Thoracic Cancer
Open Access
Thoracic Cancer ISSN 1759-7706

ORIGINAL ARTICLE

Factors relevant to the prognosis of patients with esophageal cancer who received intensity-modulated radiotherapy

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Keywords
Esophageal cancer; intensity-modulated radiotherapy; logistic regression; prognosis.

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Received: 28 May 2018;
Accepted: 16 June 2018.

doi: 10.1111/1759-7714.12800

Thoracic Cancer **9** (2018) 1215–1219

Abstract

Background: The aim of this study was to evaluate the clinical factors relevant to the prognosis of patients with esophageal cancer who received intensity-modulated radiotherapy (IMRT).

Methods: The data of 60 patients admitted to our hospital from January 2014 to December 2015 with pathologically confirmed esophageal cancer were retrospectively reviewed. All patients received IMRT. Patients were divided into groups according to two-year survival: those who survived > 2 years after treatment, and those who died within 2 years of treatment. The potential clinical factors relevant to prognosis were evaluated by logistic regression analysis.

Results: Single factor analysis showed that lesion length ($P < 0.05$), tumor diameter ($P < 0.05$), T stage ($P < 0.05$), N stage ($P < 0.05$), and combined chemotherapy ($P < 0.05$) were associated with the prognosis of esophageal cancer patients who received IMRT. Logistic regression analysis demonstrated that T stage (odds ratio = 3.62; $P < 0.05$) and N stage (odds ratio = 2.98; $P < 0.05$) were independent factors relevant to prognosis.

Conclusion: T stage and N stage influence the long-term curative effects of IMRT for esophageal cancer. The higher the stage, the lower the two-year survival rate.

Introduction

Esophageal cancer is one of the most commonly diagnosed malignant carcinomas, with incidence showing obvious regional trends.[1–3] Prognosis of esophageal cancer is generally poor, and it can easily metastasize at an early stage. Because patients often relapse after surgery, the five-year survival rate of this type of cancer is low.[4] The exact cause of esophageal cancer is not clear, but factors such as age, gender, living environment, and dietary habits have been proposed as influencing the development of the disease. Clinical symptoms of esophageal cancer mainly include dysphagia, a retrosternal burning sensation, a foreign body sensation, progressive dysphagia, and myxoid sputum. While patients with early stage esophageal cancer can be treated with radical surgery, those with advanced stages cannot be treated via the same approach; in this case, radiotherapy or radiotherapy combined with chemotherapy is generally applied. The wide application of three-dimensional conformal radiotherapy technology in clinics, especially intensity-modulated radiotherapy (IMRT), can reduce the risk of adverse reactions while improving curative effects.[5] In this study, we retrospectively analyzed the clinical data of 60 esophageal cancer patients who received IMRT treatment in our hospital and explored the factors influencing patient prognosis by logistic regression analysis.

Methods

Patients

The data of 60 patients (39 men, 21 women) diagnosed with esophageal cancer by pathology or cytology and

admitted to our hospital from January 2014 to December 2015 was reviewed in this retrospective analysis. The inclusion criteria were: (i) esophageal cancer patients clearly diagnosed by pathology or cytology; (ii) Karnofsky performance status (KPS) score > 70; (iii) no brain metastases; (iv) treated with IMRT; and (v) with complete information of the curative effects of radiotherapy. Twenty-nine patients were aged < 60 years, while 31 were aged ≥ 60 years. Thirty-seven patients had gross tumor volumes (GTV) < 64 cm^3 and 23 patients had GTVs ≥ 64 m^3. Thirty-three patients received radiotherapy combined with chemotherapy, while 27 patients were treated with radiotherapy alone. During follow-up, 22 patients survived > 2 years and 38 patients died within 2 years of treatment.

Intensity modulated radiotherapy

A computed tomography (CT) positioning machine (Philips MX 4000, Philips, Amsterdam, Netherlands) was used to conduct continuous scanning of a 5 mm thick layer of each patient's esophagus. Based on the thickened esophageal segment indicated by the CT scan, together with the lesion imaging results determined by esophagoscopy and esophagography, the tumor area was drawn. The radiotherapy target area included subclinical lesions and the drainage region caused by regional lymph nodes. The volume of the planned target area can be expanded outward by 6–7 cm on the basis of the tumor area because of peripheral expansion of the target area caused by the patient's breathing and organ activity, as well as changes in the target area volume over the course of treatment. Radiotherapy was performed using 4–7 planes five times per week at a total dose of 6–65 Gy. The patient's blood, routine liver and kidney functions, and barium test results were reviewed after three weeks of treatment, and lesions formed were checked to reduce the toxic and side effects of radiotherapy according to the patients' individual needs.

Table 1 Values assigned for univariate logistic regression analysis

Variables	Project code	Assigned value
Gender	X1	Female = 0, Male = 1
Age (year)	X2	< 60 = 0, ≥ 60 = 1
BMI ($kg \cdot m^{-1}$)	X3	< 25 = 0, ≥ 25 = 1
Lesion length (cm)	X4	< 5 = 0, ≥ 5 = 1
Tumor diameter (cm)	X5	< 4 = 0, ≥ 4 = 1
GTV (cm^3)	X6	< 64 = 0, ≥ 64 = 1
T stage	X7	T1/T2 = 0, T3/T4 = 1
N stage	X8	No = 0, N1/N2 = 1
Combined chemotherapy	X9	Yes = 0, No = 1
Tumor location	X10	Cervical = 0, thoracic = 1, abdominal = 2

BMI, body mass index; GTV, gross tumor volume.

Potential clinical factors relevant to prognosis

According to previous literature and clinical experience, the patients' age, gender, body mass index (BMI), tumor length, tumor diameter, GTV, and tumor stage were selected as potential factors related to prognosis.[6–8] Clinical data was collected from the patients' case records for statistical analysis.

Statistical analysis

SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Measurement data were expressed as $\bar{x} \pm s$ and comparisons between groups were made based on a *t*-test of the sample mean. Enumeration data were shown by a relative number, and the comparison between groups was made based on χ^2 or Fisher's exact tests. Univariate logistic regression analysis was performed for each candidate variable and $P < 0.05$ was considered to indicate a statistically significant difference. Univariate logistic regression analysis was conducted to identify the factors associated with prognosis (Table 1).

Results

Single factor analysis for prognosis

Single factor analysis showed that lesion length ($P < 0.05$), tumor diameter ($P < 0.05$), T stage ($P < 0.05$), N stage ($P < 0.05$), and combined chemotherapy ($P < 0.05$) were associated with the prognosis of esophageal cancer patients who received IMRT. However, there was no correlation between prognosis and patient gender ($P > 0.05$), age ($P > 0.05$), BMI ($P > 0.05$), GTV ($P > 0.05$), or tumor location ($P > 0.05$) (Table 2).

Logistic regression analysis

Logistic regression analysis demonstrated that T stage (odds ratio [OR] = 3.62; $P < 0.05$) and N stage (OR = 2.98; $P < 0.05$) were independent factors relevant to the prognosis of esophageal cancer patients who received IMRT (Table 3).

Discussion

Esophageal cancer presents obvious regional distribution worldwide, with morbidity and mortality clearly differing between areas.[9,10] China has a high incidence of esophageal

Table 2 Single factor analysis for prognosis

Factors	N = 60	Two-year survival		Chi-square	*P*
		Yes (*n* = 22)	No (*n* = 38)		
Gender				0.09	0.339
Male	39	16	23		
Female	21	6	15		
Age (year)				1.99	0.158
< 60	29	8	21		
≥ 60	31	14	17		
BMI ($kg \cdot m^{-1}$)				2.34	0.126
< 25	36	16	20		
≥ 25	24	6	18		
Lesion length (cm)				4.78	0.029
< 5	22	12	10		
≥ 5	38	10	28		
Tumor diameter (cm)				5.11	0.024
< 4	38	18	20		
≥ 4	22	4	18		
GTV (cm^3)				3.58	0.06
< 64	37	17	20		
≥ 64	23	5	18		
T stage				6.25	0.012
T1/T2	6	5	1		
T3/T4	54	17	37		
N stage				5.39	0.029
No	19	11	8		
N1/N2	41	11	30		
Combined chemotherapy				4.41	00.36
Yes	33	16	17		
No	27	6	21		
Tumor location				2.94	0.237
Cervical	4	0	4		
Thoracic	30	13	17		
Abdominal	26	9	17		

BMI, body mass index; GTV, gross tumor volume.

cancer,[11] particularly at the borders of Henan and Hebei and locations around the Yanshan Mountains.[12] Approximately 90% of all esophageal cancers present as squamous cell carcinoma, and the pathogenesis of the disease is believed to be related to a congenital genetic background and acquired dietary habits.[13] Unfortunately, even today, the molecular mechanisms of the occurrence and development of esophageal cancer are not completely clear.

The morbidity rates of men and women with esophageal cancer are approximately 30/100 000 and 15/100 000, respectively.[14,15] Most patients with esophageal cancer are usually diagnosed at advanced stage and thus lose the opportunity of a surgical option. Such patients are generally treated with radiotherapy, chemotherapy, or other strategies. Although radiotherapy and chemotherapy cannot achieve the goal of a radical cure for the vast majority of patients, they can remarkably prolong survival and improve quality of life.[16–18] IMRT was developed in recent years and can reduce the radiation dose to the surrounding normal tissues while significantly increasing the radiation

Table 3 Logistic regression analysis of independent factors relevant to prognosis

Factors	β	SE	Wald χ^2	OR	95% CI	*P*
Lesion length (cm)	1.11	0.71	2.47	2.1	0.55–9.66	> 0.05
Tumor diameter (cm)	0.99	0.56	2.88	2.48	0.71–10.69	> 0.05
T stage	1.41	0.32	10.33	3.62	1.52–6.66	< 0.05
N stage	1.21	0.29	8.42	2.98	1.31–7.23	< 0.05
Combined chemotherapy	1.05	0.82	2.14	2.08	0.69–8.98	> 0.05

CI, confidence interval; OR, odds ratio; SE, standard error.

dose to the tumor target area, thereby improving curative effects and reducing related side effects.[19] IMRT adjusts the irradiation intensity according to the three-dimensional shape of the target area, and the specific anatomical relationship between important organs and the target area, under the condition that the radiation fields everywhere else are consistent with the shape of the target area.

Numerous factors influence the curative effect of radiotherapy for esophageal cancer, including radiotherapy method, radiation dose, and clinical stage.[20,21] However, clinical reports are not completely consistent at present, and no prediction model of the curative effects of radiotherapy for esophageal cancer is yet available. Most reports on the curative effect of radiotherapy mainly focus on the technology applied and the irradiation intensity;[22] research on the influence of patients' clinical characteristics on the curative effect of radiotherapy is limited. Therefore, we retrospectively analyzed the data of esophageal cancer patients who were admitted to our hospital in recent years and had received IMRT to explore the influence of their clinical characteristics on the curative effects of treatment. Among the 60 patients who received radiotherapy, 22 patients survived > 2 years and 38 patients died of tumor recurrence, distant metastasis, or related complications within 2 years of treatment. Thus, the two-year survival rate was 36.7%. Logical regression analysis showed that T stage (OR = 3.62; $P < 0.05$) and N stage (OR = 2.98; $P < 0.05$) were independent factors relevant to the prognosis of esophageal cancer patients who received IMRT.

The T stage of a tumor reflects its size and invasion degree. In general, the higher the T stage, the larger the tumor and the deeper its invasion into the esophageal muscle layer. When the tumor volume is large, the central region is prone to hypoxia. At this point, the sensitivity of tumor cells in the central region to radiotherapy is reduced and the curative effect is poor. The N stage reflects regional lymph node metastasis; the later the stage, the larger the number and the wider the region of lymph node metastasis. Currently, most studies consider the N stage to be an important factor influencing the prognosis of esophageal cancer patients.

Because the number of patients included in this study is relatively small and this work is retrospective in nature, the level of clinical evidence achieved is relatively low. Prospective studies with a larger sample size are necessary to explore the relationships between the T and N stages of esophageal cancer and patient survival.

In summary, the curative effect of IMRT for advanced esophageal cancer is relatively established, and the two-year survival rate is approximately 36%. T stage and N stage influence the long-term curative effects of IMRT for esophageal cancer. The higher the stage, the lower the two-year survival rate.

Disclosure

No authors report any conflict of interest.

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