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Research Article

DOSE VOLUME RELATED ACUTE ORAL TOXICITIES DURING HEAD AND NECK CANCER IRRADIATION

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A B S T R A C T

Purpose: To study the relationship between the Dosimetric Parameters of three-dimensional conformal radiotherapy (3D-CRT) in head and neck cancers (HNC) and the resulting acute oral toxicities.

Materials and Methods: This prospective cohort study consisted of 43 HNC patients with stage (II-IVA) visiting Department of Radiation Oncology, SMS Medical College and Attached Hospitals Jaipur, Rajasthan from May 2019 to April 2020 who received definitive Concurrent Chemo-Radiotherapy (CCRT). Target volume and Organ at Risks (OARs) were identified and contoured as per Radiotherapy Guidelines DAHANCA 2019. During treatment, acute symptoms including oral mucositis, oral pain, xerostomia and dysphagia, were scored weekly during CCRT and at 1 month and 3 month post RT follow up as per CTCAE toxicity criteria (v4.03) and the accumulated scores were related individually in terms of dose–volume variables by studying dose volume histograms (DVH).

Results and Observations: Of total 43 HNC patients (34 male and 9 female), mean age of patients was 55.88 ± 12.08 years. 76% of study population was addicted with regular smoking habit and 15% were having tobacco chewing history while 9% were indulged in smoking and alcohol consumptions both. Study population comprised of 9 oral cavity, 15 oropharyngeal, 6 hypopharyngeal and 15 laryngeal cancer patients. Among the complications (grade ≥2) assessed in the study; dysphagia was the most common to be observed in 83.72% of the study population followed by mucositis and xerostomia seen in 72.09% and 69.76% of patients respectively. When comparing the mean dose and volume of OARs irradiated in the several analyzed structures, it was observed that the patients who developed lower grades (grade≤1) of complications the Dmean and volume (V%) irradiated were smaller in the parotid, oral cavity, constrictors of the pharynx than those who developed higher grades (grade ≥2) of complications. Only one patient developed grade 4 of toxicity and the same patient defaulted with the treatment at week 6 of treatment.

Conclusion: Patients undergoing CCRT treatment for HNC with techniques like 3D-CRT, by considering dosimetric parameters we can spare the OARs better without compromising dose to GTV, the early assessment of toxicities during treatment the probability of late complication of dysphagia and xerostomia can be predicted and the timely intervention of these toxicities can improve the overall quality of life (QOL) of HNC patients. Further studies should be encouraged to define a reasonable and acceptable value of normal tissue tolerance of radiation for routine clinical practice.

INTRODUCTION

Head and neck cancer (HNC) accounts for 8.04% of new cases with 5.17% of deaths worldwide of all the malignancies [1]. In INDIA head and neck cancer annual incidence is 19.35% as per GLOBACON 2018 data with lip and oral cavity cancers (10.4%) being the most common among HNC and the second most common of all malignancies after breast [2].

Tobacco and alcohol abuse are the most common etiologic factor in the cancers of oral cavity, hypopharynx, larynx, and HPV unrelated oropharynx especially in the developing countries like India where the use of these products is very common.

At our centre 1373 HNC patients visited of total 8920 cancer patients in 2019 comprising incidence of 15.39% of all cancers at SMSMC JAIPUR (Departmental Data).

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Single modality treatment with surgery or radiotherapy (RT) is generally recommended for approximately 30-40% of patients who present with early stage disease [3].

Combined modality based treatment is recommended for approximately 60% of patients who present with locally or regionally advanced disease at diagnosis. Chemoradiotherapy (CRT) is the standard approach [4] in advanced stage disease. Although, in some patients (with bulky disease where organ preservation strategies are appropriate), induction chemotherapy, followed by CRT or surgery, may be used [5].

The major goal of RT is to achieve local control of the tumor while minimizing damage to the critical organs. Radiotherapy for the patients with HNC is extremely complex because of the presence of many critical structures in close proximity to tumor.

Radiotherapy is typically associated with acute and late toxicity that can have profound effects on the patient's quality

of life. Common acute toxicities of head and neck irradiation include mucositis, dermatitis, dysphagia, odynophagia, salivary changes, and xerostomia. These complications may lead to prolongation or interruption of treatment leading to potential adverse impact on the outcome [6].

Initially the two-dimensional radiotherapy (2DRT) was the only modality available where simple shaped radiation fields based on bony anatomy were aimed at the tumor to be sure the tumor was irradiated sufficiently. Large volumes of normal tissues were irradiated resulting in considerable acute and late morbidity [7, 8].

Over the years, technological advances in treatment planning and delivery based on three-dimensional (3D) computed tomography (CT) imaging have resulted in progressive conformation of radiation dose to the target tissues while sparing adjacent organs-at-risk (OARs). Intensity-modulated radiation therapy (IMRT) defined as an advanced form of high-precision conformal technique using non-uniform beam intensities determined through computer-based optimization to achieve the desired dose-distribution, has emerged as the most preferred technique [9] and has been readily adopted by the head and neck oncology community worldwide in the curative-intent radio-therapeutic management of HNSCC.

In the early times, the radiation therapy (RT) fields/doses were selected theoretically, based largely on experiences. Physicians relied on clinical knowledge to select field sizes/dose. They understood that these empiric guidelines were imprecise, and did not fully reflect the underlying anatomy, physiology and dosimetry.

A great advantage of 3D treatment planning was quantitative correlations of doses/volumes with clinical outcomes. When 3D dosimetric information became widely available; guidelines were needed to help physicians to predict the relative safety of proposed treatment plans, though only limited data were available.

In 1991, investigators pooled their clinical experience, judgment and information regarding partial organ tolerance doses, and produced the “Emami paper” [10]. The Emami *et al*. report systematically used the dose-volume-outcome data to predict the TD5/5 and TD50/5 for the uniform irradiation of one-third, two-third, and the whole volume of an organ. This uniform approach enabled the application of “single unifying models” of dose/volume/outcome across organs. These dose/volume/outcome estimates from Emami *et al*. were used by Burman *et al*. [11], Kutcher *et al*. [12], and Lyman *et al*. [13] to generate a set of organ-specific model parameters. Such a uniform approach was attractive to clinicians and physicists. Though the paper clearly stated the limitations and uncertainities in its recommendation, it is widely admired for addressing a clinical need.

The QUANTEC (Quantitative Analysis of Normal Tissue Effects in the Clinic) article summarizes the available data to update/refine the estimates provided by “Emami”. A central goal of QUANTEC is to summarize this information in a clinically useful manner.

The commendable step to ensure the quality of life of patients after irradiation taken by the QUANTEC group was reported in 2010. The report provided a thorough review of the published clinical evidence for normal tissue dose-effect relationships [14]. The reports especially relevant to head and neck irradiation, were the reports on salivary glands, esophagus, brainstem, hearing loss, larynx and pharynx [15-19].

The relationship between radiation doses and tumor volumes and adjacent normal tissues is expressed as dose-volume histograms. The use of dose-volume histograms for treatment plan analysis has become an essential requisite for dose analysis in the tumor and in normal tissues. Thus, with the development of the three-dimensional technique, a greater individualization of treatment is possible. Radiation doses are better shaped and compared in contrast to conventional technique; safety has been increased with better visualization and evaluation of treated anatomical structures [20]. Thereafter, dosimetric data on tolerance of normal tissues began to be described in the various literatures retrospectively from these computational data of radiotherapy planning [21].
Head and neck cancer poses a particular challenge in radiation therapy, whilst being an effective treatment modality it requires very high doses of radiation to provide effective therapy. This is further complicated by the fact that the head and neck region contains a large number of radiosensitive tissues, often resulting in patients to experience debilitating normal tissue complications.

During the past decade, advancement in radiotherapy has improved the treatment outcomes of patients with head and neck cancer. Unfortunately, these improvements have been achieved at the cost of increased morbidity and compromised quality of life. Further studies are needed to define a reasonable and acceptable value of normal tissue tolerance of radiation for routine clinical practice.

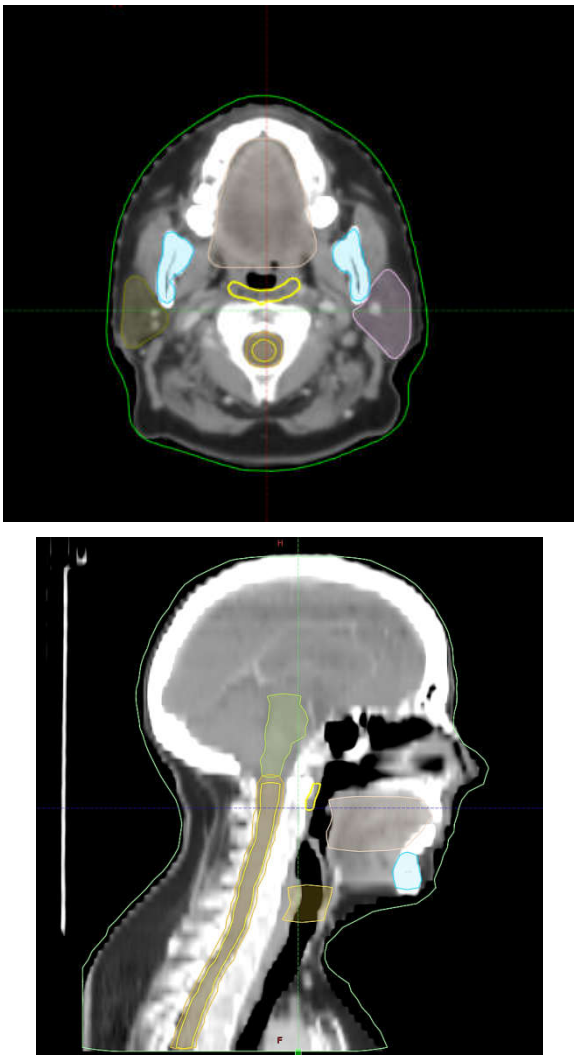
Knowing that the oral complications resulting from radiotherapy treatment directly influence the patient's quality of life and adhering to treatment, the present study is aimed to evaluate the dosimetric relationship between the established three-dimensional designed protocols and the acute oral complications of radiotherapy resulting from the treatment in HNC patients at our institute.

METHOD AND MATERIALS

A total 43 patients of whom 34 were male and 9 were female, with mean age distribution of 55.88±12.08 years (range 32-78 years) visiting department of Radiation Oncology, SMS Medical College and Attached Hospital Jaipur from May 2019 to April 2020 were included in this prospective study. All patients had pathologically confirmed squamous cell carcinoma of head and neck with prognostic stage II-IVA and received curative three-dimensional conformal radiotherapy (3D-CRT) with weekly cisplatin @ 30mg/m^2. None of the patients had undergone surgery for HNC. Patients with head and neck malignancy of nasopharynx, skin, nose, thyroid, salivary gland, sarcoma and lymphoma, distant metastases (M1), receiving unilateral neck radiotherapy and with baseline oral toxicity were excluded from the study. The ethical committee approval was received from the Ethics Committee of SMS Hospital, Jaipur and written informed consent was obtained from all patients prior to enrolment in the study.

Each patient was immobilized using a thermoplastic head and neck mask in the supine position. Shoulder retractors were used to remove shoulders from the radiotherapy field. Patients were scanned with computed tomography (CT) with intravenous contrast from the vertex to the inferior border of

the manubrium sterni with a scan thickness of 5 mm. Organs at risk (OARs) and the target volumes were identified after that contoured and defined according to the Radiotherapy Guidelines Danish Head and Neck Cancer Group (DAHANCA) 2019.

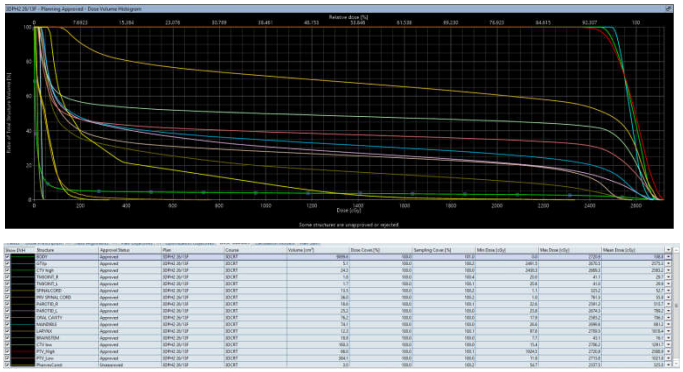


Delineation results of the oral cavity, parotid glands, and the pharyngeal constrictor muscles, projected on an axial and saggital section of CT slice.

Radiotherapy was administered by an *Ultra Modern Dual Energy Digital Linear Accelerator: Varian Vital Beam* using a complex field 3D-CRT technique. The dose prescription was according to the ICRU 62 recommendations which states that at least 95% of the prescribed dose should be delivered to at least 98% of the target volume. A total of 70Gy in 35 fractions was prescribed to the primary tumor and the involved lymph nodes (LN), and 44Gy in 22 fractions to the low-risk nodal areas (once a day, for 5 days a week @ 2Gy per fraction). The treatment plans were conducted using the *Varian Eclipse Treatment Planning System Version 13.6.*

Dosimetric Data: Extended oral cavity, and both parotid gland as defined by *Brouwer et al.[22]* and all pharyngeal constrictor muscle (PCM) superior, middle and inferior were identified and contoured as suggested by *Christianen et al.[23]*.

The mean dose in Gray (D_{mean}), the maximum dose in Gray (D_{max}) and the percentages of organ volumes receiving 20Gy, 40Gy, 60Gy 80Gy and 100Gy [V20 (%), V40 (%) and V60 (%), V80 (%) and V100 (%) respectively] were calculated from the dose volume histograms for each structure. Planning objectives required PTV coverage of 95–107%. Concerning OARs, dose constraints were set as: *Oral cavity (not involved):* V40<50%; D_{mean}<30Gy (RTOG 0920). *Oral cavity (involved):* V40<70%; D_{mean}<50Gy (RTOG 0920). *Parotid glands:* V30<45%; D_{mean} <26Gy (QUANTEC). *Pharyngeal Constrictors:* V50< 70%; D_{mean}<50Gy (QUANTEC).



Cumulative DVH was evaluated for each patient for dose received by PTV_high; PTV_low; OARs; D_{max}; D_{min}; D_{mean}.

Toxicity evaluation and follow up:

Mucosal reactions, Dysphagia, Xerostomia and oral pain were scored weekly during radiotherapy, and at 1 month and 3 month after radiotherapy, as per CTCAE Acute Morbidity Scoring Criteria for evaluation of Radiotherapy Treatments ***[24]***.Toxicities occurring within 3 months from the beginning of radiotherapy were defined as acute, and those occurring after 3 months as late toxicity. 42 patients of study population completed the intended treatment independently of the severity of toxicities while 1 patient defaulted with the treatment at 28th fraction.

RESULTS

Among the 43 patients, 34 (79.1%) were male and 9 (20.9%) were female, and the mean age on diagnosis was 55.8 years (range: 32–78).

Table 1 Patients Characteristic

	Number of Patients (n=43)	Percentage
Gender		
Male	34	79
Female	9	21
Age		
30-60	26	61
61-80	17	39
Personal Habits		
Smoking	33	76
Tobacco	6	15
Smoking + Alcohol	4	9
Primary Site		
Oral Cavity	9	21
Oropharynx	15	35
Larynx	13	30
Hypopharynx	6	14
AJCC Prognostic Stage		
II	5	12
III	15	35
IVA	23	53
Histopathology Grade		
Well Differentiated	12	30
Moderately	20	46
Differentiated	11	24
Poorly Differentiated		

Tumor localization was the oral cavity in 9 patients (21%), larynx in 13 patients (30.2%), oropharynx in 15 patients (34.8%), and hypopharynx in 6 patients (14%). The pathological diagnosis was squamous cell carcinoma in all patients. 5 patients (11.6%) had stage II disease, 15 patients (35%) had stage III disease and 23 patients (53.5%) had stage IVA disease. All patients had lymph node involvement.

Toxicity evaluation: All the patients were graded for toxicity weekly during radiotherapy and at 1 and 3 month post radiotherapy as per CTCAE v4.03 criteria. Among the complications (grade ≥2) assessed in the study; dysphagia was the most common to be observed in 83.72% of the study population following with mucositis and xerostomia presented in 72.09% and 69.76% respectively.

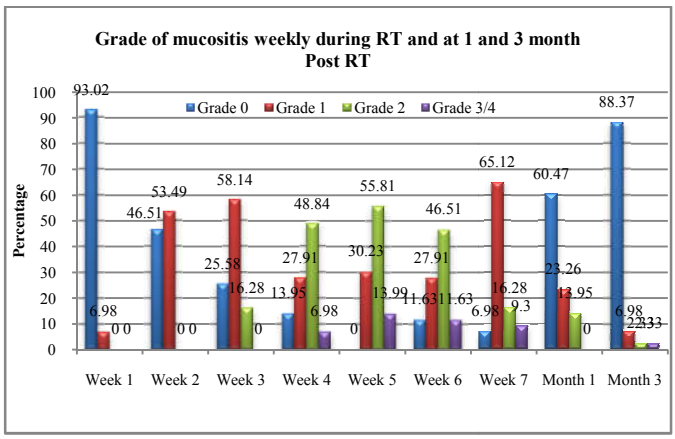
Dosimetric Parameters for Oral Cavity

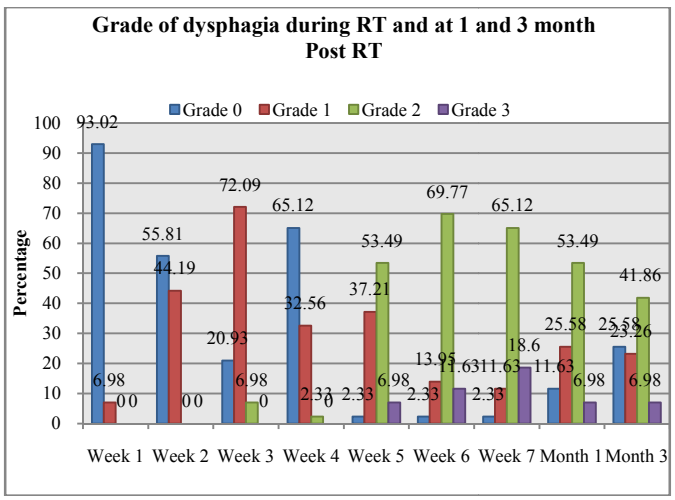
The constraints used for oral cavity in this study were as per given by RTOG 0920. Of total 43 patients studied: 5 patients were irradiated with V% in the range of 31%-40%- 4 patients presented with grade 1 toxicity and only 1 patient presented with grade 2 mucositis. No patient experienced grade 3 toxicity when volume of oral cavity irradiated was <40%. When 41%-50% volume of oral cavity irradiated- 7 patients observed grade 1 mucositis; 17 patients observed grade 2 mucositis; and 4 patients observed with grade 3 toxicity in terms of mucositis.

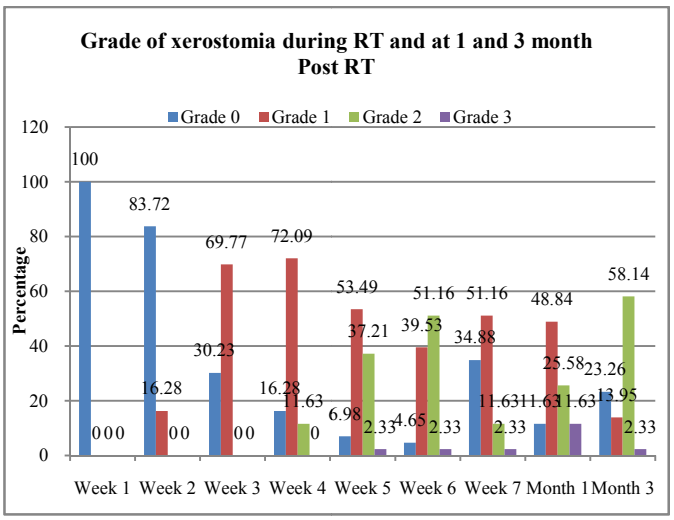
Table 2 Physician rated toxicity in terms of oral mucositis, dysphagia and xerostomia as per CTCAE v4.03 criteria

	Wk 1		Wk 2		Wk 3		Wk 4		Wk 5*		Wk 6*		Wk 7		Mnth1		Mnth3	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Mucositis																		
Grade0	40	93	20	46	11	26	6	14	0		5	12	3	7	26	60	38	88
Grade1	3	7	23	53	25	58	12	28	13	30	12	28	28	65	10	23	3	7
Grade2	0		0		7	16	21	49	24	56	20	47	7	16	6	14	1	2
Grade3	0		0		0		3	7	5	12	5	12	4	9	0		1	2
Grade4	0		0		0		0		1*	2	1*	2	0		0		0	
Dysphagia																		
Grade0	40	93	24	56	9	21	28	65	1	2	1	2	1	2	5	12	11	26
Grade1	3	7	19	44	31	72	14	33	16	37	6	14	5	12	11	26	10	23
Grade2	0		0		3	7	1	2	23	53	30	70	28	65	23	53	18	42
Grade3	0		0		0		0		3	7	5	12	8	19	3	7	3	7
Grade4	0		0		0		0		0		1*	2	0		0		0	
Xerostomia																		
Grade0	43	100	36	84	13	30	7	16	3	7	2	5	15	35	5	12	10	23
Grade1	0		7	16	30	68	31	72	23	53	17	40	22	51	21	49	6	14
Grade2	0		0		0		5	12	16	37	22	51	5	12	11	26	25	58
Grade3	0		0		0		0		1	2	1	2	1	2	5	12	1	2
Grade4			0		0		0		0		0		0		0		0	

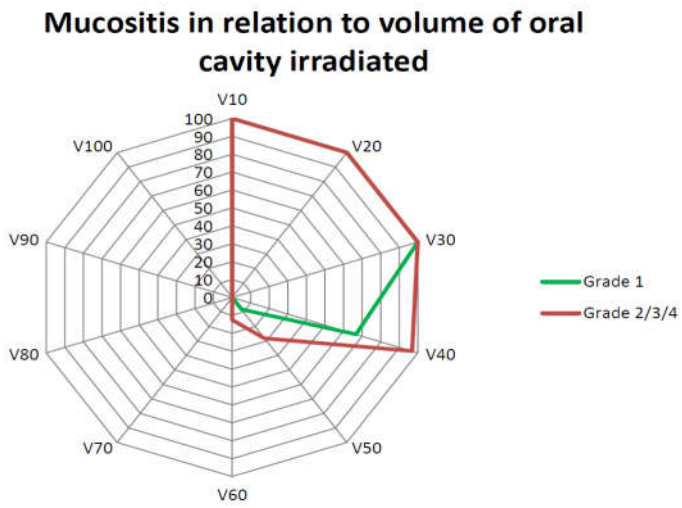
Graphical representation of toxicities observed





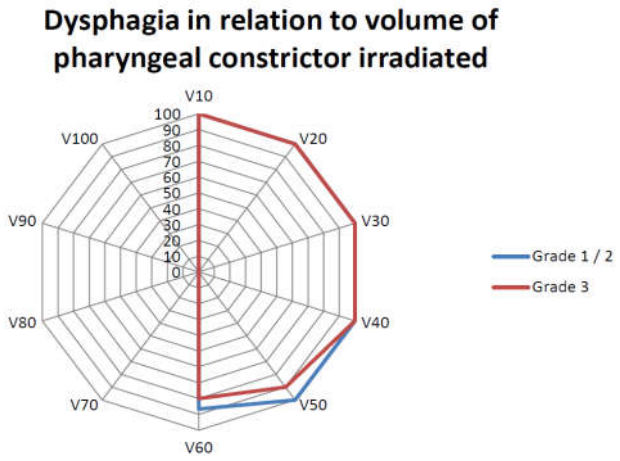


When 51%-60% volume of oral cavity irradiated- 1 patient was with grade 1 of mucositis; 4 were presented with grade 2 of toxicity; and 1 presented with grade 3 of mucositis. When considering volume of oral cavity irradiation in the range of 61%-70-; all the 4 patents presented with grade 3 of complication in terms of mucositis. Here chi square was 23.749 with 6 degrees of freedom, P<0.001 (S) was significant.



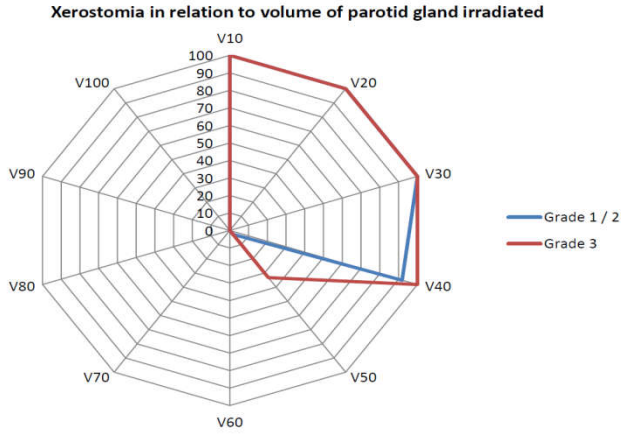
Dosimetric Parameters for Pharyngeal Constrictor Muscles (PCMs)

For the PCMs, QUANTEC recommends keeping the mean dose <50Gy to limit the risk of dysphagia to less than 20%. Here, the following constraints were associated with lower risk of dysphagia: keeping the mean dose to the PCMs <50Gy keeping V50 < 70% for the PCMs. Only one patient presented with grade 3 of complications in terms of dysphagia when 48% volume of PCMs was irradiated. ***No grade 1 and grade 2 complications was observed in 41-50% range of volume irradiated***. While ***considering V% in range of 51-60%-*** 7 (87.5%) and 1 (12.5%) patients had grade 2 and grade 3 complication in terms of dysphagia respectively. 23 (67.6%) and 8 (23.5%) patients presented with grade 2 and grade 3 toxicity ***when 61-70% volume of PCMs was irradiated.*** Here chi square= 4.806 with 4 degrees of freedom; P=0.308 (NS).



Dosimetric Parameters of Parotid Gland

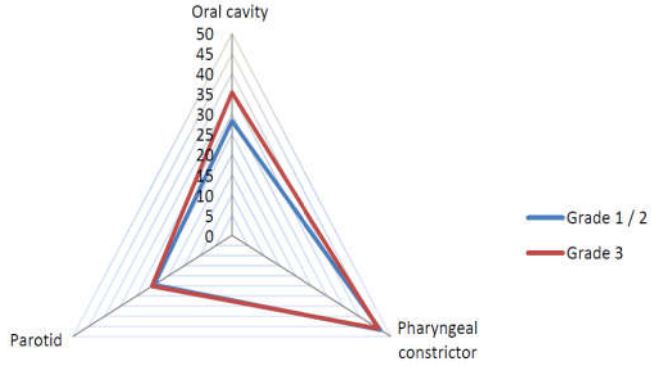
When considering *31-40% volume of parotid gland irradiation*- 2 (66.7%) patients came out with grade 1 toxicity; 1 (33.3%) patient observed grade 2 toxicity. No patient of study population came out grade 3 xerostomia when volume of parotid irradiated was limited to <40%. On comparing *41-50% volume of parotid irradiated* -7(18.9%) patients observed with grade 1 xerostomia 26 (70.3%) patients complained with grade 2 toxicity and only 4(10.8%) patients observed grade 3 of toxicity. 3 patients received *radiation to 51-60% volume of parotid* out of them 2(66.7%) patient presented with grade 3 toxicity in terms of xerostomia and 1(33.3%) patient had grade 2 xerostomia. Here chi-square = 11.434 with 4 degrees of freedom; P = 0.022(S) was significant.



Relationship between the Mean Dose (Gy) received by each structure and the Development of Complications

When comparing the mean doses (D_{mean}) in the analyzed structures, it was observed that in the patient who developed lower grades of complications (grade1/2), the D_{mean} were smaller in the oral cavity, pharyngeal constrictor muscles and in the parotid to the D_{mean} in analyzed structures of the patient who came out with higher grade of complications (grade 3).

	Grade 1 / 2	Grade 3	P value
Oral cavity	28.35 ± 7.35	35.39 ± 10.43	0.013 (S)
Pharyngeal constrictor	46.73 ± 2.636	46.17 ± 4.023	0.583
Parotid	24.41 ± 1.827	25.16 ± 2.259	0.236



DISCUSSION

All the 43 patients studied suffered with some degree of oral complication at one point of treatment; may it be of grade 1 only. But the most common grade of complications to be presented was grade 2; observed as mucositis in 23(53.5%); dysphagia in 28(65.2%); xerostomia in 23(53.5%). Oral pain as a sequential complication of oral mucositis was individually treated as according to WHO 3 step ladder and most, 33(76.7%) patient required step 2 medication of ladder i.e. opioids for mild to moderate pain ± non opioids ± adjuvant.

Dysphagia was the most common complication observed which was followed by oral mucositis and xerostomia. These findings of ours was corroborating with the study of *O Salako; O.M. Ogundana et al. [25]*

Several reports by *Christianen ME, Schilstra C, Beetz I, Muijs CT, Chouvalova O, Burlage FR, et al.[26]* and *Mazzola R, Ricchetti F, Fiorentino A, Fersino S, Giaj Levra N, Naccarato S, et al.[27]* identified the pharyngeal constrictor muscles

(PCMs) as a critical OAR for treatment-induced dysphagia. In the present study also we evaluated the dosimetric parameters of PCMs and the resulting dysphagia in the study populations.

Number of studies identified the DVH-parameters associated with both acute and late dysphagia in curative HN RT [26, 28, 29]. Furthermore acute dysphagia was a strong prognostic factor for late dysphagia [30].

Mean doses in the range of 50 to 60 Gy to the PCMs were found to be indicative of an increased risk of dysphagia in several studies by *Mazzola R, Ricchetti F, Fiorentino A, Fersino S, Giaj Levra N, Naccarato S, et al.*[27] and *Mortensen HR, Jensen K, Aksglaede K, Behrens M, Grau C.*[31]. The QUANTEC report on pharynx recommends keeping the mean dose to the pharyngeal constrictors to below 50Gy when possible, and to limit the volume receiving more than 50Gy[32]. However these recommendations are well in line with what was found for the late dysphagia at >6 months post RT.

In the present study, factor that contributed to the development of acute dysphagia is the presence of mucositis, a complication present in almost all the patients receiving concomitant radiotherapy and chemotherapy. These findings can be proven with the correlation of volume of oral cavity and pharyngeal constrictors irradiated. These findings of our study was corroborating with the findings of *Sanguineti G, Gunn GB, Parker BC, Endres EJ, Zeng J, Fiorino C.*[33] in their study "*Weekly dose-volume parameters of mucosa and constrictor muscles predict the use of percutaneous endoscopic gastrostomy during exclusive intensity-modulated radiotherapy for oropharyngeal cancer".*

Mucositis is a common and important acute toxicity of head and neck radiotherapy (RT), which may result in pain, dysphagia [33] and weight loss, and, hence, reduced quality of life [35,36]. Furthermore, severe acute reactions have been implicated in the subsequent development of 'late' radiation toxicity [37-39]. A normal tissue complication probability (NTCP) model for severe mucositis, with sufficient predictive performance, could be used for clinical decision-support [40]. Associations between RT dose metrics and mucositis could inform changes to the RT planning dose objectives to reduce the incidence of severe mucositis. It has previously been demonstrated that intensity-modulated RT can be used to spare the oral mucosa in oropharyngeal RT patients [41].

Dose objectives, such as those proposed by the Radiation Therapy Oncology Group (RTOG) clinical trials; specify varying limits for the mean dose delivered to the oral cavity in the range of 30 – 50Gy *(RTOG 0912, RTOG 0920, RTOG 1216).* In the present study dose constraints used were those as described in *RTOG 0920* [42].

Several reports with quantitative dose-response models for acute oral mucositis were identified; all based on head and neck cancer patient cohorts, with some variation in the anatomical OAR definition. The volume encompassing the oral cavity and in some cases parts of the pharynx was most commonly used [43-46], although some studies used a mucosal surface OAR definition [47-49]. In a comparative analysis ***Dean et al.*** [47, 48] concluded that models based on an oral cavity definition and mucosal surface definition performed similarly for estimating acute mucositis and they recommend using the simpler oral cavity OAR contour. Here in the present study also for the sake of simplicity and consistency, the extended oral cavity structure was defined and delineated based on Brouwer et.al. [49].

The mean dose to the oral cavity was found to be an independent predictor of oral mucositis [43,44], as well as the volume of oral cavity receiving high doses per fraction [45] and the dose to the hottest 21 cm3. [46]. These findings were consistent with findings of our study where when comparing the mean dose (Dmean) in the several analyzed structures, with the Dmean of the other patients; it was observed that in the patient who developed grade ≤1 of toxicities the Dmean were smaller in the oral cavity, parotid, and constrictors of the pharynx. Also the V% was also higher in the respective structures. One report identified concurrent chemotherapy as an independent predictor along with oral cavity dose [46], whereas for the model presented by Bhide *et al*. all patients were treated with concurrent chemo-RT [44]. In the present study also all the patients had received weekly cisplatin during radiotherapy.

It has recently become possible to spare a portion of the parotid gland by the implementation of 3-dimensional (3D) conformal RT (3D-CRT) and intensity modulated RT (IMRT) techniques in clinical practice. A high dose is administered to a small part of the parotid and is positioned close to the tumor, while the rest of the gland receives a low dose or no dose at all.

Correlation of dose with salivary flow measurements allows the production of dose/volume-response relations for parotid gland function. It became clear with the study of *Chao KSC, Deasy J, Markman J, et al.[50]* that there is an exponential relation between saliva flow reduction and mean parotid dose for each gland, suggesting that it is essential to respect a certain threshold for mean parotid dose to preserve gland function. These results were consistent with the findings of present study.

A mean parotid gland dose of ≤26Gy was initially proposed as a planning objective for substantial sparing of the gland function by *Eisbruch and colleagues* [51] from the University of Michigan. Significant reduction of xerostomia can be achieved by using a mean parotid dose of <26Gy to 30Gy as a planning criterion [52]. In the present study also the dose constraints for parotid were kept ≤26Gy as per QUANTEC and the patients who received mean doses to the higher side were having more severe grades of complications as compared to the ones who received less dose.

SUMMARY & CONCLUSION

Forty three histopathologically proven LAHNSCC patients who received curative radiotherapy with 3-DCRT technique were included in this study and further evaluated to find out the relationship between occurrence of acute oral complication and dosimetric parameters.

Clinical assessment including ENT evaluation as indicated and baseline oral health parameters assessment were done at the commencement of radiotherapy and thereafter weekly during radiotherapy and at one month and three month after radiotherapy. Oral complications in terms of mucositis, dysphagia, and xerostomia were graded as per CTCAE version 4.03 and the dosimetric parameters in terms of percent of volume (V %) receiving radiation and mean doses (D_{mean}) to the respective OAR (extended oral cavity, pharyngeal

constrictor muscles, and parotid) were evaluated by studying DVHs.

Among the complications (grade ≥2) assessed in the study; dysphagia was the most common to be observed in 83.72% of the study population following with mucositis and xerostomia presented in 72.09% and 69.76% respectively.

When comparing the mean dose and volume of OARs irradiated in the several analyzed structures, it was observed that the patients who developed lower grades (grade≤1) of complications the Dmean and volume (V%) irradiated were smaller in the parotid, oral cavity, constrictors of the pharynx than those who developed higher grades (grade ≥2) of complications. Only one patient developed grade 4 of complications and the same patient defaulted with the treatment at week 6 of treatment.
Advances in radiotherapy have improved the treatment outcomes of patients with head and neck cancer. Unfortunately, these improvements have been achieved at the cost of increased morbidity and compromised quality of life.

However, patients undergoing RT treatment for HNC with advanced technique as 3D-CRT, considering dosimetric parameters we can better spare the OAR without compromising dose to GTV, thereby reducing radiation induced acute toxicities and the assessment of acute toxicities can also predict the probability of late complication of dysphagia and xerostomia and the timely intervention for these toxicities can improve the overall quality of life of head & neck cancer patients.

Non dosimetric parameters like age, stage of disease, oral hygiene, personal habits like smoking, nutrition contribute to the toxicity observed by the patient undergoing treatment and discrepancy in the results. However, these non dosimetric parameters were not assessed in the study.

Further studies should be encouraged to define a reasonable and acceptable value of normal tissue tolerance of radiation for routine clinical practice.

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