

Original Article



Clinical Comparison of Proximal Gastrectomy With Double-Tract Reconstruction Versus Total Gastrectomy With Roux-en-Y Anastomosis for Siewert Type II/III Adenocarcinoma of the Esophagogastric Junction

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ABSTRACT


Purpose: The incidence of adenocarcinoma of the esophagogastric junction (AEG) has increased in recent years, and the optimal surgical strategy for AEG remains highly controversial. We aimed to evaluate the safety and efficacy of proximal gastrectomy with double-tract reconstruction (PG-DT) for the treatment of patients with AEG.

Materials and Methods: We retrospectively analyzed patients with Siewert type II/III AEG between January 2013 and July 2018. Clinicopathological characteristics, survival, surgical outcomes, quality of life (QOL), and nutritional status were compared between the PG-DT and total gastrectomy with Roux-en-Y anastomosis (TG-RY) groups.

Results: After propensity score matching, 33 patients in each group were analyzed. There were no statistical differences between the 2 groups in terms of disease-free survival and overall survival. The surgical option was not an independent prognostic factor based on the multivariate analysis. In addition, no differences were found in terms of surgical complications. There were no significant differences in QOL assessed by the Visick grade, Gastrointestinal Symptom Rating Scale, or endoscopic findings. Furthermore, the long-term nutritional advantage of the PG-DT group was significantly greater than that of the TG-RY group.

Conclusions: PG-DT is a safe and effective procedure for patients with local Siewert type II/III AEG, regardless of the TNM stage.

Keywords: Adenocarcinoma; Esophagogastric junction; Gastrectomy; Reconstructive surgical procedure; Nutritional status

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Conflict of Interest

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

Author Contributions

Conceptualization: M.X., W.J., X.C.; Data curation: Z.M., P.H.; Formal analysis: M.X., Z.M., W.J.; Methodology: M.X., W.J.; Supervision: W.J., X.C.; Validation: Z.M., P.H.; Writing—original draft: M.X.; Writing—review and editing: W.J., X.C.

INTRODUCTION

Gastric cancer is the fifth most common malignancy among all cancers and the third leading cause of cancer-related deaths worldwide [1]. Although the incidence of gastric cancer has decreased in recent decades, the incidence of adenocarcinoma of the esophagogastric junction (AEG) has increased [2]. AEG usually refers to adenocarcinoma involving the anatomic esophagogastric junction (EGJ), and the tumor epicenter is located between the upper and lower 5 cm of the EGJ. The criteria developed by Siewert and Stein [3] have been widely accepted and used. AEGs are divided into three types according to Siewert's classification [3]. Briefly, type I AEG defines a distal esophageal adenocarcinoma in the range of 1 to 5 cm above the EGJ, while type II is located 1 cm above to 2 cm below the EGJ, and type III is located 2 to 5 cm below the EGJ [3]. Currently, surgery is indispensable for curing this disease [4].

The optimal surgical strategy for AEG remains controversial. The surgical options for Siewert type II and III AEG are total gastrectomy (TG) or proximal gastrectomy (PG) [5]. TG achieves adequate resection margins and radical lymph node dissection; however, it is also accompanied by poor postoperative nutritional status, such as anemia and weight loss [6]. Owing to the preserved remnant stomach, which stores some food and promotes the absorption of iron, vitamin B12, and other nutrients, PG improves the nutritional status and quality of life (QOL) of patients after surgery [7]; however, its oncologic safety is in doubt. The 2018 Japanese Gastric Cancer Guidelines recommend PG as an option for cT1N0 tumors in the upper-third stomach [8]. PG can be performed for Stage-IA of Siewert type II and III AEG according to the Korean Practice Guideline for Gastric Cancer 2018 [9]. However, we noticed that most Chinese patients were diagnosed with advanced AEGs [10]. Therefore, it is necessary to explore the application of PG in advanced AEG. The critical difference between TG and PG is the dissection of No. 4d, No. 5, and No. 6 lymph node stations. A study on the distribution of lymph node metastases in AEG found that No. 4d, No. 5, and No. 6 lymph node metastases are extremely rare [11]. Sasako et al. [12] reported that resection of these lymph nodes was not beneficial for patient survival. Yun et al. [13] verified that patients with T2 or small-sized T3 tumors (≤ 5 cm) could be candidates for PG. Yura et al. [14] demonstrated that the extent of lymph node dissection in PG was sufficient for oncological radicalization in T2/T3 AEG. However, the oncological safety of PG in patients with AEG beyond stage IA remains unclear.

The ideal reconstruction method for PG is another controversial issue. The easiest method is simple esophagogastrostomy, which results in several serious complications such as reflux esophagitis and anastomotic stricture [15,16]. As these complications often lead to deterioration of the nutritional status and QOL of patients, the wide application of PG has been limited. Several other reconstruction methods have been explored to address this problem, such as gastric tube reconstruction [17], double flap technique [18], jejunal interposition [19], and double-tract reconstruction (DT) [20]. Gastric tube reconstruction has only one anastomosis, which is easy to perform; however, there is still reflux and possible anastomotic leak and stenosis [17]. The double flap technique is complex and increases the risk of anastomotic stenosis [18,21]. The jejunal interposition method is prone to emptying disturbance [19]. Some reports have indicated that DT might be the ideal reconstruction for PG despite its multiple anastomoses [22,23]. Previous studies have verified that DT is superior to esophagogastrostomy [20,24], whereas its clinical advantages over TG have not yet been established.

This study aimed to retrospectively evaluate the oncological and surgical safety, postoperative QOL, and nutritional status of patients who underwent PG with DT (PG-DT) or TG with Roux-en-Y (TG-RY) anastomosis with local Siewert type II/III AEG, regardless of the TNM stage.

MATERIALS and METHODS

Participant recruitment, inclusion criteria, and exclusion criteria

We retrospectively analyzed patients with Siewert type II/III AEG treated at the Affiliated Suqian Hospital of Xuzhou Medical University in China from January 2013 to July 2018. Data retrieved from the medical records included sex, age, tumor size, Siewert type, surgical option, histological grade, TNM stage, postoperative complications, nutritional status, disease-free survival (DFS), and overall survival (OS). The inclusion criterion was histologically confirmed Siewert type II or III AEG. The exclusion criteria were as follows: 1) Confirmed distant metastases; 2) combined organ resection; 3) palliative surgery; 4) neoadjuvant chemotherapy or radiotherapy; 5) incomplete clinical data records; and 6) PG reconstruction with esophagogastrostomy. The flowchart of patient selection is shown in **Fig. 1**.

Clinical stage was determined in accordance with the seventh edition of the guidelines of the Joint Committee on Cancer of the United States and the International Union for Cancer Control. This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Affiliated Suqian Hospital of Xuzhou Medical University. Written informed consent was obtained from all the participants.

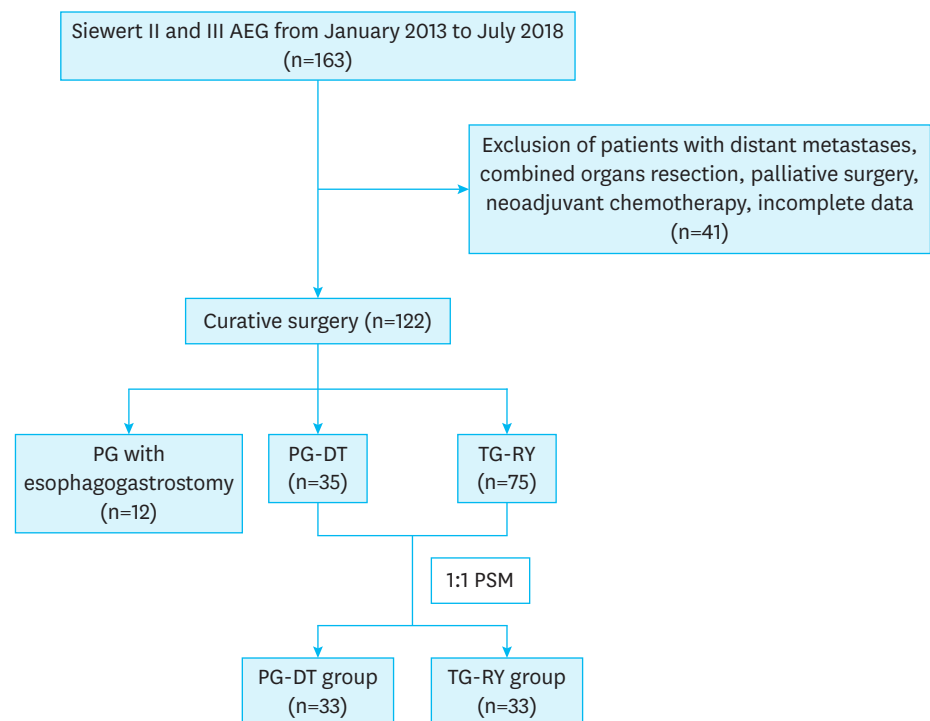


Fig. 1. Flowchart of patient selection. AEG = adenocarcinoma of the esophagogastric junction; PG = proximal gastrectomy; PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction; PSM = propensity score matching.

Surgical procedure

All patients underwent laparotomy.

PG-DT: D1+ lymph node dissection was performed according to Japanese gastric cancer treatment guidelines [8], including No. 1, 2, 3a, 4sa, 4sb, 7, 8a, 9, and 11p lymph node stations. Briefly, the omentum majus was dissociated along the transverse colon, and anterior lobe of transverse mesentery and pancreatic capsule were stripped. The roots of left gastroepiploic vessels were ligated and severed by No. 4sb lymph node dissection. The short gastric vessels were dissected with No. 4sa lymphadenectomy as dissection continued along the splenic hilum. The left side of stomach was freed up to the left crus of diaphragm, and lymph node No. 2 was removed. After the lesser omentum was severed along liver margin to right crus of diaphragm with removal of lymph nodes 1 and 3, the roots of left gastric artery and vein were dissected, and No. 8a, 7, 9, 11p lymphadenectomy was performed. The right gastric and gastroepiploic vessels were preserved to ensure blood supply to the remnant stomach. Furthermore, the adjacent lymph nodes were left untouched, including stations 5, 6, and 4d. The vagal nerve was dissected and lower esophagus was freed. The No. 110 lymph nodes were dissected via transabdominal esophageal hiatus approach in Siewert type II AEG. Subsequently, the esophagus was dissected at least 3 cm above the tumor, and a frozen section was obtained to confirm the negative incisional margin when necessary. Finally, the proximal stomach was separated by approximately 10 cm at the greater curvature and by 5 cm at lesser curvature below the tumor.

The jejunum and mesenteric vessels were severed 15 cm distal to the ligament of Treitz. The distal jejunum was moved for end-to-side esophagojejunostomy with the esophagus (esophagojejunal anastomosis) via the antecolic route, and a linear stapler was used to close the jejunum stump with a blind end of 2–3 cm. Next, 15–20 cm distal to the esophagojejunal anastomosis, a side-to-side gastrojejunostomy between the jejunum and the remnant stomach was performed mechanically using a 25-mm circular stapler (gastrojejunal anastomosis), and the stump of the stomach was closed. Finally, proximal and distal jejunal anastomoses were performed mechanically at a distance of 25 cm distal to the gastrojejunal anastomosis (jejunojejunal anastomosis). A schematic diagram and laparotomy photo of the PG-DT is shown in **Fig. 2A and B**. Upper gastrointestinal imaging after PG-DT showed that the contrast medium flowed from the proximal jejunum limb into residual stomach and distal proximal jejunum (**Fig. 2C-F**).

TG-RY: Standard D2 lymph node dissection and TG-RY were performed according to the Japanese gastric cancer treatment guidelines.

Follow-up

Patient follow-up started from the date of surgery and continued until September 2021 or until patient death. All the patients underwent postoperative follow-up every 6 months. Survival status and data were obtained through outpatient follow-up or telephone interviews with patients or family members. The median follow-up duration was 58 (2–95) months: 54 (2–94) months and 61 (6–95) months in the PG-DT and TG-RY groups, respectively. Postoperative complications, including anastomotic leakage, hemorrhage, abdominal abscess, pulmonary infection, dumping syndrome, anastomotic stenosis, anastomotic ulcer, and intestinal obstruction, were obtained from medical records and follow-up. The QOL of the patients was assessed using the Visick grade, Gastrointestinal Symptom Rating Scale (GSRS), and endoscopic findings. The Visick grade was used to assess gastroesophageal

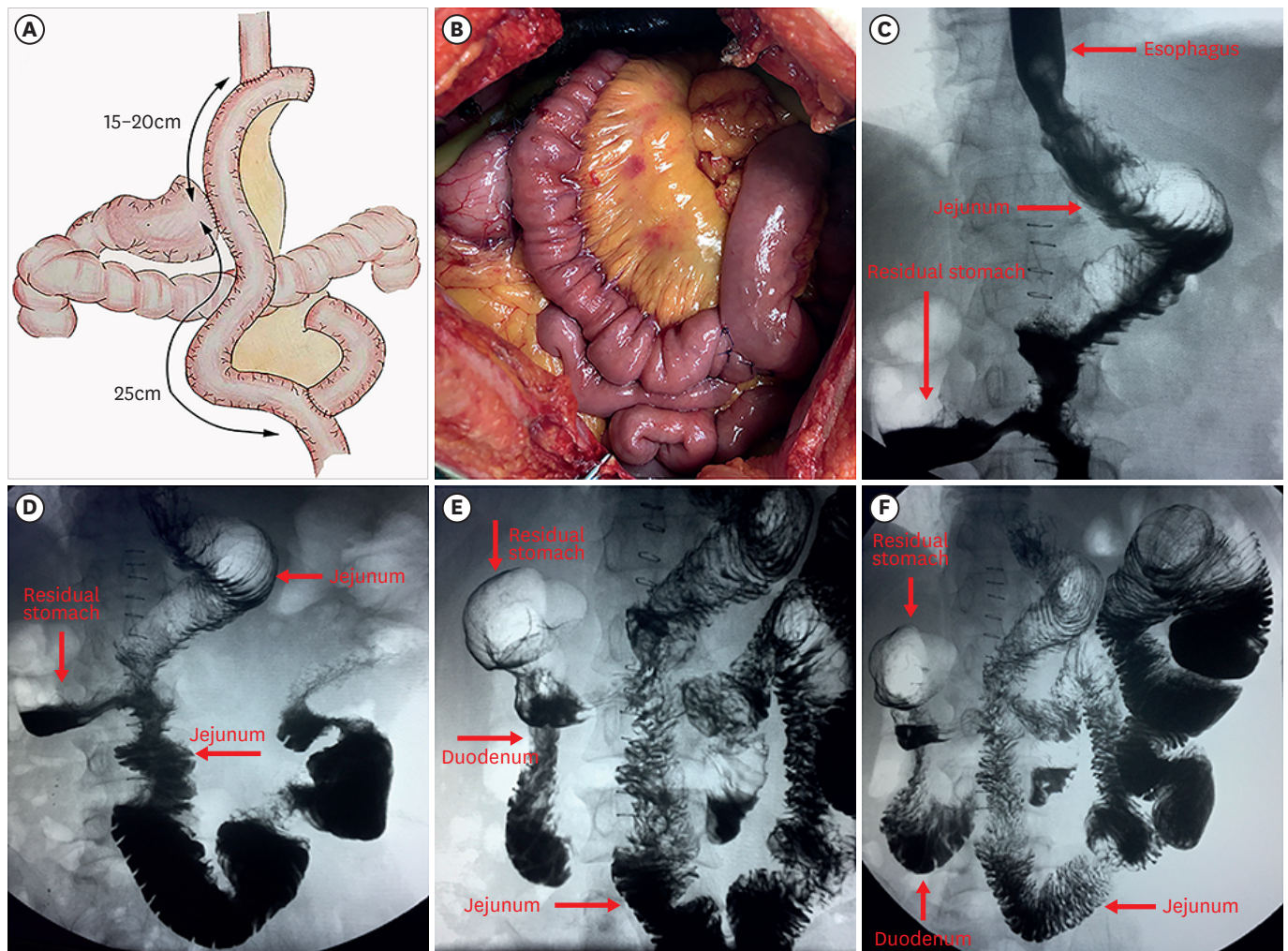


Fig. 2. Figuration of proximal gastrectomy with double-tract reconstruction. (A) Schematic diagram; (B) laparotomy photo; (C-F) upper gastrointestinal imaging showing the contrast medium flowing from the proximal jejunum limb into the residual stomach and distal proximal jejunum.

reflux symptoms approximately 12 months after surgery (Visick grade I, no symptoms; Visick grade II, occasional symptoms; Visick grade III, obvious but tolerable symptoms; and Visick grade IV, obvious and unbearable symptoms). The Gastrointestinal Symptom Rating Scale (GSRS) was used to evaluate digestive system symptoms including abdominal pain, reflux, diarrhea, dyspepsia, and constipation. Endoscopic findings were obtained from medical records approximately 12 months postoperatively, and the original images were checked for positive results. The Los Angeles (LA) classification [25] was used to evaluate endoscopic findings. Lymphocyte count, hemoglobin (Hb), serum albumin (Alb), total serum protein (TP), and body weight were collected preoperatively and at 1, 6, 12, and 36 months postoperatively to evaluate the nutritional status.

Statistical analysis

To reduce the effects of possible confounders and selection bias, propensity score matching (PSM) was used to offset the differences between the two groups. Propensity scores were estimated using a logistic regression model of the following seven variables: sex, age, tumor size, Siewert type, histological grade, positive lymph nodes, and TNM stage. One to

one matching (without replacement) according to propensity score was performed using the nearest neighbor method, with a caliper size of 0.2 standard deviations. Standardized differences were estimated before and after matching. Quantitative data are expressed as the mean ± standard deviation, while qualitative data are expressed as rates. Student’s *t*-test or the Mann–Whitney rank sum test was used to evaluate continuous data, and the χ^2 test or Fisher’s exact test was used for rates. Kaplan–Meier survival curves and the log-rank test were used to evaluate survival. Cox regression models were used to estimate the hazard ratio (HR), 95% confidence intervals (CI), and prognostic factors. A two-sided *P*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA).

RESULTS

Clinicopathological characteristics

A total of 110 patients were enrolled in this study, including 35 who underwent PG-DT and 75 who underwent TG-RY. There were no significant differences between the 2 groups in terms of sex (*P*=0.958), age (*P*=0.198), Siewert type (*P*=0.152), and histological grade (*P*=0.062), whereas statistically significant differences were found in tumor size (*P*=0.001), number of positive lymph nodes (*P*=0.013), and TNM stage (*P*<0.001). After matching, 33 patients were enrolled into each group. The 2 groups were well balanced in terms of sex (*P*=1.000), age (*P*=0.602), tumor size (*P*=0.398), Siewert type (*P*=0.802), histological grade (*P*=0.598), number of positive lymph nodes (*P*=0.811), and TNM stage (*P*=0.565). The clinicopathological characteristics of the enrolled patients before and after PSM are shown in **Table 1**.

Table 1. Clinicopathologic characteristics of patients before and after PSM

| Variables | Before PSM | | | After PSM | | |
|----------------------|--------------|--------------|--------|--------------|--------------|-------|
| | PG-DT (n=35) | TG-RY (n=75) | P | PG-DT (n=33) | TG-RY (n=33) | P |
| Sex | | | 0.958 | | | 1.000 |
| Female | 5 | 11 | | 5 | 5 | |
| Male | 30 | 64 | | 28 | 28 | |
| Age (yr) | | | 0.198 | | | 0.602 |
| ≤60 | 12 | 17 | | 10 | 12 | |
| >60 | 23 | 58 | | 23 | 21 | |
| Tumor size (cm) | | | 0.001* | | | 0.398 |
| ≤4 | 28 | 34 | | 26 | 23 | |
| >4 | 7 | 41 | | 7 | 10 | |
| Siewert type | | | 0.152 | | | 0.802 |
| II | 21 | 34 | | 19 | 20 | |
| III | 14 | 41 | | 14 | 13 | |
| Histological grade | | | 0.062 | | | 0.598 |
| Well | 6 | 3 | | 5 | 2 | |
| Moderate | 16 | 36 | | 16 | 17 | |
| Poor | 13 | 36 | | 12 | 14 | |
| Positive lymph nodes | 2.2±4.5 | 5.2±6.1 | 0.013* | 2.3±4.6 | 2.6±3.6 | 0.811 |
| TNM stage | | | 0.000* | | | 0.565 |
| I | 16 | 10 | | 14 | 10 | |
| II | 9 | 19 | | 9 | 12 | |
| III | 10 | 46 | | 10 | 11 | |

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

PSM = propensity score matching; PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction.

**P*<0.05.

Clinical outcomes

At the time of the last follow-up, the recurrence and metastasis rates in the PG and TG groups were 36.4% and 39.4%, respectively, with no significant difference ($P=0.80$). The mortality rates in the PG and TG groups were 33.3% and 39.4%, respectively, with no significant difference ($P=0.61$). The 5-year DFS rates were 60% and 53% in the PG and TG, respectively. The 5-year OS rates in the PG and TG groups were 61% and 60%, respectively. The median survival time was 44 months in both groups. The Kaplan–Meier survival curves and log-rank test showed no difference between the 2 groups in terms of DFS ($P=0.729$) and OS ($P=0.618$); however, the survival time in the PG group appeared to be slightly higher than that in the TG group (**Fig. 3**). Univariate Cox regression analysis showed that sex ($P=0.394$), age ($P=0.963$), tumor size ($P=0.123$), Siewert type ($P=0.396$), histological grade ($P=0.177$), and surgical option ($P=0.698$) were not associated with the prognosis of AEG, while lymph node metastasis (HR, 3.326; 95% CI, 1.414–7.822; $P=0.006$) and TNM stage (HR, 3.693; 95% CI, 1.610–8.469; $P=0.002$) were significantly associated with prognosis (**Table 2**). Multivariate Cox regression analysis showed that TNM stage was an independent prognostic factor (HR, 3.809; 95% CI, 1.661–8.734; $P=0.002$), while surgical option ($P=0.949$) and lymph node metastasis ($P=0.349$) were not independent prognostic factors (**Table 2**).

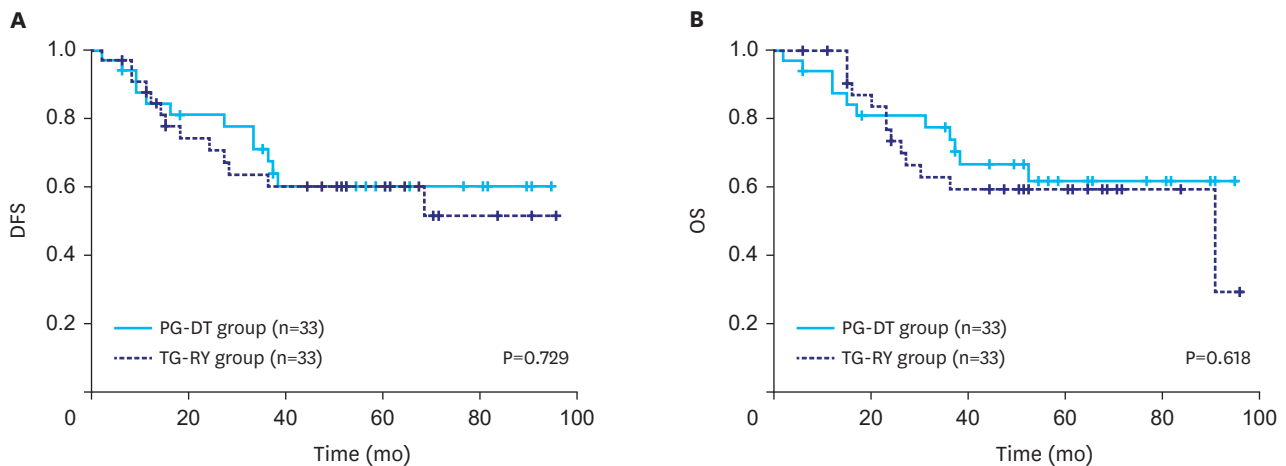


Fig. 3. Kaplan–Meier survival curves for DFS (A) and OS (B) after PG-DT and TG-RY.

DFS = disease-free survival; OS = overall survival; PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction.

Table 2. Univariate and multivariate Cox regression analysis of clinicopathological factors for overall survival in patients

| Variables | Univariate analysis | | | Multivariate analysis | | |
|--------------------------------------------|---------------------|-------------|--------|-----------------------|-------------|--------|
| | HR | 95% CI | P | HR | 95% CI | P |
| Sex: Male vs. Female | 1.880 | 0.440–8.032 | 0.394 | | | |
| Age: >60 vs. ≤60 years | 1.020 | 0.436–2.390 | 0.963 | | | |
| Tumor size: >4 vs. ≤4cm | 1.919 | 0.838–4.392 | 0.123 | | | |
| Siewert type: II vs. III | 0.706 | 0.316–1.578 | 0.396 | | | |
| Histological grade: Moderate-well vs. Poor | 0.565 | 0.247–1.293 | 0.177 | | | |
| lymph node metastasis: N+ vs. NO | 3.326 | 1.414–7.822 | 0.006* | - | - | 0.349 |
| TNM stage: III vs. I–II | 3.693 | 1.610–8.469 | 0.002* | 3.809 | 1.661–8.734 | 0.002* |
| Surgical option: PG vs. TG | 0.853 | 0.381–1.906 | 0.698 | - | - | 0.949 |

HR = hazard ratio; CI = confidence interval; PG = proximal gastrectomy; TG = total gastrectomy.

* $P<0.05$.

Table 3. Comparison of surgical outcomes between the two groups

| Variables | PG-DT (n=33) | TG-RY (n=33) | P |
|------------------------------------|--------------|--------------|--------|
| Operation time (min) | 204±37 | 205±50 | 0.928 |
| Blood loss (mL) | 171±71 | 176±96 | 0.816 |
| Number of lymph node dissection | 21.5±9.5 | 29.0±10.9 | 0.004* |
| Postoperative hospital stay (days) | 15.4±2.3 | 17.2±3.8 | 0.021* |
| Early complications | | | |
| Anastomotic leakage | 0 | 1 | ns |
| Anastomotic bleeding | 3 | 2 | ns |
| Abdominal abscess | 0 | 0 | ns |
| Pulmonary infection | 1 | 1 | ns |
| Late complications | | | |
| Dumping syndrome | 2 | 2 | ns |
| Anastomotic stricture | 2 | 1 | ns |
| Anastomotic ulcer | 0 | 1 | ns |
| Intestinal obstruction | 2 | 2 | ns |

PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction; ns = no significance.

* $P < 0.05$.

Surgical outcomes

The operation times of the PG-DT and TG-RY groups were 204±37 minutes and 205±50 minutes, respectively, and the difference was not statistically significant ($P=0.928$). The blood loss amounts in the 2 groups were 171±71 mL and 176±96 mL, respectively, with no statistical difference ($P=0.816$). The number of lymph node dissections in the 2 groups were 21.5±9.5 and 29.0±10.9, respectively, with a statistically significant difference ($P=0.004$). The mean postoperative hospital stay durations were 15.4±2.3 and 17.2±3.8 days, respectively, and the difference was statistically significant ($P=0.021$). There were no differences between the two groups in terms of early complications (anastomotic leakage, anastomotic bleeding, abdominal abscess, and pulmonary infection) or late complications (dumping syndrome, anastomotic stricture, anastomotic ulcer, and intestinal obstruction), as shown in **Table 3**. No perioperative deaths occurred in either of the groups.

Follow-up outcomes

QOL

A total of 29 patients in the PG-DT group and 31 patients in the TG-RY group were evaluated for QOL approximately 12 months postoperatively. The Visick grade results showed that there were 6 patients with Visick grade II and 2 patients with grade III in the PG-DT group, while there were 7 patients with grade II and 4 patients with grade III in the TG-RY group, with no significant difference ($P=0.846$). No patients with Visick grade IV were found in either group. The mean GSRS score of the PG-DT group (23.45±6.21) was better than that of the TG-RY group (24.74±5.99), with no statistically significant difference ($P=0.403$). However, patients in the PG-DT group had a lower incidence of diarrhea than those in the TG-RY group ($P < 0.05$). The results of LA classification showed that 27 cases were rated as grade A and 2 cases as grade B in the PG-DT group, while 27 cases were rated as grade A and 4 cases as grade B in the TG-RY group. No cases of grade C or D severe reflux esophagitis were observed in either group. There was no significant difference between the 2 groups ($P=0.731$). The details are presented in **Table 4**. Images of the endoscopic findings are shown in **Fig. 4**, and no obvious reflux esophagitis was present on any image.

Nutritional status

Lymphocyte counts were not significantly different between the 2 groups at any time point,

Table 4. Quality of life of patients at approximately 12 months postoperatively

| Variables | Total | PG-DT | TG-RY | P |
|-------------------|------------|------------|------------|-------|
| Cases | 60 | 29 | 31 | |
| Visick grade | | | | 0.846 |
| I | 41 | 21 | 20 | |
| II | 13 | 6 | 7 | |
| III | 6 | 2 | 4 | |
| IV | 0 | 0 | 0 | |
| GSRs score | 24.10±6.09 | 23.45±6.21 | 24.74±5.99 | 0.403 |
| LA classification | | | | 0.731 |
| A | 53 | 27 | 27 | |
| B | 7 | 2 | 4 | |
| C or D | 0 | 0 | 0 | |

PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction; GSRs = Gastrointestinal Symptom Rating Scale; LA = Los Angeles.

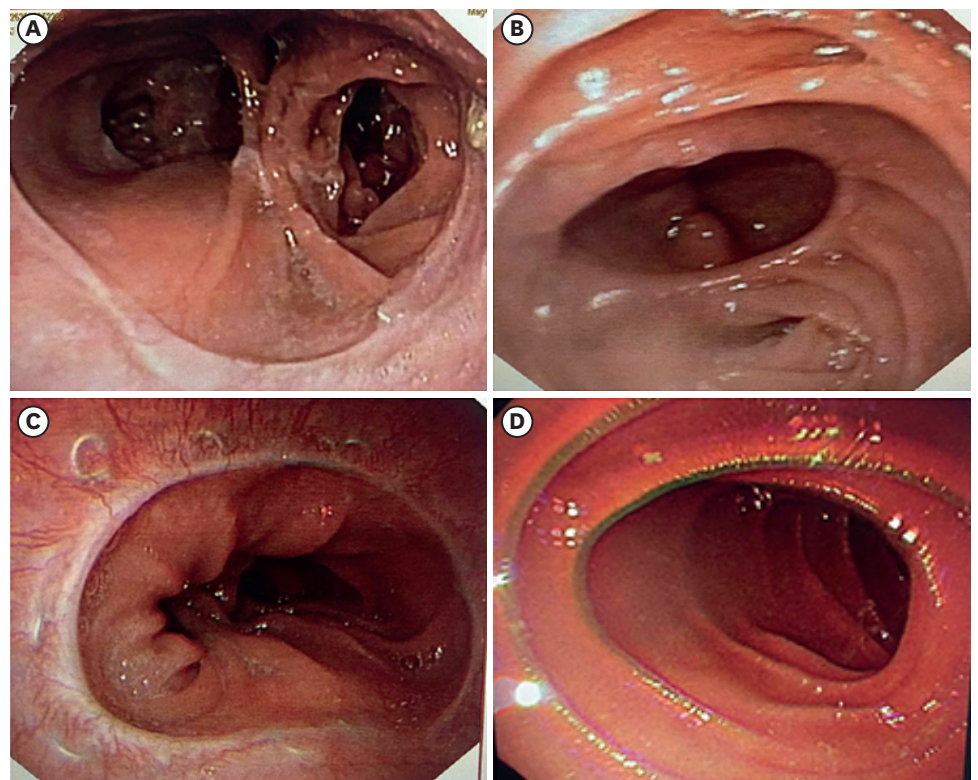


Fig. 4. Endoscopic image of the esophagojejunal anastomotic site (A) and gastrojejunal anastomotic site (B) in a PG-DT. Image of the esophagojejunal anastomotic site (C) and jejunum (D) in a TG-RY. No obvious reflux esophagitis was present in any image.

PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction.

whereas the counts of the PG-DT group appeared to be slightly better than those of the TG group at 36 months postoperatively (**Fig. 5A**). The hemoglobin, serum albumin, and total protein levels of the PG-DT group were significantly higher than those of the TG-RY group at 36 months postoperatively, with a statistically significant difference; however, no difference was present at other time points (**Fig. 5B-D**). Using the preoperative weight as the baseline, weight loss occurred after surgery compared with the preoperative weight in both groups; however, the weight loss in the PG-DT group was superior to that in the TG-RY group, with a significant difference at 36 months postoperatively (**Fig. 5E**).

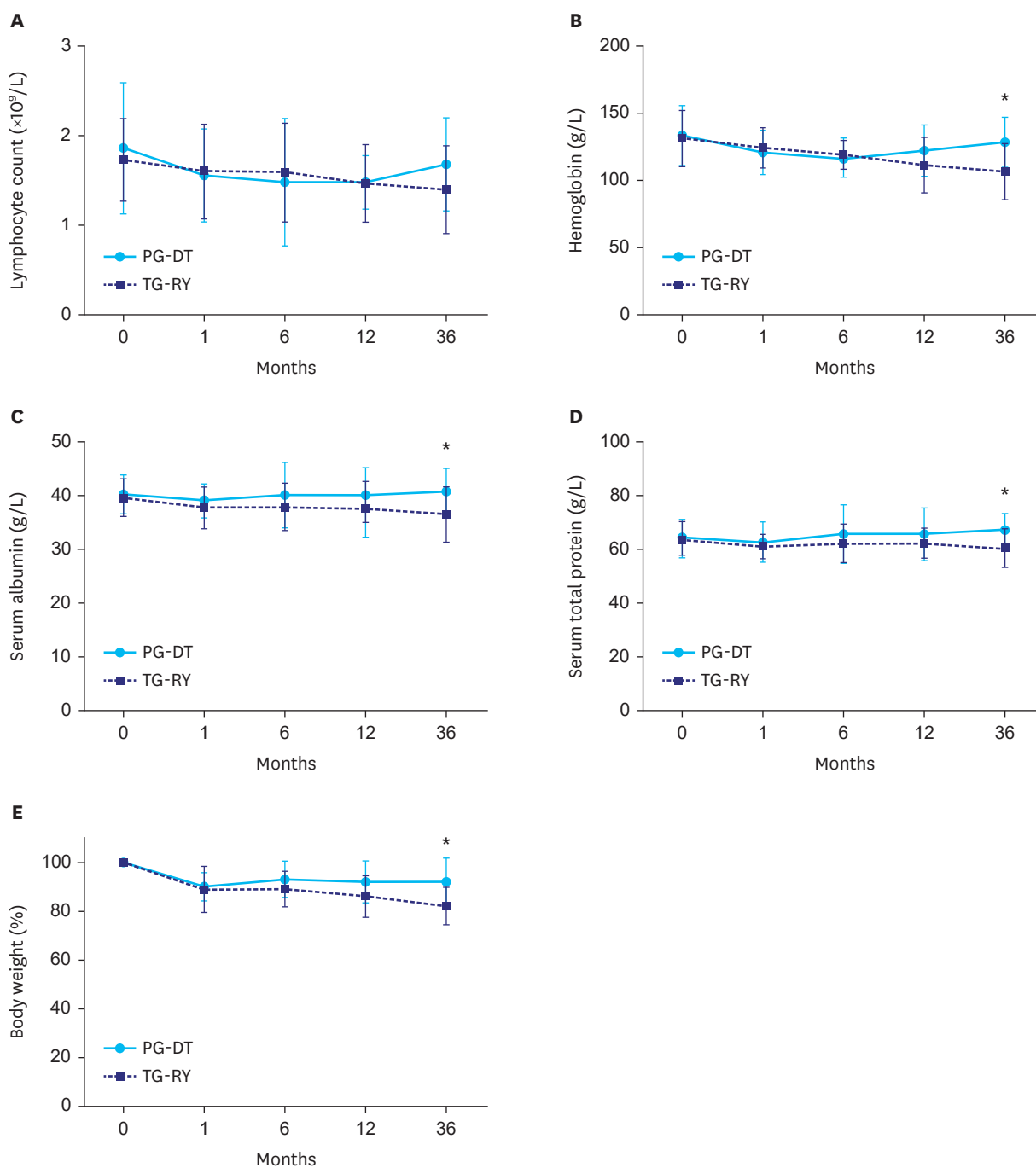


Fig. 5. Comparison of nutritional status in terms of lymphocyte counts (A), hemoglobin (B), serum albumin (C), total serum protein (D), and body weight (E) between PG-DT and TG-RY groups preoperatively and postoperative at 1, 6, 12, and 36 months.

PG-DT = proximal gastrectomy with double-tract reconstruction; TG-RY = total gastrectomy with Roux-en-Y reconstruction.

*P<0.05.

DISCUSSION

The incidence of AEG has increased in recent years, and the prognosis of AEG remains poor [2]. Currently, surgery is the preferred treatment for patients with AEG [4]. As type I AEG follows the principles of esophageal cancer treatment [26], we will only discuss the treatment

of type II/III AEG. The extent of resection, lymph node dissection, and gastrointestinal reconstruction of type II/III AEG remains controversial. Thus, there is an urgent need to establish an optimal treatment to provide more benefits to patients. In the present study, there were no significant differences in DFS, OS, surgical complications, or postoperative QOL between the PG-DT and TG-RY groups. The long-term nutritional status of the PG-DT group was better than that of the TG-RY group. To our knowledge, this is the first study to comprehensively evaluate the differences in oncological safety, surgical safety, postoperative QOL, and nutritional status between PG-DT and TG-RY groups. Our data demonstrate that PG-DT is a safe and effective procedure for local Siewert type II/III AEG, regardless of the TNM stage.

The application of PG in the treatment of early AEG is generally accepted by most surgeons [23,27]. However, there is no consensus regarding advanced disease. We believe that PG with the D1+ procedure for AEG is appropriate for the following reasons. First, according to the 5th edition of the Japanese Gastric Cancer Treatment Guidelines, lymph nodes 5 and 6 are classified as N3 lymph nodes that do not require dissection [8]. Second, No. 4d, 5, and 6 lymph node metastases in gastric cancer located at the EGJ are extremely rare [11]. Third, patients with No. 4d lymph node metastasis had a poor prognosis with or without lymph node dissection, and the therapeutic value of No. 4d resection was low [28]. Therefore, we administered PG to patients with local Siewert type II/III AEG, regardless of early or advanced disease.

In our study, the 5-year OS rates in the PG and TG groups were 61% and 60%, respectively, with no significant difference. Consistently, Rosa [5] reported no significant difference in the 5-year OS rates of 56.7% and 46.5% for the PG and TG groups, respectively. Xiao [29] found no significant difference in OS rates between the PG and TG groups (55.6% and 48.6%, respectively). The survival rate in our study appeared to be higher than that in previous studies [5,29], probably because our study included more patients with early-stage disease and excluded patients with stage IV disease. The cox regression analysis suggested that surgical option (PG or TG) was not an independent prognostic factor. It is worth noting that the P-value was 0.949, which is close to 1, indicating little effect of the surgical option on the prognosis of AEG. Consistent with our results, Harrison et al. [30] reported that surgical options for proximal gastric cancer did not affect the long-term clinical outcomes. Collectively, the above data support the notion that PG is a surgical procedure with clinical outcomes comparable to those of TG for AEG in terms of survival.

PG makes gastric contents more susceptible to reflux due to the disruption of the anatomical anti-reflux barrier. The appropriate reconstruction of the digestive tract is an important solution to this problem. Theoretically, jejunal interposition in DT could act as a buffer against reflux esophagitis to improve QOL [20,23]. However, the safety of the procedure is a concern because of increased anastomosis of the DT. We found no differences in the early and late complications between the PG-DT and TG-RY groups. No anastomotic leakage occurred in the PG-DT group, with more anastomoses observed. In addition, the PG dissected fewer lymph nodes than the TG; however, the number of lymph nodes dissected by the PG exceeded the criterion of 16. Therefore, PG-DT is considered a safe surgical procedure.

In terms of QOL, our data showed that none of the patients had serious complications, such as severe reflux or severe anastomotic stenosis. PG-DT significantly reduced PG-related reflux and achieved an antireflux effect similar to that of TG-RY. Consistently, Li et al. [31]

reported that PG-DT did not increase the incidence of reflux esophagitis and anastomotic strictures compared to TG-RY. Conversely, Sato et al. [22] reported that reflux esophagitis was more frequent in the PG-DT group than in the TG-RY group, and the incidence of anastomotic stricture did not differ. This may be due to the shorter length of the jejunal interposition (10–12 cm) in Sato's study. In this study, the length of the jejunal interposition was 15–20 cm in accordance with the size of the remnant stomach, which achieves a tension-free anastomosis and no food retention. Previous studies are in general agreement with our results [32,33]. Taken together, PG-DT is similar to TG in terms of QOL.

The intact duodenal pathway in DT appears to facilitate stimulation of gastrointestinal hormone secretion, which facilitates nutrient absorption and improves nutritional status [22,23]. Nevertheless, previous studies have reported contradictory results [34–36]. Wang et al. [34] found that PG-DT was superior to TG-RY in terms of postoperative serum albumin, total protein, and hemoglobin levels; however, the difference in weight loss was not significant. Jung et al. [35] concluded that PG-DT was more beneficial than TG-RY in terms of serum albumin level, body weight, prevention of anemia, and maintenance of serum vitamin B12 levels. Cho et al. [36] reported that postoperative hematological indices, including hemoglobin, ferritin, transferrin saturation, and anemia, showed no significant differences between the 2 groups. Our data implied the same trends in lymphocyte counts, hemoglobin, albumin, total protein, and body weight. The nutritional advantage of the PG-DT group began to emerge 12 months postoperatively, and nutritional indicators were significantly better than those of the TG-RY group 36 months postoperatively. These results suggest long-term nutritional advantages of PG-DT.

Notably, the nutritional advantage of the PG-DT group was not significant. As upper gastrointestinal imaging showed no contrast medium entering the duodenum, we speculated that the effectiveness of DT may be influenced by the amount of food passing through the physiological route (i.e., the duodenum). A 25-mm circular stapler was applied during gastrojejunal anastomosis in this study; thus, we raised the question of whether enlarging the gastrojejunal anastomosis would facilitate the entry of more food into the duodenal channel and improve nutrition. Wang et al. [34] suggested that a 60-mm linear stapler for gastrojejunostomy with an enlarged anastomosis would be better than TG-RY in terms of nutrition. However, it is unclear whether its nutritional status is better than that of a 25-mm circular gastrojejunostomy. In addition, there is a possibility of increased reflux with an enlarged gastrojejunal anastomosis. Therefore, the effect of an enlarged anastomosis needs to be clarified in further studies.

This study had several limitations. First, this was a retrospective study conducted at a single institution, with an inadequate sample size. Although PSM was used, selection bias could not be completely avoided. Second, the follow-up period did not allow for an accurate assessment of the ongoing oncologic outcomes. Third, the lack of stratified analysis of patients' postoperative chemotherapy reduced the reliability of the clinical outcomes. Further comprehensive prospective studies are required to validate these results.

In conclusion, PG-DT is nutritionally superior to TG-RY and similar to TG-RY in terms of survival, surgical complications, and QOL in patients with AEG. Therefore, PG-DT is a safe and effective procedure for patients with Siewert type II/III AEG, regardless of the TNM stage. However, the validity of these results should be verified using large-scale randomized trials.

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