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Original Research Article

To Determine Whether the Depth of Invasion is a Reliable Parameter for Predicting Regional Lymph Node Metastasis in Cases of Oral Squamous Cell Carcinomas

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Conflict of interest: Nil

Abstract:

Objective: To determine the relationship between depth of invasion and neck node metastasis in squamous cell carcinoma of the oral cavity.

Material and Methods: This was a cross-sectional retrospective study. Histopathology reports from patients who underwent neck dissection and oral squamous cell carcinoma surgery were analyzed. A total of 60 cases were studied. In each example, the depth of invasion was measured microscopically up to the point of maximum invasion. Histologically,the lymph nodes were checked for the existence of metastatic cells.

Results: This study showed no statistical significance between depth of invasion and regional lymph node metastasis ($p > 0.05$).

Conclusion: Depth of invasion might be an essential criterion for staging and determining the further management, but it is not a predictor for lymph node metastasis. According to our study, further research on this matter is advisable.

Keywords: Lymph Node, Metastasis, Staging, Depth of Invasion.

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Introduction

The most common malignancy of the head and neck is oral squamous cell carcinoma (1-3). Early-stage tumors may harbor occult metastases to neck nodes (1, 2). We must measure the depth of invasion because it is one of the most crucial elements for deciding on future management (1-4). The goal of the study is to determine whether the depth of invasion can be used as a reliable indicator of local lymph node metastasis.

Materials and Methods

This was a cross-sectional analytical study. It was conducted between January 2022 and December 2022 on 60 patients with oral squamous cell carcinoma who underwent excision with modified neck dissection. Samples were received at the histopathology department, Parul Sevashram Hospital. The information was gathered through histopathology reports, in which the depth of invasion was microscopically noted. The eighth version of the AJCC Cancer Staging Manual was used for tumor staging.

Measurement of the depth of invasion

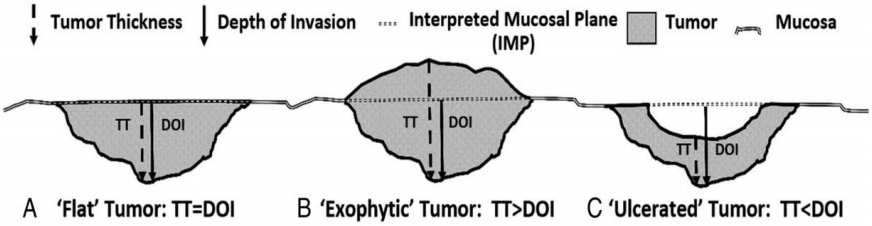

Figure 1: Depth of Invasion Measurement [2]

A: mucosal plane and tumor plane are at the same level in flat tumors (TT=DOI). [2]

B: Exophytic or bulging tumors, in which the tumor thickness is greater than the depth of invasion (TT>DOI), protrude from the mucosal plane. [2]

C: The mucosal plane and the tumor surface are separated in endophytic or ulcerated tumors, and the depth of invasion is greater than the tumor thickness (DOI > TT). [2]

Ethics

This was a cross-sectional observational study, and intervention was not done. The study was undertaken after the Institutional Ethics Committee gave its approval.

Results

Out of 60 cases, the distribution according to age, sex, tumor grade, and tumor location were done and shown in Table 1, Figure 2, Figure 3 and Table 2 respectively. In our study, there was a male predominance with a male-to-female ratio of 1.85:1, as shown in Figure 2.

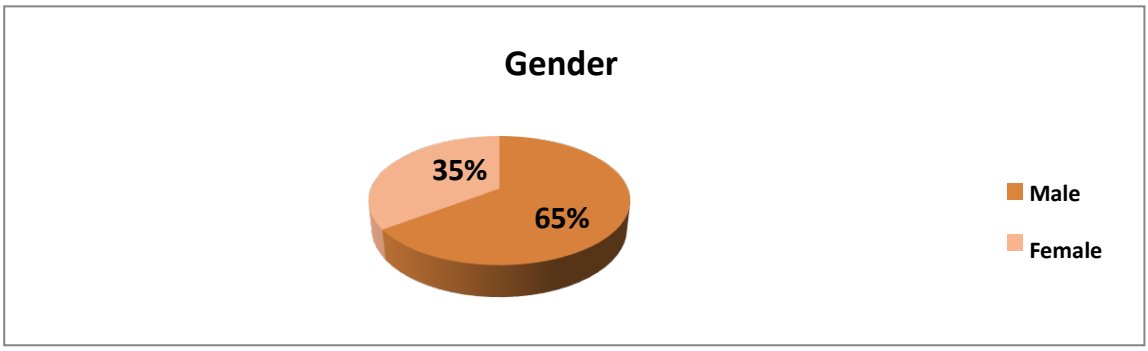

Figure 2: Sex-wise distribution of cases

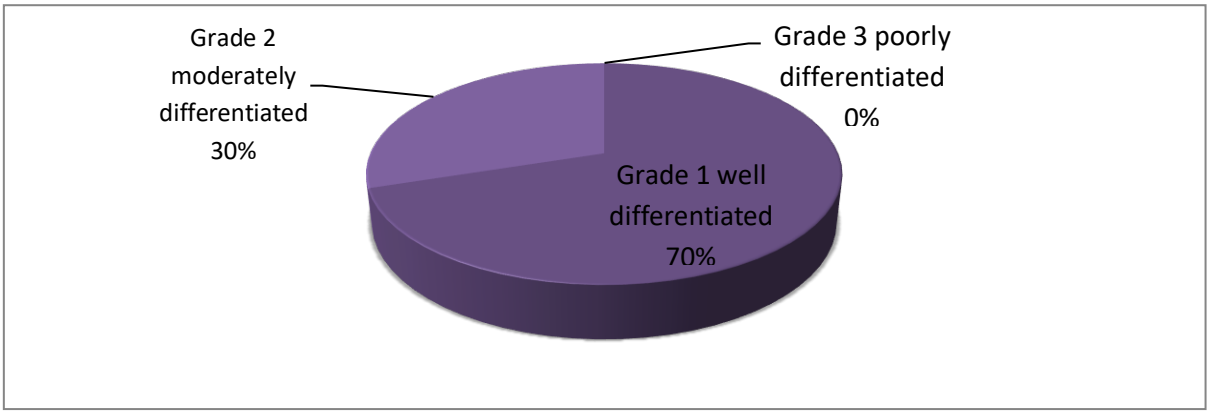

Figure 3: Grade-wise distribution of cases

As shown in Figure, 3 almost 70% of cases were be well-differentiated SCC, while the rest (30%) were moderately differentiated SCC. Instances of SCC with poor differentiation were not discovered.

Table 1: Age-wise distribution of oral squamous carcinoma (n = 60)

Age (in years)	Frequency	Percentage (%)
20-30	2	3.33%
30-40	7	11.67%
40-50	19	31.67%
50-60	20	33.33%
60-70	10	16.67%
70-80	2	3.33%

Table 1 show the age-wise distribution of cases, where the highest patients were found between 50 to 60 years of age, followed by 40 to 50. It shows the peak incidence of SCC in the middle age group.

Table 2: Distribution of oral squamous carcinoma according to the tumor site (n = 60)

Tumor site	Frequency	Percentage (%)
Tongue	24	40%
Buccal mucosa	26	43.44%
Lower alveolus	5	8.34%
Lower GBS	2	3.33%
Upper alveolus	1	1.67%
Lower lip	2	3.33%

Table 2 shows the highest number of cases were found in the buccal mucosa, followed by the tongue, which was the second most common site. Other sites for OSCC were found to be the lower alveolus, lower GBS, lower lip, and upper alveolus.

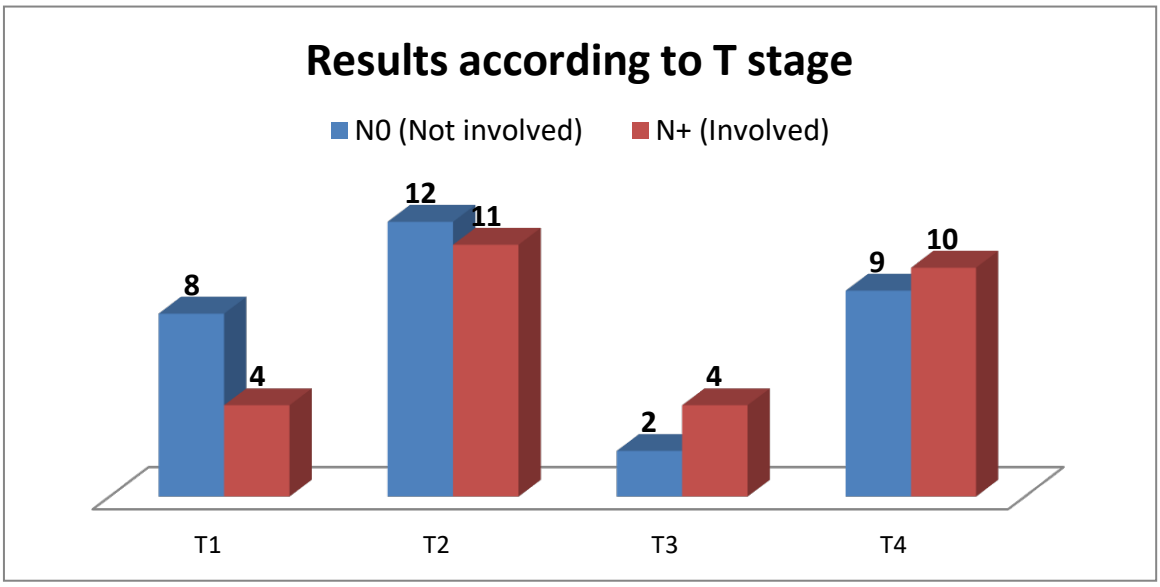

Figure 4: Involvement of lymph nodes according to T staging (n = 60)

Figure 4 shows that the nodal metastasis rate for the T1 stage is 33.33%, the T2 stage is 47.82 %, the T3 stage is 66.66%, and the T4 stage is 52.63%.

Table 3: Cross tabulation (n = 60)

DOI * Involved LN Cross-tabulation (5)					
			Involved LN		Total
			Involved	Not Involved	
DOI	< 5mm	Count	5	10	15
		ExpectedCount	7.3	7.8	15.0
	≥ 5mm	Count	24	21	45
		ExpectedCount	21.8	23.3	45.0
Total		Count	29	31	60
		ExpectedCount	29.0	31.0	60.0

The chi-square test is to be used as a test of significance to determine whether there is a link between two qualitative variables. It evaluates the statistical significance of the two qualitative variables. In our study, we divided DOI into two categories, < 5 mm and ≥ 5 mm, and created a cross-table to establish a relationship between DOI and regional lymph node metastases. The chi-square test contrasts observed and expected values, where observed values are the actual counts obtained from the sample and expected values indicate what the values of each cell in the table would be if there were no correlations between the two variables.

$$\text{Expected value} = \frac{\text{Row total} * \text{Column total}}{\text{Table total}}$$

$$\chi^2 = \Sigma \frac{(observed - expected)}{expected}$$

When values were placed into the statistical analysis algorithm, the chi-square result was 1.802. Checking if the chi-square test statistic's value is high enough to reject the null hypothesis is the last stage in the chi-square test of significance (5).

Table 4: Chi-square tests (n = 60)

Chi-Square tests (5)					
	Value	**Df**	**AsymptoticSignificance (2-sided)**	**Exact Sig.(2-sided)**	**Exact Sig.(1-sided)**
Pearson Chi-Square	1.802[a]	1	0.179	0.238	0.148
Continuity Correction	1.090	1	0.296		
Likelihood Ratio	1.832	1	0.176	0.238	0.148
Fisher's Exact Test				0.238	0.148
N of Valid Cases	60				

Table 4 is derived with the help of SPSS statistical software. The p-value for the chi-square statistic is 0.14, which is larger than the alpha-level p-value of 0.05. Thereby, the null hypothesis is accepted. The study shows no significant difference between DOI and regionallymph node metastasis (5).

Discussion

Head and neck cancers are the fifth most prevalent malignancy, according to the WHO, which tracks the global rise in cancer incidence daily [2]. Oral cancer includes malignancies of the lips, various mouth tissues, and the oropharynx; the majority of oral cancers are SCC.Males are more likely than women to develop oral cancer, and it is more lethal in males than in females. Social and economic factors significantly influence. The leading causes of oral cancer include tobacco usage, alcohol consumption, and areca nut (betel nut) use [6].

Numerous studies have demonstrated that the most crucial prognostic factor in oral cancer is nodal metastasis [2, 7, 8]. Only the primary site involving the tumor must not be treated, but cervical lymph nodes should also be treated. In the case of advanced-stage tumors with clinical or radiological evidence of positive neck nodes, neck dissection must be performed. However, there is still debate regarding handling early-stage tumors that don't exhibit clinically or radiologically detectable cervical lymph node metastases [2]. The pathologic T staging of OSCC now includes DOI, according to the AJCC 8th edition, released in 2017.

Soon after, DOI was added to important pathological and clinical care guidelines and has since evolved into a requirement for reporting OSCC [3]. Further classifications include less invasive (≤ 5 mm), moderately invasive (6–10 mm), and highly invasive (≥ 10 mm) [1]. Forthe investigation, we only used the categories of < 5 mm and ≥5 mm DOI.

Numerous investigations have revealed the association between tumor thickness, DOI, and cervical nodal metastases and the abundance of data collected in this field [1-4, 8-13, 15, 16, 18-22]. Before the publication of the AJCC 8th edition, TT and DOI were frequently used incongruously in research journals, and the majority of the studies did not explain a concise explanation of any parameter [3]. Ahmed et al. correctly described the difference between TT and DOI in terms of definition and measurement. However, studies that demented these two measurements or did not provide a clear definition went on to be reported in the literature [2].

In our study, males (65%) and people between the ages of 50 and 60 made up most OSCC cases. The majority of patients (70%) were well differentiated (Grade I), with the buccal mucosa (43%) and tongue (40%) being the most frequent sites of occurrence. According to several local studies, when compared to other regions of the oral cavity, buccal mucosal cancer is more aggressive [2]. Numerous studies, some of which are included here, have demonstrated a favorable connection between DOI and regional lymph node metastases. In a study done by Hegde P. et al., it was revealed that among OSCC, DOI was a predictive factor for nodal metastases [9]. Another survey by Odell et al. found that in this type of carcinoma, the invasion pattern had the most vital connection with metastasis and recurrence [10]. Tumor extent, DOI, and grade were found to be the three main determinants of lymph node metastasis by Wermker et al. in 2015 [11]. According to Kurokawa et al., there is a higher likelihood of occult cervical lymph node metastases if the DOI is greater than 5 mm (p-value = 0.022) [12]. Mohit-Tabatabai et al. documented a significant correlation between primary TT > 1.5 mm and the subsequent development of regional lymph node disease [13]. Khafif et al. reported that despite advanced imaging techniques, 20% to 50% of clinically N0 patients had occult metastatic disease [14]. In contrast, our study found no statistical association between DOI and regional lymph node metastasis (p-value > 0.05). Similar to our research, Rajina Sahi et al. reported that the DOI was not a predictor for cervical lymph node metastasis [15]. Chaudhary N. et al. found no significant relationship between DOI and lymph node metastasis [16].

None of the currently available advanced imaging modalities is reliable for detecting the presence of occult lymph node metastasis, even with the significant advances in technology[2].

The American Cancer Society has given treatment options for oral cavity cancers according to the stage. Cancers of stage 0 are typically solely treated with surgery; if they relapse, they may additionally require further radiotherapy. Surgery or radiation therapy treat malignancies in stages I and II. Chemoradiation is also used occasionally. Surgery and radiation are equally

effective. It can be challenging to decide whether to do a neck node dissection in early-stage oral cancer patients. High possibilities of cancer returning may exist if surgery does not eliminate it. Finding occult neck node metastases may benefit from prophylactic neck node dissection. Treatment for stage III or IV instances includes surgery, including the removal of neck nodes, as well as radiation, chemotherapy, or immunotherapy [17].

Only tumor thickness greater than 4 mm exhibited a prognostic value for cervical metastasis, according to Takahiro et al. Therefore, individuals with stage I or II tongue cancer who are thicker than 4 mm should consider a conservative neck dissection [15]. According to Muhammad Faisal et al., a depth of invasion > 10 mm is substantially linked to a higher likelihood of occult metastasis. Additionally, even in early-stage oral squamous cell carcinoma, a depth of < 5 mm carries a high chance of occult nodal metastases (> 20%), compelling surgical neck dissection [1]. In contrast to depths below 5 mm, depths greater than 5 mm had a higher likelihood of undetected neck node metastases.

Recurrent cases of OSCC were not included in the study, which is a drawback of the study. Patients were not followed up on to look for carcinoma recurrence.

Conclusion

The majority of instances were found to occur in people between the ages of 50 and 60, and the buccal mucosa was the most frequently affected site. The relationship between lymph node metastasis and the depth of invasion was not statistically significant ($p > 0.05$). In conclusion, depth of invasion may be a crucial factor in staging and deciding on subsequent care, but it is not a reliable indicator of lymph node metastases. We did not divide the depth of invasion into 6–10 mm and >10 mm categories. This may be the subject of additional research.

Author's contribution:

Dr. Labdhi Vasa was incorporated in data collection and manuscript formation. Dr. Hiren Vaghela was incorporated into the interpretation of the manuscript.

Dr. Ashish Jawarkar was incorporated in the review and interpretation of the manuscript. Dr. Premnath Hiryur was incorporated into the interpretation of the manuscript.

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Abbreviations

AJCC: American Joint Committee on Cancer, DOI: Depth of Invasion, GBS: Gingivo-buccal Sulcus, OSCC: Oral Squamous Cell Carcinoma, SCC: Squamous Cell Carcinoma, TT: Tumor Thickness

References

1. Faisal, M., Bakar, M. A., 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(8): 1–10.
2. 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. International Archives of Otorhinolaryngology, 2017; 21(3): 265–269.
3. Katabi, N., Khimraj, A., Yuan, A., Zanoni, D. K., Ganly, I., Patel, S. G., Ghossein, R., & Xu, B. Depth of invasion versus tumour thickness in early oral tongue squamous cell carcinoma: which measurement is the most practical and predictive of outcome? Histopathology, 79(3), 325–337.
4. Moore, C., Kuhns, J. G., & Greenberg, R. A. (1986). Thickness as Prognostic Aid in Upper Aerodigestive Tract Cancer. Archives of Surgery, 1986; 121(12), 1410–1414.
5. Mindrila, D., & Balentyne, P. The Chi -Square Test. Analyzing. The Basic Practice of Statistics, 2013, 23. https://www.westga.edu/academics/research/vrc/assets/docs/ChiSquareTest_LectureNot es.pdf
6. Chaturvedi, P. (2012). Effective strategies for oral cancer control in India. Journal of Cancer Research and Therapeutics, 2012; 8(SUPPL. 2), 55–57.
7. Layland, M. K., Sessions, D. G., & Lenox, J. The influence of lymph node metastasis in the treatment of squamous cell carcinoma of the oral cavity, oropharynx, larynx, and hypopharynx: N0 versus N+. Laryngoscope, 2005; 115(4), 629–639.
8. Iwai, H., Kyomoto, R., Ha-Kawa, S. K., Lee, S., & Yamashita, T. Magnetic resonance determination of tumor thickness as predictive factor of cervical metastasis in oral tongue carcinoma. Laryngoscope, 2002; 112(3), 457–461.
9. Sneha Ambwani, Arup Kumar Misra, R. K. Prucalopride: A Recently Approved Drug by the Food and Drug Administration for Chronic Idiopathic Constipation. International Journal of Applied and Basic Medical Research, 2017; 2019(November), 193–195.
10. Odell, E. W., Jani, P., Sherriff, M., Ahluwalia, S. M., Hibbert, J., Levison, D. A., & Morgan, P. R. The prognostic value of individual histologic grading parameters in small lingual squamous cell carcinomas. The importance of the pattern of invasion. Cancer, 1994; 74(3), 789–794.
11. Wermker, K., Belok, F., Schipmann, S., Klein, M., Schulze, H. J., & Hallermann, C. Prediction model for lymph node metastasis and recommendations for elective neck dissection in lip cancer. Journal of Cranio-Maxillofacial Surgery, 2015; 43(4), 545–552.
12. Kurokawa, H., Yamashita, Y., Takeda, S., Zhang, M., Fukuyama, H., & Takahashi, T. Risk factors

for late cervical lymph node metastases in patients with stage I or II carcinoma of the tongue. Head and Neck, 2002;24(8), 731–736.
13. Mohit-Tabatabai, M. A., Sobel, H. J., Rush, B. F., & Mashberg, A. Relation of thickness of floor of mouth stage I and II cancers to regional metastasis. The American Journal of Surgery, 1986; 152(4), 351–353.
14. Khafif, R. A., Gelbfish, G. A., Tepper, P., & Attie, J. N. Elective radical neck dissection in epidermoid cancer of the head and neck. A retrospective analysis of 853 cases of mouth, pharynx, and larynx cancer. Cancer, 1991; 67(1), 67–71.
15. Asakage, T., Yokose, T., Mukai, K., Tsugane, S., Tsubono, Y., Asai, M., & Ebihara, S. Tumor thickness predicts cervical metastasis in patients with Stage I/II carcinoma of the tongue. Cancer, 1998; 82(8), 1443–1448.
16. Chaudhary, N., Verma, R., 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. Journal of Head & Neck Physicians and Surgeons, 2017; 5(2), 75.
17. Survivor, O. C. (n.d.). Living as an Oral Cavity and Oropharyngeal Cancer Survivor. 1–11.
18. Weimar, E. A. M., Huang, S. H., Lu, L., O'Sullivan, B., Perez-Ordonez, B., Weinreb, I., Hope, A., Tong, L., Goldstein, D., Irish, J., De Almeida, J. R., Bratman, S., Xu, W., & Yu, E. Radiologic-pathologic correlation of tumor thickness and its prognostic importance in squamous cell carcinoma of the oral cavity: Implications for the eighth edition tumor, node, metastasis classification. American Journal of Neuroradiology, 2018; 39(10), 1896–1902.
19. Pentenero, M., Gandolfo, S., & Carrozzo, M. Importance of tumor thickness and depth of invasion in nodal involvement and prognosis of oral squamous cell carcinoma: A review of the literature. Head and Neck, 2005; 27(12), 1080–1091.
20. ahi, R., Karmacharya, D., & Rao, T. S. Oral Squamous Cell Carcinoma in Relation with Depth of Invasion and Lymph Node Metastasis. Journal of College of Medical Sciences-Nepal, 2020; 16(2), 71–73.
21. Frierson, H. F., & Cooper, P. H. Prognostic factors in squamous cell carcinoma of the lower lip. Human Pathology, 1986; 17(4), 346–354.
22. Mamelle, G., Pampurik, J., Luboinski, B., Lancar, R., Lusinchi, A., & Bosq, J. Lymph node prognostic factors in head and neck squamous cell carcinomas. The American Journal of Surgery, 1994;168(5): 494–498.