

## Original Research Article

# Treatment outcome of postoperative radiotherapy for squamous cell carcinoma of the head and neck

H. U. Ghori\*, M. Sohaib, Vivek Tiwari, Manish Ahirwar

Department of Radiotherapy, Gandhi Medical College, Bhopal, M.P., India

**Received:** 09 August 2017

**Revised:** 20 September 2017

**Accepted:** 21 September 2017

### \*Correspondence:

Dr. H. U. Ghori,

E-mail: [hughori@rediffmail.com](mailto:hughori@rediffmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Though early stage malignancy of head and neck can be cured by surgery or radiotherapy, cure of patients with locally advanced disease continues to pose a therapeutic challenge. Local regional failure is the major cause of death in head and neck cancer. As the cure of locally advanced head and neck cancer is less than expectation, a combined modality approach is generally used in these type of patients. The combination of surgery, radiotherapy and chemotherapy can improve outcome in locally advanced head and neck cancer.

**Methods:** This observational study reviewed cancer patients reported in our hospital with the following inclusion criteria: primary head and neck cancer, treatment with radical surgery, and multiple nodal metastases. The prescribed dose of postoperative radiotherapy was 60–66 Gy. Patient characteristics, treatment parameters and clinical outcome were recorded.

**Results:** The primary end point was overall survival, and the secondary endpoint was disease status.

**Conclusions:** Concurrent postoperative administration of chemotherapy and radiotherapy is a way to intensify treatment for resectable high-risk head and neck tumors.

**Keywords:** Head and neck cancer, Postoperative, Radiotherapy, Concomitant, Cisplatin

### INTRODUCTION

Head and neck cancer are common in India. It accounts for 30 percent of cancer in male and 13 percent in female. Nearly 60 percent of cases present in advanced stages. Local regional failure constitutes predominant recurrence pattern and most deaths result from uncontrolled local or regional disease. The two important main treatment modalities for patients with squamous cell carcinoma of the head and neck are surgery and radiotherapy (RT). Patients with stage I and II disease are optimally treated with one modality. Unfortunately, a large number of patients present with stage III and IV disease. The organ preservation treatment modalities using RT alone or with concomitant chemotherapy have proven to be acceptable

for patients with favorable low volume malignancies. Despite regimens that permit organ preservation in selected patients with advanced carcinomas of the head and neck, ablative surgical resection and postoperative radiotherapy are required in many patients. Various studies show that many local or regional disease recurrences occur in 30 percent of patients, and distant metastases occur in 25 percent.<sup>4</sup> Patients who have two or more regional lymph nodes involved, extracapsular spread of disease, or microscopically involved mucosal margins of resection have particularly high rates of local recurrence (27 to 61 percent) and distant metastases (18 to 21 percent) and a high risk of death (five-year survival rate, 27 to 34 percent).<sup>5</sup>

## METHODS

This observational study done in the department of Radiotherapy, Gandhi Medical College, Bhopal between July 20015 to December 2016.

### Inclusion criteria

Patients with disease involving the oral cavity, oropharynx, larynx, or hypopharynx; with histopathology of squamous-cell carcinoma, treated with macroscopically complete resection of disease were analysed. Patients having following high-risk characteristics i.e. histologic evidence of invasion of two or more regional lymph nodes, extra capsular extension of nodal disease, and microscopically involved mucosal margins of resection were analysed.

### Exclusion criteria

Patient with histopathology other than squamous cell ca., pt. with distant metastasis disease, co morbid condition,

All patients treated with postoperative radiotherapy using a conventional fractionated dose of 2 Gy single fraction every day, 5 days every week using Cobalt 60, upto total dose of 60 to 66 Gy. The initial treatment volume included the primary tumor and the regional cervical lymph nodes. Patients treated using the conventional field arrangement, including a bilateral opposing field. The spinal cord was shielded after 46 Gy. The radiotherapy treatment started immediately after adequate healing had occurred. Normally, this occurs four to six weeks after the surgical procedure. Inj cisplatin was used as concurrent chemotherapy. A continuous course of radiotherapy was maintained. Any interruptions due to adverse effects had to be kept to a minimum. Inj. Cisplatin therapy was with old if the absolute neutrophil count was below 4000 per cubic millimeter or the platelet count was below 1,00,000 per cubic millimeter. All the patients were examined regularly on weekly basis during the treatment. All the patients were evaluated for the response and toxicity at nine weeks, then every three months for the first year. All patients were followed at outpatient department. The statistical analyses of survival and disease-free interval were based on a comparison of Kaplan–Meier curves by the log-rank test. The primary end point was overall survival (OS), and the secondary end points were recurrence-free survival (RFS) and local-regional recurrence-free survival. The survival period was calculated from the date of surgery to the date of the any recurrence or death from the disease.

## RESULTS

Total 52 number of patients included in the analysis, between the ages from 25 to 65 years old. The median age was 49 years. Thirty six (69.23%) patients were male, and 16 (30.76%) were female. The buccal mucosa was the most common sub site (20, 38.46%), followed by the

tongue (18, 34.61%), alveolous (6, 11.53%), retro molar trigone (3, 5.76%), floor of mouth f (2, 3.84%), hard palate (1, 1.92%), and lips (1, 1.92%). Majority of the patients reported with pathologic stage IVa disease, and their nodal stage was among either N2 or N3. There were 1 (1.92%) patient with stage T1, 4 (7.69%) patients with stage T2, 20 (38.46%) patients with stage T3, and 27 (51.92%) patients with stage T4 disease, respectively. After radical surgery, 18 (34.61%) patients were given postoperative radiotherapy within 6 weeks, and 34 (65.38%) given postoperative radiotherapy within 8 weeks. Fifteen (28.84%) patients given 60 Gy dose of postoperative radiotherapy, and 37 (71.15%) patients given between 60 and 66 Gy dose of radiotherapy. The overall survival rate at 1-year was 85%.

**Table 1: Patients characteristics.**

Characteristic	Subcategory	Frequency
<b>Sex</b>	Male	36
	Female	16
<b>Age (Median: 49 (29–75))</b>	Less than 40 years	22
	More than 40yrs	30
<b>Smoking</b>	Yes	40
	No	12
<b>Site</b>	Tongue	18
	Mouth floor	2
	Lips	1
	Buccal mucosa	20
	Alveolous	6
	Hard palate	1
	Retromolar trigone	3
	Others	1
<b>Differentiation</b>	Well	25
	Moderate	18
	Poor	9
<b>Pathologic T stage</b>	T1	1
	T2	4
	T3	20
	T4	27
<b>N stage</b>	N1	8
	N2	25
	N3	12
	N4	7
<b>Margin involve</b>	Yes	28
	No	24
<b>Skin invasion</b>	Yes	5
	No	47
<b>Bone invasion</b>	Yes	3
	No	49
<b>Perineural invasion</b>	Yes	2
	No	50
<b>Vascular invasion</b>	Yes	2
	No	50
<b>Lymphatic invasion</b>	Yes	8
	No	42

**Table 2: Parameters of treatment.**

Characteristic	Subcategory	Frequency
RT dose	≤6000 CGy	12
	≥6000 CGY	35
RT duration	Incomplete RT	3
	≤7 weeks	12
	≥7 weeks	35
Time between OP and RT	≤6 weeks	18
	≥6 weeks	34
Chemotherapy	No chemotherapy	10
	Cisplatin	42

**Table 3: Survival and recurrence free survival for patients based on different factors.**

	1-year OS (%)	1-year RFS (%)	1-year LRRFS (%)
<b>T4</b>	35	36	40
<b>T1-3</b>	50	52	60
<b>Differentiation</b>			
Well	52	56	58
Moderate	50	52	52
Poor	42	46	48
<b>Vascular invasion</b>			
No Vascular invasion	60	62	70
<b>Lymphatic invasion</b>			
No lymphatic invasion	62	64	66
<b>With margin involvement</b>			
Without margin involvement	52	54	60
<b>With perineural invasion</b>			
No perineural invasion	52	52	50
<b>RT Dose</b>			
Less or equal to 6000 cGy	56	58	58
More than 6000cGY	65	71	74
<b>RT duration</b>			
≤7 weeks	55	55	60
≥7 weeks	65	65	68
<b>Time between OP and RT</b>			
≤6 weeks	52	52	54
≥6 weeks	48	48	50
<b>Chemotherapy</b>			
No	50	52	63
Yes	60	65	68

In the analysis, we found that pathologic T4 disease, bone invasion and lymphatic invasion were correlated with poor overall survival. The 1-year recurrence free survival rate was 85%. The most common recurrence was the nodal recurrence, then local recurrence, and then distant meets. In the analysis, we found that pathologic T4 disease, bone invasion, and skin invasion were significantly correlated with poor recurrence free survival (Table 3). Pathologic T4 disease, skin invasion, and bone invasion were significantly correlated with poor local recurrence free survival (Table 3). The effect of radiotherapy with chemotherapy was further evaluated. The OS in the patients received chemotherapy along with

RT, 60% as compare to 50% in cases without chemotherapy.

## DISCUSSION

The treatment for cancer patients has advances very much since last many years. Radiotherapy is being used for the treatment of head and neck cancers as a important modality of treatment for many years. It may be used as a preoperative setting or postoperative setting. In the advanced squamous-cell carcinoma of the head and neck, postoperative radiotherapy give the better result but the five-year rate of disease-free survival is less than expectation. Local recurrence and regional lymph nodal

recurrence are the most common form of treatment failure, concurrent chemotherapy along with radiotherapy after a macroscopically complete resection may intensify the control of the disease. Various studies have shown the better result of postoperative concomitant chemotherapy in the treatment head and neck cancers having positive margins or lymph node involvement with extra capsular spreading. In a nonrandomized, phase 2 RTOG 8824 trial, result showed that the risk of local and regional recurrence decrease in high risk patients who have been treated with post op radiotherapy and concomitant chemotherapy.<sup>5</sup> The presence of any of the below mentioned pathological features i.e. positive surgical margins, extra nodal spread of disease, perineural disease, or vascular tumor emboli are considered as high risk. In various studies, multiple-node metastases have shown higher tumor recurrence and poor overall survival.<sup>8,9</sup> The various pathologic factors are predictive for local–regional recurrence after surgery. These pathological factors i.e. close (less than 5 mm) or positive margins, extra capsular extension through the lymph node capsule, involvement of the soft tissues of the neck, subglottic invasion, two or more positive lymph nodes, perineural invasion and endothelial-lined space invasion are the important parameter.<sup>10-13</sup> The presence of multiple-node metastases is also an indication for postoperative radiotherapy for the treatment of head and neck cancers. The patients who present with advanced cancer and have no adverse pathologic factors may have an excellent prognosis with surgery alone. A number of factors are associated with an increased risk of local–regional recurrence after surgery alone. The two most unfavorable parameters are positive margins and extra capsular extension. The adjuvant concomitant radiotherapy reduces the risk of recurrence and result in better outcome. The survivals were improved by concomitant radiotherapy in each categories except patients who had no other pathologic risk factors. Because the chances of control is low after a local–regional recurrence, factors that affect the probability of disease control above the clavicles are also likely to have a negative influence on survival. According to various studies, the presence of multiple-node metastases was correlated with higher tumor recurrence and poor overall survival. A study carried out at the Medical College of Virginia where two groups of surgeons, surgical oncologist and otolaryngologists, operated on patients with head and neck cancer, general surgical oncologists used surgery alone and radiotherapy for treatment of recurrent disease only, and otolaryngologists routinely sent patients with locally advanced disease for postoperative radiotherapy For patients who are at high-risk for local–regional failure following surgery, postoperative radiotherapy may significantly improve both disease control and survival. Vikram was among the first to report a decreased chances of cure, secondary to delay in initiation of postoperative radiotherapy in patients.<sup>14</sup> The interval between surgery and postoperative radiotherapy, and the dose-fractionation schedule have influence on the overall treatment time. Various studies revealed that advanced T-

stage, extra capsular extension, positive margins, perineural invasion and vascular invasion significantly increased the risk of a local–regional failure (Table 3). Extra capsular extension, perineural invasion and advanced T-stage had an adverse impact on the survival. The addition of adjuvant chemotherapy was associated with a significant improvement in local–regional control and disease-free survival. However, overall survival was similar and acute toxicity was more pronounced in those who received chemotherapy. In a literature review, dose escalation through conventional fractionation was effective only for patients with extra capsular spreading.<sup>15</sup> Time factors, such as an elapsed time between surgery and postoperative radiotherapy of more than 6 weeks and a duration of postoperative radiotherapy of more than 8 weeks, did not result in inferior overall survival or recurrence free survival. In most studies, time factors play a critical role in tumor control. Delays in starting postoperative treatment and prolonged treatment times were found to be correlated with more local-regional recurrence in various study.<sup>15-17</sup>

## CONCLUSION

In summary, our study shows that certain pathological factors are important factors to decide further treatment with radiotherapy and concomitant chemotherapy after surgery. Concurrent postoperative administration of chemotherapy and radiotherapy is a way to intensify treatment for resectable high-risk head and neck tumors. In head and neck cancer patients with unfavorable factors have increased risk of loco regional failure after surgery, and post-operative radiotherapy have better outcome. Intensification of treatment with weekly cisplatin is now important in patient with high risk of disease. Over all treatment time should be minimized by avoiding delay in treatment between date of surgery and end of radiotherapy

## ACKNOWLEDGMENTS

We thank for the help of faculty members of my department, students and our patients.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. The Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med.* 1991;324:1685-90.
2. Lefebvre JL, Chevalier D, Luboinski B, Kirkpatrick A, Collette L, Sahnoud T. Larynx preservation in pyriform sinus cancer: preliminary results of a European Organization for Research and Treatment

- of Cancer phase III trial. *J Natl Cancer Inst.* 1996;88:890-9.
3. Forastiere AA, Goepfert H, Maor M, Pajak TF, Weber R, Morrison W, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med.* 2003;349:2091-8.
  4. Laramore GE, Scott CB, Al-Sarraf M, Haselow RE, Ervin TJ, Wheeler R, et al. Adjuvant chemotherapy for resectable squamous cell carcinomas of the head and neck :report on Intergroup Study 0034. *Int J Radiat Oncol Biol Phys.* 1992;23:706-13.
  5. Cooper JS, Pajak TF, Forastiere A, Jacobs J, Fu KK, Ang KK, et al. Precisely defining high-risk operable head and neck tumors based on RTOG #85-03 and #88-24:targets for postoperative radiochemotherapy? *Head Neck.* 1998;20:588-94.
  6. Bernier J, Domette C, Ozsahin M, Matuszewska K, Lefebvre JL. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med.* 2004;350:1945-52.
  7. Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med.* 2004;350:1937-44.
  8. Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C. Survival in squamous cell carcinoma of the oral cavity: differences between pT4 N0 and other stage IVA categories. *Cancer.* 2007;110:564-71.
  9. Fan KH, Lin CY, Kang CJ, Huang SF, Wang HM. Combined modality treatment for advanced oral tongue squamous cell carcinoma. *Int J Radiat Oncol Biol Phys.* 2007;67:453-61.
  10. Amdur RJ, Parsons JT, Mendenhall WM, Million RR, Stringer SP, Cassisi NJ. Postoperative irradiation for squamous cell carcinoma of the head and neck: an analysis of treatment results and complications. *Int J Radiat Oncol Biol Phys.* 1989;16:25-36.
  11. Peters LJ, Goepfert H, Ang KK, Byers RM, Maor MH, Guillaumondegui 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.
  12. Olsen KD, Caruso M, Foote RL, Stanley RJ, Lewis JE, Buskirk SJ, et al. Primary head and neck cancer. Histopathologic predictors of recurrence after neck dissection in patients with lymph node involvement. *Arch Otolaryngol Head Neck Surg.* 1994;120:1370-4.
  13. Zelefsky MJ, Harrison LB, Fass DE, Armstrong JG, Shah JP, Strong EW. Postoperative radiation therapy for squamous cell carcinomas of the oral cavity and oropharynx: impact of therapy on patients with positive surgical margins. *Int J Radiat Oncol Biol Phys.* 1993;25:17-21.
  14. Vikram B. Importance of the time interval between surgery and postoperative radiation therapy in the combined management of head & neck cancer. *Int J Radiat Oncol Biol Phys.* 1979;5:1837-40.
  15. Peters LJ, Goepfert H, Ang KK, Byers RM, Maor MH. 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.
  16. Ang KK, Trotti A, Brown BW, Garden AS, Foote RL. Randomized trial addressing risk features and time factors of surgery plus radiotherapy in advanced head-and-neck cancer. *Int J Radiat Oncol Biol Phys.* 2001;51:571-8.
  17. 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.

**Cite this article as:** Ghori HU, Sohaib M, Tiwari V, Ahirwar M. Treatment outcome of postoperative radiotherapy for squamous cell carcinoma of the head and neck. *Int J Otorhinolaryngol Head Neck Surg* 2018;4:127-31.