

Original Article



Impact of Tumor Location on the Quality of Life of Patients Undergoing Total or Proximal Gastrectomy

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ABSTRACT



Purpose: Most studies have investigated the differences in postgastrectomy quality of life (QOL) based on the surgical procedure or reconstruction method adopted; only a few studies have compared QOL based on tumor location. This large-scale study aims to investigate the differences in QOL between patients with esophagogastric junction cancer (EGJC) and those with upper third gastric cancer (UGC) undergoing the same gastrectomy procedure to evaluate the impact of tumor location on postoperative QOL.

Methods: The Postgastrectomy Syndrome Assessment Scale-45 (PGSAS-45) questionnaire was distributed in 70 institutions to 2,364 patients who underwent gastrectomy for EGJC or UGC. A total of 1,909 patients were eligible for the study, and 1,744 patients who underwent total gastrectomy (TG) or proximal gastrectomy (PG) were selected for the final analysis. These patients were divided into EGJC and UGC groups; thereafter, the PGSAS-45 main outcome measures (MOMs) were compared between the two groups for each type of gastrectomy.

Results: Among the post-TG patients, only one MOM was significantly better in the UGC group than in the EGJC group. Conversely, among the post-PG patients, postoperative QOL was significantly better in 6 out of 19 MOMs in the UGC group than in the EGJC group.

Conclusions: Tumor location had a minimal effect on the postoperative QOL of post-TG patients, whereas among post-PG patients, there were definite differences in postoperative QOL between the two groups. It seems reasonable to conservatively estimate the benefits of PG in patients with EGJC compared to those in patients with UGC.

Keywords: Esophagogastric Junction; Gastric cancer; Gastrectomy; Quality of life

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Conflict of Interest

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

Author Contributions

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INTRODUCTION

Despite the decreasing incidence of gastric cancer, the incidence rates of esophagogastric junction cancer (EGJC) and upper third gastric cancer (UGC) have been increasing in both Western and Asian countries [1-3]. The long-term outcomes for patients with these diseases have improved owing to early disease detection and advancements in surgical techniques; therefore, more attention is currently being paid to patient's quality of life (QOL) after they undergo gastrectomy [4]. Most patients with EGJC or UGC undergo total gastrectomy (TG) or proximal gastrectomy (PG) as curative treatment. Since TG and PG severely reduce postoperative QOL compared with other types of gastrectomies [5], patients with EGJC or UGC who undergo these procedures require special attention. Most researchers compare postoperative QOL based on the surgical procedures or reconstruction methods adopted while paying little attention to tumor location. Patients with EGJC generally undergo longer esophageal resection and more extensive mediastinal lymph node dissection than those with UGC. Trans-hiatal anastomosis is more frequent and surgical invasion tends to be greater in patients with EGJC than in those with UGC, even if the patients undergo the same gastrectomy procedure. These differences may have implications on the postoperative digestive function; however, the differences in postoperative QOL between patients with EGJC and UGC have not been extensively investigated. Therefore, we conducted the first large-scale comparison of postoperative QOL between patients suffering from the 2 diseases.

The Postgastrectomy Syndrome Assessment Scale (PGSAS)-45 is an integrated questionnaire developed by the Japan Postgastrectomy Syndrome Working Party, a volunteer group, to assess post-gastrectomy-specific clinical symptoms and QOL among patients [6]. Previous studies have shown that the PGSAS-45 is a valid and reliable questionnaire for the postoperative QOL assessment of patients who underwent a gastrectomy procedure and have identified several factors associated with postoperative QOL in these patients [6-8]. This study uses the PGSAS-45 to assess the postoperative QOL of patients with EGJC or UGC who underwent TG or PG and to clarify the impact of tumor location on postoperative QOL.

MATERIALS AND METHODS

Study protocols

This retrospective cross-sectional study used a continuous sampling method to enroll participants from a central registration system. The questionnaire was distributed to all the eligible patients, who were instructed to complete and return it to the data center by mail. All the QOL data collected from the questionnaires were matched with the individual patient data collected through case report forms. Patient data, including those on age, sex, height, body weight (BW), clinical stage, surgical approach, location of the cancer, administration of preoperative or postoperative chemotherapy, level of esophago-gastrointestinal anastomosis, distance between the diaphragm and esophago-gastrointestinal anastomosis, type of gastrectomy and reconstruction method, and other background information, were retrieved from the medical records. Data on patient race and ethnicity were not included in this study. The level of esophago-gastrointestinal anastomosis and the methods used for measuring the distance from the diaphragm to the esophago-gastrointestinal anastomosis were defined as follows. The anastomotic site was confirmed by the staple line on the axial cross-sectional computed tomography (CT) image. If there was no staple line (i.e., hand-sewn anastomosis), the anastomotic site was confirmed on the basis of morphological changes on the CT image.

The midpoint between the top slice where the esophageal hiatus of the diaphragm can be depicted and the bottom slice where it cannot be confirmed on the CT image was defined as the diaphragm level (D, 0 mm). Terminologies of the level of anastomosis were defined as follows: 1) the upper thoracic region (Tu); between the upper edge of the sternum and tracheal bifurcation: 2) the middle thoracic (Tm); the upper half between the tracheal bifurcation and diaphragm: 3) the lower thoracic region (Ti); the lower half between the tracheal bifurcation and diaphragm: 4) the abdomen (A); the abdominal cavity below the diaphragm (**Supplementary Fig. 1**). When the site was located below the diaphragm, the distance from the diaphragm reference point to the upper end of the site was measured. When the site was located above the diaphragm, the distance from the diaphragm reference point to the lower end of the site was measured. The distance between the diaphragm and esophago-gastrointestinal anastomosis was assigned a positive or negative value depending on whether the latter was located below or above the diaphragm, respectively.

This study was registered with the University Hospital Medical Information Network Clinical Trials Registry (registration number: 000032221) and approved by the ethics committees of each institution. Written informed consent was obtained from all the enrolled patients.

Seventy institutions participated in the study. Among the 2,364 patients who were provided with the questionnaire between July 2018 and December 2019, 1,950 (82.5%) responded, and 1,909 were eligible for the study. Among these, the data of 1,744 patients who underwent TG or PG were analyzed in this study (**Fig. 1**). These patients were divided into two cohorts according to their tumor location: EGJC and UGC.

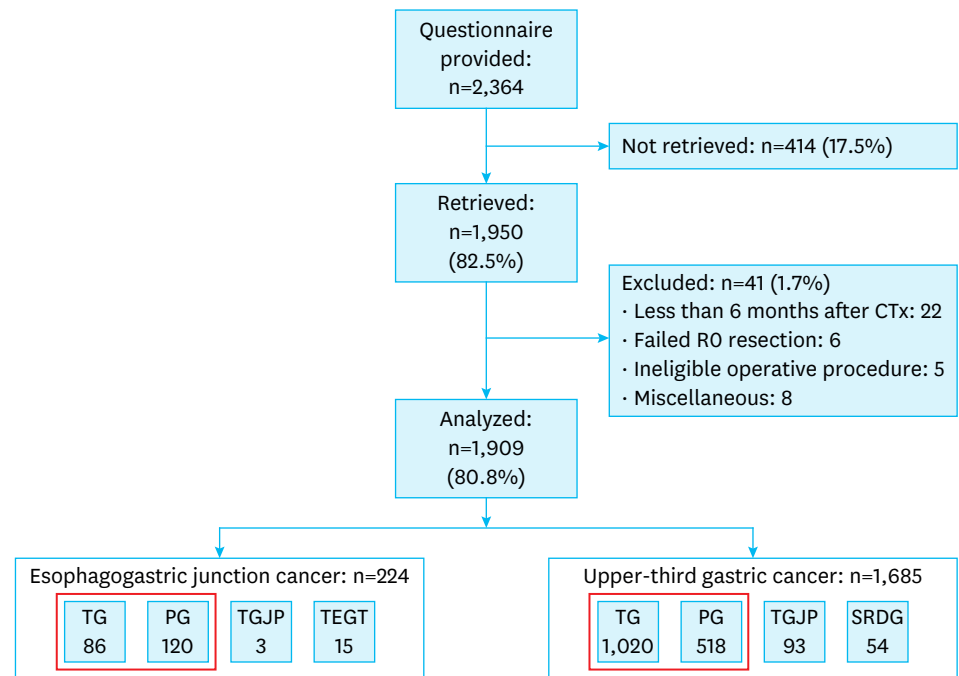


Fig. 1. Study outline. CTx = chemotherapy; TG = total gastrectomy; PG = proximal gastrectomy; TGJP = total gastrectomy with jejunal pouch reconstruction; TEGT = thoracic esophagectomy with gastric-tube reconstruction; SRDG = small remnant distal gastrectomy.

Patients

The eligibility criteria for patients were as follows: 1) cancer in the upper third of the stomach or around the esophagogastric junction (any stage or histologic type); 2) age ≥ 20 years of any sex; 3) R0 resection achieved; 4) no observed recurrence or metastasis; 5) underwent gastrectomy ≥ 6 months earlier; 6) underwent gastrectomy only once; 7) performance status 0 or 1 on the Eastern Cooperative Group Scale; 8) was able to understand the questionnaire; 9) free of any other disease or previous surgery that may influence the questionnaire results; 10) no organ failure or mental disease; and 11) spontaneous agreement to participate in the study. Patients who underwent prior chemotherapy treatments were included if more than six months had passed since the termination of their treatment. Patients with active dual malignancy or those undergoing other synchronous surgeries (except those equivalent to cholecystectomy or resection or the extraction of perigastric organs to accomplish gastrectomy or lymph node dissection) were excluded. Patients judged to be irrelevant for the analysis by the doctors conducting this study were also excluded.

QOL assessment

The PGSAS-45 questionnaire consists of 45 questions, including eight items from the Short Form-8 (SF-8) and 15 items from the Gastrointestinal Symptom Rating Scale (**Table 1**) [9-11]. The 19 main outcome measures (MOMs)—the esophageal reflux subscale (SS), abdominal pain SS, meal-related distress SS, indigestion SS, diarrhea SS, constipation SS, dumping SS, total symptoms score, change in BW, amount of food ingested per meal, necessity for additional meals, quality of ingestion SS, ability for working, dissatisfaction with symptoms, dissatisfaction at meals, dissatisfaction at working, dissatisfaction for daily life SS, and the SF-8 physical component summary (PCS) and mental component summary (MCS)—were refined through consolidation and selection and were classified into three domains: symptoms, living status, and QOL (**Table 2**).

Statistical analysis

The unpaired *t*-test and Fisher's exact test were used to compare patient characteristics and QOL between the dichotomous groups for each type of gastrectomy. Statistical significance was set at P-value of < 0.05 . In cases where P was < 0.1 , Cohen's *d*, a measure of effect size, was calculated based on the univariate analysis (interpretation of effect size: ≥ 0.2 , small; ≥ 0.5 , medium; and ≥ 0.8 , large). Patients with missing data were excluded from the analysis. All statistical analyses were performed using JMP 12.01 (SAS Institute Inc., Cary, NC, USA).

RESULTS

The characteristics of the post-TG patients are summarized in **Table 3**. The results show that the length of esophageal resection, proportion of males, frequency of open approaches, extent of esophageal resection, and level of esophago-gastrointestinal anastomosis are significantly higher; disease progression (clinical T and clinical N) is more advanced; and perioperative chemotherapy is significantly more common in the EGJC group than in the UGC group.

The characteristics of the post-PG patients are summarized in **Table 4**. The length of esophageal resection, proportion of males, ratio of division of the celiac branch of the vagus, extent of esophageal resection, and level of esophago-gastrointestinal anastomosis are significantly higher; disease progression (clinical T and clinical N) is significantly more

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Table 1. Structure of the PGSAS-45

Domains	Subdomains	Items	Scoring	Subscales						
QOL	SF-8	1 Physical functioning*	Five or six-point Likert scale	Physical component summary* (item 1-8) Mental component summary* (item 1-8)						
		2 Role physical*								
		3 Bodily pain*								
		4 General health*								
		5 Vitality*								
		6 Social functioning*								
		7 Role emotional*								
		8 Mental health*								
Symptoms	GSRs symptoms	9 Abdominal pains	Seven-point Likert scale (except items 29 and 32)	Esophageal reflux SS (items 10, 11, 13, 24) Abdominal pain SS (items 9, 12, 28) Meal-related distress SS (item 25-27) Indigestion SS (item 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								
		PGSAS original 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*	Five-point Likert scale			Quality of ingestion SS* (item 38-40)		
				35 Ingested amount of food per day*						
				36 Frequency of main meals						
			Meals (quality)	37 Frequency of additional meals						
				38 Appetite*						
			Meals (amount) 2	39 Hunger feeling*						
		40 Satiety feeling*								
	Work	41 Necessity for additional meals								
42 Ability for working										
QOL	Dissatisfaction	43 Dissatisfaction with symptoms		Dissatisfaction for daily life SS (item 43-45)						
		44 Dissatisfaction at the meal								
		45 Dissatisfaction at working								

Items or subscales with *: a higher score indicates a better condition. Items or subscales without *: a higher score indicates a worse condition. Each subscale score is calculated as the mean of composed item or subscale scores, except those for the physical component summary and mental component summary of SF-8. Items 29 and 32 do not have scores; these items were analyzed separately.

PGSAS-45 = Postgastrectomy Syndrome Assessment Scale-45; QOL = quality of life; SF-8: Short Form-8; GSRs = Gastrointestinal Symptom Rating Scale; SS = subscale.

advanced; combined resection and perioperative chemotherapy are significantly more common, and the postoperative period is significantly shorter in the EGJC group than in the UGC group.

Table 5 presents a comparison of MOMs between the 2 groups, considering post-TG patients. The quality of ingestion SS score is significantly better ($P=0.006$, Cohen's $d=0.33$) and

Table 2. PGSAS-45 domains and main outcomes measures

Domains	Main outcomes measures
Symptoms	
Subscales	Seven symptom subscales Esophageal reflux SS (items 10, 11, 13, 24), abdominal pain SS (items 9, 12, 28), meal-related distress SS (item 25-27), indigestion SS (item 14-17), diarrhea SS (items 19, 20, 22), constipation SS (items 18, 21, 23), dumping SS (items 30, 31, 33)
Total	Total symptom scale
Living status	
Body weight	Change in body weight (%)
Meals (amount)	Ingested amount of food per meal (item 34) Necessity for additional meals (item 41)
Meals (quality)	Quality of ingestion SS (items 38-40)
Work	Ability for working (item 42)
QOL	
Dissatisfaction	Dissatisfaction with symptoms (item 43), at the meal (item 44), at working (item 45) Dissatisfaction for daily life subscale SS (item 43-45)
SF-8	Physical component summary (item 1-5) Mental component summary (item 4-8)

PGSAS-45 = Postgastrectomy Syndrome Assessment Scale-45; QOL = quality of life, SF-8 = Short Form-8, SS = subscale.

constipation SS scores also tend to be better ($P=0.097$, Cohen's $d=0.17$) in the UGC group than in the EGJC group. There are no significant differences in other MOMs between the two groups.

Among the post-PG patients, several MOMs, including esophageal reflux SS score ($P=0.035$, Cohen's $d=0.22$), change in BW ($P=0.029$, Cohen's $d=0.23$), ingested amount of food per meal ($P=0.034$, Cohen's $d=0.22$), need for additional meals ($P=0.049$, Cohen's $d=0.20$), dissatisfaction with symptoms ($P=0.023$, Cohen's $d=0.23$), and SF-8 MCS ($P=0.034$, Cohen's $d=0.22$), are significantly better and dissatisfaction with daily life SS scores also tend to be better ($P=0.051$, Cohen's $d=0.20$) in the UGC group than in the EGJC group (**Table 6**).

To assess the reconstruction method-based differences among post-PG patients, we also evaluated the two groups based on the most common reconstruction methods used following PG, esophagogastrectomy, and double-tract reconstruction. The characteristics of patients who underwent PG with esophagogastrectomy (PGEG) or PG with double-tract reconstruction (PGDT) are shown in **Supplementary Tables 1 and 2**. Among both post-PGEG and post-PGDT patients, postoperative period is significantly shorter and the length of esophageal resection and level of esophago-gastrointestinal anastomosis and disease progression (clinical T) are significantly higher in the EGJC group than in the UGC group. In post-PGEG patients, the change in BW is significantly better ($P=0.035$, Cohen's $d=0.31$) and the esophageal reflux SS score is marginally better ($P=0.060$, Cohen's $d=0.28$) in the UGC group than in the EGJC group (**Supplementary Table 3**). In contrast, in post-PGDT patients, the constipation SS score is significantly better ($P=0.048$, Cohen's $d=0.33$) and SF-8 MCS is marginally better ($P=0.077$, Cohen's $d=0.29$) in the UGC group than in the EGJC group (**Supplementary Table 4**).

DISCUSSION

Several studies have evaluated post-gastrectomy QOL in patients with EGJC or UGC [12-16]. However, in most cases, the comparison is based on surgical procedures or reconstruction, and tumor locations in different cases where the same operative procedures were used have not been compared thoroughly. Comparison of the postoperative QOL of patients with EGJC with that of patients with UGC, for which various surgical procedures and reconstruction methods

Table 3. Post-TG patient characteristics

Characteristics	EGJC group (n=86)	UGC group (n=1,020)	P-value
Age (yr)	67.4±10.1	68.3±10.4	0.441
Preoperative BMI (kg/m ²)	23.4±3.5	23.1±3.1	0.495
Postoperative BMI (kg/m ²)	20.0±2.6	19.7±2.5	0.254
Postoperative period (mon)	46.5±30.2	52.9±36.5	0.114
Length of esophageal resection (mm)	25.9±14.8	7.4±10.6	<0.001
Distance from diaphragm to anastomosis (mm)	-30.1±22.0	-6.2±16.6	<0.001
Sex			0.003
Male	75	743	
Female	11	277	
Abdominal approach			<0.001
Open	69	611	
Laparoscopy	17	409	
Celiac branch of vagus			0.287
Preserved	0	19	
Divided	85	974	
Extent of esophageal resection			<0.001
Lower thoracic	29	28	
Abdominal	53	628	
None	4	358	
Level of esophago-GI anastomosis			<0.001
Tm	6	9	
Ti	64	304	
D	4	444	
A	12	241	
Clinical T*			<0.001
T1	16	450	
T2	19	172	
T3	20	176	
T4a	28	198	
T4b	2	21	
Clinical N*			<0.001
N0	36	678	
N+	49	339	
Clinical M*			0.074
M0	82	1,006	
M1	3	13	
Chemotherapy			<0.001
Preoperative	4	20	
Postoperative	34	271	
Both	14	64	
None	34	662	
Combined resection			0.414
None	56	736	
Gallbladder	22	176	
Spleen	13	144	
Pancreas	1	16	
Others	1	17	
Reconstruction procedures			0.684
Roux-en-Y (TGRY)	86	1,000	
Double-tract (TGDT)	0	13	
Jejunal interposition (TGJI)	0	2	
Others (TGX)	0	5	

Values are shown as mean±standard deviation or number of patients.

TG = total gastrectomy; EGJC = esophagogastric junction cancer; UGC = upper third gastric cancer; BMI = body mass index; GI = gastrointestinal; Tm = middle thoracic; Ti = lower thoracic; D = diaphragm; A: abdomen.

*According to the Japanese Classification of Gastric Carcinoma, 3rd English edition.

Table 4. Post-PG patient characteristics

Characteristics	EGJC group (n=120)	UGC group (n=518)	P-value
Age (yr)	67.4±10.1	69.8±9.5	0.050
Preoperative BMI (kg/m ²)	23.4±3.5	23.0±3.1	0.197
Postoperative BMI (kg/m ²)	20.0±3.0	20.1±2.7	0.684
Postoperative period (mon)	33.6±29.5	42.9±34.5	0.007
Length of esophageal resection (mm)	24.8±20.2	5.4±7.4	<0.001
Distance from diaphragm to anastomosis (mm)	-18.9±29.5	3.6±16.3	<0.001
Sex			0.017
Male	103	394	
Female	17	124	
Abdominal approach			0.251
Open	42	155	
Laparoscopy	78	363	
Celiac branch of vagus			0.041
Preserved	14	102	
Divided	102	402	
Extent of esophageal resection			<0.001
Upper thoracic	1	0	
Middle thoracic	3	0	
Lower thoracic	37	6	
Abdominal	72	288	
None	7	222	
Level of esophago-GI anastomosis			<0.001
Tu	1	0	
Tm	10	0	
Ti	59	79	
D	25	214	
A	22	216	
Clinical T*			<0.001
T1	88	439	
T2	15	63	
T3	9	11	
T4a	5	4	
T4b	3	0	
Clinical N*			0.002
N0	106	495	
N+	14	22	
Clinical M*			0.050
M0	118	516	
M1	2	1	
Chemotherapy			<0.001
Preoperative	2	0	
Postoperative	11	31	
Both	5	2	
None	102	485	
Combined resection			0.049
None	104	477	
Gallbladder	13	38	
Spleen	2	2	
Pancreas	0	1	
Others	1	0	
Reconstruction procedures			0.070
Esophagogastrostomy (PGEG)	56	300	
Double-tract (PGDT)	51	172	
Jejunal interposition (PGJI)	11	30	
Jejunal pouch interposition (PGJPI)	2	16	

Values are shown as mean±standard deviation or number of patients.

PG = proximal gastrectomy; EGJC = esophagogastric junction cancer; UGC = upper third gastric cancer; BMI = body mass index; GI = gastrointestinal; Tu = upper thoracic; Tm = middle thoracic; Ti = lower thoracic; D = diaphragm; A = abdomen.

*According to the Japanese Classification of Gastric Carcinoma, 3rd English edition.

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Table 5. Comparison of main outcome measures between EGJC and UGC group post-TG patients

Domain	Main outcome measures	EGJC group (n=86)		UGC group (n=1,020)		P-value	Cohen's <i>d</i>
		Mean	SD	Mean	SD		
Symptoms	Esophageal reflux SS	2.2	1.1	2.1	1.0	0.337	0.17
	Abdominal pain SS	1.7	0.8	1.7	0.8	0.772	
	Meal-related distress SS	2.8	1.2	2.6	1.1	0.271	
	Indigestion SS	2.2	0.9	2.2	1.0	0.856	
	Diarrhea SS	2.3	1.2	2.4	1.2	0.899	
	Constipation SS	2.4	1.2	2.2	1.1	0.097	
	Dumping SS	2.4	1.3	2.2	1.2	0.437	
	Total symptom score	2.3	0.8	2.2	0.8	0.215	
Living status	Change in BW*	-14.0%	9.0%	-14.3%	8.9%	0.758	0.33
	Ingested amount of food per meal*	5.9	2.1	6.1	2.0	0.283	
	Necessity for additional meals	2.4	0.8	2.4	0.9	0.937	
	Quality of ingestion SS*	3.3	1.0	3.6	1.0	0.006	
	Ability for working	2.2	1.0	2.2	1.0	0.681	
QOL	Dissatisfaction with symptoms	2.1	1.1	2.0	1.0	0.642	
	Dissatisfaction at the meal	2.9	1.2	2.7	1.2	0.143	
	Dissatisfaction at working	2.1	1.1	2.1	1.1	0.902	
	Dissatisfaction for daily life SS	2.4	1.0	2.3	1.0	0.389	
	PCS of SF-8*	48.9	6.6	48.7	5.8	0.697	
	MCS of SF-8*	48.6	7.0	49.3	6.3	0.302	

Outcome measures with *: a higher score indicates a better condition. Outcome measures without *: a higher score indicates a worse condition. Interpretation of effect size (Cohen's *d*): ≥0.20, small; ≥0.5, medium; ≥0.8, large.

EGJC = esophagogastric junction cancer; UGC = upper third gastric cancer; TG = total gastrectomy; SD = standard deviation; SS = subscale; BW = body weight; QOL = quality of life; PCS = physical component summary; SF-8 = Short Form-8; MCS = mental component summary.

Table 6. Comparison of main outcome measures between EGJC and UGC group post-PG patients

Domain	Main outcome measures	EGJC group (n=120)		UGC group (n=518)		P-value	Cohen's <i>d</i>
		Mean	SD	Mean	SD		
Symptoms	Esophageal reflux SS	2.2	1.0	2.0	1.0	0.035	0.22
	Abdominal pain SS	1.8	0.8	1.7	0.8	0.456	
	Meal-related distress SS	2.8	1.0	2.6	1.1	0.109	
	Indigestion SS	2.2	1.0	2.2	0.9	0.486	
	Diarrhea SS	2.3	1.2	2.2	1.2	0.488	
	Constipation SS	2.4	1.0	2.4	1.2	0.464	
	Dumping SS	2.1	1.1	2.1	1.2	0.804	
	Total symptom score	2.3	0.8	2.2	0.8	0.158	
Living status	Change in BW*	-13.9%	8.6%	-12.0%	8.1%	0.029	0.23
	Ingested amount of food per meal*	5.8	1.8	6.2	1.8	0.034	
	Necessity for additional meals	2.4	0.9	2.2	0.9	0.049	
	Quality of ingestion SS*	3.5	0.9	3.6	1.0	0.155	
	Ability for working	2.2	1.0	2.1	1.0	0.145	
QOL	Dissatisfaction with symptoms	2.2	1.0	2.0	1.0	0.023	0.23
	Dissatisfaction at the meal	2.7	1.0	2.6	1.1	0.234	
	Dissatisfaction at working	2.1	1.0	1.9	1.0	0.130	
	Dissatisfaction for daily life SS	2.3	0.9	2.2	0.9	0.051	
	PCS of SF-8*	49.0	5.8	49.1	6.1	0.786	
	MCS of SF-8*	48.4	6.2	49.7	5.9	0.034	

Outcome measures with *: a higher score indicates a better condition. Outcome measures without *: a higher score indicates a worse condition. Interpretation of effect size (Cohen's *d*): ≥0.20, small; ≥0.5, medium; ≥0.8, large.

EGJC = esophagogastric junction cancer; UGC = upper third gastric cancer; PG = proximal gastrectomy; SD = standard deviation; SS = subscale; BW = body weight; QOL = quality of life; PCS = physical component summary; SF-8 = Short Form-8; MCS = mental component summary.

can be selected, is expected to be an important issue in the near future [17]. To the best of our knowledge, this is the first large-scale study comparing the postoperative QOL of patients with EGJC to that of patients with UGC who underwent the same gastrectomy procedures.

In this study, the patient backgrounds varied significantly between groups, with more males in the EGJC group than in the UGC group for patients who underwent TG and PG.

Furthermore, more patients had higher stage progression and underwent chemotherapy in the EGJC group than in the UGC group. Until date, few studies have compared patients with EGJC to those with UGC; the differences observed in background between these two patient groups were the important findings of this study [18,19]. Similar to our results, Saito et al. [19] reported that pathological stage in patients with EGJC was more advanced than in those with UGC. In Japan, routine endoscopic screening is widespread and gastrointestinal cancer is often detected at an early stage. However, early detection of EGJC may be more difficult than that of UGC for the following reasons: 1) the tumor is located in a region where the lumen is narrow and difficult to observe; 2) the tumor often appears macroscopically flattened with a microsurface structure similar to that of the surrounding noncancerous mucosa; and 3) the tumor occasionally spreads below the squamous epithelium [20,21]. In addition, the absence of serosa in the esophagus and the complex lymphatic drainage around the esophagogastric junction may be a possible reason to explain the high-stage progression of EGJC.

Regardless of these differences, for post-TG patients, the postoperative QOL was almost the same between the two groups, and only one MOM, the quality of ingestion SS score, was slightly better in the UGC group. In contrast, among post-PG patients, postoperative QOL was significantly better for 6 of the 19 MOMs observed in the UGC group than in the EGJC group. This implies that although tumor location had only a slight effect on postoperative QOL after undergoing TG, it had a greater effect on postoperative QOL after undergoing PG. One possible reason for the worse postoperative QOL in the EGJC group post-PG could be the higher position of the esophago-gastrointestinal anastomosis, where the thoracic cavity is under negative pressure [22]. Since post-PG patients can undergo multiple reconstruction methods, we further compared the postoperative QOL in the EGJC and UGC groups based on the most common reconstruction methods adopted following PG—PGEG and PGDT. Among post-PGEG patients, weight loss was significantly greater and the esophageal reflux SS score tended to be significantly higher in the EGJC group, with a larger effect size than that in all PG patients. Conversely, among post-PGDT patients, the constipation SS score was significantly higher, and the MCS tended to be significantly poorer in the EGJC group, with a larger effect size than that for all PG patients. In view of these findings, reflux symptoms in PGEG are more likely to be affected by anastomosis height than PGDT, which may result in weight loss. It has been known that PGEG is a surgical procedure that can increase reflux symptoms even with the angle of its accentuation or fundoplication [23-25]. The results of this study indicate the need for a more potent antireflux procedure when performing PGEG in EGJC. In recent years, several techniques have been reported to be useful for reflux prevention after PGEG in UGC [22,26,27]. However, it is unclear whether these techniques are effective for EGJC, and further research is needed in this regard.

As mentioned above, the present study found significant differences in patient background between the EGJC and UGC groups. Previous studies have suggested that, of the various background factors, female sex, older age, a shorter postoperative period, and more advanced tumor progression are predictors of worse postoperative QOL [28-30]; however, a contradictory report states that a more advanced clinical stage does not affect postoperative QOL [31]. Since the proportion of female patients was lower in the EGJC group, a shorter postoperative period, more advanced tumor progression, and other unknown factors in the EGJC group may have worsened postoperative QOL. However, as the postoperative QOL in the EGJC and UGC groups post-TG was almost the same despite the large differences in the patient backgrounds in the two groups, the impact of these background factors seems relatively small. Therefore, the esophago-gastrointestinal anastomosis is at a higher position where the thoracic cavity is under negative pressure and PG may synergistically affect the postoperative QOL.

This study has some limitations. First, it was a retrospective and nonrandomized study, wherein there were substantial biases within the EGJC and UGC groups. Second, the investigation was conducted at a single time point, and the sample sizes of the two groups were dissimilar. Although as many as 1,744 patients were eligible for this study, only 206 patients with EGJC could be included in the analysis. Thus, this study did not have sufficient power for some analyses.

In conclusion, among the post-TG patients, tumor location had a minimal effect on postoperative QOL after undergoing TG, whereas among the post-PG patients, several MOMs deteriorated in the EGJC group compared to those in the UGC group. PG has been reported to prevent the severe postgastrectomy syndrome observed after TG and is a widely performed procedure for patients with UGC or EGJC. However, based on the findings of this study, it seems reasonable to conservatively estimate the benefits of PG for patients with EGJC compared with those for patients with UGC.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Post-PGEG patient characteristics

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Supplementary Table 2

Post-PGDT patient characteristics

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Supplementary Table 3

Comparison of main outcome measures between EGJC and UGC group post-PGEG patients

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Supplementary Table 4

Comparison of main outcome measures between EGJC and UGC group post-PGDT patients

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Supplementary Fig. 1

Level of esophago-gastrointestinal anastomosis.

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REFERENCES

1. 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;8:1935-1942.
[PUBMED](#) | [CROSSREF](#)
2. Yamashita H, Seto Y, Sano T, Makuuchi H, Ando N, Sasako M, et al. Results of a nation-wide retrospective study of lymphadenectomy for esophagogastric junction carcinoma. *Gastric Cancer* 2017;20:69-83.
[PUBMED](#) | [CROSSREF](#)
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;98:255-260.
[PUBMED](#) | [CROSSREF](#)
4. Nashimoto A, Akazawa K, Isobe Y, Miyashiro I, Katai H, Kodera Y, et al. Gastric cancer treated in 2002 in Japan: 2009 annual report of the JGCA nationwide registry. *Gastric Cancer* 2013;16:1-27.
[PUBMED](#) | [CROSSREF](#)
5. Nakada K, Kawashima Y, Kinami S, Fukushima R, Yabusaki H, Seshimo A, et al. Comparison of effects of six main gastrectomy procedures on patients' quality of life assessed by Postgastrectomy Syndrome Assessment Scale-45. *World J Gastrointest Surg* 2021;13:461-475.
[PUBMED](#) | [CROSSREF](#)
6. Nakada K, Ikeda M, Takahashi M, Kinami S, Yoshida M, Uenosono 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;18:147-158.
[PUBMED](#) | [CROSSREF](#)
7. Terashima M, Tanabe K, Yoshida M, Kawahira H, Inada T, Okabe H, et al. Postgastrectomy Syndrome Assessment Scale (PGSAS)-45 and changes in body weight are useful tools for evaluation of reconstruction methods following distal gastrectomy. *Ann Surg Oncol* 2014;21 Suppl 3:S370-S378.
[PUBMED](#) | [CROSSREF](#)
8. Namikawa T, Hiki N, Kinami S, Okabe H, Urushihara T, Kawahira H, et al. Factors that minimize postgastrectomy symptoms following pylorus-preserving gastrectomy: assessment using a newly developed scale (PGSAS-45). *Gastric Cancer* 2015;18:397-406.
[PUBMED](#) | [CROSSREF](#)
9. 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;12:1003-1012.
[PUBMED](#) | [CROSSREF](#)
10. Revicki DA, Wood M, Wiklund I, Crawley J. Reliability and validity of the Gastrointestinal Symptom Rating Scale in patients with gastroesophageal reflux disease. *Qual Life Res* 1998;7:75-83.
[PUBMED](#) | [CROSSREF](#)
11. Svedlund J, Sjödin 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;33:129-134.
[PUBMED](#) | [CROSSREF](#)
12. 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;44:3433-3440.
[PUBMED](#) | [CROSSREF](#)
13. Jezerskyte E, Saadeh LM, Hagens ER, Sprangers MA, Noteboom L, van Laarhoven HW, et al. Long-term quality of life after total gastrectomy versus Ivor Lewis esophagectomy. *World J Surg* 2020;44:838-848.
[PUBMED](#) | [CROSSREF](#)
14. Viklund P, Lindblad M, Lagergren J. Influence of surgery-related factors on quality of life after esophageal or cardia cancer resection. *World J Surg* 2005;29:841-848.
[PUBMED](#) | [CROSSREF](#)
15. 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;38:3152-3162.
[PUBMED](#) | [CROSSREF](#)
16. 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;18:407-416.
[PUBMED](#) | [CROSSREF](#)

17. Nakamura M, Yamaue H. Reconstruction after proximal gastrectomy for gastric cancer in the upper third of the stomach: a review of the literature published from 2000 to 2014. *Surg Today* 2016;46:517-527.
[PUBMED](#) | [CROSSREF](#)
18. Ichikura T, Ogawa T, Kawabata T, Chochi K, Sugasawa H, Mochizuki H. Is adenocarcinoma of the gastric cardia a distinct entity independent of subcardial carcinoma? *World J Surg* 2003;27:334-338.
[PUBMED](#) | [CROSSREF](#)
19. Saito H, Fukumoto Y, Osaki T, Fukuda K, Tatebe S, Tsujitani S, et al. Distinct recurrence pattern and outcome of adenocarcinoma of the gastric cardia in comparison with carcinoma of other regions of the stomach. *World J Surg* 2006;30:1864-1869.
[PUBMED](#) | [CROSSREF](#)
20. Yamamoto K, Ohnishi S, Mizushima T, Kodaira J, Ono M, Hatanaka Y, et al. Detection of early adenocarcinoma of the esophagogastric junction by spraying an enzyme-activatable fluorescent probe targeting Dipeptidyl peptidase-IV. *BMC Cancer* 2020;20:64.
[PUBMED](#) | [CROSSREF](#)
21. Omae M, Fujisaki J, Shimizu T, Igarashi M, Yamamoto N. Magnifying endoscopy with narrow-band imaging findings in the diagnosis of Barrett's esophageal adenocarcinoma spreading below squamous epithelium. *Dig Endosc* 2013;25 Suppl 2:162-167.
[PUBMED](#) | [CROSSREF](#)
22. Kuroda S, Choda Y, Otsuka S, Ueyama S, Tanaka N, Muraoka A, et al. Multicenter retrospective study to evaluate the efficacy and safety of the double-flap technique as antireflux esophagogastronomy after proximal gastrectomy (rD-FLAP Study). *Ann Gastroenterol Surg* 2018;3:96-103.
[PUBMED](#) | [CROSSREF](#)
23. Ichikawa D, Komatsu S, Okamoto K, Shiozaki A, Fujiwara H, Otsuji E. Evaluation of symptoms related to reflux esophagitis in patients with esophagogastronomy after proximal gastrectomy. *Langenbecks Arch Surg* 2013;398:697-701.
[PUBMED](#) | [CROSSREF](#)
24. Hosogi H, Yoshimura F, Yamaura T, Satoh S, Uyama I, Kanaya S. Esophagogastric tube reconstruction with stapled pseudo-fornix in laparoscopic proximal gastrectomy: a novel technique proposed for Siewert type II tumors. *Langenbecks Arch Surg* 2014;399:517-523.
[PUBMED](#) | [CROSSREF](#)
25. 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.
[PUBMED](#) | [CROSSREF](#)
26. Yamashita Y, Yamamoto A, Tamamori Y, Yoshii M, Nishiguchi Y. Side overlap esophagogastronomy to prevent reflux after proximal gastrectomy. *Gastric Cancer* 2017;20:728-735.
[PUBMED](#) | [CROSSREF](#)
27. Aizawa M, Yabusaki H, Nakada K, Matsuki A, Bamba T, Nakagawa S. A retrospective review of a single-center experience with posterolateral fundoplication during esophagogastronomy after proximal gastrectomy. *J Gastrointest Surg* 2021;25:3230-3233.
[PUBMED](#) | [CROSSREF](#)
28. Kinami S, Takahashi M, Urushihara T, Ikeda M, Yoshida M, Uenonono Y, et al. Background factors influencing postgastrectomy syndromes after various types of gastrectomy. *World J Clin Cases* 2018;6:1111-1120.
[PUBMED](#) | [CROSSREF](#)
29. Rausei S, Mangano A, Galli F, Rovera F, Boni L, Dionigi G, et al. Quality of life after gastrectomy for cancer evaluated via the EORTC QLQ-C30 and QLQ-STO22 questionnaires: surgical considerations from the analysis of 103 patients. *Int J Surg* 2013;11 Suppl 1:S104-S109.
[PUBMED](#) | [CROSSREF](#)
30. Kundes MF, Kement M, Yegen F, Alkan M, Kaya S, Kaptanoglu L. Effects of clinical factors on quality of life following curative gastrectomy for gastric cancer. *Niger J Clin Pract* 2019;22:661-668.
[PUBMED](#) | [CROSSREF](#)
31. Kinami S, Nakamura N, Zhiyong J, Miyata T, Fujita H, Takamura H, et al. Severity of postgastrectomy syndrome and quality of life after advanced gastric cancer radical gastrectomy. *Mol Clin Oncol* 2020;13:133-140.
[PUBMED](#) | [CROSSREF](#)