



## A RETROSPECTIVE AND PROSPECTIVE OBSERVATIONAL STUDY TO DETERMINE THE CORRELATION BETWEEN SIZE AND DEPTH OF ULCER IN ORAL CAVITY CARCINOMA WITH THE EXTENT OF NODAL INVOLVEMENT IN PATIENTS UNDERGOING SURGERY IN A TERTIARY CARE CENTRE

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**ABSTRACT** **Introduction:** In Asia, head and neck cancer is considered the most common neoplasm and it is the 5th most common cancer in the world. Cervical lymph node metastasis is the main mode of metastasis in various stages of oral cancer, and it is also an important factor affecting the prognosis of oral cancer. Depth of invasion of tumour is the most significant predictor of cervical node metastasis in early squamous carcinomas of the oral cavity. Patients with a tumour depth of more than or equal to 5 mm are at an increased risk of harbouring node metastasis. Aim of this study is to find whether correlation exists between tumour size and depth of invasion with extent of nodal involvement which is one of the important prognostic factors in oral malignancies. **Materials and Methods:** A retrospective and prospective observational analysis of 69 patients with buccal mucosa cancer treated in the Department of surgical oncology at Government Medical College, Aurangabad from 2022–2023. All patients underwent complete diagnostic work up. **Results:** Out of 69 patients, 47.82% OSCC showed nodal metastasis with DOI > 0.5 cm and 4.34% showed nodal metastasis present in tumours with DOI < 5 mm. Hence, according to this study DOI is a significant parameter for lymph node metastasis ( $p=0.022$ ) in OSCC. **Conclusions:** Hence it can be concluded that DOI can be used as a measure to direct elective neck therapy.

**KEYWORDS :** Oral squamous cell carcinoma (OSCC), buccal mucosa, nodal involvement, depth of invasion (DOI)

### INTRODUCTION

In Asia, head and neck cancer is considered the most common neoplasm and it is the 5th most common cancer in the world (1). In both developed and developing countries, cancer is a major cause of mortality and morbidity (2). India contributes to almost one-third of the total burden and the second country having the highest number of oral cancer cases (3). Oral cancer can develop cervical lymph node metastasis early. Sometimes the lymph nodes are negative through clinical examinations such as palpation, ultrasonography, CT and MRI, but there are micro metastases in the lymph nodes after pathological examination after neck dissection, which is called occult lymphatic metastasis. About 20% to 40% of early stage oral cancer patients have occult cervical lymph node metastasis (4). Cervical lymph node metastasis is the main mode of metastasis in various stages of oral cancer, and it is also an important factor affecting the prognosis of oral cancer. The number and size of metastatic lymph nodes, whether or not the capsular invasion, and the extent of involvement of the neck region will directly affect the prognosis of patients (5). The invasion of blood vessels and nerves by tumours has always been regarded as one of the indicators of pathological grade. Theoretically, vascular invasion indicates that a large number of tumour cells enter the blood vessel and become the first step in tumour metastasis. Nerve encroachment can exist alone without vascular invasion and is another way of tumour spread and metastasis. However, there is still controversy about the relationship between vascular nerve invasion and cervical metastasis and prognosis (6). Depth is the most significant predictor of cervical node metastasis in early squamous carcinomas of the oral cavity. Patients with a tumour depth of more than or equal to 5 mm are at an increased risk of harbouring node metastasis (7) Elective neck therapy (surgery or irradiation) is strongly indicated for tumours exceeding 5 mm invasion (8) On performing univariate analysis, the histopathological parameters that were found to be statistically significant were lymphovascular invasion ( $p = 0.004$ ) and perineural invasion ( $p = 0.003$ ) along with a cut-off depth of infiltration more than 5 mm ( $p = 0.01$ ). In an Indian setting, histopathological evaluation assumes a bigger role than other expensive and advanced techniques. (9). Ultrasound and computed tomography are of little value in predicting which patients have positive nodes. (10) Depth of invasion (DOI) was added to the staging criteria for carcinoma of the lip and oral cavity in the 8th edition of the American Joint Committee on Cancer Staging Manual (AJCC8). (11) Histological grade, WPOI, tumour

budding ( $\geq 3/\times 40$  field), LVE, and PNI were significantly associated with risk of LN metastasis. On multivariate analysis, WPOI and tumour budding were 2 most significant factors. Among the early-stage tumours with available follow up ( $n = 48$ ), DOI, WPOI, tumour budding, and LVE were associated with a shorter overall survival, although it was not statistically significant. (12) Tumour infiltration depth is an independent predictor for nodal status in pT1-2 OSCC. In pT1cN0 tumours, a cut-off at 4.59 mm results in the best predictive value (13). The combination of poor differentiation and pathologic tumour depth of 4 mm or greater identified a subset of pT1-2N0 OSCC patients with poor outcome, who may have clinical benefit from postoperative adjuvant radiotherapy (14). In this study we are trying to find whether correlation exists between tumour size and depth of invasion with extent of nodal involvement which is one of the important prognostic factor in oral malignancies.

### AIMS AND OBJECTIVES:

- To study the depth of tumour invasion in buccal mucosa carcinoma and its correlation with neck metastasis.
- To know whether the increase in depth of tumour increases the chances of cervical nodal metastasis in buccal mucosa carcinoma and derive cut-off value of depth of invasion at which the metastasis occurs.

### MATERIALS AND METHODS:

A retrospective and prospective observational analysis of 69 patients with buccal mucosa cancer treated in the Department of surgical oncology at Government Medical College, Aurangabad from 2022–2023. Institutional Ethical Board clearance approval was taken. Diagnostic work up for all patients involved prospectively were clinical examination; imaging modalities including CT scan skull base to clavicle plus chest, if required magnetic resonance imaging to evaluate regional spread and distant metastasis, biopsy to confirm the diagnosis. For retrospective patients, documented history of the above mentioned work up was taken. Post operative histopathological reports of all patients were studied and analysed.

### Measurement of depth of tumour invasion:

DOI concerns measuring the invasion of tumour mass below the epithelial surface. An objective parameter is required to meaningfully access the depth of tumour invasion. This can be effectively achieved using an ocular micrometer. DOI is measured from the basement

membrane of adjacent normal to the deepest point of invasion of the tumour. The horizon is established at the level of the basement membrane relative to the closest intact squamous mucosa. The greatest DOI is measured by dropping a “plumb line” from the horizon.

**Inclusion Criteria(s):**

1. Patients undergoing surgery in Government Cancer Hospital, Aurangabad
2. Patients having moderately differentiated squamous cell carcinoma of the buccal mucosa.
3. Operated within the time frame of Jan 2022 to march 2023.

**Exclusion Criteria(s):**

1. Extension beyond anterior tonsillar pillar
2. Carcinoma other than squamous cell carcinoma
3. Recurrent squamous cell carcinoma

**RESULTS:**

Out of 69 patients included in this study, 52 were males and 17 were females. M: F ratio was 3.05:1.

38 (55.1%) cases were seen having tumour size of 2-4cm followed by 17 (24.6%) having size <2cm followed by 14(20.3%) having size >4cm. There was no statistically significant difference found between DOI and Size of tumour (p value<0.61).

**Table 1:- Distribution of subjects according to DOI**

DOI(in cm)	Frequency	Percent (%)
<0.5	14	20.3
0.5-1	23	33.3
1-1.5	16	23.2
>1.5	16	23.2

23(33.3%) cases were seen having DOI of 0.5-1cm followed by 16(23.2%) patients each having DOI of 1-1.5 cm and >1.5 cm followed by 14(20.3%) having DOI of <0.5cm.

**Table 2:- Correlation of subjects according to DOI and T stage**

	<0.5		0.5-1		1-1.5		>1.5	
	N	%	N	%	N	%	N	%
T1	4	28.6%	0	0%	0	0%	0	0%
T2	9	64.3%	17	73.9%	0	0%	0	0%
T3	0	0%	1	4.3%	7	43.8%	5	31.3%
T4a	1	7.1%	4	17.4%	7	43.8%	10	62.5%
T4b	0	0%	1	4.3%	2	12.5%	1	6.3%

In this study T stage (AJCC 8 th edition) varies according to DOI (p<0.001)

**Table 3:- Correlation of subjects according to DOI and stage of pathological nodal status (pN)**

Pathologic al nodal status (pN)	DOI(in cm)								P Value
	<0.5		0.5-1		1-1.5		>1.5		
	N	%	N	%	N	%	N	%	
N0	11	78.6%	12	52.2%	6	37.5%	4	25.0%	0.181
N1	2	14.3%	4	17.4%	3	18.8%	3	18.8%	
N2b	1	7.1%	3	13.0%	3	18.8%	6	37.5%	
N3b	0	0%	4	17.4%	4	25.0%	3	18.8%	

**Table 4: Incidence of pathological nodal status (pN) and ENE with relation to DOI**

DOI(in cm)	N0	N+	P Value
<0.5	11	3	0.022
>0.5	22	33	
TOTAL	33	36	

ENE	Frequency	Percent
No	58	84.1%
Yes	11	15.9%

Out of 69 cases in this study, 33 cases were found to be N0 and 36 cases with N+. Out of 36 nodal metastasis (N+) cases 11 patients had extra nodal extension (ENE+).

33 patients with tumours with DOI >0.5 cm had nodal metastasis and only 3 patients had nodal metastasis present in tumours with DOI < or = 5 mm (p=0.022), that is statistically significant.

**Table 5:- Correlation of subjects according to DOI and various factors**

	<0.5		0.5-1		1-1.5		>1.5		P value
	N	%	N	%	N	%	N	%	
Bone involvement									0.016
No	14	100%	20	87.0%	11	68.8%	9	56.3%	
Yes	0	0%	3	13.0%	5	31.3%	7	43.8%	

LVI	N		%		N		%		P value
	N	%	N	%	N	%	N	%	
No	14	100%	23	100%	15	93.8%	16	100%	0.339
Yes	0	0%	0	0%	1	6.3%	0	0%	

PNI	N		%		N		%		P value
	N	%	N	%	N	%	N	%	
No	13	92.9%	17	73.9%	12	75.0%	10	62.5%	0.289
Yes	1	7.1%	6	26.1%	4	25.0%	6	37.5%	

ENE	N		%		N		%		P value
	N	%	N	%	N	%	N	%	
No	14	100%	19	82.6%	12	75.0%	13	81.3%	0.288
Yes	0	.0%	4	17.4%	4	25.0%	3	18.8%	

Tumours having DOI <0.5 cm did not show any bone involvement and 15 cases out of 55 cases i.e. 27.27% with DOI>0.5cm showed bone involvement , p value is 0.016 which is statistically significant. LVI, PNI and ENE are statistically insignificant according to DOI. Tumours having DOI <0.5 cm did not show any lymphovascular invasion and only 1 case out of 55 cases i.e. 1.81% with >0.5cm DOI showed lymphovascular invasion. Out of 14 cases having DOI <0.5 cm only 1 case i.e. 7.1% showed perineural invasion and 16 cases out of 55 cases i.e. 29.09% with DOI>0.5 cm showed perineural invasion. Tumours having DOI <0.5 cm did not show any extra lymph node extension. 11 out of 55 cases (20%) with DOI >0.5cm showed extraodal lymph node extension.

Out of 69 cases in this study, 2 (2.9%) cases were found to be of verrucous type, 10 (14.5%) cases showed skin involvement and 3 cases (4.3%) showed masticator space involvement.

**DISCUSSION**

In Asia, head and neck cancer is considered the most common neoplasm and it is the 5th most common cancer in the world. It is a major cause of mortality and morbidity. In patients with oral squamous cell carcinoma (OSCC) presence of cervical metastases is regarded as the main prognostic factor.

In the present study showed higher incidence of malignancy in males (75.36%) as compared to females (24.63%). Male to female ratio is 3.04:1. Most commonly involved age group is 41-50 years. Arjun Roy et al revealed a male to female ratio of 1.94:1 with the largest number of OSCCs developing in the 5th- 6th decades of life (18).

In the present study, we found that OSCC showed maximum tumour size ranging from 2 to 4 cm and nodal positivity is 52.17%. In this study maximum number of cases 33.3% were seen having DOI of 0.5-1cm. In this study, we found that 47.82% OSCC showed nodal metastasis with DOI>0.5 cm and 4.34% showed nodal metastasis present in tumours with DOI < or= 5 mm, p=0.022 with Yates correction that is statistically significant.

Similar to our study, Hedge P et al reported that depth of invasion was a prognostic factor for nodal metastasis in oral squamous cell carcinoma (15). Fukano et al did a study on 34 cases with a cut-off value of DOI as 5 mm. The nodal metastatic rate was 64.7% with DOI >5 mm as compared to 5.9% for DOI 5 mm (8). Ambrosch et al reported that tumour depth has a strong correlation with node metastasis. Their study showed that 2 mm depth was a valuable threshold for determining the risk of nodal metastasis (16). Shah et al reported that there is a 50% rate of node metastasis when tumour depth is between 2- and 9-mm (17). Wermker et al revealed tumour extent, depth of infiltration, and grading as the most important factors of lymph node metastasis (19). In contrast to our study, Rajina Sahi et al found no statically association between depth of invasion and lymph node metastasis (p>0.05) (20) and Chaudhary N et al also found no significant relationship between depth of invasion and lymph node metastasis(21).

Limitations of our study are that it is a single centre study and sample size is limited. Multicenter studies with large number of cases for identification of an ideal cut-off value and its relation to cervical lymph node metastasis which will direct us for elective neck therapy.

**CONCLUSION**

In this study, we showed that the DOI is a significant parameter for lymph node metastasis ( $p=0.022$ ) in OSCC. We can regard the depth of tumour invasion as a parameter before performing elective neck dissection even in the early stage of OSCC. Therefore, the role of tumour DOI as a prognostic parameter for the development of nodal metastases and for the survival of patients with OSCC is important as has been indicated in the latest NCCN guidelines.

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