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GAVIN PUBLISHERS

Journal of Surgery

Tomita R. J Surg: JSUR-1131.

Research Article

DOI: 10.29011/2575-9760. 001131

Assessment of Postprandial Abdominal Fullness in Patients after Pylorus-Preserving Gastrectomy for Early Gastric Cancer

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Citation: Tomita R (2018) Assessment of Postprandial Abdominal Fullness in Patients after Pylorus-Preserving Gastrectomy for Early Gastric Cancer. J Surg: JSUR-1131. DOI: 10.29011/2575-9760. 001131

Received Date: 07 May, 2018; **Accepted Date:** 10 May, 2018; **Published Date:** 17 May, 2018

Abstract

Background: To assess Postprandial Abdominal Fullness (PAF) in Pylorus-Preserving Gastrectomy (PPG) patients, the author investigated relationships between PAF and Postgastrectomy Disorder (PGD) and Gastric Empting Function (GEF).

Methods: A total of 22 patients 1 year after PPG for early gastric cancer were divided into 2 groups [Group A, PAF- positive (n=12); Group B, PAF-negative (n=10)]. The relationships among PAF, PGD, and GEF were studied.

Results: The Length of The Antral Cuff (LAC) was significantly shorter in group A than in group B (p=0.0245). Appetite and food consumption per meal were significantly more favorable in group B than in group A (p=0.0202, p=0.0082, respectively). Symptomatic Reflux Esophagitis (RE), early dumping syndrome, decreased percent body weight preillness, endoscopic RE and endoscopic gastritis in the remnant stomach were more frequent in group A than in group B. Gastric stasis in the remnant stomach was significantly more frequent in group A than in group B (p=0.0071). GEF with the solid diet in group A was significantly more delayed than in group B (p=0.0001). There was no significant difference in GEF with the liquid diet in either group.

Conclusions: Patients with PAF showed a short LAC, delayed GEF with the solid diet, and a more unfavorable postoperative QOL compared with those without PAF.

Keywords: Early Gastric Cancer; Gastric Empting Function; Postgastrectomy Disorder; Postprandial Abdominal Fullness; Pylorus-Preserving Gastrectomy

Introduction

Patients after Pylorus-Preserving Gastrectomy (PPG) have been reported to show an improved postoperative Quality of Life (QOL) [1-5]. PPG is correlated with significantly lower incidences of Postogastrectomy Disorders (PGD) such as Early Dumping Syndrome (EDS), bile regurgitation in the remnant stomach (i.e., alkaline gastritis), and esophagitis as well as a significant decrease in postoperative malnutrition due to a loss of appetite and postoperative body weight loss [1-3]. However, some patients after PPG compalain of Postprandial Abdominal Fullness (PAF) due to Gastric Stasis in the Remnant Stomach (GSRS) [2-9]. Frequencies of PAF after PPG have been reported about 40% [3-9]. PAF has been showed to be associated with food intake [4]. Food consumption then becomes insufficient and leads to a deterioration of the postoperative QOL which is one of the major problems in patients after PPG. Therefore, the author think that PAF may be caused by GSRS due to delay of the Gastric Emptying Function (GEF).

Generally, the radioisotope and acetaminophen methods are the most frequently used physiological and quantitative tests which are noninvasive to patients [10,11]. In Japan, for the GEF test with a solid diet, a radioisotope method using ^{99m}Tc tin colloid (short half-life of about 6 hours with a very small radiation dose of 40 MBq equivalent to the dose for one radiogram of plain abdominal radiography) has been used with rice gruel. For the GEF test with the liquid diet, the acetaminophen method has been used with orange juice. To assess PAF in patients after PPG, the author therefore studied the relationships between PAF and PGD and GEF of the residual stomach in patients who underwent PPG for early gastric cancer.

Methods

Study Population and Period

Twenty-two patients (14 men and 8 women aged from 33 to 79 years with a mean age of 64.8 years) with early gastric M (mucosa) or SM cancer of N0 (no lymph node metastasis) underwent PPG with lymph node resection preserving the pyloric, hepatic, and celiac branches of the vagal nerve (PHCV) in our hospital from January 2010 to December 2015. They were divided into 2 groups [Group A (n=12), patients after PPG with PAF; Group B (n=10), patients after PPG without PAF], and the relationship between PAF and PD and GEF were compared.

Their postoperative courses showed no complication except for one case (wound infection) in group A. No adjuvant therapies including anticancer chemotherapy were applied in either group. The past histories included no diseases of the psychoneurological, metabolic (diabetes, mellitus, hypothyroidism), or gastrointestinal systems such as functional gastrointestinal disorders (non-ulcer dyspepsia, irritable bowel syndrome, chronic constipation, and functional intestinal obstruction) or malignant tumor (Table 1). The present studies were performed in all patients at 1 year after PPG.

Factors	Group A (n=12)	Group B (n=10)	p value
Male/Female	8/4	6/4	
Age (years)	65.1 (40-79)	64.8 (33-78)	0.2710
Depth of cancer invasion			
Mucosa	75.0% (9/12)	80.0% (8/10)	0.7805
Submucosa	25.0% (3/12)	20.0% (2/10)	
Lymph node metastasis			
No	100% (12/12)	100% (10/10)	
Pathological stage			
Stage IA	100% (12/12)	100% (10/10)	
Lymph node resection			
D1	75.0% (9/12)	80.0% (8/10)	0.7805
D1+α	25.0% (3/12)	20.0% (2/10)	
PHCV preservation			
Preservation	100% (12/12)	100% (10/10)	
No preservation	0% (0/12)	0% (0/10)	
Resected stomach			
1/3	100% (12/12)	100% (10/10)	
Length of antral cuff (cm)			
Past history	1.6±0.2	2.4±0.4	0.0245
No	100% (12/12)	100% (10/10)	
Postoperative complication			
Wound infection	0% (0/12)	10.0% (1/10)	0.2621
Postoperative chemotherapy			
No	100% (12/12)	100% (10/10)	

Group A: Patients with postprandial abdominal fullness after PPG
Group B: Patents without postprandial abdominal fullness after PPG
PPG: Pylorus-Preserving Gastrectomy
PHCV: Pyloric, Hepatic, and Celiac Branches of vagal nerve
Age: Data are the median (range)

Table 1: Patients' characteristics.

Criteria for Surgery

Early M or SM cancers in the middle and/or lower third of the stomach were selected, where N0 was confirmed by ultrasonic endoscopy, computed tomography, and magnetic resonance imaging in preoperative examinations. Cases in which the remnant stomach would be 1/3 or more were also included (in the present study, the remnant stomach in both groups was 1/3). According to our data, in M cancer, the distance from the anal-side margin of the tumor to the pyloric sphincter was 3.5 cm or more and that in SM was 5.5 cm or more, and the resected margin was free from cancer cells microscopically [6]. In this surgical technique, the pyloric antrum (i.e., length of the pyloric cuff: LPC) 1.5 to 3.0 cm from the pyloric sphincter was preserved. In lymph node dissection, M cancer was excised with the D1 lymph node while preserving PHCV. SM cancer was also excised with the D1+α lymph node while preserving PHCV. Lymph node dissection, according to the general Japanese rules for Gastric Cancer Study in Surgery and Pathology [the Japanese Classification of Gastric carcinoma] [5], was classified as a D1+α dissection including the complete removal of D 1 and α (number 7 or 8 lymph nodes). D1 lymph nodes are located in the perigastric tissue along the lesser and greater curvatures and in close proximity to the primary tumor. Number 7 lymph nodes are located around the left gastric arteries. Number 8 lymph nodes are located around the common hepatic arteries.

Interview

Prior to the measurement of GET, subjects were interviewed directly by the author to obtain information on patient's, food consumption per meal compared with their normal state, symptomatic RE (heartburn, feeling of regurgitation, difficult swallowing, chest pain), EDS, percent body weight of preillness 1 year after surgery compared to normal state.

Findings of Esophagogastric Endoscopy

Patients with or without RE, GRS, and GSRS were examined by esophagogastric endoscopy.

GEF for Solid Diet (Radioisotope Method)

After ^{99m}Tc tin colloid was added to the diet (200 g of rice gruel with a raw egg) and mixed well, the total quantity was ingested by subjects within 5 minutes in a sitting position. Measurement was performed with a scintillation camera (Hitachi HARP I, Tokyo, Japan). Scanning (imaging) was performed from the abdominal (front) side in a supine position for one minute. The

scanning time was from 0 (immediately after the completion of ingestion) to 120 minutes. The data were input into a computer to count Radioactivity in The Region of Interest (ROI) of the stomach. After adjusting for the half-life of ^{99m}Tc, the time for the residual rate (%) of the radioactivity in the stomach on completing ingestion (time 0) to reach 50% of the residual rate after ingestion was calculated, considering the residual rate at time 0 as 100. Residual rates (%) at 120 min in the remnant stomach were also calculated.

GEF for 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 adopted the same supine position as for the radioisotope method for blood collection. This was considered as time 0, and blood collection was performed at 45 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.

Subjects discontinued any drugs which might affect gastrointestinal movement from one week before the examination, and did not take any food or drink from the afternoon of the day before the examination. The examination was performed from 9:00 a.m. of the following day. GEF for the solid diet was followed by the determination for the liquid diet with an interval of one week.

Statistical Analysis

Significance was determined using the non-parametric Kruskal-Wallis test with Bonferroni correction (StatView version 5.0 for Macintosh; Abacus Concepts Inc., Berkeley, CA, USA). Results are expressed as the mean±Standard Deviation (SD). For statistical analysis of the interviews, the chi-squared test was used. For statistical analysis of the percent body weight of the pre-illness weight, Student's t-test was used. A p value less than 0.05 was regarded as significant.

Ethical Considerations

Informed consent was obtained from all subjects participating in the present study. GEF in the present study was approved by the Ethical Committee of Nihon University School of Medicine. The study was performed according to the principles of the Declaration of Helsinki. Furthermore, none of the author has any financial or other conflicts of interest to declare.

Results

Patients' characteristics were showed in Table 1. There were no significant differences in patients' characteristics between groups A and B except for LAC. LAC in group A was 1.6±0.2 cm (1.5 cm, n=10; 2.0 cm, n=2) and that in group B 2.4±0.4 cm (2.0 cm, n=4; 2.5 cm, n=4; 3.0 cm, n=2). In addition, there were significant differences in LAC between groups A and B (p=0.0245).

Results of interview were showed in (Table 2).

	Group A (n=12)	Group B (n=10)	p value
Appetite			
No change vs. normal status	58.3% (7/12)	100% (10/10)	0.0202
Decreased vs. normal status	41.7% (5/12)	0% (0/10)	
Food consumption per meal compared with at normal			
2/3 or more	50.0% (6/12)	100% (10/10)	0.0087
Less than 2/3	50.0% (6/12)	0% (0/10)	
Symptomatic reflux esophagitis			
Negative	83.3% (10/12)	90.0% (9/10)	0.6500
Positive	16.7% (2/12)	10.0% (1/10)	
Early dumping syndrome (systemic symptoms)			
Negative	91.6% (11/12)	100% (10/10)	0.3501
Positive	8.4% (1/12)	0% (0/10)	
Percent body weight of preillness weight			
	91.1±4.5%	92.1±3.6%	0.5661

Group A: Patients with postprandial abdominal fullness after PPG

Group B: Patents without postprandial abdominal fullness after PPG

PPG: Pylorus-preserving gastrectomy

Table 2: Clinical symptoms 1 year after PPG.

Appetite: "No change compared with normal" was observed at a rate of 58.3% (7/12) in group A and 100% (10/10) in group B. In addition, "No change compared with normal" was significantly more frequent in group B compared with that in group A (p=0.0202). The remaining cases in both groups were "Decreased compared with normal". Food consumption per meal compared with normal: a level "2/3 or more compared with normal" was observed at a rate of 50.0% (6/12) in group A and 100% (10/10) in group B. In addition, "2/3 or more compared with normal" was significantly more frequent in group B than in group A (p=0.0087). The remaining cases in both groups were "Less than 2/3 compared with normal". Symptoms of RE (e.g., heartburn, feeling of regurgitation, difficult swallowing): Symptoms of RE occurred in 16.7% (2/12) of group A and 10.0% (1/10) of group B. In addition, they were less frequent in group B compared with group A (p=0.6500). The remaining cases in both groups showed no symptomatic RE. EDS

(systemic symptoms, see ref. 6): EDS occurred in 8.4% (1/12) of group A and 0% (0/10) of group B. They were less frequent in group B compared with group A (p=0.3501). The remaining cases in both groups showed no EDS. Percent body weight preillness: The percent body weight compared with the preillness weight was 91.1±4.5% in group A and 92.1±3.6% in group B. There was no significant difference between the groups (p=0.5661). Body weight decreased in all patients, but the decrease in the percent body weight compared to that preillness was greater in group A than in group B.

Appetite and food consumption per meal were clearly more favorable in group B than in group A. Symptomatic Reflux Esophagitis (RE), early dumping syndrome, and decreased percent body weight compared to that preillness were more frequent in group A than in group B.

Findings of esophagogastric endoscopy were showed in (Table 3).

	Group A (n=12)	Group B (n=10)	p value
Reflux esophagitis			
Negative	83.3% (10/12)	100% (10/10)	0.1757
Positive	16.7% (2/12)	0% (0/10)	
Gastritis in the remnant stomach			
Negative	75.0% (9/12)	90.0% (9/10)	0.3637
Positive	25.0% (3/12)	10.0% (1/10)	
Gastric stasis in the remnant stomach			
Negative	33.3% (4/12)	90.0% (9/10)	0.0071
Positive	66.7% (8/12)	10.0% (1/10)	

Group A: Patients with postprandial abdominal fullness after PPG

Group B: Patents without postprandial abdominal fullness after PPG

PPG: Pylorus-preserving gastrectomy

Table 3: Endoscopic findings 1 year after PPG.

Patients with or without RE, Gastritis in The Remnant Stomach (GRS), and GSRS were examined by esophagogastric endoscopy. Endoscopic RE: RE (Los Angels classification, grade A) was noted in 16.7% (2/12) of group A and 0% (0/10) of group B. It was less frequent in group B compared with group A (p =0.1757). The remaining cases in both groups had no endoscopic RE. GRS: GRS occurred at 25.0% (3/12) in group A and 10% (1/10) in group B. GRS was more frequent in group A compared with group B(p = 0.3637). The remaining cases in both groups had no GRS. GSRS: GSRS occurred at 66.7% (8/12) in group A and 10.0% (1/10) in group B. GSRS was significantly more frequent in group A than in group B (p = 0.0071). The remaining cases in both groups had no GSRS. Endoscopic RE and GRS were more frequent in group A than in group B. GSRS was clearly more prevalent in group A than in group B.

Emptying functions in the remnant stomach were showed in (Table 4) (upper side).

Parameters	Group A (n=12)	Group B (n=10)	p value
Time to 50% residual rate in the remnant stomach (minutes)			
	76.3±8.1	62.5±6.7	0.0001
The residual rate at 120 minutes in the remnant stomach (%)			
	49.3±7.8	37.8±6.3	0.0006
Blood concentration of acetomaminophen at 45 minutes (μg/mL)			
	46.3±5.8	45.6± 4.7	0.3759

Group A: Patients with postprandial abdominal fullness after PPG

Group B: Patents without postprandial abdominal fullness after PPG

PPG: Pylorus-preserving gastrectomy

Table 4: Parameters of gastric emptying functions 1 year after PPG.

GET for solid diet (radioisotope method): The time to 50% residual rates was 76.3±8.1 minutes in group A and 62.5±6.7 minutes in group B. That in group A was significantly delayed compared with that in group B (p = 0.0001). Residual rates (%) at 120 min in the remnant stomach were 49.3±7.8% in group A and 37.8±6.3% in group B. Residual rates at 120 min in group A were significantly higher than those in group B (p = 0.0006).

Gastric emptying functions with the liquid diet (acetoaminophen method) were showed in Table 4 (lower side). The blood concentration of acetoaminophen at 45 minutes was 46.3±5.8 μg/mL in group A and 45.6±4.7 μg/mL in group B. There are no significant differences in the blood concentration of acetoaminophen at 45 minutes between groups A and B (p = 0.3759). According to these results, GEF with the solid food was clearly delayed in group A compared with that in group B. However, there was no difference in the liquid-empting time in either group.

Discusssion

In early gastric cancer located in the middle and/or lower stomach, generally, the pylorus is resected with lymph node dissection without preserving PHCV (i.e., conventional distal gastrectomy) [5]. PGD (malnutrition due to loss of appetite, weight loss, EDS, RS, or GRS) are unfavorable sequelae in patients after

conventional distal gastrectomy [1-5]. To prevent PGD, PPG with preservation of the vagal nerves has been performed wordwide [12]. However, PAF has been reported in patients one year or more after PPG [1,2,6,7,9]. In this study, the author obtained similar data on PGD in patients 1 year after PPG. To clarify the causes of PAF after PPG, studies have been performed focusing on both the vagal nerve and LPC [1,7,12-15].

Sawai, et al. [16] reported that PAF with GSRS after PPG is due to damage to PHCV as a result of skeletonization of the subpyloric region with the subpyloric lymph node dissection. It was also showed that PHCV are necessary for pyloric sphincter functioning in patients after PPG [8,12,13]. In recent years, the vagal nerves, including hepatic and pyloric branches, have been preserved to prevent PGD such as PAF and endoscopic GSRS [13]. It is also 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 [7]. In contrast, it was concluded that preservation of the vagal nerve such as PHCV is not necessary for gastropyloroduodenal motility in patients after PPG [1-7]. Morita, et al. [17] showed that PAF due to GSRS can be present up to 5 years after PPG even with PHCV preservation. Therefore, the roles of PHCV in PPG are not clearly understood. By the way, it is well known that PHCV is important factors in intestinal peristalsis [18]. So, the author preserved PHCV in PPG patients.

The pyloric sphincter prevents EDS due to the rapid emptying of food and prevents alkaline RE and GRS due to the reflux of duodenal juice into the remnant stomach and esophagus [3,5]. It was reported that the remnant stomach emptying function was favorable, when a 2.0 cm or longer pyloric antrum was preserved, and favorable QOL results were obtained in PPG patients [1,13,14]. Nakane, et al. [13] demonstrated that PPG with transection 2.5 cm proximal to the pyloric ring was superior to that with transection at 1.5 cm in terms of postprandial symptoms, food intake, body weight recovery and gastric emptying. According to this data, the size of LAC may be related to the delayed gastric emptying of a solid diet. In the present study, LAC in patients with PAF was 1.6±0.2 cm and that without PAF 2.4±0.4 cm. Patients with PAF clearly showed a short LAC compared with those without PAF. Why then antropyloroduodenal coordination is important to transport gastric contents to the duodenum [19]. In this study, the author suggests that a 2 cm or longer LAC may be necessary to coordinate antropyloroduodenal motility for preventing PAF. Generally, ^{99m}Tc tin colloid or ^{99m}Tc-DTPA is used for the solid diet as a nuclide [10]. As the acetaminophen method can be safely performed at a reasonable cost, it is widely used for the determination of the emptying time of a liquid diet instead of the radioisotope method [11]. As a solid diet, the author used rice gruel, because it is familiar to Japanese people, and easy to cook and eat after gastric surgery. Previously, the author suggested that the gastric emptying curve with a rice gruel diet presented a regression line with a high regression coefficient in the control group, and the author thus considered that there was no problem associated with the use of a rice gruel diet as a solid diet [20]. In general, both the time to 50% residual rates and the residual rate at 120 minutes in the remnant stomach reveal GEF with the solid diet. In this study, the author used the time to 50% residual rates and the residual rate at 120 minutes in the remnant stomach to evaluate GEF in patients after PPG. To examine the liquid diet-emptying function with the acetaminophen method, orange juice are used. Acetaminophen is not absorbed by the stomach but is promptly absorbed by the small intestine [11].

It is well-known that the blood concentration of acetaminophen at 45 minutes shows the gastric emptying function with a liquid meal [11]. The author also used the same method in this study. Mistiaen, et al. [21] suggested that liquid diets are more appropriate for detecting possible rapid gastric emptying rates and EDS. A solid diet test, on the other hand, can be used to study gastric stasis. In the present studies, the gastric emptying of the solid diet was significantly delayed in PPG with PAF compared to PPG without PAF. However, the gastric emptying of the liquid diet showed no difference between PPG with and without PAF. According to these results, preservation of the pyloric ring in PPG is considered to be useful to prevent rapid gastric emptying rates and EDS. A feeling of PAF after PPG due to the long-term retention of solid food may occur due to delayed emptying of the solid diet. Therefore, slow emptying of a solid diet in PPG patients may contribute to the sensation of PAF and GSRS. Regarding GEF with a liquid diet (blood concentration of acetoaminophen at 45 minutes (μg/mL), there was also no significant differences between patients after PPG and normal subjects.

In conclusion, PPG patients with PAF had a clearly shorter LAC (less than 2 cm) than PPG patients without PAF. PPG patients without PAF had a greater appeteite and ate more than food, with less or a decrease in body weight, compared with patients with PAF. Patients without PAF clearly had less symptoms such as EDS and RE compared with PAF patients. Patients with PAF showed the delayed gastric emptying of solid food and a poor postoperative QOL compared with these without PAF. This was a retrospective study and sample size was small. Therefore, a randomized controlled trial of the postoperative states increased number of patients after PPG with and without PAF should be performed in the future. To prevent PAF in PPG patients, it is also necessary the author should discover a prokinetic agent for the improvement of GET of solid food.

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