Original Article
Quality of life after esophagogastrostomy plus gastrojejunostomy reconstruction following proximal gastrectomy: a comparative study of three surgical procedures

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Abstract: Objective: We have previously reported a novel reconstruction method, esophagogastrostomy plus gastrojejunostomy (EGJ), after curative proximal gastrectomy for proximal gastric cancer (PGC). The aim of this study was to evaluate the quality of life (QOL) after EGJ reconstruction in patients with PGC by comparing with other two surgical procedures during a one-year postoperative period. Methods: We investigated a total of 43 PGC patients who underwent radical gastrectomy and had no evidence of recurrence or metastasis 1 year after surgery. Of these patients, 17 were treated with proximal gastrectomy followed by esophagogastrostomy (EG) reconstruction, 12 with total gastrectomy and Roux-en Y (RY) reconstruction and 14 with proximal gastrectomy followed by EGJ reconstruction procedure. The Chinese versions of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Cancer (QLQ-C30) and the site-specific module for gastric cancer (QLQ-STO22) were used to assess changes of QOL based on three different reconstruction methods. Questionnaires were completed at the baseline (before surgery) and 1, 6 and 12 months postoperatively. Results: The mean scores for most of the functional and symptom scales deteriorated significantly at 1 month after surgery and gradually improved afterwards. Global health status, appetite loss and reflux symptoms showed significant differences among three groups at the same follow-up interval. EGJ patients suffered from the least reflux symptoms, which apparently influenced global health status of the EG group. Meanwhile, Up to 75% of RY patients at 1 month and 41.7% at 6 months postoperativelycomplained of serious appetite loss symptom and resulted in poor QOL when compared with the other two groups. Conclusions: Our study showed that EGJ patients had better QOL during a 1-year period after surgeryby not only resolving the syndrome of reflux esophagitis but alsopreserving the distal stomach as well as duodenal passage.

Keywords: Quality of life, proximal gastric cancer, esophagogastrostomy, gastrojejunostomy

Introduction

Although the rates of gastric cancer decreased substantially in most parts of the world [1], it still remains the fourth and the second most common malignancy worldwide [2] and in China [3], respectively. Moreover, the incidence of cancer in the upper third of the stomach hasincreased recently [4], and the cancer-related death rate for proximal gastric cancer (PGC) is higher than what's observed for cancers at other sites of the stomach [5, 6]. Although various treatment modalities have been developed in the last few decades, surgical resection remains the only curative approach for patients with gastric cancer [7]. Nevertheless, there is still no consensus on the choice of surgical procedures for PGC. Though total gastrectomy for PGC patients may allow more extended lymph node (LN) dissection, proximal gastrectomy has been found to yield similar recurrence and survival rates while preserving the physiological functions of the gastric remnant [8]. In addition, our studies have indicated that it is not the surgical margin and LN dissection range but rather the postoperative reflux esophagitis that hamper a widespread execution of proximal gastricin PGC [9]. Several reconstruction methods,

such as pyloroplasty, jejunal interposition and gastric tube reconstruction, have been performed after proximal gastrectomy to resolve the syndrome of reflux esophagitis. However, these reconstruction procedures appear to be more complicated and lead to more postoperative complications [10-16]. We have previously reported that esophagogastrostomy plus gastrojejunostomy (EGJ) could act as a simple and effective reconstruction method after proximal gastrectomy for PGC [9].

As earlier diagnosis and advances in treatment have prolonged the survival of patients, quality of life (QOL) has become a main oncological outcome for judging the efficacy of treatment modalities [17, 18]. Patients who underwent gastrectomy undoubtedly suffered from various gastrointestinal symptoms and malfunctionsto impact their health-related QOL [19, 20]. In this study, we sought to explore the impact of EGJ procedure on QOL after curative resection for PGC by comparing three reconstruction methods.

Patients and methods

Patients

A prospective study that followed newly diagnosed PGC patients who were expected to undergo curative resection was conducted at the Cancer Center of Guangzhou Medical University between January 2013 and December 2015. The staging of gastric cancer was conducted according to the 3rd Japanese classification of gastric carcinoma [21].

Patients were deemed acceptable for the study if they met the following eligibility criteria: 1) All of them were 18-70 years old and psychologically capable of completing the QOL questionnaires as required timely. 2) Patients with early gastric cancer were not suitable for endoscopic resection. All T4 tumors were T4a. There was no T4b case. In addition, the patients did not have distant metastasis lesions. 3) None of the patients haspreviously received an abdominal operation or preoperative chemoradiotherapy. 4) Patients did not have diabetes, moderate to severe cardiovascular disease, pulmonary or renal disease, or another malignancy. Patients who suffered from severe postoperative complications, tumor recurrence or metastasis were excluded from the study. This study protocol was approved by the Cancer Center of Guangzhou Medical University ethical committee and all patients signed a written informed consent document before the study.
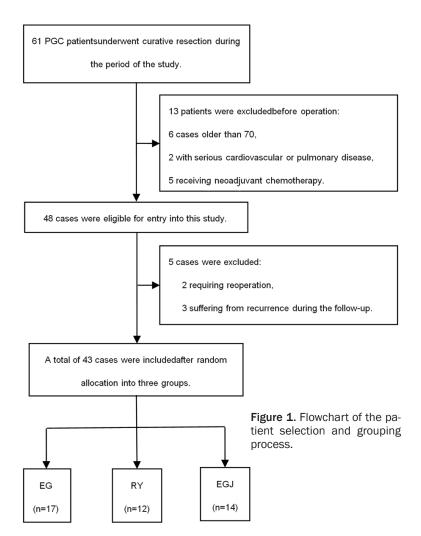
Surgical approach

All PGC patients underwent open radical surgery by the same abdominal surgery team. Three different surgical approaches: proximal gastrectomy followed by esophagogastrostomy (EG) reconstruction, total gastrectomy followed by Roux-en Y (RY) reconstruction and proximal gastrectomy followed by EGJ, were randomly conducted. The surgical procedures have been described previously [9]. Briefly, As for EG group, end-to-side direct anastomosis was executed between the esophagus and the greater curvature of the upper body of the posterior stomach wall before proximal gastrectomy. As for RY reconstruction after total gastrectomy, end-to-side esophagojejunostomy was conducted and then the RY anastomosis was made 40 cm distally.In the EGJ group, gastrojejunostomy was completed, then esophagogastrostomy and PG were performed as described in EG group.

Gastrectomy was an exclusively abdominal operation without thoracotomy. The resection margins were evaluated by frozen section biopsy intraoperatively in all patients to confirm the absence of disease. Lymph nodes were dissected according to the 3rd Japanese classification of gastric carcinoma [21]. None of the patients received combined organ resection. Patients with T3-4 tumors or any lymph node metastasis underwent six months of fluorouracil-based adjuvant chemotherapy.

Quality of life assessment

The validated Taiwan Chinese versions of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 [22] and its gastric module STO22 [23] were used to assess changes of QOL following three different reconstruction methods. The EORTC QLQ-C30 is a reliable and validated assessment of QOL [24]. The questionnaire contains 30 questions including 5 functional scales (physical, role, emotional, cognitive, and social), 3 symptom scales (fatigue, pain, and nausea), 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties), and 1 global scale. The gastric cancer module STO22 is designed to examine specific QOL of gastric cancer patients, containing 22 ques-

Figure 1. Flowchart of the patient selection and grouping process.

Statistical analysis

Statistical analysis was conducted using the statistical software SPSS13.0. The randomization was achieved using the random number table provided with SPSS software. All patients were randomly divided into 3 groups. Measurement data were compared by the One-Way ANOVA test. The associations between categorical variables were performed using the χ^2 test. The scores were expressed as means ± SD. The differences between mean values in each group were compared using the nonparametric Mann-Whitney U test or the Kruskal-Wallis test. All tests of significance were two-tailed and differences were considered statistically significant if P values <0.05.

Results

Characteristics of included population

The characteristic data for participants were showed in **Figure 1**. Sixty-one patients were intended to undergo curative resection for PGC during the period of the study. Thirteen of them were excluded before operation: 6 who were older than 70.2 with serious cardiovascular or pulmonary disease, and 5 who had received neoadjuvant chemotherapy. The remaining 48 cases were eligible for entry into this study according to the above criteria. Among them, forty-three cases were included in the end and five were excluded, including 2 requiring reoperation because of postoperative anastomotic bleeding or anastomotic fistula, and 3 suffering from recurrence during the first postoperative year.

The clinicopathological features of enrolled patients were summarized in **Table 1**. There were 17 cases of EG, 12 cases of RY and 14 cases of EGJ procedures. The average patient age of the surgical groups was as follows: EG, 53.9±12.5; RY, 51.7±12.9; and EGJ, 52.7±9.4. No significant association was found between

tions that evaluate 5 multi-item symptom scales (dysphagia, eating restrictions, pain, reflux, and anxiety) and 4 single-item symptom scales (dry mouth, taste, body image, and hair loss) [25, 26].

Patients were asked to complete the QLQ-C30 and the STO22 questionnaires before surgery and at 1, 6 and 12 months postoperatively. Time windows of ±1 weeks were applied for each postoperative assessment. All scales were linearly transformed into scores from 0 to 100 according to the scoring manual provided by the EORTC [26]. For QLQ-C30, high scores of functioning scales and lower scores of symptom scales represent better QOL. For STO22, lower scores indicate better QOL.

Patients also provided sociodemographic information including age, sex, marital status and education. Clinical information was obtained from the hospital electronic medical records.

Table 1. Clinicopathological features of patients included

Variables	EG (n=17)	RY (n=12)	EGJ (n=14)	P value
Gender				0.888
Male	10 (58.8%)	6 (50.0%)	8 (57.1%)	
Female	7 (41.2%)	6 (50.0%)	6 (42.9%)	
Age(years)	53.9±12.5	51.7±12.9	52.7±9.4	0.882
Stage				0.949
I	9 (52.9%)	5 (41.7%)	6 (42.9%)	
II	5 (29.4%)	4 (33.3%)	4 (28.6%)	
III	3 (17.6%)	3 (25.0%)	4 (28.6%)	
Adjuvant chemotherapy				0.922
Absent	6 (35.3%)	4 (33.3%)	4 (28.6%)	
Present	11 (64.7%)	8 (66.7%)	10 (71.4%)	

the surgical approach and the sex, age, or tumor stage (P>0.05). Moreover, there were no statistical differences among the three groups with regards to postoperative adjuvant chemotherapy (P>0.05).

Overall trends in QOL for all selected patients

Most of the mean scores deteriorated at 1 month after surgery and improved the reafter: For all 43 patients, the rate of missing value during the follow-up was 0.87%. For patients with the missing values, the most frequent answer from other patients was used during the analysis under the assumption of missing-at-random mechanism [27]. The mean scores for all surgical procedures, EG, RY and EGJ, were calculated in a longitudinal fashion during the first postoperative year. For most of the functional scales, the mean score was worst at 1 month postoperatively and generally improved during the course of the follow-up (**Table 2**, Figure S1A). Most of the Z values constantly increased though *P* values were <0.05. The score for the emotional functioning scale at 1 year postoperatively roughly reached the baseline level (P=0.15, **Table 2**).

Similarly, for almost all symptom scales of the EORTC QLQ-C30 and STO22 items, the mean score was worst at 1 month after surgery and generally improved thereafter (**Table 2**, Figure S1B, S1C). Particularly, the mean scores of some QLQ-C30 symptoms (dyspnea, insomnia, constipation, diarrhea and financial difficulties) after 6 months were not significantly different from those at the baseline level (P>0.05).

Changes in QOL by different surgical procedures

EGJ patients had better QOL when compared with the other two groups: The mean differences in EORTC QLQ-C30 and STO22 scores were not statistically significant at the baseline among three surgery groups (all P>0.05, **Table 3**). For almost all components of the functional scales and symptom scales in the QLQ-C30 and STO22, the mean scores deteriorated significantly at 1 month after surgery but gradually improved afterwards in each group (**Table 3**). Except for the emotional functioning scale, in all three groups most of QLQ-C30 functional scores did not return to baseline levels at 1 year after surgery. The emotional functioning scale wasworst at 1 month butgenerally increased, and there was no statistically significant difference compared to the preoperative score after 6 months (P>0.05, **Table 3**). In addition, the mean score of the global health status and QOL in the EGJ group and the role functioning in the RY group showed no statistically significant difference compared to the preoperative scores during the 12-month period postoperatively (P>0.05, **Table 3**).

For several QLQ-C30 symptom scales, such as fatigue, nausea and vomiting, and pain, in all groups the scores increased at 1 month, decreased at 6 months and did not return to baseline levels at 12 months after surgery. However, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties increased at 1 month after surgery, steadily decreased afterwards and recovered to the baseline levels at 6 months after surgery (P>0.05, **Table 3**).

As for STO22 symptom scales, chest and abdominal pain, reflux symptoms, eating restriction and anxiety, the scores were highest at 1 month after surgery without significant decrease afterwards during the one year period in three groups (P<0.01, **Table 3**). However, the scores for dysphagia, having a dry mouth, taste, body image and hair loss showed a trendto decrease after 1 month but improved to the preoperative level at 12 months in some groups.

Table 2. Mean QOL scores for all study participants

	Baseline Mean ± SD	1 Months			6 Months			12 Months		
		Mean ± SD	Z	P	Mean ± SD	Z	P	Mean ± SD	Z	P
QLQ-C30 function										
Global health status and QOL	82.2±6.7	48.4±16.9	-7.226	<0.01	71.7±11.4	-4.754	<0.01	74.6±9.6	-4.003	<0.01
Physical functioning	87.1±5.1	40.2±10.4	-8.064	<0.01	59.5±7.9	-8.086	<0.01	73.0±8.6	-6.71	<0.01
Role functioning	85.7±12.9	38.8±15.7	-7.839	<0.01	58.5±16.8	-6.397	<0.01	73.9±11.9	-3.966	<0.01
Emotional functioning	86.8±5.8	68.1±18.4	-5.431	<0.01	79.8±14.1	-2.412	<0.01	80.8±12.7	-2.425	0.15
Cognitive functioning	91.9±9.9	48.1±15.5	-7.921	<0.01	65.9±12.0	-7.152	<0.01	73.6±11.1	-6.181	<0.01
Social functioning	91.1±8.4	47.3±16.2	-8.077	<0.01	61.6±15.2	-7.459	<0.01	67.8±12.8	-7.178	<0.01
QLQ-C30 symptom										
Fatigue	13.2±8.5	69.8±18.2	-8.074	<0.01	61.5±15.8	-8.073	<0.01	49.9±11.5	-7.951	<0.01
Nausea and vomiting	15.9±13.1	55.0±15.2	-7.62	<0.01	45.3±14.7	-6.869	<0.01	33.7±11.2	-5.552	<0.01
Pain	7.4±8.4	47.7±20.4	-7.857	<0.01	36.8±17.7	-7.131	<0.01	28.7±11.1	-6.905	<0.01
Dyspnea	24.0±21.0	49.6±25.6	-4.478	<0.01	29.5±19.5	-1.291	0.197	26.4±17.5	-0.698	0.485
Insomnia	36.4±23.9	52.7±24.4	-2.926	<0.01	34.1±18.5	-0.56	0.576	33.3±16.3	-0.764	0.445
Appetite loss	20.2±19.4	44.2±21.5	-4.733	<0.01	31.8±19.2	-2.71	<0.01	27.9±16.2	-2.09	0.037
Constipation	20.9±16.3	41.9±18.0	-4.83	<0.01	27.9±17.7	-1.774	0.076	24.8±14.7	-1.155	0.248
Diarrhea	22.5±17.4	38.8±17.7	-3.909	<0.01	25.6±14.2	-0.986	0.324	21.7±16.1	-0.145	0.885
Financial difficulties	27.1±26.5	46.5±20.8	-3.438	<0.01	27.9±17.7	-0.425	0.671	24.0±15.1	-0.251	0.802
QLQ-STO22 symptom										
Dysphagia	17.6±5.7	44.7±13.6	-7.271	<0.01	38.0±11.7	-6.404	<0.01	31.3±9.8	-4.2	<0.01
Chest and abdominal pain	14.9±5.0	45.2±10.5	-8.125	<0.01	37.6±10.0	-7.857	<0.01	29.7±8.8	-7.174	<0.01
Reflux symptoms	14.2±6.2	53.0±18.1	-7.655	<0.01	45.5±16.2	-7.543	<0.01	35.4±13.1	-6.938	<0.01
Eating restriction	14.0±4.3	38.8±11.5	-8.089	<0.01	32.2±9.6	-7.875	<0.01	25.8±7.5	-6.893	<0.01
Anxiety	14.7±5.4	57.9±13.4	-8.195	<0.01	49.6±11.5	-8.211	<0.01	39.2±10.2	-7.72	<0.01
Having a dry mouth	20.9±16.3	45.0±21.7	-5.01	<0.01	36.4±16.0	-4.009	<0.01	30.2±16.0	-2.524	0.012
Taste	11.6±16.1	46.5±22.0	-6.397	<0.01	31.8±17.7	-4.784	<0.01	25.6±14.2	-3.886	<0.01
Body image	12.4±16.3	36.4±17.5	-5.43	<0.01	27.1±16.7	-3.787	<0.01	21.7±16.1	-2.574	0.010
Hair loss	2.3±8.6	29.5±24.4	-5.778	<0.01	19.4±20.9	-4.507	<0.01	14.0±16.6	-3.743	<0.01

P, Z: Compared with baseline.

When mean scores were compared among three operation groups at the same follow-up time point, most of the functional and symptom scales showed no statistically significant differences (P>0.05, **Table 3**) except for three scales, global health status, appetite loss and reflux symptoms. Significant differences were found when the mean scores of the global health status and appetite loss scales were compared among three groups at 1 and 6 months after surgery respectively. Moreover within 6 months postoperatively, the EG group indicated the worse global health status when compared with the EGJ group, while the RY group reported the worst appetite loss symptom among three groups (P<0.01, **Table 4**, Figure S2A, S2B). In detail, serious appetite loss (Quitea Bit and Very Much) was found in 75.0% (9/12) of RY grouppatients while 29.4% (5/17) of EG groupand 14.3% (2/14) of EGJ group at 1 month after surgery; when at 6 months after surgery, it was 41.7% (5/12) in RY

group while 0% (0/17) in EG groupand 7.1% (1/14) in EGJ group. In addition, patients undergoing EGJ reconstruction complained of the least reflux symptoms at various time intervals after surgery (P<0.05, **Table 4**, Figure S2C). The exception is that at 1 year postoperatively, there was no statistical difference between the RY and the EGJ groups with regard to the reflux symptoms (P=0.793, **Table 4**).

Discussion

Nowadays, gastric cancer patients and surgeons are increasingly concerned about postoperative QOL and oncological outcomes [28, 29]. Especially after patients went through gastrostomy on the upper third of stomach, the loss of lower esophageal sphincter and the acute angle of His usually lead to reflux esophagitis, which impairs postoperative QOL outcomes [30, 31]. Furthermore, reflux following proximal gastrostomy is worse than reflux after

Table 3. Mean QOL scores in patients after three different reconstruction methods

	Baseline				1 Months				6 Months				12 Months			
	EG	RY	EGJ	P*	EG (P)	RY (P)	EGJ (P)	P*	EG (P)	RY (P)	EGJ (P)	P*	EG (P)	RY (P)	EGJ (P)	P*
QLQ-C30 function																
Global health status and QOL	80.3±7.1	83.3±7.1	83.3±5.6	0.401	39.2±10.5 (<0.01)	47.2±16.7 (<0.01)	60.7±16.4 (<0.01)	0.002	66.6±9.3 (<0.01)	72.2±7.3 (<0.01)	77.3±14 (0.21)	0.041	71.5±7.8 (<0.01)	74.3±7.5 (<0.05)	78.5±12.1 (0.21)	0.229
Physical functioning	85.8±5.7	86.6±5.6	89±3.3	0.243	38.8±11.8 (<0.01)	38.8±8.4 (<0.01)	42.8±10.3 (<0.01)	0.510	58.8±8.5 (<0.01)	57.7±7.6 (<0.01)	61.9±7.1 (<0.01)	0.312	71.3±9.3 (<0.01)	72.2±8.9 (<0.01)	75.7±7.2 (<0.01)	0.375
Role functioning	86.2±13.4	83.3±14.2	86.9±11.6	0.783	34.3±16.1 (<0.01)	38.8±12.9 (<0.01)	44±16.8 (<0.01)	0.220	52.9±16.9 (<0.01)	58.3±15 (<0.01)	65.4±16.6 (<0.01)	0.162	76±12.5 (<0.05)	73.6±11.1 (0.114)	71.4±12.1 (<0.01)	0.460
Emotional functioning	85.2±3.6	86.1±4.1	89.2±8.2	0.147	68.6±16.2 (<0.01)	65.2±16.6 (<0.01)	69.8±22.9 (<0.01)	0.563	78.9±15.6 (0.231)	77.7±12.9 (0.068)	82.7±13.6 (0.21)	0.527	78.9±14.4 (0.182)	79.1±12.5 (0.114)	84.5±10.2 (0.227)	0.387
Cognitive functioning	94.1±8.2	88.8±8.2	91.6±12.6	0.282	48±13 (<0.01)	50±15.8 (<0.01)	46.4±18.6 (<0.01)	0.915	69.6±10.5 (<0.01)	66.6±14.2 (<0.01)	60.7±10.5 (<0.01)	0.092	76.4±10.3 (<0.01)	70.8±12.5 (<0.01)	72.6±10.5 (<0.01)	0.287
Social functioning	89.2±8.2	94.4±8.2	90.4±8.5	0.243	44.1±13 (<0.01)	44.4±20.5 (<0.01)	53.5±14.8 (<0.01)	0.192	63.7±17.9 (<0.01)	58.3±13.2 (<0.01)	61.9±13.7 (<0.01)	0.570	72.5±11.6 (<0.01)	68±11.1 (<0.01)	61.9±13.7 (<0.01)	0.137
QLQ-C30 symptom																
Fatigue	14.3±8.6	12±8.8	12.6±8.6	0.728	70.5±16.6 (<0.01)	72.2±21.4 (<0.01)	66.6±17.9 (<0.01)	0.759	58.1±13.9 (<0.01)	60.1±15.3 (<0.01)	66.6±17.9 (<0.01)	0.370	45.7±10.3 (<0.01)	50.9±11 (<0.01)	53.9±12.2 (<0.01)	0.164
Nausea and vomiting	16.6±13.1	16.6±12.3	14.2±14.4	0.845	54.9±15.3 (<0.01)	58.3±16.6 (<0.01)	52.3±14.4 (<0.01)	0.680	41.1±13.3 (<0.01)	43±15 (<0.01)	52.3±14.4 (<0.01)	0.111	34.3±10.9 (<0.01)	30.5±11.9 (<0.05)	35.7±11 (<0.01)	0.588
Pain	5.88±8.2	8.33±8.7	8.33±8.6	0.644	48±21.1 (<0.01)	52.7±22.2 (<0.01)	42.8±18.1 (<0.01)	0.574	32.3±17.1 (<0.01)	36.1±17.1 (<0.01)	42.8±18.1 (<0.01)	0.354	25.4±13.3 (<0.01)	27.7±8.2 (<0.01)	33.3±9.2 (<0.01)	0.163
Dyspnea	19.6±23.7	22.2±21.7	30.9±15.8	0.216	50.9±23.9 (<0.01)	50±26.5 (<0.05)	47.6±28.3 (0.094)	0.955	29.4±20 (0.205)	27.7±19.2 (0.551)	30.9±20.5 (0.982)	0.923	26.4±17.7 (0.306)	25±20.7 (0.755)	27.3±15.4 (0.769)	0.869
Insomnia	45±16.4	33.3±28.4	28.5±25.6	0.162	58.8±25 (0.079)	55.5±25.9 (0.089)	42.8±20.3 (0.164)	0.125	35.2±18.5 (0.218)	33.3±20.1 (1.00)	33.3±18.4 (0.603)	0.944	35.2±18.5 (0.218)	36.1±17.1 (0.843)	28.5±12.1 (0.91)	0.407
Appetite loss	17.6±20.8	19.4±17.1	23.8±20.3	0.655	41.1±18.7 (<0.01)	61.1±19.2 (<0.01)	33.3±18.4 (0.285)	0.003	25.4±14.5 (0.218)	47.2±17.1 (<0.01)	26.1±19.2 (0.769)	0.005	23.5±15.6 (0.339)	36.1±9.6 (0.052)	26.1±19.2 (0.769)	0.102
Constipation	19.6±16.9	22.2±16.4	21.4±16.5	0.905	45±16.4 (<0.01)	38.8±19.2 (0.089)	40.4±19.2 (<0.05)	0.664	31.3±14.2 (0.106)	27.7±19.2 (0.59)	23.8±20.3 (0.839)	0.454	27.4±13 (0.245)	25±15 (0.755)	21.4±16.5 (1.00)	0.525
Diarrhea	25.4±14.5	19.4±17.1	21.4±21.1	0.578	41.1±18.7 (<0.05)	38.8±19.2 (<0.05)	35.7±15.8 (0.094)	0.674	27.4±13 (0.786)	25±15 (0.514)	23.8±15.6 (0.701)	0.768	23.5±15.6 (0.786)	22.2±16.4 (0.755)	19±17.1 (0.874)	0.736
Financial difficulties	25.4±27.7	27.7±23.9	28.5±28.8	0.933	45±20.2 (<0.05)	47.2±22.2 (0.078)	47.6±21.5 (0.094)	0.905	27.4±17.6 (0.683)	27.7±19.2 (0.977)	28.5±17.8 (0.91)	0.984	23.5±15.6 (0.973)	25±15 (0.887)	23.8±15.6 (0.804)	0.965
QLQ-STO22 symptom																
Dysphagia	19±5.3	17.6±5.8	15.8±5.8	0.306	40.5±14.1 (<0.01)	47.2±14.3 (<0.01)	47.6±11.8 (<0.01)	0.328	36.6±10.9 (<0.01)	38.8±13.8 (<0.01)	38.8±11.3 (<0.01)	0.877	29.4±7.7 (0.099)	33.3±11.6 (<0.05)	31.7±10.5 (<0.01)	0.630
Chest and abdominal pain	15.1±4.4	13.8±5.4	15.4±5.5	0.671	47±9.7 (<0.01)	46.5±10.3 (<0.01)	41.6±11.3 (<0.01)	0.263	38.2±9.3 (<0.01)	40.2±9.9 (<0.01)	34.5±10.7 (<0.01)	0.327	30.8±8.2 (<0.01)	31.2±9.4 (<0.01)	26.7±8.7 (<0.01)	0.279
Reflux symptoms	15±5.5	12±7.4	15±5.6	0.451	66.6±14.1 (<0.01)	49±12 (<0.01)	39.6±15.5 (<0.01)	0.000	58.1±13.9 (<0.01)	43.5±8.8 (<0.01)	31.7±11.4 (<0.01)	0.000	41.8±13.9 (<0.01)	30.5±10.7 (<0.01)	31.7±11.4 (<0.01)	0.031
Eating restriction	14.2±3.9	12.5±5.6	14.8±3.5	0.472	40.6±11.3 (<0.01)	43±12.2 (<0.01)	32.7±8.9 (<0.01)	0.059	34.3±9.7 (<0.01)	34.7±10.5 (<0.01)	27.3±6.8 (<0.01)	0.076	23.5±7.3 (<0.01)	27±8 (<0.01)	27.3±6.8 (<0.01)	0.230

	EG	RY	EGJ	P	EG	RY	EGJ	P*	EG	RY	EGJ	P*	EG	RY	EGJ	P*
Anxiety	15.6±5.7	14.7±5.5	13.4±4.8	0.513	56.8±12.3 (<0.01)	58.3±15 (<0.01)	58.7±14 (<0.01)	0.931	48.3±9.5 (<0.01)	50.9±12 (<0.01)	50±13.6 (<0.01)	0.891	36.6±11.6 (<0.01)	37.9±8.8 (<0.01)	42.8±8.5 (<0.01)	0.321
Having a dry mouth	21.5±16.4	19.4±17.1	21.4±16.5	0.933	50.9±26.6 (<0.01)	44.4±16.4 (<0.05)	38±17.8 (0.056)	0.305	41.1±14.5 (<0.05)	27.7±12.9 (0.319)	38±17.8 (0.056)	0.077	33.3±11.7 (0.099)	22.2±16.4 (0.755)	33.3±18.4 (0.178)	0.121
Taste	13.7±16.9	11.1±16.4	9.5±15.6	0.763	50.9±20.8 (<0.01)	50±26.5 (<0.01)	38±17.8 (<0.01)	0.219	35.2±18.5 (<0.01)	33.3±20.1 (<0.05)	26.1±14.1 (<0.05)	0.351	27.4±13 (<0.05)	27.7±12.9 (<0.05)	21.4±16.5 (0.114)	0.413
Body image	13.7±16.9	11.1±16.4	11.9±16.5	0.905	35.2±18.5 (<0.01)	36.1±17.1 (<0.01)	38±17.8 (<0.01)	0.907	27.4±17.6 (0.062)	25±15 (0.089)	28.5±17.8 (<0.05)	0.882	21.5±16.4 (0.245)	19.4±17.1 (0.319)	23.8±15.6 (0.114)	0.787
Hair loss	1.9±8	2.7±9.6	2.3±8.9	0.968	25.4±25 (<0.01)	30.5±26.4 (<0.05)	33.3±22.6 (<0.01)	0.640	15.6±20.8 (0.079)	19.4±22.2 (0.078)	23.8±20.3 (<0.01)	0.500	9.8±15.6 (0.245)	13.8±17.1 (0.178)	19±17.1 (<0.05)	0.306

P: Compared with baseline in each group; P*: Comparison among three operation groups at the same follow-up time point.

Table 4. *P* values of every two groups were calculated by the One Way-ANOVA test after rank transformation.

	1 Months				6 Months				12 Months			
	EG	RY	EGJ	P	EG	RY	EGJ	P	EG	RY	EGJ	P
Global health status and QOL	39.2±10.5	47.2±16.7	60.7±16.4	P^1=0.049 P^2=0.000 P^3=0.002	66.6±9.3	72.2±7.3	77.3±14	P^1=0.170 P^2=0.006 P^3=0.221	-	-	-	
Appetite loss	41.1±18.7	61.1±19.2	33.3±18.4	P^1=0.004 P^2=0.225 P^3=0.000	25.4±14.5	47.2±17.1	26.1±19.2	P^1=0.002 P^2=0.914 P^3=0.003	-	-	-	
Reflux symptoms	66.6±14.1	49±12	39.6±15.5	P^1=0.000 P^2=0.000 P^3=0.040	58.1±13.9	43.5±8.8	31.7±11.4	P^1=0.001 P^2=0.000 P^3=0.010	41.8±13.9	30.5±10.7	31.7±11.4	P^1=0.010 P^2=0.016 P^3=0.793

P^1: EG vs RY, P^2: EG vs EGJ, P^3: RY vs EGJ.

total gastrostomy even though proximal gastrostomy can preserve the physiological functions of distal gastric remnant [32, 33]. In order to improve QOL after EG, several reconstruction methods were developed to lower the frequency of reflux symptoms. Zhang et al. found that esophagogastric anterior wall end-to-side anastomosis combined with pyloroplasty led to the best QOL for patients with proximal gastrostomy [34]. In another study, reconstruction after proximal gastrostomy was done with esophago-gastrostomy using a narrow gastric conduit to improve QOL [35]. Moreover, Kinoshita et al. reported that laparoscopic proximal gastrostomy with jejunal interposition had a same safety profile as theopen proximal gastrostomy with jejunal interposition did, but showed improved QOL in the short-term [36]. Shen et al. also demonstrated that most QOL scales after gastric tube reconstruction following proximal gastrostomycould gradually recover to the preoperative level [37]. Although these additional procedurescould decrease the frequency of reflux esophagitis,they were more complicated and could leadto unexpected complications when compared with EGJ reconstruction [9].

In this study, the Taiwan Chinese version of the EORTC QLQ-C30 and STO22 questionnaires, whose clinical validity, reliability and cross-cultural applicability had been previously ascertained [38], were used to detect the differences of QOL among three types of reconstruction methods after proximal gastrectomy.

For all patients, most functional scales decreased in the first postoperative month and improved over time during the one-year follow-up period, similar to other studies [39-42]. As for the emotional functioning scale, it was worst at 1 month after surgery and gradually recovered to the preoperative level during the 12-month period postoperatively, different from other studies where the emotional functional scale was worst at baseline and improved thereafter [40-42]. The reason might be that some families asked the doctors to conceal the conditions from the patients. In addition, the depression and anxiety from the operation probably overcame diagnosis of the disease and caused the lowest score, which improved afterwards along with good postoperative recovery.

All mean scores of the EORTC QLQ-C30 and STO22 symptom scales were highest at 1 month after surgery and gradually decreased thereafter. Dyspnea, insomnia, constipation, diarrhea and financial difficulties scores of the QLQ-C30 showed no statistically significant differences compared to the preoperative level by 6 months. Meanwhile, though the scores of the STO22 symptom scales showed tendency to recover, none returned to the baseline level at one year postoperatively. Therefore, further follow-up is necessary to confirm if the symptoms will fully recover as suggested by Kong et al. [41].

In this study, when mean scores of the three performed surgical procedures were respectively compared in a longitudinal fashion, most of the functional and symptom scales were worst at 1 month postoperatively but gradually improved afterwards in a similar pattern. The results were in line with above overall trends for all patients and showed similar changes as reported in a previous study [42]. Although some functional and symptom scales did not fully recover by 1 year, their tendency to decrease remained and they might return to the baseline level with further follow-up.

At the same follow-up time point, only the mean scores of global health status, appetite loss and reflux symptoms showed statistically significant differences among three operation groups. When the groups were compared with each other, the EGJ group were superior to the other two groups in reflux symptoms item, in accordance with our previous report that the EGJ reconstruction method could help to resolve the syndrome of reflux esophagitis [9]. Moreover, only the global health status of EGJ group returned to thebaseline level6 months after the surgery while the EG group showed the worse global health status than the EGJ group with in 6 months since QOL would be significantly impaired due to high rate of reflux esophagitis after EG reconstruction [43-45]. Recently, Karanicolas et al. also reported that patients who underwent proximal gastrostomy suffered worse reflux and global QOL than patients who underwent distal gastrostomy or total gastrostomy [30]. In addition, the RY group had the worst appetite loss symptom among three groups. The reason might be that total gastrectomy without duodenal passage pre-

servation would inevitably alter gastrointestinal hormone production and the elevated level of cholecystokinin (CCK) probably would have a suppressing effect on appetite [46-48], resulting in reduced QOL in RY reconstruction patients.

There are several limitations in our study. First of all, the sample size was small and the one-year follow-upwas too short. More cases withlonger follow-ups would be necessary to confirm the benefits of EGJ procedure on QOL results. Secondly, QOL from EGJ procedure could not be directly that from other reconstruction methods, such as pyloroplasty, jejunal interposition and gastric tube reconstruction because those procedures were not performed in our department. Lastly, adjuvant chemotherapy might interfere the final QOL results [49]. However, QOL measures were not conducted for patients with or without adjuvant chemotherapy in our study. Delamination study on more patients is essential to evaluate the impact of postoperative chemotherapy on QOL for patients after the gastrostomy for proximal gastric cancer.

In summary, this present study indicated a better QOL outcome in the first postoperative year for EGJ patients compared with both EG and RY groups. Long term observation with large sample size will be necessary to comprehend the tendency of QOL by comparing different types of surgery.

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Disclosure of conflict of interest

None.

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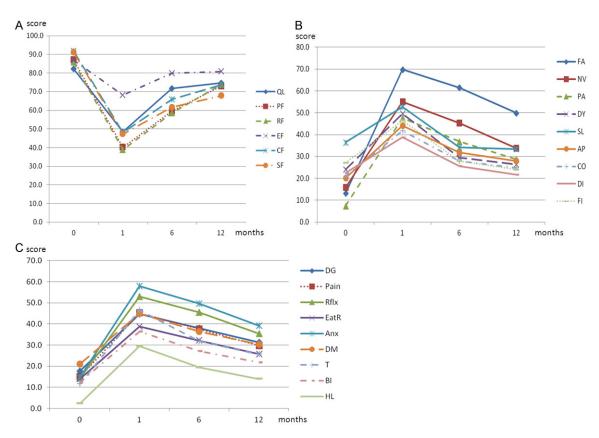
Figure S1. A. Mean scores of the QLQ-C30 functional scales; B. Mean scores of the QLQ-C30 symptom scales; C. Mean scores of the STO22 symptom scales.
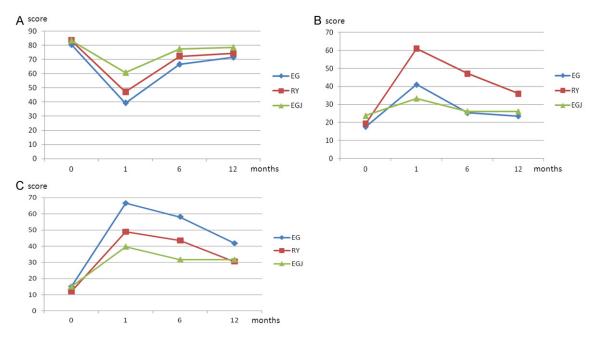

Figure S2. A. Scores of the global health status scale in each group; B. Scores of the appetite loss scale in each group; C. Scores of the reflux symptoms scale in each group.