



Laparoscopic-assisted versus open proximal gastrectomy with double-tract reconstruction for Siewert type II–III adenocarcinomas of esophago-gastric junction: a retrospective observational study of short-term outcomes

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Background: Currently, the surgical approach to adenocarcinomas of esophago-gastric junction (AEG) remains controversial. Function-preserving gastric surgeries are becoming more popular, with proximal gastrectomy with double-tract anastomosis being one of the most important for AEG. Meanwhile, with the increasing use of laparoscopic techniques in the treatment of gastric cancer, the safety and effectiveness of laparoscopic-assisted proximal gastrectomy with double-tract anastomosis for Siewert type II–III AEG need to be further clarified.

Methods: Data of patients with Siewert type II/III AEG was collected at our center from October 2010 to December 2019 were retrospectively analyzed. 61 patients underwent open proximal gastrectomy with double-tract anastomosis (OPG-DT group) and 52 underwent laparoscopic-assisted proximal gastrectomy with double-tract anastomosis (LAPG-DT group). The clinical features, surgery, and short-term outcomes of patients in these 2 groups were collected to assess the safety and feasibility of LAPG-DT.

Results: A total of 113 patients were analyzed, there were 98 males and 15 females. No death during the operation. The differences in the number of lymph nodes, time to first flatus, time to first eating, postoperative hospital stay, additional analgesics were not statistically significant between two groups. Although the operative duration of LAPG-DT group was significantly longer than that of the OPG-DT group [(217±61) vs. (161±14) min, P=0.000], while less blood loss and less stress in LAPG-DT group. Early and late postoperative complications were similar between two groups.

Conclusions: Although laparoscopic-assisted proximal gastrectomy with double-tract anastomosis requires long operative time, it is associated with less bleeding and milder stress. Therefore, it is a safe and feasible surgical method.

Keywords: Laparoscopic surgery; double-tract reconstruction; proximal gastrectomy; adenocarcinoma of the esophago-gastric junction

Submitted Feb 03, 2021. Accepted for publication Apr 20, 2021.

doi: 10.21037/jgo-21-165

View this article at: <http://dx.doi.org/10.21037/jgo-21-165>

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Introduction

The prevalence of adenocarcinoma of the esophagogastric junction (AEG) has shown a rising trend in recent years (1,2). Multidisciplinary treatment, mainly surgery, is an effective strategy for early and middle-stage AEG and remains the only possible cure for this malignancy (3). Currently, the surgical approach to AEG remains controversial. A Japanese retrospective study suggested that the short-term and long-term outcomes of laparoscopic radical surgery and open surgery in the treatment of advanced gastric cancer between were not significantly different (4). A large number of multicenter clinical studies on laparoscopic surgery for advanced gastric cancer are underway. The oncologic safety of proximal gastrectomy for stage T_{2/3} AEG has recently been found to not significantly be different from that of total gastrectomy (5). However, total gastrectomy remains the most preferred surgical procedure for Siewert type II–III AEG (6). According to the Japanese Gastric Cancer Treatment Guidelines (fifth edition) (7), the recommended digestive tract reconstruction methods following proximal gastrectomy are esophagus-gastric remnant anastomosis, jejunal interposition, and double tract anastomosis (8). Compared with total gastrectomy, proximal gastrectomy can preserve some gastric functions and improve patients' postoperative nutritional status. However, the incidence of reflux esophagitis reaches 25% one year after proximal gastrectomy plus esophagus-gastric remnant anastomosis, while the incidence of postoperative anastomotic stricture reaches to about 35% (8). A retrospective propensity score matching analysis in the Republic of Korea found that proximal gastrectomy with double-tract anastomosis lowered the incidences of these complications and might be associated with better clinical outcomes (9).

Our study retrospectively analyzed the clinical data of 113 patients who had undergone proximal gastrectomy with double-tract anastomosis in our center from October 2010 to October 2019 to assess the feasibility and safety of laparoscopically assisted proximal gastrectomy with double-tract anastomosis. We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/jgo-21-165>).

Methods

Subjects

The inclusion criteria were as follows: (I) with Siewert type II/III AGE preoperatively proven by gastroscopy

and biopsy, which was expected to be feasible for proximal gastrectomy; (II) with a diagnosis of cT₁₋₂N₀M₀ on abdominal contrast-enhanced computed tomography (CT); (III) aged 18–80 years; (IV) without a history of cancer or serious underlying disease, and with an Eastern Cooperative Oncology Group (ECOG) physical performance score of <2 and an American Society of Anesthesiologists (ASA) score of <3 points. The exclusion criteria included the following: (I) with early AEG that could be removed under endoscope; (II) with a history of malignancy; (III) with other serious comorbidities that would make surgery intolerable; (IV) previous neoadjuvant radiochemotherapy; (V) with a serious psychiatric disease; (VI) with incomplete clinical data.

The clinical outcomes of 113 consecutive Siewert type II/III AEG patients treated at our center from October 2010 to December 2019 were retrospectively analyzed. The decision to perform this procedure depended on the intraoperative findings. Laparoscopically assisted radical proximal gastrectomy with double-tract anastomosis has been carried out in our center since June 2014.

This was a retrospective case-control study and the requirement for informed consent was waived. This retrospective case-control study was approved by the ethics committee of Henan Tumor Hospital (No. 2019156) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study didn't involve the biological tissues and specimens of patients, and informed immunity.

Clinical data extraction and interpretation

Demographic and clinicopathological data including gender, age, body mass index (BMI), previous medical histories (including hypertension, diabetes, and coronary heart disease), history of surgery, lab tests, surgical procedure, operative time, intraoperative blood loss, number of lymph nodes obtained postoperatively, and postoperative complications (including reflux symptoms) were collected.

Surgical maneuvers

The scope of resection included lymph node dissection performed under open or laparoscopic conditions with reference to the Japanese Classification of Gastric Carcinoma second English Version (10), as described in detail by Ma *et al.* (11).

The reconstruction method consisted of esophagojejunostomy, gastrojejunostomy, and jejunojunction performed using

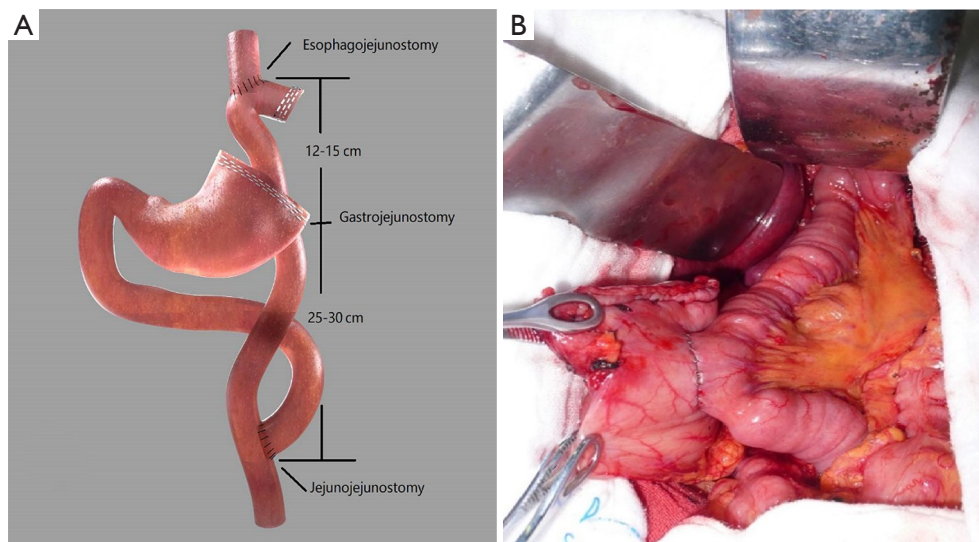


Figure 1 Schematic diagram and anastomosis of the open proximal gastrectomy with double-tract reconstruction group. (A) Schematic diagram of OPG-DT group. (B) Anastomosis in the OPG-DT group. OPG-DT, open proximal gastrectomy with double-tract anastomosis.

a circular stapler (Figure 1).

Outcome indicators and follow-up visits

Thoraco-abdominopelvic CT was performed about 3 days after surgery, and water-soluble contrast was administered about 5 days after surgery to determine the degree of healing of the reconstructed digestive tract. Patients were allowed to eat if there was no anastomotic leak or intestinal obstruction. The main outcome indicators included the occurrence of perioperative complications and the occurrence of postoperative reflux esophagitis. The postoperative complications were graded according to the Clavien-Dindo classification (12), and the postoperative gastroesophageal reflux symptoms were evaluated using the Visick scores (13). Based on the gastroscopic findings, postoperative reflux gastritis was graded according to the Los Angeles classification criteria (14).

Statistical analysis

Statistical analysis was performed by SPSS 22.0 software (IBM Corp.). The normally distributed measurement data are presented as $\bar{x} \pm SD$ and were compared using *t*-test, while the nonnormally distributed measurement data are presented using M (Q1, Q3) and were compared using Mann-Whitney U test. The generalized estimating equation was used for comparisons between groups at

different time points. Count data are expressed as cases (%). The comparisons of nonranked count data were based on χ^2 test, and the comparisons between ranked count data were performed using the Mann-Whitney U test. A P value <0.05 was considered significantly different.

Results

Surgery and recovery during the perioperative period

Radical proximal gastrectomy with double-tract anastomosis was performed in 113 patients, among whom 61 received open proximal gastrectomy with double-tract anastomosis (OPG-DT group) and 52 of whom underwent laparoscopically assisted proximal gastrectomy with double-tract anastomosis (LAPG-DT group). The clinicopathological data of these patients are listed in Table 1. The operative time in the LAPG-DT group was longer than in the OPG-DT group and stabilized with the improvement of the surgical procedure. There was no significant difference between the 2 groups in the amount of intraoperative bleeding and the number of lymph nodes obtained postoperatively. After the surgery, the time to first flatus, the time to first eating, and postoperative hospital stay also showed no significant differences (Table 2).

Postoperative complications

We defined early and late postoperative complications as

Table 1 Clinicopathological data of patients

Variable	OPG-DT (n=61)	LAPG-DT (n=52)	Statistics	P value
Age ($\bar{x} \pm s$, years)	61.2±7.2	63.2±8.6	t=-1.264	0.209
Gender, n (%)			$\chi^2=0.606$	0.542
Male	54 (88.5)	44 (84.6)		0.542
Female	7 (11.5)	8 (15.4)		
BMI	22.6±1.2	22.1±1.3	t=1.895	0.061
Comorbidities, n (%)	36 (59.0)	28 (53.8)	$\chi^2=0.306$	0.580
Hypertension	15 (24.6)	11 (21.2)		
Coronary heart diseases	2 (3.3)	1 (1.9)		
Cerebrovascular diseases	1 (1.6)	0		
Diabetes	5 (8.2)	6 (11.5)		
Chronic obstructive lung disease	1 (1.6)	0		
Differentiation degree			$\chi^2=0.206$	0.902
Highly differentiated	2 (3.3)	1 (1.9)		
Moderately differentiated	16 (26.2)	14 (26.9)		
Poorly/not differentiated	43 (70.5)	37 (71.2)		
p T, n (%)			$\chi^2=2.567$	0.277
T ₁	16 (26.2)	21 (40.4)		
T ₂	41 (67.2)	28 (53.8)		
T ₃	4 (6.6)	3 (5.8)		
p N, n (%)			$\chi^2=4.264$	0.119
N ₀	32 (52.5)	37 (71.2)		
N ₁	26 (42.6)	13 (25.0)		
N ₂	3 (4.9)	2 (3.8)		
TNM stage*, n (%)			$\chi^2=5.148$	0.272
I _A	11 (18.0)	17 (32.7)		
I _B	26 (42.6)	23 (44.2)		
II _A	18 (29.5)	9 (17.3)		
II _B	5 (8.2)	2 (3.8)		
III _A	1 (1.6)	1 (1.9)		

* , indicates tumor-node-metastasis (TNM) stage, based on the Union for International Cancer Control (UICC) TNM staging system (eighth edition). OPG-DT, open proximal gastrectomy with double-tract anastomosis; LAPG-DT, laparoscopically assisted proximal gastrectomy with double-tract anastomosis.

those occurring within or after 1 month postoperatively, respectively. Pulmonary infection was defined as high postoperative temperature (>38 °C), positive sputum culture for bacteria, cough with sputum production, and positive radiological findings. Postoperative complications were

shown in *Table 3*. Early postoperative complications were noted in 27 patients (44.3%) in the OPG-DT group and in 21 cases (40.4%) in LAPG-DT group ($\chi^2=1.366$, P=0.928); late complications were found in 1 patient in each group (1.6% vs. 1.9%, $\chi^2=2.773$, P=0.096). Each group had

Table 2 Surgeries and perioperative recovery

Variable	OPG-DT (n=61)	LAPG-DT (n=52)	Statistics	P value
Operative time ($\bar{x} \pm s$, min)	161±14	217±61	t=-6.870	0.000
Intraoperative blood loss, mL ($\bar{x} \pm s$)	243±114	186±91	t=2.883	0.005
Lymph nodes dissected, n ($\bar{x} \pm s$)	24±6	26±7	t=-1.957	0.053
Time to first flatus, days ($\bar{x} \pm s$)	3.3±0.9	2.9±0.7	t=0.608	0.544
Time to first eating, days ($\bar{x} \pm s$)	5.8±3.1	5.9±4.0	t=-0.257	0.798
Post-operative hospital stay, days ($\bar{x} \pm s$)	11.0±3.0	10.0±2.7	t=1.885	0.062

OPG-DT, open proximal gastrectomy with double-tract anastomosis; LAPG-DT, laparoscopically assisted proximal gastrectomy with double-tract anastomosis.

Table 3 Postoperative complications

Variable	OPG-DT (n=61)	LAPG-DT (n=52)	Statistics	P value
Early postoperative complications, n (%)	27 (44.3)	21 (40.4)	$\chi^2=1.366$	0.928
Anastomotic leak	1 (1.6)	1 (1.9)		
Atelectasis	25 (41.0)	20 (38.5)		
Pleural effusion	18 (29.5)	15 (28.9)		
Pulmonary infection	4 (6.6)	3 (5.7)		
Anastomotic bleeding	1 (1.6)	0		
Wound infections	2 (3.3)	1 (1.9)		
Late postoperative complications, n (%)	1 (1.6)	1 (1.9)	$\chi^2=2.773$	0.096
Anastomotic stricture	1 (1.6)	0		
Intestinal obstruction	0	1 (1.9)		
Clavien-Dindo grade, n (%)			$\chi^2=1.680$	0.641
I	44 (84.6)	34 (82.9)		
II	5 (9.6)	4 (9.8)		
IIIa	3 (5.8)	2 (4.9)		
IIIb	0	1 (2.4)		

OPG-DT, open proximal gastrectomy with double-tract anastomosis; LAPG-DT, laparoscopically assisted proximal gastrectomy with double-tract anastomosis.

1 patient with a minor anastomotic leak, which was cured by drainage and nutritional support. The patient with anastomotic leak in the LAPG group was administered cefoperazone-sulbactam for antimicrobial treatment. The patient with anastomotic leak in the OPG-DT group developed anastomotic stenosis after 1 month, which was treated with interventional dilatation; unfortunately, anastomotic leak reoccurred after dilatation, which was cured after transnasal placement of an enteral nutrition tube

and application of puncture and drainage. The condition was healed after 3 sessions of dilatation. Postoperative pulmonary atelectasis and pleural effusion were found by postoperative CT scans, and most of the patients were asymptomatic. In the OPG-DT group, 4 patients had pulmonary infection, which were treated with antibiotics; 2 patients had moderate pleural effusion, which was managed with thoracentesis and drainage. In the LAPG-DT group, 3 patients had pulmonary infection, which was

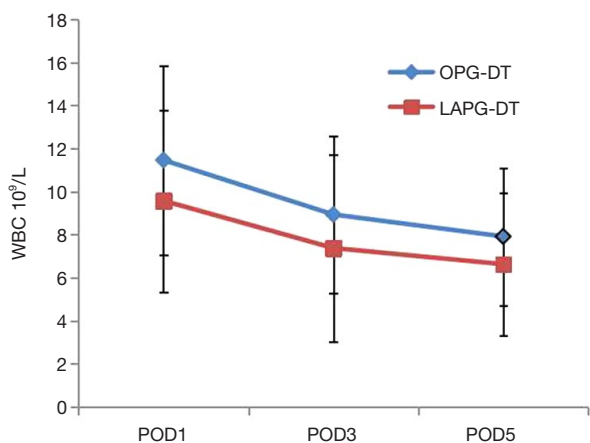


Figure 2 Postoperative change of white blood cell count. POD, postoperative day.

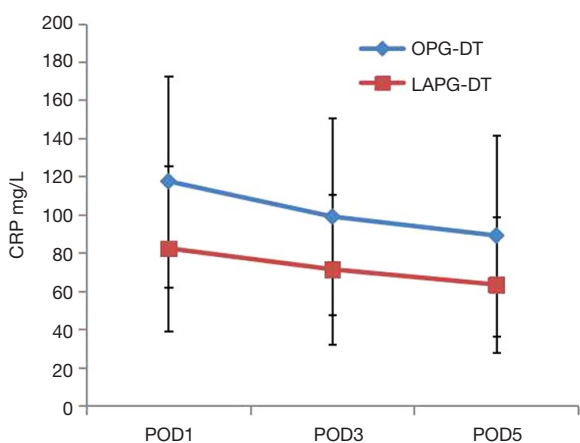


Figure 3 Postoperative change of white blood cell count. POD, postoperative day.

treated with antibiotics; 2 patients had moderate pleural effusion, which was managed with thoracentesis and drainage. One patient in the LAPG-DT group presented with sudden abdominal pain and vomiting 9 months after surgery and was diagnosed with adhesive intestinal obstruction at the Peterson's space. After laparoscopic release of the intestinal adhesion, the Peterson's space was closed. The mesenteric hiatal hernias have been closed since then.

Changes in neutrophils and C-reactive protein after surgery

As shown in *Figure 2*, the mean white blood cell (WBC)

counts in the LAPG-DT and OPG-DT groups on postoperative days 1, 3, and 5 were $9.57 \times 10^9/L$ vs. $11.46 \times 10^9/L$ ($P < 0.05$), $7.37 \times 10^9/L$ vs. $8.93 \times 10^9/L$ ($P < 0.05$), and $6.62 \times 10^9/L$ vs. $7.91 \times 10^9/L$ ($P < 0.05$), respectively. As the *Figure 3* shows, the mean levels of C-reactive protein in the LAPG-DT and OPG-DT groups on postoperative days 1, 3, and 5 were 82.4 vs. 117.5 mg/L ($P < 0.05$), 71.4 vs. 99.0 mg/L ($P < 0.05$), and 63.4 vs. 89.1 mg/L ($P < 0.05$), respectively.

Reflux esophagitis

For reflux esophagitis, 56 patients (91.8%) in the OPG-DT group and 49 patients (94.2%) in the LAPG-DT group underwent endoscopic examination 1 year after surgery. Significant symptoms were seen in 1 patient in the former group but in no patients in the latter group. However, endoscopic grading showed that 4 patients in the OPG-DT group had manifestations of esophagitis (including 3 cases of grade A and 1 case of grade B); in the LAPG-DT group, 2 patients had the manifestations of reflux esophagitis, both of which were grade A (*Table 4*).

Discussion

The extent of surgical resection and the mode of reconstruction for AEG remain controversial despite the considerable amount of research into the subject. Many studies have reported the noninferiority of proximal gastrectomy for early AEG and upper third stomach tumor in terms of oncologic safety compared to total gastrectomy (15,16). Proximal gastrectomy followed by esophagus-gastric remnant anastomosis is the simplest approach but may lead to significant reflux esophagitis (and reflux symptoms) and anastomotic stricture (17,18); nevertheless, proximal gastrectomy is superior to total gastrectomy in maintaining serum albumin and vitamin B₁₂ level, controlling body weight, and preventing anemia (19). Jung *et al.* manifested that laparoscopic proximal gastrectomy with double-tract reconstruction did not increase the risk of complications such as reflux and had significant superiority over total gastrectomy with regard to weight loss, anemia, and serum vitamin B₁₂ level (20). As laparoscopic surgery is characterized by less intraoperative bleeding and faster postoperative recovery, laparoscopic-assisted proximal gastrectomy with double-tract reconstruction may be a

Table 4 Evaluation of reflux esophagitis

Evaluation methods	OPG-DT (n=61)	LAPG-DT (n=52)	Statistics	P value
Visick score, n (%)			$\chi^2=1.241$	0.265
I	60 (98.4)	52 (100)		
II	1 (1.6)	0		
III	0	0		
IV	0	0		
Los Angeles grade, n (%)			$\chi^2=0.908$	0.341
A	3 (5.4)	2 (4.1)		
B	1 (1.2)	0		
C	0	0		
D	0	0		

OPG-DT, open proximal gastrectomy with double-tract anastomosis; LAPG-DT, laparoscopically assisted proximal gastrectomy with double-tract anastomosis.

more desirable procedure; for AEG, however, the role of laparoscopic anastomosis has not been confirmed due to the technical difficulties associated with laparoscopic reconstruction. Uyama *et al.* were the first to report 4 patients who had received completely laparoscopic proximal gastrectomy and lymphadenectomy, during which laparoscopic esophagojejunostomy, jejunum-gastric remnant anastomosis, and jejunojejunal anastomosis were also performed using a linear cutter/stapler; no patient experienced postoperative anastomotic leak or anastomotic stricture, nor did they show any symptoms of reflux or dumping syndrome (21). For early-stage upper gastric body cancer, several retrospective analyses have reported the short-term and long-term outcomes and survival quality after proximal gastrectomy with dual-tract anastomosis; however, the amount of data remains small, especially concerning comparisons between the laparoscopic-assisted or laparoscopic proximal gastrectomy with dual-tract anastomosis and the open proximal gastrectomy with dual-tract anastomosis for AEG.

The greatest advantage of proximal gastrectomy with dual-tract anastomosis is in preventing the occurrence of reflux esophagitis. In our current study, the Visick score was used to assess postoperative reflux symptoms. Only 1 of the 113 patients developed grade II reflux symptoms, which were treated with intermittent oral omeprazole, suggesting that the procedure applied had a good antireflux effect. However, 6 patients presented with reflux esophagitis (grade B in 1 patient; i.e., with occasional reflux symptoms) during

the endoscopic evaluation, indicating that the subjective symptoms do not always match perfectly with objective evidence, as described by Ronellenfitsch *et al.* (22). In the literature, the reported length of the jejunal interposition varies (23). We believe that keeping the length of jejunal interposition between 12 and 15 cm might be more helpful for reducing the occurrence of reflux and stasis (24). The operative time and difficulty of surgery are also of concern for many operators. In our current study, most patients had Siewert type II (without invasion of the dentate line) and type III tumors. The laparoscopic surgery initially lasted as long as 470 minutes, but the operative time was rapidly decreased after further optimization of the surgical processes.

Furthermore, the 2 groups showed no significant differences in postoperative complications (both short- and long-term complications) or complication grades. However, the incidences of postoperative pulmonary complications were relatively high among our patients. There are no uniform criteria for postoperative pulmonary complications, and their incidences may fluctuate from 2% to 40% (25). In our current study, 40.98% of patients in the open surgery group had varying degrees of pulmonary atelectasis, and 29.51% had varying degrees of pleural effusion; in contrast, these incidences were 38.46% and 28.85%, respectively, in the laparoscopic surgery group, which might be explained by the fact that the functional residual air volume usually reaches its valley value 1–2 days after the upper abdominal surgery and gradually

recovers 5–7 days later (26). A CT scan of the thoraco-abdominopelvic cavity performed around the third postoperative day revealed a high incidence of pulmonary atelectasis. All the patients with pleural effusion also had varying degrees of pulmonary atelectasis. However, only a small percentage of these patients developed secondary pulmonary infections, which might be associated with age, smoking history, and chronic obstructive pulmonary disease (27). All anastomotic leaks in our current study occurred at the esophagojejunostomy site, with an incidence of 1.64% and 1.92%, respectively, in the OPG and LPG groups, and the outcomes was similar to the study conducted by Nomura *et al.* (28). Although there was no statistical difference in the use of additional analgesics, patients in the open surgery group used more additional analgesics than those in the laparoscopic surgery group. In both groups, routine blood tests, biochemistry, and C-reactive protein tests performed on postoperative days 1, 3, and 5 showed that the count of WBC and level of C-reactive protein were significantly lower in the LAPG-DT group than those in the OPG-DT group, suggesting that laparoscopic-assisted surgery reduced the inflammation and stress significantly compared with traditional open surgery. These findings offered a theoretical basis for the adoption of enhanced recovery after surgery (ERAS) following laparoscopic proximal gastrectomy with double-tract anastomosis.

In conclusion, although laparoscopic proximal gastrectomy with double tract anastomosis increases the operative time, it markedly decreases the bleeding, postoperative leukocyte count, and C-reactive protein level. Meanwhile, the number of surgically obtained lymph nodes, the postoperative short- and long-term complications, and the reduction of reflux esophagitis are not significantly different from those of open surgery. This procedure also features less bleeding and reduced inflammatory response. Thus, it is a safe and feasible surgical method for early AEGs.

Acknowledgments

Funding: This study was supported by the Henan Provincial Science and Technology Key Task Program (No. 192102310311; No. 202102310414), the Henan Provincial Medical Science and Technology Key Task Program (No. LHGJ20190629), and the 1000 Talents Program of the Central Plains (No. 204200510023).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/jgo-21-165>

Data Sharing Statement: Available at <http://dx.doi.org/10.21037/jgo-21-165>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jgo-21-165>). All authors report funding supports from the Henan Provincial Science and Technology Key Task Program (no. 192102310311; no. 202102310414), the Henan Provincial Medical Science and Technology Key Task Program (no. LHGJ20190629), and the 1000 Talents Program of the Central Plains (No. 204200510023). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This was a retrospective case-control study and the requirement for informed consent was waived. This retrospective case-control study was approved by the ethics committee of Henan Tumor Hospital (No. 2019156) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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(English Language Editor: J. Gray)

Cite this article as: Zhang B, Liu X, Ma F, Peng L, Lu S, Zhang Y, Ma Q, Ji S, Zhang Z, Chai J, Hua Y, Wang H, Li Q, Luo S, Chen X. Laparoscopic-assisted versus open proximal gastrectomy with double-tract reconstruction for Siewert type II–III adenocarcinomas of esophago-gastric junction: a retrospective observational study of short-term outcomes. *J Gastrointest Oncol* 2021;12(2):249-258. doi: 10.21037/jgo-21-165