

A clinical study of thoracic esophageal carcinoma metastasis into abdominal lymph nodes

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Abstract

Objective The aim of this study was to analyze the potential of thoracic esophageal carcinoma to metastasize into abdominal lymph nodes.

Methods The data on abdominal lymph node metastasis in 164 patients who had undergone resection of thoracic esophageal carcinoma were analyzed retrospectively and grouped according to tumor position in the upper, middle, or lower thoracic esophagus. The difference in tumor infiltration depth, differentiation degree, pathological type, pathological stage, and the metastasis rate in abdominal lymph nodes among the three groups was evaluated and the correlation of abdominal lymph node metastasis with tumor infiltration depth, differentiation degree, and pathological type was analyzed.

Results Clinical characteristics such as tumor infiltration depth, differentiation degree, pathological type, and pathological stage were not significantly different between the patients with upper, middle, and lower thoracic esophageal carcinomas. Although there was a difference in the metastasis rate in abdominal lymph nodes between the three groups (6.9%, 27.4%, and 39.6% for the upper, middle, and lower thoracic esophageal carcinomas, respectively), it was not statistically significant. There was also no association between the rate of abdominal lymph node metastasis and tumor infiltration depth, differentiation degree, and pathological type.

Conclusion Esophageal carcinoma specifically metastasizes into lymph nodes. If the tumor infiltrates the upper thoracic submucosa, it could metastasize down to abdominal lymph nodes via the lymphatic capillary net. The majority of esophageal carcinomas were of T1b or higher pathological stage at the diagnosis, indicating infiltration of the submucosa. Thus, tumors of the early stage, high degree of differentiation, or position in the upper thoracic esophagus were not less prone to metastasis into abdominal lymph nodes. Therefore, routine abdominal lymph node dissection during radical surgery for esophageal carcinoma is necessary.

Key words: esophageal carcinoma; abdominal lymph node; metastasis

Received: 15 April 2015

Revised: 10 May 2015

Accepted: 25 July 2015

In recent years, lymph node dissection in the cervical, thoracic, and abdominal regions is universally accepted. The analysis of the development of lymph node metastasis in esophageal cancer revealed that the prognosis for esophageal carcinoma depends on the extent of lymph node dissection [1]. Our clinical results showed that the rates of abdominal lymph node metastasis were low in upper thoracic esophageal carcinomas, especially in the early stages of cervical esophageal cancer and upper thoracic esophageal carcinoma. Previous studies on lymph node metastasis in esophageal cancer have found that abdominal lymph node metastasis in upper thoracic esophageal carcinoma is associated with tumor location, invasion

depth, and the degree of differentiation. Thus, the early stages of cancer in the upper thoracic segment and highly differentiated esophageal carcinomas are characterized with low rates of abdominal lymph node metastasis [2]. This observation prompts the question whether selective abdominal lymph node extraction should be performed during surgery for the removal of upper thoracic esophageal carcinoma. In 2010 in our department, we developed radical resection of esophageal cancer using video-assisted thoracoscopic surgery (VATS), and since then performed many radical surgeries of esophageal carcinoma, which included lymph node dissection in the cervical, thoracic, and abdominal regions, i.e., selective three-field lymph-

adenectomy. In this study, we conducted retrospective analysis of the data obtained during radical resection of esophageal tumors and evaluated the association of clinicopathological features with abdominal lymph node metastasis.

Materials and methods

Clinical data

VATS was performed in 164 patients with esophageal carcinoma from January 2010 to November 2013. Tumors were located in the upper segment in 16 patients, middle segment in 95 patients, and lower segment in 53 patients (Table 1).

Surgery

The operative method was radical resection of esophageal cancers using VATS. All operations were conducted by the same surgeon. First, selective three-field lymphadenectomy was performed, and the decision to conduct regular cleaning or implement cervical lymph node dissection was based on the color, and Doppler ultrasound and CT results. Patients were put in the left lateral recumbent position, pitched at a 45° angle, and thoracic surgery was conducted after adequate preparation. The esophagus was freed and the corresponding lymph nodes cleaned using VATS. Then, patients were changed into the supine position and abdominal and neck surgeries were performed. During the abdominal surgery, the related abdominal lymph nodes were dissociated from the stomach and other tissues and cleaned. After a gastric tube was inserted and the esophagus was fully dissociated, mechanical cervical anastomosis was implemented for all patients to accomplish cervical esophageal reconstruction. Some abdominal lymph nodes were dissected during radical resection of esophageal tumors. Among them were lymph nodes of the peripheral cardia, gastric lesser curvature, and greater curvature of the stomach, as well as para-left gastric arterial, posterior pancreaticoduodenal, para-arteria hepatica communis, and para-truncus celiacus lymph nodes.

Pathological staging

The pathological stage was determined according to the TNM pathological classification of the Union for International Cancer Control for esophageal carcinoma (2009).

Statistical analysis

The SPSS statistical package, version 19.0, was used for statistical analyses. The chi-square test and Fisher's exact test were applied to compare the data. A *P* value less than 0.05 was considered statistically significant.

Table 1 Basic information (*n*)

Characteristics	Number of cases			Total	<i>P</i>
	Upper	Middle	Lower		
Tumor infiltration depth					
T1a	0	0	0	0	0.550
T1b	2	7	7	16	
T2	6	31	13	50	
T3	8	57	33	98	
T4	0	0	0	0	
Differentiated degree					
G1	9	43	22	74	0.733
G2	4	31	17	52	
G3	2	16	13	31	
Pathological type					
Squamous carcinoma	15	90	49	154	0.295
Adenocarcinoma	0	1	3	4	
Pathological stage					
IA	0	3	5	8	0.329
IB	4	13	8	25	
II	8	47	16	71	
IIIA	2	18	16	36	
IIIB	1	8	3	12	
IV	1	6	5	12	
Sex					
Male	10	74	44	128	0.215
Female	6	21	9	36	

Results

Lymph node dissection

In total, 1,938 abdominal lymph nodes were dissected from 164 patients with esophageal carcinoma. Among the 29 cases of thoracic esophageal carcinoma, there were 2 positive lymph nodes (metastatic rate, 6.9%) and the proportion of positive cases was 12.5% (2/16). Among the 1,138 cases of middle segment carcinoma, there were 63 positive lymph nodes (metastatic rate, 5.54%) and the proportion of positive cases was 27.4% (26/95). Among the 681 cases in the lower segment, there were 105 positive lymph nodes (metastatic rate, 15.4%) and the proportion of positive cases was 39.6% (21/53). The abdominal lymph node metastasis rate was: 10.4% for peripheral cardia lymph nodes, 18.9% for gastric lesser curvature lymph nodes, 1.2% for greater curvature of stomach lymph nodes, 3.0% for para-left gastric artery lymph nodes, 2.4% for para-arteria hepatica communis lymph nodes, 1.8% for para-truncus celiacus lymph nodes, and 0% for posterior pancreaticoduodenal lymph nodes.

Statistical analysis

Statistical analysis revealed that there was no significant difference between the upper thoracic esophageal carcinoma group, the middle thoracic esophageal carcino-

ma group, and the lower thoracic esophageal carcinoma group in sex, the depth of invasion, degree of differentiation, pathological stage, and pathological type ($P > 0.05$). The difference between these groups was observed in the metastatic rate in abdominal lymph nodes (6.9%, 27.4%, and 39.6%, respectively); however, it was not statistically significant. There was also no statistically significant association between the rate of abdominal lymph node metastasis and the depth of invasion (T stage), degree of differentiation (G stage), and pathological type (Table 2).

Discussion

Lymph node metastases are the main metastatic mode of esophageal carcinoma; therefore, the dissection of lymph nodes is important for the treatment of esophageal cancer. At present, most researchers consider selective three-field lymphadenectomy as a necessary step in the radical treatment of esophageal tumors because it can significantly improve the prognosis for cancer patients [3]. However, the incidence of surgical traumatism and postoperative complications has increased as a result of excessive three-field lymphadenectomy [4-5]. Reasonable application of lymph node dissection not only can ensure operation effectiveness and improve patients' life quality, but also can reduce postoperative complications. Therefore, it is important for clinical outcome to explore the characteristics of lymph node metastasis in esophageal cancer and to determine a reasonable rate of lymph node dissection [6]. The lymphatic capillary network in the esophagus is abundant. Submucosal lymphatic vessels not only provide horizontal transfer to the nearby lymph nodes by penetrating the esophageal wall, but also vertical transfer to the superior or inferior part of the esophagus via the submucosal lymphatic system. In addition, the number of longitudinal lymphatic vessels in the esophagus is six times greater than that of transverse lymphatic vessels. These lymphatic networks can extend to the lymphatic and blood supply systems of the neck and abdomen. In the early stage of esophageal cancer, tumor cells infiltrate the esophageal submucosa and may invade distant areas, such as abdominal lymph nodes through the lymphatic capillary network. In other words, esophageal cancer is prone to lymphatic node metastasis at the early stage, which is characterized by wide dissemination to the neck, chest, abdomen, and other areas [7-10].

Few previous studies have investigated the development of abdominal lymph node metastasis for thoracic esophageal carcinoma. Some published results suggest that in patients with upper thoracic esophageal tumors, lymph node metastasis was more likely to occur in the upper mediastinal and cervical part lymph nodes rather than in middle or lower mediastinal and abdominal lymph nodes. At the same time, patients with lower esophageal tumors

Table 2 Statistical analysis (n)

Characteristics	Metastasis	Not metastasis	P
Sex			
Male	42	86	0.151
Female	7	29	
Tumor location			
Upper	2	14	0.086
Middle	26	69	
Lower	21	32	
Tumor infiltration depth			
T1	3	13	0.507
T2	14	36	
T3	32	66	
Differentiated degree			
G1	18	56	0.323
G2	16	36	
G3	12	19	
Pathological type			
Squamous carcinoma	43	111	0.075
Adenocarcinoma	3	1	

demonstrated more frequent metastasis in lower mediastinal and abdominal lymph nodes compared to upper mediastinal and cervical part lymph nodes. The probability that tumors are vertically transferred to the superior or inferior parts of the esophagus is similar in patients with middle thoracic esophageal tumors [11]. It is also thought that abdominal lymph node metastasis of thoracic esophageal carcinoma is related to tumor position, invasion depth, and the degree of differentiation, i.e., early-stage upper thoracic segment tumors and highly differentiated esophageal cancers are less likely to metastasize into abdominal lymph nodes [2].

We analyzed the development of abdominal lymph node metastasis in patients with thoracic esophageal cancer, who underwent three-field lymphadenectomy in our department between 2010 and 2013. The results showed that abdominal lymph node metastasis occurred mainly in peripheral cardia and gastric lesser curvature lymph nodes, which is consistent with a previous report [12]. Interestingly, we also observed that abdominal lymph node metastasis of upper thoracic esophageal carcinoma appeared to be significantly lower than that of middle and lower thoracic esophageal tumors, especially of early upper thoracic esophageal carcinomas. The analysis of cancer recurrence in postoperative patients revealed that it was more frequent in upper mediastinum and perigastric area lymph nodes than in middle or lower mediastinal lymph nodes [13]. However, there was no statistically significant difference in the rates of abdominal lymph node metastasis between upper, middle, and lower thoracic esophageal carcinomas; the metastasis rate also demonstrated the lack of correlation with the depth of invasion, degree of differentiation, and pathological type. There-

fore, it cannot be concluded that the early-stage tumors of the upper thoracic segment or highly differentiated esophageal cancers are less prone to abdominal lymph node metastasis. However, a previous study has reported different results [2]. Further investigation of the mechanisms underlying possible low metastasizing potential of upper thoracic esophageal cancer compared to that of tumors in the middle and lower segments of the esophagus is required. Current data on upper thoracic esophageal cancer are not sufficient, which may lead to the lack of statistically significant conclusions regarding the migration of esophageal carcinoma cells and tumor metastasis. In the early stage of esophageal cancer, when the tumor invades esophageal submucosa, it may metastasize into distant organs, such as abdominal lymph nodes via the lymphatic capillary net. Therefore, the early stages of upper thoracic segment tumors and highly differentiated esophageal cancers have the potential to metastasize into abdominal lymph nodes. The majority of esophageal cancer patients develop T1b pathologic stage when esophageal carcinoma is diagnosed, which means that tumors have invaded the esophageal submucosa. Therefore, routine dissection of abdominal lymph nodes during radical surgery for esophageal carcinoma should be necessary irrespective of tumor position, the depth of invasion, and degree of differentiation.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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DOI 10.1007/s10330-015-0090-Z

Cite this article as: Yang QJ, Zhong L, Guo M. A clinical study of thoracic esophageal carcinoma metastasis into abdominal lymph nodes. *Oncol Transl Med*, 2016, 2: 8–11.