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TO EVALUATE THE EFFECT OF DOSE ESCALATION USING SIMULTANEOUS INTEGRATED BOOST TECHNIQUE IN UNRECECTABLE ESOPHAGEAL CANCER – A PROSPECTIVE CLINICAL STUDY

Oncology/Radiotherapy

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ABSTRACT

Background : The esophagus is one of the common sites of Malignancy in the Gastro-intestinal tract. Esophageal cancer ranks seventh in terms of incidence (604,000 new cases) and sixth in mortality overall (544,000 deaths), the latter signifying that esophageal cancer is responsible for one in every 18 cancer deaths in 2020. To achieve high dose of irradiation of on tumor without significantly increasing the exposure of organs at risk (OAR), the SIB technique is generally employed, which can give a conformable heterogeneous dose distribution inside one radiation field simultaneously. **Objective:** To evaluate the effect of dose escalation using simultaneous integrated boost technique (SIB) in unresectable esophageal cancer. **Method:** The present prospective clinical study involving 33 patients of carcinoma Esophagus with unresectable disease status conducted during June 2019 to May 2020 in Department of Radiation Oncology at Regional Cancer Centre of Pt JNM Medical College Raipur, Chhattisgarh. **Result:** In this study maximum patient 45% are between 50-60 year age group and minimum 15% are between 40-50 year age group. Maximum percentages of patient 54.54% were males and 45.45% were females. In this study maximum of lower esophageal region was involved in 51.51% cases and in 48.48% cases middle part was involved. In this study 57.57% of patients were having T4 disease, 36.36% of patients were having T3 disease, 6% of patients had T2 disease and none of patients were diagnosed of stage T1. In our study of 25 patients, in left breast ipsilateral LUNG dose data analysis was reported as the volume 1004.6 ±235.14 , Dmin 55 .21 ± 787 .82, Dmax 4187.33 ±149.1c Gy, Dmean 1869.07 ±621.64c Gy, V5 90.38 ± 8.46 %, V10 64.10 ± 12.75%, V20 25.05 ±3.69 %. **Conclusion:** With the advancement in newer radiotherapy planning and treatment techniques dose have been reduced from 60 Gy to 50 Gy, but the routine use of heterogeneity corrections may have inadvertently reduced the treatment dose still further. Not surprisingly, the GTV is at high risk of failure after chemoradiation therapy for unresectable esophageal cancer. This planning series illustrates that, theoretically, using an SIB-IMRT technique can safely increase the dose to the GTV while also reducing toxicity to critical structures.

KEYWORDS

Response, SIB, Radiation Therapy, Lung, Esophagus

INTRODUCTION

The esophagus is one of the common sites of Malignancy in the Gastro-intestinal tract. Esophageal cancer ranks seventh in terms of incidence (604,000 new cases) and sixth in mortality overall (544,000 deaths), the latter signifying that esophageal cancer is responsible for one in every 18 cancer deaths in 2020. [1] Approximately 70% of cases occur in men, and there is a 2-fold to 3-fold difference in incidence and mortality rates between the sexes. [2] Rates are higher in transitioned versus transitioning countries for men but comparable for women. Esophageal cancer is unique among the gastrointestinal tract malignancies because it embodies two distinct histopathological types, squamous cell carcinoma and adenocarcinoma. Although survival rates for all esophageal cancer patients are uniformly dismal, regardless of race and gender, 5 year survival rates have significantly improved since the 1970s based on surveillance, epidemiology, and End results (SEER) population based tumor registries reporting. African Americans mans poorly compared to women. There is no survival differences related to cell type (squamous cell carcinoma vs. adenocarcinoma). Less than 15% of patients diagnosed with esophageal carcinoma are cured, with approximately half of the patients presenting with unresectable or metastatic disease. [3] Concurrent chemoradiation has been widely recognized as a viable option for these patients specially. Local-regional recurrence of cancer after chemoradiation remains a common problem. [1] The survival outcome and local control of the tumor of CCRT are still poor, and local failure occurs in about 50% patients, indicating that the standard radiation dose (50.4 Gy) is inadequate to achieve satisfactory tumor local control. To achieve high dose of irradiation of on tumor without significantly increasing the exposure of organs at risk (OAR), the SIB technique is generally employed, which can give a conformable heterogeneous dose distribution inside one radiation field simultaneously. This technique has been successfully implemented to treat cancers of various regions such as head and neck, prostate, cervix, etc. [1] Many studies on SIB has been done for EC in terms of dosimetry , proving that it can increase the dose in high-risk areas without increasing the irradiation of normal tissues. Moreover, SIB can significantly reduce the workload for both physicians and physicists in terms of simulation, delineation and plan. [4]

OBJECTIVE

To evaluate the effect of dose escalation using simultaneous integrated boost technique (SIB) in unresectable esophageal cancer.

MATERIAL AND METHODS

The present prospective clinical study involving 33 patients of carcinoma Esophagus with unresectable disease status conducted during June 2019 to May 2020 in Department of Radiation Oncology at Regional Cancer Centre of Pt JNM Medical College Raipur, Chhattisgarh.

Patient Inclusion Criteria

- Cytologically and histopathologically proven cases of carcinoma esophagus.
- Unresectable locally advanced carcinoma mid and lower esophagus.
- Age less than 65 years.
- ECOG performance score of 0 to 2.
- T1-4 N0 M0 stage according to TNM system

Exclusion Criteria

- Already treated case of esophageal carcinoma either with surgery, radiotherapy, chemotherapy, or antineoplastic biological therapy.
- Presence of severe co morbidities that will put the patient at a significantly higher risk or will damage the protocol compliance
- Metastasis
- Age >65 year
- ECOG Score >2

Radiotherapy Planning

All Patients have been simulated with appropriate immobilization according to the standard protocol Planning CT scans is acquired with 3mm axial images from thyroid to pubic symphysis and images will be transferred to contouring station. Treatment planning was performed

using VARIAN (eclipse V.S 13.6.23) treatment planning system. TV and OARs will be contoured as per standard protocol The GTV was delineated by the using all available resources CT data, endoscopic reports, and diagnostic CT images, The GTV was expanded to the clinical target volume (CTV) by extending coverage 3 cm superiorly, 1 cm laterally, 3 cm inferiorly, and. The planning target volume (PTV) was the CTV plus a uniform 0.5-cm expansion margin. Organs at risk were outlined.

Dose Prescription

All the patients are treated with IMRT Technique Treatment plans were generated using Intensity modulated RT [IMRT] to 50.4 Gy, and SIB-IMRT to 64.8 Gy) and optimized for 33 patients with mid and distal esophageal cancer. All plans were constructed to deliver the target dose in 28 fractions using heterogeneity corrections. Isodose distributions were evaluated.

Follow up

Treatment toxicities during course of radiation and after radiation have been compared using QUANTEC data and RTOG, CTC version 5.0 respectively. Patients were followed weekly during treatment then after 1, 3 and 6 monthly. During follow up examination, any recurrence and metastasis were carefully looked for and appropriate chemotherapy was given.

RESULTS

Age

In these study maximum patients 45% are between 50-60 year age group and minimum 15% are between 40-50 year age group.

Table 1 Age Wise Distribution Of Patients

Age Groups (years)	All Patients No.	(%)
< 40	4	15
40-50	8	20
50-60	13	45
60-70	8	20

Gender

In this study maximum percentage of patient 54.54% were males and 45.45% were females

Table 2 Gender Wise Distribution

Menopausal Status	All Patients No.	(%)
Male	18	54.54
Female	15	45.45

Socioeconomic Status

Maximum patients 33.3% were belonged to upper lower socioeconomic class and minimum percentage 18.18% were belonged to lower middle socioeconomic class.

Table 3 Site Wise Distribution

Class	Frequency (n)	Percentage (%)
Lower Middle	6	18.18
Lower	11	33.33
Upper Lower	16	48.48

Site Of Disease

In this study maximum of lower esophageal region was involved in 51.51% cases and in 48.48% cases middle part was involved.

Table 4 Site Of Disease

part	Frequency (n)	Percentage (%)
Middle	16	48.48
Lower	17	51.51

Histology

In our study maximum 69.69% cases had MDSCC histology and 30.30% cases has WDSCC histology while 27.27% case were diagnosed as PDSCC histology

Table 5 Histology Wise Distribution

Class	Frequency (n)	Percentage (%)
WDSCC	1	30.30
MDSCC	23	69.69
PDSCC	9	27.27

Composite Stage Wise Distribution

In this study 57.57% of patients were having T4 disease, 36.36% of patients were having T3 disease, 6% of patients had T2 disease and none of patients were diagnosed of stage T1

Table 6 Composite Stage Wise Distribution

Composite Stage	Frequency (n)	Percentage (%)
T1N0M0(I)	0	0.0%
T2N0M0(II)	2	6.0%
T3N0M0(III)	12	36.36%
T4N0M0(IV)	19	57.57%

Dose Distribution Of PTV

In our study of 25 patients, in left breast ipsilateral LUNG dose data analysis was reported as the volume 1004.6 ±235.14 , Dmin 55 .21 ± 787 .82, Dmax 4187.33 ±149.1c Gy, Dmean 1869.07 ±621.64c Gy, V5 90.38 ± 8.46 %, V10 64.10 ± 12.75%, V20 25.05 ±3.69 %.

Table 7 Dose Distribution Of PTV

PTV	n
volume (cc)	482.58 ± 95
Minimum Dose (cGy)	6228.72 ± 49
Maximum Dose (cGy)	6917.78 ± 215
Mean Dose (cGy)	6487 ± 240

Table 8 Dose Distribution To Heart

PTV	n
volume (cc)	456 ± 108
Minimum Dose (cGy)	681 ± 189
Maximum Dose (cGy)	5800 ± 766
Mean Dose (cGy)	2356 ± 286

Table 9 Dose Distribution To Lungs And Spinal Cord

PTV	Right Lung	Left Lung	spinal cord
volume (cc)	1203 ± 246	1134 ± 272	70 ± 7.14
Minimum Dose (cGy)	145 ± 18	156 ± 84	4.64 ± 4.26
Maximum Dose (cGy)	5991 ± 332	6015 ± 392	4230.65 ± 99.02
Mean Dose (cGy)	1623 ± 246	1601± 210	4061 ± 351

RESPONSE ASSESSMENT

In our study, post radiation therapy response in term of loco regional control in 1st month follow up, all patients (100%) presented with complete response (CR), in 3rd month follow up 39(97.5%) patient presented with complete response (CR) and patient developed recurrence over post of scar in form of multiple satellite nodules, in 6th month follow up 1patient developed lung metastasis and 1 patient presented with local recurrence hence 2 (5.0%) shows progressive disease (PD) and 38 (95.0%) patients presented with complete response.

Table 10 Response Analysis

	CR	PR	PD	SD	CR %
1ST MONTH	40	0	0	0	100
2ND MONTH	39	1	0	0	97.5
3RD MONTH	38	0	2	0	95.0

DISCUSSION

In this study all histopathological confirmed cases were taken for simulation & all target volumes (PTV50.4 GY AND PTV 64.8 GY) with all OAR was drawn. Then patients were taken for radiotherapy. During radiotherapy patients were assessed for acute toxicities on weekly basis using common toxicity criteria (CTCAE Version 5.0). In our study most common age group affected by carcinoma esophagus was 5th decade of life followed by 6th decade. Several authors made similar observation. Nayak et al (1998) had 36.5% of patients in this age group. Baruah (1999) had 36.4% of his patients in this age group. Deka et al (1999) observe high incidence of esophagus in this age group. Highest incidence of the disease was observed in the upper lower socioeconomic group 48.48% of the patients were in this group. Similar incidences were reported by Desai et al (1999), Tandan (1994) and Vinod Shah et al (1999). Verma et al (1999) suggested that higher incidence in lower socioeconomic status may be due to intake of rough and bulky food deficient in vitamin & minerals over a long periods irritating the esophageal mucosa. In our study of 30 patients PTV dose data analysis were reported as average Total Volume of PTV 483 cc +/- 95, PTV Dmax 6918 cGy +/- 215 cGy, PTV Dmin 6229 cGy ± 48.8 cGy , PTV Dmean 6448 cGy +/- 240 cGy, D1% 5689.32 cGy +/- 81.91 cGy, D2% 5739.46 cGy +/- 66.32 cGy, D95% 6156.54 cGy +/- 87.03cGy , D98% 6350 cGy +/-118.85 cGy, CI 0.76 +/- 0.9 and HI 0.0016+/- 0.0004 respectvely. Minsky et al 2014 reported PTV Mean Dose (Gy) 64.6 ± 1.7, D2 (Gy) 66.4 ± 1.7, D98 (Gy) 64.5 ± 2.2, HI 0.15+/- 0.01 in VMAT respectively. [5] Chen et al reported PTV D95%

(%) 96.8±1.4 in VMAT. [6] In our study SIB-IMRT demonstrated excellent dose homogeneity, conformity and target coverage. Other international studies on SIB-IMRT also demonstrated excellent dose homogeneity, conformity and target coverage. Heart dose data analysis of our study were reported as average Total Volume of Heart is 456 cc +/- 108 cc, Min Dose received 681 cGy +/-189 cGy , Max Dose received 5800 cGy +/-766 cGy , Mean Dose received 2356 cGy ± 286 cGy , V20 56 % V30-36 % V40-15 % V50-10 % Qian Zhang et al 2014 reported Heart mean dose (Gy) 13.5 ± 5.0, V30(%) 9.9 ± 5.9,V10(%) 50.2 ± 29.0 and V5(%)78.0 ± 20.1 in VMAT respectively. [7] In this study dose data analysis of spinal cord were reported as Total Volume 70 cc +/-7.14 cc, Min Dose 4.64cGy +/- 4.26 cGy, Max Dose 4230.65 cGy +/-99.02 cGy, Mean Dose 4061 cGy +/- 1351 cGy, V10 was 27.04%+/- 9.66%, V20 12.068% +/- 7.098% ,V30 7.12% +/- 6.32% In this study spinal cord received doses within below normal tolerance limit as compare to conventional radiation technique In this study dose data analysis of liver were reported as Total Volume 99.4 cc +/-10.09 cc, Min Dose 4064cGy +/- 16.16 cGy, Max Dose 5306.65 cGy +/-571 cGy, Mean Dose 826 cGy +/- 202 cGy, this all doses ranges under below normal tolerance limit.

CONCLUSION

With the advancement in newer radiotherapy planning and treatment techniques dose have been reduced from 60 Gy to 50 Gy, but the routine use of heterogeneity corrections may have inadvertently reduced the treatment dose still further. Not surprisingly, the GTV is at high risk of failure after chemoradiation therapy for unresectable esophageal cancer. This planning series illustrates that, theoretically, using an SIB-IMRT technique can safely increase the dose to the GTV while also reducing toxicity to critical structures. Most frequently adverse event included radiation esophagitis, radiation gastritis. All toxicities were manageable with proper medications

REFERENCES

1. Brian G. et al., Esophageal cancer. In; Perez and Brady's principles and practice of Radiation oncology, Halperin EC., Wazer DE., Perez CA., and Brady LW.
2. Conteduca V, Sansonno D, Ingravallo G, Marangi S, Russi S, Lauletta G, Dammacco F (August 2012). "Barrett's esophagus and esophageal cancer: an overview". International Journal of Oncology.
3. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries Hyuna Sung, PhD 1; Jacques Ferlay, MSc, ME2; Rebecca L.
4. Chun S, Hu C, Choy H, et al. Impact of intensity-modulated radiation therapy technique for locally advanced non-small-cell lung cancer.]
5. Minsky BD, Pajak TF, Ginsberg RJ, et al. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy.
6. Wang X, Miao C, Chen Z, et al. Can involved-field irradiation replace elective nodal irradiation in chemoradiotherapy for esophageal cancer? A systematic review and meta-analysis.
7. Zhang Q., Yu X., Hu W., Chen J., Wang J., Ye J., Guo X.. Dosimetric comparison for volumetric modulated arc therapy and intensitymodulated radiotherapy on the left-sided chest wall and internal mammary nodes irradiation in treating post-mastectomy breast cancer. Radiology and Oncology. 2015;49(1): 91-98. https://doi.org/10.2478/raon-2014-0033