Clinical Research Regarding the Ratio of Lymph Node Metastasis and the Reasonable Extent of Lymphadenectomy in Middle Third Thoracic Esophageal Squamous Cell Carcinoma

OBJECTIVE To explore the extent of lymphadenectomy deemed reasonable by analyzing the influence of the regular pattern and ratio of lymph node metastasis on the prognosis of the patients with middle third thoracic esophageal squamous cell carcinoma.

METHODS Clinical data from 129 patients with middle third thoracic esophageal squamous cell carcinoma who underwent curative esophagectomy with modern two-field lymphadenectomy were retrospectively analyzed.

RESULTS The rate of lymphatic metastasis in EC patients was 56.6% in all groups, and the ratio of lymph node metastasis (RLNM, i.e. positive nodes/total dissected nodes) was 11.3%, with a lymphatic metastasis rate of 43.4% in the superior mediastinum. The most commonly involved regions included the sites around the esophagus, the right recurrent laryngeal nerve and the left-sided blood vessels of stomach, as well as the cardia and the inferior tracheal protuberance. The main factors influencing lymphatic metastasis were the depth of tumor infiltration, differentiation of tumor cells and the size of the tumor. The 5-year survival rate for patients in the groups without lymphatic metastasis, with a RLNM ≤ 20%, and a metastasis ratio > 20% was 50.4%, 31.0% and 6.8%, respectively. The differences were statistically significant among the groups (P = 0.000).

CONCLUSION The RLNM is one of the key factors affecting the prognosis of EC patients. For conventional therapy for patients with middle third thoracic esophageal carcinoma, modern 2-field lymphadenectomy, including node dissection in the bilateral superior mediastinum, should be performed.

KEY WORDS: esophagus cancer, lymph nodes, metastasis, lymphadenectomy.

Introduction

Lymphatic metastasis (LM) is one of the main routes of metastasis in esophageal carcinoma (EC). Lymphatic drainage in the esophagus is interlacing, which can easily result in regional LM or skip metastasis. However, lymph node status is the important factor affecting the prognosis of EC. Therefore, the correct staging of EC can only be achieved after performing an enlarged regional lymphadenectomy and attaining unambiguous therapeutic efficacy of surgery.

In regards to the scope of lymphadenectomy for thoracic EC, there
is at present, no accepted definition in China, and whether clearance of lymph nodes in the superior mediastinum (SM) and base of the neck is necessary remains controversial. Historically, the scope of lymphadenectomy for EC has not been well understood because the terms used to describe the scope have not been clearly delimited. Standardized terms were specifically introduced at the Conference on Common Understanding of the Diseases of Esophagus in Munich, Germany, held by the International Society of Diseases of Esophagus (ISDE)\(^\text{1}\). The scope of the EC lymphadenectomy has been classified as follows: field I (epigastric zone), field II (thoracic) and field III (inferior part of neck). Based on the scope of nodal clearance, the type of EC lymphadenectomy was divided into the 2-field lymphadenectomy (field I + II) and the 3-field lymphadenectomy (field I + II + III). Consensus has been reached on the scope of the field of lymphadenectomy, i.e., the second site of the lymphadenectomy in gastric cancer grading, with preservation of the right gastric artery, is regarded as the standard of nodal clearance.

There are 3 definitions for the scope of field II clearance, including: i) lymphadenectomy of the inferior middle mediastinum (below the tracheal protuberance), which is called “the standardized mediastinal lymphadenectomy”; ii) on the basis of the standardized mediastinal lymphadenectomy, lymph node clearance in the sites around the right trachea and right recurrent laryngeal nerve (RLN) is added, which is called “the expanded mediastinal lymphadenectomy”; iii) on the basis of the expanded mediastinal lymphadenectomy, clearance of the lymph nodes around the left trachea, left RLN chain, and aortic window is performed, which is called “the total mediastinal lymphadenectomy”. The standardized mediastinal lymphadenectomy plus field I clearance is called the traditional 2-field lymphadenectomy, and the total mediastinal lymphadenectomy plus field I clearance is called the modern 2-field lymphadenectomy. The terms quoted in the text are in agreement with those defined by the ISDE.

Patients and Methods

Patients

The data from 129 patients with middle thoracic EC in the same group, who were admitted to the Department of Thoracic Oncology, Cancer Center, Sun Yat-sen University, Guangzhou during a period from January 2001 to June 2009, were collected in our study. Resection of the partial esophagus and stomach, left neck esophageal-anastomosis, modern 2-field lymphadenectomy (total mediastinal plus abdominal lymphadenectomy) via 3 incisions of the right thorax (common posterolateral incision), left neck and upper abdomen were performed on each patient. Among the patients, 86 were male and 43 female. In all of the cases, stage-IEC occurred in 7, stage IIA in 48 (17 with T2N0M0 and 31 with T3N0M0), stage-IIB in 10 (1 with T1N1M0 and 9 with T2N1M0), stage-III in 64 (56 with T3N1M0 and 1 with T4N0M0 and 7 with T4N1M0). A final diagnosis of middle thoracic EC was made in all patients before surgery. All of the patients met the indications for surgery and were excluded by having distant metastasis or other severe complications, or by receiving preoperative chemoradiotherapy. Tumor staging was based on the standard of UICC staging for esophageal cancer, 2002 edition. Surgery was performed on all of the patients by the same group of surgeons. The pathologic diagnosis of the resected specimen from every patient was squamous cell carcinoma.

Observation indicators

These included size of tumor, the depth of tumor infiltration, degree of differentiation of tumor cells, lymph node status, ratio of lymph node metastasis (RLNM), postoperative survival rate, and the influence of modern 2-field lymphadenectomy on the prognosis of the patients with middle thoracic EC. The relationships among the above indicators were also observed.

Statistical analysis

Regular postoperative clinic visits and follow-up by phone were conducted on the study patients. Monthly visits lasted for lifetime of the patients. SPSS16.0 was used for data analysis and R × C Chi-square test for enumeration data. The COX model was employed for multifactorial survival analysis, and the Kaplan-Meier curve was applied for analyzing the overall 5-year survival rate of the patients in every group. The log rank test was used for determining the difference in the survival rates. The value of \( P \leq 0.05 \) was considered statistically significant.

Results

LM was found in 73 out of 129 patients in the group and accounted for 56.6% (LMR). A total of 2,776 lymph nodes were cleared from the study patients, with an average of 21.52 nodes in each case. Among the nodes dissected, 315 were positive and the total RLNM was 11.3%. The most common sites of lymph node involvement included the areas around the esophagus, the right RLN, the gastric cardia, the left gastric blood vessel, and at the inferior tracheal protuberance. The sites with less lymph node involvement included the areas around the left RLN and the trachea in the thoracic segment etc. (Table 1).

LM at the superior mediastinum was found in 56 of the total cases in our group (56/129, 43.4%), single metastasis of the superior mediastinum in 37 cases (37/129, 28.7%), LM of the left superior mediastinum in 18 (18/129, 14.0%), and single metastasis of the left superior mediastinum in 10 (10/129, 7.8%).

In the study patients, there was a positive correlation