IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 11 Ver. VI (Nov. 2017), PP 66-69
www.iosrjournals.org

A Comparative Study of Toxicities during Treatment With IMRT Versus 3DCRT in Locoregionally Advanced Head and Neck Carcinoma

*Ajay Singh Choudhary[1], Rameshwaram Sharma[1],Kartick Rastogi[1], Kampra Gupta[1], Shivani Gupta[1], Sushil Kumar[1]
[1]*Radiotherapy, SMS Medical College, Jaipur, Rajasthan, India*
*Corresponding Author: *Ajay Singh Choudhary*

Abstract :
Context: *Head and neck cancers represent a significant treatment challenge because the disease is located within an anatomical area that contains several critical tissues. With development of modern radiotherapy techniques, precise delivery of adequate dose of radiation to the tumor while sparing organs at risk has become possible.*
Aims: *The present retrospective study was done to compare toxicity profile of IMRT versus 3DCRT in locally advanced head and neck cancer.*
Methods and Material: *A total of 150 patients of histologically confirmed stage III to IVB squamous cell carcinoma of the oral cavity and oropharynx of either sex were evaluated in the study from July 2015 to June 2016; 58 in IMRT group and 92 in 3DCRT group. All patients received 70 Gy in 35 fractions with 2 Gy per fraction in both groups with 6MV photon beam concurrent with weekly cisplatin 30 mg/m^2.*
Results: *At median follow-up of 18 months (range, 12 to 24 months), 3D-CRT group demonstrated significantly more acute toxic effects compared with the IMRT group. Significantly higher grade III or worse acute mucositis, dysphagia, acute and late xerostomia occurred in 57.6%, 84.8%, 71.7% & 63% of patients in 3DCRT group compared with 39.7%, 56.9%, 39.7% & 20.7% of patients in IMRT group (P-value 0.23, <0.001, <0.001 and <0.001 respectively).*
Conclusions: *IMRT is associated with decreased early and late toxicities as compared to 3DCRT. It offers better normal tissue sparing, hence better quality of life.*
Keywords: *3DCRT, Head and neck, IMRT, Locally advanced, Squamous cell carcinoma*

Date of Submission: 02 -11-2017 Date of acceptance: 16-11-2017

I. Introduction

Head & neck cancer is one of the leading cancers among Indian population, with estimated incidence of about 14.3% (23.3% in males and 6.3% in females) and estimated mortality of about 15.4% (22.8% in males and 7.3% in females) for all cancer cases [1]. At our centre, SMS Medical College and attached group of hospitals; head and neck malignancies constitute approximately 25% of all cancers. Most of the diagnosed head and neck cancers are histologically squamous cell carcinomas (90-95%). Treatment for loco-regionally advanced head and neck cancers remains challenging because the disease is within an anatomic environment that contains several critical tissues, such as the spinal cord, salivary glands, mandible, major vessels and the organs of speech, swallowing, hearing and respiration. Attempts to cure such patients with aggressive multimodality treatment have not succeeded till date. More than 70% cases require radiotherapy, either as definitive or as adjuvant mode, concurrently with chemotherapy, or for palliation. Earlier used two dimensional radiotherapy techniques were associated with higher incidences of adverse effects like dermatitis, mucositis, xerostomia and dysphagia, requiring enteral or parenteral nutrition support hampering quality of life.

The reactions sometimes are severe enough warranting treatment interruptions ultimately affecting treatment outcome. With development of modern radiotherapy techniques, it became possible for us to precisely deliver radiation to the tumor sparing organs at risk (OAR) leading to decreased adverse effects. However, as we move towards higher technology, the cost of treatment also increases. So in the present study, we have compared the incidence of adverse effects in head and neck malignancies treated with Three Dimensional Conformal Radiation Therapy (3DCRT) and Intensity Modulated Radiation Therapy (IMRT).

II. Material And Methods

The present study is retrospective in nature carried out at department of Radiotherapy, SMS Medical College & attached group of hospitals, Jaipur, Rajasthan, India; during July 2015 to June 2016 on patients with locally advanced head and neck squamous cell carcinoma of oral cavity and oropharynx treated with definitive radiotherapy with curative intent either with 3DCRT or IMRT over linear accelerator and completed the prescribed dose of radiation. Patients with early stage, other than squamous histology, other than oral cavity or oropharynx location of primary, previous history of radiotherapy, non-compliance to radiotherapy and treatment with palliative intent were excluded from the study. A total of 150 patients were found eligible, 58 patients in IMRT group and 92 patients in 3DCRT group.

All patients were treated on Seimens Oncor Expression dual energy linear accelerator machine with 6 megavoltage photon energy beam with immobilization in supine position using a thermoplasticdevice. Patients received 70 Gy in 35 fractions with 2 Gy per fraction for 5 fractions per week in both groups. Planning computerized tomography (CT) scan of the area of interest was done followed by delineation of Gross Tumor Volume (GTV), Clinical Target Volume (CTV), Planning Target Volume (PTV) and organs at risk (OAR) volumes as per the RTOG atlas. All patients received injection cisplatin at 40 mg/m^2 given intravenously concurrently with radiotherapy every week. Acute toxicities like mucositis, dermatitis, xerostomia and dysphagia were assessed according to Radiation Therapy Oncology Group (RTOG) Acute and Late Radiation Morbidity Scoring Criteria and the worst grade was reported.

For statistical analysis, all data were recorded and analyzed on Microsoft Excel 2007 and Statistical Package for Social Sciences (SPSS) version 20.0 (IBM Corp., Armonk, New York, USA). Chi-square was used for all categorical data. P value reports were two tailed and an alpha level of 0.05 was used to assess statistical significance.

III. Results

The baseline patient and tumor characteristics are shown in Table 1. No statistically significant difference was found in patient and tumor characteristics between the two arms. The treatment related acute and late toxicities are shown in Table 2. The median follow-up was 18 months (range, 12 to 24 months). The 3DCRT group demonstrated significantly more grade III or higher acute mucositis (P = 0.03), dysphagia (P < 0.001), acute xerostomia (P < 0.001) and late xerostomia (P < 0.001) compared with the IMRT group. However, the difference of acute and chronic dermatitis was not statistically significant between the two groups.

IV. Figures and Tables

Table 1 Clinical characteristics of the patients

Characteristics	**IMRT group** (n=58)	**3DCRT group** (n=92)	**P-value**
	Number (%)	Number (%)	
Age (Range, years)	32-74	35-72	0.87
Gender			0.56
Male	50 (86.2)	76 (82.6)	
Female	8 (13.8)	16 (17.4)	
Site			0.42
Oral cavity	20 (34.5)	26 (28.3)	
Oropharynx	38 (65.5)	66 (71.7)	
AJCC Stage			0.44
III	11 (18.9)	26 (28.3)	
IVA	40 (69)	56 (60.9)	
IVB	7 (12.1)	10 (10.8)	

Table 2 Treatment related acute and late toxicities

Toxicity		**IMRT Group (n=58)**	**3DCRT Group (n=92)**	**P-value**
		Number (%)	Number (%)	
Acute dermatitis	< Grade III	54 (93.1)	80 (87)	0.23
	≥ Grade III	4 (6.9)	12 (13)	
Acute mucositis	< Grade III	35 (60.3)	39 (42.4)	0.03
	≥ Grade III	23 (39.7)	53 (57.6)	
Dysphagia	< Grade III	25 (43.1)	14 (15.2)	<0.001
	≥ Grade III	33 (56.9)	78 (84.8)	
Acute xerostomia	< Grade III	35 (60.3)	26 (28.3)	<0.001
	≥ Grade III	23 (39.7)	66 (71.7)	
Chronic dermatitis	< Grade II	58 (100)	90 (97.8)	0.26
	≥ Grade II	0	2 (2.2)	
Late xerostomia	< Grade II	46 (79.3)	34 (37)	<0.001
	≥ Grade II	12 (20.7)	58 (63)	

3DCRT: Three Dimensional Conformal Radiation Therapy, IMRT: Intensity Modulated Radiation Therapy

V. Discussion

Treatment of head and neck malignancy is a multimodality approach, requiring surgery, chemotherapy and radiotherapy according to site and stage of the tumor. More than two third of head and neck cancer patients require radiotherapy, which can be given either alone or concurrently with chemotherapy. Radiotherapy can be given either as definitive or adjuvant form, sometimes even for palliation. Delaney and his colleagues have described the utilisation rate of radiotherapy in head and neck carcinoma [2]. According to their study, radiotherapy was indicated at some point in 74% of all patients with head and neck carcinoma. The optimal radiotherapy utilization rates by subsite were 74% for oral cavity; 20% for lip; 87% for salivary glands; 100% for larynx, oropharynx, hypopharynx, nasopharynx, and paranasal sinuses; and 90% for unknown squamous cell carcinoma of the head and neck.

The widely used conventional radiotherapy has been associated with significant acute and late toxicities. To overcome this, newer techniques like 3DCRT and IMRT have evolved with the aim of delivering radiation precisely to the tumor while delivering minimum dose to surrounding normal tissues. The development of newer radiotherapy techniques have been described in detail by Bucci, and Ling et al [3-4]. These sophisticated techniques have advantage of adjusting radiation beam to irregularly shaped target volumes reducing the radiation to the surrounding healthy critical structures like spinal cord, brain stem, parotid glands, larynx etc. in case of head and neck cancer malignancy. IMRT represents one of the most significant technical advances in radiation therapy since the advent of the medical linear accelerator, allowing clinical implementation of highly conformal nonconvex dose distributions [5-7]. However, these advances do not come without a risk. Lee et al. have studied the target volume delineation in 150 head and neck cancer patients with IMRT delivered using three different techniques: manually cut partial transmission blocks; computer-controlled auto-sequencing segmental multileaf collimator; and sequential tomotherapy using dynamic multivane intensity-modulating collimator [8]. They have concluded that accurate target volume delineation in IMRT treatment for head-and-neck cancer is essential. Their multidisciplinary approach in target volume definition resulted in few recurrences with no marginal failures. Higher treatment failure rates were noted in the postoperative setting in which lower doses were prescribed.

Ghosh and his colleagues in a study over 80 head and neck cancer patients have concluded that IMRT was associated with a significantly lower incidence of grade III or greater xerostomia, dermatitis, mucositis and dysphagia (45%, 7.5%, 40% and 57.5% respectively) than 3DCRT (72.5%, 12.5%, 57.5% and 85% respectively) [9]. Patient in IMRT group required less feeding tube use during radiotherapy compared with 3DCRT group.

Xerostomia is the most common late side-effect of radiotherapy to the head and neck. Compared with conventional radiotherapy, IMRT can reduce irradiation of the parotid glands. Nutting et al. undertook a randomised controlled trial between 2003 and 2007, that compared conventional radiotherapy with parotid-sparing IMRT (47 patients in each group) with primary endpoint to assess the proportion of patients with grade II or worse xerostomia [10]. At 12 months follow up, grade II or worse xerostomia was significantly lower in the IMRT group than in the conventional radiotherapy group, $P = 0{\cdot}003$. At 24 months, grade II or worse xerostomia was significantly less common with IMRT than with conventional radiotherapy; $P < 0{\cdot}001$. At 12 and 24 months, significant benefits were seen in recovery of saliva secretion with IMRT compared with conventional radiotherapy. At 24 months, no significant differences were seen between the two groups in non-xerostomia late toxicities, locoregional control, or overall survival. Lambrecht and his colleagues have compared 3DCRT with IMRT in 245 patients with stage III and IV head and neck squamous cell carcinoma treated with primary radiotherapy between 2003 and 2010, 135 patients were treated with 3DCRT, 110 patients with IMRT [11]. No significant differences were found in 3-year locoregional control and overall survival rates between the IMRT group and 3DCRT group. Significantly less acute mucositis ≥ grade III (32% vs. 44%, $P = 0.03$) and late xerostomia ≥ grade II (23% vs. 68%, $P < 0.001$) was observed in the IMRT group.

Tribius and Bergelt searched English-language literature published between January 2005 and August 2010 for studies comparing IMRT versus2DRT or 3DCRT in head and neck cancers that included quality of life (QoL) evaluation and identified 14 studies; 5 prospective and 9 retrospective [12]. EORTC QLQ-C30 was the most widely used instrument, generally supplemented with the head and neck cancer module H&N35. They found that IMRT was associated with statistically significant improvements in certain QoL domains versus 2DRT and 3DCRT, particularly those relating to xerostomia, including dry mouth, sticky saliva and eating-related domains.

VI. Conclusion

The present study represents cohort of locally advanced head and neck squamous cell carcinoma patients treated with modern radiotherapy techniques in a single institute. The results of present study are matched with most of the studies cited in the literature. The present study concludes that IMRT is associated

with statistically significantly decreased acute mucosities, dysphagia, acute and late xerostomia compared to 3DCRT. The better normal tissue sparing by IMRT may lead to better quality of life in long run. Retrospective nature, small number of patients and relatively short follow up remains the major limitations of the present study.

References

[1]. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, Accessed on 17/10/2016.

[2]. Delaney G, Jacob S, Barton M. Estimation of an optimal external beam radiotherapy utilization rate for head and neck carcinoma. Cancer 2005;103:2216-27.

[3]. Bucci MK, Bevan A, Roach M 3rd. Advances in radiation therapy: conventional to 3D, to IMRT, to 4D, and beyond. CA Cancer J Clin 2005;55:117-34.

[4]. Ling CC, Humm J, Larson S, Amols H, Fuks Z, Leibel S, et al. Towards multidimensional radiotherapy (MD-CRT): biological imaging and biological conformality. Int J Radiat Oncol Biol Phys 2000;47:551-60.

[5]. Ezzell GA, Galvin JM, Low D, Palta JR, Rosen I, Sharpe MB, et al. Guidance document on delivery, treatment planning, and clinical implementation of IMRT: report of the IMRT Subcommittee of the AAPM Radiation Therapy Committee. Med Phys 2003;30:2089-115.

[6]. Nutting C, Dearnaley DP, Webb S. Intensity modulated radiation therapy: a clinical review. Br J Radiol 2000;73:459-69.

[7]. Eisbruch A. Intensity-modulated radiation therapy: a clinical perspective. Introduction. Semin Radiat Oncol 2002;12:197-8.

[8]. Lee N, Xia P, Fischbein NJ, Akazawa P, Akazawa C, Quivey JM. Intensity-modulated radiation therapy for head-and-neck cancer: the UCSF experience focusing on target volume delineation. Int J Radiat Oncol Biol Phys 2003;57:49-60.

[9]. Ghosh G, Tallari R, Malviya A. Toxicity Profile of IMRT Vs. 3D-CRT in Head and Neck Cancer: A Retrospective Study. J Clin Diagn Res 2016;10:XC01-3.

[10]. Nutting CM, Morden JP, Harrington KJ, Urbano TG, Bhide SA, Clark C, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol 2011;12:127-36.

[11]. Lambrecht M, Nevens D, Nuyts S. Intensity-modulated radiotherapy vs. parotid-sparing 3D conformal radiotherapy. Effect on outcome and toxicity in locally advanced head and neck cancer. Strahlenther Onkol 2013;189:223-9.

[12]. Tribius S, Bergelt C. Intensity-modulated radiotherapy versus conventional and 3D conformal radiotherapy in patients with head and neck cancer: is there a worthwhile quality of life gain? Cancer Treat Rev 2011;37:511-9.

*Ajay Singh Choudhary. "A Comparative Study of Toxicities during Treatment With IMRT Versus 3DCRT in Locoregionally Advanced Head and Neck Carcinoma." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.11 (2017): 66-69