

Factors that minimize postgastrectomy symptoms following pylorus-preserving gastrectomy: assessment using a newly developed scale (PGSAS-45)

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Abstract

Background Pylorus-preserving gastrectomy (PPG) is sometimes performed as a function-preserving surgery for the treatment of early gastric cancer. The aim of this study was to use an integrated assessment scale for postgastrectomy syndrome to determine the appropriate indicators and optimal methods for PPG.

Methods The Postgastrectomy Syndrome Assessment Study (PGSAS) is a multicenter survey based on an integrated questionnaire (PGSAS-45) consisting of 45 items. Questionnaire responses were retrieved from a total of 2,520 patients, each of whom had undergone one of six

different types of gastrectomy procedures; 313 responses from patients who had received PPG were analyzed here.

Results The size of the proximal gastric remnant (less than one-quarter, about one-third, or more than one-half of the original size) significantly influenced the change in body weight, the scores for dissatisfaction at the meal, and dissatisfaction for daily life subscale ($P = 0.030$, $P = 0.005$, $P = 0.034$, respectively). The nausea score in patients who underwent hand-sewn anastomosis was significantly lower than in those who underwent anastomosis with a linear stapler ($P = 0.006$). The scores for diarrhea subscale, increased passage of stools, and sense of foods

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sticking differed significantly depending on the length of the preserved pyloric cuff ($P = 0.047$, $P = 0.021$, $P = 0.046$, respectively).

Conclusions The results suggest that preservation of a sufficient proximal gastric remnant is recommended when utilizing PPG as function-preserving surgery.

Keywords Pylorus-preserving gastrectomy · Quality of life · Early gastric cancer · Function-preserving surgery · Postgastrectomy syndrome

Introduction

Pylorus-preserving gastrectomy (PPG) is a form of function-preserving surgery that preserves the quality of life (QOL) of patients requiring radical gastrectomy [1, 2]. PPG was initially reported by Maki et al. [3] as an effective modification of distal gastrectomy for the treatment of benign gastric diseases. Preserving pyloric function has several advantages, such as the prevention of dumping syndrome, protection against bile mucosal injury of the remnant stomach, and reduction in postoperative body weight loss. The low probability of lymph node metastasis in early gastric cancer (EGC) has allowed the increasing use of limited resection as a treatment option, and PPG has been demonstrated to be a viable option for patients with EGC located in the middle third of the stomach [1, 4, 5]. Moreover, it has been reported that PPG may result in a long-term survival benefit for patients diagnosed with cT1 gastric cancer (mucosal or submucosal), or cN0 gastric cancer in the middle of the body of the stomach [1]. Previous investigators have reported that the overall 5-year survival rate for patients who have undergone PPG is 95–98 % [1, 5, 6].

Evaluation of the various ways of preserving function, such as reducing the extent of gastrectomy, or conducting nerve or sphincter preservation, is very important; however, scientific assessment is not easy because there is no gold standard scale for measuring gastrointestinal function and the QOL of patients. So far, there have been few reports of long-term symptom evaluation following PPG with large numbers of cases [7, 8]. The Postgastrectomy Syndrome Assessment Study (PGSAS) is a multicenter questionnaire survey conducted from July 2009 to December 2010 by the Japan Postgastrectomy Syndrome Working Party to clarify the actual life status of patients after gastrectomy and the relationship between type of gastrectomy and postgastrectomy syndrome (PGS). Although PPG has many benefits compared with conventional distal gastrectomy with Billroth I reconstruction, debate continues regarding the clinical benefits of PPG, the effects of preserving either the celiac or the pyloric branch

of the vagal nerve, the relationship between the length of the pyloric cuff and postoperative symptoms, and the indications for PPG. Here, we analyzed responses to the survey questionnaire to determine the appropriate indicators and optimal methods for PPG and which methods of PPG reserve sufficient function to maintain a good QOL for patients with gastric cancer.

Materials and methods

The Japan Postgastrectomy Syndrome Working Party conducted a questionnaire survey by using a newly developed integrated questionnaire that is composed of 45 items (Postgastrectomy Syndrome Assessment Scale-45, PGSAS-45) to assess the effects of gastrectomy on daily life. PGSAS-45 includes the following components: (1) 8 items comprising a generic QOL questionnaire called Short Form-8 (SF-8), an instrument commonly used for measuring health-related QOL that is based on extensive previous work with the SF-36 [9]; (2) 15 items comprising the Gastrointestinal Symptom Rating Scale (GSRS), a symptom-specific instrument used to evaluate common symptoms of gastrointestinal disorders [10]; (3) 8 items regarding important postgastrectomy symptoms; (4) 2 items regarding number and type of early or late dumping symptoms; (5) 8 items regarding meal intake; (6) 1 item regarding working status; and (7) 3 items regarding degree of dissatisfaction with symptoms, meal intake, and ability to work, respectively (Table 1). For the 23 symptom items, a seven-grade (1–7) Likert scale was used, and a five-grade (1–5) Likert scale was used for all the other items except items 1, 4, 29, 32, and 34–37. Based on data from the retrieved PGSAS-45 questionnaires, outcome measures were refined through consolidation and selection [11, 12]. The main outcome measures in PGSAS are listed in Table 2, and the other outcome measures in this study are symptoms of PGSAS-45. The clinical data collected included age, sex, height, body weight, elapsed time since gastrectomy, and details of the surgical methods.

All patients enrolled in this trial fulfilled the following eligibility criteria: (1) diagnosis of pathologically confirmed stage IA or IB gastric cancer; (2) first-time gastrectomy status; (3) age >20 and ≤75 years; (4) no history of chemotherapy; (5) no recurrence or distant metastasis indicated; (6) gastrectomy conducted 1 or more years before enrollment date; (7) performance status (PS) ≤1 on the Eastern Cooperative Oncology Group (ECOG) scale; (8) full capacity to understand and respond to the questionnaire; (9) no history of other diseases or surgeries that might influence responses to the questionnaire; (10) no presence of organ failure or mental illness; and (11) written informed consent. Patients with dual malignancy or

Table 1 Structure of Postgastrectomy Syndrome Assessment Study (PGSAS)-45 (domains/subdomains/items/subscales)

Domains	Subdomains	Items	Subscales	
Quality of life	SF-8 (quality of life)	1 Physical functioning*	Physical component summary*	
		2 Role-physical*	Mental component summary*	
		3 Bodily pain*		
		4 General health*		
		5 Vitality*		
		6 Social functioning*		
		7 Role-emotional*		
		8 Mental health*		
Symptoms	GSRs (symptoms)	9 Abdominal pains	Esophageal reflux subscale (items 10, 11, 13, 24)	
		10 Heartburn	Abdominal pain subscale (items 9, 12, 28)	
		11 Acid regurgitation	Meal-related distress subscale (items 25–27)	
		12 Sucking sensations in the epigastrium	Indigestion subscale (items 14–17)	
		13 Nausea and vomiting	Diarrhea subscale (items 19, 20, 22)	
		14 Borborygmus	Constipation subscale (items 18, 21, 23)	
		15 Abdominal distension	Dumping subscale (items 30, 31, 33)	
		16 Eructation		
		17 Increased flatus	Total symptom scale (more than seven subscales)	
		18 Decreased passage of stools		
		19 Increased passage of stools		
		20 Loose stools		
		21 Hard stools		
		22 Urgent need for defecation		
		23 Feeling of incomplete evacuation		
		Symptoms	24 Bile regurgitation	
			25 Sense of foods sticking	
	26 Postprandial fullness			
	27 Early satiation			
	28 Lower abdominal pains			
	29 Number and type of early dumping symptoms			
	30 Early dumping, general symptoms			
	31 Early dumping, abdominal symptoms			
	32 Number and type of late dumping symptoms			
	33 Late dumping symptoms			
	Living status	Meals (amount) 1	34 Ingested amount of food per meal*	
			35 Ingested amount of food per day*	
36 Frequency of main meals				
37 Frequency of additional meals				
38 Appetite*			Quality of ingestion subscale* (items 38–40)	
Meals (quality)		39 Hunger feeling*		
		40 Satiety feeling*		
Meals (amount) 2		41 Necessity for additional meals		
Social activity		42 Ability for working		

Table 1 continued

Domains	Subdomains	Items	Subscales
Quality of life	Dissatisfaction (Quality of life)	43	Dissatisfaction with symptoms
		44	Dissatisfaction at the meal
		45	Dissatisfaction with working

PGSAS-45 Postgastroectomy Syndrome Assessment Scale-45, SF-8 Short Form-8, QOL quality of life, GSRS Gastrointestinal Symptom Rating Scale

In items or subscales with *, higher scores indicate better conditions. In items or subscales without *, higher scores indicate worse conditions. Each subscale is calculated as the mean of its composite items or subscales, except the physical and mental component summaries of SF-8. Items 29 and 32 do not have scores; these items were analyzed separately

Table 2 Main outcome measures in PGSAS

Domains	Main outcome measures
Symptoms	
Subscales	Esophageal reflux subscale Abdominal pain subscale Meal-related distress subscale Indigestion subscale Diarrhea subscale Constipation subscale Dumping subscale
Total	Total symptom score
Living status	
Body weight	Change in body weight (%)*
Meals (amount)	Amount of food ingested per meal* Necessity for additional meals
Meals (quality)	Quality of ingestion subscale*
Work	Ability for working
Quality of life	
Dissatisfaction	Dissatisfaction with symptoms Dissatisfaction at the meal Dissatisfaction at working Dissatisfaction with daily life subscale
Short Form-8	Physical component summary* Mental component summary*

PGSAS Postgastroectomy Syndrome Assessment Study

In items or subscales with *, higher scores indicates better conditions; in items or subscales without *, higher scores indicates worse conditions

concomitant resection of other organs (with co-resection equivalent to cholecystectomy being the exception) were excluded.

Fifty-two institutions participated in this study. The study utilized continuous sampling from a central registration system for participant enrollment. From July 2009 to December 2010, the questionnaire was distributed to all eligible patients as they presented to participating institutions. After completing the questionnaire, patients were

instructed to return forms to the data center. All QOL data from questionnaires were matched with individual patient data collected via case report forms. The study was approved by the institutional review board of the participating institutions [University Hospital Medical Information Network's Clinical Trials Registry (UMIN-CTR) registration number, 000002116]. Written informed consent was obtained from all enrolled patients, conforming to institutional guidelines.

Survey analysis

During the enrollment period, the PGSAS-45 questionnaire was handed to 2,922 eligible patients. A total of 2,520 questionnaires (86 %) were retrieved, of which 2,368 (81 %) were eligible. Respondents were 393 patients who underwent total gastrectomy, 475 patients who underwent distal gastrectomy with Roux-en-Y reconstruction, 909 patients who underwent distal gastrectomy with Billroth I reconstruction, 313 patients who underwent PPG, 193 patients who underwent proximal gastrectomy, and 85 patients who underwent local resection of the stomach. Here, we investigated the 313 patients who underwent PPG to assess the relationship between their QOL status and the size of the proximal gastric remnant, method of anastomosis, length of the pyloric cuff, and preservation of the pyloric branch of the vagal nerve.

Patients who underwent PPG were divided into three groups according to the size of the proximal gastric remnant (those with more than one-half, about one-third, or less than one-quarter of the stomach remaining) and three groups according to the length of the preserved pyloric cuff (those with less than 2.5 cm, 3.0–5.0 cm, or more than 5.5 cm of the pyloric cuff preserved).

Statistical analysis

The significance of differences between the mean values of two groups was assessed by the unpaired *t* test and that

among three groups was assessed by one-way analysis of variance (ANOVA). In the latter, Bonferroni/Dunn multiple comparisons were performed when the P value of ANOVA was less than 0.1. All data are presented as the mean \pm standard deviation. Generally, P values less than 0.05 in t tests or ANOVA were considered to be statistically significant. In a Bonferroni/Dunn multiple comparison, a P value less than 0.05/number of hypothesis was considered to be statistically significant. When P values were less than double the significant level, we calculated Cohen's d as the effect size. StatView software for Windows version 5.0 (SAS Institute) was used for all statistical analyses.

Results

Patient characteristics

Table 3 summarizes the clinical characteristics of the 313 patients who underwent PPG. One hundred and eighty-three patients (58.5 %) were men and 126 (40.3 %) were women, with a mean age of 61.5 ± 8.7 years. At the time of surgery, 136 patients (43.5 %) underwent laparoscopic PPG and 173 (55.3 %) underwent conventional open PPG. Regarding the size of the proximal gastric remnant compared with the preoperative stomach, 73 patients (23.3 %) retained more than half of the stomach, 222 patients (70.9 %) retained about one-third of the stomach, and 12 patients (3.8 %) retained less than one-quarter of the stomach. Thirty-eight patients (12.1 %) underwent mechanical anastomosis using a linear stapler, and 270 patients (86.3 %) underwent hand-sewn anastomosis. The celiac branch of the vagal nerve was preserved in 213 patients (68.1 %), and the pyloric branch of the vagal nerve was preserved in 254 patients (81.2 %).

Effect of size of the proximal gastric remnant

PGSAS scores in patients grouped according to the size of the proximal gastric remnant (more than half, about one-third, and less than one-quarter) are listed in Table 4. There were significant differences among the three groups with regard to body weight change (%) compared to preoperative weight and the scores for dissatisfaction at the meal and dissatisfaction with daily life subscale ($P = 0.030$, $P = 0.005$, and $P = 0.034$; ANOVA), respectively. When Bonferroni/Dunn comparisons between individual groups were made, the changes in body weight of patients in the "less than one-quarter" group (mean \pm SD; -11.9 ± 4.8 %) were significantly greater than those of patients in the "more than one-half" (-6.1 ± 7.1 %; $P = 0.008$, Cohen's $d = 0.94$), or "about one-third" groups (-6.8 ± 6.9 %;

Table 3 Clinical characteristics of the 313 patients who underwent pylorus-preserving gastrectomy

Number	313
Period after gastrectomy (months)	38.4 ± 27.7
Body mass index (before gastrectomy)	22.7 ± 3.0
Body mass index (at the time of study)	21.1 ± 2.6
Age (years)	61.5 ± 8.7
Gender	
Male	183 (58.5 %)
Female	126 (40.3 %)
Operation method	
Laparoscopic	136 (43.5 %)
Open	173 (55.3 %)
Size of the proximal gastric remnant	
More than half	73 (23.3 %)
Around one-third	222 (70.9 %)
Less than one quarter	12 (3.8 %)
Method of anastomosis	
Use of linear stapler	38 (12.1 %)
Hand sewn	270 (86.3 %)
Length of the pyloric cuff (cm)	
≤ 2.5	34 (10.9 %)
3.0–5.0	212 (67.7 %)
≥ 5.5	41 (13.1 %)
Preservation of celiac branch of vagal nerve	
Yes	213 (68.1 %)
No	96 (30.7 %)
Preservation of pyloric branch of vagal nerve	
Yes	254 (81.2 %)
No	40 (12.8 %)

$P = 0.014$, Cohen's $d = 0.84$), respectively. Similarly, the dissatisfaction at the meal scores in patients in the "less than one-quarter" group (3.1 ± 1.0) were significantly higher than those in the "more than half" (2.0 ± 1.0 ; $P = 0.002$, Cohen's $d = 1.04$), or "about one-third" groups (2.3 ± 1.1 ; $P = 0.013$, Cohen's $d = 0.76$), respectively. The scores for dissatisfaction for daily life subscale for patients in the "less than one-quarter" group (2.5 ± 0.8) were significantly higher than those for patients in the "more than half" group (1.8 ± 0.9 ; $P = 0.009$, Cohen's $d = 0.82$), but not those for patients in the "about one-third" group (1.9 ± 0.8). There were no significant differences among the three groups in other scales examined (Table 4).

Effect of method of anastomosis

The nausea scores in patients who underwent hand-sewn anastomosis (1.4 ± 0.9) were significantly lower than those in patients who underwent mechanical anastomosis

Table 4 Outcome measures in patients grouped according to the size of the proximal gastric remnant

	Size of the proximal gastric remnant			<i>P</i> value (ANOVA)	<i>P</i> value (B/D)	Cohen's <i>d</i>
	More than half (<i>n</i> = 73)	Around one-third (<i>n</i> = 222)	Less than one-quarter (<i>n</i> = 12)			
Main outcome measures						
Change in body weight (%)	-6.1 ± 7.1 %	-6.8 ± 6.9 %	-11.9 ± 4.8 %	0.030	0.008 ^a 0.014 ^b	0.94 0.85
Physical component summary	51.5 ± 4.8	50.9 ± 5.5	51.2 ± 3.8	≥0.1		
Mental component summary	50.2 ± 7.0	50.0 ± 5.9	49.2 ± 4.1	≥0.1		
Esophageal reflux subscale	1.7 ± 0.7	1.7 ± 0.9	1.7 ± 0.6	≥0.1		
Abdominal pain subscale	1.7 ± 0.9	1.6 ± 0.7	1.7 ± 0.6	≥0.1		
Meal-related distress subscale	2.0 ± 0.9	2.1 ± 0.9	2.2 ± 0.9	≥0.1		
Indigestion subscale	2.0 ± 1.0	2.0 ± 0.9	2.1 ± 0.9	≥0.1		
Diarrhea subscale	1.9 ± 0.9	1.8 ± 1.0	2.2 ± 1.1	≥0.1		
Constipation subscale	2.2 ± 1.0	2.2 ± 1.1	2.3 ± 1.1	≥0.1		
Dumping subscale	1.7 ± 0.9	1.8 ± 1.0	1.9 ± 0.6	≥0.1		
PGSAS total score	1.8 ± 0.7	1.9 ± 0.7	2.0 ± 0.6	≥0.1		
Amount of food ingested per meal	7.3 ± 2.0	7.0 ± 1.9	6.8 ± 1.6	≥0.1		
Necessity for additional meals	1.6 ± 0.6	1.8 ± 0.8	1.9 ± 0.6	≥0.1		
Quality of ingestion subscale	3.5 ± 1.0	3.8 ± 0.9	3.7 ± 0.8	0.064	0.021 ^c	0.31
Ability for working	1.7 ± 0.9	1.8 ± 1.0	2.0 ± 0.6	≥0.1		
Dissatisfaction with symptoms	1.8 ± 1.0	1.8 ± 0.9	2.3 ± 1.1	≥0.1		
Dissatisfaction at the meal	2.0 ± 1.0	2.3 ± 1.1	3.1 ± 1.0	0.005	0.002 ^a 0.013 ^b	1.04 0.76
Dissatisfaction at working	1.6 ± 1.0	1.7 ± 0.9	2.1 ± 1.0	≥0.1		
Dissatisfaction for daily life subscale	1.8 ± 0.9	1.9 ± 0.8	2.5 ± 0.8	0.034	0.009 ^a	0.82

In ANOVA, a *P* value less than 0.05 was considered as statistically significant

In Bonferroni/Dunn multiple comparisons, a *P* value less than 0.0167 was considered as statistically significant

Interpretation of effect size in Cohen's *d*: ≥0.20 as small, ≥0.50 as medium, ≥0.80 as large

ANOVA one-way analysis of variance, B/D Bonferroni/Dunn multiple comparisons

^a More than half vs. less than one-quarter

^b Approximately one-third vs. less than one-quarter

^c More than half vs. approximately one-third

using a linear stapler (1.9 ± 1.2; *P* = 0.006, Cohen's *d* = 0.44; unpaired *t* test). There were no significant differences between the two groups in other scales examined (Table 5).

Effect of the length of the pyloric cuff

Values for various PGSAS outcome measures in patients subgrouped according to the length of the remnant pyloric cuff (≤2.5 cm, 3.0–5 cm, or ≥5.5 cm) are listed in Table 6. There were significant differences among the three groups in terms of the scores for diarrhea subscale, increased passage of stools, and sense of foods sticking (*P* = 0.047, *P* = 0.021, and *P* = 0.046, respectively; ANOVA). Although the group with a remnant pyloric cuff of 3.0–5.0 cm showed the lowest scores for the foregoing

outcome measures, no significant differences were found between individual groups by Bonferroni/Dunn multiple comparisons tests.

Pyloric branch of the vagal nerve preservation

Patients who underwent PPG with preservation of the pyloric branch of the vagal nerve tended to complain of additional food intake necessity and nausea, whereas those without preservation of the pyloric branch of the vagal nerve tended to complain of late dumping symptoms (Table 7); however, these differences were not statistically significant by Student's unpaired *t* test. The other PGSAS scales also showed no significant differences between patients with or without preservation of the vagal nerve pyloric branch.

Table 5 Outcome measures in patients grouped according to method of anastomosis

	Method of anastomosis		<i>P</i> value	Cohen's <i>d</i>
	Linear stapler (<i>n</i> = 38)	Hand sewing (<i>n</i> = 270)		
Main outcome measures				
Change in body weight (%)	-5.7 ± 6.9	-7.0 ± 6.9	≥0.1	
Physical component summary	50.7 ± 5.0	51.1 ± 5.3	≥0.1	
Mental component summary	49.8 ± 5.9	50.0 ± 6.1	≥0.1	
Esophageal reflux subscale	1.8 ± 0.9	1.7 ± 0.8	≥0.1	
Abdominal pain subscale	1.7 ± 0.8	1.6 ± 0.7	≥0.1	
Meal-related distress subscale	2.2 ± 0.8	2.1 ± 0.9	≥0.1	
Indigestion subscale	2.1 ± 0.9	2.0 ± 0.9	≥0.1	
Diarrhea subscale	2.0 ± 0.9	1.8 ± 1.0	≥0.1	
Constipation subscale	2.1 ± 0.9	2.3 ± 1.1	≥0.1	
Dumping subscale	1.7 ± 0.9	1.8 ± 0.9	≥0.1	
PGSAS total score	1.9 ± 0.7	1.9 ± 0.7	≥0.1	
Amount of food ingested per meal	6.9 ± 2.0	7.0 ± 1.9	≥0.1	
Necessity for additional meals	1.7 ± 0.6	1.8 ± 0.8	≥0.1	
Quality of ingestion subscale	3.7 ± 0.9	3.8 ± 0.9	≥0.1	
Ability for working	1.9 ± 1.0	1.8 ± 0.9	≥0.1	
Dissatisfaction with symptoms	1.8 ± 0.9	1.8 ± 0.9	≥0.1	
Dissatisfaction at the meal	2.3 ± 1.2	2.2 ± 1.1	≥0.1	
Dissatisfaction at working	1.8 ± 1.0	1.6 ± 0.9	≥0.1	
Dissatisfaction for daily life subscale	2.0 ± 0.9	1.9 ± 0.8	≥0.1	
Other outcome measures (symptoms)				
Nausea and vomiting	1.9 ± 1.2	1.4 ± 0.9	0.006	0.44

In the unpaired *t* test, a *P* value less than 0.05 was considered as statistically significant

Interpretation of effect size in Cohen's *d*: ≥0.20 as small, ≥0.50 as medium, ≥0.80 as large

Discussion

Patients who undergo gastrectomy often suffer from PGS, resulting in a decrease in their QOL [13]. Therefore, function-preserving operations including PPG have been introduced to prevent this syndrome [1, 5, 7]. Here we examined the appropriate indicators and optimal methods for PPG and the effect of various factors on QOL.

We demonstrated that there were significant differences in terms of body weight change, dissatisfaction at the meal, and dissatisfaction with daily life subscales depending on the size of the proximal gastric remnant after PPG. It has been suggested that PGS is primarily caused by impaired function of the remnant stomach. Nomura et al. [14] reported that patients who undergo half resection rather than the more typical two-thirds resection in distal gastrectomy benefit in terms of functional outcomes such as preservation of body weight, food intake volume, and the incidence of esophagitis and gastritis; they speculated that the reservoir function of the remnant stomach is preserved in the half resection group, leading to improved postoperative nutritional status and body composition. Also, better functional outcomes have been reported in patients with a large remnant stomach than in those with a small remnant

stomach following proximal gastrectomy for gastric cancer [15]. Our finding, that several symptoms after PPG are worse when the proximal gastric remnant is a quarter the size of the preoperative stomach compared with when it is around a third or more than half the original size, indicates that the preservation of a proximal gastric remnant of sufficient size is recommended, and that careful consideration is needed before applying PPG in cases of a small-sized remnant stomach. In contrast, in patients with weakened peristalsis, an excessively large remnant stomach may render gastric emptying difficult because of the descending position below the anastomosis when it is filled with food.

A recent questionnaire survey of the status of PPG in 148 Japanese institutions reported that layer-to-layer anastomosis (defined as “two-layer anastomosis with mucosal and seromuscular sutures”) is the most representative technique for gastrogastrostomy [16]. Here, we investigated whether the method of anastomosis (hand-sewn anastomosis or mechanical anastomosis using a linear stapler) affected symptoms after PPG. The results indicated that the nausea score was significantly lower in patients who underwent hand-sewn anastomosis than in those that underwent mechanical anastomosis with small effect size

Table 6 Outcome measures according to the length of the preserved pyloric cuff

	Length of the pyloric cuff			<i>P</i> value (ANOVA)	<i>P</i> value (B/D)	Cohen's <i>d</i>
	≤2.5 cm (<i>n</i> = 34)	3.0–5.0 cm (<i>n</i> = 212)	≥5.5 cm (<i>n</i> = 41)			
Main outcome measures						
Change in body weight (%)	−7.0 ± 4.8	−6.6 ± 6.9	−7.1 ± 8.9 %	≥0.1		
Physical component summary	51.4 ± 4.9	51.2 ± 5.1	50.3 ± 6.6	≥0.1		
Mental component summary	50.0 ± 6.3	50.0 ± 6.3	49.9 ± 5.4	≥0.1		
Esophageal reflux subscale	1.9 ± 1.1	1.6 ± 0.7	1.7 ± 1.0	≥0.1		
Abdominal pain subscale	1.6 ± 0.6	1.6 ± 0.7	1.7 ± 0.9	≥0.1		
Meal-related distress subscale	2.3 ± 0.9	2.0 ± 0.8	2.3 ± 1.1	0.052	0.038 ^a	0.32
Indigestion subscale	2.0 ± 0.8	1.9 ± 0.9	2.2 ± 1.0	≥0.1		
Diarrhea subscale	2.1 ± 1.0	1.7 ± 0.9	2.0 ± 1.1	0.047	0.046 ^b	0.37
Constipation subscale	2.5 ± 1.0	2.2 ± 1.1	2.4 ± 1.2	≥0.1		
Dumping subscale	1.8 ± 0.8	1.7 ± 0.9	1.9 ± 1.2	≥0.1		
PGSAS total score	2.0 ± 0.7	1.8 ± 0.7	2.0 ± 0.8	≥0.1		
Amount of food ingested per meal	6.8 ± 1.8	7.0 ± 1.8	7.3 ± 2.3	≥0.1		
Necessity for additional meals	1.7 ± 0.8	1.7 ± 0.7	2.0 ± 0.9	≥0.1		
Quality of ingestion subscale	3.5 ± 0.8	3.8 ± 1.0	3.7 ± 0.7	≥0.1		
Ability for working	1.8 ± 1.1	1.8 ± 0.9	1.8 ± 1.0	≥0.1		
Dissatisfaction with symptoms	1.8 ± 0.7	1.7 ± 0.9	2.0 ± 1.1	≥0.1		
Dissatisfaction at the meal	2.4 ± 1.1	2.1 ± 1.1	2.6 ± 1.2	0.072	0.029 ^a	0.37
Dissatisfaction at working	1.9 ± 1.1	1.6 ± 0.8	1.9 ± 1.1	0.072	0.060 ^a	0.31
Dissatisfaction with daily life subscale	2.0 ± 0.8	1.8 ± 0.8	2.1 ± 1.0	0.062	0.026 ^a	0.36
Other outcome measures (symptoms)						
Increased flatus	2.3 ± 1.3	2.2 ± 1.3	2.7 ± 1.5	0.091	0.029 ^a	0.36
Increased passage of stools	2.1 ± 1.3	1.7 ± 1.1	2.2 ± 1.5	0.021	0.022 ^a	0.35
Sense of foods sticking	1.8 ± 0.9	1.5 ± 0.8	1.8 ± 1.2	0.046	0.031 ^a	0.33

In ANOVA, a *P* value less than 0.05 was considered as statistically significant

In Bonferroni/Dunn multiple comparisons, a *P* value less than 0.0167 was considered as statistically significant

Interpretation of effect size in Cohen's *d*: ≥0.20 as small, ≥0.50 as medium, ≥0.80 as large

ANOVA one-way analysis of variance, B/D Bonferroni/Dunn multiple comparisons

^a 3.0–5.0 cm vs. ≥5.5 cm

^b ≤2.5 cm vs. 3.0–5.0 cm

(Cohen's *d* = 0.43). This finding suggests that the delicate manipulations of hand-sewn anastomosis might avoid deformity of the proximal gastric remnant, and that insufficient flexibility in the anastomotic site caused by the use of staples might contribute to nausea. Although PPG preserves gastric function, patients occasionally have a feeling of gastric fullness after food intake, and some experience long-term retention of food in the residual stomach [16–18]. Delayed gastric emptying is the most common complaint after PPG, and it manifests as various symptoms including nausea, epigastric fullness, and poor oral intake [7, 17, 19].

Lee et al. [20] performed intracorporeal gastro-gastric anastomosis with mechanical suture devices in

laparoscopic PPG (LAPPG) operations on 12 patients, and advocated that this technique has the potential to provide a better QOL following gastric cancer surgery because of the low incidence of morbidity and no stasis; however, the sample size was small. With advances in devices for anastomosis, mechanical anastomosis using a linear stapler, including totally intracorporeal procedures, is likely to become more popular.

According to Japanese gastric cancer treatment guidelines, modification of gastric resection to PPG is recommended for cT1cN0 tumors in the middle portion of the stomach when the distal tumor border is at least 4 cm proximal to the pylorus [21]. The clinical benefits of PPG are considered to be based on the function of the

Table 7 Outcome measures depending on the pyloric branch of the vagal nerve preservation

	Pyloric branch of the vagal nerve preservation		<i>P</i> value	Cohen's <i>d</i>
	Yes (<i>n</i> = 254)	No (<i>n</i> = 40)		
Main outcome measures				
Change in body weight (%)	-6.8 ± 7.1	-6.4 ± 5.6	≥0.1	
Physical component summary	50.9 ± 5.5	51.7 ± 4.5	≥0.1	
Mental component summary	49.8 ± 6.3	50.1 ± 5.1	≥0.1	
Esophageal reflux subscale	1.7 ± 0.8	1.6 ± 0.7	≥0.1	
Abdominal pain subscale	1.7 ± 0.7	1.6 ± 0.8	≥0.1	
Meal-related distress subscale	2.1 ± 0.9	2.1 ± 0.8	≥0.1	
Indigestion subscale	2.0 ± 0.9	1.9 ± 0.7	≥0.1	
Diarrhea subscale	1.9 ± 1.0	1.7 ± 0.9	≥0.1	
Constipation subscale	2.3 ± 1.1	2.1 ± 0.7	≥0.1	
Dumping subscale	1.8 ± 0.9	1.8 ± 1.0	≥0.1	
PGSAS total score	1.9 ± 0.7	1.8 ± 0.6	≥0.1	
Amount of food ingested per meal	7.0 ± 1.9	7.1 ± 1.5	≥0.1	
Necessity for additional meals	1.8 ± 0.8	1.5 ± 0.7	0.056	0.35
Quality of ingestion subscale	3.8 ± 0.9	3.7 ± 1.0	≥0.1	
Ability for working	1.8 ± 1.0	1.6 ± 0.7	≥0.1	
Dissatisfaction with symptoms	1.8 ± 0.9	1.9 ± 1.0	≥0.1	
Dissatisfaction at the meal	2.2 ± 1.1	2.3 ± 1.1	≥0.1	
Dissatisfaction at working	1.7 ± 0.9	1.6 ± 0.9	≥0.1	
Dissatisfaction for daily life subscale	1.9 ± 0.8	1.9 ± 0.8	≥0.1	
Other outcome measures (symptoms)				
Nausea and vomiting	1.5 ± 1.0	1.2 ± 0.6	0.058	0.39
Late dumping symptoms	1.5 ± 1.0	1.9 ± 1.3	0.083	0.29

In unpaired *t* tests, a *P* value less than 0.05 was considered as statistically significant

Interpretation of effect size in Cohen's *d*: ≥0.20 as small, ≥0.50 as medium, ≥0.80 as large

preserved pylorus [22], and it has been proposed that retention of a longer pyloric cuff may be favorable to decrease postoperative symptoms such as delayed gastric emptying. Nakane et al. [23] reported that PPG with the point of transection 2.5 cm rather than 1.5 cm proximal to the pylorus was superior in terms of some postoperative symptoms and weight recovery, indicating that the length of the pyloric cuff has an important role in the motility of the pylorus following PPG. In contrast, Morita et al. [24] reported that there were no significant differences in symptoms, such as dumping syndrome or emptying disturbances, between patients with pyloric cuff lengths 3.0 cm or less and those with lengths more than 3.0 cm. Shibata et al. [17] concluded that it is uncertain what length of pyloric cuff is reasonable for PPG in terms of gastric emptying. Our results showed that there were significant differences in terms of the score for diarrhea subscale, diarrhea, and sense of foods sticking between patients grouped according to the length of pyloric cuff (<2.5, 3.0–5.0, or >5.5 cm) analyzed by ANOVA. Scores for the afore-listed symptoms were lowest in the group with a remnant pyloric cuff length of 3.0–5.0 cm, indicating that patients with cuff lengths

outside this range might have increased symptoms after PPG, although the differences between groups by Bonferroni/Dunn testing were of borderline significance. Thus, although the length of the pyloric cuff might be an important factor for PGS, its contribution is still under discussion.

It is widely accepted that the pyloric branch of the vagal nerve is important for normal pyloric function, and that preservation of the vagal nerve prevents gastric retention after PPG. One of the pitfalls of PPG for gastric cancer is considered to be the lack of suprapyloric lymph node dissection with intention to preserve the right gastric artery and the pyloric branch of the vagal nerve. Here, we compared the patients who underwent PPG with or without preservation of the pyloric branch of the vagal nerve. Although there were some differences in a few symptoms between groups with borderline significance, the effect of either preservation or division of the pyloric branch or vagal nerve was small as to effect size.

We recognize the following limitations of the present study. First, there were uneven numbers of patients among the groups because of the retrospective nature of the study, and the groups with inferior outcomes were small. Second,

the cross-sectional design of the study did not allow for the inference of cause and effect; further longitudinal studies with a greater number of subjects are required. Additional prospective randomized control studies of PPG operations should be undertaken to further evaluate the factors that minimize PGS.

In conclusion, the size of the remnant stomach following PPG is closely related to the patient's dissatisfaction with daily life and body weight change. We therefore need to consider the size of the proximal gastric remnant to obtain the optimal function-preserving benefit of PPG. In addition, having a medium length of remnant pyloric cuff may reduce some symptoms after PPG. However, further investigations, including a multicenter prospective randomized controlled trial and larger samples with longer follow-up periods, are needed to verify these conclusions.

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Conflict of interest The authors declare no conflicts of interest.

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