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Institutional experience of the multimodality treatment of cancer tongue

Mrinal Shankar[1]*, Manisa Pattanayak[1], Vipul Nautiyal[2], Sunil Saini[1]

[1]Department of Surgery, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jollygrant, Doiwala, Dehradun, Uttarakhand, India
[2]Department of Radiotherapy, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jollygrant, Doiwala, Dehradun, Uttarakhand, India

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***Correspondence:**
Dr. Mrinal Shankar,
E-mail: ms_surg@yahoo.co.in

ABSTRACT

Background: Cancer (Ca) tongue incidence has shown a rising trend in India in the last couple of years. Increasing use of tobacco being the main risk factor. Guidelines available for management of this disease include it broadly under oral cavity cancers. However, the biological behaviour of this disease is warrant of more aggressive approach to treatment. In early stage disease, treatment is mainly with single modality, surgery being the most preferred. Locally advanced disease treated with multimodality approach with surgery and adjuvant RT/chemoRT. Adverse histopathological factors are important prognostic indicators for early recurrence. Even if the mainstay of treatment in metastatic disease is palliation, multimodality approach is preferred. The aim of the study is to study clinical profile of Ca tongue ant to study outcome of multimodality management of SCC tongue and identification of treatment failure.
Methods: The study was conducted in the Department of Surgery, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India over a period of 12 months on patients attending Surgical Oncology OPD. Written informed consent and ethical committee clearance was obtained in all 64 cases included, and study type is observational.
Results: This is an observational study conducted at Himalayan Institute of Medical Sciences, Dehradun over a period of 12 months. 64 patients diagnosed with SCC tongue were included. Treatment protocols were prescribed by the multidisciplinary tumour board, and patients were followed up to 6 months after completion of the planned treatment. 68.75% patients were below 55 years of age. 87.5% were chronic tobacco chewers. 79.68% had lesion in the anterior tongue. 84.37% received treatment with curative intent (of these 16.66% patients showed early recurrence). 71.86% patients underwent definitive surgery (of these 78.26% remained disease free after 6 months of completion of treatment). Radiotherapy was used in both adjuvant and primary setting. Nodal recurrence was the commonest pattern of recurrence in patients who had underwent definitive surgery. Co-relation with adverse histopathological prognostic indicators also establish early recurrence.
Conclusions: Ca tongue was found to be commoner in individuals between 36-55 years. Tobacco users were seen to be at high risk. Surgery was the preferred modality of treatment in early stage disease. Regional lymph node metastasis is the commonest site of early treatment failure. Adverse histopathological factors were important indicators of prognosis and need consideration in planning adjuvant treatment.

Keywords: Ca Tongue, Multimodality, Recurrence

INTRODUCTION

Cancer (Ca) tongue has shown rising incidence in the last couple of years in India.[1] Most common site of involvement is anterior (lateral borders) tongue accounting for 85% of cases.[2] Tobacco is the single most important risk factor for cancers of the oral cavity including Ca tongue. There are no specific guidelines available for Ca tongue, existing guidelines include it broadily under oral cavity cancers.[3]

Early stage disease is treated with single modality with surgery being the most preferred. Locally advanced cancers are treated with multimodality approach, surgery and adjuvant RT or chemoradiation. Disease stage and presence of regional spread at the time of presentation are the most important determinants of survival. Other recognized prognostic indicators are mostly histopathological.[4]

The primary objective of this study is to assess the clinical profile and treatment outcome in cases of Ca Tongue treated with multidisciplinary protocols at our institute. The aim of the study is to study clinical profile of Ca tongue and to study outcome of multimodality management of SCC tongue and identification of treatment failure.

METHODS

The study was conducted in the Dept. of Surgery, Himalayan Institute of Medical Sciences, Dehradun, India, over a period of 12 months on patients attending Surgical Oncology OPD. Written informed consent and ethical committee clearance was obtained in all 64 cases included, and study type is observational.

The inclusion criteria were patients with diagnosed and histologically proven SCC of tongue. Patients who did not receive planned primary treatment at our Hospital and who refused to give consent, were excluded. Treatment protocols were prescribed by the multidisciplinary tumour board. Observations made were recorded in the proforma.

Patients were followed up to 6 months after completion of treatment. Qualitative data were expressed in terms of frequency and percentage. Kaplan Meier Survival curves were used to check the probability of survival at different follow-up time intervals. $P < 0.05$ was considered as statistically significant. All statistical analysis were done by using statistical software SPSS version 22.

RESULTS

In 64 patients, 51 (79.68%) were male and 13 (20.31%) were female. Young and middle age patients were commoner in present study, with 44 patients (68.75%) below 55 years of age. 56 patients (87.5%) were chronic tobacco chewers, 45 (70.31%) were chronic cigarette/bidi smokers, 23 (35.3%) were alcoholics and 12 (18.75%) were habituated to betel/areca nut.

The clinical presentation of patients varied from an asymptomatic atrophic depapillated area on the tongue to non-homogenous leucoplakia with ulceration, superficial ulcerations with induration and exophytic ulceroproliferative growths. 33 (51.56%) of cases were associated with pain.

Figure 1: Ulceroproliferative growth lesion at right lateral border of tongue.

Figure 2: Ulceroproliferative growth lesion at left lateral border of tongue (intra-op pic; with grade-I trismus).

Figure 3: Ulceroproliferative growth lesion at left lateral border of tongue (intra-op pic; without trismus).

Anterior tongue was the site of lesion in 51 (79.68%) patients. 31 (48.43%) patients had lesion over the left lateral border of tongue. 20 (31.25%) patients had lesion over the right lateral border of tongue (including one (1.56%) patient who had lesion involving the tip along with right lateral border of tongue). 13 (20.31%) patients had involvement of the posterior one third of tongue.

Figure 4: Resected (partial glossectomy) specimen of Figure 3.

Figure 5: Ulcerative lesion at posterior 1/3rd of tongue along left side (intra-op).

Figure 6: Resected specimen (of photo-5) of lesion at posterior 1/3rd of tongue on left side.

All patients were initially evaluated in the OPD by clinical examination. 12 (18.75%) patients were found to have T1 disease, 30 (46.87%) with T2 disease, 7 (10.93%) with T3 disease, and 15 (23.43%) had clinical T4 tumour size. After complete evaluation with clinical assessment, imaging and metastatic workup were done in all patients. 9 (14.06%) patients were diagnosed with Stage-I of disease. 14 (21.87%) with Stage-II, 26 (40.62%) with Stage-III, and 15 (23.43%) patients were diagnosed with advanced disease. The intent of treatment was curative in 54 (84.37%) patients and palliation in 10 (15.62%). All patients in present study were histologically proven SCC of tongue - 52 (81.25%) moderately differentiated, 7 (10.93%) well differentiated and 5 (7.81%) poorly differentiated.

Figure 7: Lesion at left lateral border of tongue extending up to posterior 1/3rd of tongue.

Treatment protocols were prescribed by the multidisciplinary tumour board (Figure 8).

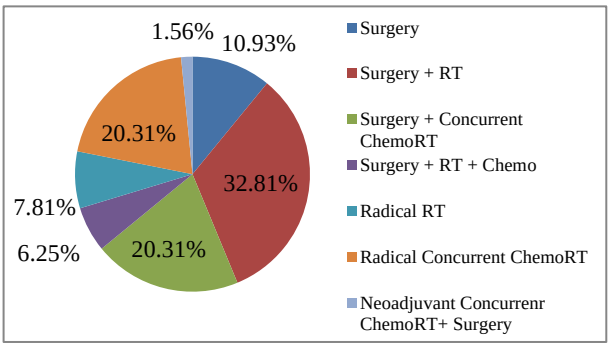

Figure 8: Modality of treatment received.

46 (71.86%) patients underwent definitive surgical procedures (Figure 9).

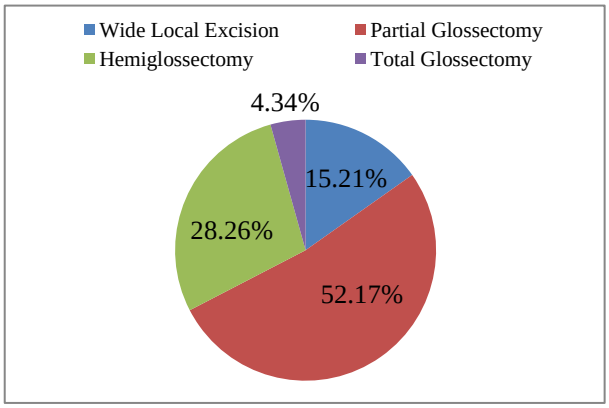

Figure 9: Surgical procedures.

Neck Dissection were done in all 46 who underwent surgery (Figure 10). 4 patients undergone an initial selective neck dissection had to undergo completion surgery (Radical Neck Dissection) for early recurrence at level V nodes. Surgical complications in the immediate post-op period was documented in 5 (10.85%) patients. One (2.17%) had bleeding into the neck wound, and was taken up for emergency re-exploration. 3 (6.51%) had surgical site infection and one (2.17%) had flap necrosis.

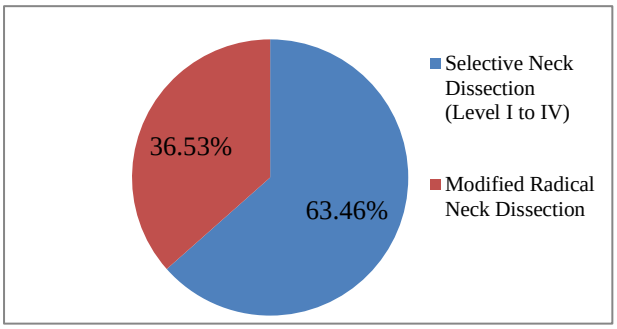

Figure 10: Neck dissection procedures.

The final histopathology report of all 46 patients undergone definitive surgery were taken into account while deciding adjuvant therapy. Surgical margins were clear in all 46. However, 10 (21.73%) patients had shown early recurrence).

Radiotherapy was used in both adjuvant and primary setting. In the adjuvant setting, the maximum dose was EBRT 60Gy/30#. And in primary/definitive/palliative setting the maximum EBRT received was 66Gy/33#. Both conventional and IMRT techniques were used for treatment.

Table 1: Mucositis grade (radiotherapy complication) in patients who had received radiation either in adjuvant or primary setting.

Mucositis	No. of cases (n=57)	Percentage
Grade I	1	1.75%
Grade II	32	56.14%
Grade III	21	36.84%
Grade IV	3	5.26%

Cisplatin was the preferred chemotherapeutic agent used concurrent with radiotherapy. IV Taxol based regimen was used in palliative setting, and oral weekly Methotrexate was used as Metronomic chemotherapy.

Table 2: Skin reaction grade (radiotherapy complication) in patients who had received radiation either in adjuvant or primary setting.

Skin reaction grade	No. of cases (n=57)	Percentage
Grade I	16	28.07%
Grade II	35	61.4%
Grade III	6	10.52%

Table 3: Other complications post-radiotherapy in patients who received radiation either in adjuvant or primary setting.

Complications	No. of cases (n=57)	Percentage
Difficulty in swallowing	47	82.45%
Xerostomia	55	96.49%
Others (fungal infection)	4	7.01%

A total of 57 (89.06%) patients out of 64 received radiation therapy, in either adjuvant or primary setting. Both early and late Radiotherapy complications were documented including grade of mucositis, skin reaction grade, difficulty in swallowing, xerostomia and fungal infection (Table 1-3). All patients were evaluated for functional disability as treatment sequelae in the study period (Table 4).

Table 4: Functional status at 6 months follow-up.

Follow-up (n=64)	Normal		Affected	
	No.	%	No.	%
Speech	31	48.43%	33	51.56%
Taste	9	14.06%	55	85.93%
Chewing/Swallowing	3	4.68%	61	95.31%
Pain	19	29.68%	45	70.31%
Shoulder Pain/ Dysfunction	3	4.68%	61	95.31%
Working status	49	76.56%	15	23.43%

Analysis of treatment outcome were done at 6 months for all 64 patients (Table 5).

Table 5: Stage of disease and early outcome at 6 months follow up after completion of treatment.

	No. of Cases	Disease free	Disease present	Chi square	P value
Stage I	9	9 (100%)	0 (0%)	8.42	0.002 Significant
Stage II	14	12 (85.71%)	2 (14.28%)	1.23	0.131
Stage III	26	20 (76.92%)	6 (23.07%)	0.34	0.557
Stage IV	15	4 (26.66%)	11 (73.33%)	15.51	0.0002 Significant
Total	64	45 (70.31%)	19 (29.68%)	6.37	0.010 Significant

Table 6: Early outcome on the intent of treatment plan and the stage of disease after 6 months of completion of treatment.

	Stage	Total	Disease free	Disease present / Residual disease / Recurrence		
				Local	Regional	Distant
Palliative	I	10	0	0	0	0
	II		0	1	0	0
	III		0	1	2	0
	IV		0	1	1	4
Curative	I	54	9	0	0	0
	II		12	0	1	0
	III		20	0	3	0
	IV		4	1	3	1
Total		64	45	4	10	5

Table 7: Treatment modality patients received in stage of disease and the early outcome / disease free status after 6 months of completion of treatment.

	Stage	Total	Disease free	Disease present
Surgery (7)	I	3	3	0
	II	4	4	0
Surgery + RT (21)	I	1	0	0
	II	4	0	0
	III	12	10	2
	IV	4	2	2
Surgery + Concurrent Chemort (13)	III	10	10	0
	IV	3	1	2
Surgery + RT + Chemo (4)	II	1	0	1
	III	1	0	1
	IV	2	0	2
RT (5)	I	1	1	0
	II	1	1	0
	III	1	0	1
	IV	2	0	2
Concurrent Chemort (13)	I	4	4	0
	II	4	3	1
	III	2	0	2
	IV	3	0	3
Neoadjuvant Concurrent Chemort + Surgery (1)	IV	1	1	0
Total (64)		64	45	19

Table 8: patterns of early recurrence (in patients undergone definitive surgery) after 6 months of completion of treatment.

Factors	No. of cases (n=46)
Recurrence in tongue	1 (2.17%)
Recurrence in neck	7 (15.21%)
Distant mets	2 (4.34%)
Total	10 (21.73%)

DISCUSSION

In the study 79.68% were male, which show concordance with the results of various previous hospital based studies conducted in India that indicates larger number of Ca Tongue in male compared to female.[5] There is higher frequency of Ca Tongue in younger and middle age patients in present study, 68.75% patients were below 55 years of age, which is a decade earlier than the findings observed in other previous studies where the commonest age group is after 5th decade of life.[6]

Observed parameters do not indicate any specific reason. In present study, 87.5% patients had a known high risk factor of chronic tobacco chewing, but again 12.5% patients were non-tobacco chewers. This is in concordance with the results of various previous studies, where more than 90% of oral cancer cases (including Ca Tongue) report using tobacco products. The commonest site of lesion in present study is in concordance with

many previous studies where around 80% lesions are also over the lateral border of tongue.[7]

The goal of treatment was curative in 84.37% patients and palliative in rest 15.62% patients. Most studies done earlier by different groups on this subject do not have defined intent of treatment and thus, the outcome of treatment modality on the basis of intent cannot be described in those. At 6 months of follow-up that we assessed patients, literature is not clear about the nomenclature of the treatment failure (presence of disease). Presence of disease in patients treated with a palliative intent is expected at 6 months and we did not include them under treatment failure. Other studies of this type had a longer follow-up time and probably did not encounter a similar problem.

Table 9: Co-relation with adverse histopathological prognostic factors in 10 of the 46 patients (who too had underwent definitive surgery) with early recurrence after 6 months of completion of treatment.

Factors	No. of case (n=10)	Percentage
Positive margins	0	0%
Lymph node positivity	9	90%
Tumour depth (in mm)		
• > 5 mm	7	70%
• ≤ 5 mm	3	30%
• pT2	4	40%
• pT3	1	10%
• pT4	5	50%
Extracapsular spread	6	60%
Lymphovascular invasion	7	70%
Perineural invasion	4	40%

In present study, Definitive Surgery was done in 71.86% of patients, Radiotherapy was given in 89.06% of patients and 48.43% of patients received Chemotherapy in different combinations. Definitive surgery is the most preferred mode of management in early stage carcinomas of tongue and has a good outcome. The smaller tumour size T has direct prognostic value. "Smaller the tumour size better the prognosis" this statement is generalized for all HNSCC but most appropriate for the tongue cancer.[8]

In present study, in 71.86% patients surgery was the most preferred primary treatment. Of these 78.26% remained disease free after 6 months of completion of treatment and 21.73% showed early recurrence. Though our follow up of 6 months is too early to comment on disease free survival, these numbers are quite encouraging.

Radical Radiotherapy or Concurrent chemoradiotherapy was used as a primary treatment modality in 28.13% patients who did not undergo surgery. This group included young patients with locally advanced disease that would otherwise require a total or near-total glossectomy.

Table 10: Poor prognostic indicators were present in the form of following (in 46 surgical patients in the final HPR).

Factors	No. of cases (n=46)	Percentage
Tumour depth (in mm)		
• >5 mm	33	71.73
• ≤5 mm	13	28.2
Positive margins	0	0
Lymph node positivity	29	63.04
• pT1	7	15.21
• pT2	25	54.34
• pT3	4	8.69
• pT4	10	21.73
Extracapsular spread	14	30.43%
Lymphovascular invasion	14	30.43%
Perineural invasion	12	26.08%

Due to small number of patients who underwent Radical RT or chemoradiotherapy as a primary treatment, the outcomes could not be compared with those of primary surgery. Moreover, such a comparison has not yet been reported for patients with SCC of tongue.

One young patient with advanced stage of disease was given neoadjuvant concurrent chemoradiotherapy followed by adjuvant surgery. This patient showed good response to treatment and remained disease free after 6 months of adjuvant surgery. More studies are the need of hour to know trends of outcomes of neoadjuvant concurrent chemoradiotherapy followed by adjuvant surgery in young patients with advanced disease.

SCC of the oral tongue remains a challenging disease to manage. Despite aggressive surgical management and adjuvant treatment including radiotherapy, patients continue to develop regional failure. Nodal metastases are frequent, particularly in patients with locally advanced disease. Even though our study includes fair number of oral tongue cancers, multi-institutional studies involving detailed databases and outcome measurement are required to determine the predictors of recurrence and overall survival.

The surgical margins, depth of tumour, nodal status, perinodal / extracapsular spread/extension, lymphovascular invasion and perineural invasion are the adverse histopathological factors which are traditionally considered indicators of early outcome, recurrence and prognosis. In present study, 21.73% patients who had underwent surgery has shown presence of disease at 6 months and these adverse histopathological prognostic factors were present in them. This is in consensus with

the available literature. The overall 6 months early outcome of our patients treated with curative intent revealed presence of disease in 29.68%. This includes both patients treated primarily with Surgery and Radiotherapy. 70.31% patients were disease free after 6 months of the completion of treatment.

Nodal recurrence were found to be the commonest site of early treatment failure in present study. The incidence of local recurrence increases with more advanced stage carcinoma and in the presence of adverse histopathological prognostic factors.

Although the combination of chemotherapy with surgery and radiotherapy has improved cure rates in some other head and neck cancers, its role in the management of oral cavity tumours is not clear. Some advocate its use in young patients, when there are multiple involved cervical nodes, and in the presence of adverse histological features. Although no survival benefit has been confirmed to date, the results of studies involving large series are awaited.[9]

The limitation in our study is the short duration of follow-up, 6 months follow-up after completion of the recommended treatment is too early to assess the outcome in terms of disease free survival, recurrence & overall survival. Early failures / recurrences likely represent progression of residual disease which remained unresponsive to primary / adjuvant treatment.

CONCLUSION

Study has a larger number of young and middle aged individuals between 36-55 years; and the youngest patients were of 25 years age; with Ca tongue. Tobacco chewers and smokers were seen to be at high risk of Ca Tongue. Other factors, however, might also be significant as deduced from the finding that 12.5% patients had no history of tobacco usage. The intent of treatment modality should be curative in patients with early stage of Ca Tongue with Surgery as the preferred primary modality. This effectively achieves local control and disease free survival.

Inspite of the use of evidence based recommendations and multimodality treatment, patients of advanced stage had only partial response. Regional lymph node metastasis is the commonest site of early treatment failure after primary surgical treatment of oral tongue carcinoma with or without adjuvant treatment. Local recurrence (Primary site) is the second common site of treatment failure. The incidence of local recurrence increases in the presence of adverse prognostic factors.

Presence of residual disease in advanced cases represent unresponsiveness to the treatment employed. Adverse histopathological factors are an important indicator of prognosis and need consideration in planning adjuvant treatment. Six months' follow-up after completion of the recommended treatment is too early to assess the disease-free survival, recurrence and overall survival.

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