



## A Single Institutional Retrospective Study to Analyze the Clinical Outcomes in Patients of $T_{1-2}N_{0-1}$ Squamous Cell Carcinoma of the Oral Tongue who Underwent Surgery with or without Post-Operative Radiotherapy

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### Abstract

**Background:** This single institutional retrospective study aims to assess the results of curative surgery with and without post-operative radiotherapy in patients with  $T_{1-2}N_{0-1}$  squamous cell carcinoma of anterior  $2/3^{rd}$  of the tongue and to evaluate the factors affecting survival in such cases.

**Methods:** Retrospective analysis of 79 cases of  $T_{1-2}N_{0-1}$  squamous cell carcinoma of anterior  $2/3^{rd}$  of the tongue who presented at the Department of Radiotherapy, Medical College and Hospital, Kolkata between January 2012 and December 2014. Patient characteristics, tumour characteristics, treatment modality and survival patterns were analysed. Statistical analysis was done using IBM SPSS Version 23.

**Results:** Mean age of presentation was 47 years with Male: Female ratio of 2.6:1. All patients underwent primary surgery, 26.58% had a WLE and the rest underwent a hemiglossectomy. Neck dissection was done in 74 of the patients, mostly supra-omohyoid. Of the factors that were assessed, close surgical margins, depth of invasion more than 5mm and poor histological grade were those that significantly affected the outcomes. Two year disease free survival was 65.8%. Post-operative radiotherapy was not found to be statistically significant in affecting survival.

**Conclusion:** In  $T_{1-2}N_{0-1}$  squamous cell carcinoma of anterior  $2/3^{rd}$  of the tongue, factors which affected prognosis were higher tumour grade, close surgical margins and depth of tumour invasion more than 5 mm. Post-operative radiotherapy should be considered in such patients with high risk pathological features.

### Introduction

The oral tongue is the most common sub site for squamous cell carcinoma of the oral cavity, excluding the lip<sup>[1]</sup>. In advanced cases, surgical resection followed by radiotherapy (RT) with or without chemotherapy is performed, and it seems to be beneficial. In early cases (T1-2), surgery is often the preferred form of treatment<sup>[2]</sup>. However, the management of cervical lymph nodes (LN) and the role of postoperative adjuvant treatment remain uncertain.

Although surgery has emerged as the preferred initial treatment approach for the majority of patients with tumours of the oral cavity, adjuvant postoperative radiation is commonly recommended to enhance the likelihood of loco-regional tumour control<sup>[3]</sup>. The results of two randomized trials suggest that postoperative chemo-radiation is beneficial in improving local-regional control and disease-free survival among patients selected for specific high-risk features of head and neck cancer<sup>[4,5]</sup>.

As with other head and neck cancers, postoperative radiation therapy (PORT) in oral tongue squamous cell carcinoma (OSCC) is recommended for patients with large primary tumours (T3, T4), close surgical margins and evidence of peri-neural invasion (PNI) while postoperative chemo-radiation is recommended for multiple positive nodes, extracapsular extension and positive margins. Data were limited for high-risk features of recurrence and PORT in early-stage OSCC. Furthermore, most series reported a mixed patient population with oral cavity cancer<sup>[6,7]</sup>. Because of the extremely low salvage rate of recurred oral tongue cancer<sup>[8]</sup>, the proper extent and modality of initial treatment is very important.

This study retrospectively evaluated patients with early stage oral cancer treated at a Government Medical College setup to investigate the pathologic prognostic factors in patients with T1-2N0-1 OSCC in terms of disease-free survival (DFS) and to verify the role of PORT.

### **Aims and Objectives**

The aim of this study was to retrospectively assess the results of curative surgery with or without postoperative radiotherapy in T1-2 N0-1 Squamous Cell Carcinoma of the anterior 2/3<sup>rd</sup> of the tongue and identify and evaluate the factors affecting survival in the treated patients.

### **Materials and Methods**

A single institutional retrospective analysis was undertaken with a study period of three years from January 2012 to December 2014. 202 patients had presented during this period with Squamous Cell Carcinoma of the anterior 2/3<sup>rd</sup> of the tongue. Among them 79 were treated by primary surgery at stage T1-2N0-1. Tumour staging was based on the pathology findings, according to the American Joint Committee on Cancer Staging System, 6<sup>th</sup> edition. In addition, the following variables were recorded: size and invasion depth of the primary tumour (tumour thickness), grade of differentiation, status of resection margins, lympho-

vascular invasion and peri-neural invasion. The grade of differentiation was also divided into two groups: well-differentiated and moderate-to-poorly differentiated. To determine the status of resection margins, the closest were labelled as positive for a margin invaded by cancer cells, negative for a safety margin not less than 0.5 cm, and close for the safety margin less than 0.5 cm. The pathologically proven metastatic lymph node was evaluated by level, diameter, and peri-nodal extension. All patients received surgery for the primary site and neck. Resection of the primary site was grouped by the extent of the resection as hemi-glossectomy and wide local excision. None of the patients underwent a total glossectomy. Neck node dissection was performed in 74 patients. The type of neck dissection used was elective supra-omohyoid except 4 cases of modified radical neck dissection. 53 patients received PORT. Because this was a retrospective study, the indication for RT had been determined by the individual physician.

Follow-up time was calculated from the date of the surgery until the date of the last hospital visit, admission, or death, and each event-free survival was calculated from the date of the surgery to the date of diagnosis of each event. The two-year disease-free survival (DFS) rate was calculated using the Kaplan-Meier method. The differences in survival rates were compared by the log-rank test.

Prognostic factors influencing survival were analyzed by univariate and multivariate analyses using Cox's proportional hazards model. A p-value  $\leq 0.05$  was considered statistically significant. Statistical analysis was done using IBM SPSS Version 23.

### **Results**

Mean age of presentation was 47 years. 73.42% were over 40 years old. The ratio of males to females was 2.6: 1. All patients underwent primary surgery, 26.58% had a WLE and the rest underwent a hemi-glossectomy. Neck dissection

was done in 74 of the patients of which 70 were supra-omohyoid.

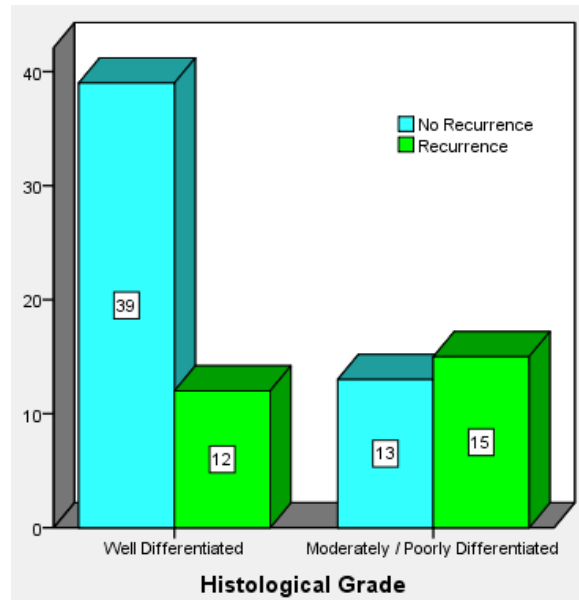
63.3% presented with stage I disease, 20.3 % presented with stage II and 16.6 % with stage III.

The baseline characteristics of the patients are shown in Table 1.

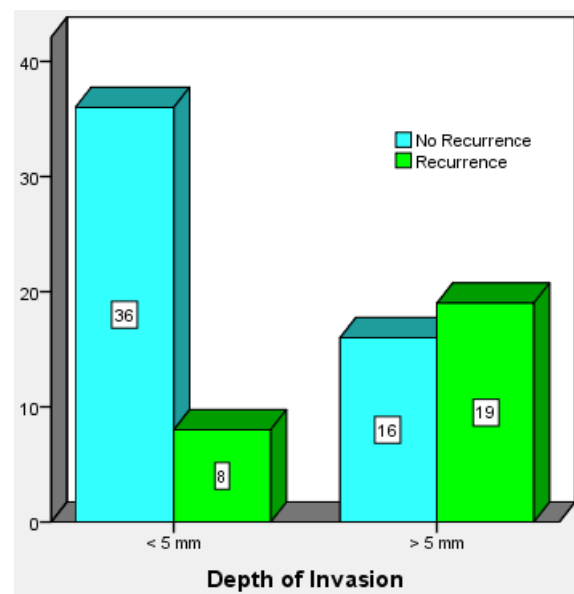
**Table 1.**

AGE GROUP	≤ 40 years	21
	> 40 years	58
T STAGE	T1	52
	T2	27
NODAL STATUS	N0	66
	N1	13
GRADE	Well differentiated	51
	Moderately/Poorly differentiated	28
DEPTH OF INVASION	≤ 5 mm	44
	> 5 mm	35
MARGINS	Free	68
	Close/Positive	11
LVI	Negative	70
	Positive	9
PNI	Negative	68
	Positive	11
TYPE OF SURGERY	Wide Local Excision	21
	Hemi-glossectomy	58
NECK DISSECTION	Not done	5
	Done	74
PORT	Not given	26
	Given	53
RECURRENCE AT 2 YEARS	No Recurrence	52
	Recurrence	27

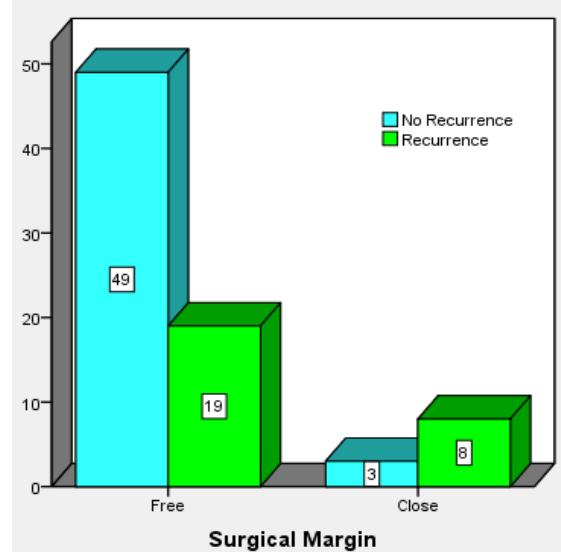
32 % of T1 tumours showed recurrence within two years compared to 37 % of T2 tumours. Recurrence was seen within 2 years in 27% no N0 disease compared to 69 % of N1 disease. For well differentiated tumours, the rate was 23.5% compared to 53.6% for moderately-poorly differentiated tumours (Fig. 1). 54.3% of tumours with depth of invasion more than 5mm recurred within two years compared to 18% for depth less than/equal to 5mm (Fig. 2). Recurrences were seen in 27% of cases with negative margins compared to 72.7% with close margins (Fig 3.)



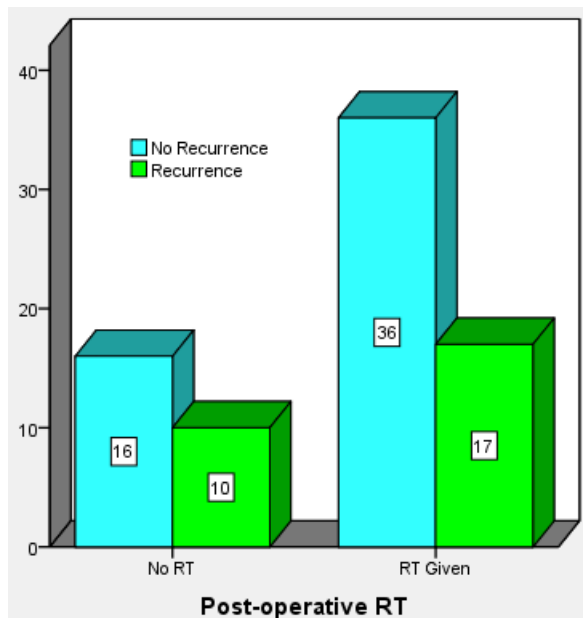
**Fig. 1**



**Fig. 2**



**Fig. 3**



**Fig. 4**

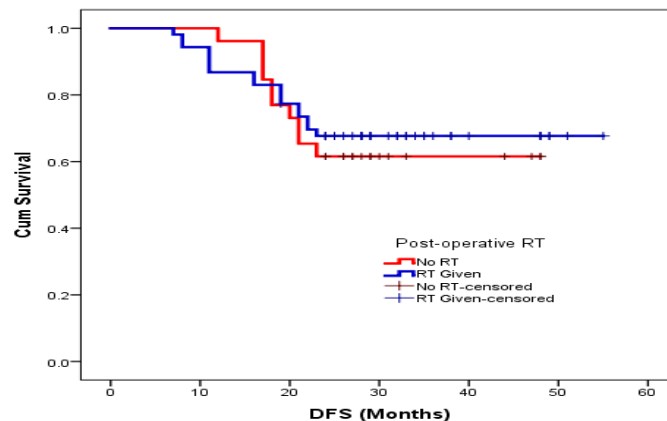
Among those patients who received PORT, 32% showed a recurrence compared to 8% among those who did not (Fig. 4)

On Univariate Analysis, histological grade, margin status, depth of invasion and post-operative radiation were found to be significant as demonstrated in Table 2.

**Table 2**

VARIABLE	P VALUE
Age group	0.193
Sex	0.447
Type of surgery	0.654
Neck dissection	0.061
T stage	0.140
N stage	0.370
Lvi	0.435
Pni	0.120
Grade	0.038
Margin	0.003
Depth of invasion	0.001
Post op rt	0.002

On multivariate analysis, Histological Grade ( $p = .007$ ), Margin Status ( $p = .003$ ) and Depth of Invasion ( $p = .001$ ) were found to retain significance.



**Table 3.**

Recurrence Within 2 Years	Frequency	Percentage
No Recurrence	52	65.8
Recurrence	27	34.3

On Kaplan Meier Survival Analysis (Fig. 5, Table 4), the two year disease free survival was found to be 65.8% which was not statistically significant with respect to delivery of PORT according to the Log Rank test ( $p = .679$ ).

**Discussion**

Oral cancer forms the fifteenth most common type of cancer worldwide with a estimated incidence rate of 2.1%<sup>34</sup>. There are about 0.2 million new cases every year worldwide with 0.1 million deaths each year. On global comparison India shows high incidence rates of oral cavity cancers forming a major health burden. Age standardized incidence rate in India is 7.5 per 100,000 population while in western Europe and USA it is 4.6 and 3.8 per 100,000 population respectively<sup>[9]</sup>. A recent national representative survey of cancer mortality in India demonstrated oral cavity cancer as the leading cause of mortality in men which was responsible for cancer-related deaths in 22.9% cases<sup>[10]</sup>. Tongue forms the most common sub-site for oral cavity cancer in western world. While gingivo-buccal complex cancer was the predominant cancer in India, the incidence of tongue cancer is slowly increasing in our country as well.

This study retrospectively observed the treatment results of patients with oral tongue cancer in relatively early stages corresponding to T1-2N0-1.

Operative treatments have been primarily performed for early oral tongue cancers, and, although there have been some reports that five-year survival rates of stage I-II diseases were 80% or higher<sup>[11]</sup>, Rusthoven et al. reported the five-year survival and cause-specific survival rates of stage I and II oral tongue cancers as 60.9% and 83.5%, respectively, and in other oral cavity subsites as 64.7% and 94.1%, respectively, based on the patient SEER database<sup>[12]</sup>.

In this study, the two year disease free survival was found to be 65.8% which appears lower than the rates suggested in published literature. This may be due to variable periods of gap between surgery and the initiation of adjuvant therapy due to both logistic reasons as well as lack of awareness among the patient population considering the setting of a Government Medical College with a high patient load.

Although primary RT and surgery are potential treatment options for oral tongue cancer, most oral tongue cancers are treated surgically<sup>[1]</sup>. Radiation therapy is used post-operatively for patients with unfavourable histological features. In your study, the decision regarding use of PORT was taken by the treating physician and although the use of PORT tended to show better outcomes, the result was not found to be statistically significant.

Risk factors for recurrence in oral tongue cancer include an infiltrating pattern of tumour growth, diffuse histological invasion, and a tumour within 5 mm of the resection margin<sup>[13]</sup>. This study has retrospectively analysed prognostic factors for patients with T1-2N0-1 SCC of the oral tongue treated primarily by surgery in an attempt to define the subgroups at a higher risk for recurrence.

In this study, depth of invasion and status of surgical margin seemed to affect the DFS rates. Al-Rajhi et al. reported that tumour thickness affected prognoses, and that lesions less than 10 mm had a comparatively favourable prognoses<sup>[14]</sup>. A meta-analysis by Huang et al demonstrated that a cut off depth of invasion of 4mm is a strong predictor of cervical lymph node metastasis<sup>[15]</sup>.

Arduino et al. reported that histological grading was related, as an independent factor, in predicting survival in patients with oral squamous cell carcinoma<sup>[16]</sup>. Shim et al. demonstrated that factors that significantly affected prognosis after primary surgery were poor tumour differentiation and deep invasion depths over 0.5 cm.

In our study, a depth of invasion less than or equal to 5mm was found to be prognostically better compared to a depth greater than 5mm. Also, tumour grades were shown to be a factor related to two year disease free survival.

There are several limitations in this study because it is retrospective. The number of patients being small, further analysis with a larger sample size may yield additional possible adverse prognostic factors which were not statistically significant in this study. Also it was difficult to evaluate the importance of PORT in early oral tongue cancer because of the small number of patients who were observed compared to those who received PORT.

### Conclusion

In T1-2N0-1 Squamous Cell Carcinoma of the anterior 2/3<sup>rd</sup> of tongue, factors that were significantly associated with prognosis after primary surgery were poor tumour differentiation, close surgical margins and depth of invasion over 0.5 cm. PORT was not found to be significantly related to clinical outcomes in this study. PORT should therefore, be considered in early oral tongue cancer patients with high-risk pathologic features.

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