

Original Article



Prospective Multicenter Observational Study on Postoperative Quality of Life According to Type of Gastrectomy for Gastric Cancer

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ABSTRACT

Purpose: This study evaluated the postoperative quality of life (QoL) after various types of gastrectomy for gastric cancer.

Materials and Methods: A multicenter prospective observational study was conducted in

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Korea using the Korean Quality of Life in Stomach Cancer Patients Study (KOQUSS)-40, a new QoL assessment tool focusing on postgastrectomy syndrome. Overall, 496 patients with gastric cancer were enrolled, and QoL was assessed at 5 time points: preoperatively and at 1, 3, 6, and 12 months after surgery.

Results: Distal gastrectomy (DG) and pylorus-preserving gastrectomy (PPG) showed significantly better outcomes than total gastrectomy (TG) and proximal gastrectomy (PG) with regard to total score, indigestion, and dysphagia. DG, PPG, and TG also showed significantly better outcomes than PG in terms of dumping syndrome and worry about cancer. Postoperative QoL did not differ significantly according to anastomosis type in DG, except for Billroth I anastomosis, which achieved better bowel habit change scores than the others. No domains differed significantly when comparing double tract reconstruction and esophagogastrostomy after PG. The total QoL score correlated significantly with postoperative body weight loss (more than 10%) and extent of resection ($P < 0.05$ for both). Reflux as assessed by KOQUSS-40 did not correlate significantly with reflux observed on gastroscopy 1 year postoperatively ($P = 0.064$).

Conclusions: Our prospective observation using KOQUSS-40 revealed that DG and PPG lead to better QoL than TG and PG. Further study is needed to compare postoperative QoL according to anastomosis type in DG and PG.



Keywords: Stomach neoplasm; Quality of life; Survey and questionnaire; Gastrectomy

INTRODUCTION

In Korea, most gastric cancers are detected through a national health screening program when patients are asymptomatic, with early gastric cancer accounting for approximately 65% of such cases [1,2]. The 5-year survival rate for early gastric cancer exceeds 90% [3], leading to an increasing number of long-term survivors. Therefore, assessing major gastrointestinal symptoms (such as dumping syndrome, dysphagia, malnutrition, and surgical wound discomfort) that arise after gastrectomy [4,5], in addition to the symptoms of the cancer itself, is crucial. As a result, clinicians are increasingly evaluating the quality of life (QoL) of patients with gastric cancer following gastrectomy.

The Korean Quality of Life in Stomach Cancer Patients Study (KOQUSS) group developed KOQUSS-40, a tool specifically designed to evaluate postoperative QoL and gastrointestinal symptoms among patients with gastric cancer who have undergone gastrectomy [6]. The goal was to create an objective measure of the outcomes of different surgical methods under similar survival conditions to predict which surgery would result in the best possible postoperative QoL for each patient based on their individual characteristics. To ensure the reliability and validity of the developed questionnaire, a large-scale, multicenter study was conducted from 2017 to 2019, involving 22 institutions, 31 surgical specialists, and more than 1,500 patients with gastric cancer [6]. That study led to improvements in and validation of the KOQUSS-40 questionnaire. The KOQUSS-40 questionnaire was found to be an effective instrument for assessing the status of patients after gastrectomy and evaluating the impact of different surgical techniques on QoL.

For this study, we used the KOQUSS-40 questionnaire to quantitatively assess changes in QoL after various gastric cancer surgeries and compare the QoL outcomes of different surgical procedures. Specifically, we aimed to provide insights into 3 contentious topics:

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QoL according to the extent of gastric resection, QoL according to anastomotic methods after distal gastrectomy (DG) and proximal gastrectomy (PG), and 1-year postoperative QoL according to clinical setting and endoscopic findings. The findings are intended to assist in the selection of surgical methods and patients' postoperative follow-up.

MATERIALS AND METHODS

Study design and participants

This prospective multicenter observational study by the KOQUSS group involved 35 surgeons from 22 hospitals in Korea and 500 patients scheduled to undergo curative gastrectomy for gastric cancer. Patients with gastric cancer aged at least 19 years who were scheduled to undergo curative gastrectomy were enrolled. The number of patients in each surgical group is shown in **Fig. 1A**. Patients with other concurrent cancers, progressive or metastatic gastric cancer requiring palliative surgery, previous abdominal surgeries, or who were pregnant or planning to become pregnant were excluded, along with those deemed unsuitable for participation by the investigators.

In prospective studies comparing surgical methods, the primary objectives often prioritize short-term outcomes, such as complications, and oncological results, such as survival rates. QoL indicators are typically collected as secondary objectives. Few studies have determined

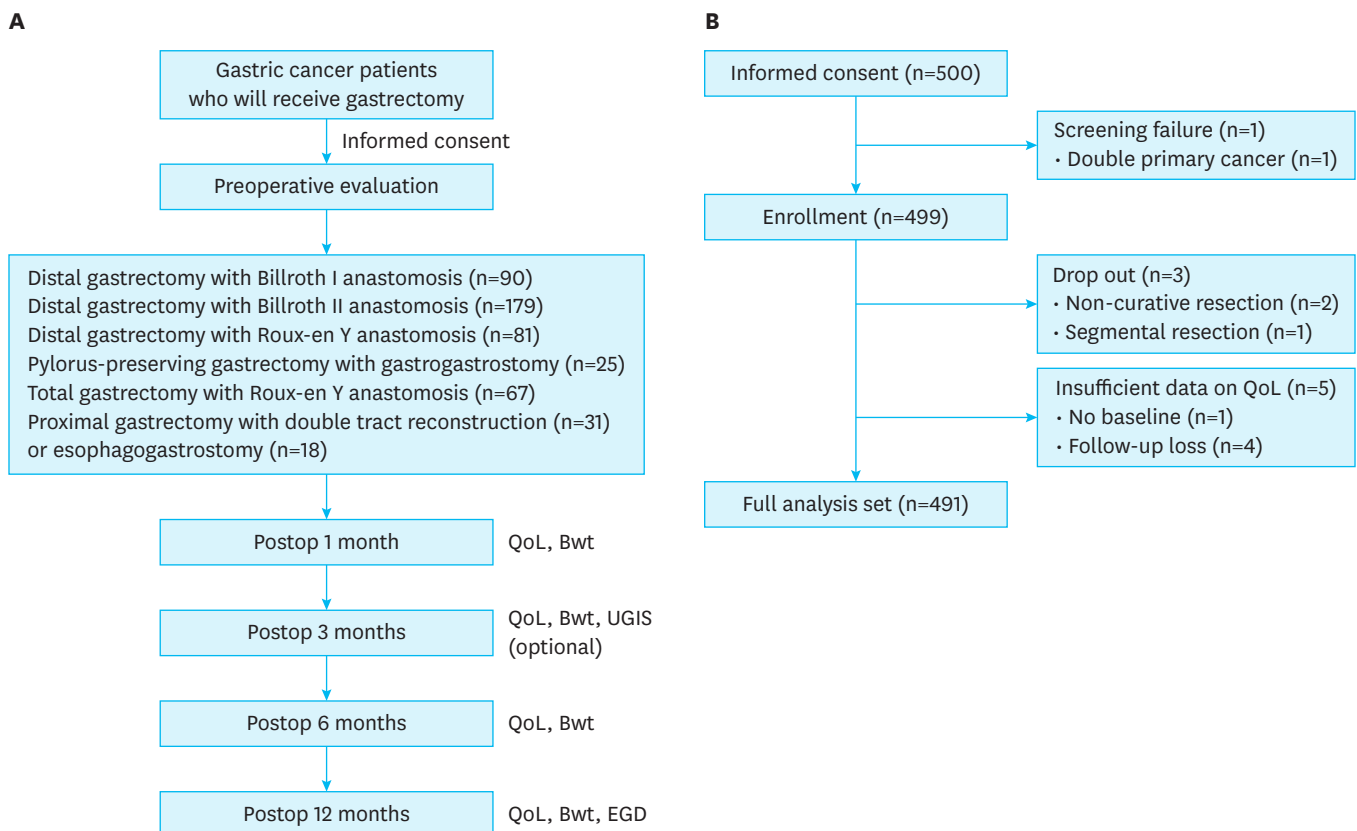


Fig. 1. Flowchart and flow diagram. (A) Study flowchart and (B) flow diagram of patient selection. QoL = quality of life; Bwt = body weight; UGIS = upper gastrointestinal series; EGD = esophagogastroduodenoscopy.

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Conflicts of Interest

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

Author Contributions

Conceptualization: E.B.W., L.J., L.H.J.; Formal analysis: E.B.W., L.J.; Investigation: E.B.W., R.K.W., A.J.Y., S.Y.S., C.I., K.S.G., P.J.H., H.H., K.H.H., A.S.H., H.S.H., Y.H.M., P.K.B., K.H.I., K.I.G., Y.H.K., S.B.J., J.S.H., K.T.H., K.O.K., A.H.S., P.J.Y., Y.K.Y., S.M.W., K.S.H., S.Y.G., S.G.J., Y.J.H., B.J.M., P.D.J., L.S., Y.J.Y., S.K.W., J.Y.J., K.S.H., L.H.J.; Writing - original draft: O.S.E., S.Y.S.

sample sizes based on QoL indicators as the primary outcome. In this study, we used the KOQUSS-40 questionnaire to measure QoL after gastrectomy; thus, we considered a realistic number of patients who could be recruited, accounting for an anticipated dropout rate of approximately 10%. Accordingly, we selected 80 participants for each surgical method. The DG group was intended to contain 240 participants (80 each for Billroth I [BI], Billroth II [BII], and Roux-en-Y gastrojejunostomy [RYGJ]), and the pylorus-preserving gastrectomy (PPG) and PG groups were each intended to have approximately 80 participants. Owing to the relatively lower disease frequency, the total gastrectomy (TG) group was intended to have 100 participants. This approach resulted in 500 participants. However, because most participants were enrolled in the BII group, enrollment was terminated before the anticipated number of patients was included in the other study groups.

Treatment

In this study, all surgical procedures adhered to stomach cancer treatment guidelines recommending radical gastrectomy with lymph node dissection [7,8]. Patients underwent DG, PPG, TG, or PG depending on tumor location and clinical stage. Following DG, either BI, BII, or RYGJ anastomosis was performed, whereas esophagogastrostomy (EG) with an anti-reflux procedure (such as the double flap technique [DFT]) or double tract reconstruction (DTR) was performed following PG, depending on the extent of the tumor and the surgeon's preference. Open, laparoscopic, and robotic approaches were all acceptable methods of surgery. Patients diagnosed with pathologic stage II or III disease were advised to undergo adjuvant chemotherapy in accordance with stomach cancer treatment guidelines [7,8].

Clinical data collection

Patients enrolled in this study had their weight measured and completed the KOQUSS-40 questionnaire during outpatient visits at 1, 3, 6, and 12 months after surgery, and endoscopy was performed one year after surgery. Patient demographic data, physical status, preoperative laboratory results, and surgical techniques were obtained from medical records. The pathological stage was determined using the Tumor Node Metastasis Classification of Malignant Tumors, 8th Edition, published by the American Joint Committee on Cancer [9].

QoL instrument and scoring

Study participants completed the KOQUSS-40 questionnaire before surgery and at 1, 3, 6, and 12 months post-surgery. KOQUSS-40 consists of 8 scales (indigestion, difficulty swallowing, acid reflux, dumping syndrome, change in bowel habits, constipation, psychological factors, and worry about cancer) containing 32 questions about symptoms that can occur after gastrectomy, along with 8 additional questions providing information deemed essential by expert agreement [6]. The scoring system for KOQUSS-40 was developed based on the methods used for the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30/STO22: raw scores (average of the questions contributing to each scale) are divided by range and then transformed into a score between 0 and 100 [10]. For KOQUSS-40, we followed the principle of summarizing scores used for EORTC QLQ-C30 [11]. The overall KOQUSS-40 score was calculated as the average of the 8 scales measuring symptoms experienced after gastrectomy, which were identified through exploratory factor analysis. Higher scores indicated better QoL or fewer symptoms after gastrectomy.

Statistical analysis

For continuous variables, descriptive statistics are reported as mean values and standard deviations, while categorical variables are expressed as numbers and percentages.

To determine statistical differences between 2 groups, we used either Student's t-test or the Wilcoxon rank-sum test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables. To examine QoL differences among groups over time, linear mixed models with a compound symmetry covariance structure were applied, as the autocorrelation function plot for the 5 measurements in each participant followed compound symmetry and was not autoregressive during the study period. These models evaluate the difference between groups as the coefficient of the group variable and the change in the difference between groups over time as the coefficient of the interaction term between group and time, which can be visualized as the slope of the difference in QoL between the 2 groups. We performed statistical analyses using R software version 4.3.0 (R Project for Statistical Computing, Vienna, Austria). All tests were 2-sided, and P-values <0.05 were considered statistically significant.

Ethical statement

The study protocol was approved by the Institutional Review Boards of 22 hospitals: National Cancer Center (NCC2021-0105), Samsung Medical Center (SMC 2021-04-084-001), Seoul National University Bundang Hospital (B-2104-676-401), Soonchunhyang University Bucheon Hospital (SCHBC 2021-03-041-001), Yeouido St. Mary's Hospital (SC21QIDI0022), Gyeongsang National University School of Medicine (GNUH 2021-03-018), Ajou University Hospital (AJIRB-MED-SUR-21-063), Pusan National University Yangsan Hospital (05-2021-056), Kyungpook National University Chilgok Hospital (KNUCH 2021-04-002), Yonsei University Severance Hospital (4-2021-1490), Gangnam Severance Hospital (4-2021-1490), Seoul National University Hospital (H-2101-198-1195), Inje University Haeundae Paik Hospital (2021-05-021-002), Gyeongsang National University Changwon Hospital (GNUCH 2021-03-028), Seoul National University Boramae Medical Center (30-2021-82), Kosin University College of Medicine (KUGH 2021-06-002), Soonchunhyang University Cheonan Hospital (SCHCA 2021-03-040), Keimyung University Dongsan Medical Center (DSMC 2021-04-128), Yeungnam University College of Medicine (YUMC 2021-03-035-001), Seoul Medical Center (SEOUL 2021-03-003), Gachon University Gil Medical Center (GAIRB2021-142), and Korea University Guro Hospital (2021GR0143).

Informed consent was obtained from all patients included in the study. All procedures were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

RESULTS

Patients

From May 2021 to April 2022, 500 participants agreed to participate in this study. Among them, one patient with double primary cancer, 2 patients undergoing non-curative treatment, one with segmental resection, and 5 with incomplete follow-up questionnaires were excluded from the analyses (**Fig. 1B**). **Table 1** shows the demographic and clinicopathological characteristics of the 491 patients. The proportion of minimally invasive surgery (MIS) was 91.0%, with open surgeries accounting for the remaining 9.0%. DG was performed in 71.3% of cases, TG in 13.7%, PPG in 5.1%, and PG in 10%. After DG, BI anastomosis was performed in 90 patients (18.3%), BII anastomosis in 179 (36.5%), and RYGI in 81 (16.5%). TG with Roux-en-Y esophagojejunostomy was performed in 67 patients (13.6%). After PG, EG was performed in 18 patients (3.7%) and DTR in 31 (6.3%).

Table 1. Demographic and clinical characteristics of the study participants (n=491)

Clinicopathologic characteristics	No. of patients
Sex	
Male	288 (58.7)
Female	203 (41.3)
Age (yr)	60.7±11.0
Height (cm)	163.2±8.4
Initial body weight (kg)	64.5±11.3
Surgical approach	
Open	44 (9.0)
Laparoscopic	403 (82.1)
Robotic	44 (9.0)
Extent of gastrectomy	
Distal gastrectomy	350 (71.3)
Total gastrectomy	67 (13.7)
Pylorus-preserving gastrectomy	25 (5.1)
Proximal gastrectomy	49 (10.0)
Reconstruction method	
Billroth-I gastroduodenostomy	90 (18.3)
Billroth-II gastrojejunostomy	179 (36.5)
Roux-en-Y gastrojejunostomy	81 (16.5)
Roux-en-Y esophagojejunostomy	67 (13.7)
Gastrogastrostomy	25 (5.1)
Esophagogastrostomy	18 (3.7)
Double tract reconstruction	31 (6.3)
Laparoscopic/robotic anastomosis	
Intracorporeal	419 (85.3)
Extracorporeal	26 (5.3)
Not described	2 (0.4)
Curative resection	
R0	490 (99.8)
R1	1 (0.2)
Resection margin	
Negative	489 (99.6)
Positive	2 (0.4)
Combined resection	
No	476 (97.0)
Yes	15 (3.1)
Gallbladder	10 (2.0)
Fallopian tubes & ovaries	2 (4.1)
Colon	1 (2.0)
Adrenal gland	1 (2.0)
Spleen	1 (2.0)
Pathologic T stage	
T1	370 (75.4)
T2	45 (9.2)
T3	50 (10.2)
T4a	26 (5.3)
Pathologic N stage	
N0	378 (77.0)
N1 (1–2)	57 (11.6)
N2 (3–6)	31 (6.3)
N3a (7–15)	20 (4.1)
N3b (16–)	5 (1.0)
Pathologic M stage	
M0	491 (100.0)
M1	0 (0.0)
Pathologic stage	
I	386 (78.6)
II	66 (13.4)
III	39 (7.9)
Adjuvant chemotherapy	
No	384 (80.5)
Yes	93 (19.5)

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

Comparison of QoL according to resection extent

Postoperative total KOQUSS-40 scores according to the type of gastrectomy (DG vs. PG vs. PPG vs. TG) are shown in **Fig. 2**. The total score decreased compared with baseline at 1 month postoperatively and then increased during the first year after surgery. However, the slopes of the total scores were not significantly different, indicating that the total scores of the groups compared did not differ significantly over time (**Table 2**). The total score was highest in the DG group during the follow-up period, followed by the PPG, TG, and PG groups (**Fig. 2**). The total QoL score did not differ significantly between the DG and PPG groups (-2.39 , $P=0.258$); however, the QoL score after DG was significantly higher than that after TG (-3.43 , $P=0.012$) and PG (-7.44 , $P<0.001$; **Table 2**).

The scores from the 9 KOQUSS-40 domains are presented according to the type of gastrectomy in **Fig. 3** and **Table 2**. The general QoL score was significantly lower after PPG (-12.27 , $P=0.010$) and PG (-8.46 , $P=0.015$) than after DG. Interestingly, the general QoL scores of the PPG and PG groups were generally lower than those of the TG group (**Fig. 3A**). Indigestion (**Fig. 3B**) and dysphagia (**Fig. 3C**) scores were significantly lower in the TG and PG groups than in the DG group (indigestion: TG, -6.09 ; PG, -12.70 ; dysphagia: TG, -7.29 ; PG, -15.40 ; all $P<0.05$). The scores for dumping syndrome (**Fig. 3E**) and worry about cancer (**Fig. 3I**) were significantly lower in the PG group than in the DG group (dumping syndrome: -4.87 , $P=0.004$; worry about cancer: -7.38 , $P=0.020$). Additionally, reflux and bowel habit change scores varied significantly over time in the PG and DG groups (reflux: slope, -0.48 , $P=0.021$; bowel habit change: slope, -0.49 , $P=0.020$). Post-hoc analysis showed that the mean score in the reflux domain for PG was significantly lower than that for DG 3, 6, and 12 months postoperatively (**Fig. 3D**, marked with an asterisk), and the mean score for bowel habit change after PG was significantly lower than that after DG at 12 months postoperatively (**Fig. 3F**, marked with an asterisk).

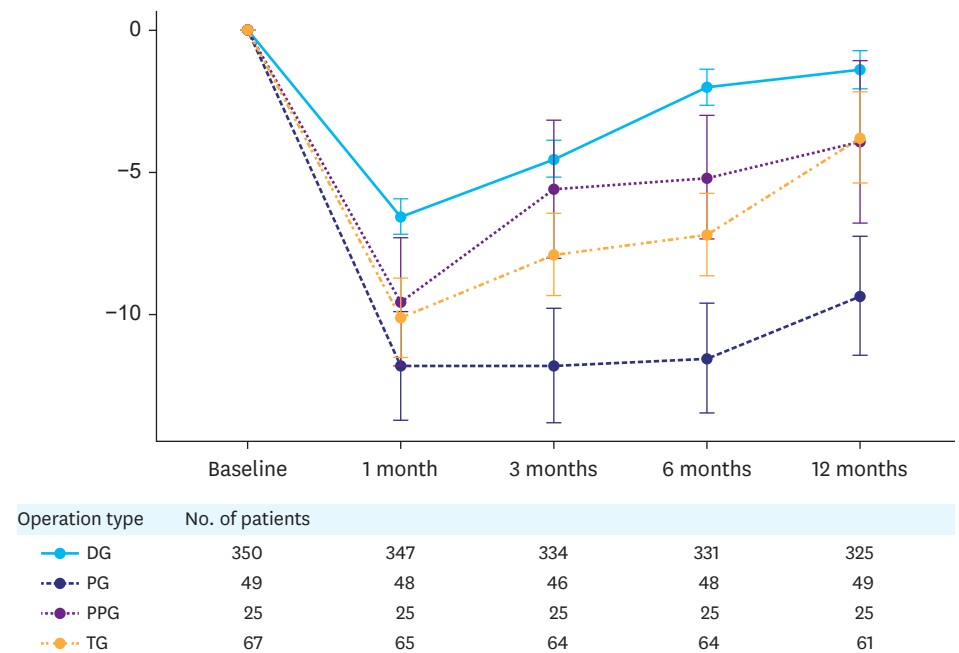


Fig. 2. Postoperative KOQUSS-40 total scores according to the type of gastric resection. Plotted with the mean difference and standard error (error bars).
DG = distal gastrectomy; PG = proximal gastrectomy; PPG = pylorus-preserving gastrectomy; TG = total gastrectomy; KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study.

Table 2. Differences in total and domain scores of KOQUSS-40 according to the type of gastric resection

Domain	Difference*	95% CI	P-value	Slope†	95% CI	P-value
Total						
DG vs. PPG	-2.39	-6.54, 1.76	0.258	-0.03	-0.38, 0.32	0.869
DG vs. TG	-3.43	-6.12, -0.75	0.012	0.08	-0.16, 0.31	0.532
DG vs. PG	-7.44	-10.51, -4.38	<0.001	-0.22	-0.48, 0.05	0.107
General QoL						
DG vs. PPG	-12.27	-21.55, -3.00	0.010	-0.52	-1.19, 0.14	0.124
DG vs. TG	-4.01	-10.01, 1.99	0.191	0.05	-0.40, 0.49	0.835
DG vs. PG	-8.46	-15.31, -1.62	0.015	0.18	-0.32, 0.67	0.485
Indigestion						
DG vs. PPG	-5.37	-13.36, 2.63	0.188	9.40×10^{-3}	-0.68, 0.70	0.979
DG vs. TG	-6.09	-11.27, -0.91	0.021	7.22×10^{-3}	-0.46, 0.47	0.976
DG vs. PG	-12.70	-18.60, -6.79	<0.001	-0.39	-0.90, 0.13	0.141
Dysphagia						
DG vs. PPG	-5.56	-11.80, 0.69	0.081	0.22	-0.38, 0.82	0.469
DG vs. TG	-7.29	-11.34, -3.24	<0.001	0.21	-0.19, 0.61	0.300
DG vs. PG	-15.40	-20.02, -10.79	<0.001	-0.07	-0.52, 0.37	0.754
Reflux						
DG vs. PPG	-2.30	-8.75, 4.15	0.484	-0.06	-0.61, 0.48	0.821
DG vs. TG	0.16	-4.02, 4.34	0.940	-0.27	-0.63, 0.10	0.148
DG vs. PG	-4.08	-8.85, 0.70	0.094	-0.48	-0.88, -0.07	0.021
Dumping syndrome						
DG vs. PPG	-1.50	-5.98, 2.97	0.511	-0.23	-0.68, 0.21	0.306
DG vs. TG	-2.61	-5.51, 0.30	0.079	0.03	-0.27, 0.33	0.862
DG vs. PG	-4.87	-8.18, -1.57	0.004	0.07	-0.26, 0.40	0.679
Bowel habit change						
DG vs. PPG	0.24	-6.53, 7.01	0.945	-0.17	-0.72, 0.38	0.536
DG vs. TG	-3.47	-7.86, 0.92	0.122	0.16	-0.21, 0.53	0.391
DG vs. PG	-2.95	-7.97, 2.07	0.249	-0.49	-0.90, -0.08	0.020
Constipation						
DG vs. PPG	-4.09	-11.90, 3.72	0.305	-0.17	-0.94, 0.60	0.668
DG vs. TG	-1.30	-6.37, 3.77	0.615	-0.05	-0.56, 0.47	0.851
DG vs. PG	-3.58	-9.35, 2.19	0.224	-0.22	-0.79, 0.36	0.460
Psychological factors						
DG vs. PPG	2.84	-3.61, 9.30	0.388	0.14	-0.43, 0.70	0.639
DG vs. TG	-3.13	-7.32, 1.06	0.143	0.36	-0.02, 0.74	0.064
DG vs. PG	-3.53	-8.30, 1.24	0.147	-8.89×10^{-3}	-0.43, 0.41	0.967
Worry about cancer						
DG vs. PPG	-2.42	-10.86, 6.02	0.574	5.18×10^{-3}	-0.67, 0.68	0.988
DG vs. TG	-3.30	-8.87, 2.28	0.247	0.17	-0.30, 0.63	0.476
DG vs. PG	-7.38	-13.61, -1.15	0.020	-0.18	-0.68, 0.33	0.493

KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study; CI = confidence interval; DG = distal gastrectomy; PPG = pylorus-preserving gastrectomy; TG = total gastrectomy; PG = proximal gastrectomy; QoL = quality of life.

*Difference: mean QoL difference between groups as the coefficient of the group variable.

†Slope: change in mean QoL difference between groups over time as the coefficient of the interaction term of group and time.

Comparison of QoL according to anastomotic method after DG and PG

We compared total KOQUSS-40 scores for the 3 anastomosis groups (BI, BII, and RYGJ) after DG (**Fig. 4**). Total scores did not differ significantly among these groups (**Table 3**). Within the 9 KOQUSS-40 domains (**Table 3** and **Supplementary Fig. 1**), only the bowel habit change score was significantly better after BI than after BII or RYGJ (BI vs. BII: -4.29, $P=0.049$; BI vs. RYGJ: -6.83, $P=0.008$).

General QoL score differences between the BI and RYGJ groups changed significantly over time (**Supplementary Fig. 1A**). One month postoperatively, the general QoL score of the RYGJ group was lower than that of the BI group; however, the score in the RYGJ group increased

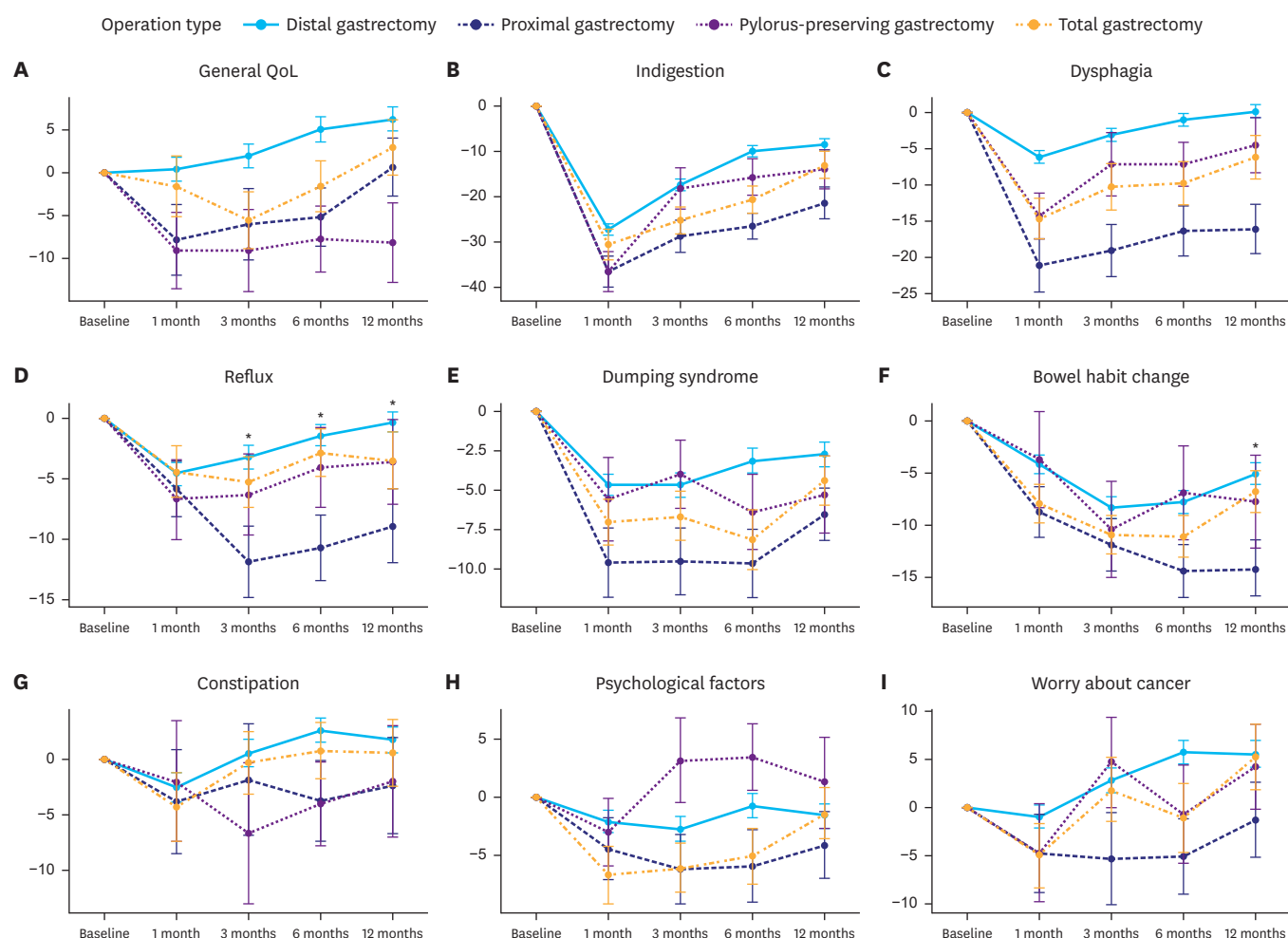
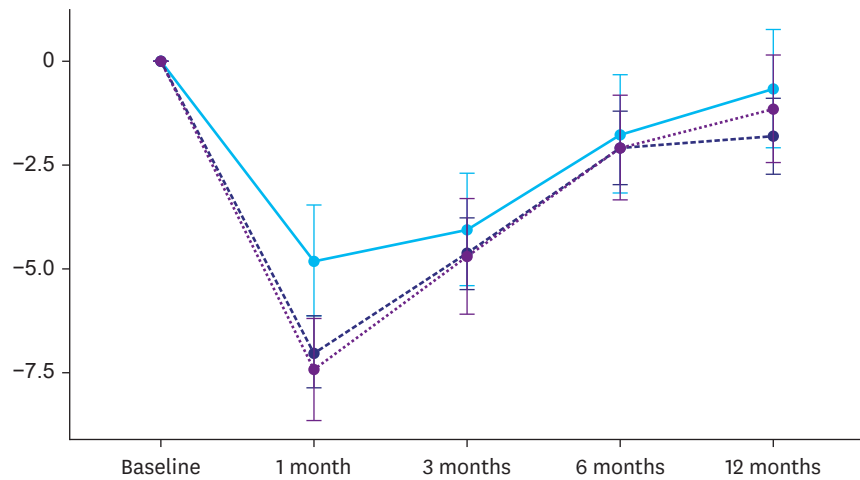


Fig. 3. Scores for the 9 KOQUSS-40 domains according to the type of gastric resection. Plotted with the mean difference and standard error (error bars). KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study.

*Distal gastrectomy vs. proximal gastrectomy ($P < 0.05$).

steeply during the follow-up period (slope, 0.61; $P = 0.020$). For indigestion (**Supplementary Fig. 1B**), the score of the BII group was lower than that of the BI group 1 month postoperatively. However, 6 months after surgery, indigestion scores were similar, and the change in scores over time between those groups was significant (slope, 0.47; $P = 0.039$). Preoperative and 1-month postoperative scores for bowel habit changes did not differ in the BI group (**Supplementary Fig. 1F**). Although the scores after BII and RYGJ were significantly lower than those for BI 1 month postoperatively (**Supplementary Fig. 1F**, marked with an asterisk), bowel habit change scores were similar 1 year after surgery. The changes in these scores over time were significant (BI vs. BII: slope, 0.49; $P = 0.009$; BI vs. RYGJ: slope, 0.66; $P = 0.003$). The remaining domains showed no significant differences or changes in scores. However, 1 year after surgery, increases in dysphagia (**Supplementary Fig. 1C**) and constipation (**Supplementary Fig. 1G**) scores were observed in all 3 groups. Reflux scores were better in the RYGJ group than in the BI or BII groups (**Supplementary Fig. 1D**). Dumping syndrome scores were lower in the RYGJ and BII groups than in the BI group at 3 months postoperatively; however, they increased and were similar at 1 year postoperatively (**Supplementary Fig. 1E**). BI consistently showed better scores than RYGJ and BII in the psychological (**Supplementary Fig. 1H**) and worry about cancer (**Supplementary Fig. 1I**) domains.



Operation type	No. of patients				
—●— B-I	90	90	87	83	90
- -●- - B-II	179	176	170	169	165
...●... RY	81	81	77	79	78

Fig. 4. Postoperative KOQUSS-40 total scores according to the type of anastomosis after distal gastrectomy. Plotted with the mean difference and standard error (error bars).

B-I = Billroth I anastomosis; B-II = Billroth II anastomosis; RY = Roux-en-Y; KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study.

Table 3. Differences in total and domain scores of KOQUSS-40 according to the type of anastomosis after distal gastrectomy (Billroth I vs. Billroth II vs. RY anastomosis)

Domain		Difference*	95% CI	P-value	Slope†	95% CI	P-value
Total	Billroth I vs. Billroth II	-1.06	-3.63, 1.51	0.419	0.12	-0.11, 0.34	0.308
	Billroth I vs. RY	-0.89	-3.93, 2.15	0.568	0.22	-0.04, 0.48	0.101
General QoL	Billroth I vs. Billroth II	-3.34	-9.55, 2.87	0.292	-0.06	-0.49, 0.38	0.805
	Billroth I vs. RY	-4.36	-11.71, 2.99	0.244	0.61	0.10, 1.12	0.020
Indigestion	Billroth I vs. Billroth II	-4.20	-9.72, 1.31	0.135	0.47	0.02, 0.91	0.039
	Billroth I vs. RY	-0.74	-7.26, 5.77	0.823	0.14	-0.38, 0.66	0.587
Dysphagia	Billroth I vs. Billroth II	0.42	-3.07, 3.90	0.814	-0.04	-0.38, 0.31	0.835
	Billroth I vs. RY	1.09	-3.03, 5.20	0.604	-0.19	-0.60, 0.21	0.351
Reflux	Billroth I vs. Billroth II	1.74	-1.78, 5.26	0.334	-0.14	-0.49, 0.21	0.424
	Billroth I vs. RY	3.84	-0.32, 8.00	0.070	0.11	-0.30, 0.52	0.595
Dumping syndrome	Billroth I vs. Billroth II	-0.10	-3.00, 2.81	0.949	0.17	-0.12, 0.45	0.250
	Billroth I vs. RY	-0.24	-3.67, 3.19	0.891	0.30	-0.03, 0.63	0.076
Bowel habit change	Billroth I vs. Billroth II	-4.29	-8.56, -0.02	0.049	0.49	0.12, 0.85	0.009
	Billroth I vs. RY	-6.83	-11.88, -1.78	0.008	0.66	0.23, 1.08	0.003
Constipation	Billroth I vs. Billroth II	-0.79	-5.42, 3.85	0.739	-0.21	-0.69, 0.27	0.397
	Billroth I vs. RY	-1.34	-6.81, 4.14	0.631	0.10	-0.47, 0.66	0.736
Psychological factors	Billroth I vs. Billroth II	-3.03	-7.17, 1.10	0.151	-0.10	-0.46, 0.26	0.601
	Billroth I vs. RY	-4.73	-9.62, 0.15	0.058	0.08	-0.34, 0.50	0.701
Worry about cancer	Billroth I vs. Billroth II	-3.45	-8.49, 1.58	0.179	0.17	-0.26, 0.60	0.440
	Billroth I vs. RY	-2.51	-8.47, 3.44	0.408	0.41	-0.10, 0.91	0.115

KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study; RY = Roux-en-Y; CI = confidence interval; QoL = quality of life.

*Difference: mean QoL difference between groups as the coefficient of the group variable.

†Slope: change in mean QoL difference between groups over time as the coefficient of the interaction term of group and time.

Table 4. Differences in total and domain scores of KOQUSS-40 according to the type of anastomosis after proximal gastrectomy (double tract reconstruction vs. esophagogastrostomy)

Domain	Difference*	95% CI	P-value	Slope†	95% CI	P-value
Total	-3.45	-10.07, 3.16	0.305	-0.43	-1.06, 0.20	0.183
General QoL	1.83	-12.09, 15.75	0.795	0.37	-0.58, 1.32	0.445
Indigestion	4.86	-7.65, 17.38	0.444	-1.23	-2.24, -0.21	0.018
Dysphagia	-3.72	-15.59, 8.14	0.537	-0.41	-1.59, 0.78	0.499
Reflux	-8.48	-17.55, 0.59	0.067	-0.80	-1.68, 0.07	0.070
Dumping syndrome	1.85	-4.25, 7.95	0.550	-0.58	-1.37, 0.21	0.151
Bowel habit change	1.94	-6.58, 10.46	0.654	-0.11	-0.91, 0.69	0.786
Constipation	1.06	-15.85, 17.98	0.901	-1.41	-2.80, -0.02	0.047
Psychological factors	-1.47	-10.78, 7.84	0.756	-0.12	-1.11, 0.88	0.814
Worry about cancer	-15.63	-31.49, 0.23	0.053	1.20	0.14, 2.26	0.027

KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study; CI = confidence interval; QoL = quality of life.
*Difference: mean QoL difference between groups as the coefficient of the group variable.

†Slope: change in mean QoL difference between groups over time as the coefficient of the interaction term of group and time.

DTR or EG anastomosis can be performed after PG. During the follow-up period, the total KOQUSS-40 score was lower in the EG group than in the DTR group (**Fig. 5**), but the difference was not significant (**Table 4**; -3.45, $P=0.305$). The change in total score over time, presented as the slope, also did not differ significantly between these groups (slope, -0.43, $P=0.183$; **Table 4**). In fact, none of the postoperative scores for any of the 9 KOQUSS-40 domains differed significantly between the EG and DTR groups (**Table 4** and **Supplementary Fig. 2**). In the DTR group, indigestion (**Supplementary Fig. 2B**) and constipation (**Supplementary Fig. 2G**) scores increased over time compared with the EG group, and this change was significant (DTR vs. EG indigestion: slope, -1.23; $P=0.018$; constipation: slope, -1.41, $P=0.047$). Conversely, in the EG group, the worry about cancer domain score increased significantly over time during the follow-up period compared with the DTR group (slope, 1.20, $P=0.027$; **Supplementary Fig. 2I**). In the remaining domains, scores and changes in scores did not differ significantly between the groups, but the following additional findings are noteworthy. During the postoperative period, both the DTR and EG groups showed an increase in general QoL scores (**Supplementary Fig. 2A**), a decrease in bowel habit change scores (**Supplementary Fig. 2F**), and no notable changes in psychological scores (**Supplementary Fig. 2H**). Dysphagia (**Supplementary Fig. 2C**) and reflux (**Supplementary Fig. 2D**) scores were higher in the DTR group than those in the EG group. Six months after surgery, the dumping syndrome score was higher in the EG group than in the DTR group (**Supplementary Fig. 2E**).

Comparison of 1-year postoperative QoL according to clinical settings and endoscopic findings

Total and domain scores for general QoL, indigestion, dysphagia, reflux, dumping syndrome, and psychological concerns all differed significantly with body weight loss from baseline to 1 year postoperatively (**Table 5**). Only bowel habit change scores varied significantly between patients treated with or without adjuvant chemotherapy. Most domains, including scarring, were not statistically correlated with the surgical approach (open vs. MIS), with the exception of financial concerns. In the 1-year postoperative endoscopic findings, the presence of reflux esophagitis showed a marginal correlation with the reflux domain. Bowel habit change scores were statistically but not clinically correlated with reflux esophagitis. The presence of residual food on the 1-year postoperative endoscopic exam did not correlate with QoL, including indigestion, dysphagia, and reflux domain scores.

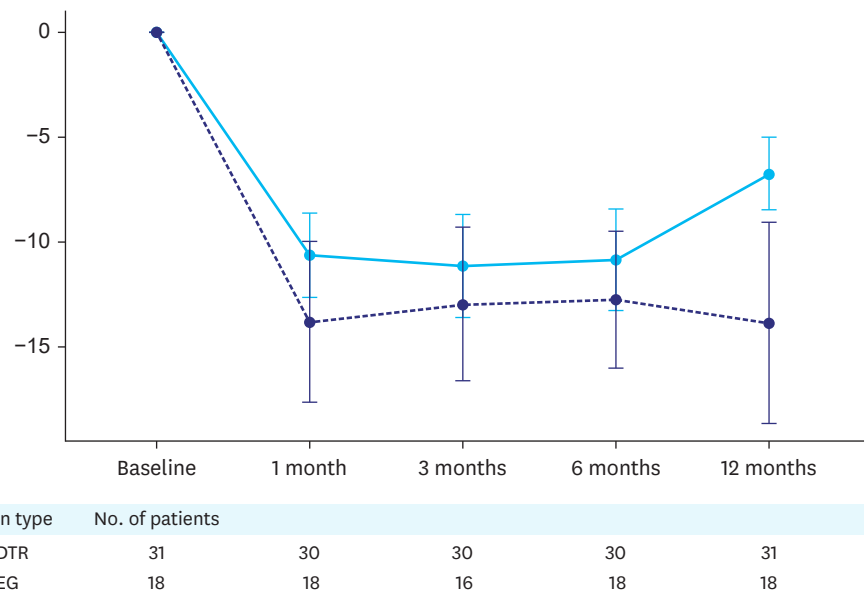


Fig. 5. Postoperative KOQUSS-40 total scores according to the type of anastomosis after proximal gastrectomy. Plotted with the mean difference and standard error (error bars). DTR = double-tract reconstruction; EG = esophagogastrostomy; KOQUSS = the Korean Quality of Life in Stomach Cancer Patients Study.

Table 5. Comparison of 1-year postoperative quality of life according to clinical setting and endoscopic findings

Clinical setting	Bwt change			Adjuvant chemotherapy			Open vs. MIS (laparoscopic/robotic)			Reflux esophagitis			Residual food		
	Bwt loss <10%	Bwt loss >10%	P-value	(-)	(+)*	P-value	Open	MIS	P-value	(-)	(+)	P-value	No residue/liquid only	Soft diet/nearly normal diet	P-value
No. of patients	285	182		380	59		45	451		420	32		407	46	
Domain															
Total	-4.3	-8.1	0.002	-3.7	-4.9	0.516	-1.7	-2.8	0.601	-2.4	-5.0	0.268	-2.6	-1.4	0.552
General QoL	2.3	-5.4	0.002	3.5	2.6	0.808	0.8	4.9	0.329	4.9	-2.5	0.115	5.1	0.7	0.261
Indigestion	-17.2	-23.5	0.004	-12.4	-18.2	0.079	-10.6	-10.6	0.987	-10	-17.6	0.073	-10.6	-8.2	0.500
Dysphagia	-3.7	-9.5	0.004	-3.9	-6.6	0.325	-1.4	-2.8	0.636	-2.1	-5.4	0.440	-2.4	0.7	0.261
Reflux	-2.7	-7.2	0.015	-4.0	0.0	0.085	1.4	-2.1	0.196	-1.3	-6.8	0.064	-1.3	-2.7	0.585
Dumping syndrome	-4.2	-7.6	0.013	-4.9	-5.4	0.805	-0.7	-3.8	0.147	-3.4	-3.9	0.785	-3.6	-1.4	0.288
Bowel habit change	-8.9	-9.9	0.560	-8.3	-15.3	0.009	-5.9	-6.5	0.794	-7.0	1.1	0.019	-6.3	-7.5	0.661
Constipation	0.1	-0.8	0.711	1.1	5.0	0.190	1.6	0.9	0.837	1.2	-3.2	0.281	0.6	4.7	0.219
Psychological factors	-1.0	-6.5	0.002	-1.4	-2.3	0.776	0.2	-1.8	0.524	-1.3	-4.9	0.292	-1.5	-1.3	0.937
Worry about cancer	3.3	-0.1	0.152	4.4	3.2	0.778	1.8	5.0	0.427	5.0	1.1	0.389	4.9	4.2	0.864
Scarring	3.4	8.1	0.392	7.1	15.3	0.347	1.7±20.2	10.1±16.7	0.115	8.8	1.9	0.385	6.6	25.9	0.448
Financial problems	2.3	5.2	0.576	6.7	0.0	0.430	-7.7	7.0	0.035	5.3	-2.4	0.411	5.0	0.0	0.619

Values are presented as mean ± standard deviation.

Change in Bwt was calculated between the preoperative baseline and 1 year postoperatively.

Reflux esophagitis and residual food were evaluated via an endoscopic examination 1 year postoperatively.

Bwt = body weight; MIS = minimally invasive surgery; QoL = quality of life.

*Patients (n=59) undergoing chemotherapy 3 months postoperatively.

DISCUSSION

In this prospective observational study, we used the newly developed KOQUSS-40 questionnaire to evaluate changes in QoL following various gastric cancer surgeries and compared the results among different surgical methods. Total, indigestion, and dysphagia scores after DG were similar to those after PPG and higher than those after TG, which were higher than those after PG. In the scores for dumping syndrome and worry about cancer, DG was similar to PPG and TG, and all 3 techniques were better than PG. After DG, the BI, BII, and RYGJ reconstruction methods had comparable scores for all parameters except bowel habit changes, with BI showing better bowel habit change scores than the others. We found no significant differences in any domains when comparing DTR and EG after PG, although the reflux and worry about cancer scores appeared worse after EG than DTR. KOQUSS-40 scores were associated with body weight loss and the extent of surgery. However, they did not strongly correlate with the use of adjuvant chemotherapy, surgical approach, or endoscopic findings such as reflux and gastric emptying.

Radical gastrectomy, including DG and TG, offers an oncological cure; however, patients experience various postgastrectomy syndromes, and their QoL deteriorates after surgery [12]. With the increased survival time of patients with gastric cancer [1,13,14], function-preserving surgeries (PPG [15] and PG [16]) have gained importance.

Previous studies using the EORTC QLQ-STO22 questionnaire [17,18] have suggested that in the early postoperative period, DG is superior to TG in terms of QoL [19-23]. Fortunately, with recent advancements in intraoperative tumor localization, good margins can be ensured during laparoscopic surgery [24]. In surgery for gastric cancers located 3–5 cm away from the gastroesophageal junction, TG can be avoided, with stomach-preserving surgery offering improved QoL for patients. PG has been adapted to compensate for the shortcomings of TG [16], but a previous study reported PG to have significantly lower QoL scores than other extents of resection [25]. The results obtained in the current study using KOQUSS-40 align with those observations. However, PG showed better QoL than TG in a recent study using the Postgastrectomy Syndrome Assessment Scale-45 [26]. To elucidate the underlying reasons for these conflicting findings, comprehensive subgroup analyses comparing TG with different anastomotic groups following PG will be required. Furthermore, future studies should account for potential confounding variables, including clinicopathologic characteristics, surgical approach, anastomotic technique after PG, and surgical outcomes (such as remnant stomach volume and food passage) to ensure more precise and reliable conclusions. PPG is associated with a lower risk of dumping syndrome and reflux owing to the preservation of the vagal nerve's hepatic and pyloric branches [27,28]. Contrary to our expectations, our study did not show that PPG led to better KOQUSS-40 QoL scores than DG, which was similar to the findings of the KCLASS-04 trial [29] and another study using the EORTC QLQ questionnaires [30]. However, in other studies using different questionnaires, PPG was associated with significantly more frequent diarrhea, dumping, and reflux than BI after DG [31,32].

Many studies have compared BI, BII, and RYGJ after DG, which is performed as a standard surgical procedure for lower gastric cancer [33-38]. Several studies have reported benefits, such as less frequent weight loss [35] and dumping syndrome [33] with BI, and a reduced occurrence of residual gastritis and reflux after RYGJ [33,35,36]. However, no definitive consensus exists on which of these reconstructive surgeries is most effective [34,37]. In this study, patients who underwent BI, BII, and RYGJ reported similar QoL scores. Only bowel habit change scores

avored BI. A previous study indicated that discoordination of the digestive tract owing to vagotomy or endocrine hypofunction, along with dysregulation of gastrointestinal hormone secretion, contributed to irregular bowel movements in gastrectomized patients [39]. Furthermore, substantial alterations in intestinal microflora and metabolite levels have been observed in many gastrectomized patients experiencing irregular bowel habits [39].

The speculation is that BI, which maintains the digestive tract's ability to pass food through the duodenum, might have led to less severe postoperative bowel habit changes compared to RYGJ or BII.

Various functional digestive-tract reconstruction methods after PG have been reported to reduce reflux esophagitis, which can severely impair postoperative QoL. A recent meta-analysis reported the incidence of reflux esophagitis after DTR, EG, and the double-flap technique to be 7.6%, 27.3%, and 9.1%, respectively [40]. In the KLASS-05 trial, the incidence of reflux esophagitis did not differ between the DTR-after-PG and TG groups. However, patients who underwent DTR showed better nutritional status and better physical and social functioning than those who underwent TG [41]. Another study comparing QoL between DTR and EG with an anti-reflux procedure showed that EG led to a higher incidence of reflux than DTR (17.8% vs. 3.4%, $P < 0.05$), with similar nutritional outcomes and QoL [42]. Similarly, we found no significant differences in any domain when comparing DTR and EG after PG, although the reflux score appeared worse after EG than after DTR. In contrast to our findings, a previous study reported that EG with DFT resulted in superior 1-year QoL, as assessed by the EORTC questionnaire, compared to DTR [43]. Postoperative weight loss is a well-established factor contributing to QoL deterioration [44], and the authors observed a significantly greater degree of weight loss in the DTR group compared to patients who underwent EG with DFT. The reduced incidence of dysphagia and fewer dietary restrictions in the EG with DFT group may have facilitated greater food intake, mitigating excessive weight loss [43]. Owing to these conflicting findings, our results should be interpreted with caution, and further analysis is warranted.

In this study, we evaluated QoL using KOQUSS-40 in various clinical situations. We expected that patients undergoing chemotherapy and those who exhibited reflux on gastroscopy after surgery would experience a decrease in QoL, but we did not find any significant differences in these measures among groups. Patients might have had mild symptoms, or their symptoms might have been well controlled by medication during the postoperative period. Furthermore, patients might have exhibited varying degrees of symptom awareness after surgery. In previous studies, MIS was preferred over open surgery in terms of QoL during the first 6 months after surgery; however, this short-term benefit tended to diminish over time, with QoL becoming similar from 6 months to one year [12,45]. One study showed no difference in QoL between patients who underwent laparoscopic surgery and those who underwent open surgery [46], which is consistent with our findings. However, our study findings should be interpreted with caution owing to certain limitations. First, the number of patients who underwent open surgery ($n=44$) was significantly smaller than that of patients who underwent MIS ($n=447$). Second, we did not assess whether the type of resection was comparable between the MIS and open surgery groups. Additionally, some studies have reported that patients who underwent totally laparoscopic gastrectomy had better QoL than those who underwent laparoscopic-assisted gastrectomy [47,48]. Therefore, future studies should not merely compare QoL between MIS and open surgery but should also evaluate QoL differences based on MIS type and anastomotic method.

This study has some limitations. First, significant inconsistencies were observed in the number of patients in each group in terms of surgical approach, extent of gastric resection, and pathological stage. More than 70% of patients underwent laparoscopic DG, were identified as pT1N0, and did not require additional chemotherapy. These potential biases reflect the clinical characteristics of patients in Eastern Asia but could impede the global generalizability of our results. Second, subgroup analysis of QoL based on the extent of gastric resection and anastomosis method might be needed to adjust for various clinical factors, such as adjuvant chemotherapy and surgical approach. Third, although gastric cancer treatment initially negatively impacts QoL, many studies have reported that overall QoL returns to baseline levels within 6 months to one year after surgery [12,49]. However, certain gastrointestinal symptoms, such as dietary restrictions, dysphagia, nausea/vomiting, reflux, and diarrhea, can persist beyond one year. For clinicians, monitoring and managing these symptoms appropriately is crucial. Therefore, a study with long-term QoL follow-up is necessary in the future.

The use of the KOQUSS-40 questionnaire revealed that DG and PPG result in better QoL than TG and PG. Although further research is needed to compare postoperative QoL according to anastomosis type in DG and PG, we expect KOQUSS-40 to be a useful method for measuring QoL after gastric cancer surgery. Based on this study, we expect it to be used in various future clinical studies. KOQUSS-40 results will provide surgeons with important information that may help in selecting the appropriate procedure and improving surgical techniques to compensate for the shortcomings of each procedure. Moreover, it will enhance postoperative care by enabling clinicians to provide relevant dietary guidance and address postgastrectomy syndromes at an early stage.

SUPPLEMENTARY MATERIALS

Supplementary Fig. 1

Scores for the 9 KOQUSS-40 domains according to type of anastomosis after distal gastrectomy. Plotted with mean difference and standard error (error bars).

Supplementary Fig. 2

Scores for the 9 KOQUSS-40 domains according to type of anastomosis after proximal gastrectomy. Plotted with mean difference and standard error (error bars).

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