The Journal of Laryngology & Otology (2016), ***130***, *474–477*.

doi:10.1017/S0022215116000931

MAIN ARTICLE

Occult level IV metastases in clinically node-negative patients with oral tongue squamous cell carcinoma

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Abstract

Objective: The present study was conducted to determine the rate of level IV lymph node involvement among node-negative (N_0) necks in patients with squamous cell carcinoma of the tongue.

Methods: The study comprised 32 patients with squamous cell carcinoma of the tongue, with tumour–node–metastasis staging of $T_{1-3}N_0M_0$, who were admitted to the Otolaryngology Department at Tehran University of Medical Sciences from March 2012 to March 2014. After a complete diagnostic evaluation, wide primary tumour excision (with 1.5–2 cm margins) and extended supraomohyoid neck dissection (levels I–IV) were accomplished.

Results: Occult metastasis was found in 28 per cent of the patients. Level I, II and III metastases were the most common (18.75, 18.75 and 15.62 per cent, respectively). Level IV metastasis was found in 6.25 per cent of patients.

Conclusion: Supraomohyoid neck dissection appears to be an appropriate treatment for N_0 tongue squamous cell carcinoma and there is no need for level IV lymph node dissection in a N_0 patient.

Key words: Metastasis; Neck Dissection; Tongue; Glossectomy; Squamous Cell Carcinoma

Introduction

Oral cavity cancers (including tongue lesions) are common worldwide.[1] The mean age of patients with an oral cavity cancer is 64 years and there is a male predominance. However, oral tongue squamous cell carcinoma (SCC) (when compared with other oral cavity SCCs) is more frequent in patients aged 35 years or younger.[2]

Nodal metastasis is one of the most important prognostic factors in oral tongue SCC.[3] Forty per cent of patients with oral tongue SCC show cervical metastases at first presentation. Even in patients with T_1 and T_2 tumours with a clinically node-negative (N_0) neck, 20–30 per cent of the specimens reveal pathological involvement.[2] The treatment of an N_0 neck in early-stage oral tongue carcinoma is controversial. In a study by Byers *et al.*, 15.8 per cent of the lateral tongue carcinoma patients had 'skip metastases' to lymph nodes of level III or IV.[4] Hence, level I–IV (extended supraomohyoid) elective neck dissection was recommended in patients with early-stage disease. However, in another study, similar outcomes were demonstrated following selective level I, II and III (supraomohyoid) neck dissection in patients with N_0 necks.[3]

The existing evidence indicates controversy regarding the extension of occult metastasis in early tongue carcinoma. It is unclear whether there is involvement of only levels I, II and III, or whether there is also frequent involvement of level IV. This study was carried out to determine the incidence of occult metastases in patients with oral tongue SCC and to detect the pattern of cervical node metastases.

Materials and methods

In this prospective study, all patients with SCC of the oral tongue, referred to Imam Khomeini Hospital Complex from March 2012 to March 2014, were investigated. Patients with a clinically and radiologically staged N_0 neck were included in the study. Neck ultrasonography and computed tomography or magnetic resonance imaging were used for radiological examinations. The exclusion criteria were: the presence of any clinically or radiologically positive cervical lymph node; a history of previous radiotherapy or neck surgery; recurrent tumour; the presence of medical contraindications for surgery; and distant metastasis. All

Accepted for publication 29 December 2015

patients filled out the formal consent form to participate in the study.

Thirty-two patients with tumours staged T_{1-3} and with an N_0 neck were included in this study. All patients were treated surgically with a partial glossectomy and extended supraomohyoid (level I–IV) neck dissection. The primary tongue lesion was excised with a margin of 1.5–2 cm; disease-free surgical margins were confirmed using frozen section analysis. The surgeon used methylene blue to mark the exact limit of levels III and IV with regard to omohyoid muscle. Immediately following the surgery, the neck dissection specimen was divided by the surgeon and the boundary of each level was determined according to anatomical landmarks. The neck specimens were sent for pathological assessment in four different containers comprising tissues from levels I to IV. The tongue lesion was also examined pathologically, and the size, thickness, margins of resection, and perineural or lymphovascular invasion of the tumour were determined. All procedures contributing to this work complied with the Helsinki Declaration of 1975, as revised in 2008.

Results

There were 32 patients in this study, including 20 men (62.5 per cent) and 12 women (37.5 per cent). The patients' ages ranged from 21 to 89 years (average, 54.41 years). The largest diameter of tongue lesions ranged from 0.7 to 6 cm (average, 1.9 cm). About 60 per cent of the patients had a lesion smaller than 2 cm. The thickness of the tumour ranged from 0.6 to 2 cm (average, 1.28 cm). The majority of the lesions (78.2 per cent) were on the lateral aspect of the oral tongue.

The primary tumour was staged as T_1 in 19 patients (59.4 per cent), T_2 in 12 patients (37.5 per cent) and T_3 in 1 patient (3.1 per cent).

Histopathological examination of the neck dissection specimens ($n = 32$) revealed lymph node metastases in 9 patients (28.12 per cent). Levels I, II and III were involved in six (18.75 per cent), six (18.75 per cent) and five patients (15.62 per cent), respectively. Two patients had metastases in level IV nodes (6.25 per cent). There was no significant relationship between tumour (T) stage and level IV involvement ($p = 0.9$), or between tumour thickness and level IV involvement ($p = 0.2$). The potential risk factors for level IV involvement are shown in Tables I–III.

TABLE I
LYMPHOVASCULAR AND PERINEURAL INVASION, AND LEVEL IV INVOLVEMENT

Invasion type	Total *n* (%)	Level IV involvement (*n*)*
Lymphovascular	6 (18.7)	0
Perineural	8 (25)	0

*There were two patients without lymphovascular invasion and without perineural invasion that had level IV involvement, but there was no significant relationship between these two parameters and level IV involvement.

TABLE II
SMOKING AND ALCOHOL CONSUMPTION, AND LEVEL IV INVOLVEMENT

Variable	Total *n* (%)	Level IV involvement (*p*-value)
Smoking	17 (53.1)	>0.05
Alcohol consumption	6 (18.7)	>0.05

There was no significant relationship between the site of the tongue lesion and the rate of level IV involvement, and no significant relationship was found in terms of sex.

One patient out of two in this series with level IV involvement had skip metastases to this level. Therefore, the rate of skip metastases was found to be 3.125 per cent.

Discussion

There is a high incidence of occult metastasis in early-stage carcinoma of tongue. A study by Samuel *et al.* reported an incidence of occult metastasis of 40 per cent (as cited in Akhtar *et al.*[3]). Yuen *et al.* reported a 27 per cent incidence of micrometastasis,[3] and Akhtar *et al.* reported a rate of 32 per cent.[3] In the present study, the incidence of occult metastasis was 28.12 per cent.

In recent years, there has been disagreement about the extension of elective neck dissection in tongue cancer patients with an N_0 neck. Before 1997, the usual procedure was supraomohyoid neck dissection which includes nodes in levels I, II and III.[4] In 1997, the term 'extended supraomohyoid neck dissection' was introduced by Byer *et al.*[4] They demonstrated skip metastases to lymph nodes in level IV in 15.8 per cent of the patients with oral tongue cancer. This finding suggests that supraomohyoid neck dissection is not sufficient for such patients. Therefore, the authors recommended dissection of level IV lymph nodes in addition to dissection of level I–III nodes in any patient with oral tongue cancer and an N_0 neck.[4] In addition, several studies have shown a low risk of occult metastases to level IV.[3]

Dogan *et al.* found out that among 40 clinically staged N_0 patients with oral tongue SCC, 7 (17.5 per cent) had metastatic lymph nodes on pathological examination, but there was no occult metastasis in level IV.[5] Akhtar *et al.* reported no skip metastases involving level IV.[3] Level IV involvement alongside other levels (I, II and III) was only observed in four patients (13 per cent). Khafif *et al.* showed metastases to level IV lymph nodes in 4 per cent of patients with T_{1-3} and N_0 oral tongue cancer, but found no skip metastases to this level.[6] In a study by Nithya *et al.*, the incidence of isolated level IV involvement was 0 per cent, and its involvement simultaneously with level III was 6.6 per cent.[7] In our study, skip metastases

https://doi.org/10.1017/S0022215116000931 Published online by Cambridge University Press

TABLE III
PATIENTS' CHARACTERISTICS ACCORDING TO LEVEL IV INVOLVEMENT

Level IV involvement	Average age (years)	Average tumour thickness (cm)	Involved lymph nodes in other levels (*n*)	Tumour (T) stage (*n*)
Involved	50.5	1.3	7.5	$T_1 = 1$; $T_2 = 1$
Not involved	54.67	1.1	0.3	$T_1 = 18$; $T_2 = 11$; $T_3 = 1$
p-value	0.75	0.2	>0.05*	0.9

*There was no significant relationship between the involvement of different levels of the neck (levels I, II and III) and the involvement of level IV.

involving level IV was found in only one patient (3.125 per cent) and the overall incidence of level IV involvement was 6.25 per cent.

Khafif *et al*. analysed the results of Byer and colleagues' study and noted that if patients with clinically positive neck nodes were excluded, the real incidence of skip metastases or subsequent recurrence in level IV might decrease to only 4.8 per cent.[6]

In a study by Woolgar, the incidence of histologically confirmed metastatic disease was 21 per cent (32 of the 152 sides of N_0 necks) in patients with oral cavity or oropharyngeal SCC.[8] Four patients with an unpredictable distribution of metastasis had tongue tumours (three cases of lateral tongue disease and one case of ventral tongue disease), including one case of microscopic 'peppering' of levels II to IV, two cases of 'skipping' to level IV, and one case of skipping from level II to IV. The author reported that about 70 patients out of 189 had oral tongue cancer, but the number of patients in this group assumed to have a clinically staged N_0 neck was not obvious.[8] The findings of Woolgar's study were used to support the necessity of level IV dissection in oral tongue SCC patients with an N_0 neck in the current study. However, the real incidence of level IV involvement in patients with oral tongue cancer and a clinically staged N_0 neck could not be estimated.

Crean *et al*. performed extended supraomohyoid neck dissection in 49 patients with oral cancer and a clinically staged N_0 neck.[9] In that series, 14 patients had oral tongue carcinoma. The authors found occult metastases of level IV in five of the pathological specimens (five patients; 10 per cent).[9] This incidence was calculated based on all the patients in the study, not just those with oral tongue cancer. Thus, it seems that our study is one of only a few to focus specifically on oral tongue cancer, and with possibly clearer results.

Kurokawa *et al*. (as cited in Wein *et al*.[2]) reported an association between occult cervical lymph node metastases and tumour depth equal to or greater than 4 mm in oral tongue SCC patients. Spiro *et al*. noted that tumour thickness, and not tumour (T) stage, is important in treatment failure and survival.[2] It is suggested that the depth of invasion can be used to determine the need for elective neck dissection in N_0 oral tongue SCC patients.[2] Perhaps it is possible to use tumour thickness as a guide for the necessity of level IV dissection in elective lymph node surgery for oral tongue cancer. In our study, no significant relationship was found between tumour thickness and level IV involvement; nevertheless, a larger sample size is needed for subsequent investigations, because the number of the patients with level IV involvement was small. In this study, there was no significant relationship between level IV involvement and tumour stage. One of the two patients with level IV involvement had positive nodes in the other levels of the neck, but there was no significant relationship between the involvement of one specific level, or the overall number of positive lymph nodes, and level IV involvement.

In this study, statistical significance was based on a small sample size. A well-designed study comprising a larger number of patients is needed to investigate this controversy further. This might entail examination of survival and recurrence rates in oral tongue cancer patients with clinically staged N_0 necks, in which patients are divided into two groups according to level IV dissection, or a systematic review.

- **Extension of elective neck dissection in tongue cancer patients with node-negative (N_0) necks is controversial**
- **In this study, level IV metastasis was found in 6.25 per cent of patients**
- **This indicates that level IV lymph node dissection is not necessary in a N_0 patient**

The present data indicate that supraomohyoid neck dissection is an acceptable surgical procedure for an oral tongue SCC patient with an N_0 neck.[10] This is because the rate of occult metastasis to level IV is less than 20 per cent, which is considered a cut-off point for elective neck treatment.[2] Therefore, the dissection of level IV in patients where there is no involvement of other levels is not yet mandatory, and can increase the risk of complications such as: thoracic or lymphatic duct injury,[9] prolonged surgical time, longer hospital stay, and elongated skin scarring.[11]

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Dr M Rabbani Anari takes responsibility for the integrity of the content of the paper
Competing interests: None declared