

Double tract reconstruction reduces reflux esophagitis and improves quality of life after radical proximal gastrectomy for patients with upper gastric or esophagogastric adenocarcinoma

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Abstract

Background: The aim of the present study was to compare the difference between double tract reconstruction and esophagogastrostomy after proximal gastrectomy.

Methods: Patients who underwent radical proximal gastrectomy with esophagogastrostomy or double tract reconstruction from December 2014 to May 2019 were included in this study.

Results: Sixty-four patients were included in this study and divided into two groups according to reconstruction method. The two groups were well balanced in terms of length of postoperative hospital stay, blood loss volume, postoperative complications, and 5-year disease-free survival (DFS). The operation duration in the double tract reconstruction group was longer than that in the esophagogastrostomy group (240 min vs 195 min, $P = 0.001$). The rates of postoperative reflux esophagitis in the double tract reconstruction group and esophagogastrostomy group were 8.0% and 30.8%, respectively ($P = 0.032$). The multivariable logistic regression analysis showed that the reconstruction method was the only independent risk factor for reflux esophagitis ($P = 0.004$). Patients in the double tract reconstruction group had better global health status ($P < 0.001$) and emotional functioning ($P < 0.001$), and complained less about nausea and vomiting ($P < 0.001$), pain ($P = 0.039$), insomnia ($P = 0.003$), and appetite loss ($P < 0.001$) based on the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire. Regarding the EORTC QLQ-STO22 questionnaire, patients in the double tract reconstruction group complained less about dysphagia ($P = 0.030$), pain ($P = 0.008$), reflux ($P < 0.001$), eating ($P < 0.001$), anxiety ($P < 0.001$), dry mouth ($P = 0.007$), and taste ($P = 0.001$). The multiple linear regression analysis showed that reconstruction method, postoperative complications, reflux esophagitis, and operation duration had a linear relationship with the global health status score.

Conclusions: Double tract reconstruction after proximal gastrectomy was comparable with esophagogastrostomy in terms of perioperative safety and 5-year DFS. Double tract reconstruction could better prevent reflux esophagitis and improve quality of life. There was a linear relationship between global health status score and reconstruction method, reflux esophagitis, postoperative complications, and operation duration.

Background

Gastric cancer is a severe threat worldwide, especially in the eastern Asian area. It has been reported that gastric cancer is the fifth most common cancer and the third leading cause of cancer-related death globally [1]. In China, gastric cancer is the third leading cause of cancer-related death, and its incidence ranks second among all malignancies. There are more than 410,000 new cases and 290,000 cancer-related deaths each year [2, 3].

In recent years, the incidence of proximal gastric cancer has steadily increased [4]. With the advancements in diagnostic techniques, an increasing number of patients with early gastric cancer are

being diagnosed. According to the Japanese Gastric Cancer Treatment Guidelines, proximal gastrectomy is recommended for patients with upper gastric adenocarcinoma at an early stage or those with adenocarcinoma of the esophagogastric junction with a tumor size less than 4 cm [5]. As a result, the number of patients needing proximal gastrectomy has increased. Moreover, perioperative safety and postoperative quality of life after proximal gastrectomy have gained increasing attention [6–8]. At present, a major problem of proximal gastrectomy is the high incidence of reflux esophagitis. Although partial function of the stomach is preserved, quality of life is impaired. Therefore, several reconstruction methods have been attempted to solve this problem. According to the Japanese Gastric Cancer Treatment Guidelines, double tract reconstruction and esophagogastrostomy are two of the recommended reconstructions for proximal gastrectomy [5]. Esophagogastrostomy is the traditional and most widely performed reconstruction method after proximal gastrectomy [9]. The main deficiency of esophagogastrostomy might be the high incidence of reflux esophagitis. It has been reported that the incidence of reflux esophagitis after esophagogastrostomy ranges from 9.1–35.3% [10, 11]. Conversely, some studies have reported that double tract reconstruction might reduce the incidence of reflux esophagitis after proximal gastrectomy [12, 13]. However, double tract reconstruction is more complicated than esophagogastrostomy, and there is a lack of high-level evidence to support the advantages of double tract reconstruction [4].

Therefore, the best reconstruction method after proximal gastrectomy is still controversial. Moreover, postoperative quality of life after proximal gastrectomy with esophagogastrostomy or double tract reconstruction is rarely investigated or reported. Thus, the purpose of the present study is to compare the differences between double tract reconstruction and esophagogastrostomy after proximal gastrectomy, and to identify the superiority of double tract reconstruction.

Methods

Patients

The patients' clinical and pathological data were retrospectively collected from a prospectively maintained database at the Peking University Cancer Hospital. Between December 2014 and May 2019, patients who underwent radical proximal gastrectomy with esophagogastrostomy, or double tract reconstruction were included in the present study. All patients were diagnosed with upper-third gastric adenocarcinoma at an early clinical stage or adenocarcinoma of the esophagogastric junction with a tumor size less than 4 cm. The diagnosis and clinical stage were confirmed by endoscopic biopsy analysis, ultrasound endoscopy, chest X-ray, abdominopelvic computed tomography scans, and laparoscopic exploration. The terminology was defined based on the Japanese classification of gastric carcinoma [14]. The clinical and pathological stages were classified based on the 8th edition Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) TNM staging system [15].

This study was performed with approval from the Ethics Committee of Peking University Cancer Hospital (reference no. 2018KT97). Informed consent was obtained from each enrolled patient.

Surgical procedure

The surgical procedure in our department was performed in accordance with the Japanese Gastric Cancer Treatment Guidelines [16]. Radical proximal gastrectomy included resection of the proximal stomach and part of the abdominal esophagus and preserved more than half of the stomach. The reconstruction method was discussed and determined by both the patients and surgeons before surgery. The degree of lymph node dissection (LND) was also performed in accordance with the Japanese treatment guidelines [16]. D1 or D1 + lymphadenectomy was chosen according to the disease stage. Esophagogastrostomy reconstruction was performed by an end-to-side anastomosis between the esophagus and remnant stomach. The anastomosis was located on the anterior wall of the remnant stomach. For double tract reconstruction, the jejunum 25 cm distal to the Treitz ligament was transected, distal limb of the jejunum was lifted to prepare the esophagojejunostomy. An end-to-side esophagojejunostomy was performed with a circular stapler, and the jejunal stump was closed with a linear stapler. Next, a side-to-side gastrojejunostomy was performed 15 cm below the esophagojejunostomy. Finally, a side-to-side jejunojejunostomy was performed 15–20 cm below the gastrojejunostomy.

Clinical and pathological characteristics

The clinical and pathological characteristics of patients collected from the database included age, gender, body mass index (BMI), tumor location, proximal and distal margins, degree of differentiation, Lauren classification, tumor size, pT stage, pN stage, pTNM stage, number of harvested lymph nodes (LNs), degree of LND, lymphovascular invasion (LVI), perineural invasion (PNI), and adjuvant chemotherapy. The intraoperative and postoperative parameters included postoperative hospital stay, blood loss volume, operation duration, postoperative complications, 30-day reoperation rate, and 30-day mortality rate. Complications were defined according to the Clavien-Dindo classification system [17].

Follow-up

All patients were recommended to go to the outpatient clinic to receive re-examinations every three months in the first three years after the operation, every six months in the next two years and every year thereafter. The re-examinations mainly included physical examination, laboratory blood tests, and computed tomography scans. Endoscopy was recommended once a year after the operation. The Los Angeles classification was applied to evaluate the degree of reflux esophagitis [18]. Patient quality of life was evaluated by the validated Chinese Mandarin edition of the EORTC QLQ-C30 version 3.0 questionnaire and EORTC QLQ-STO22 questionnaire. Permission to use these questionnaires in the

present study was obtained from the EORTC Quality of Life Group. The patients were invited to complete these two questionnaires approximately twelve months after the operation. The last follow-up date was May 2020. The follow-up assessments were conducted mainly through telephone interviews, email communication, or outpatient examinations.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 26.0 software (SPSS Inc., Armonk, NY). Continuous variables with normal or skewed distributions are expressed as the mean \pm standard deviation or median with interquartile range, respectively. Student's t-test or Mann-Whitney U test was used to compare variables with normal or skewed distributions among groups, respectively. Categorical variables are represented by the number of cases with percentage and were compared by the chi-square test or Fisher's exact test. Kaplan-Meier survival analysis and the log-rank test were used to compare DFS between the two groups. Univariate analysis and multivariate logistic regression analysis were conducted to identify the risk factors for reflux esophagitis. Simple and multiple linear regression analyses were applied to identify factors that might affect the global health status score in the EORTC QLQ-C30 questionnaire. A linear regression equation was established to describe the factors related to global health status. $P < 0.05$ (two-sided) was considered significant in the statistical analysis.

Results

Clinical and pathological characteristics

Altogether, sixty-four patients were included in this study. Thirty-nine patients underwent esophagogastrectomy reconstruction and twenty-five patients underwent double tract reconstruction. Age, gender, BMI, tumor location, proximal and distal margins, differentiation, Lauren classification, number of harvested LNs, and LVI were comparable between the two groups (Table 1). The proportion of patients with early-stage disease was higher in the double tract reconstruction group than in the esophagogastrectomy group ($P = 0.031$). The tumor size was smaller in the double tract reconstruction group than in the esophagogastrectomy group (1.5 cm vs. 3.0 cm, $P = 0.010$). The proportion of D1 + lymphadenectomy was lower in the double tract reconstruction group than in the esophagogastrectomy group (56.0% vs. 79.5%, $P = 0.045$). The rate of PNI was lower in the double tract reconstruction group than in the esophagogastrectomy group (12.0% vs. 38.5%, $P = 0.044$). Fewer patients received adjuvant chemotherapy in the double tract reconstruction group than in the esophagogastrectomy group (32.0% vs. 59.0%, $P = 0.035$).

Table 1
Clinical and pathological characteristics of the patients

Clinicopathological characteristics	EG (n = 39)	DT (n = 25)	P value
Age, mean±SD, year	62.1±9.1	64.5±8.9	0.314
Gender, n (%)			0.137
Male	31 (79.5%)	24 (96.0%)	
Female	8 (20.5%)	1 (4.0%)	
BMI, mean±SD, kg/m ²	24.5±3.7	24.5±2.6	0.983
Tumor location, n (%)			0.860
AEG	22 (56.3%)	15 (60%)	
Upper third of the stomach	17 (43.6%)	10 (40%)	
Proximal margin, median (IQR), cm	2.0 (1.5-2.0)	2.0 (1.2-3.0)	0.408
Distal margin, median (IQR), cm	5.0 (2.5-6.0)	5.0 (3.0-7.5)	0.293
Differentiation, n (%)			0.887
Well	6 (15.4%)	5 (20.0%)	
Moderate	17 (43.6%)	10 (40.0%)	
Poor	16 (41.0%)	10 (40.0%)	
Lauren classification, n (%)			0.788
Intestinal	24 (61.5%)	14 (56.0%)	
Diffuse	7 (18.0%)	4 (16.0%)	
Mixed	8 (20.5%)	7 (28.0%)	
Tumor size, median (IQR), cm	3.0 (2.0–4.0)	1.5 (1.2-3.0)	0.010
pT stage ^a , n (%)			0.033
T1a	8 (20.5%)	5 (20.0%)	
T1b	9 (23.1%)	13 (52.0%)	

EG, esophagogastrotomy; DT, double tract reconstruction; SD, standard deviation; BMI, body mass index; AEG, adenocarcinoma of the esophagogastric junction; IQR, interquartile range; LNs, lymph nodes; LND, lymph node dissection; LVI, lymphovascular invasion; PNI, perineural invasion.

^a 8th UICC/AJCC TNM staging system for gastric cancer

Statistically significant values are in bold.

Clinicopathological characteristics	EG (n = 39)	DT (n = 25)	P value
T2	8 (20.5%)	6 (24.0%)	
T3	10 (25.6%)	1 (4.0%)	
T4a	4 (10.3%)	0 (0.0%)	
T4b	0 (0.0%)	0 (0.0%)	
pN stage ^a , n (%)			0.034
N0	24 (61.5%)	23 (92.0%)	
N1	5 (12.8%)	2 (8.0%)	
N2	8 (20.5%)	0 (0.0%)	
N3a	2 (5.2%)	0 (0.0%)	
N3b	0 (0.0%)	0 (0.0%)	
pTNM stage ^a , n (%)			0.031
IA	16 (41.0%)	17 (68.0%)	
IB	5 (12.8%)	6 (24.0%)	
IIA	4 (10.3%)	2 (8.0%)	
IIB	8 (20.5%)	0 (0.0%)	
IIIA	4 (10.3%)	0 (0.0%)	
IIIB	2 (5.1%)	0 (0.0%)	
IIIC	0 (0.0%)	0 (0.0%)	
Number of harvested LNs, median (IQR)	22.5 (17.0–31.0)	19.0 (16.3–23.0)	0.055
Degree of LND, n (%)			0.045
D1	8 (20.5%)	11 (44.0%)	
D1 ⁺	31 (79.5%)	14 (56.0%)	
LVI, n (%)			0.080

EG, esophagogastrotomy; DT, double tract reconstruction; SD, standard deviation; BMI, body mass index; AEG, adenocarcinoma of the esophagogastric junction; IQR, interquartile range; LNs, lymph nodes; LND, lymph node dissection; LVI, lymphovascular invasion; PNI, perineural invasion.

^a 8th UICC/AJCC TNM staging system for gastric cancer

Statistically significant values are in bold.

Clinicopathological characteristics	EG (n = 39)	DT (n = 25)	<i>P</i> value
No	23 (59.0%)	20 (80.0%)	
Yes	16 (41.0%)	5 (20.0%)	
PNI, n (%)			0.044
No	24 (61.5%)	22 (88.0%)	
Yes	15 (38.5%)	3 (12.0%)	
Adjuvant chemotherapy, n (%)			0.035
No	16 (41.0%)	17 (68.0%)	
Yes	23 (59.0%)	8 (32.0%)	
EG, esophagogastrostomy; DT, double tract reconstruction; SD, standard deviation; BMI, body mass index; AEG, adenocarcinoma of the esophagogastric junction; IQR, interquartile range; LNs, lymph nodes; LND, lymph node dissection; LVI, lymphovascular invasion; PNI, perineural invasion.			
^a 8th UICC/AJCC TNM staging system for gastric cancer			
Statistically significant values are in bold.			

Perioperative parameters and survival

The two groups were well balanced in terms of length of postoperative hospital stay, blood loss volume, and postoperative complications (Table 2). The operation duration in the double tract reconstruction group was longer than that in the esophagogastrostomy group (240 min vs 195 min, $P = 0.001$). The 30-day reoperation rate and 30-day mortality rate were comparable between the two groups.

Table 2
Intraoperative and postoperative parameters of the patients

Perioperative parameters	EG (n = 39)	DT (n = 25)	Pvalue
Postoperative hospital stay, median (IQR), day	11 (10–14)	13 (11–18)	0.220
Operation duration, median (IQR), min	195 (170–240)	240 (210–270)	0.001
Blood loss volume, median (IQR), ml	100 (50–100)	50 (50–100)	0.189
Postoperative complication*, n (%)			1.000
No	32 (82.1%)	21 (84.0%)	
Yes	7 (17.9%)	4 (16.0%)	
Anastomotic leakage	4 (10.3%)	2 (8.0%)	
Anastomotic bleeding	0 (0.0%)	0 (0.0%)	
Anastomotic stenosis	0 (0.0%)	0 (0.0%)	
Effusion	3 (7.7%)	2 (8.0%)	
Infection	4 (10.3%)	2 (8.0%)	
Gastrointestinal dysfunction	2 (5.1%)	0 (0.0%)	
30-day reoperation rate	0 (0.0%)	0 (0.0%)	1.000
30-day mortality rate	0 (0.0%)	0 (0.0%)	1.000
EG, esophagogastrostomy; DT, double tract reconstruction; IQR, interquartile range.			
* Complications were defined according to the Clavien-Dindo classification system.			
Statistically significant values are in bold.			

As of May 2020, the median follow-up time was 23.1 months (range: 11.4–63.2 months). The 5-year DFS rates in the esophagogastrostomy group and double tract reconstruction group were 90.9% and 88.9%, respectively ($P=0.707$, Fig. 1).

Reflux esophagitis

Reflux esophagitis occurred in twelve patients (30.8%) in the esophagogastrostomy group and two patients (8.0%) in the double tract reconstruction group ($P=0.032$, Table 3). Of the twelve patients who were diagnosed with reflux esophagitis in the esophagogastrostomy group, nine patients were classified as level A and three patients were classified as level B according to the Los Angeles classification. In the double tract reconstruction group, both patients were classified as level A according to the Los Angeles classification.

Table 3
Evaluation of postoperative reflux esophagitis of the patients

	EG (n = 39)	DT (n = 25)	<i>P</i> value
Reflux esophagitis			0.032
No	27 (69.2%)	23 (92.0%)	
Yes	12 (30.8%)	2 (8.0%)	
Los Angeles classification			
A	9 (23.1%)	2 (8.0%)	
B	3 (7.7%)	0 (0.0%)	
EG, esophagogastrostomy; DT, double tract reconstruction.			
Statistically significant values are in bold.			

To identify the risk factors for postoperative reflux esophagitis, a univariate analysis was performed (Table 4). Then, all factors with a *P* value less than 0.2 were included in the multivariable logistic regression analysis. Finally, the reconstruction method was found to be the only independent risk factor for reflux esophagitis (*P* = 0.004, Table 4).

Table 4
Univariate analysis and multivariate logistic regression analysis of reflux esophagitis

Univariate analysis	<i>P</i> value	Multivariate analysis	OR (95% CI)	<i>P</i> value
Age	0.696	Reconstruction method		0.004
Gender	0.644	EG	1	
BMI	0.408	DT	0.078 (0.009–0.674)	
Tumor location	1.000			
Proximal margin	0.568			
Distal margin	0.418			
Differentiation	1.000			
Lauren classification	0.143			
Tumor size	0.689			
pT stage	0.153			
pN stage	0.518			
pTNM stage	0.405			
Number of harvested LNs	0.179			
Degree of LND	0.526			
LVI	1.000			
PNI	0.085			
Adjuvant chemotherapy	0.232			
Operation duration	0.128			
Blood loss volume	0.113			
Postoperative hospital stay	0.318			
Postoperative complication	1.000			
Reconstruction method	0.032			
EG, esophagogastrostomy; DT, double tract reconstruction; BMI, body mass index; LNs, lymph nodes; LND, lymph node dissection; LVI, lymphovascular invasion; PNI, perineural invasion; OR, odds ratio; CI, confidence interval.				
Statistically significant values are in bold.				

Quality of life

The scores of the EORTC QLQ-C30 version 3.0 questionnaire were compared between the esophagogastrectomy and double tract reconstruction groups (Table 5, Fig. 2, and Fig. 3). The global health status score was higher in the double tract reconstruction group than in the esophagogastrectomy group (83.3 vs. 50.0, $P < 0.001$). Compared with patients in the esophagogastrectomy group, patients in the double tract reconstruction group had better emotional functioning ($P < 0.001$), and complained less about nausea and vomiting ($P < 0.001$), pain ($P = 0.039$), insomnia ($P = 0.003$), and appetite loss ($P < 0.001$). The results of the EORTC QLQ-STO22 questionnaire were also compared between groups (Table 6 and Fig. 4). Patients in the double tract reconstruction group complained less about dysphagia ($P = 0.030$), pain ($P = 0.008$), reflux ($P < 0.001$), eating ($P < 0.001$), anxiety ($P < 0.001$), dry mouth ($P = 0.007$), and taste ($P = 0.001$) than those in the esophagogastrectomy group.

Table 5
The scores of the EORTC QLQ-C30 version 3.0 questionnaire

	EG, median (IQR)	DT, median (IQR)	<i>P</i> value
Global health status	50.0 (33.3–50.0)	83.3 (66.7–83.3)	< 0.001
Functional scales			
Physical functioning	80.0 (66.7–86.7)	80 (66.7–86.7)	0.600
Role functioning	66.7 (66.7–66.7)	66.7 (66.7–83.3)	0.108
Emotional functioning	50.0 (41.7–66.7)	66.7 (66.7–79.2)	< 0.001
Cognitive functioning	100.0 (66.7–100.0)	100.0 (75.0-100.0)	0.142
Social functioning	66.7 (66.7–66.7)	66.7 (66.7–83.3)	0.073
Symptom scales			
Fatigue	33.3 (33.3–33.3)	33.3 (0.0-33.3)	0.473
Nausea and vomiting	50.0 (50.0-83.3)	16.7 (16.7–16.7)	< 0.001
Pain	16.7 (16.7–33.3)	16.7 (0.0-33.3)	0.039
Dyspnea	0.0 (0.0-33.3)	0.0 (0.0–0.0)	0.072
Insomnia	33.3 (0.0-33.3)	0.0 (0.0–0.0)	0.003
Appetite loss	33.3 (33.3–33.3)	0.0 (0.0-33.3)	< 0.001
Constipation	0.0 (0.0-33.3)	0.0 (0.0–0.0)	0.082
Diarrhea	0.0 (0.0-33.3)	0.0 (0.0–0.0)	0.129
Financial difficulties	33.3 (0.0-33.3)	33.3 (0.0-33.3)	0.638
EG, esophagogastrectomy; IQR, interquartile range; DT, double tract reconstruction.			
Statistically significant values are in bold.			

Table 6
The scores of the EORTC QLQ-STO22 questionnaire

Symptom scales	EG, median (IQR)	DT, median (IQR)	<i>P</i> value
Dysphagia	22.2 (11.1–33.3)	11.1 (11.1–22.2)	0.030
Pain	33.3 (16.7–41.7)	25.0 (12.5–25.0)	0.008
Reflux	88.9 (66.7–100.0)	33.3 (0.0-44.4)	< 0.001
Eating	41.7 (33.3–66.7)	25.0 (20.8–33.3)	< 0.001
Anxiety	77.8 (66.7–100.0)	55.6 (44.4–66.7)	< 0.001
Dry mouth	33.3 (33.3–66.7)	33.3 (0.0-33.3)	0.007
Taste	66.7 (33.3–66.7)	33.3 (0.0-33.3)	0.001
Body image	66.7 (66.7–100.0)	66.7 (66.7–100.0)	0.807
Hair loss	0.0 (0.0–0.0)	0.0 (0.0-33.3)	0.494
EG, esophagogastrostomy; IQR, interquartile range; DT, double tract reconstruction.			
Statistically significant values are in bold.			

In the simple linear regression analysis of global health status, the results showed that pT stage ($P=0.035$), pN stage ($P=0.016$), pTNM stage ($P=0.015$), PNI ($P=0.022$), operation duration ($P=0.008$), reflux esophagitis ($P=0.001$), and reconstruction method ($P=0.001$) were all correlated with global health status (Table 7). All variables with a P value less than 0.1 were included in the multiple linear regression analysis. A linear regression equation was established, and the results showed a linear relationship between the global health status score and reconstruction method, postoperative complications, reflux esophagitis, and operation duration (Table 7 and Table 8).

Table 7
Simple and multiple linear regression analyses of global health status

Simple analysis	P value	Multiple analysis	P Value
Age	0.339	Reconstruction method	< 0.001
Gender	0.057	Postoperative complication	< 0.001
BMI	0.828	Reflux esophagitis	0.003
Tumor location	0.601	Operation duration	0.001
Proximal margin	0.436		
Distal margin	0.128		
Differentiation	0.703		
Lauren classification	0.416		
Tumor size	0.085		
pT stage	0.035		
pN stage	0.016		
pTNM stage	0.015		
Number of harvested LNs	0.130		
Degree of LND	0.180		
LVI	0.284		
PNI	0.022		
Adjuvant chemotherapy	0.052		
Operation duration	0.008		
Blood loss volume	0.219		
Postoperative hospital stay	0.215		
Postoperative complication	0.060		
Reflux esophagitis	0.001		
Reconstruction method	0.001		
BMI, body mass index; LNs, lymph nodes; LND, lymph node dissection; LVI, lymphovascular invasion; PNI, perineural invasion.			
Statistically significant values are in bold.			

Table 8
Multiple linear regression equation of global health status

Linear regression equation	Adjusted R-squared	F-value	P value
	0.791	22.961	< 0.001
GHS score = 23.8 · RM + 0.1 · OD - 14.3 · PC - 9.6 · RE + 44.2 RM: double tract reconstruction = 1, esophagogastrostomy = 0 OD: operation duration, expressed in minutes PC: without complication = 0, with complication = 1 RE: without reflux esophagitis = 0, with reflux esophagitis = 1			
GHS, global health status; RM, reconstruction method; PC, postoperative complication; RE, reflux esophagitis; OD, operation duration.			
Statistically significant values are in bold.			

Discussion

Esophagogastrostomy reconstruction is a traditional reconstruction method after proximal gastrectomy. However, esophagogastrostomy is associated with a high incidence of postoperative reflux esophagitis. To address this disadvantage, several modified reconstruction methods, including double tract reconstruction, have been attempted.

The safety and feasibility of double tract reconstruction after proximal gastrectomy have been of great concern in recent years. In the present study, the results showed that there was no significant difference in blood loss volume, length of postoperative hospital stay or postoperative complications between esophagogastrostomy and double tract reconstruction. The operation duration was longer in the double tract reconstruction group than in the esophagogastrostomy group in this study. Considering that the double tract reconstruction procedure is more complex than the esophagogastrostomy procedure, it is reasonable that the operation duration of double tract reconstruction was longer than that of esophagogastrostomy. On the other hand, whether double tract reconstruction causes a high rate of complications because of the technical complexity and increased number of anastomoses has been questioned [10, 11, 19]. In the present study, postoperative complications, blood loss volume and length of postoperative hospital stay were all comparable between the two reconstruction methods. These results suggest that the complexity of the surgical procedure does not increase the risk of the operation.

The anti-reflux function of double tract reconstruction after proximal gastrectomy has been investigated in previous studies [12, 13]. However, most of the results are based on studies with exceedingly small samples. In the present study, the rates of reflux esophagitis in the esophagogastrostomy group and double tract reconstruction group were 30.8% and 8.0%, respectively ($P = 0.032$). Moreover, multivariate logistic regression analysis showed that the reconstruction method was the only independent risk factor

for reflux esophagitis ($P= 0.004$). Double tract reconstruction is a protective factor against postoperative reflux esophagitis after proximal gastrectomy. Considering the reconstruction procedure, it is possible that the mechanism of anti-reflux function is mainly attributed to the lifted jejunum between esophagojejunostomy and gastrojejunostomy [20, 21].

Many studies have reported nutritional status after proximal gastrectomy [13, 22, 23]. However, postoperative quality of life after proximal gastrectomy has rarely been reported before. Thus, the present study compared quality of life after proximal gastrectomy with the EORTC QLQ-C30 version 3.0 and QLQ-STO22 questionnaires between esophagogastrectomy and double tract reconstruction. According to the EORTC scoring manual, a higher score represented a better level of functioning, or a worse level of symptoms [24]. In the present study, double tract reconstruction had obvious advantages over esophagogastrectomy based on the EORTC QLQ-C30 questionnaire, including in global health status, emotional functioning, nausea and vomiting, pain, insomnia, and appetite loss (Table 5). For the EORTC QLQ-STO22 questionnaire, symptoms including dysphagia, pain, reflux, eating, anxiety, dry mouth, and taste were much milder in the double tract reconstruction group than in the esophagogastrectomy group (Table 6). The mechanism of the anti-reflux function of double tract reconstruction has been discussed in the previous paragraph of this section. Furthermore, previous studies reported that the prevention of reflux esophagitis might improve the psychological, physical, and social functioning of patients [25]. Moreover, the prevention of reflux esophagitis could also relieve symptoms such as nausea, vomiting, pain, insomnia, appetite loss, dysphagia, eating, anxiety, and dry mouth [26–31]. Therefore, the better scores in the double tract reconstruction group might be due to the superiority of the surgical procedure itself in preventing reflux esophagitis after proximal gastrectomy.

Considering that the global health status score in the EORTC QLQ-C30 questionnaire can reflect overall quality of life, a linear regression analysis was performed to investigate the related factors [24]. The results showed that reconstruction method ($P < 0.001$), postoperative complications ($P < 0.001$), reflux esophagitis ($P = 0.003$), and operation duration ($P = 0.001$) had a linear relationship with the global health status score (Table 8). The mechanism of double tract reconstruction in preventing reflux esophagitis and improving quality of life has been discussed in the previous paragraph. Furthermore, some studies have reported that postoperative complications could induce physical and mental discomfort and impair quality of life [32, 33]. Interestingly, operation duration was also identified in the equation. The operation duration could reflect how elaborate the operation was. Theoretically, an elaborate operation could protect the nerves better, and better preserve organ function [34–36]. Therefore, a longer operation duration might improve quality of life after the operation.

The present study also has some limitations. First, selection bias was difficult to avoid because this was a retrospective study. The pathological stage was not comparable between the two groups, resulting in differences in tumor size, degree of LND, PNI, and adjuvant chemotherapy. This phenomenon was mainly caused by the different choices of the patients. In our hospital, the reconstruction method was discussed and determined by both the patients and surgeons. Patients with early-stage disease were more likely to choose double tract reconstruction after learning about its superiority because these patients might pay

more attention to quality of life after the operation. Thus, the shared decision-making method might be the cause of the bias. However, multivariable logistic regression analysis and multiple linear regression analysis could neutralize the confounding effects of these factors. Second, the sample size of the present study was not large enough, which might make the results of this study less convincing. Further large-scale, prospective, randomized controlled trial is needed to validate the results of the study.

Conclusions

Double tract reconstruction after proximal gastrectomy was comparable with esophagogastrostomy in terms of perioperative safety and 5-year DFS. Double tract reconstruction could better prevent reflux esophagitis and improve quality of life. The reconstruction method was the only independent risk factor for reflux esophagitis. There was a linear relationship between global health status score and reconstruction method, reflux esophagitis, postoperative complications, and operation duration.

Abbreviations

DFS, disease-free survival; EORTC, European Organization for Research and Treatment of Cancer; UICC, Union for International Cancer Control; AJCC, American Joint Committee on Cancer; LND, lymph node dissection; BMI, body mass index; LNs, lymph nodes; LVI, lymphovascular invasion; PNI, perineural invasion.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and had been authorized by the Ethics Committee of Peking University Cancer Hospital (Reference No. 2018KT97) before beginning the study. Each patient in this study provided signed informed consent.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions:

J-FJ and Z-DB designed this study and were in charge of its coordination. XJ, C-GJ, KJ, JZ, X-JW, X-LZ, Z-YJ, TF, BF and A-QW participated in the data collection, statistical analysis, and the interpretation of data and results. XJ, C-GJ and KJ drafted the manuscript. XJ, C-GJ and KJ are joint first authors. All authors have read and approved the final manuscript.

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Figures

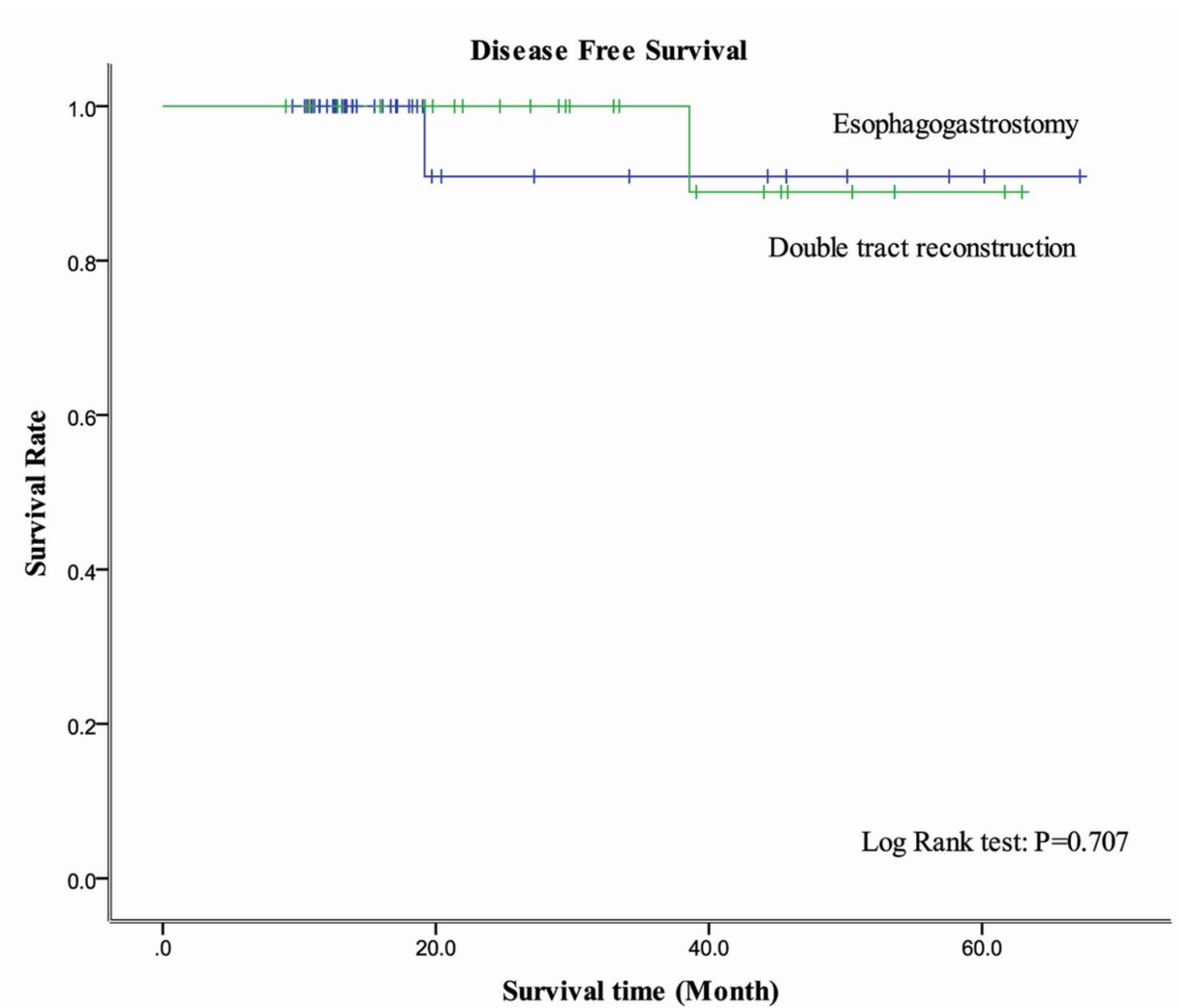


Figure 1

Five-year DFS curves of patients in the esophagogastrostomy and double tract reconstruction groups. The 5-year DFS rates were comparable between the two groups. The 5-year DFS rates of the esophagogastrostomy and double tract reconstruction groups were 90.9% and 88.9%, respectively ($P = 0.707$).

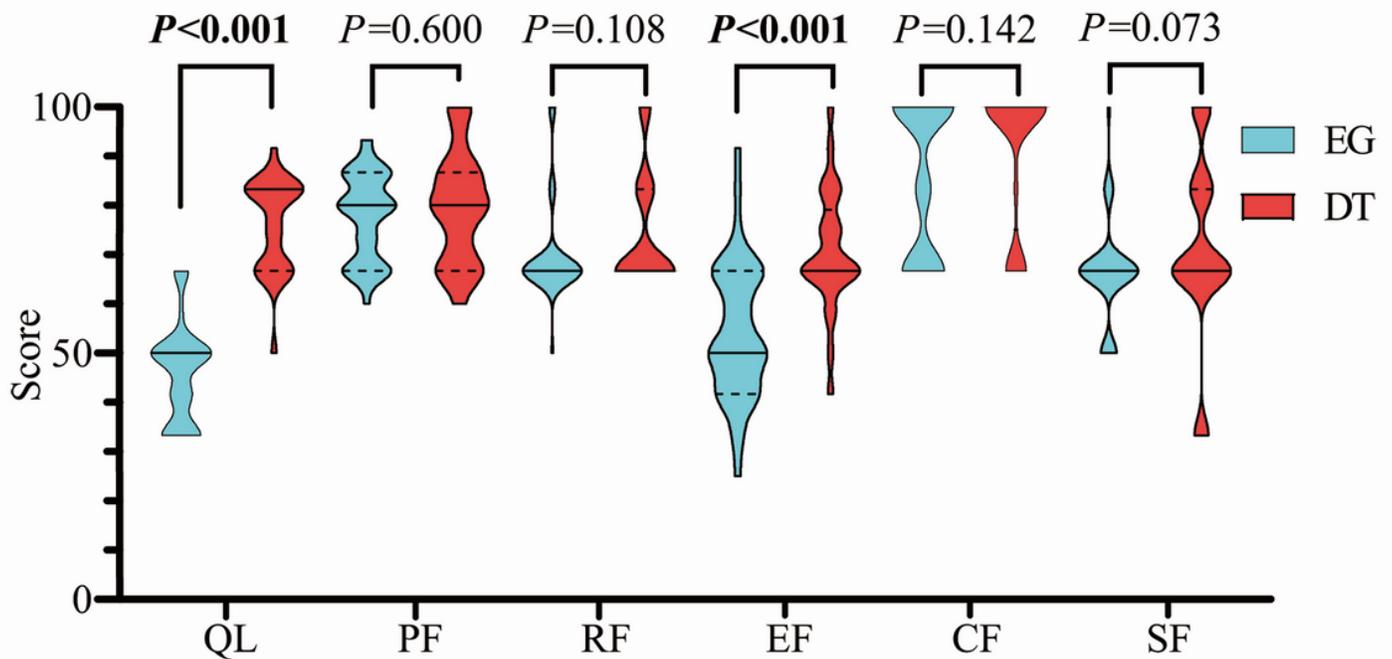


Figure 2

Violin plots of global health status and functional scales of the EORTC QLQ-C30 questionnaire. Solid lines represent medians and dotted lines represent quartiles. A high score for global health status represented a high quality of life. A high score for a functional scale represented a healthy level of functioning. The patients in the double tract reconstruction group had better global health status ($P < 0.001$) and emotional functioning ($P < 0.001$) than those in the esophagogastrostomy group. EG, esophagogastrostomy; DT, double tract reconstruction; QL, global health status; PF, physical functioning; RF, role functioning; EF, emotional functioning; CF, cognitive functioning; SF, social functioning.

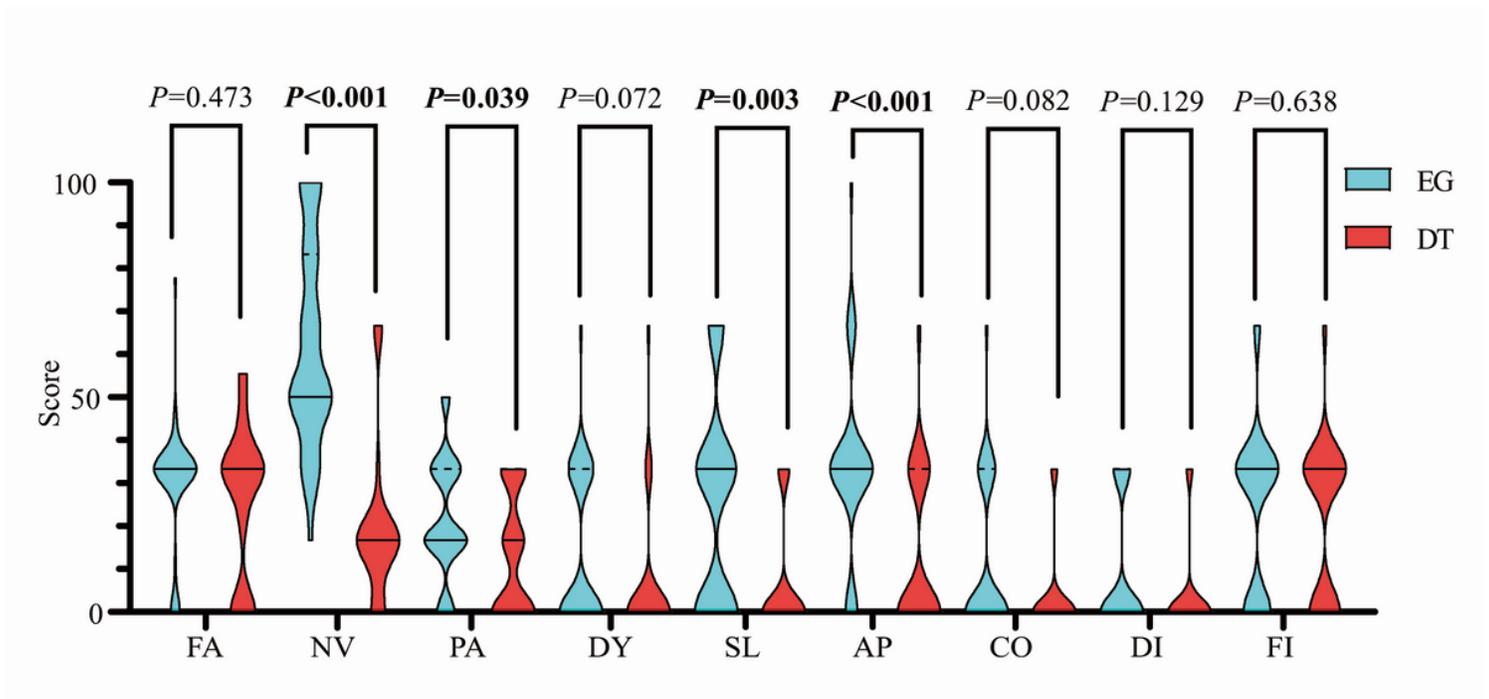


Figure 3

Violin plots of global health status and functional scales of the EORTC QLQ-C30 questionnaire. Solid lines represent medians and dotted lines represent quartiles. A high score for global health status represented a high quality of life. A high score for a functional scale represented a healthy level of functioning. The patients in the double tract reconstruction group had better global health status ($P < 0.001$) and emotional functioning ($P < 0.001$) than those in the esophagogastrostomy group. EG, esophagogastrostomy; DT, double tract reconstruction; QL, global health status; PF, physical functioning; RF, role functioning; EF, emotional functioning; CF, cognitive functioning; SF, social functioning. EG, esophagogastrostomy; DT, double tract reconstruction; FA, fatigue; NV, nausea and vomiting; PA, pain; DY, dyspnea; SL, insomnia; AP, appetite loss; CO, constipation; DI, diarrhea; FI, financial difficulties.

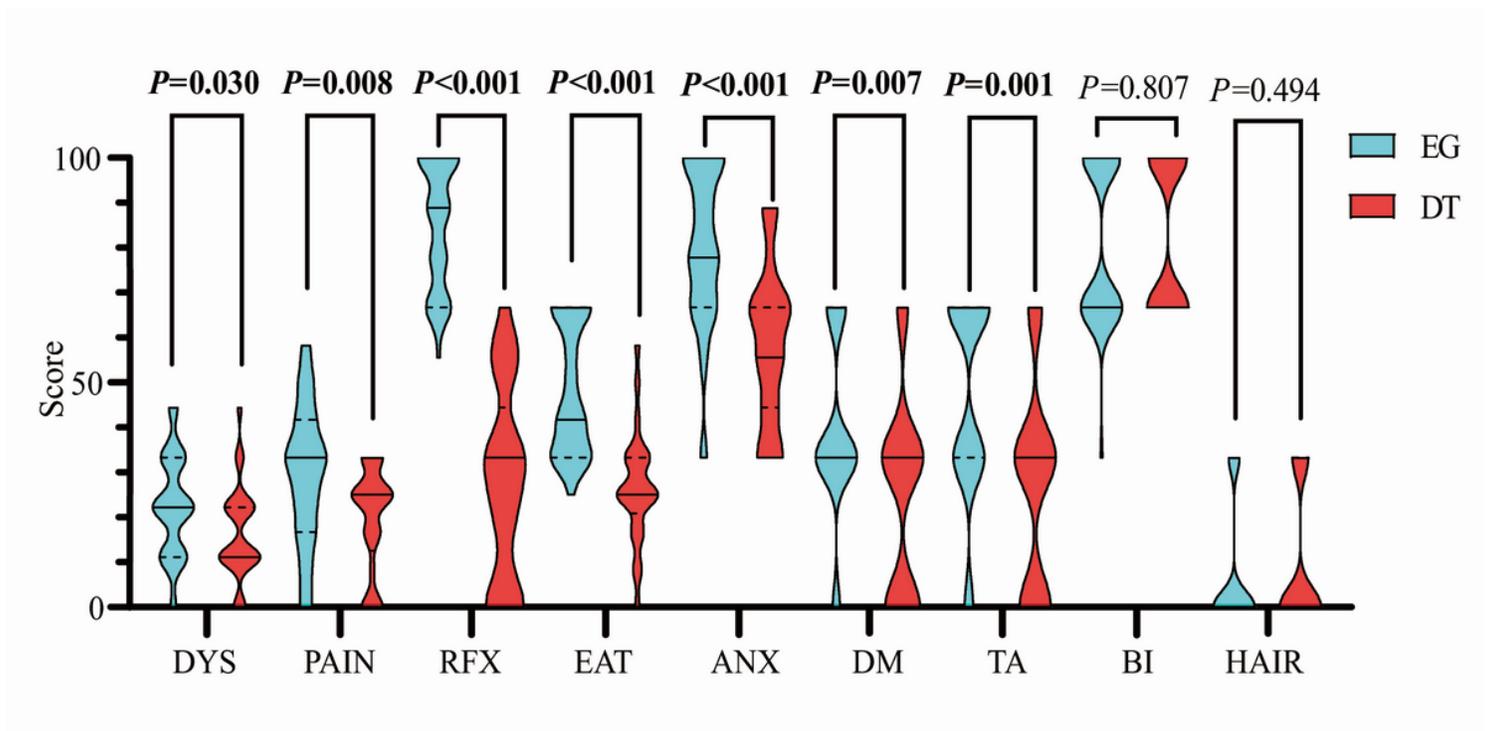


Figure 4

Violin plots of the symptom scales of the EORTC QLQ-STO22 questionnaire. Solid lines represent medians and dotted lines represent quartiles. A higher score represented worse symptoms. Patients in the double tract reconstruction group complained less about dysphagia ($P = 0.030$), pain ($P = 0.008$), reflux ($P < 0.001$), eating ($P < 0.001$), anxiety ($P < 0.001$), dry mouth ($P = 0.007$), and taste ($P = 0.001$) than those in the esophagogastrostomy group. EG, esophagogastrostomy; DT, double tract; DYS, dysphagia; PAIN, pain; RFX, reflux; EAT, eating; ANX, anxiety; DM, dry mouth; TA, taste; BI, body image; HAIR, hair loss.