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ORIGINAL RESEARCH

Clinical results of intensity-modulated radiotherapy for 250 patients with cervical and upper thoracic esophageal carcinoma

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Purpose: To evaluate and analyze the efficacy and prognostic factors of intensity-modulated radiotherapy in 250 patients with cervical and upper esophageal carcinoma.

Patients and methods: From September 2009 to September 2016, we retrospectively analyzed 250 patients with cervical and upper esophageal carcinoma treated with intensity-modulated radiotherapy (IMRT). In our study, all patients received IMRT, 54 patients with cervical esophageal carcinoma and 196 patients with upper esophageal carcinoma. Treatment response, survival status and failure modes of treatment were observed, and prognostic factors were analyzed.

Results: The median survival time was 22.60 months and 3-year survival rate was 42%. The median progress-free survival time was 14.52 months and 3-year progress-free survival rate was 29.3%. The median survival time and the median progress-free survival time for cervical esophageal carcinoma were 20.40 and 15.15 months, respectively. The median survival time and the median progress-free survival time for upper esophageal carcinoma were 25.80 and 14.52 months, respectively ($P>0.05$). The significant clinical factors associated with survival were patient age, radiotherapy dose and T stages ($P<0.05$). Radiotherapy dose and concurrent chemoradiotherapy were the significant clinical factors related to progression-free survival ($P<0.05$). Recurrence appeared in 55.2% patients, including local recurrence in 22.40%, region relapse in 10.40% and distant metastasis in 12.40%. Local recurrence was the main mode of treatment failure. During treatment, the main treatment-related acute toxicity was leukocytopenia and anemia.

Conclusion: In this study, IMRT demonstrated clinical benefit and well-tolerated toxicity in patients with cervical and upper esophageal carcinoma.

Keywords: cervical esophageal carcinoma, upper esophageal carcinoma, intensity-modulated radiotherapy, prognosis

Introduction

Esophageal cancer is one of the most common tumors in the world and is characterized by invasive growth and poor prognosis.[1] Cervical esophageal cancer accounts for 2–10% of esophageal cancer and upper thoracic esophageal cancer accounts for 5–10% of esophageal cancer.[2,3] The recurrence rate of cervical and upper thoracic esophageal cancer is higher than that of esophageal cancer in the middle and lower thoracic segments.[4,5] According to the American Joint Committee on Cancer/Union for International Cancer Control (UICC) 7th edition TNM staging criteria for esophageal cancer, cervical esophageal cancer is defined as that arising

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in the short segment range from the cricopharyngeus to the sternal notch, while the range of upper thoracic esophageal cancer is from the superior aperture of thorax to the lower edge of the arch of the azygos vein. Surgery is not the best treatment for cervical and upper thoracic esophageal cancer owing to the difficulty in surgical treatment and the high incidence of complications.[6,7]

Intensity-modulated radiotherapy (IMRT), a radiotherapeutic modality with high conformality and mild side effects, is often used for the treatment of cervical and upper thoracic esophageal cancer. Some studies demonstrate the advantages of IMRT in cervical esophageal cancer.[8,9] However, few studies have investigated the outcomes of IMRT in patients with upper thoracic esophageal cancer, and the data regarding the clinical efficacy, failure patterns and prognostic factors for cervical and upper thoracic esophageal cancer patients treated with IMRT are still limited. Therefore, in this study, we retrospectively analyzed the data of 250 patients who had cervical and upper thoracic esophageal squamous cell carcinoma and treated by IMRT. The clinical efficacy and the associated prognostic factors were evaluated.

Materials and methods

Patients

We retrospectively reviewed patients who received treatment for histologically confirmed cervical and upper thoracic esophageal squamous cell carcinoma at the Cancer Hospital of Tianjin Medical University in the period 2009–2016. The eligibility criteria for this study were as follows: (1) patients with histologically confirmed esophageal squamous cell carcinoma; (2) cervical or upper thoracic esophageal cancer confirmed by chest x-ray, CT, gastrointestinal endoscopy, endoscopic ultrasonography or positron emission tomography-CT (PET-CT) and staged according to the 2002 UICC-TNM staging system, cervical esophageal cancer was defined as tumor arising in the short segment of esophagus between the cricopharyngeus and the sternal notch, and upper thoracic esophageal cancer was defined as the main tumor located between the superior aperture of thorax and the inferior margin of the azygos arch; (3) patients treated by IMRT and had not received surgical treatment; (4) no distant metastasis at the time of treatment and (5) no other critical illness affecting treatment. Patients who did not complete the radiotherapy plan were excluded.

Treatment

Radiotherapy

All patients received definitive IMRT. Patients were placed supine, fixed and underwent radiotherapy localization under enhanced CT with images obtained at 5-mm slice intervals. The target area delineation was performed according to the following criteria: (1) gross tumor volume (GTV) including primary tumors and radiographically identified metastatic lymph nodes, (2) clinical target volume (CTV) included the radiation field which was 3–5 cm beyond the GTV in all directions and the radiation field covered both peripheral subclinical lesions. In case of tumor invasion of the lower pharynx, skull base was considered the upper boundary of the CTV; the lower boundary of the CTV was 3 cm below the tumor or 1.5 cm below the carina, and (3) in order to eliminate placement error, the planned target volume (PTV) was 5 mm outside the CTV. Planning gross tumor volume (PGTV) was 5 mm outside the tumor and metastatic lymph nodes and 1 cm above and below the tumor. The radiotherapy plan was to achieve 95% coverage of the PTV by the prescribed dose. The median prescribed dose was 54 Gy (48–70 Gy) and 1.8 Gy daily 5 times a week. Patients who simultaneously received integrated boost IMRT had 60 Gy for 95% PGTV coverage. The target dose for normal tissue involved in the target area: average dose of both lungs <13 Gy, V20%≤30%, V30%≤20%; cardiac dose V30≤40%, V40≤30%; maximum spinal cord tolerance <45 Gy.

Chemotherapy

Neoadjuvant chemotherapy consisted of 1–6 cycles of paclitaxel taxol and cisplatin before radiotherapy. Concurrent chemotherapy was started during radiotherapy and lasted for 1–5 cycles based on the paclitaxel/docetaxel plus cisplatin. Adjuvant chemotherapy was started after the radiotherapy and consisted of 1–6 cycles.

Follow-up evaluation

The patients were evaluated for the clinical efficacy starting from 1 month after the end of treatment by endoscopy, chest CT, B-ultrasound, chest MRI and PET-CT. Patients were followed every 3 months during the first year after radiotherapy, every 6 months during the second year and annually after 3 years of treatment. The initial clinical response was evaluated after completion of IMRT according to the Response Evaluation Criteria for Solid Tumors (version 1.1) by chest CT scan, upper GI and ultrasound exam.[10] The tumor progression after radiotherapy was divided into no progression, local progression, regional

progression and distant metastasis. The local progression was defined as the recurrence of the primary tumor, the regional progression was defined as patients happened lymph node metastasis, the diagnosis of lymph node metastasis was as follows: lymph nodes were considered positive if they measured ≥1 cm on the short axis; round-shaped and if lymph nodes had clearly defined boundaries or exhibited an hypoechoic pattern, and the patients who had distant metastasis showed esophageal-derived tumor metastases. Acute toxic side effects during radiotherapy were graded by Common Terminology Criteria for Adverse Events v4.0.

Statistical analysis

Results were analyzed using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The overall survival (OS) time was calculated starting from the date of initial treatment to the last follow-up or death time. The progression-free survival (PFS) time was defined as the time from the initial treatment to the first progression time or the last follow-up time. Kaplan–Meier analysis was used to calculate the OS rates and PFS rates. Log rank was performed to compare the survival differences between groups. Multivariate prognostic analysis was performed using Cox regression model. A value of $P \leq 0.05$ was considered statistically significant.

Results

Patient characteristics

A total of 250 patients (192 males and 58 females) qualified the inclusion criteria and were included in the analysis. These included 54 patients with cervical esophageal cancer and 196 patients with upper thoracic esophageal cancer. The characteristics of the patients are shown in Table 1. The median age was 61 years (range, 34–90 years). According to the UICC 8th edition TNM staging, most patients had stage IV disease. Sixty-five patients received neoadjuvant chemotherapy, 172 received concurrent chemotherapy and 106 received adjuvant chemotherapy.

Treatment outcomes

The follow-up rate was 99.2%, 108 patients died during follow-up and the median follow-up time was 13.14 months (range, 1.04–56.71 months). The median OS was 22.60 months, and the 1-, 2- and 3-year survival rates were 74.4%, 49.2% and 42.0%, respectively. The median PFS was 14.52 months, and the 1-, 2-, and 3-year PFS rates were 59.0%, 34.7% and 29.3%, respectively (Figure 1). The median OS of patients with cervical esophageal cancer was 20.37 months. The 1-, 2- and 3-year survival rates were 75.2%, 46.4% and 38.7%, respectively. The median PFS was 15.15 months and the 1-, 2- and 3-year PFS rates were 63.5%, 29.7% and 24.7%, respectively.

The median OS of patients with upper thoracic esophageal cancer was 25.82 months. The 1-, 2- and 3-year survival rates were 74.2%, 50.1% and 41.1%, respectively. The median PFS was 14.52 months, and the 1-, 2- and 3-year PFS rates were 57.6%, 36.1% and 30.5%, respectively. There was no significant difference with respect to survival rates and PFS rates between patients with cervical esophageal carcinoma and those with upper thoracic esophageal cancer (P=0.76).

For esophageal lesion, after the initial response analysis, 185 (73.9%) patients were presented with complete response (CR) and partial response (PR), 45 (17.9%) patients with a stable disease (SD) and 20 (8.2%) patients with progressive disease (PD).

According to Kaplan–Meier analysis, median OS of patients with GTV≥32 cm^3 (median value) and GTV<32 cm^3 was 20.46 and 40.44 months (P=0.046), respectively; the corresponding PFS was 10.94 and 16.70 months, respectively (P=0.108). CR and PR were observed in 93 patients with GTV≥32 cm^3 and 92 patients with GTV<32 cm^3 (P>0.05). SD and PD were observed in 38 patients with GTV≥32 cm^3 and 27 patients with GTV<32 cm^3 (P>0.05).

Patients were categorized into 2 groups based on the radiation dose: <60 Gy (28.2%) and ≥60 Gy (71.8%). The median OS in these 2 groups was 17.64 and 34.46 months, respectively (P=0.002), while the median PFS was 10.94 and 17.28 months, respectively (P=0.018). The median OS of patients who received ≥60 Gy radiation dose was significantly higher than that of patients who received <60 Gy radiation dose (P<0.05); similarly, the difference between the median PFS of patients who received ≥60 Gy and <60 Gy radiation dose was also statistically significant (P<0.05) (Figure 2). CR and PR were observed in 150 patients with ≥60 Gy and 35 patients with <60 Gy. SD and PD were observed in 35 patients with ≥60 Gy and 30 patients with <60 Gy (P<0.05).

The median OS of patients who received concurrent chemotherapy and those who did not receive concurrent chemotherapy was 30.62 and 18.60 months, respectively (P=0.013); the corresponding PFS was 15.84 and 10.94 months, respectively (P=0.039). CR and PR were observed

Table 1 Clinical characteristics of 250 patients of cervical and upper esophageal carcinoma treated with intensity-modulated radiotherapy

Clinical characteristics	Number of cases (%)	Cervical segment	Upper thoracic segment
Sex			
Male	192 (76.8%)	39 (72.2%)	153 (78.1%)
Female	58 (23.2%)	15 (27.8%)	43 (21.9%)
Age (years)			
≥65	90 (36%)	17 (31.5%)	73 (37.2%)
<65	160 (64%)	37 (68.5%)	123 (62.8%)
Clinical stage			
Stage II	40 (16%)	10 (18.9%)	30 (15.5%)
Stage III	41 (16.4%)	9 (17.0%)	32 (16.0%)
Stage IV	169 (67.6%)	35 (64.2%)	134 (68.4%)
T stage			
T2	20 (7.8%)	4 (7.5%)	16 (7.9%)
T3	65 (25.9%)	16 (30.2%)	49 (24.7%)
T4	165 (66.3%)	34 (62.3%)	131 (67.4%)
N stage			
N0	66 (26.4%)	16 (29.6%)	50 (25.5%)
N1	88 (35%)	21 (38.9%)	67 (33.9%)
N2	79 (31.7%)	16 (29.6%)	63 (32.3%)
N3	17 (6.9%)	1 (1.9%)	16 (8.3%)
Concurrent chemotherapy			
Yes	172 (67.9%)	40 (74.1%)	132 (67.3%)
No	78 (32.1%)	14 (25.9%)	64 (32.7%)
Simultaneously integrated boost			
Yes	146 (58.1%)	34 (62.3%)	112 (56.9%)
No	104 (41.9%)	20 (37.7%)	84 (43.1%)
GTV			
≥32 cm^3	130 (50.2%)	21 (40.0%)	109 (53.1%)
<32 cm^3	120 (49.8%)	33 (60.0%)	87 (46.9%)
Lesion length (cm)			
Range	3–27	3–8.6	3–27
Median length	6.5	4.2	6.5
Dose (Gy)			
Range	48–70	48–66	48–70
Median length	60	60	60

Abbreviation: GTV, gross tumor volume.

in 145 patients who received concurrent chemotherapy and 40 patients who did not receive concurrent chemotherapy. SD and PD were observed in 42 patients who received concurrent chemotherapy and 23 patients who did not receive concurrent chemotherapy (P>0.05).The median OS of patients who received adjuvant chemotherapy and those who did not receive adjuvant chemotherapy was 22.14 and 11.33 months, respectively (P=0.004); the corresponding PFS was 15.70 and 13.77 months, respectively (P=0.052). CR and PR were observed in 57 patients who received adjuvant chemotherapy and 128 patients who did not receive adjuvant chemotherapy. SD and PD were observed in 18 patients who received adjuvant chemotherapy and 47 patients who did not receive adjuvant chemotherapy (P>0.05). In addition, age, T stage and N stage were significantly associated with OS (P<0.05) (Table 2).

Results of multivariate analysis of OS and PFS are presented in Table 3. Age (HR=1.037, P=0.002), radiotherapy dose (HR=0.624, P=0.004) and the T stage of esophageal cancer (HR=1.775, P=0.011) had a significant impact on OS. Besides, radiotherapy dose (HR=0.714, P=0.008) and treatment with concurrent chemotherapy (HR=0.670, P=0.029) were independent prognostic factors for PFS of patients with cervical and upper thoracic esophageal cancer.

Treatment failure

One hundred and thirty-eight patients developed recurrent disease, and the recurrence rate was 55.2%. Local recurrence occurred in 56 patients (22.4%), lymph node recurrence occurred in 26 (10.4%) patients and distant metastasis occurred in 31 (12.4%) patients. The proportion of patients with local recurrence after IMRT was higher than other patterns of recurrence (P<0.05). The median OS of patients with lymph node recurrence, local recurrence and distant metastasis was 30.62, 16.92 and 15.84 months, respectively. OS of patients with lymph node recurrence was significantly longer than that of patients with local recurrence (P=0.038). OS of patients with lymph node recurrence was significantly longer than that of patients with distant metastasis (P=0.033); however, there was no significant difference between OS of patients with local recurrence and those with distant metastasis (P=0.79) (Table 4).

Toxicity

The acute radiotherapeutic toxicity among all patients was evaluated during treatment and during 1st 3-month post-radiotherapy, and the most serious acute responses to radiotherapy were recorded. The incidence and severity

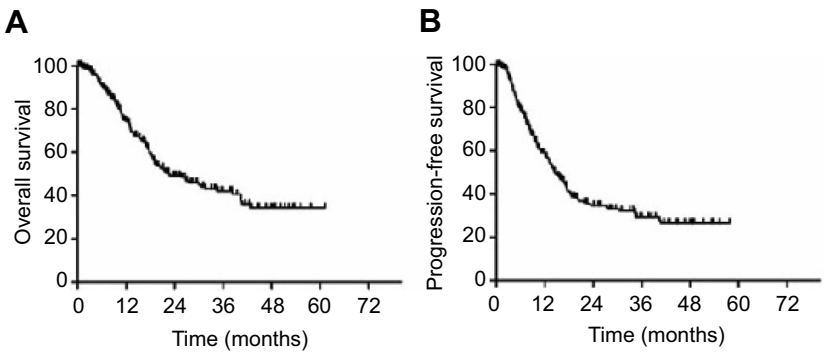

Figure 1 Survival curves of 250 patients of cervical and upper esophageal carcinoma treated with IMRT. (**A**) The overall survival of patients; (**B**) the progression-free survival of patients.

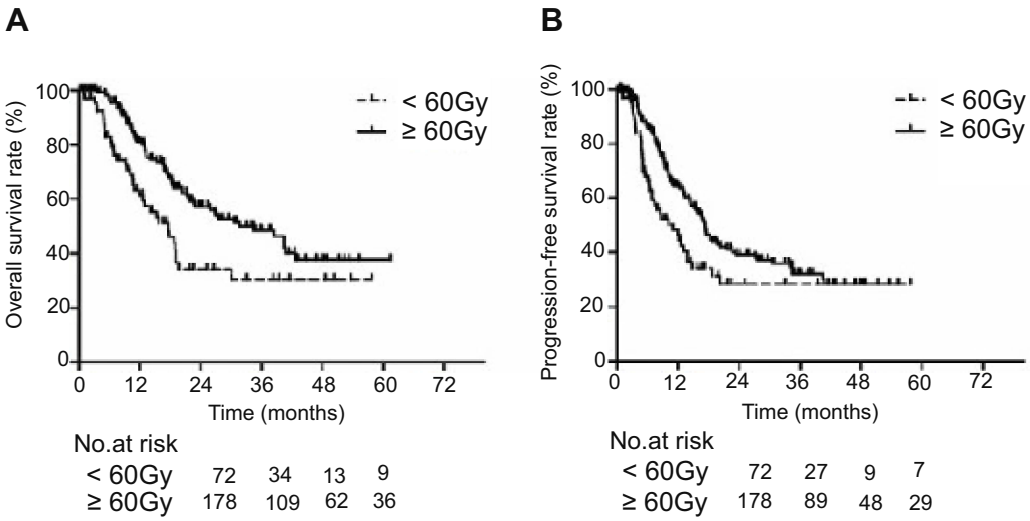

Figure 2 Comparison of survival curves of patients with different radiotherapy dose. (**A**) The overall survival of patients with different target dose; (**B**) the progression-free survival of patients with different target dose.

of acute toxicity are shown in Table 5. Patients with neck and upper thoracic esophageal cancer who received IMRT experienced mostly grade 1–2 adverse reactions. Among these, grade 1–2 radiation esophagitis and radiation pneumonitis occurred in 61 patients (24.4%) and 25 patients (10.0%), respectively; 112 (44.8%) patients experienced grade 1–2 myelosuppression. Grade 3–4 acute radiation esophagitis and radiation pneumonitis occurred in 17 (6.8%) and 7 (2.8%) patients, respectively, while 7 (2.8%) patients experienced grade 3–4 myelosuppression. All patients who experienced adverse radiotherapy reactions recovered with appropriate treatment. No patients needed esophageal dilation after treatment.

Discussion

Cervical and upper thoracic esophageal cancer accounts for approximately 15% of esophageal cancer.[11] Because of the complex anatomical structures around the cervical and upper thoracic segments (such as trachea, jugular vein, aorta and their branches), mortality of patients with cervical and upper thoracic esophageal cancer is still high and postoperative complications are liable to occur after surgery alone. In addition, several studies have shown that the 5-year OS rate of patients with cervical esophageal cancer after surgery is only 12–27% and the postoperative mortality rate is 6–20%.[3,12,13] Cervical esophageal cancer often involves the upper thoracic segment of esophagus and cervical esophageal cancer is often accompanied by upper thoracic esophageal cancer; thus, the treatment methods for these tumors are also very similar.

Surgery alone has been reported ineffective in patients with cervical esophageal cancer. Contrastively, radiotherapy and radiotherapy combined with surgery have better therapeutic efficacy.[9,14] In our study, 54 patients (24.5%) had

Table 2 Univariate analysis of 250 patients of cervical and upper esophageal carcinoma treated with IMRT

Clinical characteristics	Median OS (months)	Overall survival rate		*P*-value	Median PFS (months)	Progression-free survival rate		*P*-value
		1 year	3 year			1 year	3 year	
Age (years)				0.002				0.696
≥65	42.71	0.77	0.56		16.59	0.63	0.24	
<65	18.96	0.69	0.28		14.39	0.69	0.32	
Sex				0.586				0.209
Male	21.32	0.73	0.43		18.66	0.57	0.27	
Female	21.32	0.78	0.39		18.66	0.65	0.37	
GTV (cm^3)				0.046				0.108
≥32	20.46	0.64	0.37		10.94	0.49	0.29	
<32	40.44	0.83	0.48		16.70	0.66	0.36	
Dose				0.002				0.018
≥60 Gy	34.46	0.81	0.49		17.28	0.64	0.32	
<60 Gy	17.64	0.61	0.30		10.94	0.48	0.28	
Concurrent chemotherapy				0.013				0.039
Yes	30.62	0.79	0.47		15.84	0.63	0.35	
No	18.60	0.65	0.30		10.94	0.49	0.18	
Adjuvant chemotherapy				0.004				0.052
Yes	22.14	0.72	0.42		15.70	0.60	0.34	
No	11.33	0.75	0.42		13.77	0.59	0.29	
T stage				0.012				0.232
T2	40.48	0.81	0.53		34.20	0.70	0.38	
T3	38.41	0.86	0.50		17.45	0.67	0.29	
T4	18.76	0.69	0.36		13.14	0.54	0.29	
N stage				0.002				0.089
N0	38.41	0.83	0.50		16.72	0.65	0.31	
N1	31.70	0.77	0.46		17.54	0.62	0.36	
N2	18.27	0.68	0.21		12.03	0.52	0.22	
N3	12.58	0.53	0.13		12.58	0.40	0.20	
Clinical stage				0.004				0.168
Stage Ⅱ	38.41	0.86	0.64		20.24	0.71	0.40	
Stage Ⅲ	25.82	0.85	0.42		17.45	0.67	0.31	
Stage Ⅳ	18.76	0.69	0.36		13.14	0.53	0.29	

Abbreviation: GTV, gross tumor volume.

cervical esophageal cancer. The 1-, 2- and 3-year OS rates were 75.2%, 46.4% and 38.7% for these patients, respectively, which were superior to that of patients who received surgery alone.[15–17] In the past decade, whether radiotherapy or surgery is the better treatment for upper thoracic esophageal cancer is a hot topic. Wang et al conducted a retrospective study of 78 patients with upper thoracic esophageal cancer treated with surgery. The results showed that the median OS was 13.1 months, and the 1-, 3- and 5-year OS rates were 53.9%, 28.7% and 21.4%, respectively; the recurrence rate was 59%.[18] Manshanden et al also reported the median OS of 10.0 months for patients with upper thoracic esophageal cancer.[19] However, Zhu et al evaluated the clinical effect of IMRT in patients with upper thoracic esophageal cancer. They reported that the 1-, 3- and 5-year survival rates were 65%, 50% and 35%, respectively.[20] These studies suggested that IMRT might have superior clinical efficacy in patients with upper thoracic esophageal cancer than surgery alone.[21] In our study, 196 patients with upper thoracic esophageal cancer (78.4%) were

Table 3 Multivariate analysis of 250 patients of cervical and upper esophageal carcinoma treated with IMRT

Clinical characteristics	Median OS			Median PFS		
	95% CI	HR	*P*-value	95% CI	HR	*P*-value
Age (years) ≥65 <65	1.013–1.062	1.037	0.002			
Dose <60 Gy ≥60 Gy	0.455–0.857	0.624	0.004	0.556–0.916	0.714	0.008
GTV (cm^3) ≥32 cm^3 <32 cm^3	0.688–1.754	1.098	0.694			
Concurrent chemotherapy Yes No	0.512–1.490	0.874	0.620	0.467–0.960	0.670	0.029
Adjuvant chemotherapy Yes No	0.437–1.157	0.711	0.170			
T stage	1.140–2.763	1.775	0.011			
N stage	0.982–1.651	1.273	0.069			

Abbreviation: GTV, gross tumor volume.

Table 4 Recurrence of 250 patients of cervical and upper esophageal carcinoma treated with IMRT

	Median OS (months)	1-year survival rate	2-year survival rate	3-year survival rate	*P*-value
Overall recurrence	15.34	61.4%	26.6%	16.6%	0.012
Local recurrence	16.92	73.7%	27.5%	17.9%	
Lymph node recurrence	30.62	78.2%	56.5%	43.0%	
Distant metastasis	15.84	60.1%	28%	11.7%	

Table 5 Radiation-related complications of 250 patients of cervical and upper esophageal carcinoma treated with IMRT

Toxicity	Grade 0 (%)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)
Hematologic toxicity					
Leukocytopenia	139 (55.6%)	61 (24.4%)	30 (12%)	6 (2.4%)	1 (0.4%)
Hypohemoglobin	123 (49.2%)	98 (39.2%)	14 (5.6%)	2 (0.8%)	0
Thrombocytopenia	185 (74%)	40 (16.0%)	10 (4%)	2 (0.8%)	0
Radioactive esophagitis	159 (63.6%)	25 (10.0%)	36 (14.4%)	15 (6%)	2 (0.8%)
Radiation pneumonia	205 (82%)	22 (8.8%)	3 (1.2%)	7 (2.8%)	0

treated with IMRT. The median OS was 25.82 months, and the 1-, 2- and 3-year survival rates were 74.2%, 50.1% and 41.1%, respectively. The OS of patients treated by IMRT in our study was better than that of patients treated by surgery in Wang's study.[18] In addition, patients with upper thoracic esophageal cancer who received surgery had a high rate of complication, such as bleeding and pneumonia, and experienced a high risk of death.[22] While in our study, there is a greater incidence of grade I–II radiotherapy toxicity in patients, but treatment-related death did not happen. Compared with surgical treatment, IMRT had the advantage of a shorter duration of therapy and fewer side effects.

Table 6 Results of radiotherapy and surgery for cervical and upper thoracic esophageal

Authors	Total no. of cases	Location	Treatment	Median overall survival (months)	Overall survival rate		
					1 year	2 year	3 year
Wang et al[18]	78	Upper	Surgery	13.1	53.9%	–	28.7%
Zhu et al[20]	30	Upper	IMRT	–	65.0%	50.0%	35.0%
Manshanden et al[19]	30	Upper	Surgery	10.0	–	–	–
Esmati et al[21]	40	Cervical and upper	3DCRT	19.2	76.0%	38.0%	16.0%
Li et al[9]	92	Cervical	3D/IMRT	36.0	88.0%	66.3%	49.8%
Cao et al[17]	27	Cervical	Surgery	–	–	50.7%	–
Present study	54	cervical	IMRT	20.37	75.2%	46.4%	38.7%
Present study	196	Upper	IMRT	25.8	74.2%	50.1%	41.1%

Therefore, IMRT is an effective treatment for patients with upper thoracic esophageal cancer (Table 6).

Several studies have reported the superiority of IMRT over other radiotherapeutic modalities for treatment of esophageal cancer.[23,24] However, most of these studies pertained to patients with thoracic middle-lower segment esophageal carcinoma, and the clinical outcomes of IMRT in patients with esophageal cancer in the cervical and upper thoracic segments are not well characterized. Lachlan et al compared the efficacy of different radiotherapy methods for cervical esophageal cancer. Their results showed better 2-year and 5-year survival rates of patients with cervical esophageal cancer after IMRT (53% and 43%, respectively) as compared to that after 2-dimensional radiotherapy (33% and 14%, respectively) or 3-dimensional conformal radiotherapy (CRT) (43% and 22%, respectively).[25] In our previous study, the survival rates of patients with upper thoracic esophageal cancer after IMRT were higher than those of their counterparts treated with CRT.[26] Zhang et al compared the dose distribution of CRT and IMRT in patients with upper thoracic esophageal cancer. They found that the dose distribution of IMRT was more accurate compared with CRT and that IMRT reduced the dose of spinal cord and lung tissue, which reduced the risk of complications.[27]

Radiotherapy dose is an important prognostic factor for patients with esophageal cancer. Zhu et al compared the effects of different radiotherapy doses on the treatment of esophageal cancer; the results showed that after IMRT, patients in the high-dose group (2.13 Gy/30f) were significantly more likely to achieve complete remission (CR) than patients in the conventional dose group (2 Gy/30f). In addition, the 1-, 2- and 3-year PFS rates in the high-dose group (60%, 40% and 25%, respectively) were significantly higher than those in the conventional dose group (41.7%, 25% and 8.3%, respectively).[28] In our study, radiotherapy dose was one of the important prognostic factors in patients with cervical and upper thoracic esophageal cancer.

Concurrent chemotherapy also plays an important role in the radiotherapy of patients with esophageal cancer. Zhao et al conducted a retrospective study of 122 patients with esophageal squamous cell carcinoma; among these, 52 patients received concurrent chemoradiotherapy based on platinum and fluorouracil and 70 patients received radiotherapy alone. The OS and PFS in the concurrent chemoradiotherapy group (15.3 and 24.6 months, respectively) were significantly longer than that in the radiotherapy group (10.6 and 19.4 months, respectively) ($P<0.05$).[29] In this study, 172 patients underwent concurrent chemotherapy; the OS of patients who received concurrent chemoradiotherapy and those who received radiotherapy alone was 30.62 and 18.60 months, respectively. The results showed that concurrent chemoradiotherapy conferred a significant survival benefit in patients with neck and upper thoracic esophageal cancer ($P<0.05$).

Zhong et al found a significant difference between the 5-year survival rates of patients with stage II and III esophageal cancer ($P<0.05$); in addition, both T stage and N stage were associated with prognosis of patients.[30] This study also found that the survival time of patients with stage II disease was significantly longer than that of patients with stage IV disease ($P<0.05$).

This retrospective study has limitations. Late toxicity, such as swallowing ability, quality of voice of patients and so on, was collected in part of patients.

Conclusion

Our results indicated that IMRT had clinical benefit for patients with cervical and upper thoracic esophageal

squamous cell carcinoma. Age, radiotherapy dose and the T stages of esophageal cancer had a significant impact on OS. And radiotherapy dose and treatment with concurrent chemotherapy were independent prognostic factors for PFS of patients with cervical and upper thoracic esophageal cancer.

Ethics approval and informed consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review Board (IRB) of Tianjin Medical University Cancer Institute & Hospital (TCIH) and with the 1975 Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants included in the study.

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Author contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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