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Radiation dose to the lymph drainage area in esophageal cancer with involved-field irradiation

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Abstract. The aim of this study was to quantify the radiation dose to the corresponding lymph drainage area in esophageal cancer using three-dimensional conformal radiation therapy (3D-CRT) with involved-field irradiation (IFI) and to analyze associated factors. A retrospective analysis of 81 patients with esophageal cancer was conducted. According to the location of the lesions, the lymph drainage area was delineated and the dosimetric parameters were calculated. The 1-, 3-, 5- and 8-year survival rates of the patients were 67.90, 33.33, 20.99 and 11.11%, respectively. Based on the dose-volume histogram in the treatment plan, we calculated the volume percentage of the planning target volume including clinically positive lymph nodes (PTV-N) receiving radiation doses of 30, 35, 40, 45 and 50 Gy ($V_{PTV-N30-50}$). The median values of $V_{PTV-N30-50}$ were 73, 70, 67, 64 and 58%, respectively. The prescribed dose size exhibited no correlation with $V_{PTV-N30-35}$, but did exhibit a significant correlation with $V_{PTV-N40-50}$; the radiation field was not correlated with $V_{PTV-N30-45}$, but exhibited a significant correlation with $V_{PTV-N50}$; the length of the lesion on esophageal barium meal X-ray and the PTV were significantly correlated with $V_{PTV-N30-50}$. The analysis of variance revealed that the V_{PTV-NX} value in the upper thoracic segment was higher compared with that in the middle and lower thoracic segments; $V_{PTV-N30-35}$ values differed significantly according to the different locations of the lesions, whereas $V_{PTV-N40-50}$ values exhibited no significant differences. The value of V_{PTV-NX} exerted no significant effect on long-term patient survival. Therefore, the corresponding lymph drainage area of esophageal cancer is subjected to a certain radiation dose when patients undergo 3D-CRT with IFI, which may play a role in the prevention of regional nodal metastasis. However, this hypothesis requires confirmation by further clinical studies.

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Key words: esophageal cancer, three-dimensional conformal radiation therapy, involved-field irradiation, lymph drainage area, dosimetry

Introduction

There is significant controversy regarding target region delineation by esophageal cancer radiotherapy in different regions. In the RTOG85-01 randomized trial (1), irradiation of the entire esophagus for esophageal cancer was recommended. In the RTOG94-05 trial (2), an area with a margin of 2-5 cm surrounding the gross tumor volume (GTV) was defined as the clinical target volume (CTV). The supraclavicular nodes were included only when the tumor was located in the cervical esophageal area. However, the results of these two trials were not satisfactory, as the survival and local control rates did not improve significantly. In the RTOG01-33 trial (3), three-dimensional conformal radiation therapy (3D-CRT) technology was applied. The CTV included a 3-cm margin around the GTV, while the planning target volume (PTV) included a margin of ≤2 cm around the CTV. Over the last few years, an increasing number of studies have been conducted on elective nodal irradiation (ENI) for esophageal cancer; however, their conclusions have been inconsistent. It was previously reported that, compared with involved-field irradiation (IFI), ENI does not improve the local control rate or long-term survival of patients with esophageal cancer (4). Previous studies have indicated that ENI may prevent regional lymph node metastasis (5,6), whereas other studies (7-9) reported that the isolate out-of-field nodal failure rate was low and overall survival did not decrease when IFI was used (6,7). Ji *et al* (10) reported the results of a prospective study on 3D-CRT in 39 patients with esophageal cancer without distant metastases, and revealed that lymph node stations in close proximity to esophageal malignant tumors receive considerable incidental radiation doses with IFI, which may contribute to the elimination of subclinical lesions. The number of studies quantifying radiation dose to the corresponding lymph drainage area using 3D-CRT with IFI for esophageal cancer is currently limited. The present study aimed to determine the amount of radiation delivered to the corresponding lymph drainage area in patients with esophageal cancer treated at The Fourth Affiliated Hospital of Hebei Medical University using 3D-CRT with IFI.

Patients and methods

Clinical data. A retrospective analysis was conducted on 81 patients with pathologically confirmed esophageal squamous cell carcinoma (ESCC). All the patients received 3D-CRT and

IFI at the Department of Radiation Oncology of The Fourth Affiliated Hospital of Hebei Medical University (Shijiazhuang, China) between October, 2000 and May, 2004. All the patients were admitted for initial treatment and had complete clinical data, esophageal barium meal, chest computed tomography (CT) scans and abdominal B ultrasound or CT. For patients receiving radiotherapy, the doctors in our department and the radiologists re-examined archived esophageal barium meal films and chest CT scans. Based on case history and radiographic data, all the cases were analyzed for reclassification and staging, which was conducted according to the standards of the 2002 Union for International Cancer Control esophageal cancer staging (11), as shown in Table I.

This study's protocol conformed to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Hebei Medical University. Written informed consent was obtained from all the participants.

Conformal treatment planning. Posture fixation of the thermoplastic phantom was followed by simulation CT scanning with 3-5 mm slices (CT Brilliance; Philips Medical Systems, Amsterdam, The Netherlands). Images were collected for digital transmission and 3D reconstruction into the 3D-CRT planning system (Focus 3.0; CMS, Woodlawn, MD, USA). Based on the length of the lesion on esophageal imaging and fiber esophagoscopy, as well as the depth of invasion shown on the CT scan, lesions including the mediastinal lymph nodes were defined as GTV. The CTV was defined as the GTV plus a 0.5-0.8-cm margin in the lateral and anteroposterior directions and a 2.0-3.0-cm margin in the superoinferior direction of GTV, while PTV encompassed 0.5-0.8-cm proximal and distal margins and a 1.0-cm radial margin, based on the CTV. The PTV was also calculated. In addition, adjacent tissues and organs, including the spinal cord, trachea, heart and lungs, were delineated. The optimal treatment was designed according to the isodose curve, such as the dose-volume histogram (DVH) and two-dimensional image, and delivered by 6-MV X-rays from a linear accelerator (Elekta Precise Linear Accelerator; Elekta, Stockholm, Sweden). The prescribed dose was 56-70 Gy, delivered in 28-35 doses over 6-7 weeks, with a median dose of 64 Gy.

Delineation of lymph drainage area. According to the grouping of chest lymph nodes by the American Thoracic Society (12), the lymph drainage area in 81 patients with esophageal cancer was delineated. The upper thoracic lymph node drainage area included the bilateral supraclavicular regions, as well as regions 2, 4, 5, 6, 7 and 8, and the lower boundary was a 4-5-cm margin around the carina of the trachea; the lymph drainage area of the middle thoracic segment included regions 2, 4, 5, 6, 7 and 8 and the lower boundary was the cardiac lymph node area; the drainage area of the lower thoracic segment included regions 4, 5, 6, 7 and 8, as well as the lymph nodes of the paracardia, lesser gastric curvature and left gastric area (Fig. 1). The delineated lymph drainage area included the PTV, which was defined as the CTV including clinically positive lymph nodes (CTV-N). PTV-N was defined as the CTV-N plus a 0.3-0.5-cm margin in the lateral and anteroposterior directions and a 1.0-1.5-cm margin in the superoinferior direction. Based on the DVH in the treatment plan, we calculated the volume percentage when PTV-N received radiation doses of 30, 35, 40, 45 and 50 Gy, i.e., $V_{PTV-N30}$, $V_{PTV-N35}$, $V_{PTV-N40}$, $V_{PTV-N45}$ and $V_{PTV-N50}$, respectively.

Table I. Clinical data of esophageal cancer patients (n=81).

Observational indices	Values
Gender (no.)	
Male	59
Female	22
Age (years)	
Range	37-81
Median	63
Location of lesion (no.)	
Upper thoracic segment	25
Middle thoracic segment	44
Lower thoracic segment	12
T stage (no.)	
T1	6
T2	44
T3	25
T4	6
N stage (no.)	
N0	55
N1	26
TNM stage (no.)	
I	6
IIa	45
IIb	10
III	20
Length of lesion on X-ray (cm)	
Range	2.0-16.0
Median	6.0
Length of lesion on CT (cm)	
Range	2.7-16.0
Median	7.2
Maximal depth of invasion on CT (cm)	
Range	1.4-5.5
Median	2.8
Planning target volume (cm^3)	
Range	49.05-430.43
Median	182.0
Prescribed dose (Gy)	
Range	54-70
Median	64
IFI (Gy)	
Range	3-7
Median	3

IFI, involved-field irradiation; CT, computed tomography.

Follow-up. All the patients were followed up until December 31, 2012. Patients receiving radiotherapy were

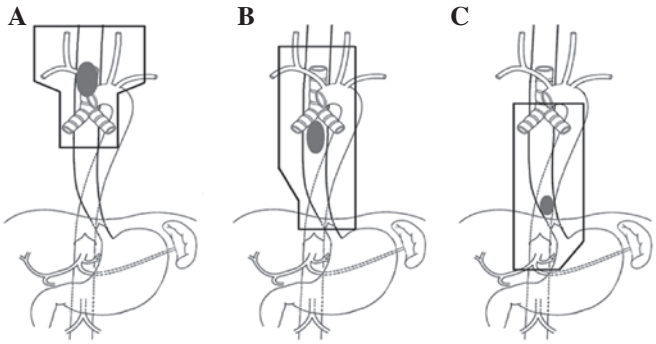

Figure 1. Delineated lymph drainage areas in patients with (A) upper, (B) middle and (C) lower thoracic esophageal cancer.

followed up for 3-118 months, with a median follow-up time of 20 months. A total of 55, 27 and 18% of the cases were followed up for 1, 3 and 5 years, respectively, with a follow-up rate of 100%.

Statistical analysis. SPSS 11.5 statistical software (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. The normal distribution of data required for observation in each group was assessed. One-way analysis of variance (ANOVA) was used for comparison among different groups and the Spearman's correlation test was used for comparison between groups. The Kaplan-Meier method was applied to analyse survival and local control rates, and the two-tailed log-rank method was used to assess significance. A multivariate analysis was conducted using the Cox proportional hazards model to assess the independent prognostic factors. $P<0.05$ was considered to indicate statistically significant differences.

Results

Overall survival. At the last date of follow-up, 9 patients remained alive, with 1-, 3-, 5- and 8-year survival rates of 67.90, 33.33, 20.99 and 11.11%, respectively. The 1-, 3-, 5- and 8-year local control rates were 76.59, 45.82, 35.81 and 20.14%, respectively. The univariate analysis revealed that the prognostic factors affecting patient survival rate included dietary intake and hoarseness prior to treatment, clinical T, N and TNM stage, length of esophageal lesions on barium meal X-ray, maximal diameter of lesions on CT and immediate curative effect (Table II). The multivariate analysis revealed that the independent prognostic factors were dietary intake prior to treatment (χ^2=12.062, P=0.001), hoarseness prior to treatment (χ^2=7.656, P=0.006), clinical TNM stage (χ^2=4.462, P=0.031) and X-ray length of esophageal lesions on barium meal X-ray (χ^2=5.360, P=0.021) (data not shown).

DVH analysis of PTV-N. The corresponding lymph drainage area in the 81 patients was delineated without altering the originally delineated GTV, CTV, PTV and prescribed dose, thereby obtaining CTV-N and PTV-N. In the absence of additional treatment, available radiotherapy planning and DVH were used to calculate the minimal, maximal and median values, as well as the mean ± standard deviation of $V_{PTV-N30}$, $V_{PTV-N35}$, $V_{PTV-N40}$, $V_{PTV-N45}$ and $V_{PTV-N50}$ (Table III).

Correlation analysis of V_{PTV-NX} and associated factors. The results demonstrated that the prescribed dose size exhibited no correlation with $V_{PTV-N30-35}$, but was significantly correlated with $V_{PTV-N40-50}$; the irradiation field exhibited no correlation with $V_{PTV-N30-45}$, but was significantly correlated with $V_{PTV-N50}$; the length of the lesion on esophageal barium meal X-ray and PTV were significantly correlated with $V_{PTV-N30-50}$ (Table IV).

Association between V_{PTV-NX} and lesion location. The ANOVA demonstrated that the values of $V_{PTV-N30}$ and $V_{PTV-N35}$ were significantly different due to the different locations of the lesions; however, no correlation was observed with $V_{PTV-N40}$, $V_{PTV-N45}$ or $V_{PTV-N50}$ (Table V). Further stratification analysis suggested that the values of $V_{PTV-N30}$ and $V_{PTV-N35}$ of the upper and middle thoracic segments exhibited significant differences compared with those of the lower thoracic segment (P-values of 0.023, 0.021 and 0.029, 0.038, respectively); the values of $V_{PTV-N40}$ of the upper/middle and the lower thoracic segments were similar, approaching statistical significance (P-values of 0.050 and 0.056, respectively), while the values of $V_{PTV-N45}$ and $V_{PTV-N50}$ of the upper/middle and the lower thoracic segments did not differ significantly (P-values of 0.094, 0.131 and 0.427, 0.525, respectively). No statistical difference was observed in $V_{PTV-N30-50}$ between the middle and lower thoracic segments (P-values of 0.449, 0.572, 0.580, 0.732 and 0.941, respectively).

Analysis results of V_{PTV-NX} and survival rate. Based on previous studies, grouping was performed according to the different values of V_{PTV-NX}, in order to compare survival rates. The results revealed no significant effect on long-term patient survival (Table VI).

Discussion

The main causes of radiotherapy treatment failure of esophageal cancer are local recurrence and distant metastasis, with the former mainly characterized by lymph node and esophageal recurrence. Therefore, radiotherapists face the challenge of identifying methods to effectively reduce the local recurrence rate, thereby improving their long-term survival rate. In recent years, a number of studies on radiotherapy combined with ENI have been conducted. ENI aims to reduce the local recurrence rate, particularly that in regional lymph nodes (5,6). However, certain studies demonstrated that, in patients who underwent radiotherapy rather than ENI, the lymph node recurrence rate outside the field was 2-8% (7,8). A number of studies in China and abroad also demonstrated that, compared with ENI, the toxicity of which was considered acceptable for the majority of the patients, the recurrence rate and distant metastasis in patients treated with IFI was not notably increased (4,13,14). Therefore, regarding patients treated with IFI, it remains unclear how they should be irradiated in order to control the recurrence of regional lymph nodes. It was previously demonstrated that, when the corresponding lymph drainage area of esophageal cancer is exposed to a lower dose of radiation, the local metastasis rate decreases and that an irradiation dose of 24 Gy may help reduce the metastasis rate by 30-50% (13,14). Ji *et al* (10) investigated 39 patients with stage $T_{0-4}N_0M_0$ ESCC who were treated with IFI and demonstrated that, when ESCC patients were treated exclusively by 3D-CRT with IFI, adjacent

Table II. Univariate analysis results of 81 esophageal cancer patients treated with involved-field irradiation.

Variables	No.	Survival rate (%)				χ^2	P-value
		1-year	3-year	5-year	8-year		
Gender						1.07	0.2999
Male	59	71.19	33.90	22.03	13.56		
Female	22	59.09	31.82	18.18	4.55		
Age (years)						0.21	0.6438
≤60	37	62.16	27.03	24.32	10.81		
>60	44	72.73	38.64	18.18	11.36		
Dietary intake prior to treatment						9.28	0.0023
Normal	24	79.17	54.17	41.67	25.00		
Abnormal	57	63.16	24.56	12.28	5.26		
Chest and back pain						2.85	0.0913
No	60	71.67	36.67	23.33	13.33		
Yes	21	57.14	23.81	14.29	4.76		
Hoarseness prior to treatment						5.76	0.0164
No	72	69.44	37.50	23.61	12.50		
Yes	9	55.56	0.00	0.00	0.00		
Location of lesion						1.47	0.4792
Upper thoracic segment	25	64.00	32.00	24.00	8.00		
Middle thoracic segment	44	72.73	38.64	20.45	13.64		
Lower thoracic segment	12	58.33	16.67	8.33	8.33		
T stage						21.55	0.0001
T1	6	83.33	83.33	33.33	33.33		
T2	44	79.55	40.91	29.55	11.36		
T3	25	52.00	16.00	8.00	8.00		
T4	6	33.00	0.00	0.00	0.00		
N stage						14.80	0.0001
N0	55	76.36	43.64	29.09	16.36		
N1	26	50.00	11.54	3.85	0.00		
TNM stage						23.29	<0.0001
I	6	83.33	83.33	33.33	33.33		
IIa	45	77.78	40.00	28.89	13.33		
IIb	10	70.00	30.00	20.00	10.00		
III	20	40.00	5.00	0.00	0.00		
Length of lesion on esophageal barium meal X-ray (cm)						21.15	<0.0001
≤5.0	24	83.33	70.83	37.50	20.83		
5.0-9.0	47	63.96	21.28	17.02	8.51		
>9.0	10	40.00	0.00	0.00	0.00		
Max diameter of lesion on CT (cm)						5.31	0.0213
≤4.0	54	72.22	42.59	27.78	12.96		
>4.0	27	59.26	14.81	7.41	7.41		
Prescribed dose (Gy)						0.06	0.8095
≤64	38	65.79	26.32	21.05	15.79		
>64	43	69.77	39.53	20.93	6.98		
Immediate curative effect						13.09	0.0114
Complete response	34	76.47	52.94	41.18	25.53		
Partial response	35	57.14	22.86	8.57	2.86		
No response	12	75.00	8.33	0.00	0.00		

CT, computed tomography.

Table III. Dose-volume histogram analysis results of PTV-N.

Values	$V_{PTV-N30}$ (%)	$V_{PTV-N35}$ (%)	$V_{PTV-N40}$ (%)	$V_{PTV-N45}$ (%)	$V_{PTV-N50}$ (%)
Minimum	16	13	10	6	0
Maximum	99	98	98	98	97
Median	73	70	67	64	58
Mean ± standard deviation	71.35±1.89	68.70±1.87	65.84±1.84	62.40±1.97	56.83±2.00

PTV-N, planning target volume with clinically positive lymph nodes.

Table IV. Correlation analysis of V_{PTV-NX} and associated factors.

	Prescribed dose		Irradiation field		Length of lesion on esophageal barium meal X-ray		PTV volume	
V_{PTV-NX}	r	P-value	r	P-value	r	P-value	r	P-value
$V_{PTV-N30}$	0.183	0.215	0.870	0.438	0.258	0.020	0.679	0.013
$V_{PTV-N35}$	0.101	0.054	0.070	0.535	0.288	0.009	0.745	0.008
$V_{PTV-N40}$	0.246	0.027	0.090	0.425	0.322	0.003	0.730	0.007
$V_{PTV-N45}$	0.336	0.002	0.114	0.313	0.339	0.002	0.851	0.001
$V_{PTV-N50}$	0.438	0.000	0.223	0.045	0.389	0.000	0.937	0.000

PTV-N, planning target volume with clinically positive lymph nodes.

Table V. One-way analysis of variance results of V_{PTV-NX} and different location of the lesions.

V_{PTV-NX} (%)	Thoracic segment	Mean ± SD	F	P-value	95% confidence interval
$V_{PTV-N30}$	Upper	78.56±11.48	3.762	0.028	73.82-83.30
	Middle	69.00±18.14			63.18-74.52
	Lower	64.92±18.65			53.07-76.77
$V_{PTV-N35}$	Upper	75.48±12.05	3.227	0.045	70.51-80.45
	Middle	66.36±17.74			60.97-71.76
	Lower	63.33±18.96			51.29-75.38
$V_{PTV-N40}$	Upper	71.88±12.05	2.659	0.076	66.90-76.86
	Middle	63.77±17.70			58.39-69.16
	Lower	60.83±18.05			49.37-72.30
$V_{PTV-N45}$	Upper	67.84±12.91	1.795	0.173	62.51-73.17
	Middle	60.39±19.63			54.42-66.35
	Lower	58.42±17.89			47.05-69.78
$V_{PTV-N50}$	Upper	59.40±13.88	0.366	0.695	63.67-65.13
	Middle	55.77±20.25			49.61-61.93
	Lower	55.33±17.66			44.12-66.55

PTV-N, planning target volume with clinically positive lymph nodes; SD, standard deviation.

lymph drainage areas were also exposed to a high dose of radiation, which may play a role in controlling subclinical metastasis.

The postoperative pathological findings of esophageal cancer play a decisive role in delineating the prophylactic irradiation range ensured by ENI. In recent years, following the analysis of the lymph node metastasis in ESCC, several studies have suggested that the level of lymph node metastasis is associated with primary tumor location. Nakamura *et al* (15) investigated 95 patients with stage $T_{1-3}N_0M_0$ esophageal cancer based on preoperative clinical staging, recommending corresponding lymph node irradiation based on primary tumor location (no prophylactic irradiation of abdominal lymph nodes in patients with upper and middle thoracic esophageal

Table VI. Analysis results of V_{PTV-NX} and survival rate.

Observational indices	Grouping (%)	n	Survival rate (%)				χ^2	P-value
			1-year	3-year	5-year	8-year		
$V_{PTV-N30}$	≥83.3	24	66.67	29.17	20.83	4.17	0.86	0.3534
	<83.3	57	68.42	35.09	21.05	17.22		
$V_{PTV-N35}$	≥71.5	40	70.00	35.00	22.50	8.57	0.05	0.8222
	≥71.5	41	65.85	31.71	19.51	17.07		
$V_{PTV-N40}$	≥62.5	51	68.63	35.29	25.49	12.83	0.17	0.6798
	<62.5	30	66.67	30.00	13.33	13.33		
$V_{PTV-N45}$	≥55.6	59	66.10	35.59	23.73	12.85	0.02	0.9002
	<55.6	22	72.73	27.27	13.64	13.63		
$V_{PTV-N50}$	≥50.0	57	70.18	36.84	26.32	15.11	1.37	0.2412
	<50.0	24	62.50	25.00	8.33	8.33		

PTV-N, planning target volume with clinically positive lymph nodes.

cancer, and no prophylactic irradiation of the supraclavicular area in patients with middle and lower thoracic esophageal cancer). Huang *et al* (5) analyzed 1,077 cases with lymph node metastasis following surgery for ESCC. The results demonstrated that the lymph node metastasis rate of upper thoracic esophageal cancer to the neck, upper, middle and lower mediastinum and abdominal area were 16.7, 38.9, 11.1, 5.6 and 5.6%, respectively; for ESCC of the middle thoracic segment, the respective rates were 4.0, 3.8, 32.9, 7.1 and 17.1%; for the lower thoracic segment, the respective rates were 1.0, 3.0, 22.7, 37.0 and 3%. That study recommended that, in the delineated lymph node drainage area, the upper boundary of the upper thoracic segment should be the cervical esophageal area and the bilateral supraclavicular area lymph nodes, whereas the lower boundary should involve the lymph nodes under the tracheal carina; the lymph nodes under the carina should be the upper boundary of the lower thoracic segment, with the stomach, hepatic artery and adjacent lymph nodes as the lower boundary. Prophylactic irradiation of the corresponding lymph node area in patients with middle thoracic esophageal cancer should be determined by tumor location, with the mediastinal lymph drainage area being included in patients in a good overall condition. In the present study, the irradiation dose to the corresponding lymph drainage area was investigated in 81 patients who received 3D-CRT with IFI. The results demonstrated that the corresponding lymph drainage areas were exposed to 30-50 Gy of radiation in varying degrees, referred to as incidental irradiation dose (IID). The results of the study also indicated that the median IID of $V_{PTV-N35}$, $V_{PTV-N40}$, $V_{PTV-N45}$ and $V_{PTV-N50}$ was >24 Gy.

Compared with patients with middle and lower thoracic esophageal cancer, patients with upper thoracic esophageal cancer exhibit a relatively early onset of clinical symptoms. Therefore, the majority of those patients seek treatment when the tumor body is small, while the majority of patients with middle or lower thoracic esophageal cancer have unresectable tumors at presentation and receive radiation therapy. As regards earlier esophageal cancer, higher clinically prescribed doses are generally administered for radical treatment. To avoid damage to normal tissues and organs, the prescribed dose is generally lower for larger tumors compared with that for smaller tumors. Furthermore, due to the anatomical structure of the lungs, the prescribed doses may be higher in patients with upper thoracic esophageal cancer compared with those with middle or lower thoracic cancer, thus preventing increased radiation dose to the lungs. The present results suggest that the mean IID in patients with upper thoracic esophageal cancer was higher compared with that in patients with middle or lower thoracic esophageal cancer, with statistically significant differences between the radiation dose of $V_{PTV-N30}$ and $V_{PTV-N35}$, which may be associated with the higher dose received by patients with upper thoracic esophageal cancer. The present findings also indicate that V_{PTV-NX} was significantly correlated with the prescribed dose. When the esophageal lesions are longer, the PTV length and volume are accordingly larger. The present study demonstrated that V_{PTV-NX} was significantly correlated with the length of esophageal lesions as determined by X-ray and the PTV. This was consistent with the results reported by Ji *et al* (10), suggesting that PTV and length of esophageal lesions exhibited a linear correlation with the equivalent uniform dose.

The results of the present study indicate that it is not beneficial for patients to expose the lymph drainage area to higher IID in terms of survival. This may be explained as follows: i) Higher IID received by patients may compromise immunity to some extent, which may be detrimental to prognosis in long-term surviving patients; ii) esophageal cancer recurrence beyond the irradiated field is not a major cause of treatment failure. Higher recurrence rate within the field and distant metastasis may be offset by the survival benefit achieved by higher IID; iii) the irradiated field is larger in patients receiving higher IID, compared with those receiving lower IID. It is likely that the larger field will result in more extensive radiation injury, which may reduce the survival benefit achieved by higher IID.

In conclusion, the curative effect of IFI on esophageal cancer was not significantly reduced. As regards dosimetry, this may be associated with the hypothesis that the corresponding lymph drainage area in patients treated with IFI

may be exposed to different radiation doses, which may play a preventive role. In the clinical setting, a proportion of patients may present with local recurrence or distant metastasis prior to regional lymph node recurrence, thereby masking the regional lymph node recurrence. Therefore, further confirmation is required as to whether IID in esophageal cancer using 3D-CRT with IFI may play a preventive role in regional lymph node metastasis.

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