



# A comparison of the effects of anti-reflux procedures during esophagogastrostomy after proximal gastrectomy on the postoperative quality of life

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## Abstract

**Purpose** To investigate the postoperative quality of life (QOL) in patients with proximal gastric cancer (PGC) or esophago-gastric junction cancer, a nationwide multi-institutional study (PGSAS NEXT trial) was conducted.

**Methods** Patients who had undergone radical resection more than 6 months previously were enrolled from 70 Japanese institutions between July 2018 and June 2020. The Postgastrectomy Syndrome Assessment Scale (PGSAS)-45 questionnaire was distributed to eligible patients, and responses were collected by mail. The main outcome measures of the PGSAS-45 were then calculated and compared.

**Results** Questionnaires were retrieved from 1950 participants, and data from 300 patients who had undergone a proximal gastrectomy (PG) with esophagogastrostomy for PGC were analyzed. The mean esophageal reflux subscale value was 1.9 among the 276 patients who underwent an anti-reflux procedure, which was significantly better than the mean value (2.6) for the 21 patients who did not undergo an anti-reflux procedure ( $p = 0.002$ ). The esophageal reflux subscale values were also compared among 3 major anti-reflux procedures: the double-flap technique ( $N = 153$ ), the pseudo-fornix and/or His angle formation ( $N = 67$ ), and fundoplication ( $N = 44$ ); no statistically significant differences were observed.

**Conclusion** An anti-reflux procedure during esophagogastrostomy after PG for PGC is necessary to improve postoperative esophageal reflux symptoms, regardless of the type of procedure.

**Trial registration** The PGSAS NEXT study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR; registration number: 000032221).

**Keywords** Proximal gastrectomy · Esophagogastrostomy · Postgastrectomy syndrome · Quality of life · Reflux esophagitis · Fundoplication

## Introduction

Because of the increase in early gastric cancer diagnosis [1, 2] and the upward trend in the incidence of adenocarcinoma of the gastric cardia [3–7], the establishment of an optimal treatment technique for gastric cancer arising in the upper third of the stomach (proximal gastric cancer, [PGC]) is becoming an important issue. Although total gastrectomy with regional lymph node dissection has been considered the standard surgical procedure, the quality of life (QOL) among

cancer survivors after this procedure is often compromised because of postgastrectomy syndrome [8, 9].

Proximal gastrectomy (PG) with the expectation of preserving the gastric function has been proposed as a surgical option for select patients with PGC who have a low risk of lymph node spread. Recently, the Postgastrectomy Syndrome Assessment Scale (PGSAS)-45 was developed as a multidimensional QOL questionnaire [10]. The superiority of PG over total gastrectomy has been reported based on a comparison of postoperative QOL scores obtained using the PGSAS-45 [11].

However, the optimal procedure for reconstruction after PG remains to be established. While esophagogastrostomy with a large remnant stomach is a simple method that allows gastric functions and the capacity to accommodate food to be

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preserved, patients undergoing this procedure often develop severe reflux esophagitis [12, 13]. At present, esophagogastrostomy with an additional anti-reflux procedure is considered the most promising reconstruction technique [14–17].

To investigate the optimal surgical procedures to improve the postoperative QOL in patients with PGC or cancer located near the esophagogastric junction, a nationwide multi-institutional prospective study (PGSAS NEXT) was conducted. We evaluated the pooled data from the PGSAS NEXT study to determine the effect of anti-reflux procedures during esophagogastrostomy after PG for PGC on the postoperative QOL.

## Patients and methods

Patients who met the relevant criteria were enrolled from a total of 70 Japanese institutions between July 2018 and December 2019. The inclusion criteria were (1) patients with PGC or cancer located near the esophagogastric junction (with any stage or histologic type), (2) achievement of R0 resection, (3) no recurrence, (4) more than 6 months elapsed since gastrectomy, (5) previous chemotherapy terminated more than 6 months ago, (6) only 1 gastrectomy procedure, (7) performance status of 0 or 1, (8) capacity to understand the questionnaire, (9) no other disease or previous surgery with the potential to influence the results of the questionnaire, (10) no organ failure or mental illness, and (11) voluntary agreement to complete the questionnaire. The exclusion criteria were (1) multiple active malignancies in other organs, (2) another simultaneous surgery with the exception of resection of peri-gastric organs required to accomplish gastrectomy or lymph node dissection or surgery equivalent to cholecystectomy, and (3) ineligibility as determined by the physician in charge of the patient's care.

The surgical procedure used to prevent postoperative esophageal reflux disease was determined by the surgeon. Pseudo-fornix and/or His angle formation was defined as the fixation of the proximal gastric stump under the esophagus so that the esophagus and remnant stomach were juxtaposed. In addition, a double-flap technique as described in the previous reports [15] and side overlap with fundoplication by the Yamashita (SOFY) method [16] were performed in some patients. Fundoplication was defined as wrapping the posterior esophageal circumference  $\geq 180^\circ$  using the anterior wall of the remnant stomach.

The PGSAS-45 questionnaire was distributed to eligible patients at the time of their visit to an outpatient clinic, and the responses were collected by mail. The PGSAS-45 questionnaire consists of 45 questions, with 8 items from the Short-Form Health Survey (SF-8) [18], 15 items from the Gastrointestinal Symptom Rating Scale (GSRS) [19], and 22 clinically important items selected by the Japan

Postgastrectomy Syndrome Working Party. The PGSAS-45 questionnaire includes 23 items pertaining to post-operative symptoms (items 9–33), including 15 items from the GSRS and 8 newly selected items. In addition, 12 questionnaire items pertaining to dietary intake, work, and level of satisfaction with daily life were included (Table 1). The dietary intake items included five questions regarding the amount of food ingested (items 34–37, 41) and three regarding the quality of ingestion (items 38–40). One questionnaire item pertained to work (item 41), while three items addressed the level of satisfaction with daily life (items 43–45). A 7-point (1–7) Likert scale was used for the 23 symptom items, and a 5-point (1–5) Likert scale was used for all other items except for items 1, 4, 29, 32, and 34–37. For items 1–8, 34, 35, and 38–40, higher scores indicated a better condition. For items 9–28, 30, 31, 33, 36, 37, and 41–45, higher scores indicated a worse condition. The score for each subscale (SS) was calculated as the mean of the scores for the items comprising the SS, and the mean scores for the main outcomes, including the seven symptom SSs, were also calculated. The details of the clinicopathological findings and surgical procedures were collected from each institution, and the QOL scores were compared.

The statistical analyses were performed using the JMP 12.0.1 software program (SAS Institute, Cary, NC, USA). The main outcome measures were compared using *t*-tests between two groups. Multigroup comparisons were conducted using an analysis of variance (ANOVA) and the Tukey's test. All the statistical tests were two-sided, and statistical significance was set at  $p < 0.05$ . In the cases with  $p < 0.1$  for the difference between the two groups in the QOL assessment, Cohen's *d* was also calculated. The effect size based on Cohen's *d* was interpreted as follows:  $0.2 \leq d < 0.5$ , small;  $0.5 \leq d < 0.8$ , moderate;  $0.8 \leq d$ , large.

The present study was conducted in accordance with the principles embodied in the 1964 Declaration of Helsinki and its later amendments and was approved by the ethics committees of all participating institutions. Written informed consent was obtained from all enrolled patients. The PGSAS NEXT study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR; registration number: 000032221).

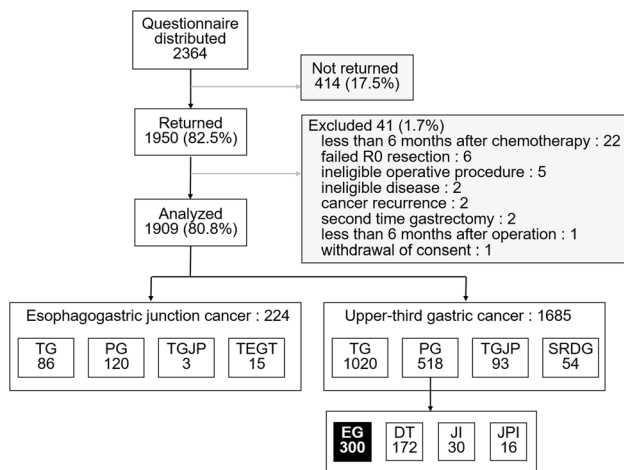
## Results

The study flow diagram is shown in Fig. 1. The PGSAS-45 questionnaire was distributed to 2364 patients, and responses were returned by 1950 patients. Of the 518 patients who underwent PG, data from 300 patients who also underwent an esophagogastrostomy were analyzed. The patient characteristics, tumor-related factors, and surgical finding are shown in Table 2. The pathological stage

**Table 1** Structure of the PGSAS-45

	Items		Subscales (SS)				
SF-8	1	Physical functioning*	Five or six-point Likert scale	Physical component summary* (items 1–8) Mental component summary* (items 1–8)			
	2	Role physical*					
	3	Bodily pain*					
	4	General health*					
	5	Vitality*					
	6	Social functioning*					
	7	Role emotional*					
	8	Mental health*					
GSRS	9	Abdominal pains	Seven-point Likert scale except for items 29 and 32	Esophageal reflux SS (items 10, 11, 13, 24) Abdominal pain SS (items 9, 12, 28) Meal-related distress SS (items 25–27) Indigestion SS (items 14–17) Diarrhea SS (items 19, 20, 22) Constipation SS (items 18, 21, 23) Dumping SS (items 30, 31, 33) Total symptom scale (above seven subscales)			
	10	Heartburn					
	11	Acid regurgitation					
	12	Sucking sensations in the epigastrium					
	13	Nausea and vomiting					
	14	Borborygmus					
	15	Abdominal distension					
	16	Eructation					
	17	Increased flatus					
	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					
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					
Meals (quality)	38	Appetite*	Five-point Likert scale	Quality of ingestion SS* (items 38–40)			
	39	Hunger feeling*					
	40	Satiety feeling*					
Meals (amount) 2	41	Necessity for additional meals		–			
Work	42	Ability for working		–			
Dissatisfaction	43	Dissatisfaction with symptoms		Dissatisfaction for daily life SS (items 43–45)			
	44	Dissatisfaction with meals					
	45	Dissatisfaction while working					

In items or subscales with \*, a higher score indicates a better condition; in items or subscales without \*, a higher score indicates a worse condition



**Fig. 1** Study flow diagram. *TG* total gastrectomy, *PG* proximal gastrectomy, *TGJP* total gastrectomy with jejunal pouch reconstruction, *TEGT* thoracic esophagectomy with gastric-tube reconstruction, *SRDG* small remnant distal gastrectomy

was Stage I, II, III, and IV in 282 (94.0%), 9 (3.0%), 7 (2.3%), and 1 (0.3%) patient, respectively. The esophagus was partially resected in half of the patients. A laparoscopic approach was used in 204 (68.0%) patients. An anti-reflux procedure was performed in 267 (93.0%) patients.

The main outcome measures of the QOL evaluation stratified according to the presence or absence of an anti-reflux procedure are shown in Table 3. On comparing the mean score of 19 main outcomes measures, the esophageal reflux SS (1.9 vs. 2.6,  $p=0.002$ , Cohen's  $d: 0.73$ ), abdominal pain SS (1.7 vs. 2.2,  $p=0.007$ , Cohen's  $d: 0.63$ ), and constipation SS (2.5 vs. 3.1,  $p=0.026$ , Cohen's  $d: 0.52$ ) were significantly better in the patients who received an anti-reflux procedure than in those who did not. The Cohen's  $d$ -value for the esophageal reflux SS was above 0.7, indicating that anti-reflux measures dramatically improved the symptoms of esophageal reflux disease. Among other surgical factors examined in the present study, the size of the remnant stomach (Supplemental Table S1) and pyloric drainage (Supplemental Table S2) significantly affected several main outcome measures. However, neither of these factors affected the esophageal reflux SS.

The most commonly used anti-reflux procedure was the double-flap technique ( $N=153$ ), followed by pseudo-fornix and/or His angle formation ( $N=67$ ) and fundoplication ( $N=44$ ). Postoperative symptoms for these three groups are compared in Table 4. No marked differences in the mean values of the esophageal reflux SS were seen. However, a significant difference in the indigestion SS was observed, with better scores observed for patients who had undergone pseudo-fornix and/or His angle formation. Significant differences in the size of the remnant stomach and the frequency

of pyloric drainage (Table 5) were also seen among the three anti-reflux procedure groups.

## Discussion

Although an esophagogastrectomy is the principal type of reconstruction after PG, reflux symptoms are common, limiting the clinical benefits of PG compared with total gastrectomy [12, 13]. To improve postoperative reflux symptoms, the formation of a mucosal flap has been attempted [20–23]; however, the complexity of this procedure has prevented it from becoming widely adopted. Reconstruction with jejunal interposition is another method of reducing the risk of reflux symptoms; however, this technique can cause dysphagia or hinder food intake because of the stagnation of food in the interposed jejunal segment [24–26]. A decade ago, many surgeons hesitated to perform PG as a standard surgical procedure. Recently, however, reflux prevention procedures have been improved, and the use of PG has been increasing. The practical utility of the double-flap method as a relatively simple mucosal flap has been reported [14, 15], making it the most effective technique for valve formation presently available. However, the hand-sewn esophagogastrectomy procedure poses some difficulty. In addition, flap valve formation by wrapping the posterior esophageal circumference  $\geq 180^\circ$  with the anterior gastric wall of the remnant stomach [16, 17, 26] has been reported. With these methods, esophagogastrectomy can be performed using mechanical devices that are technically simple to operate and easier to use under a laparoscopic approach than hand sewn anastomosis.

The present study was designed as nationwide survey, and the results showed that the double-flap method is the most widely used of the procedures (55.4%). Both fundoplication and side overlap fundoplication were classified as mechanical anastomosis with wrapping and were performed in 15.9% and 4.0% of patients, respectively. Pseudo-fornix and/or His angle formation, which is regarded as a classical method, was performed in 24.3% of cases.

The PGSAS NEXT study evaluated the long-term postoperative symptoms using the PGSAS-45 in patients who underwent curative gastrectomy for PGC. The criterion of at least 6 months since surgery was selected based on previous studies reporting that the postoperative QOL returned to preoperative baseline levels and stabilized within 6 to 12 months after gastrectomy [27–29]. According to data from a previous PGSAS study [10] with a design similar to the present study, a QOL analysis of 115 patients who underwent esophagogastrectomy following PG showed a mean esophageal reflux SS score of 2.0 [30]. In another analysis, the mean scores for the reflux SS in 82 patients who underwent miscellaneous anti-reflux procedures and 29 patients

**Table 2** Patient characteristic, tumor-related factors and surgical findings

Age, mean (SD)	(years)	70.8	(9.5)
BMI at baseline, mean (SD)	(kg/m <sup>2</sup> )	22.8	(3.0)
Sex, <i>n</i> (%)	Male	237	(79.0)
	Female	63	(21.0)
Tumor location, <i>n</i> (%)	UE	6	(2.0)
	U	284	(94.6)
	UM	8	(2.7)
	MU	2	(0.7)
Tumor stage, <i>n</i> (%)	I	282	(94.0)
	IIA/IIB	9	(3.0)
	III	7	(2.3)
	IVA/IVB	1	(0.3)
Surgical approach, <i>n</i> (%)	Open method	96	(32.0)
	Laparoscopic	204	(68.0)
Lymph node dissection, <i>n</i> (%)	D0-1	28	(9.3)
	D1 +	265	(88.3)
	D2	6	(2.0)
Resection of esophagus, <i>n</i> (%)	None	149	(49.7)
	Abdominal esophagus	144	(48.0)
	Lower thoracic esophagus	5	(1.7)
Preservation of abdominal branch of vagus nerve, <i>n</i> (%)	+	77	(25.7)
	–	216	(72.0)
Size of remnant stomach, <i>n</i> (%)	3/4 or more	57	(19.0)
	2/3	165	(55.0)
	1/2	73	(24.3)
Anti-reflux procedure, <i>n</i> (%)	None	21	(7.0)
	Double-flap technique	153	(51.0)
	Pseudo-fornix and/or His angle formation	67	(22.3)
	Fundoplication	44	(14.7)
	Side overlap with fundoplication by Yamashita	11	(3.7)
	Others	1	(0.3)
Pyloric drainage, <i>n</i> (%)	None	249	(83.0)
	Pyloric bougie	42	(14.0)
	Pyloroplasty	2	(0.7)
Period from surgery to QOL evaluation, mean (SD)	(months)	40.3	(33.8)
BMI at the time of QOL assessment, mean (SD)	(kg/m <sup>2</sup> )	20.2	(2.8)
Postoperative chemotherapy	–	278	(92.7)
	+	22	(7.3)

*SD* standard deviation, *QOL* quality of life

who underwent esophagogastrectomy without any additional anti-reflux procedure were 1.9 and 2.3, respectively [31]. However, a comparison of postoperative symptoms between PG and total gastrectomy in the literature reported the superiority of PG for maintaining food regulation, whereas the reflux symptoms were comparable [11, 32].

The characteristics and surgical findings of the present study participants showed several time-series differences from the previous study. For example, the mean age of the subjects in the present study was older (70.8 vs. 64.1 years). While the previous PGSAS study was limited to patients  $\leq 75$  years old, 34.1% of the participants in the present study were  $\geq 75$  years old (data not shown). In addition, the proportions of patients who received laparoscopic

surgery (68.0% vs. 14.8%) and an anti-reflux procedure (93.0% vs. 73.9%) were both higher in the present study than in the previous one [31]. Since these differences can be attributed to the recent trends in treating gastric cancer in Japan, the results of the present study might be more relevant to actual clinical practice than those of the previous study. The present findings showed that the use of an anti-reflux procedure significantly improved postoperative symptoms significantly, as shown by the esophageal reflux SS, abdominal pain SS, constipation SS and total symptom score. The beneficial effect on the esophageal reflux SS was consistent with the effect seen in the previous analysis.

In addition to esophagogastric reflux, the size of the remnant stomach has a strong impact on the postoperative QOL

**Table 3** Effect of anti-reflux procedures on postoperative QOL

Main outcomes measures	Present ( <i>n</i> = 276)		Absent ( <i>n</i> = 21)		<i>t</i> -test	Cohen's <i>d</i>
	Mean	SD	Mean	SD	<i>p</i> value	
Esophageal reflux SS	1.9	1.0	2.6	1.1	0.002	0.73
Abdominal pain SS	1.7	0.8	2.2	1.2	0.007	0.63
Meal-related distress SS	2.6	1.1	3.0	1.2	0.127	–
Indigestion SS	2.1	0.9	2.2	0.9	0.832	–
Diarrhea SS	2.3	1.3	2.4	1.3	0.794	–
Constipation SS	2.5	1.3	3.1	1.3	0.026	0.52
Dumping SS	2.1	1.2	2.4	1.5	0.454	–
Total symptom score	2.2	0.8	2.5	1.0	0.090	0.41
BW loss%*	–11.5%	8.3%	–9.6%	9.0%	0.317	–
Ingested amount of food per meal*	6.3	1.8	5.7	1.6	0.176	–
Necessity for additional meals	2.2	0.9	2.6	1.1	0.066	0.42
Quality of ingestion SS*	3.6	1.0	3.7	1.0	0.891	–
Ability for working	2.1	1.0	2.0	0.8	0.746	–
Dissatisfaction with symptoms	2.0	1.0	2.3	1.1	0.195	–
Dissatisfaction with meals	2.6	1.2	2.8	1.3	0.364	–
Dissatisfaction while working	1.9	1.0	1.9	1.0	0.788	–
Dissatisfaction with daily life SS	2.2	0.9	2.3	1.0	0.444	–
Physical component summary*	48.8	6.4	49.8	5.9	0.509	–
Mental component summary*	49.7	6.1	48.5	5.8	0.402	–
Esophageal reflux SS	1.9	1.0	2.6	1.1	0.002	0.73

In items or subscales with \*, a higher score indicates a better condition; in items or subscales without \*, a higher score indicates a worse condition

after PG with esophagogastrostomy. Several main outcomes of the QOL assessment in patients with a remnant stomach of 3/4 or larger were significantly better than those in patients with a remnant stomach of 2/3 or 1/2 (Supplement Table S1). The present study identified a clearer correlation between the postoperative QOL and the size of the remnant stomach than a previous study [31]. By preserving as much of the distal stomach as possible, gastric functions such as the storage capacity and gastric acid secretion can be maintained. Preservation of 3/4 or more of the remnant stomach is recommended to improve the postoperative QOL. However, no marked differences were detected between patients with a remnant stomach of 1/2 or 2/3. These results suggest that an acceptable postoperative QOL can be ensured if a remnant stomach of at least 1/2 can be preserved.

We also compared the postoperative reflux SS values of patients receiving each of the three major anti-reflux procedures. This is the first study to compare the beneficial effects of each procedure using a QOL assessment tool. The result showed no marked differences in the esophageal reflux SS scores according to the type of anti-reflux method. Although the size of the remnant stomach and frequency of pyloric drainage differed significantly among the three anti-reflux procedures (Table 5), which significantly influenced the QOL analysis, none of these factors affected the esophageal reflux SS (Supplement Tables S1 and S2) a

finding consistent with the results of a previous study [31]. These factors therefore likely did not affect the comparison of the esophageal reflux SS among the anti-reflux procedures. However, the significant differences in the indigestion SS among the procedures might have been influenced by other surgical factors. The esophageal reflux SS in patients receiving each of the anti-reflux procedures was uniformly superior to that of patients who did not receive a reflux prevention procedure. Therefore, these findings suggest that an anti-reflux procedure should be selected based on the surgeon's experience and competence. Each of these procedures is undergoing constant improvements. Therefore, when determining the optimal procedure in the future, postoperative safety and the technical simplicity of the procedure will likely be as important as the anti-reflux effect.

Unexpectedly, the addition of anti-reflux measures did not improve the weight loss, even though positive effects on the postoperative QOL were obtained. In the present study, the median weight loss in patients who underwent an anti-reflux procedure was 11.5% (Table 3), which was comparable to previously reported values of 7.4–12.5% [16, 26, 33–35]. A previous study showed that meal-related distress was the only symptom associated with weight loss, and other symptoms, such as esophageal reflux and dumping, were not [36]. Therefore, the relief of esophageal reflux symptoms through anti-reflux procedures may have little effect on improving

**Table 4** A comparison of the effect of three major anti-reflux procedures on the postoperative QOL

Main outcomes measures	A: double-flap (n = 153)		B: pseudo-formix and/ or His angle (n = 67)		C: fundoplication (n = 44)		ANOVA p value	Tukey's s-test		Cohen's d	Cohen's d	Cohen's d				
	Mean	SD	Mean	SD	Mean	SD		A vs B					B vs C		A vs C	
								p value	Cohen's d				p value	Cohen's d	p value	Cohen's d
Esophageal reflux SS	1.8	0.9	1.9	1.1	2.1	1.3	0.217									
Abdominal pain SS	1.7	0.8	1.6	0.8	1.8	1.0	0.191									
Meal-related distress SS	2.6	1.1	2.4	1.0	2.8	1.4	0.115									
Indigestion SS	2.3	0.9	1.9	0.8	2.2	1.0	0.024	0.018	0.41							
Diarrhea SS	2.4	1.3	2.1	1.3	2.3	1.4	0.346									
Constipation SS	2.5	1.2	2.4	1.3	2.5	1.5	0.910									
Dumping SS	2.3	1.3	1.9	1.1	2.1	1.3	0.091	0.075	0.34							
Total symptom score	2.3	0.8	2.0	0.8	2.3	1.1	0.105									
BW loss%*	- 11.0%	7.7%	- 12.2%	10.7%	- 12.0%	7.0%	0.583									
Ingested amount of food per meal*	6.3	1.8	6.4	1.8	5.9	1.6	0.353									
Necessity for additional meals	2.2	0.9	2.1	0.8	2.2	1.0	0.656									
Quality of ingestion SS*	3.7	0.9	3.7	1.0	3.4	1.1	0.238									
Ability for working	2.0	0.9	2.2	1.2	2.2	1.1	0.407									
Dissatisfaction with symptoms	2.1	1.0	1.8	1.0	2.2	1.1	0.064	0.070	0.33							
Dissatisfaction with meals	2.6	1.2	2.4	1.1	2.7	1.2	0.261									
Dissatisfaction while working	1.9	1.0	1.8	1.1	2.2	1.2	0.261									
Dissatisfaction with daily life SS	2.2	0.9	2.0	0.9	2.3	1.1	0.150									
Physical component summary*	49.5	5.5	48.9	7.3	46.8	7.7	0.057				0.044	0.44				
Mental component summary*	49.6	5.3	50.6	6.0	47.8	8.2	0.063			0.050	0.4					

In items or subscales with \*, a higher score indicates a better condition; in items or subscales without \*, a higher score indicates a worse condition  
 QOL quality of life, ANOVA analysis of deviation, SD standard deviation, SS subscale

**Table 5** The comparison of surgical finding among three major anti-reflux procedures

Surgical findings	Anti-reflux procedures		Double-flap ( <i>n</i> = 153)		Pseudo-fornix and/or His angle ( <i>n</i> = 67)		Fundoplication ( <i>n</i> = 44)		Fisher's exact test <i>p</i> value
	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	
Size of remnant stomach									
1/2	37	(24.2)	13	(19.4)	13	(29.5)	0.002		
2/3	93	(60.8)	32	(47.8)	22	(50.0)			
3/4	14	(9.2)	21	(31.3)	8	(18.2)			
Pyloric drainage									
–	142	(92.8)	27	(40.3)	43	(97.7)	<0.001		
+	3	(2.0)	39	(58.2)	0	(0.0)			

weight loss. Since body weight after surgery tended to be better in patients with a larger remnant stomach than in those with a smaller remnant (Supplement Table S1), weight loss might be affected by the size of the remnant stomach.

Previous reports of the PGSAS NEXT study revealed that both a double-tract procedure and esophagogastrectomy were widely selected for reconstruction after PG [37, 38], especially when the remnant stomach was small. Regarding postoperative symptoms and nutritional status, esophagogastrectomy with an anti-reflux procedure was reportedly equivalent to double-tract [39, 40]. The present study showed that the postoperative QOL in patients with esophagogastrectomy resulting in a remnant stomach size of 1/2 was comparable to that of patients with a remnant stomach size of 2/3 (Supplement Table S1). These results indicate that the QOL after esophagogastrectomy or a double-tract procedure does not differ considerably, regardless of the size of the remnant stomach. Further large-scale research is required to compare the functional outcomes of esophagogastrectomy and a double-tract procedure after proximal gastrectomy.

The present study had several limitations. First, this study was designed as an observational study, so the surgical procedure was not determined prospectively. Further comparative studies will be required to optimize the anti-reflux procedure. Second, the operational details of the anti-reflux procedure were not strictly defined, although they were classified into three major types. Bias in the surgeons' skill levels was also inevitable. Third, esophageal reflux disease was evaluated only via a questionnaire. The results of endoscopic findings during the postoperative course were not collected. Tests of the gastrointestinal function, such as esophageal pressure measurements and 24-h pH impedance monitoring, were also not performed in this study. Therefore, objective evidence supporting esophageal reflux disease was lacking. Nevertheless, the results of the present study suggest that the use of any anti-reflux procedure is clearly useful, so we expect further progress in the development of anti-reflux procedures during esophagogastrectomy, which may help clarify the optimal procedure in the future.

## Conclusion

The inclusion of an anti-reflux procedure during esophagogastrectomy after PG significantly improved postoperative esophageal reflux symptoms, regardless of the type of anti-reflux procedure.

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## Declarations

**Conflict of interest** The authors have no conflicts of interests to declare.

**Ethical approval** All procedures were in accordance with the ethical standards of the responsible committees on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. The study was conducted with the approval of the Institutional Review Boards of all the participating institutions.

**Sex-inclusive reporting** The subjects' sex was not considered as a biologic variable in this work.

## References

1. Maruyama K, Katai H. Surgical treatment of gastric cancer in Japan, trend from standardization to individualization. *Chirurgia (Bucur)*. 2014;109:722–30.
2. Katai H, Ishikawa T, Akazawa K, Isobe Y, Miyashiro I, Oda I, et al. Five-year survival analysis of surgically resected gastric cancer cases in Japan: a retrospective analysis of more than 100,000 patients from the nationwide registry of the Japanese gastric cancer association (2001–2007). *Gastric Cancer*. 2018;21:144–54.
3. Ahn HS, Lee HJ, Yoo MW, Jeong SH, Park DJ, Kim HH, et al. Changes in clinicopathological features and survival after



- gastrectomy for gastric cancer over a 20-year period. *Br J Surg.* 2011;98:255–60.
4. Blaser MJ, Saito D. Trends in reported adenocarcinomas of the oesophagus and gastric cardia in Japan. *Eur J Gastroenterol Hepatol.* 2002;14:107–13.
  5. Honda M, Wong SL, Healy MA, Nakajima T, Watanabe M, Fukuma S, et al. Long-term trends in primary sites of gastric adenocarcinoma in Japan and the United States. *J Cancer.* 2017;8:1935–42.
  6. Jang JH, Beron RI, Ahn HS, Kong SH, Lee HJ, Kim WH, et al. Clinicopathological features of upper third gastric cancer during a 21-year period (single center analysis). *J Gastric Cancer.* 2010;10:212–8.
  7. Zhou Y, Zhang Z, Wu J, Ren D, Yan X, Wang Q, et al. A rising trend of gastric cardia cancer in Gansu Province of China. *Cancer Lett.* 2008;269:18–25.
  8. Bolton JS, Conway WC 2nd. Postgastrectomy syndromes. *Surg Clin North Am.* 2011;91:1105–22.
  9. Carvajal SH, Mulvihill SJ. Postgastrectomy syndromes: dumping and diarrhea. *Gastroenterol Clin North Am.* 1994;23:261–79.
  10. Nakada K, Ikeda M, Takahashi M, Kinami S, Yoshida M, Ueno-sono Y, et al. Characteristics and clinical relevance of postgastrectomy syndrome assessment scale (PGSAS)-45: newly developed integrated questionnaires for assessment of living status and quality of life in postgastrectomy patients. *Gastric Cancer.* 2015;18:147–58.
  11. Takiguchi N, Takahashi M, Ikeda M, Inagawa S, Ueda S, Nobuoka T, et al. Long-term quality-of-life comparison of total gastrectomy and proximal gastrectomy by postgastrectomy syndrome assessment scale (PGSAS-45): a nationwide multi-institutional study. *Gastric Cancer.* 2015;18:407–16.
  12. An JY, Youn HG, Choi MG, Noh JH, Sohn TS, Kim S. The difficult choice between total and proximal gastrectomy in proximal early gastric cancer. *Am J Surg.* 2008;196:587–91.
  13. Ronellenfitsch U, Najmeh S, Andalib A, Perera RM, Rousseau MC, Mulder DS, et al. Functional outcomes and quality of life after proximal gastrectomy with esophagogastrostomy using a narrow gastric conduit. *Ann Surg Oncol.* 2015;22:772–9.
  14. Hayami M, Hiki N, Nunobe S, Mine S, Ohashi M, Kumagai K, et al. Clinical outcomes and evaluation of laparoscopic proximal gastrectomy with double-flap technique for early gastric cancer in the upper third of the stomach. *Ann Surg Oncol.* 2017;24:1635–42.
  15. Kuroda S, Nishizaki M, Kikuchi S, Noma K, Tanabe S, Kagawa S, et al. Double-flap technique as an antireflux procedure in esophagogastrostomy after proximal gastrectomy. *J Am Coll Surg.* 2016;223:e7–13.
  16. Yamashita Y, Yamamoto A, Tamamori Y, Yoshii M, Nishiguchi Y. Side overlap esophagogastrostomy to prevent reflux after proximal gastrectomy. *Gastric Cancer.* 2016;20:728–35.
  17. Aizawa M, Yabusaki H, Nakada K, Matsuki A, Bamba T, Nakagawa S. A retrospective review of a single-center experience with posterolateral fundoplication during esophagogastrostomy after proximal gastrectomy. *J Gastrointest Surg.* 2021;25(12):3230–3.
  18. Turner-Bowker DM, Bayliss MS, Ware JE Jr, Kosinski M. Usefulness of the SF-8 Health Survey for comparing the impact of migraine and other conditions. *Qual Life Res.* 2003;12:1003–12.
  19. Svedlund J, Sjodin I, Dotevall G. GSRS—a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. *Dig Dis Sci.* 1988;33:129–34.
  20. Seta K, Hatafuku T, Higuchi T, Watanabe M. A method of valvuloplastic esophagogastrostomy to prevent reflux after proximal gastrectomy. *World J Surg.* 1978;2:851–7.
  21. Tocornal JA, Snow HD, Fonkalsrud EW. A mucosal flap valve mechanism to prevent gastroesophageal reflux and esophagitis. *Surgery.* 1968;64:519–23.
  22. Redo SF, Barnes WA, Ortiz Della Sierra A. Esophagogastrostomy without reflux utilizing a submuscular tunnel in the stomach. *Ann Surg.* 1960;151:37–46.
  23. Watkins DH, Prevedel A, Harper FR. A method of preventing peptic esophagitis following esophagogastrostomy: experimental and clinical study. *J Thorac Surg.* 1954;28:367–79.
  24. Fukagawa T, Gotoda T, Oda I, Deguchi Y, Saka M, Morita S, et al. Stenosis of esophago-jejuno anastomosis after gastric surgery. *World J Surg.* 2010;34:1859–63.
  25. Tokunaga M, Ohyama S, Hiki N, Hoshino E, Nunobe S, Fukunaga T, et al. Endoscopic evaluation of reflux esophagitis after proximal gastrectomy: comparison between esophago-gastric anastomosis and jejunal interposition. *World J Surg.* 2008;32:1473–7.
  26. Nakamura M, Nakamori M, Ojima T, Katsuda M, Iida T, Hayata K, et al. Reconstruction after proximal gastrectomy for early gastric cancer in the upper third of the stomach: an analysis of our 13-year experience. *Surgery.* 2014;156:57–63.
  27. Kobayashi D, Kodera Y, Fujiwara M, Koike M, Nakayama G, Nakao A. Assessment of quality of life after gastrectomy using EORTC QLQ-C30 and STO22. *World J Surg.* 2011;35:357–64.
  28. Shan B, Shan L, Morris D, Golani S, Saxena A. Systematic review on quality of life outcomes after gastrectomy for gastric carcinoma. *J Gastrointest Oncol.* 2015;6:544–60.
  29. van den Boorn HG, Stroes CI, Zwinderman AH, Eshuis WJ, Hulshof M, van Etten-Jamaludin FS, et al. Health-related quality of life in curatively-treated patients with esophageal or gastric cancer: a systematic review and meta-analysis. *Crit Rev Oncol Hematol.* 2020;154: 103069.
  30. Yabusaki H, Kodera Y, Fukushima N, Hiki N, Kinami S, Yoshida M, et al. Comparison of postoperative quality of life among three different reconstruction methods after proximal gastrectomy: insights from the pgsas study. *World J Surg.* 2020;44(10):3433–40.
  31. Inada T, Yoshida M, Ikeda M, Yumiba T, Matsumoto H, Takagane A, et al. Evaluation of QOL after proximal gastrectomy using a newly developed assessment scale (PGSAS-45). *World J Surg.* 2014;38:3152–62.
  32. Ichikawa D, Komatsu S, Okamoto K, Shiozaki A, Fujiwara H, Otsuji E. Evaluation of symptoms related to reflux esophagitis in patients with esophagogastrostomy after proximal gastrectomy. *Langenbecks Arch Surg.* 2013;398:697–701.
  33. Omori T, Yamamoto K, Yanagimoto Y, Shinno N, Sugimura K, Takahashi H, et al. A novel valvuloplastic esophagogastrostomy technique for laparoscopic transhiatal lower esophagectomy and proximal gastrectomy for siewert type ii esophagogastric junction carcinoma—the tri double-flap hybrid method. *J Gastrointest Surg.* 2020;25(1):16–27.
  34. Hayami M, Hiki N, Nunobe S, Mine S, Ohashi M, Kumagai K, et al. Correction to: clinical outcomes and evaluation of laparoscopic proximal gastrectomy with double-flap technique for early gastric cancer in the upper third of the stomach. *Ann Surg Oncol.* 2018;25(Suppl 3):990.
  35. Sakuramoto S, Yamashita K, Kikuchi S, Futawatari N, Katada N, Moriya H, et al. Clinical experience of laparoscopy-assisted proximal gastrectomy with toupet-like partial fundoplication in early gastric cancer for preventing reflux esophagitis. *J Am Coll Surg.* 2009;209:344–51.
  36. Nakada K, Takahashi M, Ikeda M, Kinami S, Yoshida M, Ueno-sono Y, et al. Factors affecting the quality of life of patients after gastrectomy as assessed using the newly developed PGSAS-45 scale: a nationwide multi-institutional study. *World J Gastroenterol.* 2016;22:8978–90.
  37. Kunisaki C, Yoshida K, Yoshida M, Matsumoto S, Arigami T, Sugiyama Y, et al. Effects of proximal gastrectomy and various clinical factors on postoperative quality of life for upper-third gastric cancer assessed using the postgastrectomy syndrome

- assessment scale-45 (PGSAS-45): a PGSAS NEXT study. *Ann Surg Oncol.* 2022;29:3899–908.
38. Lee SW, Kaji M, Uenosono Y, Kano M, Shimizu H, Noguchi T et al. The evaluation of the postoperative quality of life in patients undergoing radical gastrectomy for esophagogastric junction cancer using the Postgastrectomy Syndrome Assessment Scale-45: a nationwide multi-institutional study. *Surg Today.* 2022;52:832–43.
39. Tominaga S, Ojima T, Nakamura M, Katsuda M, Hayata K, Kitadani J, et al. Esophagogastrostomy with fundoplication versus double-tract reconstruction after laparoscopic proximal gastrectomy for gastric cancer. *Surg Laparosc Endosc Percutan Tech.* 2021;31:594–8.
40. Eom BW, Park JY, Park KB, Yoon HM, Kwon OK, Ryu KW, et al. Comparison of nutrition and quality of life of esophagogastrostomy and the double-tract reconstruction after laparoscopic proximal gastrectomy. *Medicine (Baltimore).* 2021;100: e25453.

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