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DOSIMETRIC COMPARISON OF USING CONFORMAL RADIOTHERAPY VERSUS INTENSITY MODULATED RADIOTHERAPY IN THE TREATMENT OF MID ESOPHAGEAL CARCINOMA

Oncology

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ABSTRACT

BACKGROUND: Esophageal carcinoma accounts for 6% of all GI malignancies in the world. The treatment of cancer of the esophagus has evolved from 2 dimensional conformal radiotherapy to the present day image guided radiotherapy .Due to the presence of many vitals organs like the spinal cord, heart, lung which lie in close proximity to the esophagus, the treatment of this cancer has been challenging. In our setting most of the cases usually present with tumors in the mid and distal esophagus. Over the past few years, studies based on dosimetric parameters have revealed the efficacy of IMRT in the treatment of these cancers owing to its superior target volume coverage and conformality with decreased dose to the normal structures.

OBJECTIVES: To compare the 3D conformal and IMRT technique with respect to conformality of target coverage and to analyze the dose received by various structures around the esophagus.

METHODS: A prospective comparative study with purposive sampling of 25 patients of esophageal cancer being treated with radical chemo radiation or radiation alone were included in the study .Three plans were created for all patients, one 3DCRT and two IMRT plans using 5 beam and 7 beams were made and dosimetric parameters were compared in each of these plans to analyse the structures around the esophagus will benefit from using more advanced planning techniques.

RESULTS: Patients in our study had performance scores ranging from 70 to 90 with the mean GTV length being 8.74 cms and the mean PTV length 18.34 cms. The percentage of PTV receiving 95% of the dose was 84.23% in 3DCRT, 93.67% in 5 beam IMRT and was 94.73% in 7 beam IMRT plans thus showing statistically significant improvement in the IMRT plans as compared to 3DCRT plans ($p<0.001$). The volume of the heart that received 40Gy in the 3DCRT plans was 67.23% whereas in the 5 beam IMRT plans was 30.77% and 30.36% in the 7 beam IMRT plans, all of which was found to be statistically significant.($p<.001$). The V20 of whole lung was 23.64% in the 3DCRT plans and 39.68 in the 5 beam IMRT plans and 36.69 in the 7 beam IMRT plan.

CONCLUSION: In this study it was found that IMRT plans had significantly better PTV coverage as compared to 3DCRT plans. However the lung doses were higher in the IMRT plans as compared to 3DCRT. When the 5 beam and 7 beam IMRT plans were compared it was found that the 7 beam IMRT plans had a lower lung dose as compared to the 5 beam IMRT plans. The heart doses were significantly lower in the IMRT plans as compared to 3DCRT plans.

KEYWORDS

Esophageal cancers; Dosimetric study; 3DCRT;IMRT

INTRODUCTION

Esophageal carcinoma accounts for 6% of all GI malignancies in the world[1].

Smoking is one of the most important risk factors for esophageal carcinoma[2]. AJCC 8 has defined esophageal cancers as those arising from the cricopharyngeus muscle up to tumors arising within the proximal 5cm of the stomach extending into the esophagus.. It has been noted that there has been an increase in cases of adenocarcinoma when compared to squamous cell carcinoma over the last few decades. Symptoms of this disease usually do not appear early and hence patients present in late stages and thereby also have a poor prognosis. The treatment of cancer of the esophagus has evolved from 2 dimensional conformal radiotherapy (CRT) to the present day image guided radiotherapy. Due to the presence of many vitals organs like the spinal cord, heart, lung which lie in close proximity to the esophagus,the treatment of this cancer has been challenging. In the treatment of esophageal cancer in the cervical esophagus a study by Fenkell et al has shown that based on dosimetric parameters internsity modulated radiotherapy (IMRT) provides superior target volume coverage and conformality with decreased dose to the normal structures[3]. In our setting most of the cases usually present with tumors in the mid and distal esophagus.

The study will be using conformal radiotherapy to treat all the patients and a 5 and 7 beam IMRT plan will be simulated on the planning system for these patients and the doses received by various organs around the esophagus will be compared. The doses delivered to the heart and lung will be assessed to infer if IMRT is superior to CRT in lowering the doses and thus complications in normal organs. The target coverage will also be assessed between the three plans .Standard treatment protocols will be used on the patients delivering a dose of 54Gy as per institutional protocol.

MATERIALS AND METHODS:

SOURCE OF DATA:

Patients attending the Department of Radiotherapy, Father Muller Medical College hospital Mangalore from October 2016 to June 2018 with histological proven esophageal cancer.

INCLUSION CRITERIA:

1. Histologically diagnosed cases of carcinoma oesophagus receiving radical chemoradiation or radiation alone with a curative intent using the 3DCRT technique.
2. Oesophageal cancer originating from the middle third of the oesophagus.

EXCLUSION CRITERIA:

1. Patients on palliative intent radiotherapy
2. Patients who have received radiation before
3. Cervical and GE junction tumors

METHOD OF COLLECTION OF DATA:

- A prospective comparative study of patients coming to the hospital for carcinoma Esophagus was done. The sampling used was purposive sampling technique.
- A treatment planning CT scan with intravenous contrast was taken for all patients making 2.5mm cuts from the base to skull to the L5 vertebral level.
- The GTV was designed by diagnostic CT scan film and Upper gastoduodenoscopy findings on the planning CT scans. Contours of the gross tumor volume (GTV) were expanded by 1.5 cms laterally and by 4 cms superiorly and inferiorly to get the CTV. The CTV was cropped in anatomical boundaries to tumor spread
- The PTV was then be expanded by 5mm in order to account for setup errors

- All patients will be planned for 3DCRT to a dose of 54 Gy in 27 fractions using ECLIPSE 13 treatment planning system with analytical anisotropic algorithm that accounts for tissue inhomogenisity and photons were delivered from a **6** MV VARIAN linear accelerator. Conformal RT plans uses opposed Anterior- posterior fields till 36 Gy followed by three field technique till 54Gy (2 posterior field and 1 anterior field) where the spinal cord was shielded by using MLCs. \
- An alternate IMRT plan was performed using the ECLIPSE version 13 inverse planning algorithm and dynamic technique of IMRT to evaluate the dose conformality and dose to organ at risk and were compared to the similar parameters of the 3DCRT plan.
- There was no elective lymph nodal radiation given. A comparative plan was then generated by the planning system using and comparison was made based on the doses received by various organs around the esophagus like the lung, heart and spinal cord in the three plans.
- An analysis was made based on the dose received to various like the heart, lung, and spinal cord.
- Three plans were made for each patient and the doses received by various organs were studied and compared between these three plans. Doses received by the organs were compared with RTOG 0972/CALGB 36050 guidelines. These guidelines state that the lung V20 must be less than 35%, spinal cord point dose must be less than 45 Gy and heart dose must be less than 60, 45, 40 for 1/3, 2/3, 3/3 of the heart respectively. Plans were made such that 95% of the isodose surfaces cover at least 99% of the PTV.

RESULTS

In our study total of 25 patient with oesophageal carcinoma were taken and dosimetric evaluation of different plan were assessed. 36% of the patients were found to be in the age group 50 - 60 years. 28% in the age group of 40-50 yeras. 20 % in the age group of 30-40 years. 16% in the age group of 30-40 years.72% of the patients in the study were female and 28% were male. The performance score of all patients taken into the study was between 70 and 90. The GTV length were between 3.3cms to 13cms and the mean was 8.72cms. The PTV length was between 13.5cms to 22cms and the mean was 18.34cms.

TABLE 1: comparison of doses received by various OARs and PTV coverage

Parameters			Mean Difference (I-J)	Std. Error	p	
Left Lung	@3DCRT	IMRT5	-15.511	2.078	p<0.001	HS
		IMRT7	-12.805	1.761	p<0.001	HS
	IMRT5	IMRT7	2.706	1.133	.075	
95% PTV	@3DCRT	IMRT5	-9.441	1.138	p<0.001	HS
		IMRT7	-10.499	1.019	p<0.001	HS
	IMRT5	IMRT7	-1.058	.644	.341	
Heart	@3DCRT	IMRT5	36.464	2.573	p<0.001	HS
		IMRT7	36.869	2.547	p<0.001	HS
	IMRT5	IMRT7	.405	.543	1.000	
Right Lung	@3DCRT	IMRT5	-16.566	1.053	p<0.001	HS
		IMRT7	-13.297	.823	p<0.001	HS
	IMRT5	IMRT7	3.269	.937	p<0.001	HS

The above table shows that the PTV coverage is significantly better in the IMRT plans as compared to 3DCRT plans. (p<0.001). The heart dose is significantly lower in the IMRT plans s compared to 3DCRT plans. (p<0.001).The lung doses is significantly higher in the IMRT plans as compared to the 3DCRT plans.

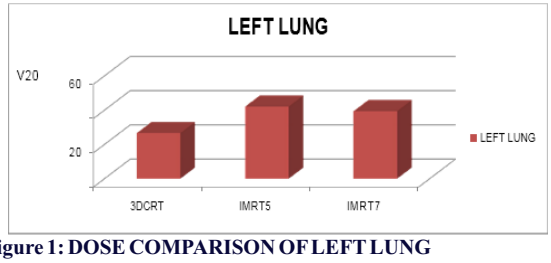

Figure 1: DOSE COMPARISON OF LEFT LUNG

There was a statistically significant(p<0.001) reduction in the dose to the left lung in the 3DCRT plans when compared to the IMRT plans ,where the mean V20 of left lung was 26.69% in the 3DCRT plans as compared to 42.20% in 5 beam IMRT and 39.50% in 7 beam IMRT plans. (p<0.001) There was no statistically significant difference between the doses to the left lung in both the IMRT plans.

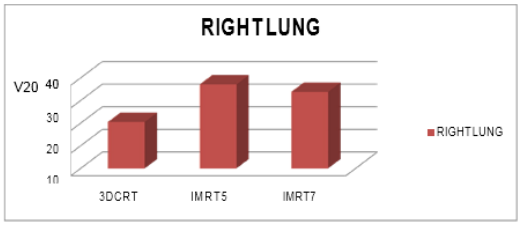

Figure 2: DOSE COMPARISON OF RIGHT LUNG

There was a statistically significant reduction in the doses to the right lung in the 3DCRT when compared to the IMRT plans where the V20 was 20.59% in 3DCRT as compared to 37.16% in 5 beam IMRT and 33.89% in the 7 beam IMRT plan..(p<0.001) There was also a statistically significant reduction in the doses to the right lung in the 7 beam IMRT plan as compared to the 5 beam IMRT plan (p<0.01).

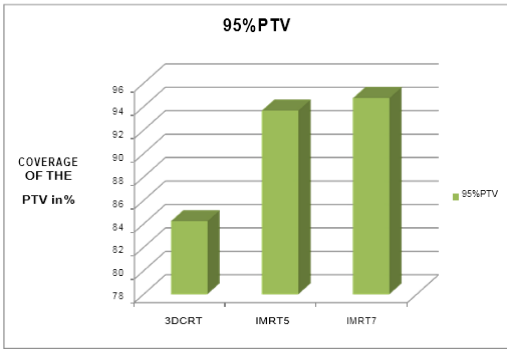

Figure 3: 95% PTV COVERAGE

The 95% PTV coverage i.e. the percentage of the PTV receiving 95% of the prescribed dose was 84.23% in the 3DCRT plans and 93.67% in 5 beam IMRT and 94.73% in 7 beam IMRT plans. (p<0.001) There was a statistically significant better coverage of the PTV in IMRT plans as compared to 3DCRT plans. (p<0.001) As mentioned in the methodology the 3DCRT plans were planned in two phases. Phase one was given up to 36GY in 18 # which was delivered by placing beams in the AP/PA portals. The 3 field oblique plans were created after 36GY in order to meet the dose constraints of the spinal cord and when doing this PTV coverage had to be compromised by shielding the spinal cord by the MLCs. Hence the PTV coverage was significantly lower in the 3DCRT plans as compared to the IMRT plans.

There was a statistically significant increase in the dose received by the heart in the 3DCRT plan as compared to the IMRT plans. .(p<0.001) Volume of the heart receiving 40 Gy was 67.33% in the 3DCRT plans as compared to 30.77% and 30.36% in the 5 beam and 7 beam IMRT plans. There was no significant difference in the heart dose between the two IMRT plans.

TABLE 2: whole lung V20 and mean lung dose

		N	Mean	Std. Deviation	95% Confidence Interval for Mean		Anova F	p
					Lower Bound	Upper Bound		
Lung V20	3DCRT	25	23.642	6.473	20.970	26.314	114.644	p<0.001
	IMRT 5	25	39.681	7.237	36.693	42.668		HS
	IMRT 7	25	36.693	6.761	33.902	39.484		
Mean Lung	3DCRT	25	12.762	3.495	11.319	14.204	114.503	p<0.001
Dose	IMRT 5	25	21.422	3.907	19.809	23.035		HS
	IMRT 7	25	19.817	3.654	18.308	21.325		

The mean of the V20 was 23.64% in the 3DCRT arm and 39.68% in the 5 beam IMRT arm and 36.69% in the 7 beam IMRT arm. The whole lung V20 was also found to be lower in the 3DCRT plans as compared to the IMRT plans. .(p<0.001) When the whole lung V20 was compared between the two IMRT plans it was found to be statistically lower in the 7 beam IMRT plan as compared to the 5 beam IMRT plan . The mean of the whole lung dose was 12.76 in 3DCRT

plans and 21.422 in 5 beam IMRT plans and 19.81 in the 7 beam IMRT plans .the mean lung dose was also lower in the 3DCRT plan as compared to the IMRT plans. (p<0.001) There was also a statistically significant reduction in the mean lung dose of the 7 beam IMRT plans as compared to 5 beam IMRT plan.(p<0.01).

DISCUSSION

A total number of 25 patients treated at the department of Radiation Oncology, Father Muller Medical College Hospital were included in this study.

Patients in our study had performance scores ranging from 70 to 90 with the mean GTV length being 8.74cms and the mean PTV length 18.34cms.The range of GTV length was between 3.3cms and 13cms and that of PTV between 13.5cms to 22cms. Most dosimetric studies as well as clinical trials have not mentioned the mean length of the GTV or PTV. This was found to be an important factor especially in mid esophageal cancers as the length of the PTV had a correlation to the dose received by the lung. Higher the PTV length more amount of lung volume would need to be irradiated to achieve adequate PTV coverage.

In a study in Manchester by Griffiths et al, it was found that tumor length greater than 3.5 cm was associated with increasing T stage (p<0.0001), N stage (p<0.032), overall stage (P<0.003), and involvement of the longitudinal resection margins (P<0.02)[11]. Univariate analysis found tumor length greater than 3.5 cm was associated with worse overall survival compared with shorter tumors (P<0.0002). Tumor length remained a significant prognostic factor on multivariate analysis (P<0.04)[11]. These findings were confirmed by study in china by Wu et al who concluded that Esophageal tumor length is a predictive factor for long- term survival especially for lower tumor stage, absence of metastatic lymph nodes and lower TNM stage patients[12].

The above studies show that tumor length in addition to stage of the tumor is important prognostically in the treatment of esophageal cancer. Also, dosimetrically larger the treatment length, larger will be the lung volume that will need to be treated and hence larger will be the lung dose in the IMRT plans.

The PTV coverage was better in the IMRT plans and was found to be highly statistically significant when 3DCRT was compared to IMRT plans. It was 84.23% in 3DCRT, 93.67% in 5 beams IMRT and was 94.73% in 7 beam IMRT plans. There was no statistically significant difference in between the two IMRT plans. This is in concurrence with a study by Wu et al in Hong Kong where they found that the PTV coverage and conformity index was far superior in IMRT plans as compared to 3DCRT plans[13].

The dose received by the heart was significantly lower in the IMRT plans as compared to the 3DCRT plans. The mean dose in the 3DCRT plans was 67.23% whereas in the 5 beam IMRT plans was 30.77% and 30.36% in the 7 beam IMRT plans. There was a statistically significant reduction in the dose to the heart in the IMRT plans as compared to the 3DCRT plans but there were no significant differences between the 5 and 7 beam IMRT plans.

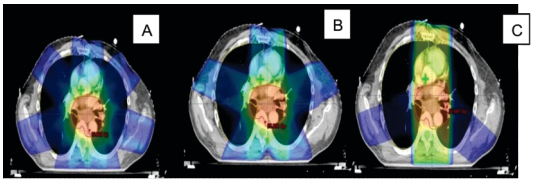

Figure 4: : DOSE COLOR WASH OF 7 BEAM IMRT, 5 BEAM IMRT AND 3DCRT (PLAN SUM)

This was in accordance with a a study done by Kole at al where it was found that there was a significant reduction in the mean heart dose in the IMRT plans as compared to a 3DCRT.[141] They also found that in the dose volume histograms there was a reduction in the volume of the heart exposed to doses above 10 Gy which was also found to be true in this study. This has an important clinical significance as the doses to the heart have been correlated with both acute toxicities like pericardial effusion where if the V30 is more than 46% there is a 73% chance of pericardial effusion as compared to V30 less than 46 % where the effusion chances are 13% .This was reported by Wei et al in a study on risk factors of pericardial effusion in esophageal cancers treated with definitive radiotherapy[10].

The doses received by the lungs were significantly higher in the IMRT plans when compared to the 3DCRT plans in our study. The mean V20 of the left lung dose was 26.69% in the 3DCRT plans, 42.20% in the 5 beam IMRT plans and 39.50% in the 7 beam IMRT plans. There was a statistically significant difference between the 3DCRT plans and the IMRT plans. There was no statistically significant difference between the 5 beam and the 7 beam IMRT plans in regards to the left lung dose

The right lung dose was also significantly lower in the 3DCRT plans as compared to the IMRT plans. The mean V20 was 20.59% in 3DCRT, 37.16% in the 5 beam IMRT plan and 33.89% in the 7 beam IMRT plans. The dose were statistically highly significantly low in 3DCRT as compared to IMRT plans. There was also a statistically significant reduction the doses to the right lung when 7 beam IMRT was compared to 5 beam IMRT.

The V20 of whole lung was 23.64% in the 3DCRT plans and 39.68 in the 5 beam IMRT plans and 36.69 in the 7 beam IMRT plan. There was a highly significant reduction in the doses received by the lungs in the 3DCRT plans when compared to the IMRT plans with p<0.001. there was also a significant reduction in the whole lung V20 in the 7 beam IMRT plan as compared to 5 beam IMRT with p<0.01.

This was also found to be similar to another study done in new Delhi by Kumar G et al in Rajiv Gandhi cancer institute where they found that the V20 was higher in the IMRT arm as compared to the 3DCRTarms and they found that there was a statistically significant increase in the pneumonitis rates too were higher in the IMRT arms as compared to 3DCRT arms[15].

CONCLUSION

To conclude, it can be said that there are benefits when compared to better coverage of the PTV and lower heart doses with IMRT plans, however the lung doses were higher in IMRT plans as compared to 3DCRT plans. Thus in patients where dose constraints can be met IMRT looks like an attractive option that needs to be further analyzed with toxicity scoring and overall survival analysis of patients in future studies.

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