Optimal Extent of Lymph Node Dissection for Siewert Type II Esophagogastric Junction Adenocarcinoma

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Background. The optimal surgical approach and extent of lymphadenectomy for Siewert type II adenocarcinoma of the esophagogastric junction (AEG) is controversial. The aim of this study was to identify its optimal extent of thoracic and abdominal lymph node dissection, and the appropriate surgical approach.

Methods. The clinicopathologic data of 192 patients with Siewert type II AEG who were admitted to our center during January 2007 through October 2011 were retrospectively analyzed. We used the index of estimated benefit from lymph node dissection to assess the therapeutic value of lymph node dissection of each station.

Results. Overall, for the thoracic lymph node dissection, the left thoracic route and Ivor-Lewis procedure are better choices than the abdominotranshiatal route. While for the abdominal lymph node dissection, the abdominotranshiatal achieved a better dissection extent. No significant difference was found in metastatic frequency for each station except the 16th station. The multivariate analysis found only N stage ($p = 0.000$) and number of resected lymph nodes of 12 or more ($p = 0.035$) were prognostic factors for Siewert type II AEG. Furthermore, we identified two thoracic lymph node stations (8M and 8L) and six abdominal lymph node stations (16, 17, 19, 20, G3, G4) that have a high therapeutic value for the patients.

Conclusions. We recommend the 8M, 8L, 16, 17, and G3 should be excised for Siewert type II AEG. Considering the lymphadenectomy, the Ivor-Lewis procedure is the optimal choice for patients with Siewert type II AEG.

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Adenocarcinoma of the esophagogastric junction (AEG) is defined as adenocarcinoma involving the anatomic border between the esophagus and the proximal stomach. AEG is further classified into three distinct entities (types I, II, and III) according to Siewert's proposal based on anatomic location of the tumor center [1]. Siewert type I AEG was reported to be the most prevalent type in Western countries, whereas in Eastern countries types II and III are the predominant ones [2–4].

Surgical resection is still the cornerstone for the treatment of AEG [5]. The Siewert classification provides a useful tool for the selection of the appropriate surgical procedure [6]. Briefly, the standard procedure for Siewert type I AEG is en bloc superior polar esophagogastrectomy through the transthoracic approach with extended two-field lymphadenectomy (abdominal and thoracic), whereas total gastrectomy with transhiatal resection of the distal esophagus is recommended for type III tumors. Still, no final conclusion has been reached for type II AEG, and both of the surgical procedures could be chosen [7]. Ivor-Lewis esophagogastrectomy is the frequently recommended surgical approach to treat carcinoma of the lower esophagus and proximal tumor of the gastroesophageal junction [8].

The lymph node involvement status is the most important prognostic factor for Siewert type II AEG, and the seventh American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) classification of the esophageal carcinoma had been reported to be more compatible with Siewert type II AEG [9, 10]. Previously, some studies had reported the optimal extent of lymphadenectomy of Siewert type II AEG, but none of them discussed the value of thoracic lymph node dissection in detail [11, 12]. In this study, we retrospectively analyzed the clinicopathologic characteristics of patients with Siewert type II AEG who underwent surgery using three different approaches, to explore and identify its optimal extent of thoracic and abdominal lymph node dissection and surgical approach.

Material and Methods

Patients

This study was approved by the Ethics Committee of the West China Hospital of Sichuan University, which waived the requirement for written informed consent of individual patient owing to the retrospective nature of this study. Patients with Siewert type II AEG who had undergone curative radical surgery from January 2007 to

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October 2011 in the thoracic surgery and gastrointestinal surgery departments were retrospectively analyzed from the database. The Siewert type II AEG was precisely defined based on the following methods: the preoperative computed tomography scan, esophagogram and endoscopic findings, intraoperative observation, and postoperative pathology examination.

According to the different surgical approaches used, we categorized the patients into three groups: the left thoracic approach (LT) group, the Ivor-Lewis approach (IL) group, and abdominotranshiatal approach (AT) group. Clinicopathologic variables, including tumor stage according to the esophageal cancer TNM classification (seventh edition) [13], were retrieved from the patient's hospital records. Lymph node stations were numbered according to the AJCC first [14], as well as the Japan Esophageal Society lymph node numbered system if no corresponding lymph node stations existed in AJCC [15]. The definitions of each lymph node station are demonstrated in Figure 1. All patients were followed up until death or until July 2014.

Surgical Procedures

The patients in the LT and IL groups were operated by thoracic surgeons. For LT patients, only one incision of left posterolateral thoracotomy was deployed, and subtotal esophagectomy with superior polar gastrectomy was adopted. The lymphadenectomy was performed mainly in the thorax and lymph node around the stomach. For IL patients, an en bloc esophagectomy with two-field lymphadenectomy (right thoracic and abdominal) was performed. The surgery of the AT group was performed by gastrointestinal surgeons. Total gastrectomy with distal esophagectomy through the abdominal incision and limited two-field (abdominal and lower mediastinal) lymphadenectomy was adopted.

Evaluation of Therapeutic Value of Lymph Node Dissection

To evaluate the therapeutic value of lymph node dissection for each station, we adopted the index of estimated benefit from lymph node dissection (IEBLD), a concept proposed by Sasako and colleagues [16]. In brief, this index was calculated by multiplying the incidence of metastasis by the 5-year survival rate of patients with positive nodes at that station. The incidence of metastasis to each station was determined by dividing the number of patients with metastasis at each station by the number of patients in whom the station was dissected. The cumulative 5-year overall survival rate of patients with metastasis at each nodal station was calculated irrespective of the presence/absence of metastasis at other nodal stations.

Statistical Analysis

Continuous data were presented as the mean ± SD, and compared by one-way analysis of variance or Kruskal-Wallis H test. Categoric data were compared by χ^2 test or Fisher's exact probability test. Cumulative survival rates were generated by the Kaplan-Meier method.

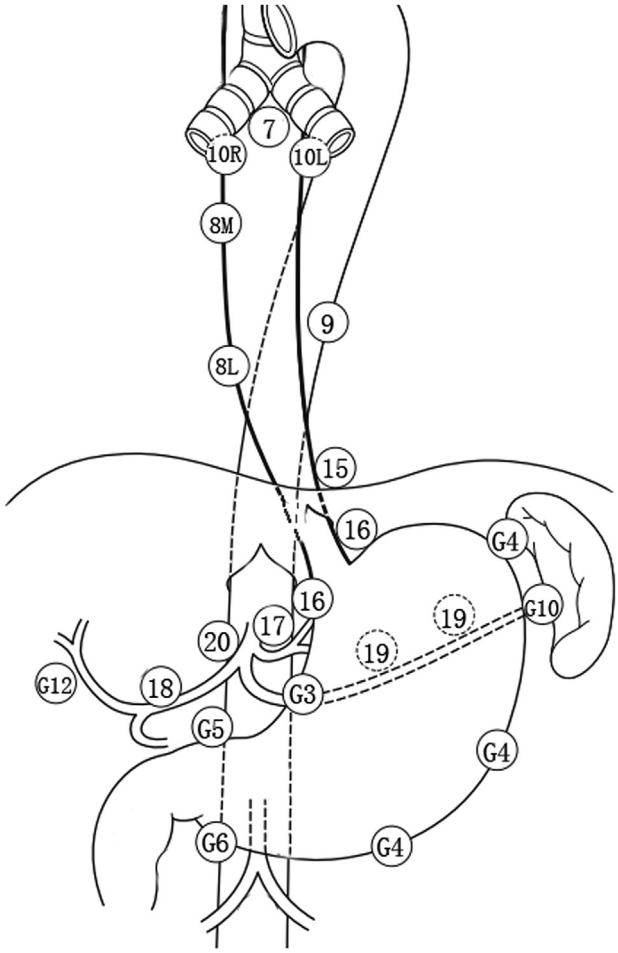

Fig 1. Definition of lymph node stations: 7 = subcarinal lymph nodes; 8M = middle thoracic paraesophageal lymph nodes; 8L = lower thoracic paraesophageal lymph nodes; 9 = pulmonary ligament lymph nodes; 10 = main bronchus lymph nodes; 15 = supradiaphragmatic lymph nodes; 16 = paracardial lymph nodes; 17 = lymph nodes at the root of the left gastric artery; 18 = lymph nodes along the common hepatic artery; 19 = lymph nodes along the splenic artery; 20 = lymph nodes along the celiac artery; G3 = lesser curvature lymph nodes; G4 = greater curvature lymph nodes; G5 = suprapyloric lymph nodes; G6 = infrapyloric lymph nodes; G10 = lymph nodes around the splenic hilum; and G12 = lymph nodes in the hepatoduodenal ligament.

Survival curves and univariate significant factors were compared with the log rank test. Multivariate analysis for overall survival was performed using stepwise Cox's proportional hazard regression model. All statistical tests were two-sided, and p values less than 0.05 were considered to be statistically significant. All statistical analyses were carried out using SPSS version 16.0 (SPSS, Chicago, IL).

Results

Patient Characteristics

In the current study, we included 192 patients with Siewert type II AEG (LT group 106, IL group 31, AT group