

Tomita et al. [21] reported that the gastric emptying curve of a solid diet is presented as a regression line because emptying decreases linearly. Instead of a solid diet we used rice gruel because it is familiar to Japanese people; it is also easy to eat after gastric surgery as well as to cook and prepare for the experiment. In this study the gastric emptying curve drawn using this diet presented as a regression line with a high regression coefficient in the control group. Thus we believed there was no problem associated with the use of this semisolid diet instead of a solid diet. To evaluate the liquid diet emptying function by the acetaminophen method, diets such as milk, liquid food, elemental diet, and orange juice were used. Acetaminophen is not entirely absorbed from the stomach but is promptly absorbed from the small intestine. The acetaminophen method is used in regular clinical practice because it requires no special equipment [13]. Mistiaen et al. [12] reported that liquid diets are more appropriate for detecting possible rapid gastric emptying rates and dumping; a solid test diet, on the other hand, can be used to study gastric stasis. We measured gastric emptying for semisolid (instead of solid) and liquid diets.

Gastric emptying of the semisolid diet after PPG was slower than that in normal subjects, and the emptying curve for the liquid diet was satisfactory, similar to that of the normal subjects. Emptying for the liquid diet was significantly faster throughout the study for the patients who had undergone CDG compared with those with PPG and the control subjects. There was no statistically significant difference between the PPG and CDG patients regarding gastric emptying of the semisolid diet. The gastric emptying study of the semisolid diet was performed in a supine position. If gastric emptying time of a semisolid diet is conducted not supine but in the seated position, there may be a significant difference between the PPG and CDG patients. Slow emptying of a semisolid diet in patients after PPG is thought to contribute to the sensation of

epigastric fullness after meals. Fast gastric emptying of a liquid diet in patients after CDG may be related to the early dumping syndrome.

Recently, according to clinicopathologic findings in patients with early gastric cancer at our clinic, the criteria for performing PPG are the following [22]: Early mucosal gastric cancers in the lower third of the stomach are selected. It must be confirmed by ultrasonic endoscopy, W-computed tomography, and magnetic resonance imaging preoperatively and by the findings of abdominal exploration during the surgery that there are no lymph node metastases (N0). The distance from the anal-side margin of the cancer to the pylorus ring must be 2 cm or more. The cases must not be suitable for endoscopic mucosa excision or partial excision of the stomach. Finally, PPG is performed only on patients in whom the upper third of the stomach can be preserved. For patients in whom PPG is inappropriate based on these criteria, CDG is performed.

We previously reported that as the delayed gastric emptying function in patients after CDG is improved by mosapride citrate, this drug may be recommended for prophylactic use in patients after PPG [23]. Mosapride citrate improves gastrointestinal movement and so may prevent the feeling of epigastric fullness after meals due to retention of content in the residual stomach. Hence it should be prescribed for PPG patients for as long as possible.

Conclusions

For the PPG procedure, without preservation of the hepatic and pyloric branches of the vagal nerve, preservation of the pyloric ring is thought to be useful for preventing rapid emptying of the liquid content and the development of early dumping syndrome. The pyloric sphincter also prevents alkaline reflux esophagitis and alka-

line gastritis in the remnant stomach due to regurgitation of intestinal contents. However, it is possible that a feeling of epigastric fullness after surgery due to long-term retention of solid or semi-solid food may occur because of delayed emptying. In the present study we were unable to determine the cause of the gastric stasis of semisolid diet in the remnant stomach, producing the sensation of epigastric fullness.

Shibata et al. [16] concluded that postprandial gastric emptying may be slower after PPG than after CDG, and this phenomenon was unchanged even after vagal denervation. Hotta et al. [7] showed that indigestible solids are emptied by coordinated efforts of the gastric body and pylorus after PPG. Mistiaen et al. [12] suspected that removal of the gastric pacemaker is responsible for the decreased gastric emptying of a solid diet, whereas preservation of this pacemaker leads to the presence of gastric common cavity waves and hence to a normal or increased emptying rate [24]. From this point of view, we think that the size of the remnant stomach may be related to the delayed gastric emptying of the semisolid diet. The ventriculus upper part of the greater curvature side includes the pacemaker [24]. Therefore to prevent delayed gastric emptying of a semisolid diet in patients after PPG more than one-third of the stomach may have to be preserved to not lose the gastric pacemaker. It is well known that receptive relaxation of the gastric fundus is controlled by the vagal nerve. The postoperative states after PPG with and without preservation of the vagal nerve should be compared in future.

Résumé. Afin de prévenir le syndrome postgastrectomie après gastrectomie distale conventionnelle (GDC), on préconise au Japon pour le cancer au début, la gastrectomie distale avec conservation du pylore (GDPC). Cependant, la qualité de vie (QdV) postopératoire à long terme et la fonction de vidange gastrique après GDPC n'ont pas été évaluées en détail. Afin de préciser la place de la GDPC dans le traitement du cancer au début, nous avons examiné le rapport entre le syndrome post-gastrectomie et la fonction de vidange 5 ans après GDPC; ces résultats ont été comparés à ceux à 5 ans après GDC. Nous avons étudié les dossiers de 35 patients ayant eu à titre curatif une gastrectomie pour cancer au début (cancer de la sous-muqueuse sans métastase ganglionnaire) dans notre clinique. Dix patients ayant eu une GDPC avec une lymphadénectomie D2 sans conservation des branches hépatiques ou pyloriques du nerf vague (groupe A: 8 hommes et deux femmes, âge moyen de 60.7 ans (extrêmes: 33 et 70) ont été interrogés en ce qui concerne l'appétit, la perte de poids, la sensation de plénitude gastrique, l'existence de symptômes d'oesophagite de reflux et le syndrome de dumping précoce, et comparés aux patients ayant eu une GDC (groupe B; âge moyen de 63.6 (extrêmes 36 à 72) ans. Les résultats de l'endoscopie oesophagogastrique, de l'échographie abdominale et de l'étude de la fonction de vidange gastrique (temps de vidange gastrique pour les semi-solides: grauu de riz étiqueté par la méthode des radio-isotopes ^{99m}Tc , étude de vidange pour des liquides: méthode d'acétaminophène avec le jus d'orange) ont été consignés. 18 volontaires (10 hommes et 8 femmes) d'âge moyen de 60.8 (extrêmes 38-68) ans, sans symptômes gastro-intestinaux, ont servi de groupe de contrôle (groupe C). Les résultats ont été les suivants: comparé au groupe B, l'intervention dans le groupe A a amélioré l'appétit, les symptômes d'oesophagite de reflux, le syndrome de dumping précoce, la perte de poids et la gastrite du moignon endoscopique ainsi que la lithiase biliaire postgastrectomie. Le seul point faible de la GDPC a été la sensation de plénitude épigastrique. En ce qui concerne la vidange gastrique pour les semi-solides, la courbe de vidange a été pratiquement la même pour les groupes A, B, et C, mais la vidange gastrique tardive a été constatée plus fréquemment chez les patients du groupe A par rapport aux groupes B et C ($p < 0.05$). La vidange des liquides a été significativement plus rapide dans le groupe B que dans les groupes A et C ($p < 0.01$). La vidange gastrique était similaire dans les groupes A et C. Ces résultats montrent que la GDPC améliore la QdL, mais que la vidange tardive des semi-solides après GDPC provoque une sensation de plénitude épigastrique postprandiale en raison de la rétention du contenu dans le moignon gastrique, constatée chez plusieurs patients. Le seul point faible

de la GDPC est la plénitude épigastrique et la stase gastrique en rapport avec la vidange gastrique prolongée des semi-solides.

Resumen. En Japón, para tratar los cánceres gástricos precoces, con objeto de prevenir el síndrome postgastrectomía tras gastrectomía distal convencional (CDG) se efectúan, cada vez más, gastrectomías con preservación del píloro (PPG). Sin embargo, se desconocen los resultados tardíos postoperatorios tras PPG de la calidad de vida (QOL) y del funcionamiento del vaciado gástrico. Para aclarar el valor de la PPG tras resección por cáncer gástrico precoz, se efectúa un estudio comparativo entre el síndrome postgastrectomía y la función de vaciamiento gástrico en pacientes a los 5 años de haber sufrido una PPG o una CDG. Estudiamos 32 pacientes que fueron sometidos a una gastrectomía curativa por cáncer gástrico precoz (Cáncer submucoso sin metástasis linfáticas). En 10 casos se realizó una PPG con linfadenectomía D2 sin preservar las ramas hepática y pilórica del nervio vago. (Grupo A: 8 varones y 2 mujeres; edad comprendida entre 33 y 70 años: media 60.7 años). A todos ellos se les inquirió sobre: apetito, pérdida de peso, plenitud epigástrica, reflujo esofágico y síndrome precoz de dumping (síndrome de evacuación gástrica rápida). Los resultados de la encuesta se compararon con los obtenidos tras CDG (grupo B, $n = 24$, de edades comprendidas entre 36–72 años; media 63.6 años). También se realizaron otras pruebas como: endoscopias esofágicas, ecografía abdominal y estudios sobre la función de vaciamiento gástrico (tiempo de vaciamiento de una dieta semisólida, empleando radiosítopos: gachas de arroz radiomarcadas con ^{99m}Tc ; tiempo de vaciamiento de una dieta líquida, utilizando el método de acetaminofen con zumo de naranja). El grupo control (grupo C) estaba constituido por 18 voluntarios sanos (10 varones y 8 mujeres) sin sintomatología gastrointestinal y edades comprendidas entre 38–68 años: media 60.8 años. Los resultados obtenidos fueron los siguientes. Comparando el grupo A con el B, la técnica operatoria del grupo A mejora los síntomas gastrointestinales del postoperatorio tales como: inapetencia, esofagitis de reflujo, síndrome precoz de rápido vaciamiento gástrico, pérdida de peso, esofagitis de reflujo detectable endoscópicamente al igual que la gastritis del muñón gástrico y colelitiasis postgastrectomía. El único punto débil de la PPG es la sensación de plenitud, pesadez en epigastrio. La curva de vaciamiento gástrico para una dieta semisólida fue semejante en los grupos A, B, y C, pero en el A, se registró, con más frecuencia un retardo en el vaciado ($p < 0.05$) que en los grupos B y C. Por lo que a la dieta líquida se refiere el vaciado gástrico fue significativamente más rápido en el grupo B que en el A y C ($p < 0.01$), siendo en estos dos últimos similar. Los resultados demuestran que el PPG mejora la QOL postoperatoria, pero retrasa el vaciamiento gástrico de dietas semisólidas, por lo que el paciente aqueja una sensación de pesadez postprandial debido a la retención del contenido en el estómago residual. El único inconveniente de la PPG es la pesadez y la estasis gástrica por vaciamiento retardado con dietas semisólidas.

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