ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 01 | January - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY TO EVALUATE CLINICOPATHOLOGICAL ASSOCIATION BETWEEN DEPTH OF INVASION AND NECK NODE METASTASIS IN ORAL CAVITY CARCINOMA

ENT

Dr. Yash Agrawal	Junior Resident, Department of ENT, Sawai Man Singh Medical College, Jaipur
Dr. Siddharth Nirwan	Assistant Professor, Department of ENT, Sawai Man Singh Medical College, Jaipur
Dr. Purnima	Assistant Professor, Department of ENT, Sawai Man Singh Medical College, Jaipur
Dr. Kailash Singh Jat	Assistant Professor, Department of ENT, Sawai Man Singh Medical College, Jaipur
Dr. Pawan Singhal	Senior Professor, Department of ENT, Sawai Man Singh Medical College, Jaipur
Dr. Man Prakash Sharma	Senior Professor, Department of ENT, Sawai Man Singh Medical College, Jaipur
Dr. Vikas Rohila*	Assistant Professor, Department of ENT, Sawai Man Singh Medical College, Jaipur *Corresponding Author

ABSTRACT

Objective: To evaluate association between depth of invasion and neck node metastasis. **Methods:** A prospective observational study was carried at Department of ENT, Sawai Man Singh Medical College over a period of one year in which 102 patients of oral carcinoma were included that underwent wide local excision with neck dissection. **Results:** The mean depth of invasion was 10.59 with 7.44 standard deviation (range 2-45 mm). Lymph node metastasis was present in 3 out of 27 patients with a DOI < 5mm (11%), in 13 out of 39 with a DOI 5.1-10 mm (34%) and in 8 out of 36 with DOI >10mm (22%). Chi square value was 30.79 and the p-value was<0.001. **Conclusion:** The risk of lymph node metastasis increased with increased depth of invasion.

KEYWORDS

oral carcinoma, depth of invasion, neck node metastasis.

INTRODUCTION

Head and neck cancers are the most common cancers in the developing countries especially in Southeast Asia. Oral cavity cancer is the most common cancer in India, as four out of ten of all cancers are oral cavity cancers.[1] An estimated 135,929 new cases of intraoral cancer are diagnosed annually in India[2] In the developed world, tongue and floor of mouth cancers are common while gingivobuccal cancers are the most common oral cavity cancers in india.[3] Histologically, more than 90% of all oral cavity cancers are squamous cell carcinoma (OCSCC). The most common risk factors for developing OCSCC are tobacco and alcohol consumption. In Southern Asia (India, Sri Lanka, China, and Thailand), the incidence of OCSCC is even higher due to the chewing of tobacco with or without betel quid.[4]

Factors that contribute to a patient prognosis are tumor size, regional lymph node involvement and distance metastasis, tumor differentiation grade, perineural invasion, and lymphovascular invasion.[4] Knowledge of the patterns of nodal metastasis has practical implications in the design of neck dissection for patients with oral cancer. The patient with a clinically negative neck is at highest risk of metastasis to levels I–III. Skip metastases to level IV do occur, especially in cancer of the anterior tongue. Metastases to level V are extremely rare (1%) even in patients with clinically positive neck.[5] An elective neck dissection increases the disease-specific survival and overall survival compared to watchful waiting, supported by a therapeutic lymph node dissection when needed. A neck dissection can be associated with several adverse effects such as edema, pain, and disability of the shoulder.[4]

Histopathological studies of resected lymph node have shown that even small lymph node metastasis which are neither palpable during surgery nor obvious on imaging studies can have extracapsular extension, including lymph-vascular and peri-neural invasion.[6-9]

Cervical lymph node metastasis has remained the most important prognostic factor. However, many previous studies have studied different predictive factors for cervical nodal metastasis in oral carcinoma among which depth of tumor invasion (DOI) is the most important.[10]

The 8th Edition of TNM staging was recently updated and depth of invasion (DOI), was introduced as a fundamental staging criterion to define T1, T2, and T3 categories as it shows significant correlation with disease specific survival (DSS). Moreover, DOI correlates well with the risk of nodal metastasis and loco-regional recurrence, especially in tongue SCC.[11]

Depth of invasion means the extent of cancer growth into the tissue beneath an epithelial surface. In cases in which the epithelium is destroyed, some investigators reconstruct a surface line and measure from this line. However, the infiltration depth is sometimes expressed by referring to the microscopic, anatomic deep structures that are reached, rather than by referring to objective micrometer measurements in millimeter.[12]

The risk of occult nodal metastasis is 27–40% for early-stage squamous cell carcinoma of oral tongue (ESSCOT). Neck dissection is mandatory if the risk of nodal metastasis is more than 15–20%.

Chances of occult metastasis increase with-[13-15]

1) Increase in the size of the tumor to >2cm.
2) Increase in the depth of invasion >1cm
3) Unfavorable histological differentiation.

Surgical resection is the treatment of choice for SCCOC. Surgical resection allows accurate pathologic staging, with information about the status of margins, tumor spread and histopathologic characteristics which can then be used to inform subsequent management based upon assessment of risk versus benefit.[16]

OBJECTIVES

Primary objective:

1) To evaluate association between depth of invasion and neck node metastasis.

Secondary objectives:

1) To assess the necessity of neck dissection by preoperative radiological depth of invasion.
2) To correlate preoperative radiological depth of invasion with postoperative histopathological depth of invasion.

MATERIALS AND METHODS

102 patients of oral carcinoma presenting to Sawai Man Singh Medical College that underwent wide local excision with neck dissection were evaluated. Surgical specimens were oriented and labeled by surgeons and fixed in 10% buffered formalin by pathologists. The specimens were then processed and examined under microscopic vision. Paraffin was applied a day after fixation. Information on the presence or absence of cervical lymph node metastasis, tumor size, degree of differentiation, and depth of invasion was obtained from the pathology reports. The depth of invasion was calculated as the distance between the basal membrane and the deepest point of the invaded stromal tissue.

OBSERVATION AND RESULTS

All 102 cases of oral cavity cancer were evaluated and postoperative histopathological reports studied thoroughly to evaluate association between depth of invasion and neck node metastasis.

In our study, mean age of presentation was 45.06 with standard deviation of 11.830. Minimum age of presentation was 23 year and maximum age of presentation was 79 years. Maximum patients were in 41-50 year of age group. In present study, 86.3% were males and 13.7 % were females. In present study, 37.25% patients have buccal mucosa as primary site of cancer and 36.3% patients have tongue as primary site of cancer.

In present study, out of 102 patients, WDSCC were 52.94% and MDSCC were 42.15%.

Table 1: Frequency distribution of preoperative HPE diagnosis

Preoperative HPE	Frequency	Percent
WDSCC	54	52.94
MDSCC	43	42.15
PDSCC	2	1.9
SQUAMOUS PAPILLOMA	2	1.9
Verrucous CA	1	0.98
	102	100.0

Preoperative T and N stages

In our present study, on clinical examination;16 cases were T1 (N0=15), 35 cases were T2(N0=25 cases), 5 cases were T3(3 case N+), 46 cases were 46 (26 cases N+) which states that with higher T stage, chances of positive N stage increased.

Table 2: Comparison of preoperative T and N categories

		cN						Total
		N0	N1	N2	N2a	N2b	N2c	
cT	T1	15	1	0	0	0	0	16
	T2	25	10	0	0	0	0	35
	T3	2	1	0	0	1	1	5
	T4a	20	20	3	1	1	0	45
	T4b	0	0	1	0	0	0	1
Total		62	32	4	1	2	1	102

cT stands for preoperative clinical T stage and cN stands for preoperative clinical N stage

Chi square analysis suggests that with higher T grades chances of positive N grades are increased. The chi square value was 69.330 and the p-value was <0.001.

Postoperative T and N stage

In our present study, on Histopathological examination;20 cases were T1 (N0=17), 35 cases were T2(N0=18 cases), 13 cases were T3(9 case N+), 44 cases were 46 (28 cases N+) which states that with higher T stage, chances of positive N stage increased.

Table 3: Comparison of postoperative T and N categories

		pN				Total
		N0	N1	N2a	N2b	
pT	T1	17	3	0	0	20
	T2	18	14	0	3	35
	T3	4	3	1	5	13
	T4a	6	20	0	7	33
	T4b	0	0	0	1	1
Total		45	40	1	16	102

pT stands for pathological T stage and pN stands for pathological N stage.

Chi square analysis suggests that with higher T grades chances of positive N grades are increased. The chi square value was 42.687 and the p-value was <0.001.

Table 4: Comparison of cT and pT

	cT	pT
T1	16	20
T2	35	35
T3	5	13
T4a	45	33
T4b	1	1

Chi square analysis suggests that cT and pT are significantly similar. The chi square value was 78.221 and the p-value was <0.001.

Table 5: Comparison of cN and pN

	cN	pN
N0	62	45
N1	32	40
N2a	5	1
N2b	2	16
N2c	1	0

Chi square analysis suggests that cN and pN are significantly similar. The chi square value was 44.691 and the p-value was <0.001.

Postoperative HPE

In our study, 34.3% patient were MDSCC and 64.7 % patient were WDSCC.

Table 6: Frequency Distribution Of Post Op HPE

	HPE POST OP				Total
	MD	PD	WD		
Mets in LN	No	13	0	32	45
	Yes	22	1	34	57
Total		35	1	66	102

Depth of invasion

In our study, mean DOI was 10.59 with standard deviation of 7.440. Minimum DOI was 2 mm and maximum DOI was 45 mm. Out of 102 patients, 27(26.5%) shows DOI <5mm, 39 (38.2%) shows DOI 5-10 mm and 36 (35.3%) shows DOI >10mm.

Table 7: Descriptive statistics of depth of invasion of the subjects

		Frequency	Percent
Depth of Invasion in mm	<5	27	26.5
	5.1-10	39	38.2
	>10	36	35.3
	Total	102	100.0

Table 8: Correlation between depth of invasion and number of metastatic lymph nodes

		Depth of Invasion in mm			Total
		<5mm	5.1-10mm	>10.1mm	
Mets in LN	No	24	13	8	45
	Yes	3	26	28	57
Total	27	39	36		102

In our study, out of 27 patients with DOI<5mm (24 were negative LN), out of 39 cases with DOI 5.1-10mm (26 were positive LN) and out of 36 cases of DOI >10mm (28 were positive LN).

Chi square analysis suggest that with increase in depth of invasion the number of metastatic lymph node also increases. The chi square value was 30.79 and the p-value was <0.001.

DISCUSSION

Treatment of the neck should always be performed when there are obvious clinically detectable lymph nodes in a patient with squamous cell carcinoma of the oral cavity. But in patients with a clinically negative neck or with early-stage oral cavity carcinoma (T1/T2, N0), treatment of the neck remains controversial. The two options for managing the neck in these cases are elective neck dissection and a

wait-and-see approach.[17] END is recommended based on risk of occult metastasis and for this, depth of invasion is regarded as an independent parameter.[18,19]

Tumor thickness and depth of invasion (DOI) are predictors for lymph node metastasis. Many studies have investigated tumor thickness and DOI in OCSCC as predictor for prognosis. However, in the literature, the definitions of DOI and tumor thickness are often used inconsistently.[19]

In current AJCC TNM classification (8th edition), depth of invasion (DOI) has been incorporated into T staging and has shown to be an important factor in redefining the staging system resulting in up gradation based on depth of invasion cut off 5 mm and 10 mm.[10]

In our study, out of 102 patient, post-operative reports of 66 patients showed well differentiated squamous cell carcinoma (64.7%), out of which 52% had lymph node metastasis. Out of total 102 patients, 22 patients showed moderately differentiated squamous cell carcinoma (34.3%) with 63% lymph node metastasis which states that most of the oral cavity tumor have well differentiated cells with risk of lymph node metastasis more in MDSCC. Vijaykumar G et al studied 100 patient and 63% patient graded as WDSCC and 37% patient graded as MDSCC.[20]

Trehan SS et al studied 196 patient and found node involvement in 15 of 71 patients with well-differentiated carcinoma (21.4%), in 20 of 50 with moderately differentiated disease (40.0%), and in 15 of 20 cases with poorly differentiated cancer (75.0%) which is statistically significant p<0.001.[4] However, Fukano et al found no significant association between the degree of tumor differentiation and pN0 and pN+ status.[4]

In our study, on comparison of postoperative T (Tumor size) and N (Lymph node status) stage shows that out of 55 cases of early stage (T1/T2) cancer, 35 were lymph node negative and out of 47 cases of Late stage (T3/T4) cancer, 37 patients were lymph node positive. This comparison concluded that with increasing T stage, N stage will also increase with p=<0.001 and chi square value=18.445 which is significant. Same results were shown by Sharma A et al study, which stated that out of 55 early stage cancer patients (T1/T2), 45 patients were lymph node negative and out of 21 patient of late stage cancer, 7 patient were lymph node positive which is significant p=0.014.[21]

In our study, on preoperative examination 63 patient were node positive and 39 patients were node negative. However, on postoperative pathology 57 patients were node positive and 45 patients were node negative. Sharma A et al studied in 76 patient of oral cavity cancer and found 52 patients were clinically node positive and 24 were clinically node positive and 59 patients were pathologically negative and 17 patients were pathologically positive.[21]

The prevalence of occult metastasis was low in our study because maximum patient presented in advance stage. In our study mean depth of invasion was 10.59 with 7.44 standard deviation (range 2-45 mm). According to AJCC 8, we have classified accordingly in which 26.5% specimen < 5mm DOI, 38.2% specimen 5.1-10mm DOI and 35.3 % specimen have >10mm depth of invasion.

Lymph node metastasis was present in 3 out of 27 patients with a DOI < 5mm (11%), in 13 out of 39 with a DOI 5.1-10 mm (34%) and in 8 out of 36 with DOI >10mm (22%). Chi square analysis suggest that with increase in depth of invasion the number of metastatic lymph node also increases. Chi square value was 30.79 and the p-value was<0.001.

Venugopalan S et al studied in 30 patient and stated that for oral tongue and buccal mucosa, 8 mm of depth of tumor invasion was calculated as the cut-off depth, above which incidence of nodal metastasis increases to 13.34% in T1 and T2 lesions.[1]

Muhammad AY et al studied 80 patient of tongue cancer, out of which 31 (38.75%) patients have DOI < 5mm and 49 (61.25%) patients have DOI >5mm and they concluded that DOI >5mm was significantly associated with occult neck node metastasis (p=0.004).[22]

Fukano H et al studied 34 patients of tongue cancer and concluded that depth of invasion was a statistically significant predictor of regional metastasis at p=0.0003. In the group in which tumor depth exceeded 5 mm, the metastatic rate was 64.7% (11/17). In contrast, when the depth of invasion was less than 5 mm, the incidence of cervical metastasis was 5.9% (1/17).[23]

So, after going through various studies, we can conclude that with increasing depth of invasion, lymph node metastasis also increases.

REFERENCES

1. Venugopalan S et al. Pathoradiological association between depth of invasion and neck node metastasis in oral cavity tumors. Int J Otorhinolaryngol Head Neck Surg. 2019 Sep;5(5):1240-1243.
2. https://gco.iarc.fr/today/data/factsheets/populations/356-india-fact-sheets.pdf (Globocan)
3. Shah AH, Parikh RP. Clinicopathological correlation between depth of tumor and neck node metastasis in oral (Tongue and Buccal Mucosa) Carcinoma. Int J Head Neck Surg 2021; 12 (1):6-10.
4. Aaboubout Y et al. Is the Depth of Invasion a Marker for Elective Neck Dissection in Early Oral Squamous Cell Carcinoma? Front Oncol. 2021;11: 628320. doi: 10.3389/fonc.2021.628320
5. Lydiatt DD, Robbins KT, Byers RM, Wolf PF. Treatment of stage I and II oral tongue cancer. Head & neck. 1993 Jul;15(4):308-12.
6. Alvi A, Johnson JT. Extracapsular spread in the clinically negative neck (N0): implications outcome. Otolaryngol Head Neck Surg. 1996;114: 65-70.
7. Mamelle G, Pampurik J, Luboinski B, Lancar R, Lusinchi A, Bosq J. Lymph node prognostic factors in head and neck squamous cell carcinomas. AM J Surg. 1994;168: 494-498.
8. Rassekh CH, Johnson JT, Myers EN. Accurancy of intraoperative staging of the N0 neck in squamous cell carcinoma. Laryngoscope. 1995;105: 1334-1336.
9. Hughes CJ, Gallo O, Spiro RH, Shah JP. Management of occult neck metastasis in oral cavity squamous carcinoma. Am J Surg 1993;166: 380-3.
10. Sahi R et al. Study of Oral Squamous Cell Carcinoma in Relation with Depth of Invasion and Lymph Node Metastasis. JCMS Nepal. 2020;16(2):71-3
11. Piazza C, Bresciani L et al. Depth of invasion for prognostic stratification in oral cavity cancer:do we need further validation? Ann Transl Med 2019;7(Suppl 3): S84.
12. Padmaraj H, Satadru R et al. Tumor Infiltration Depth as a Prognostic Parameter for Nodal Metastasis in Oral Squamous Cell Carcinoma. Int J Appl Basic Med Res. 2017 Oct-Dec; 7(4): 252–257
13. Yuen AP, Ho CM, et al. Prospective randomized study of selective neck dissection versus observation for N0 neck of early tongue carcinoma. Head Neck 2009;31: 765-72. Shear M, Harkins DM, Fart HW. The prediction of sentinel lymph node metastasis from oral squamous cell carcinoma Cancer 1976;37: 1901-07.
14. Martinez Gimeno C, Rodriguez EM, Vila CN, Varela CL. Squamous cell carcinoma of oral cavity: a clinicopathological scoring system for evaluating risk of cervical lymph node metastasis. Laryngoscope. 1995;105: 728-33.
15. Braams JW, Pruium J, Freling NJM, et al. Detection of lymph node metastases of squamous-cell cancer of the head and neck with FDG-PET and MRI.J Nucl. Med. 1995;36: 211-216.
16. Lydiatt DD, Robbins KT, Byers RM, Wolf PF. Treatment of stage I and II oral tongue cancer. Head & neck. 1993 Jul;15(4):308-12.
17. Trehan S, et al. The effect of depth of invasion and tumor size on risk of neck node metastasis in squamous cell carcinoma of oral cavity: retrospective analysis. J Res Med Den Sci 2015;3(3):1-6.
18. Melchers LJ, Schuuring E, Van Dijk BA, De Bock GH, Witjes MJ, Van der Laan BF, van der Wal JE, Roodenburg JL. Tumor infiltration depth≥ 4 mm is an indication for an elective neck dissection in pT1cN0 oral squamous cell carcinoma. Oral Oncology. 2012 Apr 1;48(4):337-42.
19. Van lanschot CGF, Klazen YP et al. Depth of invasion in early-stage oral cavity squamous cell carcinoma: The optimal cut-off value for elective neck dissection, Oral Oncology, Volume 111, 2020, 104940, ISSN 1368-8375, https://doi.org/10.1016/j.Oraloncology.2020.104940.
20. Vijayakumar G, Narwal A, Kamboj M, Sen R. Association of SOX2, OCT4 and WNT5A Expression in Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma: An Immunohistochemical Study. Head Neck Pathol. 2020 Sep;14(3):749-757. doi: 10.1007/ s12105-019-01114-1. Epub 2020 Jan 4.
21. Sharma A, Kim JW, Paeng JY. Clinical analysis of neck node metastasis in oral cavity cancer. J Korean Assoc Oral Maxillofac Surg. 2018 Dec;44(6):282-288. doi: 10.5125/ jkaoms. 2018.44.6.282. Epub 2018 Dec 28.
22. Muhammad AY, Dhanani R, Salman S, Shaikh Z, Ghaloo SK, Ikram M. Depth of Invasion as a Predictor of Cervical Nodal Metastasis of Oral Tongue Squamous Cell Carcinoma: Findings from a Tertiary care center in Pakistan. Cureus. 2021 Oct 22;13(10): e18976. doi: 10.7759/cureus.18976
23. Fukano H, Matsuura H, Hasegawa, Nakamura S. Depth of invasion as a predictive factor for cervical lymph node metastasis in tongue carcinoma. Head Neck 1997; 19:205-10.