Article published online: 2022-04-25

Head and Neck Cancer

Concurrent Weekly Cisplatin and Simultaneous Integrated Boost-IMRT in Locally Advanced Head and Neck Squamous Cell Carcinoma—An Institutional Experience

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South Asian J Cancer 2022;11(3):235–242.

Abstract

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Introduction Concurrent chemoradiation with weekly cisplatin in locally advanced head and neck squamous cell carcinoma (LA-HNSCC) is widely practiced in India. Radiation with simultaneous integrated boost intensity-modulated radiotherapy (SIB-IMRT) has the advantage of executing IMRT in single phase with better dose distribution.

Material and Methods 150 patients with LA-HNSCC treated between April 2015 and December 2019 were retrospectively evaluated. All patients received 70Gy in 33 to 35 fractions with SIB-IMRT and concurrent weekly cisplatin at a dose of 40 mg/m^2. Treatment compliance and toxicities were assessed. Overall survival (OS) was evaluated using Kaplan-Meier estimates; univariate and multivariate analysis of prognostic factors were also evaluated.

Results Median age was 58.5 years. Forty-five percent had primary oropharyngeal cancer. Sixty-two percent had T3 disease, 41% had N2 disease, and 51% had stage IV disease. All patients received 70Gy dose of RT. Median chemotherapy cycles were six, 84.7% received 200 mg/m^2. Acute grade 2 xerostomia was seen in 79%, grade 3 neutropenia, mucositis and pharyngitis were seen in 11, 15, and 21%, respectively. Complete response was seen in 66.6%. At median follow-up of 21.4 months (3–71) OS was 60% and median OS was 33.2 months. Estimated 2 and 3 year OS was 56 and 48%. On univariate analysis, absence of node, N0–N1, stage III, cisplatin use, dose per fraction 2.12Gy ,and complete response showed good OS (p <0.05). On multivariate analysis dose per fraction 2.12Gy and complete response showed good OS (p <0.05).

Conclusion Definitive chemoradiation with weekly cisplatin and SIB-IMRT in LA-HNSCC is well tolerated with good clinical outcomes.

Keywords

- chemoradiation
- head and neck cancer
- India
- SIB-IMRT
- weekly cisplatin

DOI https://doi.org/10.1055/s-0042-1743578 ISSN 2278-330X

How to cite this article: Ahmed I. Krishnamurthy S, Bhise R, et al. Concurrent Weekly Cisplatin and Simultaneous Integrated Boost-IMRT in Locally Advanced Head and Neck Squamous Cell Carcinoma—An Institutional Experience. South Asian J Cancer 2022;11(3):235–242.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Squamous cell carcinomas of the head and neck region are the most common cancers in India. Cancers of the oral cavity, larynx, oropharynx, and hypopharynx account for more than 2,00,000 cases, with an annual incidence of 16.7%.[1] Use of tobacco in its various forms is the most common etiological factor[2] and human papilloma virus (HPV)-related cancers are less common.[3] A vast majority of patients present with advanced disease require multimodality treatment. Locally advanced head and neck squamous cell carcinomas (LA-HNSCC) of the pharynx and larynx are treated with definitive concurrent chemoradiotherapy (CCRT) with the advantage of functional organ preservation. It is important to consider cancers of the oral cavity as separate entity as they behave differently and surgery is the primary modality of treatment followed by adjuvant RT with or without chemotherapy.

With the results of updated meta-analysis of chemotherapy in head and neck cancer (MACH-NC),[4] CCRT with cisplatin-based chemotherapy is the current standard of care with a 5-year overall survival (OS) of 33.6% with an absolute benefit of 6.5%. But this benefit is overshadowed by the increased probability of treatment toxicities. These toxicities lead to poor compliance and treatment breaks, affecting the clinical outcomes and quality of life. Hence, the primary goal of the management should be to combine chemotherapy and RT in a way that is better tolerated and at the same does not compromise the treatment outcomes.

Since radiotherapy is the primary modality of treatment, in this era of advanced technology, use of IMRT should be the first step forward. Simultaneous integrated boost intensity-modulated radiotherapy (SIB-IMRT) technique has the advantage of single phase planning with better dose distribution and slight dose escalation with mild hypo-fractionation. While choosing the appropriate chemotherapy with RT, the current evidence suggests that cisplatin is the drug of choice[4] and cisplatin-based chemotherapy cannot be replaced by even anti-EGFR targeting agents like cetuximab[5] or nimotuzumab[6] or newer chemotherapy agents like paclitaxel.[7] Though high-dose cisplatin (100 mg/m^2) given in 3 weekly interval is considered standard and reinforced by recent evidence,[8] the optimal schedule is still open to discussion.

The use of IMRT with cisplatin incorporated in a simpler manner seems to be a logical approach, provided it translates to an acceptable therapeutic ratio. This prompted us to evaluate weekly cisplatin and SIB-IMRT in the management of patients with LA-HNSCC treated at our institution. The initial data was presented in ECHNO/ICHNO 2021 conference.[9]

Materials and Methods

This is a retrospective study evaluating compliance and outcomes in head and neck carcinoma patients treated with definitive SIB-IMRT and weekly cisplatin. A total of 150 consecutive patients with non-metastatic locally advanced cancer of oropharynx, larynx, and hypopharynx treated in a single unit between April 2015 and December 2019 at our institution were included in the study.

All had biopsy proven histology of squamous cell carcinoma and Karnofsky Performance Status (KPS) of more than 70. Baseline demographic and tumor-related parameters were documented. All 150 patients underwent baseline clinical and radiological evaluation of loco-regional disease with endoscopy and contrast-enhanced computed tomography (CECT) scan of head and neck region. Staging was done according to American Joint Committee on Cancer (AJCC), 7th edition.[10]

Radiotherapy

With the patient in supine position, head and neck regions were immobilized with four clamp thermoplastic mask CECT simulation was done with 2.5-mm slice thickness and images were acquired. Gross tumor volume, clinical target volume, high (70Gy), intermediate (59.4Gy), low risk (54–56Gy) planning target volumes (PTV-HR, PTV-IR, and PTV-LR) and organs at risks were contoured and constraints were defined. Treatment was planned with seven or nine field SIB-IMRT technique, to a total dose of 70Gy in 33 to 35 fractions at a dose of 2.12Gy or 2Gy per fraction over 6.5 to 7 weeks in Eclipse Version 11 treatment planning system. Treatment verification was done with weekly electronic portal imaging device images.

Chemotherapy

Concurrent chemotherapy consisted of cisplatin given every week at a dose of 40 mg/m^2, administered intravenously with pre-medications and adequate hydration protocol. Weekly carboplatin at area under curve-2 was given in patients with deranged renal function test (RFT). Weekly complete blood count and RFT were done each time before the start of chemotherapy.

Toxicity Evaluation and Response Assessment

Acute hematological and non-hematological toxicities were assessed every week, at the end of treatment and at every visit till 3 months post treatment, using RTOG-EORTC toxicity grading.[11] Weight loss, need for supportive care (analgesics, IV fluids, and antibiotics), and treatment breaks were documented.

Loco-regional response was assessed with CECT scan of head and neck region at 3 months post treatment and documented as per Response Evaluation Criteria in Solid Tumors (RECIST) criteria version 1.1.[12] Patients were followed up for every 3 to 6 months.

Statistics

Data was collected retrospectively; the results were prospectively evaluated and analyzed using SPSS version 16. OS was defined as the time between the dates of the start of treatment to the date of death/last seen in clinic/last telephonic information. Loco-regional control (LRC) was defined as the time between the dates of the start of treatment to the date of local or regional recurrences; in patients who did not achieve complete response (CR) it was taken as a failure at

the time of assessment. Kaplan-Meier estimates were performed to calculate the OS and LRC. Potential prognostic factors affecting the survival were identified. Univariate analysis with log rank test was performed on them to study correlation to survival and a $p < 0.05$ was considered statistically significant. Those prognostic factors with significant p-value on univariate analysis were further evaluated with multivariate analysis using Cox Regression model.

Results

Baseline Patient Characteristics

Median age at presentation was 58.5 years (range 29–81). In total, 73% were male, 70% had a history of tobacco use either in the form of chewing or smoking and 13% had associated co-morbidities like diabetes and hypertension. All had KPS of >70. Baseline hemoglobin, weight, need for feeding jejunostomy (FJ), and tracheostomy (TT) and other demographic details are as shown in ►Table 1.

Tumor and Treatment Characteristics

Sixty-eight patients (45%) had primary oropharyngeal cancer, 93 (62%) had T3, 102 (68%) had node positive, and 74 (49%) had stage III disease. All patients (100%) completed planned radiotherapy dose of 70Gy in 33 to 35 fraction, equal number of patients (50%) received 2.12 and 2Gy per fraction. Median chemotherapy cycles were six (IQR 5–6), 125 patients (83.2%) received five or more cycles. A total of 118 patients (78.6%) received cisplatin chemotherapy, and 100 (84.7%) of them received >200 mg/m^2 of cumulative dose of cisplatin.

Acute Toxicity and Treatment Compliance

Median overall treatment time was 50 days (IQR 48–54). Median treatment interruption was 4 days (IQR 1–8), 39 (26%) patients had treatment break: 18 (11.3%) due to hematological toxicities, 9 (6%) due to non-hematological toxicities, and 12 (8%) due to logistic reasons. Overall, 18 patients (11.3%) had grade 3 hematological toxicity. Fifteen patients (10%) had grade 3 neutropenia, only one patient had grade 3 anemia. Twenty-three patients (15.3%) and 28 patients (18.7%) had grade 3 mucositis and pharyngitis, respectively. In total, 119 patients (79.3%) had grade 2 xerostomia. Overall grade 3 non-hematological toxicities were seen in 54 patients (36.6%). No treatment-related deaths were reported. Mean weight loss was 9.8% (IQR 6–12%). Two patients gained weight. Details are given in ►Table 2.

Survival Outcomes

At the last follow-up, a total of 72 patients were alive. Seventy-one patients were alive and disease-free and one patient was alive with disease. Of the total 150 patients, 99 (66%) achieved CR, 40 (26.6%) had partial response, nine (6%) had progressive disease and two (1.4%) had stable disease. With a median follow-up of 21.7 months (range 3–71) and 36 months in surviving patients (range 16–71 months) the OS was 60%. Median OS was 33.2 months. Estimated 2-year, 3-year, and 5-year OS were 56, 48, and 42%, respectively. Estimated 2-year OS for stage III and IV oropharynx, hypopharynx, and larynx was 55, 59.9, 71.9% and 48.8, 44.1, 66.7%, respectively. Estimated 2 year LRC was 62.4%. Survival curves for OS and LRC are shown in ►Figs. 1 and 2.

Prognostic Factors

On univariate analysis of the potential prognostic factors, N0 status, N0–N1 nodal group (low nodal burden), stage III disease, RT dose per fraction: 2.12Gy, use of cisplatin chemotherapy and CR to treatment showed good OS with statistically significant p-value (<0.05), as depicted in ►Table 3.

These prognostic factors were further evaluated with multivariate analysis. RT dose per fraction: 2.12Gy showed significant median OS benefit of 59.2 versus 21.9 months ($p = 0.01$); in patients who had CR to treatment, median OS was not reached ($p = 0.00$).

Patterns of Failure

Of the 99 patients who had CR, 29 patients have expired. Of the 29 patients, five developed second primary cancer after 2 to 5 years post treatment—two had esophageal cancer treated with CCRT, two had oral cavity cancers treated with re-irradiation in one patient, and one had lung cancer treated with palliative RT. Six had local only, one had local-regional-distal, two had distal (bone only) failures, all of them subsequently succumbed to disease. In total, 15 patients expired of unknown causes.

Of the 51 patients who did not achieve CR, forty-nine patients (96%) had local, eight (15.6%) had loco-regional, and four (7%) had distal failure. A total of 56.8% were of primary oropharyngeal cancer. None of them were considered for salvage surgery also many refused further intervention.

Late Toxicity

Of the 71 patients who are alive and disease free, with a median follow-up of 36 months (range 16–71) in these patients, 28 did not report any form of late toxicity and late toxicity was not documented in 17 patients. Most common late toxicity was xerostomia (19 patients—26%) and only seven (9.7%) among them had grade 2 xerostomia; followed by spicy intolerance in eight patients (11%). No grade-3 late toxicities were reported. None of the patients reported any grade of dysphagia, feeding tube dependence, renal toxicity, or symptomatic hearing loss. Feeding jejunostomy (FJ) and Tracheostomy tube (TT) were removed in two and three patients, respectively.

Discussion

At a median follow-up of 21.7 months, the OS in our study was 60%. With an estimated 2-year OS of 56% and 5-year OS of 42%, our outcomes are similar to that of MACH-NC,[4] where the 2-year OS was in the range of 50 to 55% and 5-year OS was 33.6%.

While comparing our results with the standard trials, the OS data across these have to be interpreted with caution. There is heterogeneity in patient selection with regard to primary site owing to geographical variation (oral cavity

Table 1 Patient and treatment characteristics

Characteristic	Number = 150	Percentage
Age (years) Median	58.5 y (range 29–81)	
Sex Male/Female	109/41	73%/27%
Co-morbidities	19	13%
Addiction to tobacco	105	70%
KPS >70	150	100%
Histology Grade 1/2 Grade 3/NOS	19/71 16/44	13%/47% 11%/29%
Baseline hemoglobin (gm/dL) Mean	12.6 (range 5.2–19.6)	
Baseline weight (kg) Mean	48.5 (range 29–86)	
Baseline feeding tube	15	10%
Tracheostomy	7	05%
Site of primary		
Oropharynx	68	45%
Hypopharynx	54	36%
Larynx	28	19%
Tumour stage		
T2/T3	24/93	16%/62%
T4a/T4b	30/03	20%/02%
Nodal stage		
N0/N1	48/35	32%/23%
N2/N3	62/05	41%/03%
Stage group		
III	73	49%
IVA	67	45%
IVB	10	06%
Radiotherapy 70Gy	150	100%
Chemotherapy		
Cisplatin	118	78.6%
Carboplatin	32	21.3%
Chemotherapy (cycles)		
Median	6 (IQR 5–6)	83.2%
5 cycles or more (>200 mg/m^2)	125	
OTT (days) Median	50 (IQR 48–54)	
Weight loss Mean		9.8%

Abbreviation: NOS, Not otherwise specified.

cancers are common in India, nasopharyngeal cancers in China); tumor biology (HPV positive vs. negative, tobacco related cancers); fractionation of RT used (accelerated RT vs. conventional RT); chemotherapy used (cisplatin 30 mg vs. 40 mg, carboplatin: 5FU, Docetaxel, MAbs), and cisplatin regimen used (weekly Cisplatin vs. 3 weekly Cisplatin). Our

Table 2 Acute toxicities

Toxicity	Grade 0	Grade 1	Grade 2	Grade 3	Overall
Hematological					
Anemia	97 (64.7%)	42 (28%)	10 (6.7%)	1 (0.7%)	Grade 3 11.3%
Leucopenia	69 (46%)	38 (25.3%)	26 (17.3%)	17 (11.3%)	
Neutropenia	97 (64.7%)	23 (15.3%)	15 (10%)	15 (10%)	
Thrombocytopenia	131 (87.3%)	14 (9.3%)	5 (3.3%)	0	
Non hematological					
Mucositis	24 (16%)	24 (16%)	79 (52.7%)	23 (15.3%)	Grade 3 36.6%
Dermatitis	0	143 (95.3%)	5 (3.3%)	2 (1.3%)	
Xerostomia	14 (9.3%)	17 (11.3%)	119 (79.3%)	NA	
Pharyngitis	7 (4.7%)	15 (10%)	100 (66.7%)	28 (18.7%)	
Laryngitis	14 (9.3%)	73 (48.7%)	53 (35.3%)	10 (6.7%)	

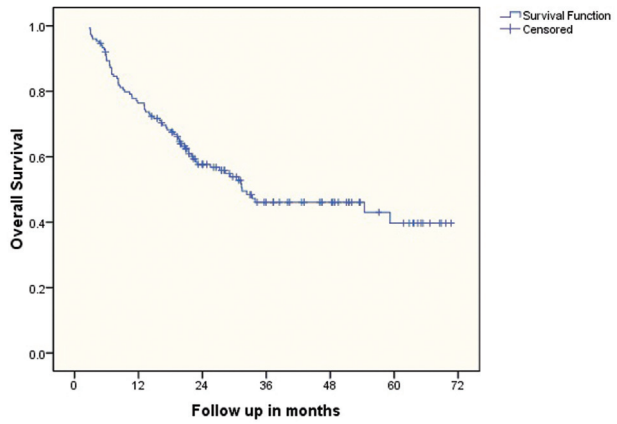

Fig. 1 Overall survival.

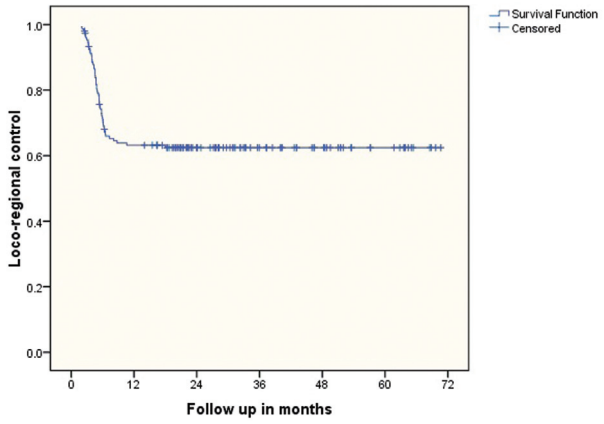

Fig. 2 Loco-regional control.

OS data are compared with some of these studies as shown in ►**Table 4**.

Most of the recent western studies that used 3 weekly[13,14] or weekly cisplatin[15] regimen, had significant number of HPV positive patients (>70% of oropharyngeal cancers). The 5-year OS here was overwhelming, in the range of 75 to 85% which cannot be compared with our patient population where HPV positivity rate is less than 10%.[3] Since RTOG 0129 study,[13] most of the RTOG studies use accelerated fractionation with 6 fractions/wk and two cycles of 100 mg/m^2 cisplatin[5,14] further making the comparison difficult and challenging. While in these studies, accelerated fractionation was used to compensate for the third cisplatin cycle, GORTEC 9902 study did not show any benefit with accelerated fractionation and chemotherapy.[16]

Table 3 Univariate analysis of prognostic factors

Variable	Prognostic factor	Median OS in months	*p*-Value
Node	Negative or Positive	NR or 21.9	**0.002**
N stage	N0–1 or N2–3	59.2 or 21.3	**0.005**
Stage	III or IVa-b	NR or 20.8	**0.001**
Dose in Gy	2.12 or 2	59.2 or 21.9	**0.03**
Chemotherapy	Cisplatin or carboplatin	54.4 or 19.4	**0.03**
Response	CR or others	NR or 9.1	**0.000**

Note: *p*-Value was >0.05 (NS) for—age, sex, co morbidities, addiction, tumor grade, site, T stage, hemoglobin, OTT, chemotherapy dose, feeding tube, and weight loss.

Table 4 Overall survival across studies

	Studies	Salient features	Overall survival	Comments
Present study	Institutional	IMRT and weekly cisplatin	42% (5 y)	Retrospective study, Weekly Cisplatin—40 mg/m^2
Meta-analysis	MACH-NC[4]	107 studies	33.6% (5 y)	Level 1 evidence
3 weekly vs. Weekly cisplatin	Meta-analysis[17]	52 studies	40% (5 y)	Included adjuvant RT cases also
	TMH[8]	RT + 3W cisplatin[a] vs. RT + W cisplatin	NR vs. 39.5 (median) p = NS	Adjuvant RT (93%), oral cavity primary and MUO (95% cases), 2 y LRC 73 vs. 58%(p = 0.01) Weekly Cisplatin dose—30 mg/m^2
	JCOG 1008[18]	RT + 3W cisplatin[a] vs. RT + W cisplatin	71 vs. 59% (3 y) p = 0.002	Adjuvant RT only, oral cavity only primary Weekly Cisplatin dose: 40 mg/m^2 (ASCO abstract)
Altered fractionation (AFRT)	Meta-analysis[19]	AFRT + 3W cisplatin vs. AFRT + W cisplatin	33 vs. 57% (5 y) p = 0.01	Different fractionation schedules, Except for RTOG studies, all were phase 2 single arm trials
	RTOG 0129[12]	AFRT + 3W cisplatin[b] vs. RT + 3W cisplatin	48 vs. 48% (8 y) p = NS	HPV positive: 73% of oropharynx Similar rate of toxicities
	RTOG 0522[13]	AFRT + 3W cisplatin[b] vs. AFRT + 3W cisplatin + cetuximab	73 vs. 76% (3 y) p = NS	HPV positive: 70% of oropharynx 3Y OS in HPV negative: 60 vs. 86%
	GORTEC 9902[16]	RT + CT vs. AFRT + CT vs. VAFRT alone[c]	–	3Y PFS: 37 vs. 34 vs. 32% (p = NS) AFRT—6#/week, very AFRT—64·8Gy in 3.5 wk-1.8Gy twice a day
RT + MAB	GORTEC 2007–01[20]	RT + CT + cetuximab[c] vs. RT + cetuximab	61 vs. 55% (3 y) p = NS	Limited nodal disease—up to N2a PFS: 52.3 vs. 40.5
	GORTEC 2007–02[22]	TPF-RT + cetuximab[c] vs. CCRT	50 vs. 52% (2 y) p = NS	Heavy nodal burden disease N2b-N3, PFS-42 (NS) Toxicities more in TPF arm
	TMH[6]	RT + W cisplatin vs. RT + W cisplatin + nimotuzumab	64 vs. 58% (2 y) p = NS	2Y DFS 48.5 vs. 60.2% (p = 0.008) HPV positive were 7.5–10%, Cisplatin dose 30 mg/m^2, 2 y OS in HPV NEG 57 vs. 34%
Induction CT→ CCRT	TAX 324[23]	TPF→ RT + W carboplatin vs. PF→ RT + W carboplatin	62 vs. 48% (3 y) p = 0.002	No direct CCRT comparison arm
	PARADIGM[24]	TPF→ RT + W docetaxel/carboplatin v/s RT + 3W cisplatin	73 vs. 78% (3 y) p = NS	HPV pos—more, toxicity more in TPF regimen RT—concurrent boost schedule Slow accrual—early halting of study

[a]Cisplatin—100 mg/m^2 D1, D22, D43.
[b]Cisplatin—100 mg/m^2 D1, D22.
[c]CT in GORTEC—carboplatin + 5FU.

While concurrent three weekly 100 mg/m^2 cisplatin is considered standard, meta-analysis of three weekly versus weekly cisplatin by Szturz et al[17] failed to show any survival difference (5-year OS of 40%) and weekly regimen was more compliant with less toxicity especially in the definitive setting. This meta-analysis was published before the publication of the study by Noronha et al.[8] It is this study which re-iterated that weekly cisplatin is inferior to three weekly regimen, with 2 year LRC of 58 versus 73% (p = 0.014). But this study itself had major pitfalls—93% of patients were treated in adjuvant RT setting; 90% had oral cavity primary, oropharyngeal, hypopharyngeal and laryngeal primaries constituted only 5% cases

in whom definitive RT was used; weekly cisplatin dose was 30 mg/m^2, wherein the adequacy of dose is questionable. Also it did not show any OS benefit ($p = 0.48$). Similar data was presented by JCOG in ASCO 2020,[18] comparing 40 mg/m^2 of weekly cisplatin with three weekly cisplatin in adjuvant setting which showed results favoring weekly cisplatin with 3-year OS of 72 versus 59% ($p = 0.002$). These two studies again do not throw any light on the definitive CCRT. Another meta-analysis assessing altered fractionation with weekly versus 3 weekly cisplatin showed 5-year OS benefit of 57 versus 33% ($p = 0.01$) favoring 3 weekly regimen.[19] Here except for RTOG studies all were small phase 2 studies using different fractionation schedules and different doses of weekly cisplatin. Hence, the debate of three weekly cisplatin versus weekly cisplatin is still unsettled.

While monoclonal antibodies like cetuximab has completely failed to compete with standard chemotherapy,[5,14,15,20] there are claims that combination of nimotuzumab with weekly 30 mg/m^2 cisplatin is the standard in comparison with weekly 30 mg/m^2 cisplatin, especially in HPV negative, tobacco using population like in ours.[3,6] In this study, 2-year LRC (67 vs. 57%, $p = 0.006$) and DFS (61.8 vs. 50%, $p = 0.003$) benefits were seen without any OS benefit (63 vs. 58%, $p = 0.16$). Irony is, while there are still questions regarding the dose adequacy of 30 mg/m^2 cisplatin, novel strategies are being compared with this schedule.

In our study, all patients completed planned RT dose (70Gy) without any significant treatment breaks. Nearly 80% patients received cisplatin and among them 85% received a cumulative dose of >200 mg/m^2 in a day care setting. Only 11.3% had grade 3 hematological toxicities; grade 3 mucositis or dysphagia was seen in less than 20% of the patients, most of them were managed on OPD basis. None of them had grade 3 late toxicity and most of them did not report impaired activities of daily living. In the standard fractionation and three cycles of high dose cisplatin arm of the RTOG 0129,[13] the overall grade 3 acute toxicity was 74% and oral mucositis was seen in 40% of the patients; in RTOG 0522 study[14] which used AFRT and two cycles of high dose cisplatin, overall grade 3 acute toxicity was 87% and oral mucositis was seen in almost 60% of the patients. This probably suggests that weekly cisplatin regimen has a better toxicity profile.

Classical prognostic factors like node negative, low nodal burden, and stage III disease showed better OS benefit on univariate analysis in our study too. Cisplatin chemotherapy fared well in comparison to carboplatin on univariate analysis with a median OS of 54.4 versus 19.4 months (0.03), showing that the single agent carboplatin is less efficacious than cisplatin. On multivariate analysis, dose per fraction of 2.12Gy and CR to treatment showed statistically significant OS benefit. This indicates that, with SIB-IMRT if the goal of CR is achieved, many patients continue to survive long time. Surprisingly, while evidence pushes us to achieve a minimum cumulative target dose of 200 mg/m^2 of cisplatin,[21] the median OS in our patients receiving >200 mg/m^2 was 54.4 versus 20 months, which was not statistically significant ($p = 0.12$).

The patterns of failure in our study indicates that local and loco-regional failures are more common, distal failures, even if occur, are usually not isolated. Studies like GORTEC 2007–02,[22] TAX 324,[23] PARADIGM,[24] and DeCIDE[25] looked into the role of neo-adjuvant chemotherapy followed by CCRT, assuming that LA-HNSCC might have more distant failures requiring aggressive systemic therapy. Treatment-related toxicities in the induction arms of these studies were high. More importantly 20 to 30% patients after induction chemotherapy did not enter CCRT especially in TPF.[22,23] These studies also failed to show any difference in survival or patterns of failure (distant failure rates 7 vs. 11%). Hence, it is imperative that CCRT alone is the treatment of choice.

Five patients (3.3%) developed second primary cancers, which are comparable to the historical data where the incidence of second primary cancer was 10 and 15% at 3 and 5 years, respectively.[26]

In the present day oncology practice, there is not only a wide array of chemotherapy drugs to choose from, but the regimen that gives best results also has to be carefully chosen. Entangled in all these issues, the primary modality of treatment—radiotherapy is completely submerged in the wave of chemotherapy. Like systemic therapies, radiotherapy has also taken a big leap keeping in pace with the ever evolving technology ameliorating toxicities backed by evidence.[27] Yet it is not explored to its full potential and its contribution is masked. It is very surprising that, even in the recent studies like the Noronha et al study[8] or the nimotuzumab study[6] significant number of patients were treated by two-dimensional RT technique (99% and 86%, respectively).

The major drawback of our study is its retrospective nature, though most of the data were prospectively well maintained. But our study is currently relevant especially for the Asian population where weekly cisplatin is more commonly used owing to potential differences in demography, resources, and compliance.[28,29] This approach has to be studied in a well-conducted RCT in a definitive setting answering all the gray areas. Till then, CCRT with weekly cisplatin in LA-HNSCC is here to stay.

Conclusion

Definitive SIB-IMRT and weekly cisplatin in locally advanced head and neck cancer are relatively simpler to deliver culminating to a combination which is better tolerated with good toxicity profile and good clinical outcomes.

Conflict of Interest

None declared.

Acknowledgments

The authors are thankful to all their patients and their caregivers.

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