Section: Pathology

Original Research Article

DEPTH OF INVASION(DOI) AS A PREDICTOR OF LYMPHNODE METASTASIS IN ORAL SQUAMOUS CELL CARCINOMAS(OSCC) CONTRIBUTION AND CONTRAVERSIES: A HISTOPATHOLOGICAL ANALYSIS.

Korra Sree Lakshmi[1], Ravuri Swarupa[2], Mareedu Radhika Rani[3], Othuluru Hema Radhika Krishna[4], Dondapati Aruna Chaithanya[5]

[1]Assistant Professor: Department of Pathology, MNJ institute of Oncology and Regional Cancer Center, Lakdikapul, Hyderabad, Telangan, India
[2]Assistant Professor: Department of Pathology, MNJ institute of Oncology and Regional Cancer Center, Lakdikapul, Hyderabad, Telangana, India
[3]Associate Professor: Department of Radiation Oncology, MNJ institute of Oncology and Regional Cancer Center, Lakdikapul, Hyderabad, Telangana, India
[4]Professor: Department of Pathology, MNJ institute of Oncology and Regional Cancer Center, Lakdikapul, Hyderabad, Telangana, India
[5]Blood bank Medical Officer: Department of Pathology, MNJ institute of Oncology and Regional Cancer Center, Lakdikapul, Hyderabad, Telangana, India

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Corresponding Author:
Dr. Othuluru Hema Radhika Krishna,
Email: othululuradhika@gmail.com

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Abstract

Background: This study is done to correlate depth of invasion (DOI) in isolation as a predictor for lymph node metastasis in squamous cell carcinomas (SCC) of oral cavity. **Materials and Methods:** It is retrospective study in100 cases of primary Oral SCCs treated surgically along with elective neck dissection (END). FFPE tissues were taken, H&E slides were reviewed and data for LN metastasis, DOI and other relevant findings were collected and tabulated. DOI measurement was done using Graduated Mechanical Microscope X-Y Stage. **Result:** Mean age of incidence of SCC oral cavity was 46 years, OSCC was more common in males than females. The most common site within the oral cavity was Buccal mucosa. Incidence of LN metastasis increases with DOI in early stage OSCC. A significant P value of 0.01919 was observed when studied for DOI > 5mm with respect to lymph node metastasis. A significant p value of 01 was obtained when calculated for LN metastasis against DOI >10mm, implying that there is correlation. **Conclusion:** DOI is a reliable parameter for predicting regional LN involvement in early stage OSCC(T1-2). Cut off value of 5mm and 10mm to upstage tumors is well supported by our study.

INTRODUCTION

The depth of invasion (DOI) - independent risk factor for - occult lymph node (LN) metastasis- in oral cavity squamous cell carcinoma (OSCC), 8th edition of the cancer staging manual from the American Joint Committee on Cancer (AJCC), 2017, categorized tumors with DOI even if tumor dimension is lesser than the corresponding T stage criteria. Validation of the association between DOI and lymphnode metastasis on OSCCs has been a research question for many studies.[1-4] Contradicting statistical data was published, when they studied DOI as considered to be the actual mass present beneath the basement membrane, or in case of ulceration or exophytic lesions the theoretical reconstruction of the basement membrane. No longer used synonymous to tumor thickness (TT). Tumor emboli are easily formed in wider lymphatics of the deeper tissue, than in the small-caliber lymphatics of superficial areas.[5-8] DOI in isolation , inspiried us to take up this study for correlation of DOI in isolation as a predictor for lymph node metastasis in squamous cell carcinomas of oral cavity.

MATERIALS AND METHODS

It is retrospective study from January to August, 2022, at MNJIO & RCC, Hyderabad. 100 cases of primary Oral SCCs treated surgically along with elective neck dissection (END) FFPE tissues were taken, H&E slides were reviewed and data for LN metastasis, DOI and other relevant findings were collected and tabulated. DOI measurement was done using Graduated Mechanical Microscope X-Y Stage.

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Inclusion Criteria

All primary well differentiated OSCCs treated by surgery along with END

Exclusion Criteria

OSCCs with recurrences, OSCCs treated with adjuvant radiation therapy, autoimmune / immunodeficient cases and moderate / poorly differentiated OSCCs

Multiple sections of pathology slides were examined with a digital microscope to identify the deepest part of tumor invasion. The histopathological measurement of DOI and TT were repeated three times for each slide, where the average was ultimately used as the final value. A double board-certified pathologist confirmed the results. Patients were divided into three groups for each part: (1) classification according to DOI: group A = DOI ≤ 5 mm, group B = 5 mm < DOI ≤ 10 mm, and group C = DOI > 10 mm; and (2) classification according to TT: group A = TT ≤ 5 mm, group B = 5 mm < TT ≤ 10 mm, and group C = TT > 10 mm.

A descriptive analysis was performed for categorical and continuous variables with summary measures. For continuous variables, mean values were reported, whereas percentages were used for categorical variables. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 22.0; SPSS, Chicago, IL, USA).

RESULTS

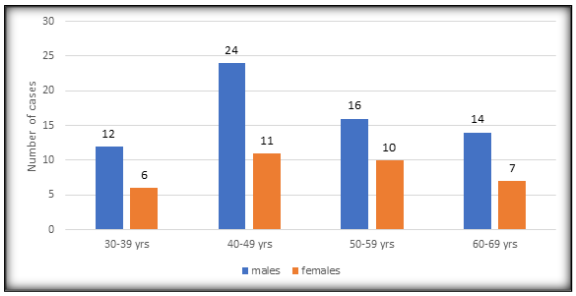


Figure 1: Age distribution in present study.

Mean age of incidence of SCC oral cavity was 46 years, OSCC was more common in males than females.

The most common site within the oral cavity was Buccal mucosa. Incidence of LN metastasis increases with DOI in early stage OSCC. A significant P value of 0.01919 was observed.

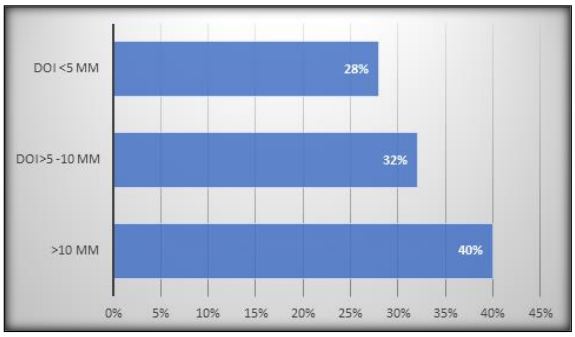


Figure 2: Distribution under tumor stage(T1-3) bases on DOI.

when studied for DOI > 5mm with respect to lymph node metastasis. A significant p value of 01 was obtained when calculated for LN metastasis against DOI >10mm, implying that there is correlation.

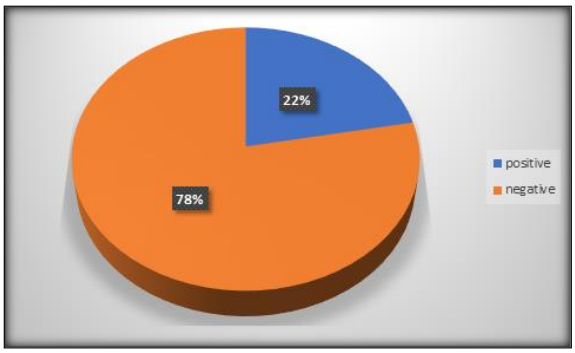
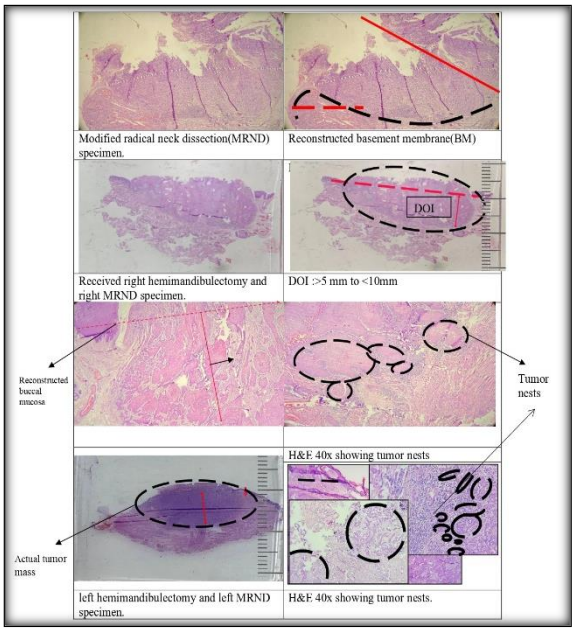


Figure 3: Cases with lymphnode metastasis

Pattern of invasion (POI) type 4 and 5 grouped together, i.e, infiltrative type * was more common among the cases showing lymph node metastasis.

Both the cut off levels to upstage the tumors are statistically significant. Lymphnode metastasis was seen to be increasing with DOI.



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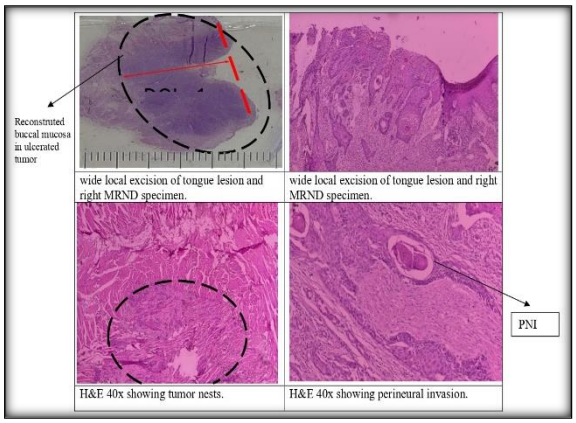

Figure 4: Cases in present study.

Table 1: Site distribution.

Site	Number of cases(n=100)	Percentage
Buccal mucosa	42	42 %
Tongue	28	28%
Alveolus	16	16%
Lip	14	14%

Table 2: Lymphnode Metastasis in relation to DOI

DOI	Number of cases (n=100)	LN Positive		LN Negative	
< 5mm	28	0	0%	28	100%
< 5mm - <10 mm	32	8	25%	24	75%
<10 mm	40	14	35%	26	65%

DISCUSSION

We also observed pattern of invasion (POI) type 4 and 5 grouped together, i.e, infiltrative type was more common among the cases showing lymph node metastasis. Primary mode of treatment in OSCCs has been surgery. Surface/exophytic tumors vs endophytic tumors (deeper invasion) displace the normal anatomy planes to make way. The presence of occult lymph node metastasis is the most important prognostic factor for patient survival. END is done – if > 20 % risk of LN metastasis. T1 vs T2 differentiation is important because of decision between wait and watch vs END. DOI is a reliable parameter for predicting regional LN involvement in early stage OSCC(T1-2). Cut off value of 5mm and 10mm to upstage tumors is well supported by our study. Other histopathological factors also come into play along with DOI. DOI to be clearly reported and synonymous usage to TT is not recommended. Studies to compare significance of DOI among cases with similar POI may add value. We recommend that POI can add value if included as an addendum to DOI into tumor staging for OSCC.

Kano et al. (2018) suggested that the possibility of nodal metastasis in patients with T1-2N0 was not different for the criteria in the 7th and 8th editions.[9] Therefore, the same management is needed for patients with N0 disease. According to the results of this study, it was demonstrated that the T category of the 7th edition of the AJCC was more robust than that of the 8th edition. There was no significant evidence that the T category of the 8th edition is a better prognostic factor compared with the 7th edition.

Piazza et al. (2019) and Bjerkli et al. (2020) suggested that the 8th edition of the AJCC staging system improved the prognostic value of the T category than the previous one in early-stage oral tongue SCC.[10,11] Contrary to Piazza et al. (2019) and Bjerkli et al. (2020), our results are more relevant to Kano et al. (2018) As this study included a relatively small number of patients and all oral cavity subsites, additional studies using a larger patient population are needed.

CONCLUSION

The most common site within the oral cavity was Buccal mucosa. Incidence of LN metastasis increases with DOI in early stage OSCC. The previous studies also included all subsites, such as tongue, mouth floor, retromolar trigone, gingiva, buccal mucosa, hard palate, and even lip.[5] However, many studies performed analyses only on oral tongue cancer,[12,13] or the buccal cheek.[5] As the tongue is the most common subsite of oral squamous cell carcinoma (OSCC) and has a higher risk of cervical lymph node metastasis than other subsites with regard to its abundant lymphatics and mouth floor,[8] lots of studies analyzed the pathology of oral tongue squamous cell carcinoma (OTSCC). As shown in the study by Brockhoff et al. (2017), each oral subsite has different considerations, and the cut-off point for each treatment plan may be different.[14] A sufficient population size for each subsite is needed to analyze the site-specific characteristics and design a more specific treatment plan.

The findings in our study are in accordance with those of Studies that are showing contradictory

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results as Hegde P et al, Chaudhary et al, Wermker et al and Anuj H shah et al.[15-19]

REFERENCES

1. Kennedy, R.A. WHO is in and WHO is out of the mouth, salivary glands, and jaws sections of the 4th edition of the WHO classification of head and neck tumours. Br. J. Oral Maxillofac. Surg. 2018, 56, 90–95.
2. Müller, S. Update from the 4th edition of the World Health Organization of head and neck tumours: Tumours of the oral cavity and mobile tongue. Head Neck Pathol. 2017, 11, 33–40.
3. Ahmed, S.Q.; Junaid, M.; Awan, S.; Choudhary, M.M.; Kazi, M.; Masoom, A.; Khan, H.U. Relationship of tumor thickness with neck node metastasis in buccal squamous cell carcinoma: An experience at a tertiary care hospital. Int. Arch. Otorhinolaryngol. 2017, 21, 265–269.
4. Berdugo, J.; Thompson, L.D.; Purgina, B.; Sturgis, C.D.; Tuluc, M.; Seethala, R.; Chiosea, S.I. Measuring depth of invasion in early squamous cell carcinoma of the oral tongue: Positive deep margin, extratumoralperineural invasion, and other challenges. Head Neck Pathol. 2019, 13, 154–161.
5. Dirven, R.; Ebrahimi, A.; Moeckelmann, N.; Palme, C.E.; Gupta, R.; Clark, J. Tumor thickness versus depth of invasion–Analysis of the 8th edition American Joint Committee on Cancer Staging for oral cancer. Oral Oncol. 2017, 74, 30–33.
6. Faisal, M.; Abu Bakar, M.; Sarwar, A.; Adeel, M.; Batool, F.; Malik, K.I.; Jamshed, A.; Hussain, R. Depth of invasion (DOI) as a predictor of cervical nodal metastasis and local recurrence in early stage squamous cell carcinoma of oral tongue (ESSCOT). PLoS ONE 2018, 13, e0202632
7. Liu, B.; Amaratunga, R.; Veness, M.; Wong, E.; Abdul-Razak, M.; Coleman, H.; Gebski, V.; Sundaresan, P. Tumor depth of invasion versus tumor thickness in guiding regional nodal treatment in early oral tongue squamous cell carcinoma. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. 2020, 129, 45–50.
8. Tam, S.; Amit, M.; Zafereo, M.; Bell, D.; Weber, R.S. Depth of invasion as a predictor of nodal disease and survival in patients with oral tongue squamous cell carcinoma. Head Neck 2019, 41, 177–184.
9. Kano, S.; Sakashita, T.; Tsushima, N.; Mizumachi, T.; Nakazono, A.; Suzuki, T.; Yasukawa, S.; Homma, A. Validation of the 8th edition of the AJCC/UICC TNM staging system for tongue squamous cell carcinoma. Int. J. Clin. Oncol. 2018, 23, 844–850.
10. Piazza, C.; Bresciani, L.; Giannini, L. Depth of invasion for prognostic stratification in oral cavity cancer: Do we need further validation? Ann. Transl. Med. 2019, 7 (Suppl. 3), S84.
11. Bjerkli, I.H.; Laurvik, H.; Nginamau, E.S.; Søland, T.M.; Costea, D.; Hov, H.; Uhlin-Hansen, L.; Hadler-Olsen, E.; Steigen, S.E. Tumor budding score predicts lymph node status in oral tongue squamous cell carcinoma and should be included in the pathology report. PLoS ONE 2020, 15, e0239783.
12. Tan, W.J.; Chia, C.S.; Tan, H.K.; Soo, K.C.; Iyer, N.G. Prognostic significance of invasion depth in oral tongue squamous cell carcinoma. ORL 2012, 74, 264–270.
13. Almangush, A.; Bello, I.O.; Coletta, R.D.; Mäkitie, A.A.; Mäkinen, L.K.; Kauppila, J.H.; Pukkila, M.; Hagström, J.; Laranne, J.; Soini, Y.; et al. For early-stage oral tongue cancer, depth of invasion and worst pattern of invasion are the strongest pathological predictors for locoregional recurrence and mortality. Virchows Arch. 2015, 467, 39–46.
14. Brockhoff, H.C.; Kim, R.Y.; Braun, T.M.; Skouteris, C.; Helman, J.I.; Ward, B.B. Correlating the depth of invasion at specific anatomic locations with the risk for regional metastatic disease to lymph nodes in the neck for oral squamous cell carcinoma. Head Neck 2017, 39, 974–979.
15. Hegde et al,. Tumor Infiltration Depth as a Prognostic Parameter for Nodal Metastasis in Oral Squamous Cell Carcinoma. International Journal of Applied and Basic Medical Research: Oct–Dec 2017 - Volume 7 - Issue 4: p 252-257.
16. Chaudhary N, Verma RK, Agarwal U, Gupta S, Jaitly S. Incidence of occult metastasis in clinically N0 oral tongue squamous cell carcinoma and its association with tumor staging, thickness, and differentiation. J Head Neck Physicians Surg 2017;5:75-8.
17. Pimenta Amaral TM, Da Silva Freire AR, Carvalho AL, Pinto CA, Kowalski LP. Predictive factors of occult metastasis and prognosis of clinical stages I and II squamous cell carcinoma of the tongue and floor of the mouth. Oral Oncol 2004;40:780-6.
18. 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.
19. Kai Wermker, Friederike Belok, Stephanie Schipmann, Martin Klein, Hans-Joachim Schulze, Christian Hallermann, Prediction model for lymph node metastasis and recommendations for elective neck dissection in lip cancer,Journal of Cranio-Maxillofacial Surgery, Volume 43, Issue 4, 2015, Pages 545-552,

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