Prognostic Value of Different Lymph Node Staging Methods in Esophageal Squamous Cell Carcinoma After Esophagectomy

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Background. **This study aimed to investigate the prognostic value of number of involved lymph nodes, number of removed lymph nodes, ratio of involved to removed nodes (lymph node ratio), and number of negative lymph nodes in esophageal squamous cell carcinoma (ESCC) patients after esophagectomy.**

Methods. **A retrospective review of 603 patients receiving esophagectomy for ESCC was made. Cox regression analysis was performed to identify significant prognostic factors.**

Results. **The median follow-up time was 36.7 months, and the 5-year overall survival (OS) was 43.5%. Patients with negative lymph node count ≥14 had better survival ($p < 0.001$). Univariate Cox analysis showed that the number of involved lymph nodes, number of removed lymph nodes, lymph node ratio, and number of negative lymph nodes influenced OS ($p < 0.05$ for all). Multivariate Cox analysis indicated that the number of involved lymph nodes and number of negative lymph nodes were independent prognostic factors for OS, and a higher number of negative lymph nodes was associated with lower mortality. The number of removed lymph nodes and lymph node ratio had no significant effect on OS. The number of negative lymph nodes had prognostic value in different lymph node stages and in two-field or three-field lymphadenectomy.**

Conclusions. **For ESCC patients after esophagectomy, the number of involved lymph nodes and the number of negative lymph nodes had a better prognostic value than did the number of removed lymph nodes and lymph node ratio.**

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Esophageal cancer (EC) is a common malignancy and has a high incidence [1]. In China, EC is the fifth most common cancer and the fourth leading cause of cancer-related deaths [2]. Interestingly, EC has different characteristics in Eastern and Western countries: 90% of EC in China is squamous cell carcinoma, whereas in Western countries, adenocarcinoma is predominant [3]. This implies that there might be differences in the prognosis and therapeutic strategies for EC patients in Eastern countries and Western countries.

Radical esophagectomy is a major treatment modality for resectable EC. Lymph node (LN) metastasis is an important prognostic factor for patients with EC, and clinicians increasingly emphasize evaluating the status of lymph nodes. In the 2009 staging system for EC of the International Cancer Control/American Joint Committee on Cancer, the pathologic nodal (pN) stage is redefined based on the number of involved lymph nodes [4]. In recent years, studies have revealed that other factors related to the status of lymph nodes, such as the number of removed lymph nodes (RLNs) and the ratio of involved to removed nodes (lymph node ratio, LNR), have a significant impact on the prognosis of EC patients [5–8]. However, there is still controversy about the prognostic value of the number of RLNs and LNR.

Regional lymph nodes have been the most common initial site of EC recurrence. Theoretically, resecting more lymph nodes or finding more negative lymph nodes (NLNs) may reduce the risk of occult lesions and thus increase the survival rate. Currently, there is still controversy about the role of the number of NLNs in EC. In studies on EC patients from Eastern countries, the results indicate that the number of NLNs may influence the survival of patients with esophageal squamous cell carcinoma (ESCC) [9–11]. However, although studies on EC patients from Western countries showed that the NLN count may influence the survival of patients with esophageal adenocarcinoma [12, 13], they have no prognostic

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Table 1. Correlation Between Number of Negative Lymph Nodes and Clinicopathologic Characteristics

Characteristic	n	No. of NLNs (quartiles) 0–8 NLNs n = 160 (%)	9–13 NLNs n = 167 (%)	14–18 NLNs n = 125 (%)	19–55 NLNs n = 151 (%)	*p* Value
Age, y						
≤60	480	126 (78.8)	135 (80.8)	99 (79.2)	120 (79.5)	0.970
>60	123	34 (21.2)	32 (19.2)	26 (20.8)	31 (20.5)	
Sex						
Male	454	125 (78.1)	122 (73.1)	87 (69.9)	120 (79.5)	0.192
Female	149	35 (21.9)	45 (26.9)	38 (30.4)	31 (20.5)	
Tumor location						
Upper third	44	12 (7.5)	12 (7.2)	12 (9.6)	8 (5.3)	0.741
Middle third	251	61 (38.1)	72 (43.1)	55 (44.0)	63 (41.7)	
Lower third	308	87 (54.4)	83 (49.7)	58 (46.4)	80 (53.0)	
Tumor stage						
pT1	25	10 (6.3)	3 (1.8)	3 (2.4)	9 (6.0)	0.243
pT2	176	40 (25.0)	51 (30.5)	41 (32.8)	44 (29.1)	
pT3	402	110 (68.7)	113 (67.7)	81 (64.8)	98 (64.9)	
Node stage						
pN0	330	85 (53.1)	91 (54.5)	74 (59.2)	80 (53.0)	0.387
pN1	155	39 (24.4)	37 (22.2)	31 (24.8)	48 (31.8)	
pN2	93	26 (16.3)	31 (18.5)	17 (13.6)	19 (12.6)	
pN3	25	10 (6.3)	8 (4.8)	3 (2.4)	4 (2.6)	
Histologic grade[a]						
G1	109	22 (13.8)	39 (23.4)	25 (20.0)	23 (15.2)	0.068
G2	304	74 (46.2)	83 (49.7)	63 (50.4)	84 (55.6)	
G3	190	64 (40.0)	45 (26.9)	37 (29.6)	44 (29.2)	
No. of fields dissected						
Two-field	464	141 (88.1)	134 (80.2)	91 (72.8)	98 (64.9)	<0.001
Three-field	139	19 (11.9)	33 (19.8)	34 (27.2)	53 (35.1)	

[a] G1 = well-differentiated; G2 = moderately differentiated; G3 = poorly differentiated.

NLNs = negative lymph nodes.

effect in ESCC [13]. Thus, we performed this study to investigate the prognostic value of different lymph node staging methods, including the number of involved lymph nodes, number of removed lymph nodes, lymph node ratio, and number of negative lymph nodes in patients with ESCC.

Material and Methods

Patients

A total of 603 EC patients who received radical esophagectomy were enrolled from October 2002 to March 2007. The inclusion criteria were as follows: (1) resectable ESCC with radical esophagectomy and lymph node dissection, (2) staging of ESCC as pT1-3N0-3M0 according to the 7th edition of the UICC/AJCC TNM staging system, (3) negative surgical margin (R0), (4) no preoperative radiotherapy or chemotherapy, and (5) location of ESCC in the thoracic esophagus. The study was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee of Sun Yat-Sen University Cancer Center. All patients provided written consent for storage of their information in the hospital database and for use of this information in our research.

Surgical Procedures

The surgical operations were performed according to our previously reported study [5]. In brief, all patients received radical esophagectomy with primary tumor resection and lymph node dissection. The most common surgical procedures were left thoracotomy, the Ivor-Lewis approach, and the cervicothoracoabdominal procedure. The left thoracotomy and the Ivor-Lewis procedure (right thoracotomy) with anastomosis of the upper chest were performed for all tumors in the lower third of the esophagus and some tumors in the middle third. The cervicothoracoabdominal procedure was used for all tumors in the upper third of the esophagus and some tumors in the middle third. Extensive lymph node resection in the posterior mediastinum and abdomen was routinely performed. For lymph node dissection, the thoracic lymphatics were resected through the posterior mediastinum; in other words, the middle and lower mediastinal nodes, including the periesophageal, parahiatal, subcarinal, and aortopulmonary window nodes were completely