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Original Article

Analysis of prognostic factors for esophageal squamous cell carcinoma with distant organ metastasis at initial diagnosis

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Abstract

Background: Esophageal cancer is the eighth most common malignancy and sixth most fatal disease worldwide. However, it is the fourth most common cause of death in China. Although surgery is currently the recommended course of treatment, there are some patients that do not receive radical treatment due to the presence of distant organ or lymph node metastasis. There is at present no established treatment standard for esophageal cancer patients with distant organ metastasis. The purpose of this study was to investigate the prognostic factors involved in determining survival of esophageal cancer patients with distant organ metastasis at initial diagnosis, and to provide a reference for the planning of a clinical treatment strategy.

Methods: The data of 57 evaluable esophageal squamous cell carcinoma patients with distant organ metastasis at initial diagnosis were studied retrospectively. The survival rate was calculated using the Kaplan–Meier method, and the log-rank test was used to test the differences. Multivariable analysis was performed using the Cox proportion hazards model.

Results: The median survival time for all patients was 6 months (range, 1–55 months), and the 1- and 2-year survival rates were 21.1% and 11.8%, respectively. The median survival time for patients with single metastasis was 10 months with 1- and 2-year survival rates of 47.4% and 28.1%, respectively. For patients with multiple metastases, the survival duration was 5 months, with 1- and 2-year survival rates of 7.9% and 3.9%, respectively (p < 0.001). The 1- and 2-year survival rates with multimodality treatment were 70% and 45%, respectively, which were significantly better than chemotherapy alone (13.3% and 8.9%, respectively, p = 0.003) and best supportive care (5.9% and 0%, p < 0.001), but there was no significant difference between the latter two groups (p = 0.061).

Conclusion: For esophageal squamous cell carcinoma patients with distant organ metastasis upon initial diagnosis, the presence of a single metastasis appeared to favor overall survival compared to multiple metastases. Multimodality treatment may also improve patient survival, but chemotherapy alone has not been established as a favorable prognostic factor.

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Keywords: esophageal neoplasms; neoplasm metastasis; prognosis; therapy

1. Introduction

Esophageal cancer has an extraordinary impact on worldwide health, with ~460,000 new diagnoses and >380,000

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deaths annually.¹ It also has a significant effect on the health of Chinese people, in whom it represents the fourth most common cause of death. Surgery is currently the mainstay of esophageal cancer treatment; however, >30% of patients do not qualify for surgical resection due to advanced cancer stage or concomitant diseases.² Furthermore, about 18% of patients present with distant organ or lymph node metastasis and miss the opportunity for radical treatment.³

Although there are numerous available case reports regarding the treatment of newly diagnosed distant organ metastasis of esophageal cancer,^{4,5} there is currently no established standard

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treatment. Due to the dismal long-term patient survival rate of 0.3% at 3 years and a median survival time (MST) of 7 months,^{6,7} treatment commonly includes palliative esophageal stent implantation or improvement of symptoms by palliative chemotherapy and radiotherapy.

In the present study, the clinical data of 57 esophageal squamous cell carcinoma patients with distant organ metastasis at initial diagnosis were collected and retrospectively reviewed. The outcomes were evaluated and the factors affecting prognosis were analyzed to provide reference for the planning of a clinical treatment strategy.

2. Methods

2.1. Patient characteristics

The data of 57 esophageal squamous cell carcinoma patients with distant organ metastasis at initial diagnosis, who were treated at Fujian Medical University Union Hospital, Fujian, China between January 1, 2007 and December 31, 2010, were collected. The retrospective analysis was approved by Fujian Medical University Union Hospital Institutional Review Board. All information had been anonymized and de-identified prior to its analysis. The clinical characteristics of these patients are summarized in Table 1. The patients included 47 men and 10 women (male: female ratio, 4.7:1), with a median age of 57 years (range, 37-78 years). All patients had been diagnosed with squamous cell carcinoma. Furthermore, 50 (87.7%) patients had an Eastern Cooperative Oncology Group (ECOG) score of <1. Pulmonary, hepatic, bone, brain, and gastric body metastases were diagnosed in 29 patients, 17 patients, four patients, one patient, and one patient, respectively, whereas five patients presented with multiple organ metastases.

2.2. Exclusion criteria

The exclusion criteria were as follows: (1) history of other tumors; (2) adenocarcinoma, neuroendocrine or small-cell

Table 1 Clinical characteristics of 57 patients.	
Sex (M/F), n	47/10
ECOG performance status, n	
0	19
1	31
≥ 2	7
Organ of metastasis (solitary-metastasis), n	
Lung	29 (10)
Liver	17 (5)
Bone	4 (2)
Brain	1 (1)
Gastric body	1 (1)
Multiorgan	5
Treatment, n	
Best supportive care	17
Chemotherapy alone	30
Surgery and chemotherapy	6
Radiotherapy and chemotherapy	4

ECOG = Eastern Cooperative Oncology Group.

esophageal carcinoma, or other malignant tumors of special or uncertain biological behavior; and (3) other concomitant medical condition requiring treatment.

2.3. Pretreatment workup and diagnosis of metastases

The pretreatment workup of all patients included a physical examination, standard laboratory tests, chest radiography, upper gastrointestinal endoscopy, barium swallow, cervical and abdominal ultrasound, chest computed tomography (CT), bone scan, and magnetic resonance imaging. Additionally, bronchoscopy was performed if considered necessary. The diagnostic criteria for metastasis were: (1) metastatic lesions pathologically confirmed by surgical or biopsy samples; (2) multiple metastases on CT or ¹⁸F-fluorodeoxyglucose positron emission tomography/CT; and (3) a single metastatic lesion confirmed by two or more types of imaging modalities. The presence of a single metastatic lesion was defined as solitary metastasis (19 patients; 33.3%), whereas two or more metastatic lesions were defined as multiple metastases (38 patients; 66.7%).

2.4. Statistical analysis

All patient outcomes were evaluated in December 2011. Survival was calculated from the 1st day of treatment to the date of death or the last follow-up. The survival data were analyzed with SPSS software, version 17.0 (SPSS, Inc., Chicago, IL, USA).

Survival curves were created with the Kaplan–Meier method and compared with the log-rank test. A multivariable analysis by sex, age, ECOG score, metastasis site, number of metastases, and treatment model was performed using the Cox proportional hazards model. The relevant inspection level was bilateral, where $\alpha \leq 0.05$.

2.5. Treatment

The patients were classified into three categories by treatment method: best supportive care, chemotherapy alone, and multimodality treatment (surgery combined with chemotherapy, or radiotherapy combined with chemotherapy; Table 1). Seventeen patients received best supportive care (2 cases, esophageal stenting; 1 case, referred for gastric fistula; 1 case, traditional Chinese medicine treatment; and 13 cases, nutritional supportive treatment). Thirty patients received chemotherapy alone [6 cases, calcium folinate + ftorafur + lobaplatin or oxaliplatin; 11 cases, taxol + cisplatin (lobaplatin or oxaliplatin or nedaplatin); 4 cases, S1 + lobaplatin; 1case, gemcitabine + cisplatin; 1 case, irinotecan + cisplatin; 3 case, single-agent Xeloda or carmofur; and 4 cases, outpatient chemotherapy]. The mean number of chemotherapy cycles was 1.8 (range, 1–9 cycles). Multimodality treatment was administered to 10 patients [6 cases, surgery + chemotherapy (5 cases, esophageal tumor resection and 1 case, esophageal tumor and concomitant solitary lung metastasis resection); 4 cases, radiotherapy + chemotherapy (1 patient underwent

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