Original Article

Concurrent cisplatin-based chemotherapy versus radiotherapy alone as adjuvant therapy for squamous cell carcinoma of the oral cavity bearing high-risk features

Anis Bandyopadhyay, Surendranath Senapati[1], Deepti Rani Samanta[2], Sarthak Mohanty[3], Prafulla Kumar Das[4]

Department of Radiotherapy, Medical College and Hospital, Kolkata, West Bengal, Departments of [1]Radiation Oncology, [2]Medical Oncology and [4]Surgical Oncology, Acharya Harihar Regional Cancer Center, Cuttack, Odisha, [3]Department of Radiation Oncology, Tata Memorial Hospital, Mumbai, Maharashtra, India

ABSTRACT

Background: To compare concurrent cisplatin-based chemoradiation in an adjuvant setting for high-risk squamous cell carcinoma of oral cavity terms of toxicity, local-regional control, and overall survival. **Materials and Methods:** A total of 54 patients of postoperative squamous cell carcinoma of oral cavity with high-risk features were randomized into two groups; postoperative radiation (60 Gy/30#/6 weeks) or postoperative concurrent chemoradiation (60 Gy/30#/6 weeks with weekly concurrent cisplatin 50 mg) arms. **Results:** Buccal mucosa was the most common sub site (44.4%) affected, followed by lower alveolus/alveolar ridge (37%) and most tumors (64.3%) were well-differentiated. About 67.3% of the patients completed their course of radiation within 6 weeks with only 69 patients receiving the scheduled 60 Gy of external beam radiation therapy dose. Only 6 patients out of 22 completed the 6 cycles of weekly chemotherapy with compliance decreasing most after 3 cycles. Mucositis and dysphagia were significantly higher in the chemoradiation arm. After a median follow-up of 47 months, the loco-regional control rate was 51.4% in the postoperative chemoradiation arm as compared to 35.56% in the postoperative radiation arm. The 5 years overall survival was 56.4% in postoperative chemoradiation arm as compared to 51.3% in the postoperative radiation only. **Conclusion:** Postoperative concurrent chemoradiation with weekly cisplatin in high-risk oral cancer gave an advantage in the loco-regional control rate and overall survival at the end of 47 months, with significant increase in acute toxicities Grade III and Grade IV toxicities.

Key words: Chemoradiation, oral cancer, postoperative

INTRODUCTION

Annually about 600,000 squamous cell carcinomas of head and neck are diagnosed worldwide. In India, it accounts for one-fourth of all male cancers, with the oral cavity being the most common site.[1] Chewing betel quid and nonsmoke tobacco consumption along with smoking are the biggest risk factor for these cancers in the country.[2] The majority (60%) of these patients clinically present with the locally advanced disease with surgery and/or radiotherapy (RT) being the mainstay of treatment. Locoregional recurrences and distant failure are frequent after surgery of Stage III or IV squamous cell carcinoma of the head and neck. Most multi-institutional trials, including patients treated with surgery followed

Address for correspondence: Dr. Anis Bandyopadhyay, Department of Radiotherapy, Medical College and Hospital, College Street, Kolkata, West Bengal, India.
E-mail: anish_b123@yahoo.com

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.164719

Cite this article as: Bandyopadhyay A, Senapati S, Samanta DR, Mohanty S, Das PK. Concurrent cisplatin-based chemotherapy versus radiotherapy alone as adjuvant therapy for squamous cell carcinoma of the oral cavity bearing high-risk features. Clin Cancer Investig J 2015;4:610-6.

RT for advanced head and neck squamous cell carcinoma yielded local-regional recurrence, distant metastasis, and 5-year survival rates of 30%, 25%, and 40%, respectively.[3]

Various strategies have been proposed to improve the outcome among patients who have resectable, locally advanced squamous cell carcinoma of the head and neck with a high risk of recurrence or metastases. From late 1970s to the early 1990s, promising results emerged from the use of various combinations of postoperative chemotherapy and RT in randomized and nonrandomized studies.[4-6] In 2004, two large studies, European Organization for Research and Treatment of Cancer (EORTC) trial 22931 and Radiation Therapy Oncology Group (RTOG) 9501/intergroup trial evaluated the role of concurrent cisplatin-based chemoradiation in an adjuvant setting for high-risk head and neck cancer. Both trials resulted in a substantial and significant increase in local, regional control and a short-term increase in survival with postoperative adjuvant chemo-RT in poor prognosis patients.[7,8] However, there was no impact on the rate of distant metastases, which represented greater the 40% of the failures in both studies.

Oral cavity cancers in them are an aggressive subgroup with much worse outcomes with both radical (conventional or altered) and postoperative RT. Above studies which have demonstrated improved control with addition of concurrent chemotherapy in the form of cisplatin (weekly or 3 weekly) had a very small subset of patients of oral cancers and thus generalization of the overall effects on these smaller subset warrants caution. Moreover, the widely prevalent poor oral hygiene, malnutrition, tobacco chewing are added factors to be taken into consideration for feasibility of such an aggressive therapy. Thus, the study aims to evaluate the effect of cisplatin-based postoperative adjuvant concurrent chemoradiation as compared to postoperative radiation alone for squamous cell carcinoma of oral cavity alone regarding toxicity, compliance, and loco-regional control.

MATERIALS AND METHODS

Patients of nonmetastatic oral cavity squamous cell carcinoma fulfilling the eligibility criteria were accrued for the longitudinal prospective nonrandomised cell carcinoma arising from the oral cavity, who underwent radical surgery with histopathological evidence of the disease and having high characteristics and did not receive any prior chemotherapy or RT. High-risk features described were any of the following: pT3 or pT4, more than two metastatic neck node, extracapsular extension (ECE), lymphovascular or perineural invasion and surgical positive margin. The other inclusion criteria were single lesion, age more than 20 but <70 years, hemoglobin level minimum 10 g/dl, minimum performance (Karnofsky Performance Score [KPS]) status of 70 and above, total leucocyte count minimum 4000, serum creatinine level <1.5 and serum urea level 40mg/dl. Patients fulfilling the above criteria were randomly allocated into chemoradiation or radiation only arm. Twenty six patients in the Arm A were treated with postoperative RT alone by Co-60 Machine, using conventional fractionation, dose 58–60 Gy over 6 and 28 patients with high-risk features received postoperative RT (58–60 Gy, conventional fractionation) along with weekly cisplatin (6 cycles) at the rate of 35–40 mg/m^2, to be completed 2 h prior to the start of RT. Radiation was started after minimum 3 weeks postsurgery, but not beyond 6 weeks, using unilateral fields (single or antero-lateral wedge pair portals) for lateralized disease and bilateral portals for midline structures such as tongue and floor of mouth. All patients were evaluated by a postoperative computed tomography of the head and neck. Radiation was planned using the conventional simulator. The treatment portal included the primary site and the draining nodal region. All patients underwent selective/modified neck dissection. For pathological N0 disease, elective nodal irradiation was done up to level II, and for pN+ disease with the well lateralized primary disease, radiation portal included ipsilateral nodal station one level lower than the extent of the dissection. For midline disease with pN+ status, bilateral neck was included one level lower than the extent of the dissection. For pN+ disease in level III/IV levels I-V was included.

The patients were first evaluated postsurgery just before the start of radiation therapy, during each week of treatment and at the end for acute toxicity as per RTOG toxicity criteria, and for compliance, both for RT and chemotherapy. Routine hematological and biochemical parameters were monitored every week and at the end of the therapy. Care was taken not to discontinue radiation, due to acute toxicity, but limiting or delaying subsequent doses of chemotherapy. Cisplatin was postponed till the absolute neutrophil count reached ≥1000/cc and renal function normalized. Patients were followed up posttherapy first at 6 weeks, thereafter every 3 months till 2 years, thereafter every 6 months till 5 years for toxicity and loco-regional control. Loco-regional control was defined as the absence of any disease above the clavicle. The time period for loco-regional control rate was measured from the date of completion of postoperative adjuvant radiation therapy.

Statistical analysis

Pretreatment patient and tumor characteristics of the two groups were compared using frequency table with counts and percentages. Variability between the groups was determined using Student's *t*-test for numerical values and Chi-square test for categorical values. A confidence interval of 95% was taken for detecting a significant difference between groups. The prevalence of various risk factors treatment-related factors and acute toxicity were compared

between the two groups. Compliance to chemotherapy was defined as the ability to receive at least five out of six planned weekly doses of cisplatin within the period of radiation. Compliance to RT was defined as the ability to complete the planned radiation dose within 6 weeks. The loco-regional recurrence rate/failure-free survival was calculated using Kaplan–Meier statistics and compared using log-rank test. A (*post hoc*) multivariate analyses of various cofactors was undertaken using cox's proportional hazard model.

RESULTS

During the period of September 2006 to August 2008, 282 cases of oral cavity cases were treated with definitive surgery. Ninety-two of these had any of the high-risk features and were eligible for the study, of which three patients had associated comorbid conditions, and 12 patients received preoperative chemotherapy. Among the rest only 54 patients gave consent for the study and included in the analysis. The baseline characteristics of these 54 patients are enlisted in Table 1. The median age was 52 years. Buccal mucosa was the most common subsite (44.4%) affected, followed by lower alveolus/alveolar ridge (37%) and oral tongue (11.1%), and most tumors (64.3%) were of well differentiated. Most patients underwent wide excision along with adjacent bony resection (segmental/marginal mandibulectomy or maxillectomy) and flap repair with selective supra omohyoid neck dissection as the surgical procedure. The distribution of high risk features were comparable in both the Arms [Table 2]. Four patients in the chemoradiation arm started radiation after 6 weeks as compared to 6 patients in the radiation arms (3 in the intermediate and 3 in the high-risk group). 67.3% of the patients completed their course of radiation within 6 weeks and 29.6% had treatment break and delay due to toxicity with only 69 patients receiving the scheduled 60 Gy of external beam radiation therapy (EBRT) dose and 4 patients receiving <40 Gy. The median duration of treatment was 43 days in the chemoradiation arm and 42 days in the radiation arms. Only 6 patients out of 22 completed the 6 cycles of weekly chemotherapy, and 11/22 patients received at least 5 cycles of concurrent weekly cisplatin with compliance decreasing most after 3 cycles. Twenty-eight (52%) patients had pT3/pT4 disease, 17 (31.5%) had close or positive margins, 16 (29.6%) had >2 nodes, 9 (16.7%) had ECE, 10 and 11 patients had perineural and perivascular invasion, respectively [Table 2]. 57.7% in the chemoradiation arm (Arm A) and 71% of the radiation arm completed their course of radiation within 6 weeks ($P = 0.39$). Three patients in Arm A received of EBRT dose less than the scheduled 58–60 Gy. Only 9 patients out of 26 completed the 6 cycles of weekly chemotherapy.

Table 1: Background characteristics of the two arms

Background characteristics	CTRT arm (*n*=26)	RT arm (*n*=28)	*P*
Age (median) in years	52	56.5	0.16
>50 years of age (%)	46.9	53.1	0.24
Sex			
Males	18	24	0.19
Females	8	4	
Hemoglobin level (median) in g/dl	11.4	11.7	0.81
KPS score			
90	0	0	0.66
80	75.9	75	
70	24.1	25	
Interval between surgery and start of RT (median) in days	32	31	0.61
Lymph node dissection			
SOND	21	19	0.53
MND	3	6	
Not done	2	3	
Subsite			
Buccal mucosa	11	13	0.71
Lower alveolus	11	13	
Oral tongue	3	3	
Floor of mouth	3	1	
Gingiva (GBS)	1	1	
Upper alveolus	1	2	
pT			
T2	9	17	0.07
T3	5	6	
T4a	12	5	
pN			
pN0	8	11	0.57
pN1	11	8	
pN2	7	9	

CTRT: Computed tomography radiotherapy, GBS: Gingivobuccal sulcus, KPS: Karnofsky Performance Score, RT: Radiotherapy

Mucositis and dysphagia were the major dose-limiting toxicity in the both arms [Table 3], with significantly higher incidence Grade III or higher mucositis in the chemoradiation arm. Four patients in the chemoradiation arm as compared to two patients the radiation arm had Grade IV neutropenia, with one patient dying on the 4th week of chemoradiation due to febrile neutropenia. There were more incidence of severe dysphagia in the chemoradiation arm; 5 patients were put on nasogastric tube feeding during the course of the treatment, who had a weight loss of more than 10% during the course of radiation. Significantly higher incidence of nausea and vomiting in the chemoradiation arm was observed. Overall the incidence of severe adverse effects was significantly higher in the chemoradiation arm, which however, was well-managed, except for one patient having toxicity-related death.

After a median follow-up of 47 months, the loco-regional control rate was 51.4% in the postoperative chemoradiation arm as compared to 35.56% in the postoperative radiation arm ($P = 0.39$) [Figure 1]. During this period, 27 loco-regional recurrences were observed. Of the loco-regional failure majority (6/15) were in the supraclavicular fossa, with three cases failing at the host graft site and four within the primary radiation field. The rest failed above clavicle but outside the radiation field used. There was no difference in the pattern of failure between the treatment arms. Of the above

Table 2: Distribution of risk factors in the two treatment arms

Risk characteristic*	Number of patients receiving postoperative chemoradiation (%)	Number of patients receiving postoperative radiation only (%)	*P*
Stage III, Stage IV disease	21 (95.5)	22 (93.7)	0.37
Two or more pathologically positive nodes	5 (22.7)	6 (29.2)	0.82
Extracapsular extension	4 (18.1)	8 (36.2)	0.59
Perinueral or lymphovascular invasion	7 (31.8)	5 (22.7)	0.32
Surgical positive margin	5 (22.7)	3 (12.5)	0.23
Level IV or level V nodal involvement	4 (18.1)	2 (8.3)	0.32

*Total more than 100%, since presence of more than one type of risk factors in single patient

Table 3: Acute toxicity comparison of two treatment arms

Acute toxicity	CTRT (*n*=26)	RT (*n*=28)	*P*
Mucositis			
Grade I/Grade II	9	21	0.00
Grade III	10	6	
Grade IV	3	1	
Hematologic			
Grade I/Grade II	17	21	0.01
Grade III	5	4	
Grade IV	4	3	
Dysphagia			
Low grade	14	23	0.07
Grade III	8	5	
Upper GI			
Low grade	20	27	0.01
Grade III	6	1	
Skin			
Low grade	19	20	0.07
Grade III	6	7	
Grade IV	1		
Renal			
Low grade	24	28	0.2
Grade III	2		
Neurologic			
Low grade	22	25	0.04
Grade III	4	3	

CTRT: Computed tomography radiotherapy, RT: Radiotherapy, GI: Gastrointestinal

27 patients, eight patients in each group received salvage chemotherapy, platinum-based or taxane-based, 2 patient in the RT arm and 1 in the concurrent chemoradiation (CTRT) arm received reirradiation and 4 patients were salvaged surgically (3 in the CTRT arm and one in the RT arm). The rest received either oral tyrosine kinase inhibitors or metronomic chemotherapy based on their performance status as salvage therapy. The 5 years overall survival was 56.4% in postoperative chemoradiation arm as compared to 51.3% in the postoperative radiation only (P = 0.482, log-rank test) [Figure 2]. There were in total 22 recorded deaths during this period, 12 in the RT arm and 10 in the CTRT arm, of which death due to disease were in 18 cases, two patients died of cardiac causes, one due to renal failure and one patient committed suicide.

On multivariate analysis, it was found that among various covariates presence of pathological positive nodal disease, suboptimal RT dose received, and positive margin status was associated with significant high hazard ratio [Table 4]. Other factors like age more than 50 years, Hb level <10 mg/dl, moderate and poorly differentiation of tumors, KPS ≤80,

Table 4: Multivariate (*post hoc*) analysis of factors for LR failure free survival

Covariate	Hazard ratio	Significance (*P*)
Age (more than 50 vs. <50)	1.5	0.3
Hemoglobin level (more than 10 vs. <10 mg/dl)	0.8	0.6
Tumor differentiation		
Moderate	2.7	0.3
Poor	3.9	0.2
KPS		
≤80	1.8	0.2
Positive nodal status	2.1	0.03
Tumor size >4 cm (advanced T stage)	1.15	0.5
Margin positive	3.4	0.07
Absence of perineural involvement	0.2	0.15
Suboptimal RT dose (<60 Gy)	4.6	0.01

KPS: Karnofsky Performance Score, RT: Radiotherapy, LR: Loco-regional

tumor size and presence perineural involvement, though had hazard ratio of more than one but this was not found to be statistically significant.

DISCUSSION

The potential benefit of postoperative concurrent chemoradiation using cisplatin-based chemotherapy for head and neck cancer with poor prognosis was well established by the two large randomized trials published in 2004.[9,10] Both trials resulted in a substantial and significant increase in local, regional control and short-term survival with postoperative adjuvant chemo-RT in poor prognosis patients although only the European trial proved to have significant and sustained increase in long-term survival.[9] The fact that the eligibility criterion and the definition of high-risk factors were different in the two trials did not reflect in the results as both studies had similar outcomes, with the estimated increase in 5 years disease free survival from 36% to 47% in the EORCTC arm and 45% to 54% 3 years disease free survival in the RTOG arm with addition of cisplatin. This study consolidated the evidence supporting the use of concurrent chemoradiation in postoperative setting for oral cavity cancers, which constituted only a minor subgroup of the above two studies, associated mostly with chewing tobacco and betel nuts, with an absolute benefit of 16% in loco-regional control rate at 47 months median follow-up and a 13% advantage in 4 years overall survival, with manageable increase acute toxicity.

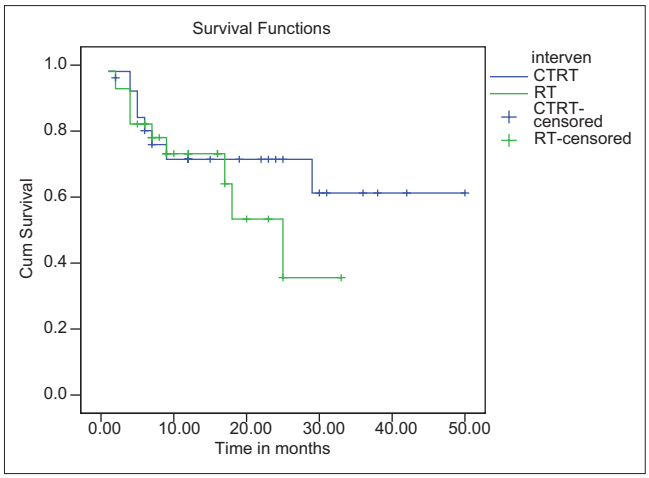

Figure 1: Loco-regional recurrence free survival (*P* = 0.39, log-rank test)

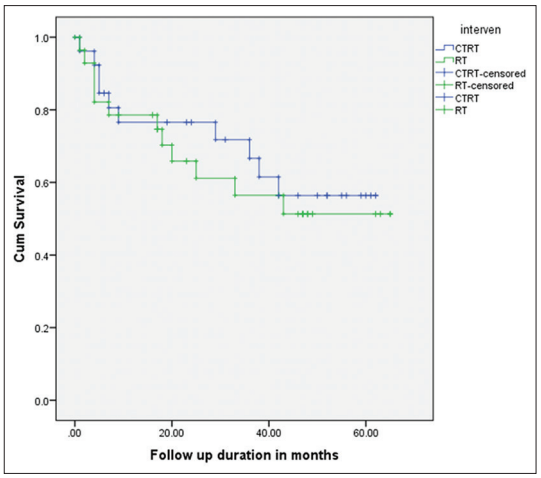

Figure 2: Five years overall survival comparison of the two treatment arms (*P* = 0.489, log-rank test)

The categorization of pathologic risk factors of head and neck cancers was described by Peters *et al*. in the 1990s, who clarified which patients needed postoperative RT depending on the risk of recurrence.[6] The presence of pathological two or more lymph nodes and/or ECE of tumor were independent variables linked to a significantly increased risk of recurrence in this study, and these were also taken as high-risk factors in the above two randomized trials. Combinations of two or more risk factors were associated with a progressively higher risk of local failure. For oral cancers, the simultaneous presence of three or more risk factors, which included additional risk factors such as degree of histologic differentiation, skin invasion, bone invasion, and invasion depth, was associated with severe prognosis.[12] In another retrospective data of oral cancers of over 35 years poor loco-regional control was associated with positive margins, vascular invasion, perineural invasion, ECE, and T classification.[12,13] In the present study, however, presence any of the risk factors was qualifiers for high risk since this criterion was validated in the larger two randomized trials.

In contrast to the EORTC and the RTOG trials, and other trials we used a weekly cisplatin schedule at the dose of 40 mg/m^2 on the basis of the results of the trial reported by Bachaud *et al*. and the more favorable toxicity profile of the weekly cisplatin schedule compared to the 100 mg/m^2 3 weekly schedule.[5] Furthermore, this has enabled us to measure the compliance to concurrent chemotherapy since 6 weekly doses can be given instead of only two to three in the later schedule. The disadvantage of the combination of chemo and RT is the potential increase of acute and late radiation toxicity by the chemotherapy. Our study showed a higher overall severe acute toxic effect rate in the concurrent chemoradiation group than in the RT group as was observed by Bouchard *et al*. (41 vs. 18%). Mucositis, dysphagia, nausea, and vomiting were the most frequent adverse effects in both the groups; however, neutropenia was the only fatal toxicity in CCRT group.

Barring one, all the patients eventually completed the scheduled RT, however only 27% (7/26) completed the full course of six cycles of chemotherapy; much in contrary to what was observed by earlier authors, Bouchard *et al*. and Porceddu *et al*.[8] The possible explanation could be a combination of low nutritional status and low motivation of the patients in the study.

Though the median follow-up period of this study was short, there was definite increase (16%) in the loco-regional control rate at 47 months with addition of concurrent weekly cisplatin, in spite of the fact that only 50% of patients received at least 5 cycles of weekly cisplatin. This corroborates with earlier studies like Bouchard *et al*. and the EORTC and RTOG study. However, the 24 months LCR rate of 57.8% in the concomitant arm is much inferior to 73% observed by Porceddu *et al*, Smid *et al* 69% and the RTOG study (79%).[7,8,10] There could be various possible explanations to this fact, first and foremost is that the present study included only oral cavity cancers, which are shown to have inferior loco-regional control rates. The other possible reasons include the greater rate of high-grade acute toxicity observed leading to lower compliance to chemotherapy. Also, the overall low nutritional status and probably the lack of prophylactic nutritional interventions like percutaneous endoscopic gastrostomy might have also contributed. This study has various strengths and limitations. This is probably one of the few studies, where the effect of concurrent chemoradiation in postoperative setting was tested for exclusively oral cavity cancers. There is very little clarity regarding the choice of adjuvant therapy according to histopathological risk factors for oral cavity cancers. A randomized control trial (The OCAT trial) is ongoing, and the results from the same would provide the required level I evidence to this end.[14] Although a single institutional nonrandomized study, the present one has provided some vital clues. First it has validated the role

Table 5: Comparison of studies using concurrent chemoradiation for head and neck squamous cell carcinomas in the postoperative settings

Study/ author	Eligibility criteria	Percentage of oral cavity	Arms	Chemotherapy	LR disease free survival year	OS	LR versus distant metastases	Acute toxicity
Bachaud *et al.*, 1996	Stage III/Stage IV ECE		Arm 1: RT 65-70 Gy, Arm 2: RT 65-70 Gy plus CT	50 mg cisplatin weekly	2 years RT - 59%, CTRT - 84%; 5 years RT - 55%, CTRT - 70%,	2-year (P<0.01) RT - 46, CTRT - 72%, 5 years RT - 13%, CTRT - 36%	LR: RT - 18/44, CTRT - 9/39 DM: RT - 13/44, CTRT - 15/39	
Porceddu *et al.* 2004	High risk factors ECE Positive or close (5 mm) margins LR after surgery alone	24/47	Single arm, RT - 60-66 Gy plus CT	40 mg/m^2 weekly cisplatin	2 years - 73%,* LRc	2 years OS - 56%		6% Grade III/IV neutropena
RTOG Cooper *et al.*, 2004	High risk factors Two or more regional lymph nodes ECE Positive or close (5 m) margins	112/416	Arm 1: 60 Gy in 30#±6 Gy boost Arm 2: Same as above plus CT	Cisplatin (100 mg/m^2 days 1, 22, and 43)	2 years LRc: RT - 72%, CTRT - 82%	5 years; (P=NS) RT - 41%, CTRT - 50%	LR: RT - 61/210, CTRT - 33/206 DM: RT - 23%, CTRT - 20%	RT - 34% Grade III/IV acute toxicity CTRT - 77% Grade III/IV acute toxicity
EORTC Bernier *et al.*, 2004	pT3/pT4, except T3N0 larynx ECE Positive margin PNI LVSI Oral cavity/oropharynx primary with level IV/V N+	87/334	Arm 1: 54-66 Gy cf Arm 2: Same as above plus CT	Cisplatin (100 mg/m^2 days 1, 22, and 43)	5 years pfs: RT - 36%, CTRT - 47%	5 years OS: (P=0.02) RT - 40%, CTRT - 53%	LR: RT - 52/137, CTRT - 31/137 DM	RT - 21% Grade III/IV acute toxicity CTRT - 41% Grade III/IV acute toxicity
Smid *et al.* 2003		21/114	Arm 1 (55): RT 56-70 Gy cf Arm 2 (59): RT 56-70 Gy plus CT	Mitomycin c (15 mg/m^2 single dose) and bleomycin 5 mg twice weekly	2 years; RT - 69%, CTRT - 86%	2 years (P=0.037) RT - 64%, CTRT - 74%	LR: RT - 15/55, CTRT - 7/59 DM: RT - 8, CTRT - 6	
Present study	pT3/pT4, except T3N0 larynx ECE Positive margin pNI LVSI Level IV/V N+	54/54	Arm 1: 58-66 Gy cf Arm 2: Same as above plus CT	50 mg cisplatin weekly	DFS (47 m): RT - 35.5% CTRT - 51.4%	OS 5 year: (P=NS) RT - 51.3% CTRT - 56.4%	LR: RT - 15/28 CTRT - 12/28	CTRT - 62%, RT - 47% Grade III/IV toxicity

* P=0.05. OS: Overall survival, CTRT: Computed tomography radiotherapy, RT: Radiotherapy, CT: Computed tomography, ECE: Extra capsular extension, DM: Distant metastasis, LR: Loco-regional recurrence, EORTC: European organization for research and treatment of cancer, RTOG: Radiation therapy oncology group

of weekly cisplatin-based concurrent chemotherapy in the postoperative setup of this subset of head and neck cancers by demonstrating a significant improvement in loco-regional control. It also raises the question of proper scheduling of concurrent chemotherapy since only 27% actually completed the six scheduled cycles. The major limitation of this study is it that is a nonrandomized one. The sample size was also too small to allow for any subgroup analysis regarding the effect of various individual high-risk features on loco-regional control and progression-free survival. Another major drawback of this study was that all patients were treated using conventional planning using a conventional simulator, and no dose constraints were applied for organs at risks. This may have resulted in higher acute and late toxicities. However, with all its limitation this study produced comparable results in terms of loco-regional control rate and overall survival to previous studies [Table 5], there reemphasizing the benefit of use of concurrent cisplatin with RT for those selected group of patients with some clinical or pathological high risk features.

CONCLUSION

Postoperative concurrent chemo RT with weekly cisplatin for patients with high-risk oral cavity cancer gave an advantage in the loco-regional control rate at the end of 24 months, though there were significant higher toxicity and less compliance with this protocol as compared to postoperative RT only. A longer follow-up and a larger sample may be needed to assess the survival advantage provided by this intense schedule in high-risk oral cavity cancer in this part of the world.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Gupta PC, Nandakumar A. Oral cancer scene in India. Oral Dis 1999;5:1-2.
2. Subapriya R, Thangavelu A, Mathavan B, Ramachandran CR, Nagini S. Assessment of risk factors for oral squamous cell carcinoma in Chidambaram, Southern India: A case-control study. Eur J Cancer Prev 2007;16:251-6.
3. Pai V R, Mazumdar AT, Deshmukh CD, Bakshi AV, Parikh DM, Parikh PM, *et al*. Two-versus three-drug combination chemotherapy in advanced or recurrent head and neck cancer: A single institution experience of 361 patients. Med Oncol 2004;21:305-8.
4. Vikram B, Strong EW, Shah JP, Spiro R. Failure at the primary site following multimodality treatment in advanced head and neck cancer. Head Neck Surg 1984;6:720-3.
5. Bachaud JM, Cohen-Jonathan E, Alzieu C, David JM, Serrano E, Daly-Schveitzer N. Combined postoperative radiotherapy and weekly cisplatin infusion for locally advanced head and neck carcinoma: Final report of a randomized trial. Int J Radiat Oncol Biol Phys 1996;36:999-1004.
6. Peters LJ, Goepfert H, Ang KK, Byers RM, Maor MH, Guillamondegui O, *et al*. Evaluation of the dose for postoperative radiation therapy of head and neck cancer: First report of a prospective randomized trial. Int J Radiat Oncol Biol Phys 1993;26:3-11.
7. Smid L, Budihna M, Zakotnik B, Soba E, Strojan P, Fajdiga I, *et al*. Postoperative concomitant irradiation and chemotherapy with mitomycin C and bleomycin for advanced head-and-neck carcinoma. Int J Radiat Oncol Biol Phys 2003;56:1055-62.
8. Porceddu SV, Campbell B, Rischin D, Corry J, Weih L, Guerrieri M, *et al*. Postoperative chemoradiotherapy for high-risk head-and-neck squamous cell carcinoma. Int J Radiat Oncol Biol Phys 2004;60:365-73.
9. Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, Saxman SB, *et al*. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 2004;350:1937-44.
10. Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefèbvre JL, Greiner RH, *et al*. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004;350:1945-52.
11. Bernier J, Cooper JS. Chemoradiation after surgery for high-risk head and neck cancer patients: How strong is the evidence? Oncologist 2005;10:215-24.
12. Fan KH, Wang HM, Kang CJ, Lee LY, Huang SF, Lin CY, *et al*. Treatment results of postoperative radiotherapy on squamous cell carcinoma of the oral cavity: Coexistence of multiple minor risk factors results in higher recurrence rates. Int J Radiat Oncol Biol Phys 2010;77:1024-9.
13. Hinerman RW, Mendenhall WM, Morris CG, Amdur RJ, Werning JW, Villaret DB. Postoperative irradiation for squamous cell carcinoma of the oral cavity: 35-year experience. Head Neck 2004;26:984-94.
14. Al-Sarraf M, Pajak TF, Byhardt RW, Beitler JJ, Salter MM, Cooper JS. Postoperative radiotherapy with concurrent cisplatin appears to improve locoregional control of advanced, resectable head and neck cancers: RTOG 88-24. Int J Radiat Oncol Biol Phys 1997;37:777-82.