Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.47750/jptcp.2023.30.06.024

Histological depth of invasion and its correlation in oral squamous cell carcinoma- a retrospective study

Reenu Joshy[1], Palati Sinduja[2*], Priyadharshini[3]

[1]Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-600077.

[2]Senior Lecturer, Department of Oral and Maxillofacial Pathology, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University,Chennai-600077

[3]Senior Lecturer, Department of Oral and Maxillofacial Pathology, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University,Chennai-600077

***Corresponding author:** Palati Sinduja, Senior Lecturer, Department of Oral and Maxillofacial Pathology, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-600077, Email: sindujap.sdc@saveetha.com

Submitted: 11 February 2023; Accepted: 14 March 2023; Published: 03 April 2023

ABSTRACT

Introduction: Oral squamous cell carcinoma is the most prevalent head and neck tumour, which is also one of the main causes of cancer-specific mortality. The most often impacted area of OSCC is the tongue. Occult nodal metastasis is the most significant indicator for prognosis of early-stage OSCC with a clinically negative neck. It was discovered that depth of invasion was a highly accurate indicator of occult nodal metastasis in OSCC, making it potentially a very valuable tool for predicting the incidence of nodal dissemination and, consequently, prognosis.

Aim: To determine the correlation between depth of invasion and staging of cancer.

Materials and methods: Evaluated the records of OSCC patients retrospectively. Depth of invasion for 30 excision specimens were measured using the magna software. The data was statistically analysed using SPSS software.

Results: DOI less than 5mm can be considered as stage one of OSCC. Similarly DOI of 6-10 mm as stage 2 and 11-15 mm as stage 3. Furthermore, depth of invasion above 16mm can be considered as stage 4 which involves nodal metastasis.

Conclusion: The study concludes that there is correlation between depth of invasion and staging of OSCC, thus DOI can be considered as an important prognosis factor.

Keywords: *Depth of invasion, nodal metastasis, oral squamous cell carcinoma, prognosis, Good health and well being*

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is a type of malignant oral epithelial neoplasia, which represents the most frequent of all oral neoplasms. About 90% of all oral cancers are OSCCs (1). Oral cancers that affect the salivary glands, pharynx, and oral cavity account for 2% to 4% of all cancer cases globally (2,3).

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2021 Muslim OT et al.

OSSC most commonly develops on the sites such as lips, tongue and floor of the mouth, while some OSCCs arise in apparently normal mucosa and some may be preceded by clinically obvious premalignant lesions like leukoplakia and erythroplakia (4,5). Typically, OSCC often presents as an ulcer with prominent exophytic margins or fissures(6). It can also develop as a lump, an enlarged, hard, or fixated cervical lymph node, a white or mixed white and red lesion, an extraction socket that won't heal, or a red lesion (erythroplakia)(7,8). If any of these characteristics last for longer than two weeks, OSCC should be taken into consideration(9).

The two biggest risk factors for oral cancer are smoking and alcohol consumption. 75% of all incidences of oral cancer are related to tobacco use. Smokers are six times more likely to get oral cancer than non-smokers.(10). Alcohol drinkers are also six times more likely than non-drinkers to acquire oral cancer. Users of cigarettes and alcohol have an oral cancer risk that is fifteen times greater than non-users. While smoking and drinking are typically the biggest risk factors, it's vital to take into account other aspects as well, like betel quid chewing in some ethnic groups. Chewing betel nut is common among Indian and Taiwanese people, and it raises your risk of mouth cancer substantially (11). Use of cannabis, areca nuts, and opioids leads to a higher risk of oral cancer. Older men, people from poorer socioeconomic backgrounds, and members of ethnic minorities are most likely to have OSCC. There are additional considerations at play. These consist of decreased capacity to repair mutagen-induced DNA damage, an inability to digest cancer-causing substances, vitamins A, E, or C, or trace element deficiencies and immunity problems (12).

Oropharyngeal and oral SCC are becoming more common. Globally, there are about 263,000 new cases of oral cancer each year, and the illness claims 127,000 lives (13). It is the third most prevalent malignancy in India and causes close to 40% of fatalities. In India it is the second most frequent site in men and the fourth in women. Male incidence rates were 10.1 per 100,000 in 2012, while female incidence rates were 4.3 per 100,000 (14). Numerous single or multicenter studies have consistently shown a relationship between a number of prognostic markers and disease-specific survival, local and regional recurrence, and lymph node metastasis. The prognosticators are extranodal extension (ENE), lymphovascular invasion (LVI), perineural invasion (PNI), depth of invasion (DOI), and pattern of invasion (POI)(1,3,5) .

DOI is regarded as an objective metric that has been examined by numerous researchers for the prognosis of OSCC. Although the majority of writers mostly concur that DOI is a crucial factor in determining nodal metastasis and survival, there is no set threshold for when neck dissection should be performed because the outcomes in the research differ. The aim of the present is to analyse the correlation between DOI and staging of OSCC.

MATERIALS AND METHODS

The Department of Oral and Maxillofacial Pathology's archives provided access to 30 formalin fixed paraffin embedded tissue blocks that represented the core specimens of excision specimens. The excision of oral squamous cell carcinoma and the removal of lymph nodes were both inclusion criteria for the study.

Staining Protocol

The sections were rehydrated with alcohol for 10 minutes after being deparaffinized with Xylene for 20 minutes. During the differentiation process the slides were dipped in acid alcohol and ammonia each for one dip, and then washed in running water for bluing. Harris's haematoxylin stain was used to stain the sections for 5 minutes after which it was rinsed in running tap water for 3-5 minutes. Slides were dehydrated using progressively stronger alcohol, after being dipped once in eosin. The slides were mounted with DPX after being cleaned in xylene.

The slides were observed under a microscope and the DOI was recorded and tabulated. Magna Software was used to measure the DOI. The patient's information was recorded using the patient data. Measurements were taken in millimetres by an experienced pathologist.

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2021 Muslim OT et al.

Statistical analysis

The SPSS software was used to analyse the data. To summarise qualitative data, descriptive statistics expressed as percentage was generated.

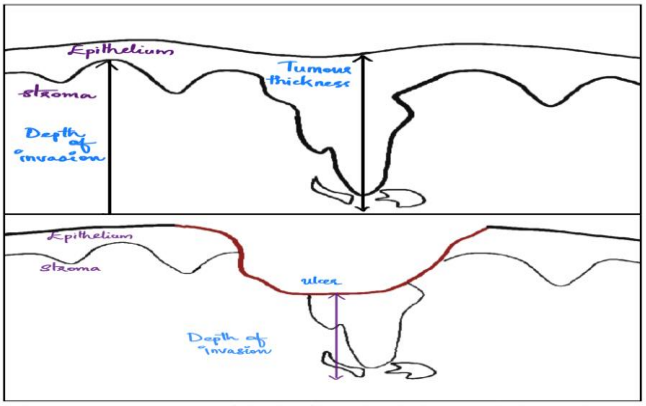

Figure 1: Measurement of depth of invasion in intact and ulcerated carcinomas.

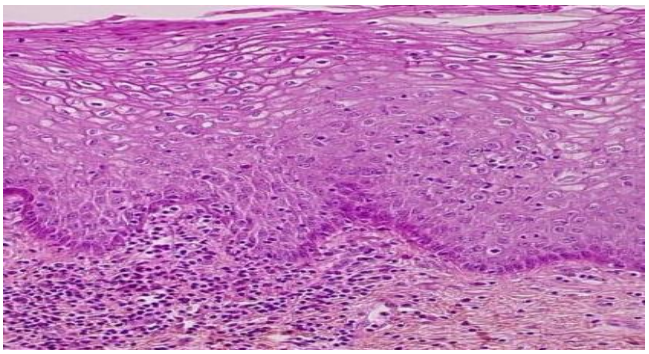

FIGURE 2: DOI analysis in invasive SCC

RESULTS

The depth of invasion and staging of oral squamous cell carcinoma is correlated. DOI less than 5mm can be considered as stage one of OSCC. Similarly DOI of 6-10 mm as stage 2 and 11-15 mm as stage 3. Furthermore, depth of invasion above 16mm can be considered as stage 4 which involves nodal metastasis.

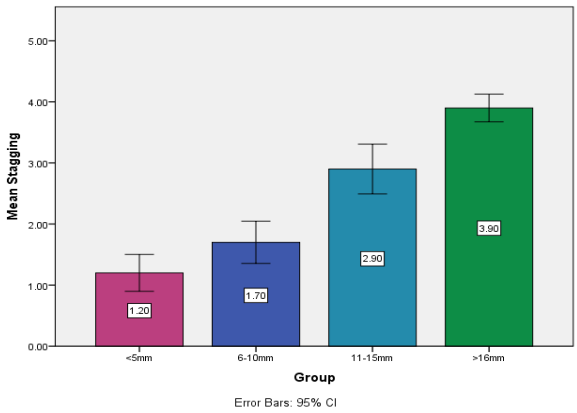

FIGURE 3: Bar graph depicting the correlation between DOI and mean stagging. X axis represents the depth of invasion in millimetres and Y axis represents mean staging of OSCC.

J Popul Ther Clin Pharmacol Vol 30(6):e183–e188; 03 April 2023.
This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2021 Muslim OT et al.

		Group	Stagging
Group	Pearson Correlation	1	.914**
	Sig. (2- tailed)		.000
	N	40	40
Stagging	PearsonCorrelation	.914**	1
	Correlation	.000	
	Sig. (2- tailed)	40	40
	N		

**. Correlation is significant at the 0.01 level (2- tailed).

DISCUSSION

Radical neck dissections have been conducted since the late 1800s to prevent cancer recurrences despite the fact that they resulted in serious postoperative problems such as shoulder dislocation. The lymph nodes that drained the tumour's initial site were removed during more focused neck dissections in the 1980s. Even with conservative care, shoulder dysfunction might still occur occasionally(15).

The size of the primary tumour, the location, the T stage, the grade, the depth of invasion, the biological tumour markers, the perineural invasion, and patient compliance are a few of the variables that can influence the rate of cervical metastasis and survival from oral cavity cancer (16)(17). Since the tumour breadth and the site were once thought to be the key prognostic determinants, numerous prognostic models were developed to determine the amount of metastasis dissemination. Recently, DOI has gained importance as a prognostic factor for early detection of OSCC.

The term "depth of invasion" refers to the extent cancer penetrated into the tissue below an epithelial surface. Some investigators restore a surface line after the epithelium has been damaged and measure along this line. However, rather than using precise millimetre measurements from a micrometre, the depth of invasion is frequently described in terms of the microscopic, deep anatomical structures that are reached.

In the present study we have assessed the depth of invasion of 30 excisional specimens and the correlation with staging and nodal metastasis. The lateral margin of the tongue and buccal mucosa are the two most frequent locations for tumours. Males are more likely to get cancer of the tongue, according to numerous research. Indian men are exposed to both smokeless and smoked tobacco, which explains why this is the case. But recently, some cases without any prior history of habits that can contribute to the emergence of oral cancers, including tongue cancer, have been identified.

In our study we have found that depth of invasion less than 5 mm can be considered as stage one of OSCC. Similarly DOI of 6-10 mm as stage 2 and 11-15 mm as stage 3. Furthermore, depth of invasion above 16mm can be considered as stage 4 which involves nodal metastasis.

When the depth of invasion is greater than 5 mm, it was found that the cutoff threshold is most significantly associated with neck metastasis. Therefore, predicting the occult cervical lymph node metastases using the depth of invasion may be helpful. Similar investigations have shown that in cases of carcinomas of the lateral border of the tongue, level II nodes are the most frequently involved site, followed by level III nodes(6,18,19).

Depth of invasion also has its limitations; in some circumstances, particularly when there has been perineural invasion, it can be challenging to ascertain the depth of invasion. The fundamental issue with measuring tumour thickness in mucosal tumours, when there is frequently no mucosal surface on the slide to utilise as a reference point, is the difference in complexity (20). This issue was also brought up by several publications. Another drawback is that multiple cutoff values have been used to determine elective neck dissection for clinically negative necks due to the lack of a consistent way of assessing tumour thickness/depth of

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2021 Muslim OT et al.

invasion(21). Despite these drawbacks, it is evident from our research that there is a connection between the depth of invasion and nodal metastasis, which would provide us with newer perspectives when coordinating the patients' treatment plan.

CONCLUSION

The study concludes that there is correlation between depth of invasion and staging of OSCC, thus DOI can be considered as an important prognosis factor for the early detection of oral squamous cell carcinoma.

ACKNOWLEDGMENTS

We would like to thank Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University for providing us support to conduct the study.

CONFLICT OF INTEREST

The author declares that there were no conflicts of interests in the present study.

Authorship Criteria

Reenu Joshy, Dr. R.Priyadharshini and Dr. Palati Sinduja framed the Concept, design of study or acquisition of data or analysis and interpretation of data

Drafting the article or revising was done by Dr.R.Priyadharshini and Dr.Palati sinduja

Final approval of the version to be published was done by Dr. R.Priyadharshini and Dr. Palati Sinduja

Source Of Funding

The present project is supported by Saveetha Institute of Medical and Technical Sciences Saveetha Dental College and Hospitals, Saveetha University.

REFERENCE

1. Markopoulos AK. Current aspects on oral squamous cell carcinoma. Open Dent J. 2012 Aug 10;6:126–30.
2. Williams HK. Molecular pathogenesis of oral squamous carcinoma [Internet]. Vol. 53, Molecular Pathology. 2000. p. 165–72. Available from: http://dx.doi.org/10.1136/mp.53.4.165
3. Jain A. Molecular Pathogenesis of Oral Squamous Cell Carcinoma [Internet]. Squamous Cell Carcinoma - Hallmark and Treatment Modalities. 2020. Available from: http://dx.doi.org/10.5772/intechopen.85650
4. Farhood Z, Simpson M, Ward GM, Walker RJ, Osazuwa-Peters N. Does anatomic subsite influence oral cavity cancer mortality? A SEER database analysis [Internet]. Vol. 129, The Laryngoscope. 2019. p. 1400–6. Available from: http://dx.doi.org/10.1002/lary.27490
5. Almangush A, Mäkitie AA, Triantafyllou A, de Bree R, Strojan P, Rinaldo A, et al. Staging and grading of oral squamous cell carcinoma: An update [Internet]. Vol. 107, Oral Oncology. 2020. p. 104799. Available from: http://dx.doi.org/10.1016/j.oraloncology.2020.104799
6. Wu J, Kong L, Field X, Ebrahim AK. The incidence of occult level IV nodal metastasis in tongue squamous cell carcinoma: a 20 year review. ANZ J Surg [Internet]. 2022 Oct 5; Available from: http://dx.doi.org/10.1111/ans.18090
7. Rabin M. Oral Squamous Cell Carcinoma: From Diagnosis to Treatment. Nova Science Publishers; 2021. 261 p.
8. Oral Squamous Cell Carcinoma: New Insights for the Healthcare Professional: 2013 Edition. ScholarlyEditions; 2013. 128 p.
9. Sankaranarayanan R, Duffy SW, Padmakumary G, Day NE, Krishan Nair M. Risk factors for cancer of the buccal and labial mucosa in Kerala, southern India [Internet]. Vol. 44, Journal of Epidemiology & Community Health. 1990. p. 286–92. Available from: http://dx.doi.org/10.1136/jech.44.4.286
10. Sankaranarayanan R, Duffy SW, Krishnan Nair M, Padmakumary G, Day NE. Tobacco and alcohol as risk factors in cancer of the larynx in Kerala, India [Internet]. Vol. 45, International Journal of Cancer. 1990. p. 879–82. Available from: http://dx.doi.org/10.1002/ijc.2910450517
11. Shield KD, Ferlay J, Jemal A, Sankaranarayanan R, Chaturvedi AK, Bray F, et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. CA Cancer J Clin. 2017 Jan;67(1):51–64.
12. Aaboubout Y, van der Toom QM, de Ridder MAJ, De Herdt MJ, van der Steen B, van Lanschot CGF, et al. Is the Depth of Invasion a Marker for Elective Neck Dissection in Early Oral Squamous Cell Carcinoma? Front Oncol. 2021 Mar 12;11:628320.
13. Franco EL, Rohan TE. Cancer Precursors: Epidemiology, Detection, and Prevention.

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2021 Muslim OT et al.

Springer Science & Business Media; 2007. 430 p.
14. Panta P. Oral Cancer Detection: Novel Strategies and Clinical Impact. Springer; 2019. 314 p.
15. Meghji S. Creating a Prognostic Model to Assess the Multivariate Predictors of Neck Metastasis in Oral Cavity Squamous Cell Carcinoma. 2017.
16. Jones KR, Lodge-Rigal RD, Reddick RL, Tudor GE, Shockley WW. Prognostic Factors in the Recurrence of Stage I and II Squamous Cell Cancer of the Oral Cavity [Internet]. Vol. 118, Archives of Otolaryngology - Head and Neck Surgery. 1992. p. 483–5. Available from: http://dx.doi.org/10.1001/archotol.1992.01880050029006
17. Sinduja P, Ramani P, Gheena S, Ramasubramanian A. Expression of metallothionein in oral squamous cell carcinoma: A systematic review. J Oral Maxillofac Pathol. 2020 Jan;24(1):143–7.
18. Piotrowicz O, Jia HN, Blazak J. F18-FDG PET/CT accuracy in nodal staging of head and neck squamous cell carcinoma and correlation of SUV to the likelihood of a confirmed nodal metastasis. J Med Imaging Radiat Sci [Internet]. 2022 Oct 19; Available from: http://dx.doi.org/10.1016/j.jmir.2022.09.016
19. Wicks C, Zubair F, Ogunbowale A, McMahon J. The relative propensity for regional metastasis in floor of mouth squamous cell carcinoma versus other oral cavity subsites. Br J Oral Maxillofac Surg [Internet]. 2022 Aug 2; Available from: http://dx.doi.org/10.1016/j.bjoms.2022.07.012
20. 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 Neck. 2005 Dec;27(12):1080–91.
21. Silva RKD, De Silva RK, Siriwardena BSM, Samaranayaka A, Abeyasinghe WAMU, Tilakaratne WM. A model to predict nodal metastasis in patients with oral squamous cell carcinoma [Internet]. Vol. 13, PLOS ONE. 2018. p. e0201755. Available from: http://dx.doi.org/10.1371/journal.pone.0201755

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. ©2021 Muslim OT et al.