

Proximal gastrectomy with double-tract reconstruction versus total gastrectomy for proximal early gastric cancer

A systematic review and meta-analysis

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Abstract

Background: The incidence of proximal gastric cancer in the gastric fundus, cardia, and other parts is increasing rapidly. The purpose of this study was to systematically compare the short-term and long-term clinical effects of proximal gastrectomy with double tract reconstruction (PG-DTR) to total gastrectomy (TG) for proximal early gastric cancer (EGC).

Methods: A systematic review and meta-analysis was conducted through searching the literature in PubMed, Web of Science, Cochrane Library, EMBASE, CNKI, WAN FANG, and VIP databases. All clinical controlled trials and randomized controlled trials (RCTs) of PG-DTR and PG were included. Simultaneously, the relevant data were extracted, and the software RevMan version 5.1 was used for the meta-analysis.

Results: Eight studies with a total of 753 patients were eligible for the meta-analysis. There were no significant differences in the operation time, intraoperative blood loss, postoperative hospital stay, early complications (anastomotic fistula and anastomotic bleeding), late complications (reflux symptoms and anastomotic stenosis), and 5-year survival rate between PG-DTR and TG. However, the levels of partial nutritional indicators (vitamin B12 supplements and vitamin B12 deficiency) were significantly higher in the PG-DTR group than in the TG group.

Conclusion: This study showed ample evidence to suggest that PG-DTR improved the postoperative nutritional status without compromising patient safety while providing the same surgical characteristics and postoperative morbidity as TG.

Abbreviations: AAP = acetaminophen, CCT = clinical controlled trial, CI = confidence interval, DTR = double tract reconstruction, EG = esophagogastrectomy, EGC = early gastric cancer, JI = jejunal interposition, JPI = jejunal pouch interposition, NOS = Newcastle-Ottawa Scale, OR = odds ratio, PG = proximal gastrectomy, PG-DTR = proximal gastrectomy combined with double tract reconstruction, QoL = quality of life, RCT = randomized controlled trial, SMD = standard mean difference, TG = total gastrectomy, WMD = weighted mean difference.

Keywords: double tract reconstruction, meta-analysis, proximal early gastric cancer, proximal gastrectomy, total gastrectomy

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The authors report no conflicts of interest.

All data generated or analyzed during this study are included in this published article [and its supplementary information files];

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1. Introduction

Gastric cancer is a highly malignant tumor and the third-leading cause of cancer-related deaths worldwide.^[1,2] Over the years, with the standardization of screening procedures and the development of endoscopic technology, the detection rate of gastric cancer has gradually increased, whereas the incidence of proximal gastric cancer in the fundus and cardia has increased sharply.^[3,4] Presently, surgery is still the main method of treatment, which can be supplemented by preoperative neo-adjuvant chemotherapy or postoperative chemoradiotherapy according to the different TNM stages of the tumor. Proximal early gastric cancer (EGC) is mainly treated by proximal gastrectomy (PG) and total gastrectomy (TG). However, the reconstruction of PG is complicated and diverse; including esophagogastrectomy (EG), EG combined with pyloroplasty, jejunal interposition (JI), jejunal pouch interposition (JPI), double-tract reconstruction (DTR), and JI with DTR.^[5–8] These reconstruction methods have varying effects on the postoperative recovery, nutritional status, and quality of life (QoL) of the patients. Some recent randomized controlled trials (RCTs) and

retrospective comparative studies have concluded that PG has certain advantages in the retention of function and is superior to TG in the recovery of weight after the operation and the prevention of anemia,^[9–11] although several postoperative complications of PG still plague patients, particularly reflux esophagitis and anastomotic stenosis. Fortunately, several studies have demonstrated that PG combined with DTR (PG-DTR) yields excellent results in improving the reflux symptoms and reducing anastomotic stenosis.^[12–16] This study was designed to systematically compare the surgical features, postoperative complications, long-term survival, nutritional status, and QoL of PG-DTR and PG in the treatment of proximal EGC.

2. Materials and methods

2.1. Inclusion criteria

The inclusion criteria were: proximal EGC patients (stage I) who needed laparoscopic, robotic, or open surgery, PG-DTR or TG as the initial treatment method. The patients enrolled in the study were divided into PG-DTR and TG groups. The clinical parameters included intraoperative situations, postoperative complications, nutritional status, recurrence, and survival time. These were compared between PG-DTR and TG by retrospective or prospective clinical controlled trials (CCTs) and RCTs.

2.2. Exclusion criteria

The exclusion criteria were: case reports, letters, comments, and reviews; articles without a control group or a rigorous design, missing data, duplicate publications, sample sizes <20, and follow-up time <12 months; if 2 studies were published by the same institution, the one with a smaller sample size was excluded, non-English and Chinese publications, articles that did not mention important information or data such as the clinicopathological characteristics.

2.3. Literature search strategy

The PubMed, Web of Science, Cochrane Library, and EMBASE databases were used to search for English literature, whereas the databases CNKI, WAN FANG, and VIP were used for Chinese literature. Articles published until August 1, 2019, were selected. According to the Cochrane Handbook, the search terms were [(proximal gastrectomy) or (subtotal gastrectomy)] and (double tract reconstruction) and/or [(early gastric cancer) or (proximal early gastric cancer) or (upper third gastric cancer)] and/or (total gastrectomy) and/or [(gastric cancer) or (stomach cancer) or (gastric neoplasms) or (stomach neoplasms)]. We also retrospectively analyzed the references included in the quantitative analysis to avoid missing hidden articles. Finally, we searched 47 articles in PubMed, 46 articles in the Web of Science, eight articles in the Cochrane Library, 34 articles in EMBASE, 25 articles in CNKI, 85 articles in WAN FANG, and 144 articles in VIP. Ethical approval was not required for this study as all the data were obtained from previously published literature.

2.4. Data extraction

Relevant data were extracted by 2 evaluators according to the pre-designed data extraction form. If there was a disagreement, a consensus was reached through discussion. The content included basic information (the first author's name, date of publication, and nationality), sample size, surgical-related features (operation

time, intraoperative blood loss, the number of lymph nodes, and duration of hospital stay), postoperative complications (reflux symptoms, anastomotic stenosis, anastomotic leakage, and bleeding), 5-year survival time, nutritional status (weight loss, hemoglobin deficiency, iron deficiency or anemia, hypoalbuminemia, Vitamin B12 deficiency, and supplements), and QoL (functional scores and gastrointestinal symptom scores).

2.5. Literature selection and quality evaluation

Two researchers searched and screened the literature independently. Initially, after reading the title and abstract, the articles that did not meet the inclusion criteria were excluded. Then, the literature that initially appeared to meet the inclusion criteria was selected after reading the full text. Finally, the quality was independently evaluated, and cross-checks were performed by both the researchers. In case of a disagreement, a decision would be taken following discussion. The risk-bias assessment tool in the Cochrane Reviewer's Handbook was used to evaluate RCTs from four aspects (sequence generation, concealment of allocation, blinding, loss of follow-up), and literature graded B or above was considered high-quality literature. The Newcastle-Ottawa Scale (NOS), which was composed of the selection of study population (4 items), comparability between groups (2 items), and outcome indicators (3 items), was used to evaluate the quality of CCTs. Each item was scored for one point, and CCTs with ≥ 6 points were considered high-quality CCTs, with a maximum of 9 points.^[17]

2.6. Statistical analysis

The meta-analysis was conducted using the software RevMan version 5.1 published by Cochrane Collaboration. The statistical analysis included the test for heterogeneity, meta-analysis, funnel chart analysis, and sensitivity analysis. Initially, the chi-square test was used for testing the heterogeneity. If no heterogeneity was determined at $P > .1$ and $I^2 < 50\%$, the fixed-effect model was selected for the meta-analysis. Moreover, if heterogeneity was determined at $P < .1$ and $I^2 > 50\%$, a random-effect model was used. When $P < .1$ and heterogeneity could not be determined, a descriptive analysis was chosen instead of the meta-analysis. Odds ratio (OR) and weighted mean difference (WMD) or standard mean difference (SMD) was used as comprehensive statistics of the quantitative data and qualitative data, respectively. A confidence interval (CI) of 95% was calculated for all statistics, and a P value of $< .05$ indicated statistically significant differences. A funnel chart was utilized to evaluate the publication bias, and the sensitivity was analyzed.

3. Results

3.1. Search results

A total of 389 articles were retrieved from the selected databases, of which 40 articles were excluded because of duplication, 329 articles were excluded after reading the title and abstract, and 10 articles were excluded after reading the full text and evaluating the quality. Finally, 8 CCTs were selected for the meta-analysis. The process for the selection of the CCTs is presented in Figure 1.

3.2. Results of data acquisition and quality evaluation

Eight studies involving 753 patients were enrolled into the meta-analysis, with the number of patients in each study varying from

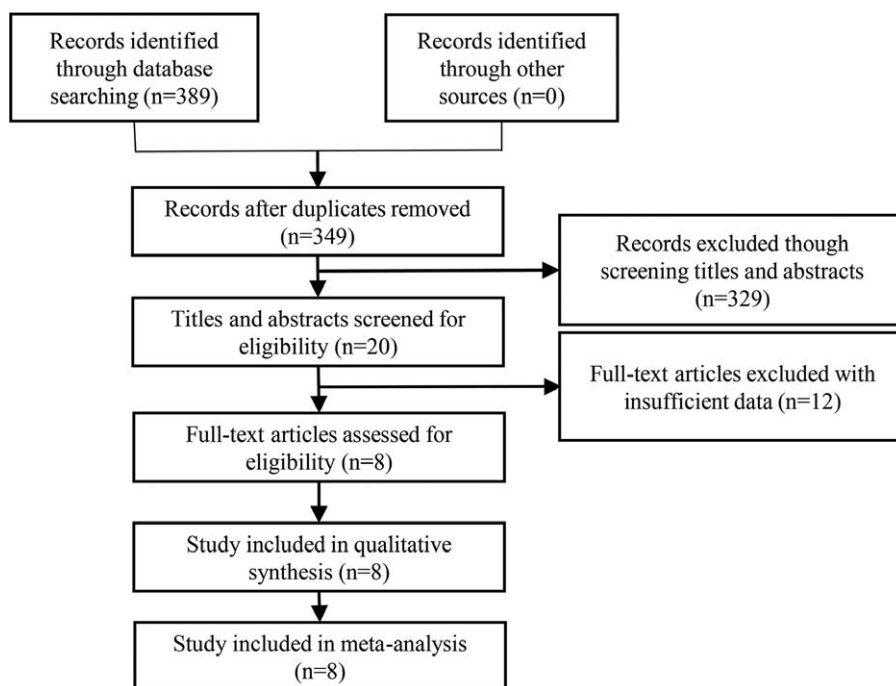


Figure 1. Flow chart of this study.

30 to 248. Among these studies, 5 were conducted in South Korea, 2 in Japan, and one in China. Besides, 7 studies described the surgical-related characteristics and early complications; 5 reported late complications, 2 reported the 5-year survival time, and 4 evaluated postoperative nutritional status. According to NOS, 6 articles scored 8 points, and 2 articles scored nine points. The detailed basic characteristics and quality evaluation are presented in Table 1.

3.3. Comparison of surgical-related features

3.3.1. Operation time. In total, 7 studies^[12-16,18,19] reported the operation time. Due to the heterogeneity ($\chi^2=24.19, P < .1, I^2=75\%$) in the reported results, a random effect model was selected, which showed no statistical significance between the 2 groups (WMD=-8.55, 95% CI: -22.70 to 5.59, $P=.24$, Table 2).

3.3.2. Intraoperative bleeding. Five included studies^[12-15,19] reported data on intraoperative bleeding loss. Because of the

heterogeneity ($\chi^2=25.85, P < .1, I^2=85\%$) in the reported results, a random effect model was applied, which indicated no significant differences between PG-DTR and TG (WMD=-3.91, 95% CI: -52.09 to 44.27, $P=.16$, Table 2).

3.3.3. Number of lymph node dissections. Six homogenous articles^[12-14,16,18,19] ($\chi^2=10.82, P=.06, I^2=54\%$) reported the number of lymph node dissections. The meta-analysis demonstrated that the PG-DTR was associated with lesser lymph node dissections (WMD=-12.26, 95% CI: -15.70 to -8.82, $P < .01$, Figure 2).

3.3.4. Postoperative hospital stay. Seven eligible studies^[12-16,18,19] reported data regarding postoperative hospital stay. There was no heterogeneity between the 2 groups ($\chi^2=6.96, P=.22, I^2=28\%$). Therefore, the meta-analysis was conducted using the fixed-effect model, which demonstrated no significant difference between the 2 groups (WMD=-0.78, 95% CI: -1.91 to 0.35, $P=.18$, Table 2).

Table 1
Data acquisition and quality evaluation of 8 studies.

Author	Time	Nationality	Total cases	Cases (DTR/R)	Sex (male/female)	Procedure	PG-DTR follow-up	TG follow-up	Scores
Jung et al ^[12]	2017	Korea	248	92/156	197/51	L	26.6±10.3	43.5±23.2	8*
Cho et al ^[14]	2018	Korea	80	38/42	63/17	L, R	18~30	18~30	8*
Park et al ^[18]	2018	Korea	80	34/46	48/32	L	29.6 (2.9~39.5)	47.5 (7.0~67.4)	8*
Nomura et al ^[15]	2018	Japan	45	15/30	34/11	L	12	12	8*
Sugiyama et al ^[19]	2018	Japan	30	10/20	24/6	L	12	12	8*
Kim and Kim ^[16]	2016	Korea	34	17/17	24/10	L	—	—	9*
Ko et al ^[13]	2019	Korea	104	52/52	70/34	L, O	22.7±15.4	36.3±23.1	9*
Fan et al ^[20]	2019	China	132	51/81	117/15	Unclear	26 (1~110)	26 (1~110)	8*

—= no data, L=laparoscope, NOS=Newcastle-Ottawa Scale, O=open, PG-DTR=proximal gastrectomy with double-tract reconstruction, R=robot, RY=Roux-en Y reconstruction, TG=total gastrectomy.
* Newcastle-Ottawa Scale scores.

Table 2
Meta-analysis of surgical features, complications, survival, and partial nutritional status.

Subgroup	No. of studies	No. of Patients	Heterogeneity test		OR, WMD (95% CI)	P
			I ²	P		
Operation time	7	621	75%	.0005	-8.55 (-22.70 to 5.59)	.24
Surgical bleeding	5	507	85%	<.0001	-3.91 (-52.09 to 44.27)	.87
Hospital stay	7	591	28%	.22	-0.78 (-1.91 to 0.35)	.18
Early complication	8	753	22%	.25	0.71 (0.48 to 1.05)	.08
Anastomotic fistula	7	673	0%	.76	0.63 (0.26 to 1.51)	.30
Anastomotic bleeding	6	643	0%	.68	1.59 (0.52 to 4.87)	.41
Late complication	4	401	13%	.33	0.73 (0.37 to 1.43)	.36
Reflux symptom	5	511	0%	.73	1.61 (0.61 to 4.22)	.33
Anastomotic stenosis	—	401	0%	.42	1.42 (0.48 to 4.19)	.52
5-y survival	2	352	74%	.05	3.03 (0.14 to 66.08)	.48
Weight loss	3	358	0%	.73	0.83 (0.42 to 1.65)	.60
Hemoglobin deficiency	—	—	—	—	—	—
1 y	4	490	11%	.34	0.66 (0.39 to 1.12)	.13
2 y	2	328	30%	.23	0.64 (0.29 to 1.41)	.27
Iron deficiency anemia	2	110	0%	.35	1.42 (0.59 to 3.38)	.43
Hypoalbuminemia	2	278	0%	.52	0.80 (0.17 to 3.67)	.77

—=no data, CI=confidence interval, No=number, OR=odds ratio, WMD=weighted mean difference.

3.4. Comparison of early complications

3.4.1. Total early complications. The meta-analysis of the combined data of early complications from 8 articles,^[12-16,18-20] which was performed using a fixed-effect model ($\chi^2=8.99$, $P=.25$, $I^2=22\%$) indicated no significant differences between the 2 groups (OR=0.71, 95% CI: 0.48 ~ 1.05, $P=.08$, Table 2).

3.4.2. Anastomotic fistula. The incidence of anastomotic fistula described by seven studies^[12-16,19,20] was similar between the 2 groups (OR=0.63, 95% CI: 0.26 ~ 1.51, $P=.30$, Table 2), as determined using a fixed effect model ($\chi^2=3.38$, $P=.76$, $I^2=0\%$).

3.4.3. Anastomotic bleeding. The fixed effect model ($\chi^2=2.29$, $P=.68$, $I^2=0\%$) for the meta-analysis of 6 studies^[12,13,15,16,18,20] revealed that there was no difference in the frequency of anastomotic bleeding (OR=1.59, 95% CI: 0.52 ~ 4.87, $P=.41$, Table 2) between the 2 groups.

3.5. Comparison of late complications

3.5.1. Total late complications. A total of 5 articles^[12,13,15,16] reported the occurrence of late complications. The comprehensive data showed a strong homogeneity ($\chi^2=3.44$, $P=.33$, $I^2=13\%$) between the 2 groups. Therefore, the meta-analysis was

conducted using a fixed-effect model, which demonstrated no significant differences between the 2 groups (OR=0.73, 95% CI: 0.37 ~ 1.43, $P=.36$, Table 2).

3.5.2. Reflux symptoms. Five homogenous ($\chi^2=2.04$, $P=.73$, $I^2=0\%$) studies reported data on reflux symptoms.^[12-16] According to the fixed effect model, there were no significant differences between PG-DTR and TG (OR=1.61, 95% CI: 0.61 ~ 4.22, $P=.33$, Table 2).

3.5.3. Anastomotic stenosis. Four homogenous articles^[12,13,15,16] reported anastomotic stenosis ($\chi^2=2.79$, $P=.42$, $I^2=0\%$). Based on this, a fixed-effect model was computed, which confirmed that there was no significant difference between the 2 groups (OR=1.42, 95% CI: 0.48 ~ 4.19, $P=.52$, Table 2).

3.6. Comparison of long-term survival outcomes

3.6.1. Five-year survival rate. Two qualified studies^[12,13] reported data on the 5-year survival rates. Because of the heterogeneity ($\chi^2=3.91$, $P=.05$, $I^2=74\%$), a random-effect model was used for the meta-analysis, which confirmed that the 2 groups had similar 5-year survival rates (OR=3.03, 95% CI: 0.14 ~ 66.08, $P=.48$, Table 2).

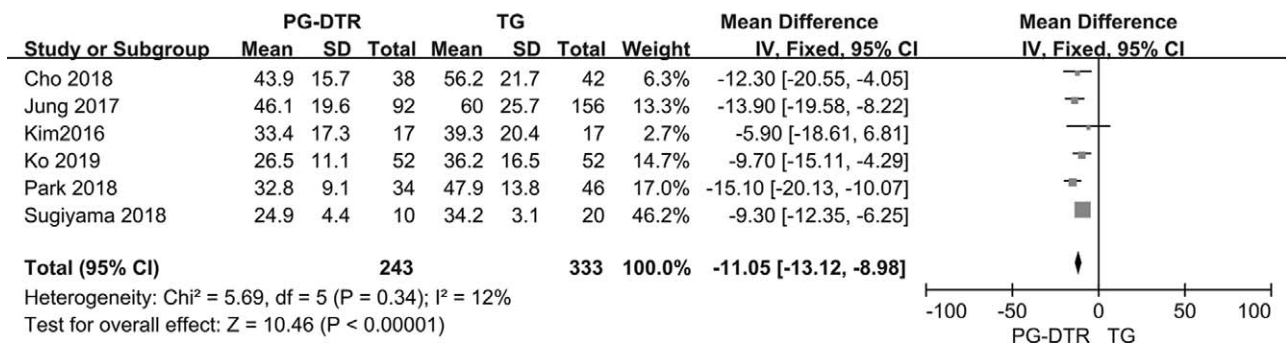


Figure 2. Comparison of the number of lymph node dissection between PG-DTR and TG. PG-DTR=proximal gastrectomy combined with double tract reconstruction, TG=total gastrectomy.

3.7. Nutritional status

3.7.1. Weight loss. Three of the included studies^[12,18,19] reported weight loss among patients at one-year after surgery and the results were homogenous ($\chi^2=0.64, P=.73, I^2=0\%$). Thus, a fixed-effect model was selected for the meta-analysis, which reported no significant difference in the incidence rate of 1-year weight loss between the 2 groups (OR=0.83, 95% CI: 0.42 ~ 1.65, $P=.60$, Table 2).

3.7.2. Hemoglobin deficiency. Four eligible studies^[12,14,19,20] investigated the one-year incidence of hemoglobin deficiency after surgery. Since there was no heterogeneity ($\chi^2=3.37, P=.34, I^2=11\%$) between the studies, a fixed-effect model was chosen for the meta-analysis, which showed no statistical significance between PG-DTR and TG (OR=0.66, 95% CI: 0.39~1.12, $P=.13$, Table 2). Moreover, the data on 2-year hemoglobin deficiency were analyzed using a fixed-effect model^[12,14] ($\chi^2=1.43, P=.23, I^2=30\%$) and the same results were obtained (OR=0.64, 95% CI: 0.29 ~ 1.41, $P=.27$, Table 2)

3.7.3. Iron-deficiency anemia. Two articles^[14,19] reported information on iron-deficiency anemia. Because of the strong homogeneity ($\chi^2=0.88, P=0.35, I^2=0\%$), the fixed-effect model was chosen, which demonstrated that the incidence of iron-deficiency anemia in the 2 groups was similar (OR=1.42, 95% CI: 0.59 ~ 3.38, $P=.43$, Table 2).

3.7.4. Hypoalbuminemia. Two homogenous^[12,19] studies reported information on patients with hypoalbuminemia for one year. According to a fixed-effect model ($\chi^2=0.41, P=.52, I^2=0\%$), there was no obvious difference between the 2 groups (OR=0.80, 95% CI: 0.17 ~ 3.67, $P=.77$, Table 2).

3.7.5. Vitamin B12 deficiency. Comprehensive analysis of the data from three studies^[12,14,19] using a random-effect model ($\chi^2=5.73, P=.06, I^2=65\%$, Fig. 3) demonstrated that the incidence of vitamin B12 deficiency in the PG-DTR group was significantly lower than that in TG after 2 years (OR=0.03, 95% CI: 0.00 ~ 0.32, $P=.003$)

3.7.6. Vitamin B12 supplements. Three homogenous^[1,9] studies provided data on the number of patients taking vitamin B12 supplements within 2 years. According to the random-effect model ($\chi^2=25.83, P<.00001, I^2=92\%$), the number of PG-DTR patients requiring vitamin B12 supplementation was significantly lower (OR=0.06, 95% CI: 0.00 ~ 0.89, $P=.04$, Fig. 4).

3.8. Evaluation of publication bias and analysis of sensitivity

The funnel chart analysis of each result showed a symmetrical inverted funnel chart (Fig. 5 presents lymph node dissection as an example), which indicated that there was no publication bias. Moreover, the eight studies included in the meta-analysis were deleted one-by-one, sensitivity analysis was carried out, and then the data were reorganized, which did not affect the results. Finally, the random-effect model was used for the analysis, and the results were still stable.

4. Discussion

Recently, the incidence of proximal EGC has increased rapidly.^[4] The Japanese Gastric Cancer Treatment Guidelines^[21] suggest the implication of PG and the adoption of more than half of the

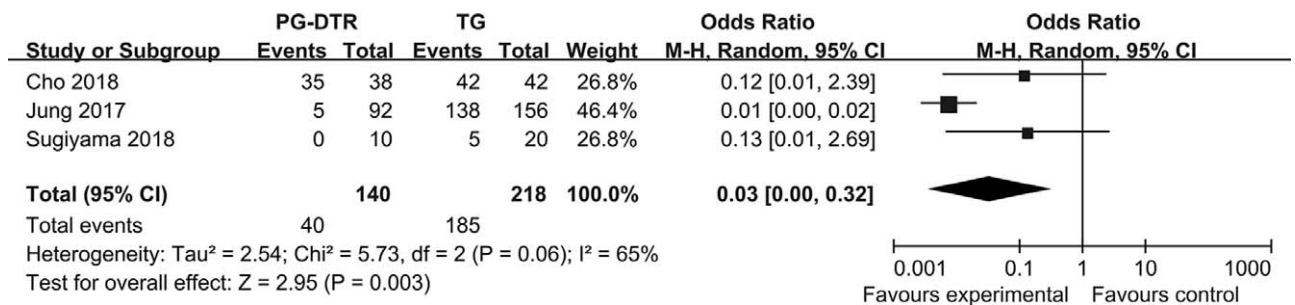


Figure 3. Comparison of the incidence of vitamin B12 deficiency between PG-DTR and TG. PG-DTR=proximal gastrectomy combined with double tract reconstruction, TG=total gastrectomy.

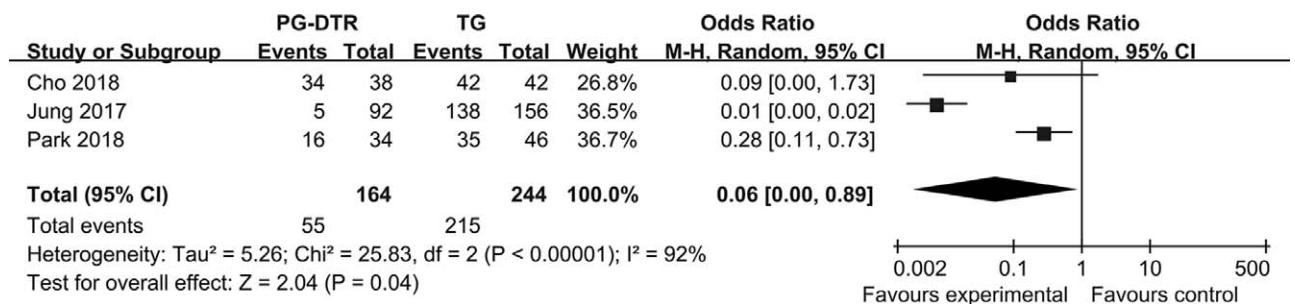


Figure 4. Comparison of the number of people taking vitamin B12 supplements between PG-DTR and TG. PG-DTR=proximal gastrectomy combined with double tract reconstruction, TG=total gastrectomy.

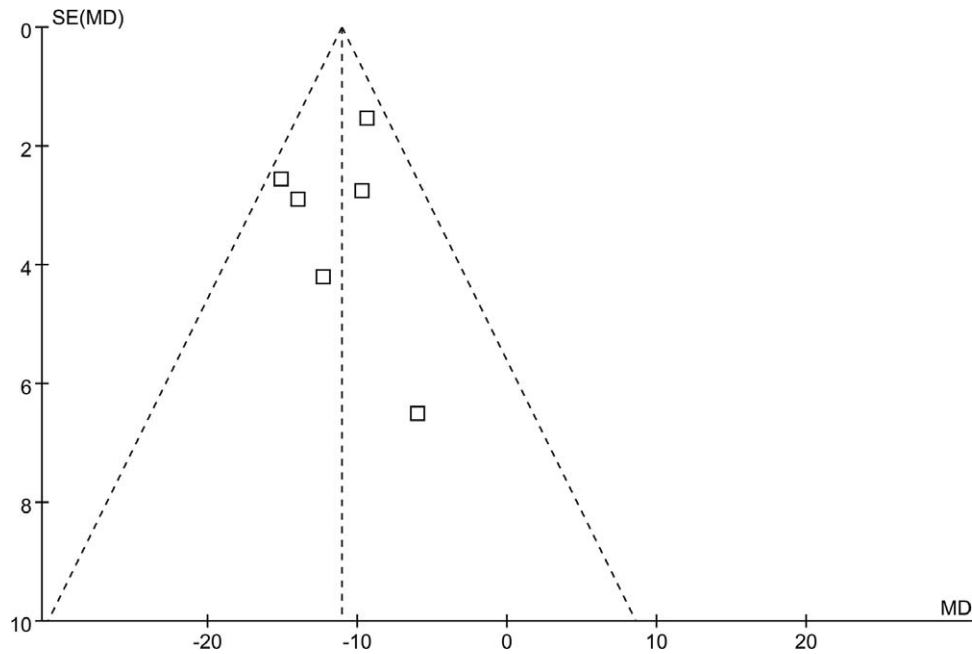


Figure 5. The funnel chart of the number of lymph node dissection.

distal stomach for proximal EGC. PG somewhat retains the physiological functions of the stomach and duodenum, which can significantly improve the long-term nutritional status of the patients. However, due to the loss of the anti-reflux effect of the lower esophageal sphincter and His angle, patients usually suffer reflux esophagitis caused by gastric acid or food reflux after PG, which seriously affects their QoL.^[9,22–24] Therefore, researchers have adopted numerous methods for the reconstruction of the digestive tract after PG, which can be divided into 2 categories: the direct and indirect esophagogastric anastomosis.

The direct anastomosis methods consist of EG, gastric tube reconstruction, pyloroplasty, preservation of the lower esophageal sphincter, and PG with a double-flap technique.^[5,6,9,23,25–31] As a traditional and classic method for the reconstruction of the digestive tract, EG retains the physiological channel from the residual stomach to the duodenum, which does not affect the endoscopic examination or the treatment of the residual stomach, gallbladder, and pancreas.^[9,22,23] Besides, EG has more advantages than TG regarding the long-term nutritional status and QoL, although there is a higher incidence of reflux esophagitis and anastomotic stenosis.^[9,11,22] Reconstruction of the gastric tube was firstly developed by Uyama et al,^[32] which allows food to pass quickly and avoids retention, whereas the removal of most of the stomach can reduce the secretion of gastric acid, thus objectively reducing the material basis of reflux and effectively preventing the occurrence of reflux.^[33] However, the procedure requires a long cut, which increases the risk of bleeding. Moreover, the narrow lumen of the tubular stomach leads to an increase in the anastomotic tension, which increases the risk of anastomotic leakage and anastomotic stenosis.^[26] Simple PG destroyed the anatomical structure of the gastroesophageal junction, but PG combined with pyloroplasty can accelerate residual gastric emptying, which alleviates gastric retention and reduces the degree of reflux to some extent. Unfortunately, bile reflux readily occurs after pyloroplasty, which increases the material basis of gastric acid reflux to the esophagus. Several studies^[25,27,28]

indicate that the preservation of the lower esophageal sphincter is a safe and feasible technique for preventing reflux and stenosis, but the indications for surgery are more strict, and the tumor needs to be located on the larger curved side of the upper and middle stomach. Furthermore, the rapid pathological examination of the cutting edge should be performed during the operation, and the lower esophageal sphincter can be retained when the test result is negative. PG with double-flap technique is similar to reconstructive cardia, which acts as a 1-way flap to reduce the incidence of reflux esophagitis.^[30,31,34] Moreover, the anastomotic stoma was covered by the anterior gastromyocutaneous flap, which strengthens the anastomotic stoma and reduces the risk of anastomotic leakage. However, the operation is extremely complicated, and the technique of endoluminal suture is also high, which leads to a prolonged operation time.^[29]

The indirect anastomosis methods consist of JI with single-tract reconstruction and DTR. The single-tract reconstruction can be further divided into JI, JPI, and jejunal interposition. In this method, a section of the jejunum is anastomosed between the esophagus and residual stomach, and an anti-reflux barrier is formed due to the tolerance of the jejunum to the gastric acid, as well as the natural peristalsis of the intestine. Meanwhile, it reduces the tension of anastomosis and is safer.^[7,16,35,36] However, the procedures of JI and JPI are complicated, and the intracavitary operation is difficult, limiting its application in clinical practice.

The main difference between PG-DTR and jejunal interposition is that the former does not close the channel under gastrojejunostomy, which was originally applied by Aikou et al^[37] with a primary purpose to promote the smooth passage of food. During the past few years, various studies have confirmed that DTR has the dual advantages of EG and Roux-en-Y reconstruction simultaneously.^[12,13,15,16,18,19] Since its introduction, some studies have compared PG-DTR and TG in proximal EGC surgery. So far, to the best of our knowledge, no meta-analysis has compared PG-DTR and TG for proximal EGC.

The results of this systematic review and meta-analysis revealed that the treatment of PG-DTR for proximal EGC patients has significant advantages in improving the long-term nutritional status without compromising the safety of the patients.

Regarding the safety of surgery, our research has demonstrated that the operation time, intraoperative blood loss, and postoperative hospital stay between the 2 groups were similar, which is consistent with the results of all included studies.^[12–16,18,19] Besides, the number of lymph node dissections in TG was lower than that in PG-DTR, although there were no significant differences in the 5-year survival rates between the 2 groups, indicating that the lymph nodes of proximal EGC do not metastasize downward. This finding is consistent with that of Kitamura et al.^[38] These results confirm that the surgical safety of PG-DTR and TG is similar.

Regarding the similarity in surgical safety between PG-DTR and TG, the 2 surgical methods are gradually favored by surgeons in terms of postoperative complications, nutritional status, and QoL. As for postoperative complications, the study demonstrates that there is no obvious difference in the reflux symptoms between the 2 groups, which may be related to the anti-acid reflux by the antegrade peristalsis of the jejunum and alkaline intestinal fluid-neutralizing gastric acid. Moreover, the incidence of anastomotic stenosis in the 2 groups may be related to the independent double tract, food can be diverted, and the residual stomach and pylorus can effectively reduce the incidence of the dumping syndrome. This conclusion has laid the theoretical foundation for the replacement of traditional EG with DTR and further clinical comparison between DTR and TG.

Regarding nutritional status, as the levels of serum iron and vitamin B12 are affected by additional supplementation during the treatment, our research incorporated the supplementary population, which may make the results more reliable. It was observed that in the PD-DTR group, the rate of vitamin B12 deficiency and vitamin B12 supplementation was significantly lower. Several studies have shown that in the case of serum vitamin B12 levels, PG-DTR patients are superior to TG patients. Moreover, a lower proportion of PG-DTR patients requires supplementation of iron and vitamin B12 at lower average levels.^[12,13,16,18] Our findings are consistent with these results, which are closely related to the storage of the remnant stomach, retention of the pylorus, and the stimulation of the duodenum to food. The gastric acid and castle intrinsic factors secreted by the remnant stomach contribute to the absorption of vitamin B12. The meta-analysis in our study demonstrated that the incidences of weight loss, hemoglobin deficiency, iron deficiency anemia, and hypoalbuminemia were similar between the 2 groups. However, several studies have shown that PG-DTR patients show better recovery of serum iron levels and weight compared with TG patients,^[12,13,15,16,18] which may be the reason of extra supplement that changes the actual biochemical index of patients and promotes the early recovery of weight. In the end, the results showed some reasonable differences.^[39–41]

Regarding QoL, the descriptive analysis is chosen because of the different analytic methods and the lack of scoring data. Two studies evaluated the postoperative QoL of patients with PG-DTR and PG using questionnaires (QLQ-C30 and QLQ-STO22). Park et al.^[18] reported no statistical differences between the 2 groups in the functional scores of physical/role/cognitive functions, as well as the scores of gastrointestinal symptoms, such as nausea, vomiting, diarrhea, dysphagia, reflux, dietary restrictions, and taste sensation. Nomura et al.^[15] reported that

the food intake of the PG-DTR group was slightly better, although no statistical difference was observed. Moreover, none of the 2 groups had any obvious advantages in the abdominal symptoms such as abdominal fullness/distension/pain. Furthermore, the intestinal absorption by acetaminophen (AAP) and the secretion kinetics of hormones was evaluated.^[15] The change in plasma AAP concentration in the DTR group was lower, although none of the groups were affected by the sitting or supine positions. The plasma insulin levels and gastrin levels in both groups were not affected by different body positions, except for the blood glucose level, which was significantly lower than that in the DTR group. These results may be the influence of gravity movement of the intestinal tract in the sitting position. According to these 2 studies, there appears to be no significant difference in the QoL between the 2 groups after surgery, although more research is needed to confirm the findings.

This study has some limitations. First, all the included studies were retrospective CCTs, and there was a lack of RCTs. Second, there were few studies on the QoL; so, our conclusions may not be reliable. Finally, all the included studies were from South Korea, Japan, and China; hence, it is unclear whether the results will also apply to other countries or regions.

5. Conclusions

In summary, PG-DTR is similar to TG in terms of surgical safety, postoperative complications, and 5-year survival rate but is better in improving the long-term nutritional status. Therefore, PG-DTR is an ideal method for proximal EGC reconstruction and requires further prospective studies by surgeons.

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References

- [1] Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65:87–108.
- [2] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394–424.
- [3] Saito T, Kurokawa Y, Takiguchi S, et al. Current status of function-preserving surgery for gastric cancer. *World J Gastroenterol* 2014;20:17297–304.
- [4] Nunobe S, Hiki N. Function-preserving surgery for gastric cancer: current status and future perspectives. *Transl Gastroenterol Hepatol* 2017;2:77.
- [5] Wang S, Lin S, Wang H, et al. Reconstruction methods after radical proximal gastrectomy: a systematic review. *Medicine (Baltimore)* 2018;97:e0121.
- [6] Nakamura M, Yamaue H. Reconstruction after proximal gastrectomy for gastric cancer in the upper third of the stomach: a review of the literature published from 2000 to 2014. *Surg Today* 2016;46:517–27.
- [7] Namikawa T, Oki T, Kitagawa H, et al. Impact of jejunal pouch interposition reconstruction after proximal gastrectomy for early gastric

- cancer on quality of life: short- and long-term consequences. *Am J Surg* 2012;204:203–9.
- [8] Fan KX, Xu ZF, Wang MR, et al. Outcomes for jejunal interposition reconstruction compared with Roux-en-Y anastomosis: a meta-analysis. *World J Gastroenterol* 2015;21:3093–9.
- [9] Ushimaru Y, Fujiwara Y, Shishido Y, et al. Clinical outcomes of gastric cancer patients who underwent proximal or total gastrectomy: a propensity score-matched analysis. *World J Surg* 2018;42:1477–84.
- [10] Nishigori T, Okabe H, Tsunoda S, et al. Superiority of laparoscopic proximal gastrectomy with hand-sewn esophagogastrostomy over total gastrectomy in improving postoperative body weight loss and quality of life. *Surg Endosc* 2017;31:3664–72.
- [11] Xu Y, Tan Y, Wang Y, et al. Proximal versus total gastrectomy for proximal early gastric cancer: A systematic review and meta-analysis. *Medicine (Baltimore)* 2019;98:e15663.
- [12] Jung DH, Lee Y, Kim DW, et al. Laparoscopic proximal gastrectomy with double tract reconstruction is superior to laparoscopic total gastrectomy for proximal early gastric cancer. *Surg Endosc* 2017;31:3961–9.
- [13] Ko HJ, Kim KH, Lee SH, et al. Can proximal gastrectomy with double-tract reconstruction replace total gastrectomy? A propensity score matching analysis. *J Gastrointest Surg* 2019;24:516–24.
- [14] Cho M, Son T, Kim HI, et al. Similar hematologic and nutritional outcomes after proximal gastrectomy with double-tract reconstruction in comparison to total gastrectomy for early upper gastric cancer. *Surg Endosc* 2019;33:1757–68.
- [15] Nomura E, Kayano H, Lee SW, et al. Functional evaluations comparing the double-tract method and the jejunal interposition method following laparoscopic proximal gastrectomy for gastric cancer: an investigation including laparoscopic total gastrectomy. *Surg Today* 2019;49:38–48.
- [16] Kim DJ, Kim W. Laparoscopy-assisted proximal gastrectomy with double tract anastomosis is beneficial for vitamin B12 and iron absorption. *Anticancer Res* 2016;36:4753–8.
- [17] Lo CK, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC Med Res Methodol* 2014; 14:45.
- [18] Park JY, Park KB, Kwon OK, et al. Comparison of laparoscopic proximal gastrectomy with double-tract reconstruction and laparoscopic total gastrectomy in terms of nutritional status or quality of life in early gastric cancer patients. *Eur J Surg Oncol* 2018;44:1963–70.
- [19] Sugiyama M, Oki E, Ando K, et al. Laparoscopic proximal gastrectomy maintains body weight and skeletal muscle better than total gastrectomy. *World J Surg* 2018;42:3270–6.
- [20] Fan JY, Qian F, Liu JJ, et al. Comparison of clinical efficacy between proximal gastrectomy with double tract reconstruction and total gastrectomy with Roux-en-Y reconstruction for proximal gastric cancer. *Zhonghua Wei Chang Wai Ke Za Zhi* 2019;22:767–73.
- [21] Japanese Gastric Cancer A. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer* 2011;14:113–23.
- [22] Hosoda K, Yamashita K, Katada N, et al. Potential benefits of laparoscopy-assisted proximal gastrectomy with esophagogastrostomy for cT1 upper-third gastric cancer. *Surg Endosc* 2016;30:3426–36.
- [23] Ahn SH, Lee JH, Park DJ, et al. Comparative study of clinical outcomes between laparoscopy-assisted proximal gastrectomy (LAPG) and laparoscopy-assisted total gastrectomy (LATG) for proximal gastric cancer. *Gastric Cancer* 2013;16:282–9.
- [24] Huh YJ, Lee HJ, Oh SY, et al. Clinical outcome of modified laparoscopy-assisted proximal gastrectomy compared to conventional proximal gastrectomy or total gastrectomy for upper-third early gastric cancer with special references to postoperative reflux esophagitis. *J Gastric Cancer* 2015;15:191–200.
- [25] Kim DJ, Lee JH, Kim W. Lower esophageal sphincter-preserving laparoscopy-assisted proximal gastrectomy in patients with early gastric cancer: a method for the prevention of reflux esophagitis. *Gastric Cancer* 2013;16:440–4.
- [26] Aihara R, Mochiki E, Ohno T, et al. Laparoscopy-assisted proximal gastrectomy with gastric tube reconstruction for early gastric cancer. *Surg Endosc* 2010;24:2343–8.
- [27] Tomita R. Surgical techniques to prevent reflux esophagitis in proximal gastrectomy reconstructed by esophagogastrostomy with preservation of the lower esophageal sphincter, pyloric and celiac branches of the vagal nerve, and reconstruction of the new His angle for early proximal gastric cancer. *Surg Today* 2016;46:827–34.
- [28] Tomita R, Sakurai K, Fujisaki S. Significance of the lower esophageal sphincter preservation in preventing alkaline reflux esophagitis in patients after total gastrectomy reconstructed by Roux-en-Y for gastric cancer. *Int Surg* 2014;99:174–81.
- [29] Hayami M, Hiki N, Nunobe S, et al. Clinical outcomes and evaluation of laparoscopic proximal gastrectomy with double-flap technique for early gastric cancer in the upper third of the stomach. *Ann Surg Oncol* 2017;24:1635–42.
- [30] Muraoka A, Kobayashi M, Kokudo Y. Laparoscopy-assisted proximal gastrectomy with the hinged double flap method. *World J Surg* 2016;40:2419–24.
- [31] Kuroda S, Choda Y, Otsuka S, et al. Multicenter retrospective study to evaluate the efficacy and safety of the double-flap technique as antireflux esophagogastrostomy after proximal gastrectomy (rD-FLAP Study). *Ann Gastroenterol Surg* 2019;3:96–103.
- [32] Uyama I, Sugioka A, Matsui H, et al. Laparoscopic side-to-side esophagogastrostomy using a linear stapler after proximal gastrectomy. *Gastric Cancer* 2001;4:98–102.
- [33] Nordby T, Ikdahl T, Bowitz Lothe IM, et al. Improved survival and quality of life in patients undergoing R1 pancreatic resection compared to patients with locally advanced unresectable pancreatic adenocarcinoma. *Pancreatol* 2013;13:180–5.
- [34] Kuroda S, Nishizaki M, Kikuchi S, et al. Double-flap technique as an antireflux procedure in esophagogastrostomy after proximal gastrectomy. *J Am Coll Surg* 2016;223:e7–13.
- [35] Ichikawa D, Komatsu S, Kubota T, et al. Long-term outcomes of patients who underwent limited proximal gastrectomy. *Gastric Cancer* 2014; 17:141–5.
- [36] Takagawa R, Kunisaki C, Kimura J, et al. A pilot study comparing jejunal pouch and jejunal interposition reconstruction after proximal gastrectomy. *Dig Surg* 2010;27:502–8.
- [37] Aikou T, Natsugoe S, Shimazu H, et al. Antrum preserving double tract method for reconstruction following proximal gastrectomy. *Jpn J Surg* 1988;18:114–5.
- [38] Kitamura K, Nishida S, Yamamoto K, et al. Lymph node metastasis in gastric cancer in the upper third of the stomach—surgical treatment on the basis of the anatomical distribution of positive node. *Hepatogastroenterology* 1998;45:281–5.
- [39] Liu K, Yang K, Zhang W, et al. Changes of esophagogastric junctional adenocarcinoma and gastroesophageal reflux disease among surgical patients during 1988-2012: a single-institution, high-volume experience in China. *Ann Surg* 2016;263:88–95.
- [40] Hu Y, Kim HI, Hyung WJ, et al. Vitamin B(12) deficiency after gastrectomy for gastric cancer: an analysis of clinical patterns and risk factors. *Ann Surg* 2013;258:970–5.
- [41] Lee JH, Hyung WJ, Kim HI, et al. Method of reconstruction governs iron metabolism after gastrectomy for patients with gastric cancer. *Ann Surg* 2013;258:964–9.