

# Lymph node dissection for Siewert II esophagogastric junction adenocarcinoma

## A retrospective study of 3 surgical procedures

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### Abstract

The present study was aimed to investigate the application of right transthoracic Ivor–Lewis (IL), left transthoracic (LTT), and left thoracoabdominal (LTA) approach in Siewert type II adenocarcinoma of esophagogastric junction (AEG).

The data of 196 patients with Siewert type II AEG received surgical resection in our cancer center between January 2014 and April 2016 was retrospectively analyzed. Finally, 136 patients met the inclusion criteria were enrolled in the study and divided into the IL (47 cases), LTT (51 cases), and LTA group (38 cases). Clinical and short-term treatment effects were compared among the 3 groups.

The patients with weight loss, diabetes, and heart disease increased in the LTT group ( $P=0.054$ ,  $P=0.075$ , and  $P=0.063$ , respectively). Operation time was significantly longest in the IL group ( $P<0.001$ ), but the amount of bleeding and tumor size did not significantly differ among the 3 groups ( $P=0.176$  and  $P=0.228$ , respectively). The IL group had the significantly longest proximal surgical margin ( $P<0.001$ ) and most number of total ( $P<0.001$ ) and thoracic lymph nodes ( $P<0.001$ ) dissected. Both the IL and LTA groups had more abdominal lymph nodes dissected than the LTT group ( $P<0.001$ ). In general, the IL and LTT groups had the highest dissection rates of every station of thoracic ( $P<0.05$ ) and lower mediastinal lymph nodes ( $P<0.05$ ), respectively. The dissection rate of the paracardial, left gastric artery, and gastric lesser curvature lymph nodes did not differ significantly among the 3 groups ( $P>0.05$ ), but the dissection rate of the hepatic artery, splenic artery, and celiac trunk lymph nodes was significantly highest in the IL group ( $P<0.05$ ). Postoperative hospital stay, perioperative complications, and mortality did not differ significantly among the 3 groups ( $P>0.05$ ).

Compared with the traditional left transthoracic approach, the Ivor–Lewis approach did not increase the perioperative mortality and complication rates in Siewert type II AEG, but obtained satisfactory length of the proximal surgical margin, and was better than the left transthoracic approach in thoracic and abdominal lymph node dissection. However, the advantages of Ivor–Lewis procedure requires further follow-up and validation through prospective randomized controlled trials.

**Abbreviations:** AEG = adenocarcinoma of the esophagogastric junction, AJCC = American Joint Committee on Cancer, CT = computed tomography, IL = Ivor–Lewis, LTA = left thoracoabdominal, LTT = left transthoracic, PET = positron emission tomography, TNM = tumor–node–metastasis.

**Keywords:** adenocarcinoma, esophagogastrectomy, esophagogastric junction, Ivor–Lewis, left transthoracic, lymphadenectomy

### 1. Introduction

Adenocarcinoma of the esophagogastric junction (AEG) is divided into 3 types according to the anatomical position of the tumor center as follows<sup>[1,2]</sup>: Siewert type I, in the distal esophagus 1 to 5 cm above the esophagogastric junction; Siewert type II, within 1 cm above and 2 cm below the esophagogastric junction; and Siewert type III, in the proximal stomach, 2 to 5 cm below the esophagogastric junction. Siewert type II is actually the

carcinoma of gastric cardia, which has high prevalence in Asian countries, including China.<sup>[3]</sup>

Although surgical resection is still the main treatment of AEG, recent studies indicate that neoadjuvant chemotherapy or chemoradiotherapy can provide significant survival benefits for local advanced esophageal or esophagogastric junction cancer.<sup>[4–6]</sup> The efficacy of neoadjuvant chemoradiation for patients with adenocarcinoma of the distal esophagus and AEG was established in the chemoradiotherapy for esophageal cancer followed by the surgery study (CROSS study), which demonstrated that neoadjuvant treatment resulted in longer mean survival than surgery alone.<sup>[6]</sup> A recent database analysis of 4996 patients for Siewert type II AEG showed that preoperative therapy was used in as few as 10% of cases in 1998, rising to 25% in 2010.<sup>[7]</sup> With the accumulation of evidence, patients with AEG are increasingly treated with neoadjuvant therapy.

Siewert classification provides a reference for the choice of the appropriate surgical approach.<sup>[8]</sup> Siewert type I mainly uses esophagectomy through the transthoracic approach. Siewert type III mainly uses total gastrectomy through the abdominal/transhiatal and distal esophageal resection.<sup>[9]</sup> Several studies compared the short- and long-term efficacy of treatment with the transthoracic and abdominal/transhiatal approaches in Siewert type II AEG.<sup>[10–14]</sup> Although some literatures have claimed that

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the incidence of pulmonary complications in the transthoracic approach group is higher than that in the abdominal/transhiatal approach group,<sup>[10,13]</sup> esophagogastrectomy through the transthoracic approach provides better thoracic lymph node dissection,<sup>[12–14]</sup> improves the R0 resection rate and acquires survival benefit in patients with 1 to 8 positive lymph nodes<sup>[12]</sup> or T3 AEG,<sup>[13]</sup> which is in accordance with the principle of oncology treatment.

Esophagogastrectomy through the left thoracic approach is commonly used in the resection of tumors at the end of the esophagus and esophagogastric junction.<sup>[15]</sup> Ivor–Lewis esophagogastrectomy through the right thoracic approach is the most commonly used operation approach for esophageal cancer of the lower thorax and can attain a more extensive thoracic and abdominal lymph node dissection.<sup>[16]</sup> The seventh edition of the American Joint Committee on Cancer/tumor-node-metastasis (AJCC/TNM) esophageal cancer staging system is more applicable to the AEG.<sup>[17]</sup> The Ivor–Lewis approach may be the best surgical resection approach for Siewert type II AEG.<sup>[18]</sup> This study retrospectively analyzed the clinical data of patients with Siewert type II AEG, compared the application of 3 surgical approaches in Siewert type II AEG, and investigated the optimal surgical approach for lymph node dissection.

## 2. Methods

### 2.1. Patients

The study was approved by the ethics committee of the Tianjin Medical University Cancer Hospital, and patients who signed the informed consent form were enrolled in the study. We retrospectively analyzed the clinical pathological data of patients with Siewert type II AEG who received radical resection at the Department of Esophageal Cancer of Tianjin Medical University Cancer Hospital between January 2014 and April 2016. The inclusion criteria were as follows: (1) adenocarcinoma, (2) not undergone neoadjuvant therapy, (3) undergone transthoracic esophagogastrectomy, (4) at >3 months of postoperative follow-up.

The patients were divided into 3 groups according to the operative approach as follows: right transthoracic Ivor–Lewis (IL), left transthoracic (LTT), and left thoracoabdominal (LTA) approach groups. The epidemiological characteristics, clinical pathological data, and information on perioperative mortality and complications were obtained by examining the clinical records of the patients. The lymph node stations were grouped as previously described.<sup>[18]</sup> Paracardiac lymph nodes were divided into left and right groups. In addition, an upper mediastinal lymph node group was included in the present study.

### 2.2. Surgical procedures

All the patients were confirmed via gastroscopic and pathological diagnosis before surgery. They received preoperative type-B ultrasonography (neck and abdomen), enhanced computed tomography (CT; chest and upper abdomen), upper gastrointestinal radiography, and endoscopic ultrasonography. Some patients were also examined by using positron emission tomography (PET) or PET/CT for preoperative staging. All thoracic and abdominal surgeries were performed independently by thoracic surgeons.

The IL group: The right thoracic incision through the fifth or sixth intercostal space and central abdominal incision were used. In the abdominal area, the stomach was dissociated, a tubular stomach was made, and perigastric lymph nodes were dissected.

In the thoracic area, the lower esophagus was dissociated, thoracic lymph nodes were dissected, and gastroesophageal anastomosis was performed.

The LTT group: The seventh intercostal incision in the left chest was used. In the thoracic area, the lower esophagus was dissociated and thoracic lymph nodes were dissected. In the abdominal area, the stomach was dissociated, a tubular stomach was made, and perigastric lymph nodes were dissected. Gastroesophageal anastomosis was performed.

The LTA group: A continuous abdominal and left thoracic incision through the seventh intercostal space was used. In the thoracic area, the lower esophagus was dissociated and thoracic lymph nodes were dissected. In the abdominal area, the stomach was dissociated, a tubular stomach was made, and perigastric lymph nodes were dissected. Gastroesophageal anastomosis was performed.

### 2.3. Outcomes and statistical analysis

The main outcome were (1) the number of total dissected lymph nodes, thoracic lymph nodes and abdominal lymph nodes, (2) the lymph node dissection frequency of each station. Secondary outcomes included surgical time and bleeding amount, length of proximal resection margin, hospital stay, postoperative death, and complications.

Data were processed and analyzed by using the SPSS18.0 statistical software (SPSS Standard version 18.0; SPSS, Chicago, IL). Measurement data were presented as  $\bar{x} \pm s$  and compared among the groups by using ANOVA analysis. Count data were presented by using frequency and percentage and were compared among the groups by using the chi-square test or Fisher exact probability test. A *P* value of <0.05 was considered statistically significant.

## 3. Results

### 3.1. Patient characteristics

Between January 2014 and April 2016, 196 patients with Siewert type II AEG received surgical resection, including 31 cases of esophagogastrectomy through the abdominal/transhiatal approach, 15 cases of neoadjuvant chemoradiotherapy or chemotherapy, and 2 nonadenocarcinoma cases. Eventually, 136 patients who met the inclusion criteria were enrolled in the study and divided into the IL (47 cases), LTT (51 cases), and LTA groups (38 cases) according to the operative approach.

The clinical pathological characteristics of the 136 patients with Siewert type II AEG are shown in Table 1. The median age of the 136 patients was 64 years (range, 34–80 years), and the male-to-female ratio was 128:8. Lymph node metastasis occurred in 92 patients (67.6%), among whom 2 (1.5%) had thoracic metastasis, 79 (58.1%) had abdominal lymph node metastasis, and 10 (7.4%) had thoracic and abdominal lymph node metastases.

The LTT group had more patients with concurrent weight loss, diabetes, and heart disease than the IL and LTA groups (*P* = 0.054, *P* = 0.075, and *P* = 0.063, respectively), although no statistical difference was observed. The operation time in the IL group was significantly longer than that in the LTT and LTA groups (223.8 vs 149.2 vs 166.2 min, *P* < 0.001), but the amount of bleeding did not significantly differ among the 3 groups (*P* = 0.176). Tumor size did not significantly differ among the 3 groups (*P* = 0.228), but the isolated proximal surgical margin in the IL

**Table 1****Clinicopathologic characteristics of patients.**

Patient characteristics	IL (n=47)	LTT (n=51)	LTA (n=38)	P
Age, y	63.6±9.3	63.7±7.8	61.6±8.4	0.455
Sex				0.320
Male	43 (91.5)	50 (98.0)	35 (92.1)	
Female	4 (8.5)	1 (2.0)	3 (7.9)	
Weight loss				0.054
Yes	29 (61.7)	37 (72.5)	18 (47.4)	
No	18 (38.3)	14 (27.5)	20 (80.0)	
Drinking	29 (61.7)	31 (60.8)	20 (52.6)	0.452
Smoking	29 (61.7)	37 (72.5)	23 (60.5)	0.470
Comorbidity				
Hypertension	12 (25.5)	9 (17.6)	5 (13.2)	0.472
Diabetes	1 (2.1)	7 (13.7)	2 (5.3)	0.075
Heart disease	4 (8.4)	7 (13.7)	0 (0.0)	0.063
Surgical time, min	223.8±34.2	149.2±21.9	166.2±25.2	<b>0.000</b>
Surgical blood loss, mL	194.3±116.2	160.7±60	168.3±62.3	0.176
Histology				0.229
Adenocarcinoma	37 (78.7)	42 (82.4)	24 (63.2)	
With other differentiation	10 (21.3)	9 (17.6)	14 (36.8)	
Tumor length, cm	5.4±2.0	4.7±1.9	5.2±2.4	0.228
Proximal marginal length, cm	3.8±1.6	2.4±1.3	1.9±1.3	<b>0.000</b>
pT category				0.191
T1-2	4 (8.5)	7 (13.7)	6 (15.8)	
T3-4	43 (91.5)	44 (86.3)	31 (84.2)	
pN category				0.461
N0	10 (21.3)	19 (37.3)	15 (39.5)	
N1	27 (57.4)	23 (45.1)	14 (36.8)	
N2	8 (17.0)	7 (13.7)	6 (15.8)	
N3	2 (4.3)	2 (3.9)	3 (7.9)	
pTNM stage				0.174
I	4 (8.5)	13 (25.5)	10 (26.3)	
II	31 (66.0)	29 (56.9)	19 (50.0)	
III	12 (25.5)	9 (7.6)	9 (23.7)	
pG category				0.491
G1	4 (8.5)	7 (13.7)	4 (10.5)	
G2	21 (44.7)	19 (37.3)	12 (31.6)	
G3	22 (46.8)	25 (49.0)	22 (58.0)	
Number resected lymph nodes				
≥12	41 (87.2)	20 (39.2)	19 (50)	0.000
Total	21.2±9.3	10.7±6.1	14.3±7.9	0.000
Thoracic	7.8±5.4	2.6±2.7	1.0±2.1	0.000
Abdominal	13.7±7.8	8.0±4.7	13.3±7.2	0.000
Postoperative days	15.4±4.8	16.9±10.0	14.4±3.2	0.227
Postoperative death	0 (0)	1 (2.0)	0 (0)	0.432
Postoperative complications	6 (12.8)	8 (15.7)	3 (7.9)	0.545
Pulmonary complication	3 (6.4)	2 (3.9)	0 (0)	0.297
Anastomotic leakage	0 (0)	1 (2.0)	0 (0)	0.321
Incision complication	1 (2.1)	1 (2.0)	0 (0)	0.673
Others	2 (4.3)	4 (4.0)	3 (7.9)	0.723

Values are mean±SD or n (%).

IL=Ivor-Lewis, LTA=left thoracoabdominal, LTT=left transthoracic.

group was significantly longer than those in the LTT and LTA groups (3.8 vs 2.4 vs 1.9 cm,  $P < 0.001$ ).

### 3.2. Postoperative complications

Postoperative death due to anastomotic leak, pneumonia, and multiorgan failure occurred in 1 patient. The incidence of total postoperative complications was 12.5% (17/136), including 5 cases of pulmonary complications, 2 cases of incision complications, 1 case of anastomotic leak, and 9 cases of other complications (3 cases of fever of unknown origin, 2 cases of fibrillation combined with heart failure, 1 case of stress

hyperglycemia, 1 case of bacteremia, 1 case of diaphragmatic hernia, and 1 case of incomplete intestinal obstruction). Postoperative hospital stay, mortality, and incidence of complications did not differ significantly among the 3 groups ( $P > 0.05$ ). See Table 1 for details.

### 3.3. Lymph node dissection

A total of 2083 lymph nodes were dissected in 136 patients, including 537 thoracic and 1546 abdominal lymph nodes. The lymph node metastasis frequency was 20.7% (431/2083), and the lymph node metastasis rate was 67.6% (92/136).

**Table 2**  
**Lymph node dissection frequency in 3 surgical procedures.**

Lymph node stations	IL (n=47)	LTT (n=51)	LTA (n=38)	P
Thoracic stations				
Superior mediastinum	9 (19.1)	1 (2.0)	0 (0)	0.001
Subcarinal	36 (76.6)	4 (4.0)	0 (0)	0.000
Middle paraesophageal	30 (63.8)	13 (25.2)	2 (5.3)	0.000
Lower paraesophageal	42 (89.4)	36 (70.6)	18 (47.4)	0.000
Pulmonary ligament	6 (12.8)	11 (21.6)	4 (10.5)	0.297
Left main bronchus	31 (66.0)	0 (0)	0 (0)	0.000
Right main bronchus	20 (42.6)	0 (0)	0 (0)	0.000
Supradiaphragmatic	10 (21.3)	5 (9.8)	0 (0)	0.004
Abdominal stations				
Left paracardial	44 (93.6)	50 (98.0)	37 (97.4)	0.469
Right paracardial	42 (89.4)	49 (96.1)	37 (97.4)	0.223
Left gastric artery	46 (97.9)	48 (94.1)	37 (97.4)	0.567
Common hepatic artery	25 (53.2)	5 (9.8)	7 (18.4)	0.000
Splenic artery	25 (53.2)	8 (15.7)	10 (26.3)	0.000
Celiac artery	15 (31.9)	6 (11.8)	8 (21.1)	0.052
Lesser curvature	46 (97.9)	47 (92.2)	34 (89.5)	0.273
Greater curvature	16 (34.0)	9 (17.6)	16 (42.1)	0.035
Suprapyloric	1 (2.1)	0 (0)	4 (10.5)	0.022
Infrapyloric	0 (0)	0 (0)	5 (13.2)	0.001
Splenic hilum	2 (4.2)	1 (2.0)	1 (2.6)	0.833

Values are n (%).

IL=Ivor-Lewis, LTA=left thoracoabdominal, LTT=left transthoracic.

A mean of 21.2 lymph nodes were dissected in the IL group, which was significantly more than the 14.3 lymph nodes dissected in the LTA group ( $P < 0.001$ ) and the 10.7 lymph nodes dissected in the LTT group ( $P < 0.001$ ). The number of dissected lymph nodes in the LTA group was significantly higher than that in the LTT group ( $P = 0.031$ ).

A mean of 7.8 thoracic lymph nodes were dissected in the IL group, which was significantly more than the 2.6 lymph nodes dissected in the LTT group ( $P < 0.001$ ) and the 1 lymph node

dissected in the LTA group ( $P < 0.001$ ). The number of dissected thoracic lymph nodes in the LTT group was significantly higher than that in the LTA group ( $P = 0.045$ ).

A mean of 13.7 and 13.3 abdominal lymph nodes were dissected in the IL and LTA groups, respectively, which show an insignificant difference between the 2 groups ( $P = 0.756$ ) but were significantly higher than the 8 lymph nodes dissected in the LTT group ( $P < 0.001$  vs  $P < 0.001$ ).

### 3.4. Lymph node dissection in each group

The rates of lymph node dissection in all the groups are shown in Table 2. The dissection rates of lymph nodes in the upper mediastinum ( $P = 0.001$ ), subcarina ( $P < 0.001$ ), main bronchi ( $P < 0.001$ ), middle esophagus ( $P < 0.001$ ), lower esophagus ( $P < 0.001$ ), and upper diaphragm ( $P = 0.004$ ) in the IL group were higher than those in the LTT and LTA groups. The dissection rates of lymph nodes in the middle ( $P = 0.012$ ) and lower esophagus ( $P = 0.027$ ) in the LTT group was higher than that in the LTA group ( $P = 0.069$ ).

The dissection rates of lymph nodes in the cardia, left gastric artery, and gastric lesser curvature did not differ significantly among the 3 groups ( $P > 0.05$ ), but the dissection rates of lymph nodes in the hepatic artery ( $P < 0.001$ ) and splenic artery ( $P < 0.001$ ) in the IL group were significantly higher than those in the LTT and LTA groups. The dissection rates of lymph nodes in the superior pyloric ( $P = 0.022$ ) and inferior pylorus ( $P = 0.001$ ) in the LTA group were significantly higher than those in the IL and LTT groups. The dissection rates of lymph nodes on the greater curvature side in the IL and LTA groups were higher than that in the LTT group ( $P = 0.035$ ).

### 3.5. Lymph node metastasis in each group

The lymph node metastasis rates in all the groups are shown in Table 3. The lymph node metastasis rates at the celiac trunk were significantly different among the groups ( $P = 0.010$ ). The

**Table 3**  
**Lymph node metastatic frequency in 3 surgical procedures.**

Lymph node stations	IL (n=47)	LTT (n=51)	LTA (n=38)	P
Thoracic stations				
Superior mediastinum	1/9 (11.1)	0/1 (0)	–	1.000
Subcarinal	1/36 (2.8)	0/4 (0)	–	1.000
Middle paraesophageal	0/30 (0)	1/13 (7.7)	0/2 (0)	0.333
Lower paraesophageal	4/42 (9.5)	6/36 (16.7)	0/18 (0)	0.185
Pulmonary ligament	0/6 (0)	0/11 (0)	0/4 (0)	1.000
Left main bronchus	2/31 (6.5)	–	–	–
Right main bronchus	0/20 (0)	–	–	–
Supradiaphragmatic	0/10 (0)	0/5 (0)	–	–
Abdominal stations				
Left paracardial	19/44 (43.2)	17/50 (34.0)	12/37 (32.4)	0.596
Right paracardial	8/42 (19.0)	15/49 (30.6)	10/37 (27.0)	0.408
Left gastric artery	23/46 (50.0)	18/48 (37.5)	19/37 (51.4)	0.346
Common hepatic artery	6/25 (24.0)	0/5 (0)	0/7 (0)	0.317
Splenic artery	6/25 (24.0)	2/8 (25.0)	3/10 (30.0)	0.892
Celiac artery	0/15 (0)	3/6 (50.0)	1/8 (12.5)	0.010
Lesser curvature	14/46 (30.4)	12/47 (25.5)	11/34 (32.4)	0.738
Greater curvature	2/16 (12.5)	2/9 (22.2)	1/16 (6.25)	0.334
Suprapyloric	0/1 (0.0)	–	1/4 (25.0)	1.000
Infrapyloric	–	–	1/5 (20.0)	–
Splenic hilum	0/2 (0.0)	1/1 (100.0)	0/1 (0.0)	0.500

Values are n (%).

IL=Ivor-Lewis, LTA=left thoracoabdominal, LTT=left transthoracic.

metastasis rates in all the other groups of lymph nodes did not significantly differ ( $P > 0.05$ ).

#### 4. Discussion

The surgical approaches for Siewert type II AEG include transthoracic and abdominal/transhiatal esophagogastrectomy. Theoretically, the transthoracic approach can obtain a better lower mediastinal lymph node dissection and safer upper surgical margin, and the abdominal approach can prevent the increase in the risk of perioperative pulmonary complications caused by thoracotomy.<sup>[19]</sup> The incidence of pulmonary complications in transthoracic esophagogastrectomy in large domestic medical centers has been reduced to around 6%,<sup>[14,18]</sup> which is not significantly different from the incidence in esophagogastrectomy through the abdominal approach. In the present study, the incidence of total pulmonary complications was only 3.7% (5/136). A recent meta-analysis that included 2 prospective and 4 retrospective studies between 1996 and 2012 compared the clinical effects between surgical resections with the transthoracic and abdominal approaches for adenocarcinoma of the lower esophagus and AEG. The meta-analysis showed that the transthoracic approach can dissect more lymph nodes, obtain better 5-year disease-free survival rate, and 5-year overall survival rate ( $P=0.001$ ,  $P=0.05$ , and  $P=0.03$ , respectively).<sup>[20]</sup> The transthoracic approach can obtain better lymph node dissection, improve the R0 resection rate, and improve long-term patient survival. In experienced medical centers, thoracotomy does not increase the incidence of perioperative complications. Therefore, transthoracic esophagogastrectomy should be chosen as the first surgical approach for most patients with Siewert type II AEG.

Transthoracic esophagogastrectomy includes right and left transthoracic approaches, and the decision is mainly based on tumor size, disease stage, position, and surgeon experience and preference. The left transthoracic approach is a commonly used surgical method for Siewert type II AEG by thoracic surgeons in our country. This approach can obtain better thoracic lymph node dissection than the abdominal/transhiatal approach.<sup>[14]</sup> Chen et al retrospectively analyzed the clinical results of 3 surgical approaches (right transthoracic, left transthoracic, and abdominal approaches) for the treatment of Siewert type II AEG. They found that the right transthoracic approach was the most effective in terms of achieving thoracic and abdominal lymph node dissection.<sup>[18]</sup> The left transthoracic approach includes the LTT and LTA approaches. The present study compared short-term efficacy among 3 different transthoracic approaches and further investigated the best surgical approach for lymph node dissection.

This study found that the operation times in the IL and LTA groups were significantly longer than that in the LTT group, and the tumor size and disease stage did not significantly differ among the 3 groups. Generally, the left transthoracic approach may be easy to perform and have fewer complications. Epidemiological data show that patients in the LTT group tended to have more patients with weight loss, diabetes, and heart disease. Thus, the general condition and comorbidity of patients may be considered before the surgery, and the left thoracic approach with fewer traumas may be chosen as the operation approach. This study found that the amount of bleeding during operation did not differ significantly among the 3 groups, and the Ivor-Lewis approach did not increase the patients' mortality and risk of complications.

Of the 136 patients in this study, 119 had pT3-4 cancer, 92 had pN1-3 cancer, 89 had abdominal lymph node metastases,

and 12 had thoracic lymph node metastases. AEG is usually diagnosed in advanced stage, and its lymph node metastasis rate is high. Complete resection of suspicious affected lymph nodes is of clinical significance in accurate staging and improvement of prognosis.<sup>[21]</sup> Studies have found that lymph node metastasis and the number of lymph nodes dissected are independent risk factors that influence the long-term survival of patients with Siewert type II AEG.<sup>[18,22-23]</sup> This study found that the total number of dissected lymph nodes and the numbers of dissected thoracic and abdominal lymph nodes in the IL group were higher than those in the LTT approach group. In addition, 87.2% of the patients in the IL group had  $> 12$  dissected lymph nodes, which was significantly higher than those in the LTT and LTA groups. Chen et al reported that dissection of number  $< 12$  lymph nodes is an independent prognostic factor that influences the long-term survival of patients with Siewert type II AEG.<sup>[18]</sup>

Previous studies investigated the optimal extent of abdominal lymph node dissection in patients with Siewert type II AEG.<sup>[21,24-25]</sup> Yamashita et al<sup>[25]</sup> believe that dissection of the abdominal proximal perigastric lymph nodes, including the paracardiac, lesser curvature of the stomach, left gastric artery, and splenic artery lymph nodes, has great survival benefits. Fujitani et al<sup>[24]</sup> reported that dissection of the lymph nodes at the cardia and lesser curvature of the stomach is necessary for staging or survival. Goto et al<sup>[21]</sup> also believe that dissection of the lymph nodes at the cardia, lesser curvature of the stomach, and left gastric artery is significant in the treatment of Siewert type II AEG. Chen et al<sup>[18]</sup> believe that dissection of the lymph nodes at the cardia, lesser curvature of the stomach, and the left gastric artery has high therapeutic value, and that dissection of the lymph nodes at the greater curvature of the stomach, hepatic artery, splenic artery, and celiac trunk has some therapeutic value. In our study, we found that the metastatic rates of lymph nodes in the cardia, lesser curvature of the stomach, and left gastric artery in the patients in all the 3 groups were high, and that the 3 surgical approaches provided good dissection of lymph nodes in these regions. IL provided better dissection of lymph nodes in the greater curvature of the stomach, hepatic artery, splenic artery, and celiac trunk than the LTT approach. Many literatures reported that dissection of distal gastric and splenic hilar lymph nodes does not have much prognostic value for Siewert type II AEG.<sup>[18,21,24-27]</sup> Therefore, proximal subtotal gastrectomy is more beneficial for Siewert type II AEG than total gastrectomy and extended lymph node dissection.<sup>[18,21,24]</sup>

Three studies discussed the optimal extent of the thoracic lymph node dissection for Siewert type II AEG and reported that dissection of the middle and lower esophageal lymph nodes under the inferior mediastinum had significant survival benefits.<sup>[18,26-27]</sup> Our study found that the IL approach had a significant advantage in the dissection of middle and lower esophageal lymph nodes.

Parry et al<sup>[28]</sup> reported that the superior mediastinal lymph node metastasis rate in Siewert II type AEG is 11%. Our study found 1 case of superior mediastinal lymphatic metastasis, 1 case of subcarinal lymphatic metastasis, and 2 cases of left main bronchus lymphatic metastasis in the IL group. Therefore, in addition to the dissection of common lymphatic metastasis sites, evaluation and dissection of lymph nodes in the above-mentioned regions are also needed in the surgical treatment of Siewert type II AEG to ensure a radical resection. The right transthoracic approach has significant advantages in the dissection of lymph nodes in these regions.

In addition, the length of the proximal resection margin has been reported to be a risk factor of recurrence and mortality in

patients with AEG.<sup>[29–30]</sup> Mine et al believe that a 2 cm proximal surgical margin in situ is sufficient for AEG.<sup>[29]</sup> Barbour et al<sup>[30]</sup> reported that the radical resection for T2+ stage AEG should include at least 5 cm in situ and 3.8 cm isolated proximal surgical margins. In this study, we found that the mean length of the isolated proximal surgical margins in the right thoracic IL group was 3.8 cm and the lengths of the proximal surgical margins in the LTT and LTA approach groups were 1.9 and 2.4 cm, respectively. Therefore, the IL approach can obtain a satisfactory length of the surgical margin, which has a certain clinical value for preventing subclinical metastasis and improving prognosis.

## 5. Conclusion

Right transthoracic Ivor–Lewis esophagogastrectomy does not increase perioperative mortality and the incidence of complications in Siewert type II AEG compared with the traditional left transthoracic approach. The Ivor–Lewis procedure can obtain a satisfactory length of the proximal surgical margin and is superior to left transthoracic approach in thoracic and abdominal lymph node dissections. However, the advantages need further follow-up and validation through prospective randomized controlled trials.

## References

- [1] Rudiger Siewert J, Feith M, Werner M, et al. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. *Ann Surg* 2000;232:353–61.
- [2] Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. *Br J Surg* 1998;85:1457–9.
- [3] 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.
- [4] Duan XF, Tang P, Yu ZT. Neoadjuvant chemoradiotherapy for resectable esophageal cancer: an in-depth study of randomized controlled trials and literature review. *Cancer Biol Med* 2014;11:191–201.
- [5] Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. *Lancet Oncol* 2011;12:681–92.
- [6] Shapiro J, van Lanschot JJ, Hulshof MC, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. *Lancet Oncol* 2015;16:1090–8.
- [7] Martin JT, Mahan A, Zwischenberger JB, et al. Should gastric cardia cancers be treated with esophagectomy or total gastrectomy? A comprehensive analysis of 4,996 NSQIP/SEER patients. *J Am Coll Surg* 2015;220:510–20.
- [8] Siewert JR, Feith M, Stein HJ. Biologic and clinical variations of adenocarcinoma at the esophago-gastric junction: relevance of a topographic-anatomic subclassification. *J Surg Oncol* 2005;90:139–46. discussion 46.
- [9] Mariette C, Piessen G, Briez N, et al. Oesophagogastric junction adenocarcinoma: which therapeutic approach? *Lancet Oncol* 2011;12:296–305.
- [10] Hulscher JB, van Sandick JW, de Boer AG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med* 2002;347:1662–9.
- [11] Sasako M, Sano T, Yamamoto S, et al. Left thoracoabdominal approach versus abdominal-transhiatal approach for gastric cancer of the cardia or subcardia: a randomised controlled trial. *Lancet Oncol* 2006;7:644–51.
- [12] Omloo JM, Lagarde SM, Hulscher JB, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. *Ann Surg* 2007;246:992–1000. discussion-1.
- [13] Kutup A, Nentwich MF, Bollschweiler E, et al. What should be the gold standard for the surgical component in the treatment of locally advanced esophageal cancer: transthoracic versus transhiatal esophagectomy. *Ann Surg* 2014;260:1016–22.
- [14] Zheng B, Chen YB, Hu Y, et al. Comparison of transthoracic and transabdominal surgical approaches for the treatment of adenocarcinoma of the cardia. *Chin J Cancer* 2010;29:747–51.
- [15] Forshaw MJ, Gossage JA, Ockrim J, et al. Left thoracoabdominal esophagogastrectomy: still a valid operation for carcinoma of the distal esophagus and esophagogastric junction. *Dis Esophagus* 2006;19:340–5.
- [16] Visbal AL, Allen MS, Miller DL, et al. Ivor Lewis esophagogastrectomy for esophageal cancer. *Ann Thorac Surg* 2001;71:1803–8.
- [17] Kawaguchi T, Komatsu S, Ichikawa D, et al. Comparison of prognostic compatibility between seventh AJCC/TNM of the esophagus and 14th JCGC staging systems in Siewert type II adenocarcinoma. *Anticancer Res* 2013;33:3461–5.
- [18] Peng J, Wang WP, Yuan Y, et al. Optimal extent of lymph node dissection for Siewert type II esophagogastric junction adenocarcinoma. *Ann Thorac Surg* 2015;100:263–9.
- [19] Wong J, Law S. Two approaches to cancer of the cardia. *Lancet Oncol* 2006;7:613–5.
- [20] Aurello P, Magistri P, Berardi G, et al. Transthoracically or transabdominally: how to approach adenocarcinoma of the distal esophagus and cardia. A meta-analysis. *Tumori* 2016;102:352–60.
- [21] Goto H, Tokunaga M, Miki Y, et al. The optimal extent of lymph node dissection for adenocarcinoma of the esophagogastric junction differs between Siewert type II and Siewert type III patients. *Gastric Cancer* 2015;18:375–81.
- [22] Zhang H, Chen C, Yue J, et al. Effect of number of metastatic lymph nodes and metastatic lymph node ratio on the prognosis in patients with adenocarcinoma of the esophagogastric junction after curative resection. *Zhonghua Zhong Liu Za Zhi* 2014;36:141–6.
- [23] Wang JQ, Wei DZ, Xie MR, et al. Prognostic significance of the number of dissected lymph nodes in Siewert type adenocarcinoma of the esophagogastric junction without lymphatic metastasis. *Zhonghua Zhong Liu Za Zhi* 2016;38:300–4.
- [24] Fujitani K, Miyashiro I, Mikata S, et al. Pattern of abdominal nodal spread and optimal abdominal lymphadenectomy for advanced Siewert type II adenocarcinoma of the cardia: results of a multicenter study. *Gastric Cancer* 2013;16:301–8.
- [25] Yamashita H, Katai H, Morita S, et al. Optimal extent of lymph node dissection for Siewert type II esophagogastric junction carcinoma. *Ann Surg* 2011;254:274–80.
- [26] Mine S, Sano T, Hiki N, et al. Lymphadenectomy around the left renal vein in Siewert type II adenocarcinoma of the oesophagogastric junction. *Br J Surg* 2013;100:261–6.
- [27] Hasegawa S, Yoshikawa T, Rino Y, et al. Priority of lymph node dissection for Siewert type II/III adenocarcinoma of the esophagogastric junction. *Ann Surg Oncol* 2013;20:4252–9.
- [28] Parry K, Haverkamp L, Bruijnen RC, et al. Surgical treatment of adenocarcinomas of the gastro-esophageal junction. *Ann Surg Oncol* 2015;22:597–603.
- [29] Mine S, Sano T, Hiki N, et al. Proximal margin length with transhiatal gastrectomy for Siewert type II and III adenocarcinomas of the oesophagogastric junction. *Br J Surg* 2013;100:1050–4.
- [30] Barbour AP, Rizk NP, Gonen M, et al. Adenocarcinoma of the gastroesophageal junction: influence of esophageal resection margin and operative approach on outcome. *Ann Surg* 2007;246:1–8.