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Nodal skip metastasis is associated with a relatively poor prognosis in thoracic esophageal squamous cell carcinoma

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Abstract

Background: Nodal skip metastasis (NSM) is common in esophageal carcinoma, even with different lymph node classification criteria. The prognostic impact of NSM in esophageal carcinoma has been unclear. Some studies found no impact on survival and others found a positive impact. This research was to further investigate the incidence of NSM in patients with thoracic esophageal squamous cell carcinoma (ESCC), and assess its prognostic value in thoracic ESCC.

Methods: We retrospectively analyzed the clinical data of 340 consecutive patients with solitary lymph node metastasis who underwent esophagectomy with three-field lymph node dissection for ESCC at the First Affiliated Hospital of Zhengzhou University from January 2005 to December 2013. The survivals of the patients with NSM or adjacent node metastasis were compared.

Results: There were 216 patients with NSM, and 124 patients with adjacent node metastasis. The incidence of NSM in this cohort was 63.5%. No significant difference was found between the patients with NSM and the patients with adjacent node metastasis in age, sex, tumor location, pathologic T stage, histologic grade, tumor length, and the number of resected lymph nodes (all $p > 0.05$). Patients with NSM had 5-year cumulative survival of 29.2%, which was significantly worse than the 45.6% survival in those with adjacent node metastasis ($p < 0.05$).

Conclusion: In conclusion, NSM is associated with a relatively poor prognosis in thoracic ESCC.

Keywords: Esophageal squamous cell carcinoma; Nodal skip metastasis; Prognosis

Introduction

Esophageal carcinoma is one of the most tedious malignancies in the digestive system. Squamous cell carcinoma (SCC) accounts for most of the esophageal malignant tumors in China, in contrast to the predominance of adenocarcinoma in the Western world.[1] The outcome of patients with esophageal squamous cell carcinoma (ESCC) continues to be poor, with a 5-year survival rate ranging from 26.2% to 49.4%.[2–7] Lymph node metastasis is a common pathway for the spread of esophageal cancer; nodal stage is considered the most reliable predictor of survival after esophagectomy with lymphadenectomy in esophageal cancer patients without systemic metastasis, and the presence of nodal metastasis is indicative of high risk for disease recurrence.[8–10]

Nodal skip metastasis (NSM) is not a rare event in esophageal carcinoma, even with different lymph node classification criteria.[11–15] However, its relevance for esophageal carcinoma was only assessed in a few studies, and the findings have been inconsistent; some studies found no impact on survival and others found a positive impact.[11–15] Therefore, we conducted a retrospective study to further investigate the incidence of NSM in patients with ESCC, and assess its prognostic value in thoracic ESCC.

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Patients and methods

Study cohort

This retrospective study was approved by the ethics committees of the First Affiliated Hospital of Zhengzhou University, which waived the requirement for written, informed consent of individual patients given the retrospective nature of this study. The records of all patients with solitary lymph node metastasis who underwent esophagectomy with three-field lymph node dissection for ESCC at the First Affiliated Hospital of Zhengzhou University from January 2005 to December 2013 were identified. We excluded patients with non-SCC, multiple lymph node metastases, neoadjuvant chemotherapy or radiotherapy, or both, other concurrent malignant diseases, previous primary cancers, cervical esophageal carcinoma, and gastroesophageal junction carcinoma. Tumor, node, and metastasis descriptors, as well as the staging classification used for this analysis, were those defined in the American Joint Committee on Cancer (AJCC) Staging Manual (7th edition).[16] The lymph nodes were grouped according to Casson's lymph node map of esophageal cancer.[17] (Tables 1 and 2). NSM was defined as follows: there was no continuous tumor cell spread from the primary tumor into the adjacent lymph node levels (station 1), but firstly appears in further one level (station 2) or more than one level (station 3).[13] The primary endpoint of this research was survival time, and the secondary endpoints were the incidence of NSM and relevant clinicopathological factors.

Table 1
The grouping and naming of regional lymph node drainage for esophageal cancer.

Group	Name	Group	Name
1	Supraclavicular nodes	8L	Lower paraesophageal nodes
2R	Right upper paratracheal nodes	9	Pulmonary ligament nodes
2L	Left upper paratracheal nodes	10R	Right tracheobronchial nodes
3P	Posterior mediastinal nodes	10L	Left tracheobronchial nodes
4R	Right lower paratracheal nodes	15	Diaphragmatic nodes
4L	Left lower paratracheal nodes	16	Paracardial nodes
5	Aortopulmonary nodes	17	Left gastric nodes
6	Anterior mediastinal nodes	18	Common hepatic nodes
7	Subcarinal nodes	19	Splenic nodes
8M	Middle paraesophageal nodes	20	Celiac nodes

For Group 8: M = middle, L = lower; for other Groups: R = right, L = left, P = posterior.

Table 2
The lymph nodes drain station according to the location of the tumor.

Tumor location	Station 1	Station 2	Station 3
Upper thoracic	3P	2, 4, 7, 8M	Others
Middle thoracic	8M	3P, 2, 4, 7, 8L, 9, 15, 16	Others
Lower thoracic	8L	8M, 9, 15, 16, 17	Others

Surgical procedure

Esophagectomy and three-field lymph node dissection were performed through a right thoracotomy, laparotomy, and bilateral cervical collar incision. The patient was placed in the left lateral decubitus position, which was inserted via the fifth intercostal space after posterolateral thoracotomy. We dissected the esophagus and adjacent tissue from the apex of the chest to the diaphragmatic hiatus, then closed the thoracic incision. For the second stage, the patient was placed in the supine position. We dissected the stomach and abdominal lymph nodes via laparotomy, which preserved the right gastroepiploic vessels and vascular arcades. A gastric tube of 4–5 cm in diameter was made. We returned to the neck, and bilateral cervical collar incision was made to expose the cervical esophagus and dissect the cervical lymph nodes. The gastric conduit was brought to the neck and an esophagogastric anastomoses were done. Finally, we closed the cervical and abdominal incisions. Lymph node dissection included 5 anatomical groups (cervical, upper mediastinal, middle mediastinal, lower mediastinal, and abdominal lymph nodes).

Follow-up assessment

A follow-up examination was generally scheduled every 3 months for the first year, every 4 months for the second year, and twice yearly thereafter. The regular follow-up assessment included physical examination, blood chemistry analysis, tumor markers (carcinoembryonic antigen, SCC antigen), computed tomography scan, esophagography, ultrasonography, and endoscopy. However, examinations were performed sooner if the patient had specific symptoms. Operative death was defined as death within 30 days after operation or at any time postoperatively if the patient did not leave the hospital alive. April 2015 was the last contact date for survival. The median time from the operation to the last contact date for the entire cohort was 25.0 months (range, 1.0–159.0 months).

Statistical analysis

Continuous variables were compared by independent samples t test. The mean values were described as mean ± standard deviation. The Pearson chi-squared test was used to determine the significance of differences between groups for dichotomous variables. Survival was calculated by the Kaplan–Meier method, and the log-rank test was used to assess differences in survival between groups. A two-sided $p < 0.050$ was considered statistically significant. Survival time was measured from the date of