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ASSOCIATION OF THE DEPTH OF TUMOR & LYMPHATIC METASTASIS IN ORAL TONGUE CANCER

Otolaryngology

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ABSTRACT

Carcinoma of tongue is one of the most notorious cancer of head and neck region. It constitutes about 36.5% of all oral malignancies. Neck node status is the single most important prognostic factor in oral tongue cancers and other head and neck cancers . Another important parameter which has the greatest influence on survival is the tumor thickness especially in carcinoma tongue . In this study, we assessed the association between tumor thickness & lymphatic metastasis in oral tongue cancer. The optimal cut-off point for tumor thickness was 4mm. Total 126 cases were studied of which maximum cases were between 40-49 years of age .Cases were more prevalent in males (69.05%) than females(30.95%) . As the T-stage of cancer progressed , the incidence of nodal metastasis also progressively advanced. It was also observed that as the tumor thickness increased , the proportion of positive lymph node cases also significantly increased. There was significant positive correlation between the tumor thickness measured on MRI and histopathology ($r=0.709$, $p<0.001$)

KEYWORDS

Tongue cancer , nodal staging , tumor thickness, radiological evaluation ,histopathogy

INTRODUCTION

Carcinoma of tongue is one of the most notorious cancer of head and neck region. The tongue cancer is the most common of all oral malignancies (36.5% of all oral malignancies).[1]

Neck node status is the single most important prognostic factor in oral tongue cancers and other head and neck cancers .

The five years survival rate in patients with neck metastasis decreases according to the number & level of the nodes involved & if extracapsular spread is present.[2]

The incidence of lymph node metastases of these cancers depends largely on histo-pathologic factors like tumour thickness, peri-neural and micro-vascular invasions, lymphocytic inflammatory infiltration, pattern of tumour-invasion and differentiation, and molecular tumour markers.[3,4,5,6]

Apart from this multivariate analysis have shown that the parameter with greatest influence on survival is tumor thickness especially in carcinoma tongue.

Most studies have suggested that TT is a strong predictor for lymph-node involvement in Oral tongue malignancies [7-11]. However, controversy exists about the optimal TT cutoff point for a clinically relevant risk to the neck of harboring microscopic disease .

Accurate and consistent assessment of tumor thickness is essential for optimal preoperative planning . A recent description of sentinel lymph node biopsy suggests that the 4-mm tumor thickness cutoff point is potentially most appropriate for the risk stratification for cervical lymphadenopathy [12]

MRI has been shown to satisfactorily depict oral tongue carcinoma because the tumor has higher signal intensity than the normal tongue tissue .

AIM & OBJECTIVES

- To assess the association between tumor thickness & lymphatic metastasis in oral tongue cancer.
- To assess the accuracy of clinical assessment of lymph node involvement against histopathological assessment in oral tongue cancer.
- To determine the correlation between findings of tumor thickness measured by MRI & HPE in oral tongue cancer patients.

MATERIAL & METHODS

- The study was done between April 2014 to November 2015 on 126 patients presenting with squamous cell carcinoma of oral tongue who presented to the ENT department, SMS Medical College and Hospital, a tertiary care referral.

Sample Size

- The sample size required is 42 to verify the expected minimum difference of 26.7% in proportion to cases with lymph node metastasis (33% vs. 40%) in all three groups of different level of tumor thickness at 95% confidence and 80% power.
- This sample size is also adequate for assessing other variables.

Sampling procedure

- All eligible patients of oral tongue cancer were included & categorized as per the depth of tumor till the sample size of 42 in all three groups were achieved

INCLUSION CRITERIA-

- All histopathologicaly proved pateints attending ENT OPD with squamous cell carcinoma of oral tongue who had given the consent & fit for surgery.

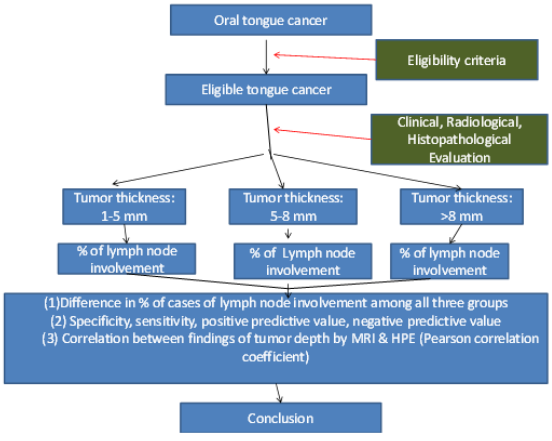
Exclusion criteria-

- Patients who had taken neo-adjuvant treatment.
- Patients in which growth extended beyond the oral tongue.
- Patients who had not given the consent for surgery.
- Patient in which growth was extending up to or crossing the midline .

STATISTICALANALYSIS

Statistical analysis was performed with the SPSS, Trial version 20 for Windows statistical software package (SPSS inc., Chicago, il, USA) and PRIMER. The Categorical data were presented as numbers (percent) and were compared among groups using Chi square test. Groups were compared for demographic data were presented as mean and standard deviation and were compared using by students t-test Relationships between variables in the patient group was assessed by using Pearson's correlation coefficient. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cutoff values of significant variable. The study was approved by the ethics committee, SMS Medical college .Probability P value <0.05 was considered statistically significant A detailed history is taken with special reference to age, sex, place of origin, occupation any addictive habits, family history etc.

These cases are subjected to routine laboratory tests beside the indirect laryngoscopy , direct laryngoscopy , MRI , FNAC, X-ray soft tissue neck ,Biopsy and all investigations required for pre anaesthetic check-up .



- The measurement for depth of invasion preoperatively done by MRI of tongue & neck.
- All patients were examined with a 1.5-T MRI system at a median of 5 days (range 0–23 days) before glossectomy.
- Coronal gadolinium-enhanced T1-weighted imaging (short TR/TE, 3- mm slice thickness, and no spacing) and coronal T2-weighted imaging with fat suppression (long TR/TE, 3-mm slice thickness, and no spacing) were performed.
- A horizontal line joining the two tumor–mucosa junctions was drawn as a reference line. We measured the tumor thickness by drawing perpendicular lines from the reference line to the point of maximal tumor projection and invasion and then calculated the greatest radiologically determined tumor thickness by adding these two parameters.(FIG. 1)

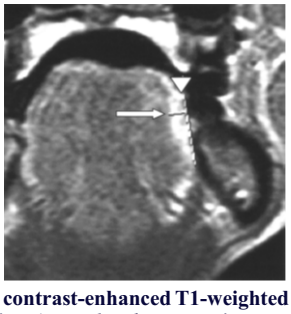


FIG. 1 - Coronal contrast-enhanced T1-weighted spin-echo image shows vertical line (*arrowhead*) connecting two tumor–mucosa junctions as reference line. Horizontal line (*arrow*) drawn perpendicular to it represents radiologically determined tumor thickness of 3 mm

- The measurement of depth of invasion post-operatively done by histopathological examination.
- Each glossectomy specimen was pinned on a foam board during formalin fixation to prevent shrinkage of the tissue. The preserved specimen was cut into 3-mm sections in the coronal plane and stained with H and E.
- The tumor border was outlined, and the image on each slide was analyzed using a computerized image analyzer (Metamorph Imaging System, Universal Imaging, Downingtown, PA).
- The tumor thickness was assessed in the same way as it was measured on coronal MR images.
- We drew a horizontal line to connect the two tumor–mucosa junctions and then drew vertical lines perpendicular to the horizontal line to measure the maximal thickness of both exophytic and endophytic parts of the tumor. We then calculated the greatest histologically determined tumor thickness by adding these two parameters.(FIG. 2)

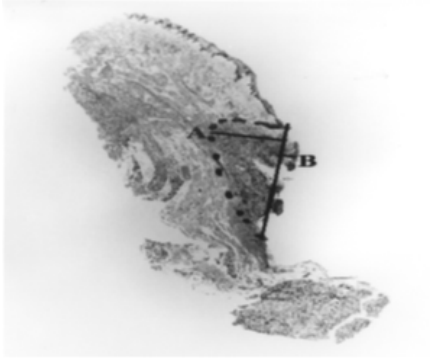


FIG. 2-Photograph of histologic slide obtained in 43-year old man with oral tongue cancer. We calculated tumor thickness by adding measurements of largest exophytic (A) and largest endophytic (B) parts of tumor

- Surgeries performed for the tumor are wide excision or hemiglossectomy along with modified neck dissection , selective neck dissection or radical neck dissection depending on the clinical stage of the disease , location & size of the tumor.

OBSERVATIONS

Maximum cases were in 40 to 49 years of age group (34.92 %) followed by 50 to 59 years (27.78%) .

Proportion of the males (69.05%) were more than females (30.95%) .M:F ratio was 2.23:1. Cases were more (58.73%) on right lateral border of tongue than left lateral border of tongue (41.27%).

56 cases out of 126 were T1(Tumor </=2cm size) lesions, 70 were T2 (Tumor 2-4cm size) type.

There were 52 patients (48.41%) with clinically palpable neck disease but 55 patients (43.65%) were radiological palpable neck disease .Histopathological palpable neck disease was found in 50 patients (39.68%%)

No significant difference was observed within T staging and histopathological staging. Although with T 2 stage , 44.29% cases were positive while 33.93% nodes were positive in T1 staging .

No significant difference was observed within observation in pre-operative biopsy and histopathological staging. Cases with PDSCC, 45.54 % cases were with node positive while 40.85 % nodes were positive in MDSCC and 36.36% were in WDSCC. [TABLE 1]

Table 1- Association of Degree of differentiation with Nodal Staging (pN)

	Pn+		Pn0		Total	
	No.	%	No.	%	No	%
MDSCC	29	40.85	42	59.15	71	56.35
PDSCC	5	45.45	6	54.55	11	8.73
WDSCC	16	36.36	28	63.64	44	34.92
Total	50	39.68	76	177.34	126	100.00

PDSCC-Poorly differentiated squamous cell carcinoma

MDSCC- Moderatly differentiated squamous cell carcinoma

WDSCC- Well differentiated squamous cell carcinoma

Table 2 - Distribution Of The Cases According To Thickness In Mri

Tumor thickness on MRI (mm)	No	%
<5	48	38.10
5 to 8	51	40.48
>8	27	21.43
Total	126	100.00

Cases with tumor thickness less than 5mm as measured by MRI were maximum (38.10%) .[TABLE 2]

Tumor thickness on HPE (mm)	No	%
<5	42	33.33
5 to 8	42	33.33
>8	42	33.33
Total	126	100.00

Table 3- Distribution Of The Cases According To Thickness In Hpe

Depth **(Thickness)** of tumour were equal in number measured by HPE (histopathogical examination) .[TABLE 3]

Depth of tumor (HPE) in mm	pN+		pN0		Total	
	No	%	No	%	No	%
<5	5	11.90	37	88.10	42	33.33
5 to 8	17	40.48	25	59.52	42	33.33
>8	28	66.67	14	33.33	42	33.33
Total	**50**	39.68	**76**	60.32	**126**	100

Table 4- Distribution Of The Cases According To Depth Of Tumor Hpe With Nodal Staging

Proportion of the nodal positive cases significantly increase with the depth of tumor .11.90% cases were nodal positive in tumor with depth of <5mm while it was 66.67% in tumor depth of >8mm .[TABLE 4]

Diagnostic accuracy of Clinically diagnosed Lymph node status against the Gold Standard (HPE finding) was 77.78% while that of radiologically diagnosed lymph node status was 81.75% .

	Mean	SD	N	R	R Square	
Depth of Tumor (MRI)	5.99	3.700	126			Sig. F Change
Depth of Tumo (HPE)	7.20	3.620	126	.709[a]	.502	.000

Table 5 - Correlation Between Depth Of Tumor(hpe And Mri)

A significant positive correlation existed between the Depth of Tumor(MRI)and HPE (r= 0.709 $p < 0.001$) by using Pearson's correlation coefficient . The R2= 0.502 ,it means 50.2 % of the total variation in MRI was explained by the linear relation with HPE . The relationships between the variables in the patient group were considered by using Pearson's correlation coefficient .[TABLE 5]

DISCUSSION

Neck dissections are performed as an elective or therapeutic procedure in the treatment of carcinomas of head and neck especially in squamous cell carcinoma. During neck dissection lymph nodes of one side of neck and several important surrounding non lymphatic structures are resected which is the cause of considerable morbidity (physical, emotional and social) in postoperative patients and affect the overall quality of life. It is presumable that quality of life postoperative is poor in patients undergoing neck dissection as part of primary surgical procedure.

The main dilemma arises in treating an N0 neck in squamous cell carcinoma of tongue. The question, which arise while treating such patients are:

Should the neck be treated or observed?

Are there any tumor factors which affect nodal metastasis and help us make a decision on whether to treat N0 neck or not?

Is there any non-invasive modality to assist in diagnosing cervical lymphnode metastasis?

What is the optimal surgery for neck?

After assessing 126 patients of carcinoma oral tongue who underwent surgery for primary tumor excision and ipsilateral neck dissection done at Department of Otorhinolaryngology and head and neck surgery, Sawai Man Singh Medical College, Jaipur Rajasthan.

Sensitivity and specificity of lymph node metastasis with each group thickness was calculated. 4 mm came as cut off tumor thickness for presence/ absence of cervical nodal metastasis. The results are comparable to those mentioned in other studies on similar subject. Thus in all patients with tumor thickness more than 4 mm should undergo neck dissection.

Relation of Cellular differentiation with nodal metastases

There is high incidence of moderately differentiated tumours in the present study (56.34%), while 34.92% cases were with well differentiated and 8.73% were with poorly differentiated tumors.

It was observed in our study that 45.45% (5 cases) of the 11 poorly differentiated lesions had a pathologically positive neck at the time of presentation as compared to 40% (29 cases) of the 72 moderately differentiated lesions and 36.36% (16 cases) of the 44 well differentiated lesions. Thus, it can be concluded that as the anaplasia increases and the degree of differentiation of the tumor decreases, the incidence of nodal metastases progressively increase.

T Stage of Primary Lesions

On clinical examination we observed that 56 cases were of T1 stage (44.44%), 70 cases of T2 stage (55.66%).

Cancers of oral tongue were seen in the early stage because of easy accessibility of the tumors by the patients as well as by a general practitioner.

Clinical Evaluation of Nodal Metastasis

In this series, the proportion of nodal metastasis was found to be 39.68% (50 cases) and 60.32% (70 cases) patients had a clinically negative neck at the time of presentation.

Correlation of T Stage with Nodal Metastasis

It was observed in our study that as the T stage progressively advanced, the incidence of nodal metastasis also progressively increased.In T1 and T2 stage cervical metastasis was noted in 33.93% and 44.29% cases respectively.

Comparison of Clinical Examination, Radiological Evaluation and Histopathology

Diagnostic efficacy of clinical examination of lymph nodes (77.78%) is less than that of radiological evaluation of lymph nodes (81.75%).

Correlating MRI and Histologic Tumor Thickness in the Assessment of Oral Tongue Cancer

In our study, we investigated the reliability MRI in assessing tongue tumour thickness as an in-vivo preoperative measure of tumour depth of invasion.

We included STIR sequences in the measurement protocol as it has been shown to be a reasonable alternative to T1-weighted fat-suppressed contrast-enhanced sequences[13]

We found a high degree of concordance for both studied sequences with histologic tumour thickness (R value of 0.71 for STIR axial sequences).

This is in agreement with data in published literature where R values of 0.609–0.94 have been reported[14,15,16]

Summary And Conclusion

An association between tumor thickness and cervical lymph-node involvement was confirmed in this study . The optimal cutoff point for tumor thickness is 4mm . For oral tongue cancers thicker than 4mm , prophylactic neck management should be considered .

The assessment of tumor thickness on MRI before surgery can assist one in deciding whether the patient who has oral tongue cancer but no nodal involvement in the neck should be placed under observation or treated with prophylactic neck dissection .

Tongue tumor thickness can be measured reliably on MRI ,and has a significant bearing on patient prognosis.Our study suggested the significant positive correlation between the tumor thickness measured on MRI and histopathologically ($r = 0.709$ $p < 0.001$).

STIR sequences are more sensitive in detection of small tongue tumors.

Clinical evaluation of neck nodes have high false negative rate and low sensitivity than radiological (MRI) evaluation so we recommend radiological evaluation of neck as a method of staging for oral tongue cancer.

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