Clinicopathological Correlation between Depth of Tumor and Neck Node Metastasis in Oral (Tongue and Buccal Mucosa) Carcinoma

Anuj H Shah¹, Rupa P Parikh²

ABSTRACT

Aims and objectives: (1) To study the depth of tumor invasion in an oral (tongue and buccal mucosa) carcinoma and its correlation with neck metastasis. (2) To know whether the increase in depth of tumor (depth of invasion) increases the chances of cervical nodal metastasis in the oral tongue and buccal mucosa carcinoma and derive cutoff value of depth of invasion at which the metastasis occurs.

Materials and methods: The study was carried out on 14 tongue and 22 buccal mucosa cases to know the correlation between the depth of tumor and neck node metastasis in the oral (tongue and buccal mucosa) carcinoma.

Results: Among 36 cases, 10 cases were pN+. Out of 10 cases, 7 (70%) were having depth ≥ 12 mm and 30% cases (pN+) having depth between 8 and <10 . We found it statistically significant and so as the depth of tumor increases the chances of nodal metastasis increases. We found the cutoff for a depth of invasion in both tongue and buccal mucosa carcinomas as 8 out of 22 patients had DOI >10 mm and among them 4 were pN+ and among 14 tongue cases, 3 cases had DOI >8 mm and all of them were pN+.

Conclusion: For tongue 8 mm and for buccal mucosa, 10 mm of the depth of tumor invasion was calculated as the cutoff depth, above which the incidence of nodal metastasis increases to 75% and 66.66%, respectively.

Clinical significance: Depth of tumor is an important prognostic indicator in the tongue and buccal mucosa carcinoma to know the cervical nodal metastasis. Hence for an increase in depth of tumor cases, neck must be addressed along with primary tumor excision. Radiological investigations [ultrasonography (USG), magnetic resonance imaging (MRI), computed tomography (CT) scan] play an important role in nodal metastasis detection hence should be considered in carcinoma of the oral tongue and buccal mucosa especially in clinically N0 neck.

Keywords: Buccal mucosa carcinoma, Depth of tumor, Nodal metastasis, Tongue carcinoma.

International Journal of Head and Neck Surgery (2021): 10.5005/jp-journals-10001-1423

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 In India, 4 in 10 of all cancers are oral cancers as it is the most common cancer.³ In the developed world, tongue and floor of mouth cancers were common while gingivobuccal cancers were the most common oral cavity cancers in India. However, the incidence of oral tongue cancers has been increasing in India and today it is as common as gingivobuccal cancers in most cancer registries in India.⁴ In head and neck carcinoma, cervical lymph node metastasis is the most important prognostic factor. As cancer grows, they invade the surrounding tissue and metastasize to cervical lymph nodes due to the rich lymphatic system in the neck.⁵⁻⁸ Currently, tumor thickness is considered as a factor for doing adjuvant neck dissection in oral cavity cancers.⁹ So many times these tumor thickness and depth of invasion are used synonymously but in reality, both are different and should be clearly differentiated.¹⁰⁻¹⁶

"Tumor thickness" is the thickness of the entire tumor mass.

"Depth of invasion" is the extent of tumor growth into the tissue beneath an epithelial surface.⁹⁻¹⁶

There are so many studies that have found a significant correlation between depth of invasion and cervical nodal

^{1,2}Department of ENT, Surat Municipal Institute of Medical Education and Research, Surat, Gujarat, India

Corresponding Author: Anuj H Shah, Department of ENT, Surat Municipal Institute of Medical Education and Research, Surat, Gujarat, India, Phone: +91 8238935656, e-mail: anujhshah.1989@gmail.com

How to cite this article: 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.

Source of support: Department of ENT, Department of Radiology, and Department of Pathology, Surat Municipal Institute of Medical Education and Research, Surat, Gujarat, India

Conflict of interest: None

metastasis, we also planned to conduct a similar study in our institute to find whether a similar correlation exists or not.

AIMS AND OBJECTIVES

- To study the depth of tumor invasion in an oral tongue and buccal mucosa carcinoma and its correlation with neck metastasis.
- To know whether the increase in depth of tumor increases the chances of cervical nodal metastasis in the oral (tongue and buccal mucosa) carcinoma and derive cutoff value of depth of invasion at which the metastasis occurs.

CONCLUSION

We conclude our study by saying that in the (tongue and buccal mucosa) carcinoma, depth of tumor (depth of invasion) is an important prognostic indicator.

As the depth of tumor invasion increases chances of cervical lymph node metastasis increases significantly.

For oral tongue 8 mm and for buccal mucosa, 10 mm of the depth of tumor invasion was calculated as the cutoff depth, above which incidence of nodal metastasis increases to 75% and 66.66%, respectively.

Hence, the neck in these patients must be addressed along with primary tumor excision.

Radiological investigations [ultrasonography (USG), magnetic resonance imaging (MRI), computed tomography (CT) scan] play an important role in nodal metastasis detection hence should be considered in carcinoma of the oral (tongue and buccal mucosa) especially in clinically N0 neck.

Development of future technologies for more accurate assessment of DOI will further assess to solve the controversies of management (Figs 1 to 5).

The study was carried out on 14 tongue and 22 buccal mucosa cases coming to the ENT department of the tertiary care center and who underwent surgery to know the correlation between the

depth of the invasion and neck node metastasis in the oral (tongue and buccal mucosa) carcinoma. The lymph nodes were considered metastatic or positive histologically only.

Study Population

All the patients presenting with ulcer or growth on the tongue and buccal mucosa were examined in ENT OPD.

Study Design

Observational cross-sectional.

Study Period

From September 2015 to November 2016.

Sample Size

The sample size was calculated using openepi version 2.

$$P = \text{prevalence} = 9.9\% = 0.099$$

$$q = (1 - p) = 0.901$$

$$I = 10\% = 0.1$$

(*National Cancer Registry Programme, ICMR: 3-year report of PBCRs 2006–2008.)

Sample size of 34 is calculated using openepi version 2.

Fig. 1: Case distribution according to sites

Fig. 2: Distribution of subsites in tongue cases

Fig. 3: Distribution of subsites in buccal mucosa (BM) cases

Fig. 4: Cutoff value of DOI for tongue

$$n = \frac{(1.96) * (1.96) * p * q}{I * I}$$

$$= \frac{3.84 * 0.099 * 0.901}{0.01}$$

$$= 34.25$$

$$= 34$$

Statistical Method

Descriptive analysis and Chi-square test.

Inclusion Criteria

- All patients with biopsy-proven oral (tongue and buccal mucosa squamous cell) carcinoma operated in the ENT department of our institute.

Exclusion Criteria

- Patient with an ulcer over the tongue and buccal mucosa but biopsy negative.
- Patients with non-squamous cell carcinoma of tongue and buccal mucosa.
- Patients with a traumatic ulcer over the tongue.

Fig. 5: Cutoff value of DOI for buccal mucosa

- Patient with advanced stage making it inoperable.
- Patients with biopsy-proven oral cavity carcinoma except for tongue and buccal mucosa.
- Patients with tongue and buccal mucosa carcinoma previously treated with chemotherapy or radiotherapy.
- Patients with residual or recurrent lesions of squamous cell carcinoma of the oral tongue and buccal mucosa.

Depth of tumor invasion (DOI) is a strong predictor for cervical lymph node involvement in squamous cell carcinoma of the oral cavity but the precise cutoff point is still variable. Two of the most important variable for neck metastasis are depth of invasion histologically and tumor thickness. Thickness measurement: Moore et al.¹⁷ explained the difference between the depth of invasion and tumor thickness (Figs 5 to 8).

Depth of Invasion¹⁸

Depth of invasion is the extent of cancer growth into the tissue beneath an epithelial surface. In cases, if epithelium is destroyed, some investigators reconstruct a surface line and measure it from this line.

Tumor Thickness

Tumor thickness means entire tumor mass and it is measured by using an ocular micrometer.¹⁸ Tumor thickness is used for the measurement of a tumor's vertical bulk and it includes both the exophytic and endophytic portions of the tumor.¹⁹

There is a big difference in the concept of tumor thickness, e.g., by Giacomarra et al.,²⁰ who says that "tumor thickness is commonly used as a synonym of depth of invasion and it shows the part of the tumor which is under the line of the basal membrane" compared with authors who adopted the technique proposed by Breslow,²¹ which measures tumor thickness from either the tumor surface or from the base of the ulcer. Moore et al. reported about the reconstruction of a "normal mucosal line" as the basement membrane line in case of both exophytic and/or verrucous tumors. Ambrosch et al. and Woolgar et al.²² both used techniques based on the "normal mucosal line". Ambrosch et al. interpreted it as the basement membrane line, whereas Woolgar et al. used the surface line of the surrounding healthy mucosa.¹⁸

Hoçal et al. reported that patients having a tumor depth of <9 mm showed significantly better outcome than those whose depth was >9 mm ($p < 0.05$) and so tumor depth should always be taken into consideration while deciding on neck management.²³

Figs 6A and B: Methods of measuring tumor thickness. (A to D) Tumor surface/base of the ulcer up to the deepest point of invasion; (B to E) Adjacent intact mucosa up to the deepest point of invasion; (C to F) Basal membrane up to the deepest point of invasion

Figs 7A to C: Depth of invasion of the lip and oral cavity tumors. AJCC manual, 6th edition; (A) Exophytic tumors: Measure the "tumor thickness from surface (A) to the deepest area of invasion (B); (B) Ulcerated tumors: Measure from the ulcer base (A) to the deepest area of invasion (B) as well as from the surface of the most lateral extent of the invasive carcinoma (C) to the deepest area (D); (C) Endophytic tumors: Measure from the perpendicular surface of the invasive squamous cell carcinoma (A) to the deepest area of invasion (B)

Fig. 8: Measurement of depth of invasion histologically in our study

Ambrosch et al. reported that tumor 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.²⁴ Shah et al. reported that there is a 50% rate of node metastasis when tumor depth is between 2 mm and 9 mm.²⁵

Fukano et al. did a study on 34 cases with a cutoff 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. Hence, elective neck dissection is strongly indicated for DOI >5 mm.¹²

Yuen et al. also suggested tumor thickness was the only significant factor for the prediction of local recurrence, nodal metastasis, and survival and proved the cutoff value for DOI as 3 mm.²⁶

For DOI >8 mm in carcinoma oral tongue cases, the cervical nodal metastasis rate (pN+) was found to be 75% while for DOI >10 mm in carcinoma buccal mucosa, cervical nodal metastasis rate (pN+) was 66.66%.

A similar study was published by Samanta, Surendra Nath Senapati, and Ashish Upadhyaya in the Journal of Clinical Oncology

at ASCO annual meeting in 2016. In this study for DOI >6 mm in carcinoma tongue cases, cervical nodal metastasis rate (pN+) was 73.68% while for DOI >8 mm in carcinoma buccal mucosa cases, cervical nodal metastasis rate (pN+) was 62.79%.²⁷ This is comparable to our study.

Although we faced the problem of small sample size, our study also found a significant cutoff for tongue and buccal mucosa carcinoma and so we suggest END at depth 8 and 10 mm for tongue and buccal mucosa carcinoma, respectively.

Depth of tumor invasion is a more important parameter than tumor thickness *per se*, as in exophytic growth the tumor spreads in the available space which does not affect the normal anatomy much, whereas in endophytic growth the tumor cells replace the normal cells or displace them to make space for rapidly progressing mitosis of tumor cells. Therefore, we must measure the depth of tumor invasion rather than tumor thickness before deciding for performing elective neck dissection.

REFERENCES

- Parkin DM, Bray F, Ferlay J, et al. Global cancer statistics, 2002. CA: a cancer. J Clinici 2005;55(2):74–108. DOI: 10.3322/canjclin.55.2.74.
- Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer, 2013 <http://globocan.iarc.fr> (accessed Dec 23, 2013).
- Incidence And Prevalence [Internet]. Available from: <http://ocf.org.in/professional/IncidenceAndPrevalence.aspx>.
- National Cancer Registry Programme. Three year report of the population based cancer registries: 2009-2011. Indian Council of Medical Research, India.
- Sessions DG, Spector GJ, Lenox J, et al. Analysis of treatment results for oral tongue cancer. Laryngoscope 2002;112(4):616–625. DOI: 10.1097/00005537-200204000-00005.
- Le Tourneau C, Velten M, Jung GM, et al. Prognostic indicators for survival in head and neck squamous cell carcinomas: analysis of a series of 621 cases. Head Neck 2005;27(9):801–808. DOI: 10.1002/hed.20254.
- De Zinis LO, Bolzoni A, Piazza C, et al. Prevalence and localization of nodal metastases in squamous cell carcinoma of the oral cavity: role and extension of neck dissection. Eur Arch Otorhinolaryngol 2006;263(12):1131–1135. DOI: 10.1007/s00405-006-0128-5.
- Ferlito A, Rinaldo A, Devaney KO, et al. Detection of lymph node micrometastases in patients with squamous carcinoma of the head and neck. Eur Arch Otorhinolaryngol 2008;265(10):1147–1153. DOI: 10.1007/s00405-008-0715-8.
- Pfister DG, Ang K, Briezel D. NCCN clinical practice guidelines in oncology – head and neck cancer. J Natl Compr Canc Netw 2011;9(6):596–650. DOI: 10.6004/jnccn.2011.0053.
- Close LG, Burns DK, Reisch J, et al. Microvascular invasion in cancer of the oral cavity and oropharynx. Arch Otolaryngol Head Neck Surg 1987;113(11):1191–1195. DOI: 10.1001/archotol.1987.01860110057008.
- Fakih AR, Rao RS, Borges AM, et al. Elective versus therapeutic neck dissection in early carcinoma of the oral tongue. Am J Surg 1989;158(4):309–313. DOI: 10.1016/0002-9610(89)90122-0.
- Fukano H, Matsuura H, Hasegawa Y, et al. Depth of invasion as a predictive factor for cervical lymph node metastasis in tongue carcinoma. Head Neck 1997;19(3):205–210. DOI: 10.1002/(SICI)1097-0347(199705)19:3<205::AID-HED7>3.0.CO;2-6.
- Godden DR, Ribeiro NF, Hassanein K, et al. Recurrent neck disease in oral cancer. J Oral Maxillofac Surg 2002;60(7):748–753. DOI: 10.1053/joms.2002.33240.
- Jones KR, Lodge-Rigal RD, Reddick RL, et al. Prognostic factors in the recurrence of stage I and II squamous cell cancer of the oral cavity. Arch Otolaryngol Head Neck Surg 1992;118(5):483–485. DOI: 10.1001/archotol.1992.01880050029006.
- Kurokawa H, Yamashita Y, Takeda S, et al. Risk factors for late cervical lymph node metastases in patients with stage I or II carcinoma of the tongue. Head Neck 2002;24(8):731–736. DOI: 10.1002/hed.10130.
- O-charoenrat P, Pillai G, Patel S, et al. Tumour thickness predicts cervical nodal metastases and survival in early oral tongue cancer. Oral Oncol 2003;39(4):386–390. DOI: 10.1016/S1368-8375(02)00142-2.
- Moore C, Kuhns JG, Greenberg RA. Thickness as prognostic aid in upper aerodigestive tract cancer. Arch Surg 1986.
- 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;27(12):1080–1091. DOI: 10.1002/hed.20275.
- Kane SV, Gupta M, Kakade AC, et al. Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. Eur J Surg Oncol 2006;32(7):795–803. DOI: 10.1016/j.ejso.2006.05.004.
- Giacomarra V, Tirelli G, Papanikolla L, et al. Predictive factors of nodal metastases in oral cavity and oropharynx carcinomas. Laryngoscope 1999;109:795–799.
- Breslow A. Prognostic factors in the treatment of cutaneous melanoma. J Cutan Pathol 1979;6:208–212.
- Woolgar JA, Scott J. Prediction of cervical lymph node metastasis in squamous cell carcinoma of the tongue/floor of mouth. Head Neck 1995;17:463–472.
- Hoçal AS, Unal OF, Ayhan A. Possible prognostic value of histopathologic parameters in patients with carcinoma of the oral tongue. Eur Arch Otorhinolaryngol 1998;255(4):216–219. DOI: 10.1007/s004050050046.
- Ambrosch P, Kron M, Fischer G, et al. Micrometastases in carcinoma of the upper aerodigestive tract: detection, risk of metastasizing, and prognostic value of depth of invasion. Head Neck 1995;17(6):473–479. DOI: 10.1002/hed.2880170604.
- Shah AR, Spiro RH, Shah JP, et al. Squamous carcinoma of the floor of the mouth. Am J Surg 1984;148(4):455–459. DOI: 10.1016/0002-9610(84)90369-6.
- Yuen APW, Lam KY, Wei WI, et al. A comparison of the prognostic significance of tumor diameter, length, width, thickness, area, volume, and clinicopathological features of oral tongue carcinoma. Am J Surg 2000;80(2):139–143. DOI: 10.1016/S0002-9610(00)00433-5.
- Samanta DR, Senapati SN, Upadhyaya A. Histopathology correlation between depth of invasion and cervical lymph node metastasis in post operative patients of carcinoma buccal mucosa and tongue. In ASCO Annual Meeting Proceedings 2016 May 20 (vol. 34, No. 15_suppl, p. e17542).