



Esophageal cancer

The pattern of cervical lymph node metastasis in thoracic esophageal squamous cell carcinoma may affect the target decision for definitive radiotherapy



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ABSTRACT

Background: Metastasis to lymph nodes is a key determinant of thoracic esophageal squamous cell carcinoma (TE-SCC) prognosis. We sought to identify factors linked with cervical lymph node metastasis, which could be used to inform the decision of surgical and definitive radiotherapy.

Methods: We retrospectively reviewed records from 1715 patients who had had radical esophagectomy with three-field lymphadenectomy between January 1993 and March 2007 in our hospital. All patients included in the study had pathologically confirmed TE-SCC and no clinical evidence of cervical metastasis. **Results:** Cervical node metastases were found in 547 patients (31.9%); rates of cervical-node positivity were 44.2% for those with upper-thoracic tumors, 31.5% for mid-thoracic tumors, and 14.4% for lower-thoracic tumors. Univariate analysis showed that cervical node metastasis was associated with tumor site, differentiation, and length, pathologic T status, and pN status ($P < 0.05$); however, only tumor site and pN status retained significance in multivariate analysis ($P < 0.05$). Positive cervical nodes were most often found in the paraesophageal region (72.3%), followed by supraclavicular (24.4%); involvement of deep cervical (2.4%) or retropharyngeal nodes (0.9%) was rare ($P < 0.0001$). Positive cervical nodes were most often associated with upper TE-SCCs (60.1%), followed by middle TE-SCCs (31.2%) and lower TE-SCCs (10.6%).

Conclusions: Upper TE-SCC with multiple involved nodes at any site was associated with a high rate of cervical node metastasis. These findings provide critical information for clinical decision-making regarding the extent of nodal dissection or the size of radiation fields in definitive radiotherapy.

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Esophageal squamous cell carcinoma (SCC) is one of the most aggressive forms of gastrointestinal carcinomas and metastasis to lymph nodes is a determinant factor of prognosis severity. The reported frequency of cervical lymph node metastasis ranges from 23.4% to 49.5% [1–4]. Three-field lymphadenectomy (3FL), including thoracic, abdominal, and cervical (with supraclavicular) nodes, is considered the mainstay of surgical treatment for esophageal SCC, given its significant contribution to improved patient survival [1–5].

Radiation therapy, often in combination with chemotherapy, is the alternative treatment plan for patients who cannot undergo

surgery. However, the topic of whether and when the cervical node basin should be included in the radiation treatment plan has been discussed extensively in the radiation oncology community. Understanding the patterns of cervical node metastases and the risk factors underlying them, is critical for answering these questions. Few reports, all evaluating a small number of patients, have described the specific characteristics associated with cervical node metastasis in esophageal SCC. In this study, we retrospectively analyzed patterns of cervical node metastasis in patients with biopsy-proven thoracic esophageal (TE) SCC who had undergone extended esophagectomy with 3FL. We identified factors associated with and predictive of cervical node metastasis; this information could prove valuable in deciding the extent of nodal dissection or the size of radiation fields in definitive radiotherapy.

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Methods

Patient selection

Medical records from patients with biopsy-proven TE-SCC, treated at Fujian Provincial Tumor Hospital from January 1993 to March 2007, were reviewed. All patients received clinical examination and neck/chest/abdomen CT scanning before surgery. The following inclusion criteria were used: diagnosis and extended esophagectomy plus 3FL performed in our hospital; minimum 15 dissected lymph nodes; no palpable enlarged nodes in the cervical area (including supraclavicular) during the presurgical physical examination; and lymph nodes with a diameter smaller than 1 cm (by computed tomography). Exclusion criteria were: chemotherapy or radiation therapy received before esophagectomy and presence of distant metastasis. During this period of time, a total of 2635 cases of thoracic esophageal squamous cell carcinoma received radical surgery in our hospital, of which 320 cases that received left chest and upper abdominal two FL esophageal cancer radical surgery and had less than 15 total lymph nodes removed were excluded from this study. 79 patients with other types of cancer and 521 cases that received preoperative radiotherapy or chemotherapy or postoperative chemotherapy were also excluded from this study. In total, 1715 cases were included in this study, of which 547 patients had cervical lymph node metastases.

This study protocol was approved by the institutional review board of the hospital. The requirement for informed consent was waived.

Surgical procedures

Details of the surgical procedure were described elsewhere [1]. Briefly, TE tumors were resected through cervical incision, right thoracotomy, or laparotomy. According to the guidelines for esophageal carcinomas issued by the Japanese Society for Esophageal Diseases, the cervical nodes were classified as being in the 101 (paraesophageal), 102 (deep cervical), 103 (retropharyngeal) and 104 (supraclavicular) areas, with each area divided into left and right sections (Fig. 1) [6].

Statistical analysis

Differences among groups were analyzed using a χ^2 test (for continuous variables) or a one-way analysis (for categorical variables). Multivariate logistic regression analysis was used to analyze factors influencing the likelihood of cervical metastasis. *P* values <0.05 were considered statistically significant. All statistical analyses were done using the software package SPSS 15.0.

Results

Characteristics of cervical node metastasis

A total of 44,237 lymph nodes were dissected from the 1715 patients reviewed (Table 1). The average number of dissected nodes per patient was 25.8 (range 15–73) and did not vary with the location of the primary tumor (26.8 nodes per patient for those with upper TE-SCC, 25.7 for middle, and 24.7 for lower TE-SCC, *P* = 0.069). A total of 3487 nodes were positive for metastasis, at a metastatic ratio of 7.9%, which did not differ among tumor sites (6.5% upper, 8.2% middle, and 8.1% lower, *P* = 0.287). However, the rates of cervical lymph node metastases differed greatly based on to the location of the tumor: 60.1% upper, 31.2% middle, and 10.6% lower (*P* < 0.0001). Similarly, rates of positive mediastinal and abdominal nodes were also different depending on tumor location: rates of mediastinal metastases were 34.8% for upper, 46.3%

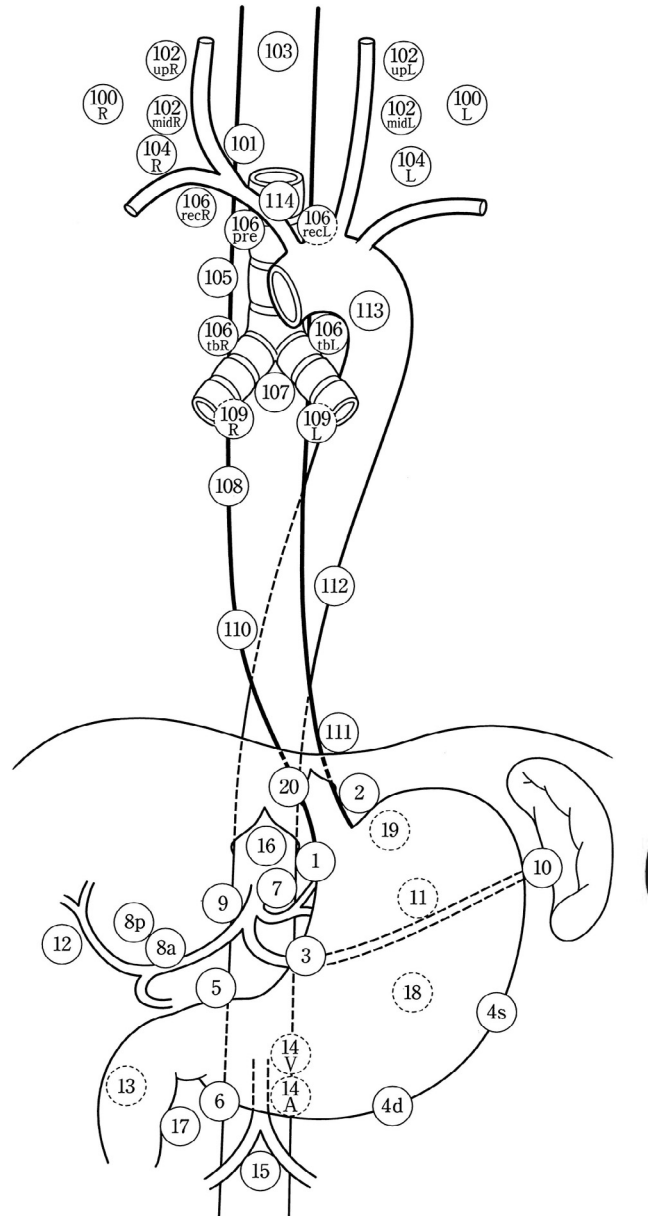


Fig. 1. Station numbers of regional lymph nodes according to the guidelines for esophageal carcinoma as issued by the Japanese Society for Esophageal Diseases. The cervical nodes were classified as being in the 101 (paraesophageal), 102 (deep cervical), 103 (retropharyngeal) and 104 (supraclavicular) areas, with each area divided into left and right sections. This figure was adapted from Ref. [6].

for middle, and 34.4% for lower TE-SCC (*P* = 0.002); and the ones for abdominal metastases were 5.1% for upper, 22.5% for middle, and 55.0% for lower esophageal tumors (*P* < 0.0001) (Table 1).

The highest rates of positive cervical nodes (Table 2) were in the paraesophageal (101) region (72.3%), followed by the supraclavicular (104) region (24.4%); nodes in the deep cervical (102) or retropharyngeal (103) areas were rarely positive (2.4% and 0.9%, respectively). As noted above, upper TE tumors were most often associated with positive cervical nodes. The location of the tumor also affected the percentage of positive cervical nodes at each sub-site; rates of positive nodes in the left paraesophageal (101L) area varied significantly for upper (24.9%), middle (21.1%), and lower (26.5%) tumors (*P* < 0.0001), as did the rates of positive nodes in the right paraesophageal (101R) area (48.4% upper, 50.6% middle, and 52.9% lower, *P* < 0.0001), the retropharyngeal (103) area (3.2% upper, 0.1% middle, and 0.0% lower, *P* = 0.012), and the right

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