

Evaluation of Occult Lymph Node Metastases in Cases of T1 and T2 Tongue Squamous Cell Carcinoma

Original
Article

Mosaad Abdaljawwad Khalifah Khalifah

Associate Professor at Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Kafrelsheikh University, Kafrelsheikh, Egypt

ABSTRACT

Background: Squamous cell carcinoma (SCC) is associated with a high risk for lymph node (LN) metastases even for T1 and T2 patients even in clinically and radiologically negative neck. However, little data are provided in the literature about each type separately.

Objectives: therefore, the current study tries to present more specific data about the level of LN metastases for each stage.

Material and methods: This is a retrospective study that was conducted on 67 patients diagnosed with tongue SCC. Patients' records were reviewed who were previously untreated T1 or T2 patients and were operated by radical resection of the primary tumour and neck dissection (level I-IV). cases with multiple tumours or recurrent or with distant metastases were excluded. The level of LN metastases was evaluated and compared to clinical and histopathological data.

Results: T1 patients showed positive cLN up to level IB with occult LN metastases up to level III, T2 patients had clinically positive LN metastases up to level II, but occult metastases up to level IV. In T1 and T2 patients with cLN0, the occult involvement extended to level II. (not statistically significant). However, primary tumours with more than 3mm depth of penetration were associated with pathologically positive LN metastases.

Conclusion: The distal-most level for occult LN metastases can be at least two levels ahead of the last clinically detectable evidence of the disease, however not statistically significant. Nevertheless, the depth of invasion is more important predictor for LN metastases rather than the size of the primary lesion.

Key Words: Tongue SCC; T1; T2; Occult LN metastases, Depth of penetration.

Received: 9 December 2022, **Accepted:** 13 December 2022.

Corresponding Author: Mosaad Khalifah, Associate Professor at Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Kafrelsheikh University, Kafrelsheikh, Egypt, **Tel :** 0452738074, **Mobile:** 01008603084, **E-mail:** mosaad_khalifa@den.kfs.edu.eg

ISSN: 2090-097X, July 2022, Vol. 13, No. 3

INTRODUCTION

Squamous cell carcinoma (SCC) of the tongue is one of the highest incidence oral cancers. Moreover, it raises a high suspicion for regional and distant spread. [1], [2] Lymph node (LN) metastases is an immensely powerful indicator for the prognosis since it is correlated with a 50% reduction of the survival rate. [2]-[4] Although T1 and T2 are collectively considered early-stage tongue carcinomas, they are related to occult LN metastases even in clinically and radiologically negative neck (N0). Little data are provided in the literature about each type separately.

[5], [6] Moreover, no consensus exists to correlate each type with the presence of occult LN metastases. Therefore, the current study tries to present more specific data about the level of LN metastases, either clinically evident or occult, for each stage of the disease.

MATERIALS AND METHODS

The current study is a retrospective study that was conducted on consecutive 67 patients diagnosed with tongue SCC who presented at the department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Kafrelsheikh University, and the National Oncology Institute during the period from October 2018 through October 2022. Patients' records with tongue SCC were reviewed including the clinical, radiographical and other diagnostic aids, and pathological reports.

All patients were examined clinically and with the aid of CT, MRI, PET-CT, and ultrasound-guided fine needle aspiration biopsy (FNAB) when other diagnostic aids were inconclusive. Inclusion criteria included previously untreated tongue SCC, T1 or T2 as diagnosed according to the seventh edition of TNM Classification of Malignant Tumours (UICC), [7] and who were operated by radical resection of the primary tumour lesions and neck dissection (level I-IV).

Moreover, inclusion criteria included five years follow up through the clinical examination every month for the first

year, bimonthly in the second year, and then every three months; given that CTs were taken every six months and PET-CT every year. Exclusion criteria included patients with multiple tumours, recurrent tumours, and patients with distant metastases. The level of LN metastases was evaluated and compared to clinical TNM staging, depth of penetration and to the histopathological reports.

This study was approved by the ethical committee of Kafrelsheikh University and written informed consent was obtained from all the patients. Statistical analysis was done using SPSS 13 for Windows (SPSS Chicago, IL).

RESULTS:

Only 41 patients out of the 67 patients with tongue SCC fulfilled the inclusion criteria. Age range was 37-72 years (with an average of 54 year). Gender distribution was 29 males and 12 females ($P=1$; insignificant Fisher's exact test at $p<0.05$).

As depicted in tables 1 and 2, out of the 16 patients who had T1 lesions, only two patients showed clinically positive LN at the level IB, however, on histopathological examination, occult LN metastases were revealed up to level III. Other than these two patients, there were three patients with clinically negative neck but with occult metastases up to levels II. That means that the distal-most level for the occult LN metastases was at least two levels ahead of the last clinically detectable evidence of the disease. Regarding patients with T2 lesions, out of the 25 patients, there were 16 patients with clinically positive LN metastases up to level II with occult metastases up to level IV.

Moreover, for two with clinically negative necks, there were occult metastases to level IB and level II. For the remaining patients, there was no evidence of regional or distant metastases. Therefore, the distal-most level for the occult LN metastases was at least two levels ahead of the last clinically detectable evidence of the disease. Nevertheless, these differences were statistically insignificant.

Table 1: Clinical and pathological neck involvement in relation to the size of the primary tumour.

T stage	Total No.	cLN	pLN	Significance*
T1	16	2	5	Insignificant
T2	25	16	18	Insignificant

cLN: clinically positive LN; pLN: pathologically positive LN.
*: logistic regression analysis

Table 2: Distribution of the clinical and pathological neck involvement in relation to the size of the primary tumour

T stage	Involvement type	The level of the distal-most LN metastases					Significance*
		Level IA	Level IB	Level II	Level III	Level IV	
		T1	cLN	0	2	0	
T2		2	9	5	0	0	Insignificant
T1	pLN	1	1	2	1	0	Insignificant
T2		0	1	2	14	2	Insignificant

cLN: clinically positive LN; pLN; pathologically positive LN; IA, AB, II, III, IV: the levels of the neck; *: logistic regression analysis.

With regards to the depth of penetration, pathologically positive LN metastases was related to a depth of penetration of the primary tumour larger than 3mm with a statistically significant difference at $P<0.05$.

Table 3: The relationship between the depth of penetration and pathologically positive LN metastases.

T stage	DIV<3mm	DIV>3mm	pLN	Fisher's exact test	Significance
T1	6	10	5	0.0438	Significant
T2	4	21	18	0.0295	Significant

DIV: Depth of invasion; pLN; pathologically positive LN

DISCUSSION

Squamous cell carcinoma (SCC) of the tongue is a high-incidence, high-risk oral cancer. [1], [2] Since positive LN metastases reduced the survival rate by about 50%, [2]-[4] a meticulous effort has to be spent to assess the LN metastases status and to correlate it with the treatment plan for the patients. nevertheless, little data are provided in the literature about accurate correlation; particularly most reports deal with the early-stage SCC of the tongue collectively as T1-T2 stage. [5], [6] Therefore, the current study tries to provide more specific data about the level of LN metastases in the early-stage SCC of the tongue separately, and to correlate the incidence of occult LN metastases to each stage of the disease. Therefore, the current retrospective study was conducted on previously untreated primary tongue SCC, T1 or T2 who were operated by radical resection of the primary tumour lesions and neck dissection (level I-IV) with the exclusion of patients with multiple tumours, or distant metastases.

In the current study, patients with T1 lesions showed positive cLN up to level IB with occult LN metastases up to level III. Moreover, patients with T2 lesions showed clinically positive LN metastases up to level II, but occult metastases up to level IV. Furthermore, in T1 and T2 patients with cLN0, the occult involvement extended to level II.

This may clarify that distal-most level for occult LN metastases was at least two levels ahead of the last clinically detectable evidence of the disease. Although this notice was constant in both groups, it failed to show a statistical significance. In addition, there was no statistical significance to correlate the level of neck involvement with size of the primary tumour. On the other hand, primary tumours with more than 3mm depth of penetration were associated with pathologically positive LN metastases with a statistically significant difference at $P < 0.05$.

Hence, in the view of the current study, the depth of penetration was an important predictor and risk factor for the loco-regional spread of the tumour, thus positive cervical LN involvement, rather than the size of the primary tumour.

However, distal-most level for occult LN metastases was at least two levels ahead of the last clinically detectable evidence of the disease irrespective of the size of the primary tumour. However, in other studies the size of the primary tumour was correlated to lymph node metastases.^[8-10] However, some of these studies employed another basis for size determination such as dividing patients into a group with less than 1cm lesions and another with more 1cm lesions.^[10] On the other hand, other reports were in agree with findings of the current study.^[11]

Moreover, the current study and many other studies showed that occult LN metastases takes places in cases of T1 and T2 even in clinically negative necks. Also, they have emphasized that the depth of invasion is more important predictor rather than the size of the primary lesion which may reflect the aggressiveness of the tumour and so the increases LN metastases. This predictor can alter the treatment plan towards more conservative neck dissection or more extensive dissection according to the risk. More conservative dissections serve in reducing the operative time and blood loss, and in preserving shoulder function and phneric nerve for an enhanced postoperative quality of life.^{[12]-[14]}

CONCLUSION:

Squamous cell carcinoma of the tongue is a high-incidence, high-suspicion cancer. Patients with T1 and T2 tumours with cLN0 can have occult LN metastases to level II. However, T1 and T2 patients with clinically positive necks can have occult metastases up to level III, and IV respectively.

The distal-most level for occult LN metastases was at least two levels ahead of the last clinically detectable evidence of the disease, however not statistically significant. Nevertheless, the depth of invasion is more important predictor for LN metastases rather than the size of the primary lesion.

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES

- [1] A. Jemal, F. Bray, M. M. Center, J. Ferlay, E. Ward, and D. Forman, "Global cancer statistics," *CA Cancer J Clin*, vol. 61, no. 2, pp. 69–90, Mar. 2011, doi: 10.3322/CAAC.20107.
- [2] A. Ferlito et al., "Prognostic significance of microscopic and macroscopic extracapsular spread from metastatic tumor in the cervical lymph nodes," *Oral Oncol*, vol. 38, no. 8, pp. 747–751, Dec. 2002, doi: 10.1016/S1368-8375(02)00052-0.
- [3] A. A. Arain et al., "Occult Nodal Metastases in Oral Cavity Cancers," *Cureus*, vol. 12, no. 11, Nov. 2020, doi: 10.7759/CUREUS.11640.
- [4] K. Y. Choi, S. C. Park, J. H. Kim, and D. J. Lee, "The occult nodal metastases rate of early tongue cancer (T1–T2): A protocol for a systematic review and meta-analysis," *Medicine*, vol. 100, no. 3, Jan. 2021, doi: 10.1097/MD.00000000000024327.
- [5] L. L. de Matos et al., "Tumor thickness as a predictive factor of lymph node metastases and disease recurrence in T1N0 and T2N0 squamous cell carcinoma of the oral tongue," *Oral Surg Oral Med Oral Pathol Oral Radiol*, vol. 118, no. 2, pp. 209–217, 2014, doi: 10.1016/J.OOOO.2014.03.023.
- [6] E. A. Dik, S. M. Willems, N. A. Ipenburg, A. J. W. P. Rosenberg, E. M. van Cann, and R. J. J. van Es, "Watchful waiting of the neck in early stage oral cancer is unfavourable for patients with occult nodal disease," *Int J Oral Maxillofac Surg*, vol. 45, no. 8, pp. 945–950, Aug. 2016, doi: 10.1016/J.IJOM.2016.03.007.
- [7] L. Bertero et al., "Eighth Edition of the UICC Classification of Malignant Tumours: an overview of the changes in the pathological TNM classification criteria—What has changed and why?," *Virchows Archiv*, vol. 472, no. 4, pp. 519–531, Apr. 2018, doi: 10.1007/S00428-017-2276-Y/TABLES/2.

- [8] A. Sparano, G. Weinstein, A. Chalian, M. Yodul, and R. Weber, "Multivariate predictors of occult neck metastases in early oral tongue cancer," *Otolaryngology - Head and Neck Surgery*, vol. 131, no. 4, pp. 472–476, Oct. 2004, doi: 10.1016/j.otohns.2004.04.008.
- [9] K. Sagheb et al., "Cervical Metastases Behavior of T1-2 Squamous Cell Carcinoma of the Tongue," *J Maxillofac Oral Surg*, vol. 16, no. 3, pp. 300–305, Sep. 2017, doi: 10.1007/S12663-016-0936-0.
- [10] S. Vishak and V. Rohan, "Cervical node metastases in T1 squamous cell carcinoma of oral tongue- pattern and the predictive factors," *Indian J Surg Oncol*, vol. 5, no. 2, pp. 104–108, 2014, doi: 10.1007/S13193-014-0301-Z.
- [11] A. Warshavsky et al., "Assessment of the Rate of Skip Metastases to Neck Level IV in Patients With Clinically Node-Negative Neck Oral Cavity Squamous Cell Carcinoma: A Systematic Review and Meta-analysis," *JAMA Otolaryngol Head Neck Surg*, vol. 145, no. 6, pp. 542–548, Jun. 2019, doi: 10.1001/JAMAOTO.2019.0784.
- [12] H. Inoue et al., "Quality of Life After Neck Dissection," *Arch Otolaryngol Head Neck Surg*, vol. 132, no. 6, pp. 662–666, Jun. 2006, doi: 10.1001/ARCHOTOL.132.6.662.
- [13] S. O. Short, J. N. Kaplan, G. E. Laramore, and C. W. Cummings, "Shoulder pain and function after neck dissection with or without preservation of the spinal accessory nerve," *The American Journal of Surgery*, vol. 148, no. 4, pp. 478–482, 1984, doi: 10.1016/0002-9610(84)90373-8.
- [14] D. Remmler et al., "A prospective study of shoulder disability resulting from radical and modified neck dissections," *Head Neck Surg*, vol. 8, no. 4, pp. 280–286, 1986, doi: 10.1002/HED.2890080408.