Original Article

Intensity-modulated radiotherapy does not decrease the risk of malnutrition in esophageal cancer patients during radiotherapy compared to three-dimensional conformal radiation therapy

Cong Wang[1#], Ming Lu[2#], Tingting Zhou[1], Shasha Zhao[3], Shanghui Guan[1]

[1]Department of Radiation Oncology, [2]Department of Thoracic Surgery, [3]Department of Clinical Nutrition, Qilu Hospital of Shandong University, Jinan 250012, China

Contributions: (I) Conception and design: S Guan; (II) Administrative support: S Guan; (III) Provision of study materials or patients: C Wang, M Lu; (IV) Collection and assembly of data: C Wang, T Zhou, S Zhao; (V) Data analysis and interpretation: C Wang, M Lu, S Guan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work and should be considered co-first authors.

Correspondence to: Shanghui Guan. Department of Radiation Oncology, Qilu Hospital of Shandong University, Jinan 250012, China. Email: guanshanghui@163.com.

Background: Esophageal cancer is a lethal disease of global scope. Radiotherapy is the main method to treat esophageal cancer; however, it concurrently leads to malnutrition. Intensity-modulated radiotherapy (IMRT) is superior to three-dimensional conformal radiation therapy (3D-CRT) in dosimetry and clinical outcomes. In this cohort study, we aimed to compare the effect of 3D-CRT and IMRT on malnutrition status.

Methods: We retrospectively included 79 esophageal cancer patients (IMRT: n=27, 3D-CRT: n=52) who received radiotherapy. We collected nutrition indexes at the beginning, the second week, and the end of radiotherapy. Paired-T test was used to evaluate the nutrition status during radiotherapy in each group. Chi-square test and independent-sample *T*-test were applied to compare the dynamic changes of indexes between IMRT and 3D-CRT groups.

Results: The baselines of the two groups are comparable. Nutrition Risk Screening 2002 (NRS-2002) score, body weight, BMI, hemoglobin, lymphocyte, total protein, and albumin values were significantly reduced during radiotherapy in both groups. The dynamic changes of nutrition indexes during radiotherapy were not significantly different between the IMRT and 3D-CRT groups. Besides, no difference was found for radiation esophagitis or treatment completion between the two groups.

Conclusions: Malnutrition occurs in esophageal cancer patients during radiotherapy. IMRT did not significantly decrease the risk of malnutrition compared to 3D-CRT.

Keywords: Intensity-modulated radiotherapy (IMRT); three-dimensional conformal radiotherapy (3D-CRT); malnutrition; esophageal cancer; radiotherapy

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Introduction

Esophageal cancer is a serious malignancy with regards to mortality and prognosis. Squamous cell carcinoma is the most common histological type of esophageal cancer worldwide, with a higher incidence in developing nations (1). Although treatment technologies have improved in recent years, the five-year survival rate remains low (ranging from 15% to 25%) (2). Radiotherapy plays a crucial role in the management of esophageal cancer (3,4). Three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) are the most common technologies used for esophageal cancer treatment. 3D-CRT realizes the distribution of radiation fields in polyhedral and non-concentric areas, which contributes to better target coverage and decreased toxicity to normal organs compared to 2D-CRT. IMRT has become increasingly popular for the treatment of esophageal and other cancers (5). The superiority of the dosimetry distribution of IMRT leads to superiority in clinical efficacy. It has been reported to significantly reduce the dosage to the lung (5) and heart (6) in esophageal cancer radiotherapy. Furthermore, IMRT is associated with a lower risk of grade 3 or higher non-hematologic toxicity (7) and a higher five-year survival rate than 3D-CRT (8,9).

Nutrition status is of great importance for tumor patients' survival. Malnutrition frequently occurs in cancer patients and has negative effects on clinical outcomes (10). A moderate degree of malnutrition and a severe degree of malnutrition were observed in 76% and 12% of cancer patients, respectively (11). The prevalence of malnutrition in esophageal cancer patients has been reported to be about 60.2% (12). However, only 28.4% of non-malnourished patients and 57.6% of malnourished patients received nutrition support (12).

Radiotherapy increases the risk of malnutrition. One study showed that 74% of patients were malnourished at the end of radiotherapy while this proportion was only 10% before radiotherapy (13). The increase of malnutrition during radiotherapy was also reported in breast, lung, stomach, and colorectal cancer patients (14). Brown *et al.* (15) compared the difference of 3D-CRT and helical-IMRT in body weight change and the need for tube feeding. It was found that both groups had a median weight loss of 45%, a high incidence of tube feeding, and severe weight loss. Nutrition intervention remains critical despite advances in radiotherapy techniques. However, no research has been reported in esophageal cancer patients. In this study, we aimed to compare the effect of IMRT and 3D-CRT on the nutritional status of esophageal cancer patients.

Methods

Subjects

We retrospectively included 95 esophageal cancer patients receiving radiotherapy between January 2018 and August 2018 in the Qilu Hospital of Shandong University. All patients received standardized nutritional management. Nutrition Risk Screening 2002 (NRS-2002) screening was performed on a regular basis, and patients with nutritional risk were given a PG-SGA score. For patients at risk, we consulted the nutrition department and gave nutritional intervention. After nutrition screening and examination, a five-step nutritional treatment was given according to the specific nutritional risk of patients, including modification of basic nutrition, oral nutritional supplements (ONS), enteral nutrition (EN), and parenteral nutrition (PN). The most common nutritional approach is the modification of regular nutritional intake due to dysphagia. If the intake of food with a normal diet is insufficient despite these adjustments, we opt for an additional nutritional intake using ONS. EN is the least invasive form of artificial nutritional therapy. Nutrient solutions are delivered through a tube or a stoma. When a patient being treated for esophageal cancer experiences a partial or complete gastrointestinal failure and sufficient nutritional and energy intake cannot be administered by means of EN, we opt for a supplementary or complete PN (16). Patients included who had malnutrition received individualized dietary counseling and ONS and no patients received EN or PN. Nutrition Risk Screening 2002 (NRS-2002), body weight, blood routine, and liver function are examined every week during radiotherapy to assess the patient's metabolic state, response to nutritional therapy, and utilization of nutrients. For comparison, we included the NRS-2002 score, body weight, body mass index (BMI), hemoglobin (Hb), lymphocyte, pre-albumin, total protein, albumin, and globulin at the beginning, the second week, and the end of radiotherapy from the medical records. Prevalence of radiation esophagitis and treatment completion were also included for analysis. The esophagitis grade standard, as defined by the Acute Toxicity Grading System of The Radiation Therapy Oncology Group (RTOG), was used. We divided esophagitis grades 0 to 1 into one group, and radioactive esophagitis of grade 2 or greater into the other group.

The same dosimetric constraints were used for IMRT and 3D-CRT. The main dosimetric constraints were as follows: the prescribed dose contains 95% of the target area, the V20 of the lung is less than 30%; the V30 is less than 20%, and the other organs at risk (OARs) are in accordance with RTOG's 0615 protocols [the dose-volume histogram parameter of Vx was defined as the percentage of total organ volume receiving a radiation dose of x (Gy) or more]. For radical radiotherapy, gross tumor volume (GTV) includes imaging and gastroscopy of visible primary tumors and any positive lymph nodes. Clinical tumor volume (CTV) consists of a longitudinal area 3–5 cm away from esophageal tumors, 0.8 cm outside the esophagus and any positive lymph nodes, and area delineation. For postoperative adjuvant radiotherapy for esophageal cancer, CTV consists of the area of the tumor

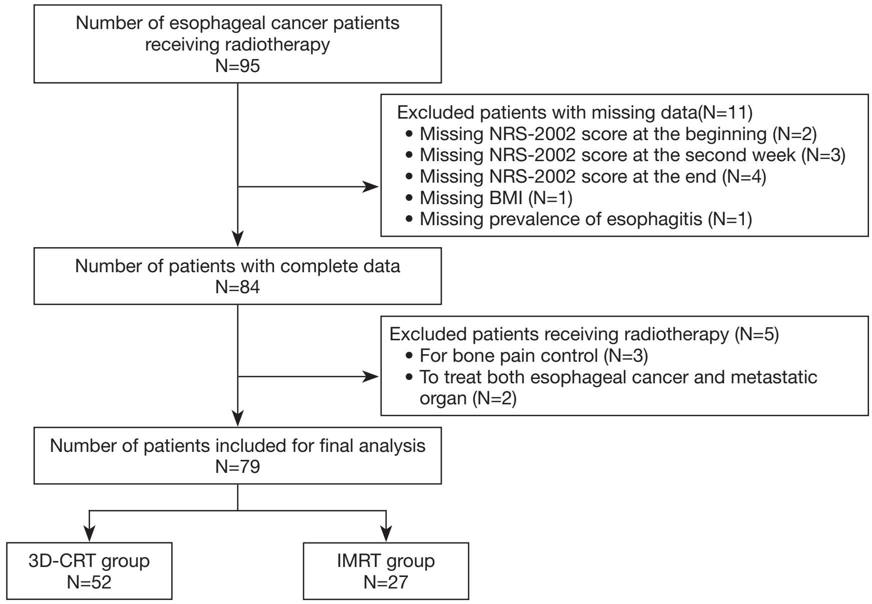

Figure 1 The flow chart of participants: 95 patients were screened at first, 11 were excluded for missing data, and 5 were excluded for that they received radiotherapy not only for esophageal cancer treatment, but also for bone pain control or other metastatic organs treatment. Finally, 79 patients were included for finally analysis. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy, NRS-2002, Nutrition Risk Screening 2002.

bed, positive lymph nodes, and area delineation.

The staging standard we adopted (including pathological staging and clinical staging) is the 8th edition of the TNM staging criteria for esophageal cancer co-published by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) (17,18). Neoadjuvant radiotherapy patients were not involved in our study. We included definitive and adjuvant radiotherapy patients. For patients who could not receive surgery or refused surgery, definitive radiotherapy was adopted. Adjuvant radiotherapy was used for patients receiving surgery. In regards to chemotherapy methods, monotherapy, doublet therapy, and triple therapy were adopted. Docetaxel or Tegio capsules were used for monotherapy. The combination of docetaxel and platinum was used for doublet therapy. The triple therapy was a combination of docetaxel, Tegio, and irinotecan. We defined concurrent chemoradiotherapy as the completion of 2 cycles of chemotherapy during radiotherapy. All concurrent chemoradiotherapy patients in our study completed 2 cycles of chemotherapy during radiotherapy. Patients with missing data or receiving radiotherapy not only for esophageal cancer control were excluded. None of the patients received a blood transfusion.

This study was approved by the Ethics Committee of Qilu Hospital. All participants were informed about the purpose, procedures, benefits, and potential risks of the study and their written consents were obtained.

Statistical analysis

Paired-T test was used to evaluate the nutrition status during radiotherapy in each group. Chi-square test and independent-sample *T*-test were applied to compare the nutrition status changes between the IMRT and 3D-CRT groups. P values <0.05 were considered statistically significant. All tests were two-sided. Statistical analyses were performed by using SPSS software (version 19.00; SPSS Inc., Chicago, IL, USA).

Results

Ninety-five esophageal cancer patients receiving radiotherapy were first included. Eleven patients with missing data were excluded, while 3 patients receiving radiotherapy for bone pain control, and 2 for esophageal cancer along with metastatic organ treatment were excluded. Finally, 79 patients (52 in the 3D-CRT group and 27 the in IMRT group) were included in this study (*Figure 1*).

Table 1 The characteristics of patients in 3D-CRT and IMRT groups[a]

Indexes	Group	3D-CRT (N=52)	IMRT (N=27)	P*
Age	<60	27	15	0.759
	≥60	25	12	
Gender	Male	47	25	0.743
	Female	5	2	
Smoking index (number of cigarette/d per year)	<400	31	17	0.622
	≥400	21	9	
Drinking index (g/d per year)	<658	32	22	0.071
	≥658	20	5	
Chronic disease history	None	34	18	0.924
	Yes	18	9	
Family history	None	46	25	0.564
	Yes	6	2	
Tumor site	Cervical	1	6	0.008
	Upper thoracic	5	4	
	Middle thoracic	38	11	
	Lower thoracic	8	4	
T stage	T1	2	2	
	T2	24	9	0.691
	T3	24	15	
	T4	2	1	
N stage	N0	9	4	
	N1	4	2	0.990
	N2	25	13	
	N3	14	8	
M stage	M0	32	16	
	M1	9	6	0.975
	Unclear	11	5	
cTNM stage	I	4	0	0.346
	II	7	6	
	III	34	16	
	IV	7	5	
Pathological type	Squamous cell cancer	50	26	0.975
	Adenocarcinoma	2	1	
Distant metastasis	None	32	16	0.860
	Yes	9	6	
	Not clear	11	5	
Received surgery	None	11	10	0.130
	Yes	41	17	
Chemoradiotherapy	Radiotherapy only	11	10	0.130
	Chemoradiotherapy	41	17	
Chemotherapy	Monotherapy	14	6	
	Doublet therapy	25	10	0.982
	Triple therapy	2	1	

Table 1 (continued)

[a], values are number in each group; *, Chi-square test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy.

Table 2 Radiotherapy doses and times in 3D-CRT and IMRT groups[a]

Index	Groups	Mean ± SD	P*
Doses (Gy)	3D-CRT	50.44±11.86	0.332
	IMRT	53.45±13.45	
Times	3D-CRT	25.69±5.91	0.784
	IMRT	25.22±7.74	

[a], values are mean ± SD in each group; *, independent sample *T*-test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; SD, standard deviation; N, number.

Firstly, we compared the baseline characteristics of the two groups. There was no difference in gender, age, smoking, drinking, chronic disease history, family history, TNM stage, distant metastasis, pathological type, and treatments. However, the difference was significant in the tumor site. Patients with cervical esophageal cancer in the IMRT group were more in number than those in the 3D-CRT group (P=0.008) (*Table 1*). The radiotherapy doses in the IMRT and 3D-CRT groups were 50.44±11.86 and 53.45±13.45 Gy (P=0.332), respectively, and the total radiotherapy times were 25.69±5.91 and 25.22±7.74 (P=0.784), respectively (*Table 2*).

Table 3 Comparison of nutrition associated indexes during radiotherapy[a]

Index	Groups	Beginning of RT	End of RT	P*
NRS-2002 score	3D-CRT	2.50±1.24	2.83±1.20	0.037
	IMRT	1.81±1.00	2.48±1.19	<0.001
Body weight (kg)	3D-CRT	61.07±12.69	57.06±12.45	<0.001
	IMRT	67.19±10.11	62.30±9.75	<0.001
BMI	3D-CRT	21.60±4.13	20.11±4.05	<0.001
	IMRT	23.31±3.06	21.06±3.04	<0.001
Hb (g/L)	3D-CRT	130.91±17.56	123.19±16.00	<0.001
	IMRT	133.19±18.37	116.52±24.63	<0.001
Lymphocyte ($\times 10^9$/L)	3D-CRT	1.72±0.68	0.68±0.60	<0.001
	IMRT	1.61±0.72	0.51±0.25	<0.001
Pre-albumin (g/L)	3D-CRT	21.92±6.01	19.79±6.88	0.092
	IMRT	20.81±6.15	18.36±5.07	0.056
Total protein (g/L)	3D-CRT	68.71±5.26	65.49±5.82	0.003
	IMRT	68.20±5.31	64.78±5.75	0.049
Albumin (g/L)	3D-CRT	42.25±3.56	38.55±6.63	0.005
	IMRT	42.46±4.25	39.32±5.07	0.001
Globulin (g/L)	3D-CRT	26.48±4.16	25.53±3.29	0.100
	IMRT	25.74±5.65	25.64±3.99	0.942

[a], values are mean ± SD in each group; *, paired-T test. 3D-CRT, three-dimensional conformal radiotherapy; Hb, hemoglobin; IMRT, intensity-modulated radiotherapy; NRS-2002, Nutrition Risk Screening 2002; RT, radiotherapy.

NRS-2002 score

According to NRS-2002 nutritional screening criteria, patients with an NRS-2002 score ≥3 were regarded as having malnutrition. Paired-T test indicated that the NRS-2002 score increased during radiotherapy treatment in both the 3D-CRT and IMRT groups (P=0.037 and P<0.001) (*Table 3*). Furthermore, we found that the malnutrition status did not differ in both groups at the baseline (40.4% *vs.* 22.2%, P=0.106). In the second week, 3D-CRT generated higher malnutrition probability than IMRT (57.7% *vs.* 33.3%, P=0.040). At the end of radiotherapy, there was no statistically significant difference between the two groups (55.8% *vs.* 37.0%, P=0.114). We further compared the changes in NRS-2002 scores during radiotherapy between the two groups. However, no significant statistical differences were found (all P>0.05) (*Table 4*).

Table 4 Comparison of NRS-2002 scores between 3D-CRT and IMRT groups[a]

Time points	Nutrition status	3D-CRT	IMRT	P*
Beginning of RT	Good nutrition	31 (59.6%)	21 (77.8%)	0.106
	Malnutrition	21 (40.4%)	6 (22.2%)	
Middle of RT	Good nutrition	22 (42.3%)	18 (66.7%)	0.040
	Malnutrition	30 (57.7%)	9 (33.3%)	
End of RT	Good nutrition	23 (44.2%)	17 (63.0%)	0.114
	Malnutrition	29 (55.8%)	10 (37.0%)	
End *vs.* beginning		0.32±1.09	0.67±0.83	0.129
Middle *vs.* beginning		0.38±1.08	0.62±0.97	0.310
End *vs.* middle		0.33±1.09	0.04±0.65	0.211

[a], values are number (percentage) or reduction rate of NRS-2002 score (mean ± SD) in each group; *, for continuous variables: by using Independent sample T-test; for enumeration data: by using Chi-square test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; NRS-2002, Nutrition Risk Screening 2002; RT, radiotherapy.

Body weight

Body weight decreased at the end of radiotherapy compared with the beginning in both the 3D-CRT and IMRT groups (both P<0.001) (*Table 3*). The baseline of body weight in the IMRT group was higher than that in the 3D-CRT group (67.19±10.11 *vs.* 61.07±12.69, P=0.023), which might have led to the difference between the two groups in the second week (64.11±9.66 *vs.* 59.00±12.23, P=0.046) and the end of radiotherapy (62.30±9.75 *vs.* 57.06±12.45, P=0.044). To compare the dynamic changes of weight during radiotherapy, we divided each group into three subgroups according to the boundaries of 5% and 10% between any two-time points (the end *vs.* the beginning, the second week *vs.* the beginning, and the end *vs.* the second week). However, no significant statistical differences were found (all P>0.05) (*Table 5*).

BMI

BMI index was compared between the two groups. Firstly,

Table 5 Comparison of body weight and BMI between 3D-CRT and IMRT groups[a]

Time points	Body weight (kg)			BMI (kg/m^2)		
	3D-CRT	IMRT	P*	3D-CRT	IMRT	P*
Beginning of RT	61.07±12.69	67.19±10.11	0.023	21.59±4.13	23.31±3.15	0.062
Middle of RT	59.00±12.23	64.11±9.66	0.046	20.79±3.99	22.29±2.96	0.090
End of RT	57.06±12.45	62.30±9.75	0.044	20.11±4.05	21.66±3.04	0.083
Reduction rate						
End *vs.* beginning			0.597			0.740
<5%	43	21		10	6	
5–10%	9	6		31	17	
≥7%	0	0		11	4	
Middle *vs.* beginning			0.740			0.663
<5%	12	5		41	19	
5–10%	30	18		9	7	
≥80%	10	4		2	1	
End *vs.* middle			0.659			0.592
<5%	43	24		40	23	
5–10%	8	3		11	4	
≥10%	1	0		1	0	

[a], values are number or mean ± SD in each group. *, for continuous variables: by using Independent sample T-test; for enumeration data: by using Chi-square test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; BMI, body mass index; RT, radiotherapy.

we found that BMI was reduced at the end of radiotherapy than at the beginning (both P<0.001) (*Table 3*). Then, we compared the IMRT and 3D-CRT groups. We found that there were no significant differences in BMI between the two groups at the beginning, middle, and end of radiotherapy. For the dynamic change of BMI during radiotherapy, we looked for the difference between any two time points. No statistical differences between the two groups were found (all P>0.05) (*Table 5*).

Hb

Hb level was also significantly reduced during radiotherapy in both groups (both P<0.001) (*Table 3*). We also analyzed its difference between the two groups, and found that the differences in Hb levels between the two groups at the beginning, middle, and end of radiotherapy were not significant, and there were also no statistical differences for the dynamic changes of Hb during the process of radiotherapy between the two groups (all P>0.05) (*Table 6*).

Lymphocyte count

Lymphocyte count was decreased during radiotherapy in both groups (both P<0.001) (*Table 3*). No difference was found for lymphocyte count at each point of radiotherapy between the two groups. Moreover, there were no statistical differences when comparing the dynamic changes during radiotherapy (all P>0.05) (*Table 6*).

Pre-albumin

No significant decrease was found during radiotherapy in both groups (P=0.092 in the 3D-CRT group and P=0.056 in the IMRT group) (*Table 3*). Moreover, we found that there were no significant differences when comparing pre-albumin level at the beginning, middle, or endpoints during radiotherapy nor were there any dynamic changes during

Table 6 Comparison of Hb, lymphocyte and pre-albumin levels between 3D-CRT and IMRT groups[a]

Time points	Hb (g/L)			Lymphocyte ($\times 10^9$/L)			Pre-albumin (g/L)		
	3D-CRT	IMRT	P*	3D-CRT	IMRT	P*	3D-CRT	IMRT	P*
Beginning of RT	131.52±17.84	133.00±17.39	0.736	1.69±0.65	1.65±0.76	0.796	22.08±5.69	20.54±5.96	0.353
Middle of RT	129.90±12.51	124.25±15.56	0.279	0.75±0.44	0.61±0.30	0.240	19.63±6.04	17.16±5.24	0.239
End of RT	124.28±16.55	116.52±24.63	0.142	0.67±0.58	0.51±0.25	0.234	19.81±6.97	18.26±4.80	0.348
Reduction rate									
End *vs.* beginning			0.107			0.681			0.130
<5%	19	4		3	1		15	5	
5–10%	7	5		0	0		1	3	
≥10%	15	12		37	20		18	7	
Middle *vs.* beginning						0.510			0.579
<5%	13	5	0.691	1	0		7	2	
5–10%	4	3		0	0		1	0	
≥10%	9	3		25	11		10	6	
End *vs.* middle			0.582			0.706			0.035
<5%	15	5		9	4		11	2	
5–10%	2	2		1	1		0	1	
≥10%	6	2		13	4		2	4	

[a], values are number or mean ± SD in each group. *, for continuous variables: by using Independent sample T-test; for enumeration data: by using Chi-square test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; Hb, hemoglobin; RT, radiotherapy.

radiotherapy between the 3D-CRT and IMRT groups (all P>0.05) (*Table 6*).

Total protein

Total protein level was significantly reduced during radiotherapy in both the 3D-CRT and IMRT groups (P=0.003 and 0.049, respectively) (*Table 3*). No differences were found when comparing its levels at the 3-time points, and no differences were found in dynamic changes during radiotherapy between 3D-CRT and IMRT (all P>0.05) (*Table 7*).

Albumin

Albumin levels were significantly reduced during radiotherapy in both the 3D-CRT and IMRT groups (P=0.005 and 0.001, respectively) (*Table 3*). No differences were found when comparing its levels at the beginning, middle or endpoints, nor were there any dynamic changes during radiotherapy between the IMRT and 3D-CRT groups (all P>0.05) (*Table 7*).

Globulin

No significant decrease was found during radiotherapy in both groups (both P>0.05) (*Table 3*). Furthermore, no differences were found when comparing its level at the 3 time points, nor were there any dynamic changes during radiotherapy (all P>0.05) (*Table 7*).

Radiation esophagitis

We compared the prevalence of radiation esophagitis at the end of radiotherapy. In all, 28 of 52 (53.8%) patients were diagnosed with radiation esophagitis in the 3D-CRT group, while 13 of 27 (48.1%) patients were diagnosed in the IMRT group. No difference between 3D-CRT and IMRT

Table 7 Comparison of total protein, albumin and globulin levels between 3D-CRT and IMRT groups[a]

Time points	Total protein (g/L)			Albumin (g/L)			Globulin (g/L)		
	3D-CRT	IMRT	P*	3D-CRT	IMRT	P*	3D-CRT	IMRT	P*
Beginning of RT	68.37±5.00	68.55±5.29	0.892	42.21±3.40	42.54±3.77	0.727	26.17±3.82	25.98±5.33	0.881
Middle of RT	68.05±4.04	66.28±4.09	0.252	40.11±2.69	40.42±3.27	0.790	27.95±3.37	25.86±4.36	0.184
End of RT	65.42±5.75	64.53±5.44	0.581	38.26±6.63	39.33±4.79	0.541	25.69±3.38	25.37±3.87	0.767
Reduction rate									
End *vs.* beginning			0.777			0.889			0.822
<5%	13	5		11	5		14	5	
5–10%	4	1		4	1		3	1	
≥10%	3	2		5	2		3	2	
Middle *vs.* beginning			0.535			0.206			0.482
<5%	16	8		14	7		20	9	
5–10%	12	3		5	5		3	3	
≥10%	8	5		17	4		13	4	
End *vs.* middle			0.549			0.138			0.283
<5%	6	5		6	6		3	4	
5–10%	3	1		1	1		5	1	
≥10%	4	1		5	0		26.17±3.82	25.98±5.33	0.881

[a], values are number or mean ± SD in each group. *, for continuous variables: by using Independent sample T-test; for enumeration data: by using Chi-square test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; RT, radiotherapy.

Table 8 Comparison of radiation esophagitis and radiotherapy completion between 3D-CRT and IMRT groups[a]

Items	3D-CRT	IMRT	P*
Radiation esophagitis			0.631
Grade 0–1	24 (46.2%)	14 (51.9%)	
Grade ≥2	28 (53.8%)	13 (48.1%)	
Radiotherapy completion			0.386
None	12 (23.1%)	4 (14.8%)	
Yes	40 (76.9%)	23 (85.2%)	

[a], values are number (percentage) in each group; *, Chi-square test. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy.

was found (P=0.631) (*Table 8*).

Treatment completion

The treatment completion rate was analyzed. In all, 40 of 52 (76.9%) patients completed the radiotherapy plan in the 3D-CRT group, while 23 of 27 (85.2%) patients finished the treatment plan in the IMRT group. There was no significant difference between the two groups (P=0.386) (*Table 8*).

Discussion

Radiation therapy is a double-edged sword, but the relevant technological innovations can reduce the side effects of normal organs and improve treatment efficacy. However, side effects will still inevitably occur over the course of treatment. It has been reported that more than 70% of esophageal cancer patients experience malnutrition, which is caused mainly by anorexia and dysphagia, before the treatment starts (19). Dysphagia-related nutrition deficiency may be even worse during the treatment, and, as a result, weight loss may occur. During RT, nutritional interventions positively influence outcomes, including improving nutritional intake and status, decreasing morbidity of RT toxicity , and improving quality of life (20). A systematic review showed the beneficial effects of individualized dietary counseling on nutritional status and quality of life, compared to no counseling or standard nutritional advice (21). It was also reported that after preforming enteral tube feeding with the energy of 25 kcal × kg/d in esophageal cancer patients during radiotherapy, prognostic nutritional index and the key nutritional index reflecting prognosis, significantly decreased (22). Cong *et al.* (23) found that nutritional status was significantly improved in a nutrition support group. Meanwhile, nutritional interventions improved the completion of radiotherapy and decreased the average length of hospital stay of esophageal cancer patients. The major goal of nutrition intervention is to favorably influence body composition, with the potential to improve cancer therapy outcomes, morbidities, and ultimately, prognosis. To be effective, individualized counselling has to be based on a thorough assessment of various nutritional and clinical parameters: nutritional status and dietary intake, usual dietary pattern, intolerances or food aversions, patients' psychological status, autonomy, cooperation, and need for help or support of others in the act of eating (24). A five-step nutritional treatment was applied to malnutrition patients. In our department, we carry out nutrition intervention for all malnutrition patients. Therefore, we did not specifically analyze the role of nutrition intervention.

IMRT technology achieves better target dosimetry distribution compared to 3D-CRT and improves clinical outcomes. It improves the local control rate and long term survival while reducing side effects in various cancers like nasopharyngeal carcinoma (25,26), head and neck cancer (27), and pancreatic cancer (28). We investigated whether IMRT generates advantages in nutrition status. However, this study indicates that IMRT technology did not decrease malnutrition risk compared to 3D-CRT.

The esophagus is a string organ. The radiation field covers cancerous tissues and part of the normal esophageal tissues. The radiation dose is relevant to radiation esophagitis, which is the main cause of eating pain and further malnutrition. It always appears at about 2–3 weeks from the beginning of radiotherapy and lasts for more than 2 weeks after radiotherapy (29). In our study, the incidence of radiation esophagitis between the two groups was not significant, which may be the main reason for the unobvious difference in nutritional status between the two groups. Advances in IMRT technology manifest in the reduction in dosimetry distribution on surrounding normal tissues, but not the effect on nutritional status during radiotherapy. A similar conclusion has been reported in head and neck cancer (15), as mentioned previously.

The proportion of cervical esophageal cancer patients was higher in the IMRT group than the 3D-CRT group. IMRT is recommended for cervical esophageal cancer treatment because normal radiosensitive structures in the head and neck are close to the radiation area, and higher radiation doses are commonly required in this area (3). In cervical esophageal cancer, IMRT provides superior target volume coverage and conformity, with decreased dose to normal structures (30). It was reported that higher RT doses were associated with a borderline improved OS (31). However, the number of patients in the 3D-CRT group was not enough for statistical analysis, so we did not compare the effect of the two technologies on cervical esophageal cancer.

There are some limitations to this study. Firstly, this study is retrospective, not prospective, and has a small sample size. Secondly, all patients come from the same hospital which may lead to selection bias. Thirdly, chemotherapy methods of concurrent chemoradiotherapy are not uniform, but we did not compare different chemotherapy methods because of the small sample size. Moreover, in this study, ONS were used for all patients with an NRS-2002 score less than 3. PN and EN treatments were not used in our study. Therefore, we did not analyze the effect of different nutrition intervention methods. A multi-center study with a large sample is required to validate these findings.

In conclusion, malnutrition occurs during radiotherapy, and IMRT did not significantly decrease the risk of this malnutrition in esophageal cancer patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of Qilu Hospital. All participants were informed about the purpose, procedures, benefits and potential risks of the study, and their written consents were obtained.

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