

Original Article



OPEN ACCESS

Received: Sep 21, 2022

Revised: Dec 16, 2022

Accepted: Dec 26, 2022

Published online: Feb 28, 2023

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Effect of Four Main Gastrectomy Procedures for Proximal Gastric Cancer on Patient Quality of Life: A Nationwide Multi-Institutional Study

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ABSTRACT


Purpose: This study aimed to examine the effects of 4 main types of gastrectomy for proximal gastric cancer on postoperative symptoms, living status, and quality of life (QOL) using the Postgastrectomy Syndrome Assessment Scale-45 (PGSAS-45).

Materials and Methods: We surveyed 1,685 patients with upper one-third gastric cancer who underwent total gastrectomy (TG; n=1,020), proximal gastrectomy (PG; n=518), TG with jejunal pouch reconstruction (TGJP; n=93), or small remnant distal gastrectomy (SRDG; n=54). The 19 main outcome measures (MOMs) of the PGSAS-45 were compared using the analysis of means (ANOM), and the general QOL score was calculated for each gastrectomy type.

Results: Patients who underwent TG experienced the lowest postoperative QOL. ANOM showed that 10 MOMs were worse in patients with TG. Four MOMs improved in patients with PG, while 1 worsened. One MOM was improved in patients with TGJP versus 8 MOMs in patients with SRDG. The general QOL scores were as follows: SRDG (+39 points), TGJP (+6 points), PG (+3 points), and TG (-1 point).

Conclusions: The TG group experienced the greatest decline in postoperative QOL. SRDG and PG, which preserve part of the stomach without compromising curability, and TGJP, which is used when TG is required, enhance the postoperative QOL of patients with proximal gastric cancer. When selecting the optimal gastrectomy method, it is essential to understand the characteristics of each and actively incorporate guidance to improve postoperative QOL.

Keywords: Gastrectomy; Postgastrectomy syndromes; Quality of life; Patient reported outcome measures; Gastric cancer

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Funding

This study was supported by a grant from Jikei University and the Japanese Gastric Cancer Association.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Conceptualization: N.K.; Data curation: O.A., N.K.; Formal analysis: O.A., N.K.; Funding acquisition: N.K.; Investigation: N.K., K.A., Y.K., F.N., M. K., A.K., F.Y., T.K., K.H., O.A., K.Y.; Methodology: N.K.; Project administration: N.K.; Resources: N.K., K.A., Y.K., F.N., M. K., A.K., F.Y., T.K., K.H., O.A., K.Y.; Supervision: N.K.; Validation: N.K.; Visualization: N.K.; Writing - original draft: N.K.; Writing - review & editing: N.K., K.A., Y.K., F.N., M.K., A.K., F.Y., T.K., K.H., O.A., K.Y.

INTRODUCTION

The incidence of proximal gastric cancer and gastroesophageal junction cancer is increasing due to the decline in *Helicobacter pylori* infections, widespread use of eradication therapy, and Westernization of diets [1-3]. Due to improved diagnostic and therapeutic techniques, most patients with gastric cancer can now be detected and treated early enough to guarantee a cure or long-term survival [4]. However, postgastrectomy complications that negatively impact patients' lives are common and constitute clinical problems [5-7]. In addition to surgery curability, emphasis should be placed on improving postoperative quality of life (QOL).

According to the Japanese clinical practice guidelines for gastric cancer, the standard surgical treatment for proximal gastric cancer is total gastrectomy (TG) [8]; however, since all gastric functions are lost during this procedure, severe postgastrectomy impairments persist [9]. Therefore, proximal gastrectomy (PG) [10-12] or small remnant distal gastrectomy (SRDG) [13-15], which preserve part of the stomach, is frequently performed. TG with jejunal pouch reconstruction (TGJP) remains an option if TG is unavoidable [16-19]. Several procedures are used to treat proximal stomach cancer; however, the procedure that can best reduce postgastrectomy sequelae and improve postoperative QOL is unknown.

Due to a lack of questionnaires that specifically evaluate postgastrectomy syndrome (PGS), it is difficult to assess how gastrectomy impacts a patient's life. The Postgastrectomy Syndrome Assessment Scale-45 (PGSAS-45) [20] is a new patient-reported outcome measure useful for evaluating patients' postoperative symptoms, living status, and QOL [21,22]. Therefore, we conducted a nationwide multicenter Postgastrectomy Syndrome Assessment Study NEXT (PGSAS NEXT) using the PGSAS-45 to compare the severity and characteristics of PGS among the 4 most common types of gastrectomy for proximal gastric cancer.

MATERIALS AND METHODS

Patients

In this cross-sectional observational study, the PGSAS-45 was administered to 2,364 patients at 70 participating hospitals between July 2018 and December 2019, and we retrieved the PGSAS-45 questionnaire from 1,950 (82.5%) patients. Of the 1,950 patients, 1,909 (80.8%) patients were included in the analysis, and 41 (1.7%) patients were excluded because they: received chemotherapy within the preceding 6 months (n=22), failed R0 resection (n=6), undergone an ineligible operative procedure (n=5), had an ineligible disease (n=2), had cancer recurrence (n=2), undergone a second gastrectomy (n=2), a period of less than 6 months after surgery (n=1), and withdrawal of consent (n=1). Of the 1,909 included patients, 1,685 patients who underwent gastrectomy for proximal gastric cancer were examined: 1,020 underwent TG, 518 underwent PG, 93 underwent TGJP, and 54 underwent SRDG, where the remnant proximal stomach size was equal to or less than one-fifth (**Fig. 1**). Reconstruction procedures were not regulated by the protocol; however, it depended on the institutional guidelines or the discretion of each surgeon.

Patient eligibility criteria

The patient inclusion criteria were as follows: 1) woman or man above 20 years; 2) pathologically confirmed upper one-third gastric cancer or esophagogastric junction cancer, defined as having its epicenter within 2 cm of the anatomical esophagogastric junction regardless of the histologic

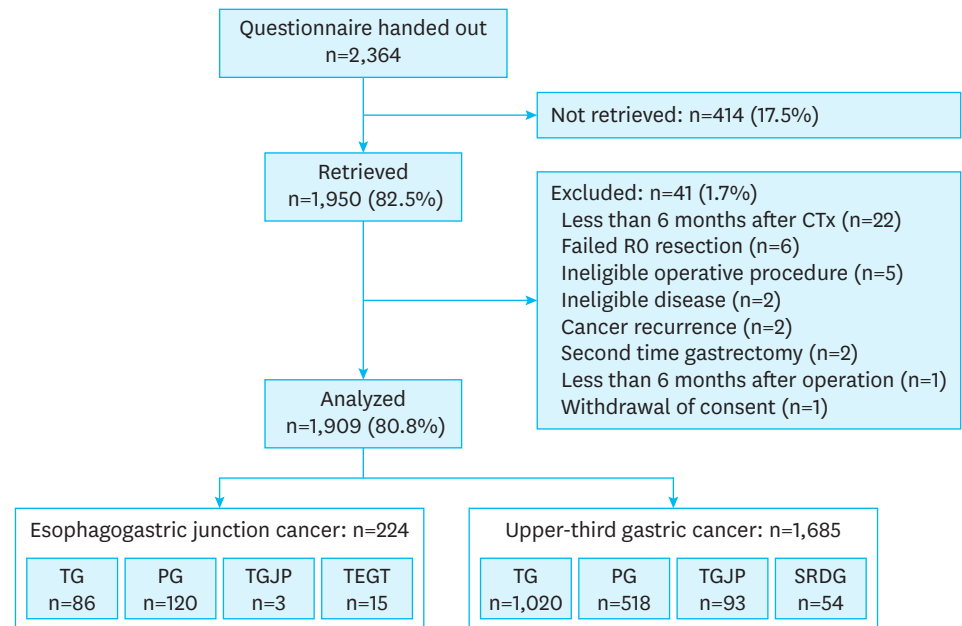


Fig. 1. Outline of the study.

CTx = chemotherapy; 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.

type; 3) R0 resection was achieved; 4) no recurrence or distant metastasis; 5) gastrectomy performed at least 6 months before registration; 6) adjuvant chemotherapy administered at least 6 months before the enrollment date; 7) first-time gastrectomy; 8) performance status of 0 or 1 on the Eastern Cooperative Oncology Group scale; 9) sufficient ability to understand and respond to the questionnaire; 10) no history of other diseases or surgical procedures that may influence the response to the questionnaire; 11) no organ failure or mental illness; 12) provision of written informed consent. Patients with dual malignancy or concomitant resection of other organs were excluded, except for patients undergoing resection of the perigastric organs to undergo radical gastrectomy or cholecystectomy.

QOL assessment

In this study, PGS was measured using the PGSAS-45 [20], a multidimensional QOL questionnaire based on the 8-Item Short-Form Health Survey (SF-8) [23] and the Gastrointestinal Symptom Rating Scale (GSRS) [24]. The PGSAS-45 questionnaire contains 45 questions, including 8 items from the SF-8, 15 from the GSRS, and 22 clinically important items selected by the Japan Postgastrectomy Syndrome Working Party (Table 1). The PGSAS-45 questionnaire includes 23 questions on postoperative symptoms (9–33), 15 questions from the GSRS and 8 newly selected questions. Additionally, 12 questions on diet, work, and life satisfaction were included. The dietary intake items included 5 questions regarding the amount of food consumed (34–37 and 41) and 3 questions about the quality of food consumed (38–40). One question relates to work (42), while 3 address life satisfaction (43–45). Factor analysis was used to reduce the 23 questions on postoperative symptoms into 7 symptom subscales (SSs), including esophageal reflux, abdominal pain, meal-related distress, indigestion, diarrhea, constipation, and dumping (20). Following consolidation and selection, 19 main outcome measures (MOMs) were refined through consolidation and selection and classified into 3 domains: symptoms, living status, and QOL (Table 2).

Except for questions 29 and 32 a seven-point Likert scale (1–7) was used for the 23 symptom questions, except for questions 29 and 32. Except for questions 34–37, a five- or six-point Likert scale was used for all items. For items 1–8, 34, 35, and 38–40, higher scores indicated better conditions, while for questions 9–28, 30, 31, 33, and 41–45, higher scores indicated worse conditions. Each SS score was calculated as the mean of the composed items, except for the physical component summary (PCS) and mental component summary (MCS) of SF-8, and the total symptom score was calculated as the mean of the 7 SSs. The details of PGSAS45 have been previously reported [20].

Table 1. Structure of PGSAS-45

Domains	#		SSs
SF-8	1	Physical functioning*	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	Emotional role*	
	8	Mental health*	
GSRS	9	Abdominal pains	Esophageal reflux SS (items 10, 11, 13, and 24) Abdominal pain SS (items 9, 12, and 28) Meal-related distress SS (items 25–27) Indigestion SS (items 14–17) Diarrhea SS (items 19, 20, and 22) Constipation SS (items 18, 21, and 23) Dumping SS (items 30, 31, and 33) Total symptom scale (above 7 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*	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
44		Dissatisfaction with meal	
45		Dissatisfaction with working	

PGSAS-45 = Postgastrectomy Syndrome Assessment Scale-45; SS = symptom subscale; GSRS = Gastrointestinal Symptom Rating Scale; SF-8 = 8-Item Short-Form Health Survey.

Items or subscales with *: higher score indicating better condition; Items or subscales without *: higher score indicating worse condition.

Table 2. Main outcomes measures of PGSAS-45

Domains	Subdomains	Main outcome measures
Symptoms	Subscales	7 symptom subscales Esophageal reflux (10, 11, 13, and 24), Abdominal pain (9, 12, and 28), Meal-related distress (25–27), Indigestion (14–17), Diarrhea (19, 20, and 22), Constipation (18, 21, and 23), Dumping (30, 31, and 33)
	Total	Total symptom score (above 7 subscales)
Living status	Body weight	Change in body weight (%)*
	Meals (amount)	Ingested amount of food per meal* (34) Necessity for additional meals (41)
	Meals (quality)	Quality of ingestion subscale* (38–40)
	Work	Ability for working (42)
QOL	Dissatisfaction	Dissatisfaction with symptoms (43), at the meal (44), at working (45) Dissatisfaction for daily life subscale (43–45)
	SF-8	Physical component summary* (1–8)
		Mental component summary* (1–8)

PGSAS-45 = Postgastrectomy Syndrome Assessment Scale-45; QOL = quality of life; SF-8 = 8-Item Short-Form Health Survey
Outcome measures with *: higher score indicates better condition; Outcome measures without *: higher score indicates worse condition.

General QOL score

The percentage of the MOM score of each surgical procedure divided by the overall mean score was calculated for 19 MOMs of the PGSAS-45. One point was added for every 5% deviation from the overall mean score if the change indicated an improvement and subtracted if the change indicated a deterioration. The total number of points on the 19 MOMs for each gastrectomy type was used to calculate the overall QOL score [9].

Study methods

This study used continuous sampling from a central registration system for participant enrollment. The questionnaire was distributed to all eligible patients. Patients were instructed to return the completed forms to the data center. All QOL data from the questionnaires were matched with patient-specific data collected using case report forms. The following are the methods for measuring the distance between the diaphragm and the esophagogastrointestinal anastomosis: A staple line on axial cross-sectional computed tomography (CT) images was used to confirm the anastomotic site. The diaphragm level was defined as the midpoint between the top slice where the esophageal hiatus of the diaphragm could be depicted and the bottom slice where it could not be confirmed on the CT image (D, 0 mm). The distance between the diaphragm and esophago-gastrointestinal anastomosis was given a positive or negative value, depending on whether it was below or above the diaphragm. This study was registered in the University Hospital Medical Information Network Clinical Trials Registry (trial number 000032221). The study was conducted with the approval of the Institutional Review Boards of all the participating institutions. All procedures were in accordance with the ethical standards of the responsible committees on human experimentation (institutional and national), the Helsinki Declaration of 1964 and later versions. Written informed consent was obtained from all the enrolled patients.

Statistical analyses

Analysis of means (ANOM) and Fisher’s exact test, followed by residual analysis, were used to compare patients’ backgrounds and QOLs. $P < 0.05$ were considered statistically significant. JMP 12.0.1 software (SAS Institute Inc., Cary, NC, USA) was used to perform statistical analysis.

RESULTS

Patient characteristics

Table 3 shows the characteristics of the study participants. The mean age of the patients was 68.7 years, with PG patients being much older (69.8 years). The mean postoperative period was 50.3 months, with TGJP (69.8 months) and TG (52.9 months) being significantly longer and that of PG (42.9 months) being significantly shorter. The postoperative period after SRDG was the shortest at 38.8 months. However, it did not differ significantly between gastrectomy types. In this cohort, 74% were men, and 26% were women, with no sex differences in the procedures. The mean preoperative body mass index (BMI) was 23.1 kg/m², with no significant differences between the procedures. The mean postoperative BMI was 19.9 kg/m², with PG patients having a significantly higher BMI (20.1 kg/m²) and TG patients having a significantly lower BMI (19.7 kg/m²). Although the difference was not statistically significant, the SRDG group had the highest postoperative BMI of 20.4 kg/m².

Of these procedures, 49% were open, while 51% were laparoscopic. The rate of laparoscopic surgery was significantly higher in SRDG (85%) and PG (70%) and significantly lower in TG (40%). The celiac branch of the vagus nerve was preserved and resected in 8% and 92% of the cases, respectively. The celiac branch of the vagus nerve was preserved at a higher rate in PG (20%) and a lower rate in TGJP (1%) and TG (2%). The cancer sites were the upper third of the stomach extending into the esophagus (UE; 3%), upper third of the stomach (U; 70%), upper third of the stomach extending into the middle third (UM; 15%), and middle third of the stomach extending into the upper third (MU; 12%). With PG, the proportion at the U site was significantly higher than that at the other sites for PG, whereas the proportions at the UM and MU sites were significantly higher for TGJP and TG. The central thoracic region (1%), inferior thoracic region (25%), near the diaphragm (43%), and abdomen (31%) had the highest anastomosis of the esophagus and digestive tract (remnant stomach or jejunum). The proportion of anastomoses in the inferior thoracic region (Ti) was significantly higher in TG (30%) than in the other groups. However, the proportion in the abdomen was significantly higher in TGJP (49%) and PG (42%). The length of the esophageal resection was significantly longer in the TG group (7.4 mm) and significantly shorter in the PG group (5.4 mm). The distance from the anastomosis of the esophagus and distal digestive tract to the diaphragm was significantly higher with TG at 6.2 mm on the chest cavity (upper) side of the diaphragm, while it was significantly lower with PG on the abdominal cavity (lower) side of the diaphragm with PG (3.6 mm) and TGJP (3.9 mm).

Overall, the clinical stages (cStage) in patients were I (67%), IIA/IIB (15%), III (16%), and IVA/IVB (2%). There were significantly more cStage IIA/IIB and III patients with TG, cStage I patients with PG, and cStage IIA/IIB patients with TGJP. Patients who had undergone chemotherapy were 25% of all the patients (20% postoperative, 1% preoperative, 4% both). The chemotherapy rates were significantly higher in the TG group (35%); however, it was significantly lower in PG (6%). The extents of lymph node dissection were D0 (0.2%), D1 (3%), D1+ (55%), D2 (39%), and D2+ (2%). There were significantly more D2 with TG (57%), D1 (9%), D1+ (88%) with PG, and D2+ (4%) with TGJP. Other organ resection was performed in 23% of the patients, with TGJP (66%), TG (28%), PG (8%), and SRDG (2%).

QOL assessment

ANOM assessment

The results of the ANOM assessment were as follows.

Optimal Gastrectomy Procedures

Table 3. Patient characteristics

Characteristics	TG (n=1,020)	PG (n=518)	TGJP (n=93)	SRDG (n=54)	P-value	Overall
Age (yr)	68.3±10.4	69.8±9.5*	66.7±11.2	67.8±8.9	0.007 [‡]	68.7±10.2
Postoperative period (mon)	52.9±36.5*	42.9±34.5*	69.8±51.5*	38.8±23.6	<0.0001 [‡]	50.3±37.1
Sex					0.238 [§]	
Male	743 (72.8)	394 (76.0)	74 (79.6)	37 (68.5)		1,248 (74.1)
Female	277 (27.2)	124 (24.0)	19 (20.4)	17 (31.5)		437 (25.9)
Preoperative BMI (kg/m ²)	23.1±3.1	23.0±3.1	23.2±2.7	23.0±2.8	0.744 [‡]	23.1±3.1
Postoperative BMI (kg/m ²)	19.7±2.5*	20.1±2.7*	19.7±2.1	20.4±2.8	0.004 [‡]	19.9±2.6
Abdominal approach					<0.0001 [§]	
Open	611 (59.9) [†]	155 (29.9) [†]	44 (47.3)	8 (14.8) [†]		818 (48.5)
Laparoscopy	409 (40.1) [†]	363 (70.1) [†]	49 (52.7)	46 (85.2) [†]		867 (51.5)
Celiac branch of vagus					<0.0001 [§]	
Preserved	19 (1.9) [†]	102 (20.2) [†]	1 (1.1) [†]	4 (7.7)		126 (7.7)
Divided	974 (98.1)	402 (79.8) [†]	92 (98.9)	48 (92.3)		1,516 (92.3)
Tumor location (JGCA 14th)					<0.0001 [§]	
UE (Siewert type III)	33 (3.2)	15 (2.9)	2 (2.2)	0 (0.0)		50 (3.0)
U	609 (59.8) [†]	476 (91.9) [†]	47 (51.6) [†]	46 (88.5)		1,178 (70.1)
UM	203 (19.9) [†]	18 (3.5) [†]	22 (24.2) [†]	2 (3.8)		246 (14.6)
MU	173 (17.0) [†]	9 (1.7) [†]	20 (22.0) [†]	4 (7.7)		207 (12.3)
Extent of esophageal resection					0.017 [§]	
Lower thoracic	28 (2.8)	6 (1.2)	1 (1.1)	-		35 (2.2)
Abdominal	628 (61.9)	288 (55.8)	58 (62.4)	-		974 (60.0)
None	358 (35.3)	222 (43.0)	34 (36.6)	-		614 (37.8)
Level of esophago-GI anastomosis					<0.0001 [§]	
Tm	9 (0.9)	0 (0.0)	0 (0.0)	-		9 (0.6)
Ti	304 (30.5) [†]	79 (15.5) [†]	10 (10.8) [†]	-		393 (24.5)
D	444 (44.5)	214 (42.0)	37 (39.8)	-		695 (43.4)
A	241 (24.1) [†]	216 (42.4) [†]	46 (49.5) [†]	-		504 (31.5)
Length of esophageal resection (mm)	7.4±10.6*	5.4±7.4*	7.2±9.0	-	0.001 [‡]	6.8±9.7
Distance from diaphragm to anastomosis (mm)	-6.2±16.6*	3.6±16.3*	3.9±10.2*	-	<0.0001 [‡]	-2.6±16.8
cStage (JGCA 14th)					<0.0001 [§]	
A/ B	547 (53.8) [†]	488 (94.4) [†]	42 (45.7) [†]	43 (79.6)		1,120 (66.7)
A/ B	196 (19.3) [†]	19 (3.7) [†]	29 (31.5) [†]	8 (14.8)		252 (15.0)
A/ B	240 (23.6) [†]	9 (1.7) [†]	16 (17.4)	3 (5.6)		268 (16.0)
A/ B	33 (3.2)	1 (0.2) [†]	5 (5.4)	0 (0.0)		39 (2.3)
Chemotherapy					<0.0001 [§]	
None	662 (65.0) [†]	485 (93.6) [†]	61 (65.6)	47 (87.0)		1,255 (74.5)
Yes	357 (35.0) [†]	33 (6.4) [†]	32 (34.4)	7 (13.0)		429 (25.5)
Preoperative	20 (2.0) [†]	0 (0.0) [†]	1 (1.1)	0 (0.0)		21 (1.2)
Postoperative	271 (26.6) [†]	31 (6.0) [†]	26 (28.0)	7 (13.0)		335 (19.9)
Both	64 (6.3) [†]	2 (0.4) [†]	5 (5.4)	0 (0.0)		71 (4.2)
Extent of lymph node dissection					<0.0001 [§]	
D0	1 (0.1)	3 (0.6)	0 (0.0)	0 (0.0)		4 (0.2)
D1	10 (1.0) [†]	45 (8.7) [†]	3 (3.2)	0 (0.0)		58 (3.5)
D1+	403 (39.7) [†]	453 (87.8) [†]	41 (44.1)	34 (63.0)		931 (55.4)
D2	579 (57.0) [†]	15 (2.9) [†]	45 (48.4)	20 (37.0)		659 (39.2)
D2+	23 (2.3)	0 (0.0) [†]	4 (4.3) [†]	0 (0.0)		27 (1.6)
Combined resection					<0.0001 [§]	
None	736 (72.2)	477 (92.1) [†]	32 (34.4) [†]	53 (98.1)		1,298 (77.0)
Yes	284 (27.8) [†]	41 (7.9) [†]	61 (65.6) [†]	1 (1.9) [†]		387 (23.0)
Gallbladder	176 (17.3)	38 (7.3)	58 (62.4)	1 (1.9)		273 (16.2)
Spleen	144 (14.1)	2 (0.4)	25 (26.9)	0 (0.0)		171 (10.1)
Pancreas	16 (1.6)	1 (0.2)	7 (7.5)	0 (0.0)		24 (1.4)
Other	17 (1.7)	0 (0.0)	2 (2.2)	0 (0.0)		19 (1.1)

Values are presented as mean ± standard deviation or number (%).

TG = total gastrectomy; PG = proximal gastrectomy; TGJP = TG with jejunal pouch reconstruction; SRDG = small remnant distal gastrectomy; BMI = body mass index; JGCA = Japanese Gastric Cancer Association; UE = upper third of the stomach extending into the esophagus; U = upper third of the stomach; UM = upper third of the stomach extending into the middle third; MU = middle third of the stomach extending into the upper third; GI = gastrointestinal; Tm = middle thoracic; Ti = lower thoracic; D = diaphragm; A = abdomen; ANOM = analysis of mean; ANOVA = analysis of variance.

*P<0.05 ANOM, †P<0.05 residual analysis. ‡ANOVA, §Fisher's exact test.

Table 4. Comparison of main outcome measures of PGSAS-45 among 4 gastrectomy types for proximal gastric cancer using ANOM

Domain	Main outcome measures	TG (n=1,020)		PG (n=518)		TGJP (n=93)		SRDG (n=54)		ANOVA P-value	Overall	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	N
Symptoms	Esophageal reflux SS	2.1 [†]	1.0	2.0	1.0	1.9	0.9	1.5 [†]	0.6	0.000	2.0	2
	Abdominal pain SS	1.7	0.8	1.7	0.8	1.6	0.7	1.5	0.7	0.171	1.7	0
	Meal-related distress SS	2.6	1.1	2.6	1.1	2.4	0.9	2.1 [†]	0.9	0.003	2.6	1
	Indigestion SS	2.2	1.0	2.2	0.9	2.1	1.0	2.1	0.8	0.417	2.2	0
	Diarrhea SS	2.4	1.2	2.2	1.2	2.5	1.3	2.4	1.3	0.189	2.3	0
	Constipation SS	2.2	1.1	2.4 [†]	1.2	2.2	0.9	2.1	0.9	0.090	2.3	1
	Dumping SS	2.2 [†]	1.2	2.1	1.2	2.1	1.0	1.9	1.0	0.038	2.2	1
	Total symptom score	2.2	0.8	2.2	0.8	2.1	0.7	2.0	0.6	0.152	2.2	0
Living status	Change in BW*	-14.3% [†]	0.1	-12.0% [†]	0.1	-15.6%	0.1	-10.9%	0.1	<0.0001	-13.5%	2
	Ingested amount of food per meal*	6.1 [†]	1.9	6.2	1.8	6.5	2.0	7.6 [†]	1.6	<0.0001	6.2	2
	Need for additional meals	2.4 [†]	0.9	2.2 [†]	0.9	2.1 [†]	0.8	2.2	0.9	<0.0001	2.3	3
	Quality of ingestion SS*	3.6	1.0	3.6	1.0	3.6	1.0	3.8	1.0	0.631	3.6	0
	Ability for working	2.2 [†]	1.0	2.1 [†]	1.0	2.0	0.9	1.8 [†]	0.8	0.000	2.1	3
QOL	Dissatisfaction with symptoms	2.0	1.0	2.0	1.0	1.9	1.0	1.7	0.8	0.045	2.0	0
	Dissatisfaction with meal	2.7 [†]	1.2	2.6	1.1	2.5	1.1	2.1 [†]	1.0	0.001	2.6	2
	Dissatisfaction with working	2.1 [†]	1.1	1.9 [†]	1.0	1.9	1.1	1.6 [†]	0.8	<0.0001	2.0	3
	Dissatisfaction for daily life SS	2.3 [†]	1.0	2.2	0.9	2.1	0.9	1.8 [†]	0.7	0.000	2.2	2
	PCS of SF-8*	48.7 [†]	5.7	49.1	6.1	49.7	5.6	51.6 [†]	4.4	0.002	49.0	2
	MCS of SF-8*	49.4	6.2	49.7	5.9	49.0	5.6	51.1	4.7	0.151	49.5	0

PGSAS-45 = Postgastrectomy Syndrome Assessment Scale-45; ANOM, analysis of mean; TG = total gastrectomy; PG = proximal gastrectomy; TGJP = total gastrectomy with jejunal pouch reconstruction; SRDG = small remnant distal gastrectomy; ANOVA = analysis of variance; SD = standard deviation; N = mean number of gastrectomy type differs from overall mean; SS = symptom subscale; BW = body weight; QOL = quality of life; PCS = physical component summary; MCS = mental component summary; SF-8 = 8-Item Short-Form Health Survey.

Outcome measures with *: higher score indicates better condition; Outcome measures without *: higher score indicates worse condition.

[†]P<0.05 ANOM.

Symptoms

Among the postgastrectomy symptoms, TG had significantly more severe esophageal reflux SS scores and dumping SS scores than the overall mean, while PG had more severe constipation SS scores (P<0.05). However, the SRDG had significantly less severe esophageal reflux SS scores and meal-related distress SS scores than the overall mean (P<0.05) (Table 4).

Meal-related distress was the most severe symptom among the SSs. The esophageal reflux SS score had the largest impact (2 of 4 procedures) according to the number of procedures, with mean values that differed from the overall mean, the esophageal reflux SS score had the greatest impact (2 of 4 procedures) (Table 4).

Living status

The postgastrectomy living status score for all MOMs was significantly lower than the overall mean with TG, excluding the quality of ingestion SS, body weight (BW) loss, ingested amount of food per meal, need for additional meals, and ability to work (P<0.05). However, PG had significantly better outcomes for BW loss, the need for additional meals, and ability to work, TGJP for the need for additional meals, and SRDG for the ingested amount of food per meal and ability to work (P<0.05) (Table 4).

The living status MOMs with the greatest impact based on the number of procedures with mean values that differed from the overall mean, were the need for additional meals and the ability to work (3 of 4 procedures), followed by BW loss and amount ingested per meal (2 of 4 procedures) (Table 4).

QOL

In the TG, postgastrectomy QOL regarding dissatisfaction with the meal, job dissatisfaction, life dissatisfaction, and SF-8 PCS was significantly lower than the overall mean (P<0.05). However, QOL regarding Job dissatisfaction with PG and QOL regarding meal dissatisfaction, job dissatisfaction, life dissatisfaction, and SF-8 PCS with SRDG was significantly better (P<0.05) (Table 4).

After surgery, the most notable change among MOMs in the QOL domain was dissatisfaction with meals. Based on the number of procedures with mean values that differed from the overall mean, dissatisfaction at work (3 of 4 procedures) had the greatest impact on the QOL, followed by dissatisfaction with the meal, dissatisfaction with daily life, and SF-8 PCS (2 of 4 procedures) (Table 4).

General QOL score evaluation

According to the general QOL score, TG was -1 point lower due to BW loss (Table 5). PG was +2 points higher for BW loss and +1 point higher for job dissatisfaction (Table 5). The TGJP was +2 points higher for the need for additional meals and +1 point higher for esophageal reflux SS, meal-related distress SS, ability to work, dissatisfaction with symptoms, dissatisfaction with the meal, dissatisfaction with work, and dissatisfaction with daily life SS, while BW loss (-2 points) and diarrhea (-1 point) were lower (Table 5). The SRDG was +4 points higher for esophageal reflux SS, the amount ingested per meal, and dissatisfaction with work; +3 points higher for meal-related distress SS, BW loss, the ability to work, dissatisfaction with symptoms, dissatisfaction with the meal, and dissatisfaction with daily life SS; +2 points higher for abdominal pain SS, dumping SS, and total symptom score;

Table 5. Percentage and points against overall mean of the main outcome measures of PGSAS-45 among gastrectomy types for proximal gastric cancer

Domain	Main outcome measures	TG (n=1,020)			PG (n=518)			TGJP (n=93)			SRDG (n=54)			Overall Mean
		Mean	%†	Point‡	Mean	%†	Point‡	Mean	%†	Point‡	Mean	%†	Point‡	
Symptoms	Esophageal reflux SS	2.1	103		2.0	98		1.9	94	1	1.5	75	4	2.0
	Abdominal pain SS	1.7	100		1.7	102		1.6	96		1.5	89	2	1.7
	Meal-related distress SS	2.6	101		2.6	100		2.4	93	1	2.1	82	3	2.6
	Indigestion SS	2.2	101		2.2	98		2.1	96		2.1	97		2.2
	Diarrhea SS	2.4	101		2.2	96		2.5	106	-1	2.4	103		2.3
	Constipation SS	2.2	98		2.4	104		2.2	97		2.1	94	1	2.3
	Dumping SS	2.2	103		2.1	96		2.1	96		1.9	88	2	2.2
	Total symptom score	2.2	101		2.2	100		2.1	97		2	90	2	2.2
Living status	Change In BW*	-14.3%	106	-1	-12.0%	89	2	-15.6%	114	-2	-10.9%	81	3	-13.5%
	Ingested amount of food per meal*	6.1	98		6.2	100		6.5	104		7.6	122	4	6.2
	Need for additional meals	2.4	103		2.2	96		2.1	89	2	2.2	94	1	2.3
	Quality of ingestion SS*	3.6	100		3.6	100		3.6	100		3.8	105		3.6
	Ability to work	2.2	104		2.1	95		2.0	93	1	1.8	84	3	2.1
QOL	Dissatisfaction with symptoms	2.0	102		2.0	100		1.9	93	1	1.7	84	3	2.0
	Dissatisfaction with meal	2.7	102		2.6	98		2.5	93	1	2.1	80	3	2.6
	Dissatisfaction with working	2.1	104		1.9	95	1	1.9	94	1	1.6	78	4	2.0
	Dissatisfaction for daily life SS	2.3	103		2.2	98		2.1	93	1	1.8	81	3	2.2
	PCS of SF-8*	48.7	99		49.1	100		49.7	101		51.6	105	1	49.0
	MCS of SF-8*	49.4	100		49.7	100		49.0	99		51.1	103		49.5
General QOL score (total points)					-1		3		6		39			

PGSAS-45 = Postgastrectomy Syndrome Assessment Scale-45; SS = symptom subscale; BW = body weight; PCS = physical component summary; MCS = mental component summary; SF-8 = 8-Item Short-Form Health Survey; QOL = quality of life.; TG = total gastrectomy; PG = proximal gastrectomy; TGJP = total gastrectomy with jejunal pouch reconstruction; SRDG = small remnant distal gastrectomy

Outcome measures with *: higher score indicates better condition; Outcome measures without *: higher score indicates worse condition.

†Percentage (%) to the overall mean.

‡If the QOL is better than 5% versus overall mean, +1 point is given for every 5%. If the QOL is worse than 5% versus overall mean, -1 point was given for every 5%.

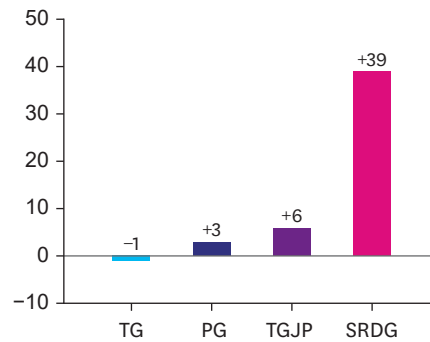


Fig. 2. General QOL scores after the 4 gastrectomy procedures for proximal gastric cancer. QOL = quality of life; TG = total gastrectomy; PG = proximal gastrectomy; TGJP = total gastrectomy with jejunal pouch reconstruction; SRDG = small remnant distal gastrectomy.

and +1 point higher for constipation SS, the necessity for additional meals, and SF-8 PCS (Table 5). Calculating the general QOL score from the total points of the 19 MOMs for each gastrectomy procedure revealed that the TG had the lowest score at -1 point, while the PG had the highest score at +3 points and TGJP, had the lowest score at +6 points. The SRDG had the highest score among the procedures, with +39 points (Table 5, Fig. 2).

DISCUSSION

The rate of proximal gastric and gastroesophageal junction cancers has increased in recent years [1-3]. TG is the standard surgical treatment for proximal gastric cancer [8]; however, this procedure can result in the loss of all stomach functions and cause the most severe postgastrectomy impairments, causing clinical problems [5-7,9]. Therefore, PG [10-12] and SRDG [13-15] can be performed to improve the QOL when curability is maintained. Furthermore, TGJP may be an option if TG cannot be avoided [16-19]. However, no study has simultaneously compared the extent to which these procedures improve postoperative QOL. In this study, we evaluated postoperative QOL using the PGSAS-45 in several cases enrolled in the PGSAS NEXT, a nationwide multicenter study, comparing the effects of the 4 main procedures for proximal gastric cancer on postoperative QOL. The findings revealed that SRDG significantly improved postoperative QOL. Furthermore, postoperative QOL with PG and TGJP was significantly higher than with TG.

It is important to identify and improve gastrectomy and reconstruction methods that lead to better postoperative QOL to improve patients' postgastrectomy QOL. To accomplish this, a questionnaire that can clearly and appropriately measure the effect of gastrectomy on a patient's daily life is required. Although many studies have compared different gastrectomy procedures using existing questionnaires, including a combination of the SF-36 and GSRS or the EORTC QLQ-C30 and STO-22 [18,25-27], evaluating their impact on postoperative QOL has been difficult due to lack of a questionnaire for assessing the effects of gastrectomy. The Japan Postgastrectomy Syndrome Working Party recently developed the PGSAS-45 as a new questionnaire to evaluate postgastrectomy QOL. The usefulness of this questionnaire has been previously reported [21,22]. Therefore, in the PGSAS NEXT study, we used the PGSAS-45 to compare the effects of the 4 main proximal gastric cancer procedures on patients' postoperative lives. Recently, the Korean Quality of Life in Stomach Cancer Patients Study Group (KOQUSS) developed the KOQUSS-40 QOL questionnaire for postgastrectomy patients [28]. It is hoped

that by disseminating these questionnaires for assessing postgastrectomy QOL, optimal surgical procedures will be identified and further improvements will be promoted.

According to the Japanese Clinical Practice Guidelines on Gastric Cancer, TG is the standard surgical treatment for proximal gastric cancer [8]. However, because this procedure leads to the loss of all stomach functions, it has the most severe impact on daily life [9]. Therefore, various other gastrectomy procedures can be used to ensure cure depending on the location and stage of the cancer.

Postoperative QOL in PG [10-12], SRDG [13-15], and TGJP [16-19] have been reported to be higher than in TG. Based on this study, the PGSAS NEXT study found that postoperative QOL was better with PG [29], SRDG [30], and TGJP [31] than with TG, even after adjusting for the effects of various confounders using multiple regression analysis, supporting a previous report. However, no study has simultaneously compared these procedures for proximal gastric cancer to determine the severity and characteristics of their impact on postoperative QOL. Understanding the extent to which these gastrectomy procedures affect patients' postoperative lives and their characteristics may help in the selection of the optimal procedure for gastric cancer based on its location and stage, considering not only curability but also postoperative QOL.

ANOM was used to analyze the effects of each procedure on postoperative QOL with 19 MOMs from the PGSAS-45. The findings revealed that, when compared to the overall mean, 10 MOMs performed significantly worse in the TG. Four MOMs performed significantly better with PG, while one performed significantly worse. One MOM was significantly better with TGJP, whereas 8 MOMs were significantly better with SRDG.

Furthermore, for each procedure, we examined the shift in each MOM from the overall mean for the better (positive points) or worse (negative points) to calculate a general QOL score for the 19 MOMs. The TG was worse in one MOM with a general QOL score of -1 PG was better in 2 MOMs with a general QOL score of +3, TGJP was better in 8 MOMs (+9); however, it was worse in 2 MOMs (-3) with a general QOL score of +6, and SRDG was better in 15 MOMs with a general QOL score of +39. Thus, comparing the 4 main procedures for proximal gastric cancer showed that patients who underwent SRDG had the best postoperative QOL compared with the other procedures. The results also showed that patients who underwent PG and TGJP had significantly better postoperative QOL than those who underwent TG.

In terms of the magnitude of the effect on the 19 MOMs of PGSAS-45 in cases of proximal gastric cancer, of the 7 SSs, the meal-related distress SS was the most affected, while dissatisfaction with daily life had the greatest impact on dissatisfaction with the meal. Therefore, procedures to make meals more enjoyable should be developed in the future.

Of the 19 MOMs of PGSAS-45, large differences between procedures were observed for the necessity for additional meals, the ability to work, and dissatisfaction at work (3 of 4 procedures) and for esophageal reflux SS, BW loss, the amount of food ingested per meal, dissatisfaction with the meal, dissatisfaction with daily life SS, and SF-8 PCS (2 of 4 procedures). It is important to understand and consider the characteristics of each procedure when choosing a surgical method and actively incorporate guidance to improve the amount of food ingested and physical activity.

This study had some limitations. First, this study was retrospective; hence, there was some bias in the location of cancer, as measured by distance from the esophagogastric junction, clinical backgrounds, and a number of cases for each procedure. Some of the indications for these gastrectomy procedures overlapped, while others are distinct. However, understanding how gastrectomy procedures affect patients' postoperative QOL can provide insights into the broader perspective of the gastrectomy burden. Nevertheless, this study significantly contributes to the existing literature, as other reports comparing gastrectomy procedures for proximal gastric cancer and the severity and characteristics of the corresponding PGS, are limited. Second, the reconstruction methods used for each gastrectomy method were not controlled and were left to the policy of the institution or the preferences of the surgeon, which created a selection bias. A prospective, randomized controlled trial with a large sample size should be conducted to eliminate these effects,

Postoperative QOL was the worst with TG among the 4 main procedures for proximal gastric cancer. The postoperative QOL of patients with proximal gastric cancer can be improved by selecting SRDG if a small remnant of the proximal stomach remains, PG if no proximal part of the stomach remains, or TGJP if TG cannot be avoided. These procedures should be improved to reduce postgastrectomy sequelae, and appropriate postoperative guidance and care should be provided based on an understanding of PGS characteristics associated with each procedure.

ACKNOWLEDGMENTS

The authors would like to thank all the physicians and patients who participated and cooperated with this study.

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