Review Article

Comparative evaluation of oral mucositis in oral cancer patients undergoing 3-dimensional conformal radiation therapy and intensity modulated radiation therapy with or without chemotherapy

Shirin H. Harnekar[1], Nilima Prakash[1], Raj Nagarkar[2], Pradeep GL[1], Aarti Mahajan[1], Roshan Kumar A. Patil[3]

[1]Oral Pathology and Microbiology, MGV's KBH Dental College and Hospital, Nashik, Maharashtra, [2]Chief Robotic Surgeon and Surgical Oncologist, HCG Manavata Cancer Centre, Nashik, Maharashtra, [3]Consultant Radiation Oncologist, Cancer Centers of America, Nashik, Maharashtra, India

Abstract

Context: Oral cancer is a significant cause of death across the world. A combined multimodal approach integrating surgery and radiation therapy (RT) with or without chemotherapy (CT) is commonly employed in advanced oral cancer to prevent recurrences and locoregional spread. Oral mucositis is a common acute toxicity reported in patients undergoing RT and CT. The delivery of optimal cancer therapy protocols is compromised due to morbidity caused by oral mucositis.

Aims: To compare the severity of oral mucositis in oral cancer patients undergoing 3-Dimensional Conformal Radiation Therapy (3DCRT) and Intensity Modulated Radiation Therapy (IMRT) with or without concomitant CT.

Settings and Design: This was a prospective, unicentric and longitudinal study conducted in a cancer centre.

Methods and Material: One hundred four patients with locally advanced oral cancer were enrolled in this study. Fifty-two patients were treated with IMRT and 52 patients with 3DCRT to a dose of >60 Gy, along with concurrent cisplatin weekly CT. Mucositis was recorded before the start, in the end, 1 month, and 3 months post-chemoradiotherapy treatment.

Statistical Analysis Used: Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software (v. 21.0, Chicago. 2012). Descriptive and frequency statistics were performed for different parameters assessed in 3DCRT and IMRT group.

Results: Grade 3 mucositis was the most predominant grade observed in both groups at the end of treatment. Thirty-six patients (69.3%) versus 24 patients (46.1%) developed grade 3 mucositis in 3DCRT and IMRT group, respectively ($P = 0.013$). Healing was better with IMRT group when compared to 3DCRT group 1 month and 3 months post-RT. Mucositis was severe in patients undergoing concomitant CT.

Address for correspondence: Dr. Shirin H. Harnekar, Post – Morba, Taluka – Mangaon, District - Raigad, 402 117, Maharashtra, India.
E-mail: shirinhharnekar@gmail.com

Submitted: 22-Jan-2023, **Revised:** 09-Nov-2023, **Accepted:** 15-Nov-2023, **Published:** 20-Dec-2023

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JPAT/

DOI: 10.4103/jomfp.jomfp_31_23

How to cite this article: Harnekar SH, Prakash N, Nagarkar R, Pradeep GL, Mahajan A, Patil RK. Comparative evaluation of oral mucositis in oral cancer patients undergoing 3-dimensional conformal radiation therapy and intensity modulated radiation therapy with or without chemotherapy. J Oral Maxillofac Pathol 2023;27:720-6.

Conclusions: IMRT reduced the incidence of severe mucositis and also improved the treatment-compliance compared to 3DCRT in locally advanced head neck cancer patients treated by chemoradiotherapy.

Keywords: Acute toxicity, oral mucositis, radiation therapy

INTRODUCTION

Oral cancer is a significant cause of death across the world.[1] Oral squamous cell carcinoma (OSCC) accounts for 84–97% of oral cancer.[2] The primary treatment for OSCC is greatly influenced by the stage and grade of the disease. For advanced stage disease, multidisciplinary treatment including radiation therapy (RT) with or chemotherapy (CT) is commonly employed. The treatment of oral cancer should be tailored individually to the patient's needs and consider the quality of life as well as the survival of the patient.[3]

RT and CT are employed with an aim to destroy rapidly dividing cells. However, along with tumour cells, normal cells are also destroyed by RT and CT, leading to toxicities. Radiation treatment has progressed dramatically from non-site-specific two-dimensional RT to highly conformal RT methods, such as intensity-modulated RT (IMRT), intensity-modulated arc therapy (IMAT) and stereotactic RT (SRT), that allows modulation of beam shape that conforms to target volume by escalating the dose to the tumour and minimizing the toxicity to normal tissue and critical organs.[4]

When compared to 3DCRT, the cost of treating HNC patients with IMRT is approximately 2.3 times higher.[5] As India is a socioeconomically diversified country with a large proportion of the population living below the poverty line, 3DCRT is routinely used in the majority of OSCC patients.

The prevalence of OM varies greatly in the available literature and is most likely underreported because of the heterogeneity of reporting and grading criteria.[6] Thus, the purpose of this study was to evaluate and compare the severity of oral mucositis in oral cancer patients undergoing 3DCRT and IMRT with or without CT.

SUBJECTS AND METHODS

Settings and design

This prospective, unicentric and longitudinal study was conducted in a cancer centre in our city.

The objective of the present study was to compare the severity of oral mucositis in oral cancer patients undergoing 3-Dimensional Conformal Radiation Therapy (3DCRT) and Intensity Modulated Radiation Therapy (IMRT) with or without concomitant CT.

Inclusion criteria were oral cancer patients undergoing curative RT with or without CT, non-metastatic oral cancers, patients aged 18 years or older and patients with Karnofsky score performance status not less than 60. Exclusion criteria were patients receiving radiation doses less than 60 Gy, having a history of prior curative RT to the oral region, receiving palliative radiotherapy and/or CT, recurrent oral cancer and HIV positive patients. An ethical clearance was obtained from the institutional ethical committee and informed consent was obtained from patients participating in the present study. A sample size of 52 patients in each group was required for our study with 80% power and 5% level of significance.

All patients were assessed for oral mucositis at the start of treatment, end of treatment, 1 month post-treatment and 3 months after completion of the treatment. Grading of oral mucositis was done using Radiation Therapy Oncology Group Grading (RTOG).

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software (v. 21.0, Chicago. 2012). Intergroup comparison of different parameters between 3DCRT and IMRT groups was assessed using an unpaired *t*-test or independent samples *t*-test to assess significant differences. One-way Analysis of Variance (ANOVA) and *post hoc* test was used to assess significant differences at different time intervals in individual 3DCRT and IMRT groups. The Chi-Square Test of Association was used to determine any statistically significant relationship between different parameters among different groups. All statistical tests were performed at 95% confidence intervals; keeping a *P* value of less than 0.05 as statistically significant.

RESULTS

From December 2019 to December 2021, a total of 104 patients were enrolled and analysed prospectively from the IMRT or 3DCRT group.

The median age of the patients was 45 years. Hundred patients (96.2%) were male and four patients were

female (3.8%). Buccal mucosa, tongue, alveolus, gingivobuccal sulcus, lip and floor of the mouth was the site of primary tumour in 60 patients (57.8%), 32 patients (30.8%), 7 patients (6.7%), 2 patients (1.9%), 2 patients (1.9%) and 1 patient (0.9%), respectively. Clinically, Stage IV carcinoma accounted for the majority of cases, comprising of 38 cases (36.5%). This was followed by 28 (26.9%) cases each of Stage II and Stage III and 10 (9.7%) cases of Stage I cancer.

Baseline patient and tumour characteristics (sex, history of tobacco use, age, primary tumour site, stage and number of CT cycles received) [Table 1].

Fifty-seven (54.8%) of a total of 104 patients completed a full course of planned six cycles of concurrent weekly cisplatin CT [Table 1].

On comparison of severity of oral mucositis in 3DCRT with or without concomitant CT at baseline, end of treatment, 1 month after treatment and 3 months after treatment showed that out of 52 patients, features of grade 3 mucositis were reported in 36 (69.2%) patients, grade 2 mucositis in 10 (19.2%) patients and grade 4 (11.5%) mucositis in 6 patients.

The grade of oral mucositis was less severe 1 month post-treatment, with 29 (55.8%) patients presenting without mucositis. Twenty (38.4%) patients presented with features of grade 1 mucositis, while 3 (5.8%) patients had features of grade 2 mucositis.

Table 1: Baseline characteristics between both the groups

Characteristics	3DCRT (52 patients)	IMRT (52 patients)
Median age	40.5	48.5
Tobacco user		
Smokeless tobacco	31	35
Smokeless tobacco with smoking and/or alcohol	16	15
None	5	2
Gender		
Male	48	52
Female	4	-
Primary site		
Buccal mucosa	29	31
Tongue	18	14
Lip	-	2
Alveolus	1	5
GBS	3	-
FOM	1	-
Stage		
Stage I	4	6
Stage II	16	12
Stage III	15	13
Stage IV	17	21
Grade		
MDSCC	48	47
WDSCC	4	5
Concurrent chemotherapy weekly	36	21

Majority of the patients, that is, 50 (96.2%) patients showed complete healing on 3 months post-treatment follow-up. Two (3.8%) patients presented with grade 1 mucositis [Table 2].

Comparison of severity of oral mucositis in IMRT with or without concomitant CT at baseline, end of treatment, 1 month after treatment and 3 months after treatment showed that out of 52 patients, grade 2 mucositis was observed in 25 (48.1%) patients, grade 3 mucositis in 24 (46.1%) patients and grade 4 mucositis in 3 (5.8%) patients when examined at the end of treatment.

The grade of mucositis was less severe 1 month post-treatment, with 45 (86.5%) patients presenting without mucositis and 7 (13.5%) patients presenting with features of grade 1.

Complete healing was observed in all the patients (52, 100%) 3 months post-treatment [Table 2].

Out of 36 patients undergoing 3DCRT with concomitant CT, grade 3 mucositis was noted in 29 (55.8%) patients, grade 4 mucositis in 5 (9.7%) patients and grade 1 mucositis in 2 (3.8%) patients. Among the 16 patients undergoing 3DCRT without CT, grade 2 mucositis was noted in 8 (15.4%) patients, grade 3 mucositis in 7 (13.5%) patients and grade 4 mucositis in 1 (1.9%) patient.

The severity of oral mucositis in patients who underwent 3DCRT with and without concomitant CT showed statistically significant differences ($P = 0.001$) at the end of treatment as the number of patients in the two groups was variable [Table 3].

Out of 21 patients, undergoing IMRT with concomitant CT, grade 3 mucositis was observed in 16 (25%) patients, grade 2 mucositis in 6 (11.5%) patients and grade 4 mucositis in 2 (3.8%) patients.

Among the 31 patients, undergoing IMRT without CT, grade 2 mucositis was observed in 19 (36.5%) patients, grade 3 mucositis in 11 (21.2%) patients and grade 4 mucositis in 1 (1.9%) patient.

The severity of oral mucositis in patients who underwent IMRT with and without concomitant CT showed statistically significant differences ($P = 0.013$) at the end of treatment [Table 4].

Patients in IMRT group had better compliance with the treatment when compared to 3DCRT group as the

Table 2: Grades of oral mucositis in patients undergoing 3DCRT and IMRT with or without chemotherapy at different time intervals using unpaired *t*-test

Grade of oral mucositis	At the end of treatment		*P*	1 month post-treatment		*P*	3 months post-treatment		*P*
	3DCRT	IMRT		3DCRT	IMRT		3DCRT	IMRT	
0	0 (0%)	0 (0%)	0.013*	29 (55.8%)	45 (86.5%)	0.001*	50 (96.2%)	52 (100%)	0.041*
1	0 (0%)	0 (0%)		20 (38.5%)	7 (13.5%)		2 (3.8%)	0 (0%)	
2	10 (19.2%)	25 (48.1%)		3 (5.8%)	0 (0%)		0 (0%)	0 (0%)	
3	36 (69.3%)	24 (46.1%)		0 (0%)	0 (0%)		0 (0%)	0 (0%)	
4	6 (11.5%)	3 (5.8%)		0 (0%)	0 (0%)		0 (0%)	0 (0%)	

**p* value of less than 0.05 is statistically significant

Table 3: Grades of mucositis in patients undergoing 3DCRT with or without concomitant chemotherapy at the end of treatment using Chi-Square Test of Association

Grade of oral mucositis	With chemotherapy	%	Without chemotherapy	%	*P*
0	0	0	0	0	*P*=0.001*
1	0	0	0	0	
2	2	3.8	8	15.4	
3	29	55.8	7	13.5	
4	5	9.7	1	1.9	

**p* value of less than 0.05 is statistically significant

Table 4: Grades of mucositis in patients undergoing IMRT with or without concomitant chemotherapy at the end of treatment using Chi-Square Test of Association

Grade of oral mucositis	With chemotherapy	%	Without chemotherapy	%	*P*
0	0	0	0	0	0.013*
1	0	0	0	0	
2	6	11.5	19	36.5	
3	13	25	11	21.2	
4	2	3.8	1	1.9	

**p* value of less than 0.05 is statistically significant

grades of mucositis were lower. Treatment interruption/gap in the radiotherapy of more than 7 days was observed in 11 patients (21.53%) in 3DCRT group versus 2 patients (3.84%) in IMRT group.

DISCUSSION

OSCC represents about 95% of all forms of head and neck cancers. The 5-year survival rate of OSCC patients has been reported to be approximately 50%, which is not satisfactory despite new treatment modalities.[7]

The demographic data and clinical and histopathological data were recorded and subjected to descriptive analysis. The oral mucositis was recorded at the end of the treatment as it reflects the peak of mucositis during anticancer therapy. Oral mucositis was recorded 1 month post-treatment to evaluate the healing of the mucosal lesions in both groups. Oral mucositis was recorded 3 months post-treatment to evaluate the residual damage on oral mucosa.

In the present study, majority of the patients, that is, 60 (57.7%) belonged to the age group 41–60 years, 33 (31.7%) to 20–40 years and 11 (10.6%) belonged to >61 years. The mean age of the patients was found to be 46.8 years [Table 1].

Similarly, Singh *et al.* (2016)[8] found that the most common age of occurrence of OSCC was in the 4th to 5th decade in a clinico-epidemiological study of OSCC. In a study by Ghosh *et al.* (2016),[9] majority of patients belonged to the 3rd to 6th decade.

Majority of study subjects were males 100 (96.2%) and a few females 4 (3.8%) [Table 1].

Similar results were obtained by Kucha *et al.* (2020)[10] where male patients outnumbered females. Ghosh *et al.* (2016)[9] also reported male predominance in their study. Similarly, Lambrecht *et al.* (2013)[11] and Vergeer *et al.* (2009)[12] also found a male predominance in their studies.

The gender disparity can be explained by cultural trends in our country where males practice the habit of tobacco chewing or smoking whereas females refrain from adopting such habits due to social and traditional stigma. Sociocultural norms and values favour easy availability of tobacco products to males. However, females from lower socioeconomic strata practise the use of mishri (a smokeless form of tobacco) since a very young age for teeth cleansing, thus, explaining the occurrence of oral cancer in young females.

In our study, buccal mucosa was found to be the most predominant site for the occurrence of OSCC with 60 (57.8%) cases followed by 32 (30.8%) involving tongue, 7 (6.7%) alveolus, 2 (1.9%) each of GBS and lip and 1 (0.9%) involving floor of the mouth [Table 1].

Our findings are in accordance with Chen *et al.* (2009),[13] Ghosh *et al.* (2016),[9] Singh *et al.* (2016)[8] and Ghosh *et al.* (2018).[14] Carcinoma alveolus was the second most predominant site of cancer in a study by Gopa Ghosh *et al.* (2016),[9] Ghosh *et al.* (2018),[14] unlike the present study where tongue carcinoma was the second most common site of occurrence of OSCC.

On the contrary, Minhas *et al.* (2021)[15] reported tongue to be the most predominant site for the occurrence of OSCC.

The lower gingivobuccal complex is comprised of buccal mucosa, gingivobuccal sulcus, lower gingiva and retromolar trigone. It is the most common site for oral cancer in the Indian subcontinent due to the habit of chewing tobacco, which has been aptly described as the Indian oral cancer.[8] The placement of tobacco quid in the gingivobuccal sulcus region has been attributed to the development of carcinoma.

Most patients in our study were diagnosed in the advanced stages of the disease with 36.5% (38) of the total patients diagnosed with stage IV, 26.9% (28) each with stage II and III and 9.7% (10) of the patients diagnosed with stage I. [Table 1]

Our results are in accordance with Singh MP *et al.* (2016),[8] Ghosh *et al.* (2018),[14] Minhas S *et al.* (2021).[15]

Conversely, stage III cancer was predominant in a study by Kucha *et al.* (2020).[10]

Oral cancer is a major problem in the Indian subcontinent where it ranks among the top three types of cancer mostly attributable to tobacco use. Oral cancer affects those from the lower socioeconomic groups (high-risk population), due to a higher exposure to risk factors such as the use of tobacco. This high-risk population also have inadequate access to trained providers and limited health services.

In our study, we found MDSCC predominated with 95 (91.3%) cases followed by 9 (8.7%) cases with WDSCC. No cases of PDSCC were present in our study [Table 1].

Similar results were reported by Abdulla *et al.* (2018)[16] and Minhas *et al.* (2021).[15]

The frequency of oral cancer was highest in patients with history of smokeless tobacco chewing 66 (63.5%) followed by individuals with history of a combination of smokeless tobacco with smoking and/or alcohol 31 (29.8%). Habit history was not reported in 7 (6.7%) cases.

In India, estimates reveal that roughly one-third of women and two-thirds of men use tobacco in one form or another.[17] Tobacco contains many carcinogens which make the oral cavity more vulnerable to cancer. The combined effect of chewing and smoking is known to be greater in increasing the risk of cancer than that with chewing or smoking alone. Alcohol consumption has a markedly synergistic effect with smoking.

Our results are in accordance with Abdulla *et al.* (2018),[16] Tripathi *et al.* (2021)[18] who found that oral cancer is highly prevalent in patients with history of smokeless tobacco use.

On estimation of the incidence of oral mucositis among oral cancer patients undergoing 3DCRT and IMRT with or without concomitant CT all the 104 (100%) patients presented with features of oral mucositis at the end of the treatment [Table 2 and Figures 1–5].

Similar results were obtained by Trotti *et al.* (2003),[19] Chen *et al.* (2009)[13] and Gupta *et al.* (2012)[20] where the incidence of acute toxicities in patients receiving conventional 3DCRT at the end of treatment is 100%.

On the contrary, the prevalence of radiation-induced OM in a study by Pereira *et al.* (2019)[21] was 41.9%.

Comparison of severity of oral mucositis between 3DCRT and IMRT with or without CT at the end of treatment showed grade 4 oral mucositis in 6 (11.5%) patients, grade 3 in 36 (69.3%) patients and grade 2 in 10 (19.2%) patients from 3DCRT group whereas only 3 (5.8%) patients from IMRT group had grade 4 mucositis, 24 (46.1%) patients had grade 3 and 25 (48.1%) had grade 2 mucositis at the end of treatment ($P = 0.013$).

On assessment of oral mucositis 1 month after treatment, oral mucositis was not observed in 29 (55.8%) patients of 3DCRT and 45 (86.5%) patients of IMRT, grade 1 mucositis was recorded in 20 (38.5%) and 7 (13.5%) patients of 3DCRT and IMRT, respectively. ($P = 0.001$).

Oral mucositis was completely healed in IMRT group and only 2 (3.8%) patients from 3DCRT

Figure 1: Normal appearing oral mucosa- Grade 0 Mucositis. (RTOG)

Figure 2: Mild Erythema- Grade 1 Mucositis. (RTOG)

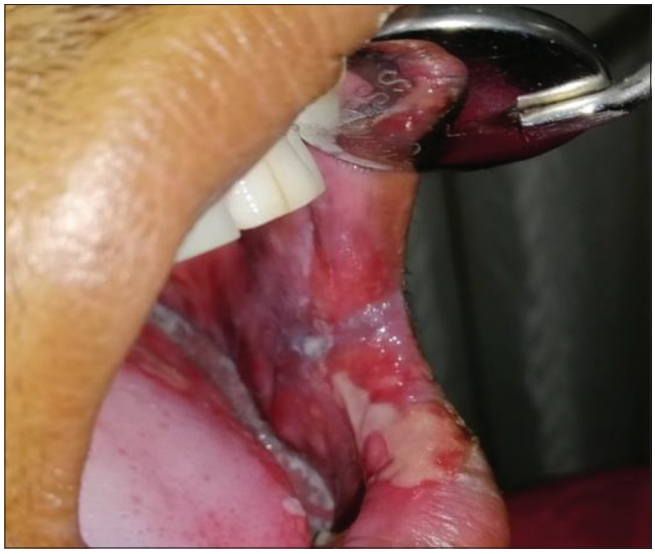

Figure 4: Patchy mucositis- Grade 3 Mucositis. (RTOG)

group exhibited grade 1 mucositis 3 months post-treatment ($P = 0.041$).

Oral mucositis in oral cancer patients undergoing 3DCRT and IMRT with or without concomitant CT at the end of treatment showed that out of 36 patients undergoing 3DCRT with concomitant CT, grade 3 mucositis was noted in 29 (55.8%) patients, grade 4 mucositis in 5 (9.7%) patients and grade 1 mucositis in 2 (3.8%) patients. Among the 16 patients undergoing 3DCRT without CT, grade 2 mucositis was noted in 8 (15.4%) patients, grade 3 mucositis in 7 (13.5%) patients and grade 4 mucositis in 1 (1.9%) patient. The results were statistically significant at end of treatment ($P = 0.001$) [Table 3].

Out of 21 patients undergoing IMRT with concomitant CT, grade 3 mucositis was noted in 16 (25%) patients, grade 2 mucositis in 6 (11.5%) patients and grade 4 mucositis in 2 (3.8%) patients. Among the 31 patients undergoing IMRT without CT, grade 2 mucositis was noted in 19 (36.5%)

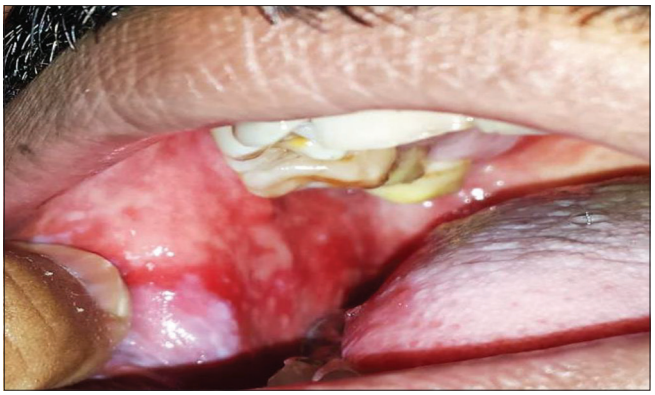

Figure 3: Severe erythema with ulcers- Grade 2 Mucositis. (RTOG)

Figure 5: Deep ulcerations with bleeding- Grade 4 Mucositis. (RTOG)

patients, grade 3 mucositis in 11 (21.2%) patients and grade 4 mucositis in 1 (1.9%) patient. The results were statistically significant at the end of treatment ($P = 0.013$) [Table 4].

Similar results were obtained by Al Mamgani *et al.* (2013)[22] and Dragan *et al.* (2019)[23] who reported an increase in the incidence and severity of oral mucositis by the addition of CT to RT.

The prevalence of OM among patients having undergone CT as adjuvant treatment was approximately 50% higher compared to those who did not undergo CT. In addition to the direct aggression caused by RT, CT systematically compromises the body, leaving the patient more prone to complications.[21]

CONCLUSION

Oral mucositis is an unavoidable, dose-limiting acute complication of cancer therapy. Although the search for new alternative treatment strategies and prevention of this debilitating complication is still on, for a country like India where the majority of people belong to low socioeconomic strata affording this treatment is difficult. Acute toxicity in the form of severe mucositis compels patients to opt for unplanned treatment breaks to allow the lesions to

heal. However, multiple unplanned treatment gap allows repopulation of tumour cells, which may result in the regrowth of CT resistant populations.

The significant differences in the severity of oral mucositis with respect to two modalities of RT warrant the need to carry out research directed towards prevention and providing symptomatic relief for patients with oral mucositis. IMRT is a safer alternative to 3DCRT in reducing these treatment related toxicities but is not cost-effective.

Limitations and future prospects

The sample size was relatively small. Since OM is considered an acute toxicity secondary to RT and CT, it is recommended to assess the patients for the onset of OM, that is, 2 weeks after the RT and/or CT has been initiated. The correlation of locoregional recurrence on long-term follow-up in patients who had unplanned treatment breaks due to severe morbidity caused by OM should be assessed.

Despite all the caveats and limitations, ours is the first prospective study comparing the severity of oral mucositis in two modern radiotherapy techniques (3DCRT and IMRT) for oral cancer at four intervals. We have been able to demonstrate not only a statistically significant but also clinically meaningful reduction in oral mucositis with IMRT compared to 3DCRT.

We recommend further study to determine the association of treatment breaks due to acute toxicity and recurrence/disease free survival.

Acknowledgement

We are thankful to the medical physicists and receptionists of the hospital for their help and constant support.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Chaturvedi P, Singh A, Chien CY, Warnakulasuriya S. Tobacco related oral cancer. BMJ 2019;365:l2142. doi: https://doi.org/10.1136/bmj.l2142.
2. Borse V, Konwar AN, Buragohain P. Oral cancer diagnosis and perspectives in India. Sens Int 2020;1:100046. doi: 10.1016/j.sintl.2020.100046.
3. Omura K. Current status of oral cancer treatment strategies: Surgical treatments for oral squamous cell carcinoma. Int J Clin Oncol 2014;19:423-30.
4. Garibaldi C, Jereczek-Fossa BA, Marvaso G, Dicuonzo S, Rojas DP, Cattani F, *et al*. Recent advances in radiation oncology. Ecancermedicalscience 2017;11:785.
5. Chauhan AS, Prinja S, Ghoshal S, Verma R, Oinam AS. Cost of treatment for head and neck cancer in India. PloS One 2018;13:e0191132. doi: 10.1371/journal.pone.0191132.
6. Blakaj A, Bonomi M, Gamez ME, Blakaj DM. Oral mucositis in head and neck cancer: Evidence-based management and review of clinical trial data. Oral Oncol 2019;95:29-34.
7. Taghavi N, Yazdi I. Prognostic factors of survival rate in oral squamous cell carcinoma: Clinical, histologic, genetic and molecular concepts. Arch Iran Med 2015;18:314-9.
8. Singh MP, Kumar V, Agarwal A, Kumar R, Bhatt MLB, Misra S. Clinico-epidemiological study of oral squamous cell carcinoma: A tertiary care centre study in North India. J Oral Biol Craniofacial Res 2016;6:31–4.
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. doi: 10.7860/JCDR/2016/21457.8583.
10. Kucha N, Soni TP, Jakhotia N, Patni N, Singh DK, Gupta AK, *et al*. Alter. Cancer Treat Res Commun 2020;25:100223.
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. Vergeer MR, Doornaert PAH, Rietveld DHF, Leemans CR, Slotman BJ, Langendijk JA. Intensity-modulated radiotherapy reduces radiation-induced morbidity and improves health-related quality of life: Results of a nonrandomized prospective study using a standardized follow-up program. Int J Radiat Oncol Biol Phys 2009;74:1-8.
13. Chen WC, Hwang TZ, Wang WH, Lu CH, Chen CC, Chen CM, *et al*. Comparison between conventional and intensity-modulated post-operative radiotherapy for stage III and IV oral cavity cancer in terms of treatment results and toxicity. Oral Oncol 2009;45:505-10.
14. Ghosh G, Gupta G, Malviya A, Saroj D. Comparison three-dimensional conformal radiotherapy versus intensity modulated radiation therapy in local control of head and neck cancer. J Cancer Res Ther 2018;14:1412-7.
15. Minhas S, Sajjad A, Chaudhry RM, Zahid H, Shahid A, Kashif M. Assessment and prevalence of concomitant chemo-radiotherapy-induced oral mucositis in patients with oral squamous cell carcinoma. Turk J Med Sci 2021;51:675-84.
16. Abdulla R, Adyanthaya S, Kini P, Mohanty V, D'Souza N, Subbannayya Y. Clinicopathological analysis of oral squamous cell carcinoma among the younger age group in coastal Karnataka, India: A retrospective study. J Oral Maxillofac Pathol 2018;22:180-7.
17. Prabhakar B, Narake SS, Pednekar MS. Social disparities in tobacco use in India: The roles of occupation, education and gender. Indian J Cancer 2012;49:401-9.
18. Tripathi A, Agarwal AK, Mahore R, Bhadoriya SS, Saraswat S. A clinico-epidemiological hospital based study of oral cancer patients in Gwalior district. Indian J Forensic Community Med 2021;8:132-8.
19. Trotti A, Colevas AD, Setser A, Rusch V, Jaques D, Budach V, *et al*. CTCAE v3.0: Development of a comprehensive grading system for the adverse effects of cancer treatment. Semin Radiat Oncol 2003;13:176-81.
20. Gupta T, Agarwal J, Jain S, Phurailatpam R, Kannan S, Ghosh-Laskar S, *et al*. Three-dimensional conformal radiotherapy (3D-CRT) versus intensity modulated radiation therapy (IMRT) in squamous cell carcinoma of the head and neck: A randomized controlled trial. Radiother Oncol 2012;104:343-8.
21. Pereira IF, Firmino RT, Meira HC, DO Egito Vasconcelos BC, DE Souza Noronha VRA, Santos VR. Radiation-induced oral mucositis in Brazilian patients: Prevalence and associated factors. In Vivo 2019;33:605-9.
22. Al-Mamgani A, van Rooij P, Verduijn GM, Mehilal R, Kerrebijn JD, Levendag PC. The impact of treatment modality and radiation technique on outcomes and toxicity of patients with locally advanced oropharyngeal cancer. Laryngoscope 2013;123:386-93.
23. Dragan T, Beauvois S, Moreau M, Paesmans M, Vandekerkhove C, Cordier L, *et al*. Clinical outcome and toxicity after simultaneous integrated boost IMRT in head and neck squamous cell cancer patients. Oral Oncol 2019;98:132-40.