Original Article

Pattern of subcarinal lymph node metastasis and dissection strategy for thoracic esophageal cancer

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Background: This study aimed to assess the role of subcarinal lymph nodes in lymph node metastasis in thoracic esophageal squamous cell carcinoma (ESCC) and to investigate the adequate range of lymph node dissection during esophagectomy.

Methods: This study included 782 thoracic ESCC patients who underwent esophagectomy between July 2008 and December 2010. The metastatic rate of subcarinal lymph nodes and their influencing factors were investigated. The outcome of subcarinal lymph node dissection was assessed using the efficacy index (the incidence of metastasis to a lymph node station (%) multiplied by the 5-year survival rate (%) of patients with metastasis to that lymph node station and divided by 100). Additionally, postoperative complications were compared between the subcarinal lymph node resection and reservation groups.

Results: The metastatic rates of subcarinal lymph nodes in the upper, middle, and lower thoracic ESCC were 8.3% (4/48), 19.1% (79/414), and 16.2% (23/142), respectively (χ^2=3.669, P>0.05) and in T1, T2, T3, and T4 tumors were 0% (0/71), 4% (4/100), 22.2% (85/383), and 34% (17/50), respectively (χ^2=42.859, P<0.05). Tumor invasion and size were significantly correlated with metastasis. For upper thoracic ESCC with positive subcarinal lymph nodes, metastasis tendency was mainly to the lower mediastinum. In middle third esophageal cancer, after subcarinal lymph nodes were involved, metastasis to the lower mediastinal lymph nodes increased by nearly 50%, and bidirectional metastasis increased by nearly three times compared with that before involvement. For lower third cancer with positive subcarinal lymph nodes, metastasis tendency was mainly to the upper mediastinum. The postoperative complication rates in the resection and reservation groups were as follows: overall, 19% and 14.6%, respectively (P>0.05), and pulmonary, 10.3% and 7.3%, respectively (P>0.05). The efficacy indexes of lymph node dissection at the upper, middle, and lower third esophagus were 0%, 7.6%, and 27.5%, respectively.

Conclusions: Dissection of subcarinal lymph nodes, which does not increase postoperative complications, should be performed routinely in lower thoracic ESCC after submucosal invasion of tumor; meanwhile, tumors larger than 3cm should also result in subcarinal lymph node dissection in patients with a tumor located in the upper esophagus and T1-T2 ESCC.

Keywords: Esophageal carcinoma; metastasis; lymph node dissection; subcarinal lymph node; efficacy index; complication

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Introduction

Esophageal cancer is one of the most common malignancies worldwide, especially in some areas of Asia (1). In 2012, it was reported as the fourth lethal alimentary tract cancer in the United States (2). Currently, operation is the mainstay treatment, especially for resectable tumor patients (3). Presently, the 5-year survival rate has increased from 17.1% to 32% (3-5). However, 5–10% mortality and 50% morbidity after operation make the prognosis even more grim (6). Among various plausible causes, lymphadenectomy-induced complications and lymph node metastasis after operation should not be ignored. Many studies support the hypothesis that lymph node metastasis is responsible for postoperative relapse because the lymphatic route is one of the most important pathways for esophageal cancer metastasis (7). Theoretically, the more suspicious lymph nodes are removed, the more potential benefits such as more accurate staging, lower postoperative relapse, and higher survival rate may be achieved (8). However, postoperative complications and mortality might increase accordingly (9). Specifically, subcarinal lymph nodes are beneath the bronchial bifurcation near the pulmonary plexus of the vagus nerve. Hence, resection of these lymph nodes is associated with potential trauma to the trachea, such as thermal radiation injury possibly caused by electronic devices. In addition, the vagus nerve can be injured, resulting in sputum retention. This is detrimental for postoperative pulmonary function restoration. Additionally, the bronchial artery may be ligated during the lymphadenectomy procedure. Consequently, blood supply to the trachea and bronchus may be reduced partially. Practitioners are concerned about all these potential risks. Thus, there is dispute concerning whether extensive lymphadenectomy should be performed (10). An adequate range of lymph nodes dissection can maintain the balance between operative effects and postoperative complications/mortality. Therefore, exploring a normative lymphadenectomy based on reasonable consideration is much significant.

Unfortunately, several lymph nodes surround the esophagus and specific metastatic rule is obscure. Lymphatic vessels in the thoracic esophageal cancer are extensive, connecting the lymph nodes in the neck, mediastinum, and abdomen. Subcarinal lymph nodes, which are adjacent to bronchial bifurcation, might be a metastatic station. Hsu *et al.* reported that the metastatic rate of subcarinal lymph nodes was 23.8% (11). However, Li *et al.* found the rate to be 10.4% (12). Generally, subcarinal lymph nodes should be resected because they are regional lymph nodes of the esophagus (13), and their metastases are more likely to be associated with postoperative recurrence and metastasis (14). However, Li *et al.* suggested that the resection may be unnecessary in early stage and upper thoracic esophageal cancer (12). This inconclusiveness regarding lymphadenectomy of subcarinal lymph nodes has been a long-standing concern for practitioners.

Few studies have focused on these concerns and no standard dissection guideline is available for practitioners. Therefore, this study assessed the role of subcarinal lymph nodes in lymph node metastasis in thoracic esophageal squamous cell carcinoma (ESCC) and investigated the adequate range of lymph node dissection during esophagectomy. We present this article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-1776).

Methods

This study retrospectively evaluated patients with esophageal carcinoma who were admitted to our department and underwent esophagectomy. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the human participants committee of West China Hospital of Sichuan University (the ethical number: 2005-126). Preoperatively, permission for the use of patients resected specimens and written informed consents were obtained.

Inclusion criteria

We included patients with histologically confirmed thoracic ESCC who underwent radical esophagectomy as the primary therapy and had complete clinicopathological data.

Exclusion criteria

We excluded patients who had cervical esophageal cancer, had received neoadjuvant chemo/radiotherapy, or had ESCC combined with other malignancies.

Patients

A total of 931 patients with ESCC were admitted into our department from July 2008 to December 2010, of which only 782 (men: 656 and women: 126) were eligible

for analysis. The median age of the patients was 59 years (range: 33–82 years). The clinicopathological stage of ESCC complied with the seventh edition American Joint Committee on Cancer tumor-node-metastasis staging criteria (2009) (15).

Surgical procedure and pathology

The surgical approach and lymphadenectomy's selection were depended on patients' preoperative examinations, at the same time, surgeons evaluated the patients' general condition and finally supplied for the patients the most appropriate surgical procedures. Generally, the McKeown esophagogastrectomy with three-filed lymph node dissection, the Sweet and Ivor-Lewis esophagogastrectomy with two-filed lymph node dissection may be performed. The lymph node identification and dissection for each patient were strictly followed by American Joint Committee on Cancer tumor-node-metastasis staging criteria (2009). Two experienced pathologists would fix the resected specimens, embedded and stained them with diaminobenzidine chromogen counterstained solution [1:50, EnVision TM Detection Kit, Gene Tech (Shanghai) Company Limited] and hematoxylin (Zhongshan Golden Bridge Biotechnology Co., Ltd, Beijing, China) subsequently. The routine way of assessing each specimen was adopted histologically, and the pathologists documented the extent and location of metastatic lymph nodes by examining the largest cross section of dissected lymph nodes.

Spectrum of postoperative complications

Postoperative pulmonary complication was defined as occurrence of any one of the following complications not because of anastomotic leak, massive pleural effusion, or nonpulmonary origin of infection (16): pneumonia, atelectasis/effusions, pleural effusion requiring placement of additional chest tubes, chylothorax, adult respiratory distress syndrome, respiratory failure requiring mechanical ventilation, and pulmonary embolism.

Anastomotic leakage was defined as the extravasation of water-soluble contrast medium and/or appearance of orally ingested methylene blue in the thoracic drainage (17).

Chylothorax was defined as a pleural effusion with presence of chylomicrons on lipoprotein electrophoresis or a triglyceride level higher than 110 mg/dL (18).

Recurrent laryngeal nerve paresis or palsy was diagnosed by the presence of hoarseness and aphonia (19).

Postoperative arrhythmias included sinus tachycardia, atrial fibrillation, multifocal atrial tachycardia, reentrant supraventricular tachycardia, atrial flutter, ventricular tachycardia, and heart blocks (20).

Wound infection, deep infection, wound hemorrhage, deep hemorrhage, chest infection, urinary infection, septicemia, wound dehiscence, deep venous thrombosis and pulmonary embolus, cardiac failure, impaired renal function, and hypotension were defined based on the Physiological and Operative Severity Score (21).

Follow-up

All patients were followed-up by telephone or interview at 3-month intervals for the first 2 postoperative years, at 6-month intervals for the following 3 years, and thereafter annually. Data regarding tumor status (tumor metastasis and recurrence), patient status (survival and death), and patients lost to follow-up were documented through outpatient follow-up as well as through telephone and letter follow-ups. Survival time was measured from the date of operation to the date of death or last follow-up. The last general follow-up of survivors was conducted in the end of March 2016. The median follow-up time was 30.41 months (range: 1.06–62.86 months).

Efficacy index

The efficacy index (22,23) is calculated as the incidence of metastasis to a lymph node station (%) multiplied by the 5-year survival rate (%) of patients with metastasis to that lymph node station and divided by 100.

Statistical analysis

Categorical data are expressed as numbers (percentage) and compared using the chi-square test or Fisher exact probability test. Continuous data are expressed as means ± standard deviation and analyzed using grouped *t*-test. We performed the Kendall rank correlation test to determine intergroup differences in the rank data. A difference was considered statistically significant if the P value was <0.05. Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 13 (SPSS, Chicago, IL, USA).

Table 1 Comparison of clinicopathological demographics of patients between the resection and reservation groups

Items	Resection group (n=604)	Reservation group (n=178)	Statistics	P value
Age			χ^2=0.072	0.437
<55	145	41		
≥55	459	137		
Sex			χ^2=8.653	0.003
Male	494	162		
Female	110	16		
Esophagectomy			χ^2=0.017	0.631
McKeown	193	56		
Sweet	370	110		
Ivor-Lewis	41	12		
TNM-stage			χ^2=6.314	0.097
0-I	61	9		
II	258	90		
III	270	76		
IV	15	3		
Lymph nodes	17±8	11±7	t=9.064	<0.001

χ^2: Chi-square test; t: Grouped *t*-test.

Results

Patient characteristics and the effect of subcarinal lymph node metastasis

Among 782 esophagectomy patients, 604 (77.2%) patients underwent resection of subcarinal lymph nodes (resection group). The total number of subcarinal lymph nodes removed was 2,566, with an average of five nodes per patient (range: 1–22). In the remaining 178 (22.8%) patients, subcarinal lymph nodes were reserved (reservation group; *Table 1*).

Subcarinal lymph node metastasis was correlated with the length of tumor (P<0.001) and the depth of cancer invasion (P<0.001), among which we found patients with tumor size larger than 3 cm or T3-T4 ESCC got higher subcarinal lymph node metastasis than those with tumor size less than 3 cm or T1-T2 ESCC. In addition, pathological differentiation was an important factor in subcarinal lymph node metastasis. Although tumor location was not statistically significantly associated with subcarinal lymph node metastasis, the incidence of metastasis in upper thoracic ESCC was lower than that in middle and lower thoracic ESCC (*Table 2*).

The role of subcarinal lymph nodes in lymph node metastasis

Among 604 patients who underwent resection of subcarinal lymph nodes, 106 (17.5%) patients had metastatic subcarinal lymph nodes. Fifty-six of 106 patients with positive subcarinal lymph nodes underwent subcarinal lymph nodes dissection. Among the 498 patients with negative subcarinal lymph nodes, 276 patients underwent subcarinal lymph nodes dissection. To evaluate the role of subcarinal lymph nodes in lymph nodes metastases, we summarized the data of 332 patients with subcarinal lymph nodes dissection. Considering subcarinal lymph nodes as the point of reference, the metastatic directions of other regional lymph nodes were divided as follows: upper mediastinum, lower mediastinum, both, and none (no other metastasis except the subcarinal nodes; *Table 3*). Additionally, the metastasis rate of the left gastric artery (No. 17), paraesophageal (No. 8M and 8L), gastric cardia (No. 16), upper paratracheal (No. 2L and 2R), lower

Table 2 Correlation between subcarinal lymph node metastasis and pathological characteristics

Pathological characteristics	Number of patients	Metastatic subcarinal LN (%)	Correlation coefficient (r)	Statistics	P value
Position of tumor			−0.015	χ^2=3.669	0.160
Upper	48	4 (8.3)			
Middle	414	79 (19.1)			
Lower	142	23 (16.2)			
Length of tumor (cm)			−0.142	χ^2=16.887	<0.001
<3.0	133	8 (6.0)			
3.0–5.0	276	53 (19.2)			
5.1–7.0	153	35 (22.9)			
>7.0	42	10 (23.8)			
Depth of invasion			−0.251	χ^2=42.859	<0.001
T1	71	0 (0)			
T2	100	4 (4.0)			
T3	383	85 (22.2)			
T4	50	17 (34.0)			
Differentiation			−0.054	χ^2=4.750	0.093
Well	76	7 (9.2)			
Moderately	397	78 (19.6)			
Poorly	131	25 (19.1)			

paratracheal (No. 4L and 4R) and pulmonary ligament lymph nodes (No. 9) were 31% (134/432), 28.2% (128/454), 24.9% (87/350), 8.6% (18/209), 3.9% (6/155), and 3.9% (5/129), respectively.

Postoperative complications between two groups

A total of 141 (18%) patients experienced postoperative complications. Pulmonary complication was the most frequently encountered complication, occurring in 75 patients. No significant difference was not in the postoperative complication rates between both the groups (*Table 4*).

Effect of subcarinal lymph node metastasis on survival

The median follow-up time for resection group and reservation group are 30.30 months (range, 1.06–62.86 months) and 23.06 months (range, 1.53–61.80). The overall survival was 48.337±1.698 months in the resection group and 38.113±2.849 months in the reservation group (P<0.001, *Figure 1*). With regard to tumor location, all patients in the resection group had a significantly better prognosis than those in the reservation group (all P<0.001, *Figure 2*). The significantly better prognosis observed in the resection group was among patients with negative subcarinal lymph nodes rather than among those with positive subcarinal lymph nodes (52.305±1.821 *vs.* 19.918± 1.698 months, P<0.001, *Figure 3*).

However, for subcarinal lymph nodes at the upper, middle, and lower thirds of the esophagus in all patients, the resection rates were 70%, 74.9%, and 76.9%, respectively; the mean numbers (± SD) of nodes resected were 3.9 (±2.8), 3.6 (±2.9), and 3.8 (±2.5), respectively; the frequencies of metastasis were 8.3%, 19.1%, and 16.2%, respectively; and the efficacy indexes of lymph node dissection were 0%, 7.6%, and 27.5%, respectively (*Table 5*).

Discussion

The metastatic rate of subcarinal lymph nodes in thoracic ESCC was found to be 17.5%, which is lower than that

Table 3 Relationship between the metastatic direction of other regional lymph nodes and subcarinal lymph nodes

Metastatic direction	Subcarinal lymph nodes		Statistics	P value
	Negative (%) (n=276)	Positive (%) (n=56)		
Upper third	33	3	–	–
Upper mediastinum	6 (18.2)	0 (0)		
Lower mediastinum	2 (6.1)	2 (66.7)		
Both	2 (6.1)	0 (0)		
None	23 (69.7)	1 (33.3)		
Middle third	194	45	χ^2=39.473	<0.001
Upper mediastinum	18 (9.3)	3 (6.7)		
Lower mediastinum	45 (23.2)	21 (46.7)		
Both	14 (7.2)	14 (31.1)		
None	117 (60.3)	7 (15.6)		
Lower third	49	8		
Upper mediastinum	1 (2.0)	2 (25.0)	–	–
Lower mediastinum	26 (53.1)	6 (75.0)		
Both	1 (2.0)	0 (0)		
None	21 (42.9)	0 (0)		

Table 4 Comparison of postoperative complications between the resection and reservation groups

Complications	Resection group (n=604) (%)	Reservation group (n=178) (%)	Statistics	P value
Pulmonary complications	62 (10.3)	13 (7.3)	χ^2=1.391	0.238
Pulmonary infection	43	7		
Respiratory failure	6	2		
ARDS	13	4		
Anastomotic leakage	17 (2.8)	8 (4.5)	χ^2=1.254	0.263
Chylothorax	14 (2.3)	2 (1.1)	χ^2=0.978	0.323
Other complications	22 (3.6)	3 (1.7)	χ^2=1.701	0.192
Overall	115 (19.0)	26 (14.6)	χ^2=1.828	0.176

reported by Hsu *et al.* (23.8%) (11) and higher than that reported by Li *et al.* (10.4%) (12). The plausible reason is the proportion of T3 and T4 patients in the study population. The proportion of T3 and T4 patients in Li *et al.* study was 61.9% (305/492), in Hus *et al.* study was 79.2% (80/101), and in our study was 71.7% (433/604). Moreover, Li *et al.* reported absence of positive subcarinal lymph nodes in upper esophageal cancer, which contrasted with the metastatic rate of 8.3% in our study. However, compared with metastasis of the paraesophageal lymph nodes among mediastinal lymph nodes, metastasis of the subcarinal lymph nodes in upper ESCC was less frequent. In addition, we demonstrated that both deeper tumor invasion and longer tumor length were correlated with high rate of subcarinal lymph node metastasis; however, histological differentiation did not

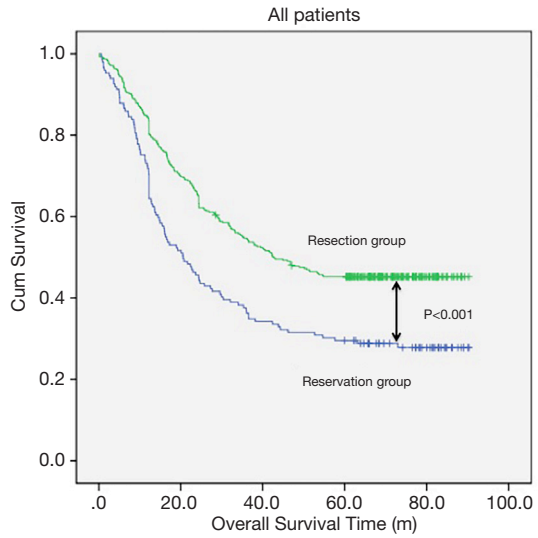

Figure 1 Survival analysis of Resection group & Reservation group for all patients: 48.337±1.698 months for dissection group *vs.* 38.113±2.849 months for non-dissection group (Chi-square =10.312, P<0.001).

affect the metastatic rate. Although some studies have reported the same findings (12), a multivariate analysis by Zhu *et al.* denied the correlations (24). However, a further study with 1,812 consecutive patients confirmed the relationship (25). These discrepancies may have resulted from the complexity of subcarinal lymph nodes or limitation and differences in sample size. However, we found eight patients with tumor length <3 cm and seven patients with histologically well-differentiated ESCC who had positive subcarinal lymph nodes and T3 or T4 stage. Therefore, tumor invasion rather than tumor length and differentiation might be a more prominent factor influencing the metastasis rate, which is consistent with the findings of Matsubara *et al.* (26). The possibility of lymph node metastases is low if the lesion is limited to the mucosa (27). However, the possibility of metastasis is highly elevated after submucosal invasion (28). Overall, subcarinal lymph nodes should be given prominence, especially in higher T-stage patients, regardless of the tumor location.

However, merely based on the metastatic rate, neither this nor other related studies could prove that subcarinal lymph nodes are sentinel lymph nodes (14). Because the distribution of lymph nodes in ESCC was unpredictable, we further investigated to clarify the role of subcarinal lymph nodes in lymph node metastasis, and believed it to be noteworthy.

We summarized the metastatic direction of lymph nodes surrounding subcarinal lymph nodes, considering subcarinal lymph node as the point of reference. In upper esophageal cancer, metastatic tendency was found to be downward after the subcarinal lymph nodes were involved, however, the number of patients with positive subcarinal lymph nodes was small, therefore, the tendency requires to be evaluated. In middle esophageal cancer patients with positive subcarinal lymph nodes, it was noted that both downward metastasis and increase in bidirectional metastatic tendency were highest. However, only upward metastasis decreased by nearly one third. Natsugoe *et al.* reported the reason for decrease in only upward metastasis as tumor invasion might be blocking the lymphatic pathway (29). The reason seems plausible and further study focused on this problem should be conducted. In lower ESCC patients, if the subcarinal lymph nodes were positive, both upward and downward metastasis increased and the former was found to be the main tendency, whereas the latter was found to be the main pattern. Moreover, if subcarinal lymph nodes were negative, other examined regional lymph nodes were rarely positive regardless of tumor location. Based on these obvious differences, it can be concluded that subcarinal lymph nodes are an important station in the lymphatic metastatic route. In addition, we found eight patients with solitary positive subcarinal lymph nodes. This can be explained as bidirectional or skip lymph node metastasis in esophageal cancer (30). The flow of lymph in the extramural lymphatic system from the distal esophagus was bidirectional, and the intramural lymphatic system communicated with different segments of the esophagus in the middle layer of muscularis mucosa. Moreover, the lymphatic pathway may be blocked by tumor invasion (29). Nevertheless, to some extent, it was still reasonable to consider subcarinal lymph node as a dependable indicator of other regional lymph node metastasis.

Lymphadenectomy may cause tissue injury and prolong operative time unavoidably. Postoperative complications resulting from the resection of subcarinal lymph nodes due to the special anatomic location should be considered. Li *et al.* reported that pulmonary complications in the resection group were considerably higher than those in the reservation group (12). On the contrary, in this study, no statistically significant differences were noted between the two groups for pulmonary complications

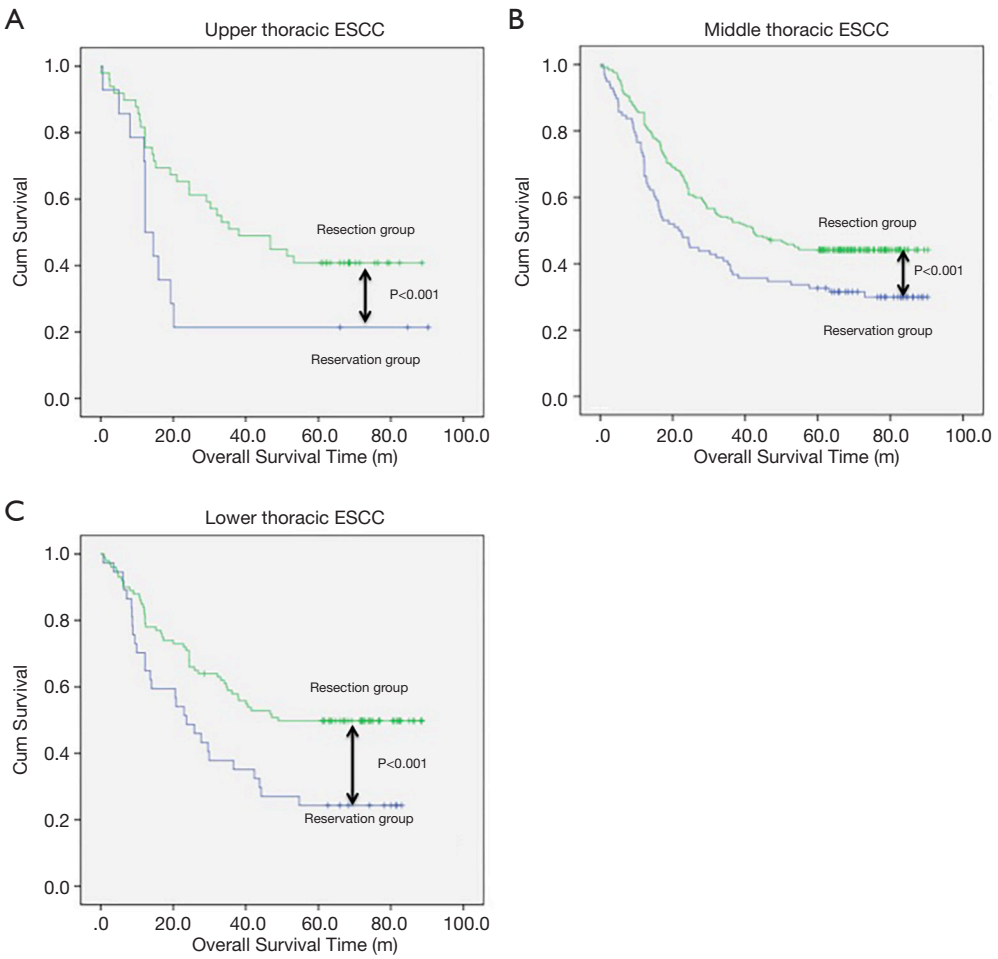

Figure 2 Survival analysis of Resection group & reservation group for thoracic ESCC patients with regard to tumor location. (A) Patients with upper thoracic ESCC: 45.832±4.590 months for dissection group *vs.* 28.743±8.691 months for non-dissection group (Chi-square =10.1931, P<0.001). (B) Patients with middle thoracic ESCC: 48.249±2.173 months for dissection group *vs.* 39.892±3.592 months for non-dissection group (Chi-square =27.0464, P<0.001). (C) Patients with lower thoracic ESCC: 48.747±3.259 months for dissection group *vs.* 35.085±4.897 months for non-dissection group (Chi-square =19.5780, P<0.001).

as well as overall complications. This indicated that the special anatomic location of subcarinal lymph nodes and prolonged operative time might not be the main causes of postoperative complications. Actually, postoperative complications can be well prevented through meticulous maneuvers during operation and appropriate perioperative treatment strategies (31,32). Many studies have reported no increase in complication rates after subcarinal lymphadenectomy (33).

In this study, the survival time was significantly better in the resection group than in the reservation group. In addition, the same trend was found when the patients were divided into three groups based on the tumor location. Similarly, the total number of lymph nodes removed was significantly higher in the resection group than in the reservation group. Therefore, we cannot judge the value of lymph node dissection. The low efficacy index (0%) for subcarinal lymph nodes dissection in patients with upper thoracic ESCC indicates that subcarinal lymph node dissection does not contribute to the improved survival for these patients. The efficacy index in patients with middle thoracic ESCC was higher (7.6%) and in those

with lower thoracic ESCC was the highest (27.5%). Based on our calculated efficacy index, subcarinal lymph node dissection can be omitted for patients with upper thoracic ESCC. However, Yukiko found that the characteristics of efficacy index were same in upper ESCC and lower ESCC patients (17).

Our study has some limitations. First, our study was a single-center retrospective study; therefore, analytical and selection biases were inevitable, however, in order to eliminate the interobserver variability of lymph nodes identification of our study, firstly, surgeons identified every station of lymph node and dissect them strictly followed by American Joint Committee on Cancer tumor-node-metastasis staging criteria (2009), which guarantee the precise dissection of each station of lymph nodes. Secondly, the two experienced pathologists examined the resected lymph nodes histologically, which make sure the exact definition of subcarinal lymph nodes in our study. Second, the specific role of subcarinal lymph nodes in lymph node metastasis has not been investigated previously. In addition, the numbers of upper and lower ESCC patients were inadequate in this study. Thus, further investigation with a larger study population is warranted. Third, the prognostic significance of subcarinal lymph node metastasis was mainly focused on ESCC patients because esophageal cancer in most of the Chinese patients is squamous cell carcinoma; however, in most of the patients of the Western countries, esophageal cancer is adenocarcinoma. Thus, a large-scale multicenter, prospective study is warranted to verify the findings.

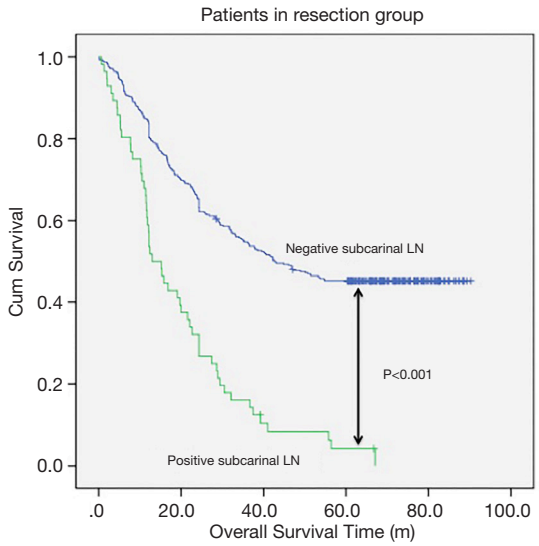

Figure 3 Survival analysis of Negative subcarinal LN & Positive subcarinal LN for patients in Resection group: 52.305± 1.821 months for patients with negative subcarinal LN *vs.* 19.918±1.698 months for patients with positive subcarinal LN (Chi-square =125.4935, P<0.001).

Conclusions

High incidence of subcarinal lymph node metastasis is observed in thoracic ESCC, especially among those with middle and lower esophageal cancer. The efficacy index of subcarinal lymph nodes dissection was higher for cancer of the lower esophagus than of the upper esophagus. The metastasis rate was obviously higher in T3-T4 stage patients than in T1-T2 stage patients. Therefore, we propose that in lower esophageal cancer, subcarinal lymph nodes dissection is necessary if the tumor has invaded the adventitia of the esophagus. However, whether the subcarinal lymph nodes dissection can be performed selectively in the upper esophageal cancer is still needed to be confirmed, but if the upper thoracic ESCC or T1-T2 stage patients with tumor size larger than 3 cm, the subcarinal lymph node dissection will be strongly recommended.

Table 5 Efficacy index of subcarinal lymph node stations in upper, middle, and lower thoracic ESCC patients

Tumor location	AJCC 7th edition		Lymphadenectomy rate (%)	Total number of lymph nodes retrieved (mean ± SD)	Metastatic rate (%)	5-year DSS rate (%)	Efficacy index (%)
	Number	Lymph node station					
Upper third	7	Subcarinal	70	3.9±2.8	8.3	0	0
Middle third	7	Subcarinal	74.9	3.6±2.9	19.1	0.4	7.6
Lower third	7	Subcarinal	76.9	3.8±2.5	16.2	1.7	27.5

AJCC, American Joint Committee on Cancer; ESCC, esophageal squamous cell carcinoma; JES, Japan Esophageal Society; SD, standard deviation; DSS, disease-specific survival.

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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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the human participants committee of West China Hospital of Sichuan University (the ethical number: 2005-126). Preoperatively, permission for the use of patients resected specimens and written informed consents were obtained.

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