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MAIN ARTICLE

Patterns of cervical lymph node metastases in oral tongue squamous cell carcinoma: implications for elective and therapeutic neck dissection

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Abstract

Objectives: To determine the patterns of lymph node metastases in oral tongue carcinomas, and examine the implications for elective and therapeutic neck dissection.

Method: The study entailed a retrospective analysis of 67 patients with previously untreated oral tongue squamous cell carcinoma who had undergone simultaneous glossectomy and neck dissection.

Results: Of the 40 clinically node-negative patients, 7 patients had metastatic lymph nodes on pathological examination. No occult metastasis was found at level IV. Of the 27 clinically node-positive patients, the incidence rate of level IV metastasis was 11.1 per cent (3 out of 27 patients). No 'skip metastases' were found at level IV. Level IV metastases were significantly related to clinically staged nodes categorised as over 2a ($p = 0.03$) and metastasis to level III ($p = 0.01$).

Conclusion: Routine inclusion of level IV in elective neck dissection is not necessary for clinically node-negative patients with oral tongue squamous cell carcinoma. Furthermore, extended supraomohyoid neck dissection with adjuvant radiotherapy can be sufficient in the treatment of selected patients with clinically node-positive necks.

Key words: Tongue; Squamous Cell Carcinoma; Neck Dissection; Neoplasm Metastasis; Pathology

Introduction

The presence of lymph node metastasis diminishes locoregional control rates, and is the most important factor for prognosis in head and neck cancer.[1,2] Accurate clinical staging of the neck and the appropriate choice of neck dissection type are crucial in treatment planning.

Radical or modified radical neck dissections that include levels I–V are widely used treatments for patients with clinically positive lymph nodes (N_+). However, selective neck dissections are increasingly being used to treat select N_+ patients in order to avoid the functional and cosmetic morbidities associated with comprehensive neck dissections.

An elective neck dissection is often proposed for oral tongue cancer patients with clinically negative lymph nodes (N_0), regardless of the tumour (T) stage.[2–5] However, in patients with clinically staged N_0 oral tongue cancer, there is controversy regarding whether supraomohyoid neck dissection or extended supraomohyoid neck dissection should be performed. Supraomohyoid neck dissection is a selective neck dissection in which the submandibular lymph nodes (level I), upper jugular lymph nodes (level II) and middle jugular lymph nodes (level III) are removed.[6] Extended supraomohyoid neck dissection encompasses dissection of the lower jugular lymph nodes (level IV) in addition to supraomohyoid neck dissection. Dissection of the lower jugular lymph nodes (level IV) has been advocated as part of an elective neck dissection for oral cavity cancers because of the possibility of 'skip metastases' to level IV.[7–9] Skip metastasis is defined as metastasis to level IV without involvement of levels I–III.

An oncologically sound surgical procedure with minimum morbidity can only be achieved when the pattern of lymphatic spread is known and the type of neck dissection is chosen accordingly. In this study, we retrospectively analysed the distribution of nodal metastasis according to levels of the neck, focusing on the frequency of metastases in levels IV and V, and isolated level IV metastases, in clinically staged N_0 and N_+ patients with oral tongue squamous cell carcinoma. We aimed to investigate whether routine inclusion of level IV is necessary in elective neck dissections performed on patients with N_0 necks, and

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whether routine inclusion of level V is needed in therapeutic neck dissections performed for N_+ necks.

Materials and methods

This study was approved by the Ethical Committee for Non-Invasive Human Research at Dokuz Eylul University School of Medicine, Turkey.

The medical records of the patients who had undergone simultaneous glossectomy and neck dissection for oral tongue squamous cell carcinoma at the Department of Otorhinolaryngology Head and Neck Surgery, Dokuz Eylul University School of Medicine, between 1990 and 2011 were reviewed retrospectively. Only those patients who had neck dissections that involved levels I–IV were included in the study. Patients who had previously undergone therapy (surgery, irradiation and/or chemotherapy) were excluded.

Clinical and pathological tumour–node staging was performed according to the 2010 American Joint Committee on Cancer staging system.[10] Clinical staging of the primary tumour involved both physical examination and imaging study findings. All patients underwent computed tomography (CT) with contrast. Magnetic resonance imaging was also performed on: patients with advanced tumours, patients with infiltrative tumours with extensive induration around the tumour on palpation, or patients in whom the floor of the mouth was involved. Neck nodal staging was based on physical examination and contrast CT findings. The lymph nodes were considered metastatic if their maximum diameter was more than 10 mm, and/or if central necrosis, heterogeneous contrasting, irregular contours or peripheral soft tissue invasion were present.

The patients underwent extended supraomohyoid neck dissection that included levels I–IV, or radical or modified radical neck dissection that included levels I–V. In patients who had extended supraomohyoid neck dissection, the lymph nodes at level IV – which was bordered by the clavicle inferiorly, the sternocleidomastoid muscle posteriorly and the deep cervical fascia medially – were removed (in addition to those at levels I–III). The material dissected behind the posterior border of the sternocleidomastoid muscle was labelled as level V in patients who underwent dissection at levels I–V.

After completion of the neck dissection, the dissected material was divided into pieces according to neck levels using anatomical landmarks. It was then put into different boxes and sent for histopathological examination. All surgical specimens were examined at the Department of Pathology, Dokuz Eylul University School of Medicine, by a group of pathologists with special expertise in head and neck pathology. The sections were stained with haematoxylin and eosin, and examined under light microscopy. Immunohistochemical staining was not performed. The distributions of the lymph nodes were determined for each level of the neck. For the purposes of this study, skip metastasis was defined as cervical metastasis at level IV without involvement at levels I, II and III.

Adjuvant radiotherapy (RT) was administered to patients pathologically staged as N_+, T_3 or T_4, as well as those with positive surgical margins and those with tumours close to the surgical margins.

The follow-up data of the patients were analysed in terms of minimum, maximum and mean follow-up durations. The rate of local or regional recurrences was determined, as was the location of the recurrences.

Statistical analysis was performed using the Statistical Package for the Social Sciences version 15.0 software (SPSS, Chicago, Illinois, USA). A Fisher's exact test was used to assess the statistical significance of the relationship between the clinicopathological features of the tumour and metastases at level IV. Statistical significance was defined as $p < 0.05$.

Results

A total of 67 patients (34 males and 33 females) aged between 19 and 82 years (mean age of 58 years) underwent simultaneous primary tumour resection and neck dissection. Forty patients were clinically staged as N_0 and 27 as N_+. The distribution of patients according to T and N clinical staging is shown in Table I.

A total of 71 neck dissections were performed (67 ipsilateral and 4 contralateral). Thirty-two of these were radical or modified radical neck dissections that included levels I–V, and 39 were extended supraomohyoid neck dissections that included levels I–IV. Of the 40 elective ipsilateral neck dissections performed on the N_0 (clinically staged) necks, extended supraomohyoid neck dissection and modified radical neck dissection were performed in 29 and 11 cases, respectively. Of the 27 therapeutic ipsilateral neck dissections conducted, extended supraomohyoid neck dissection, modified radical neck dissection and radical neck dissection were performed in 7, 9 and 11 cases, respectively. Of the four contralateral neck dissections performed, two were elective (two extended supraomohyoid neck dissections) and two were therapeutic (one extended supraomohyoid neck dissection and one modified radical neck dissection).

Of the 71 neck dissection specimens evaluated, 27 indicated metastasis. Examination of the distribution

TABLE I
PATIENT DISTRIBUTION ACCORDING TO CLINICAL STAGE

Clinical tumour (T) stage	Clinical nodal (N) stage						Total
	N_0	N_1	N_{2a}	N_{2b}	N_{2c}	N_3	
T_1	17	5	0	0	0	0	22
T_2	20	9	1	2	0	0	32
T_3	3	3	0	3	1	0	10
T_4	0	1	0	1	1	0	3
Total	40	18	1	6	2	0	67

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TABLE II
DISTRIBUTION OF OCCULT LYMPH NODE METASTASES*

Metastatic level	Patients (*n*)
I only	1
II only	5
III only	1

*Distribution of pathologically positive nodes in patients with clinically negative nodes.

TABLE III
DISTRIBUTION OF IPSILATERAL LYMPH NODE METASTASES*

Metastatic level	Patients (*n*)
I only	2
II only	9
I + II	1
I + II + III	1
II + III	2
II + IV	1
III + IV	1
II + III + IV	1

*Distribution of pathologically positive nodes in patients with clinically positive nodes.

of lymph node metastases (in the 27 specimens) revealed that level II was the most commonly involved region, followed by levels III and I. The frequency of metastasis was: 81.5 per cent (22 out of 27) at level II, 25.9 per cent (7 out of 27) at level III, 18.5 per cent (5 out of 27) at level I, 11.1 per cent (3 out of 27) at level IV and 0 per cent at level V.

Of the 40 clinically staged N_0 patients, 7 (17.5 per cent) had metastatic lymph nodes on pathological examination. There was no occult metastasis in the two contralateral clinically staged N_0 necks. Occult node metastases were most commonly located in level II. Occult metastasis was found in level II only in five patients, in level I only in one patient and in level III only in one patient. No occult metastasis was found in level IV. The distribution of occult lymph node metastases in clinically staged N_0 patients is shown in Table II. Five patients with occult metastases were pathologically staged as T_2 and two were T_1.

Of the 27 clinically staged N_+ patients, 18 (66.66 per cent) had metastatic lymph nodes on pathological examination. Level II was the most commonly involved region, followed by levels III and I. The distribution of ipsilateral lymph node metastases in clinically staged N_+ patients is shown in Table III. Level IV metastasis occurred in the ipsilateral neck in three patients. Among them, one patient had level II and IV metastases, another had level III and IV metastases, and the other had level II, III and IV metastases; however, there was no isolated (skip) level IV metastasis. The characteristics of patients with level IV metastasis are shown in Table IV. There was no level IV metastasis in the two contralateral (clinically staged) N_+ necks. Of the 27 clinically staged N_+ patients, the incidence rate of level IV metastasis was 11.1 per cent (3 of 27).

Level IV metastases were significantly related to clinically staged nodes categorised as over N_{2a} ($p = 0.035$) and metastasis to level III ($p = 0.019$). The correlations between clinicopathological features and level IV metastases are shown in Table V.

Surgical margins were positive in four patients. Adjuvant RT was administered to 33 patients (49.3 per cent). The follow-up period was defined as the time from surgery to the last follow-up day or the day the patient died. The mean follow-up period was 53.6 months (range of 5–192 months). Four patients had local recurrences and two had regional recurrences during their follow-up period. Both regional recurrences occurred in the dissected neck; one was in level I and the other was in level III. There were no recurrences in levels IV or V. Distant metastasis to bone and lung developed in two patients.

Discussion

Although the distributions of lymph node metastases in clinically staged N_0 oral tongue cancers have been investigated previously, controversy still exists regarding the type and extent of the elective neck dissection that should be performed in such patients, specifically concerning whether supraomohyoid neck dissection or extended supraomohyoid neck dissection should be carried out.[11,12]

Studies investigating the lymphatic drainage pattern in oral tongue carcinoma reported that lymphatic drainage was most frequently related to metastasis at levels I–III, and occult metastasis was most commonly seen in levels I–III.[13,14] However, dissection of level IV has been recommended as part of elective neck dissection for oral tongue cancers because of the possibility of skip metastases at level IV. Although the

TABLE IV
CHARACTERISTICS OF PATIENTS WITH LEVEL IV METASTASIS

Tumour location	Clinical stage	Pathological stage	Tumour differentiation	Metastatic levels
Posterolateral	T_3N_{2c}	T_2N_{2c}	Moderate	II + IV
Lateral	T_2N_1	T_1N_{2b}	Well	III + IV
Posterolateral	T_3N_{2b}	T_2N_{2b}	Well	II + III + IV

T = tumour; N = node

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TABLE V
CLINICOPATHOLOGICAL FACTORS AFFECTING LEVEL IV METASTASIS

Factor	No level IV metastasis (*n*)	Level IV metastasis (*n*)	*p**
Clinical stage			
– T_{1-2}	53	1	0.093
– T_{3-4}	11	2	
– $\leq N_{2a}$	58	1	0.035
– $> N_{2a}$	6	2	
Level II metastasis			
– Absent	46	1	0.210
– Present	18	2	
Level III metastasis			
– Absent	60	1	0.019
– Present	4	2	
T differentiation			
– Well	41	2	1.00
– Moderate or poor	23	1	

*Fisher's exact test. T = tumour; N = node

dissection of level IV in addition to supraomohyoid neck dissection is a simple surgical procedure that can be performed in a short period of time, several authors have questioned the necessity of dissecting level IV because of the potential complications such as chyle leak and phrenic nerve injury.

Byers *et al*. studied 277 patients and reported that the rate of level III and IV metastasis without any metastasis in levels I and II was 15.8 per cent.[7] This result suggested that supraomohyoid neck dissection was not the most appropriate elective treatment for all clinically staged N_0 necks, and the inclusion of level IV dissection was recommended.

Other studies have shown quite low rates for the risk of metastasis at level IV in clinically staged N_0 patients.[12,14–18] Khafif *et al*. determined the rate of level IV metastasis as 4 per cent in clinically staged $T_{1-3}N_0$ oral tongue carcinoma.[12] Dias *et al*. reported a rate of 1.5 per cent, and found that the rate of isolated level IV metastasis was 0.5 per cent in clinically staged $T_{1-2}N_0$ oral tongue carcinoma.[15]

In our study, we did not find level IV metastasis in any of the 40 patients clinically staged as $T_{1-3}N_0$. However, we found five cases of isolated level II metastasis, one case of isolated level I metastasis and one case of isolated level III metastasis in these patients. There was no metastasis or skip metastasis at level IV in clinically staged $T_{1-3}N_0$ patients. Similar to previous studies, the incidence of metastasis and skip metastasis in level IV were quite low for the clinically staged N_0 patients in our study. Table VI summarises level IV involvement and skip metastasis rates for different series of patients with oral tongue carcinoma. With regard to $T_{1-3}N_0$ patients, our results suggest that supraomohyoid neck dissection is sufficient for the elective treatment of a clinically staged N_0 neck; routine inclusion of level IV dissection is not mandatory.

In our study, level IV metastasis was found in 3 out of 27 clinically staged N_+ patients (an incidence rate of 11.1 per cent, compared with 0 per cent for N_0 patients). One of the patients with level IV metastasis had level II and IV metastases, another had level III and IV metastases, and the other had level II, III and IV metastases; none of the patients had isolated level IV metastasis. Correlational analyses revealed that level IV metastases were significantly related to nodes clinically staged as over N_{2a} ($p = 0.035$) and metastasis at level III ($p = 0.019$). These results suggest that it is mandatory to include level IV in therapeutic neck dissection, especially where there is suspicion of metastasis at levels II and/or III.

The feasibility of selective neck dissections in lieu of comprehensive dissections for the therapeutic management of clinically staged N_+ necks has not been clarified sufficiently. Some investigators have reported similar results for supraomohyoid neck dissection and modified radical neck dissection in obtaining disease control, and have suggested that supraomohyoid neck dissection should be used in selected $T_{1-2}N_+$ patients as well as in the elective neck management of clinically staged N_0 patients.[19,20] In our study, two patients with level IV metastasis were pathologically staged as T_2 and one as T_1. The presence of level IV metastases in pathologically staged T_{1-2} patients suggests that the routine dissection of level IV is necessary in the

TABLE VI
PREVALENCES OF LEVEL IV AND SKIP METASTASES IN ORAL TONGUE CARCINOMA

Study	Year	Site	Clinical stage	Patients (*n*)*	Level IV involvement (%)	Skip metastasis (%)
Byers *et al*.[7]	1997	OT	T_{1-4}, N_0 & N_+	270	–	15.8 (for level III & IV)
Khafif *et al*.[12]	2001	OT	$T_{1-3}N_0$	17	5.9	0
Kaya *et al*.[17]	2001	OT	$T_{1-4}N_0$	58	2.8	–
Dias *et al*.[15]	2006	OT + FOM	$T_{1-2}N_0$	192	1.5	0.5
Huang *et al*.[11]	2007	OT	$T_{1-2}N_0$	37	5.4	2.7
Akhtar *et al*.[18]	2007	OT	$T_{1-2}N_0$	94	4.2	0
Balasubramanian *et al*.[16]	2012	OT	$T_{1-4}N_0$	52	3.8	1.9
Present study	2014	OT	$T_{1-3}N_0$	40	0	0
Present study	2014	OT	$T_{1-4}N_+$	27	11.1	0

*Number of patients in the study who had neck dissections that included level IV. OT = oral tongue; T = tumour; N = node; FOM = floor of the mouth

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management of N_+ necks in oral tongue cancers, regardless of T stage. However, as no level V metastasis was found in the patients who underwent radical or modified radical neck dissection, and there were no recurrences at this level, the necessity of level V dissection as part of a therapeutic neck dissection in N_+ necks is questionable.

- **The extent of neck dissection in patients with oral tongue carcinoma remains controversial**
- **In this study, isolated level IV ('skip') metastasis was not present in node-negative (N_0) or node-positive (N_+) necks**
- **Routine inclusion of level IV is not mandatory in elective neck dissection for N_0 oral tongue squamous cell carcinoma**
- **There was no level V metastasis in patients who underwent therapeutic neck dissections that included levels I–V**
- **Extended supraomohyoid neck dissection with adjuvant radiotherapy can be sufficient for selected N_+ necks**

Post-operative shoulder function can be adversely affected after modified radical neck dissection due to nerve traction or iatrogenic nerve injury, despite conservation of the spinal accessory nerve. Studies have shown significantly poorer shoulder function in patients who have undergone modified radical neck dissection, compared with those who have had selective neck dissections.[21] Selective neck dissections that do not include level V are being used with increasing frequency in lieu of comprehensive neck dissections, in order to provide the most suitable curative therapy with minimal morbidity. Lim *et al*. found level V metastasis in 5 per cent of patients who had undergone comprehensive neck dissection for oral cavity or oropharyngeal carcinoma.[22] Naiboğlu *et al*. determined level V metastasis in 6.2 per cent of clinically staged N_+ patients with oral cavity carcinoma.[23] The authors stated that selective neck dissections excluding level V could be performed in clinically staged N_+ patients in order to avoid morbidities such as shoulder dysfunction following comprehensive neck dissection. Although the results of our study suggest that extended supraomohyoid neck dissection with adjuvant RT might be sufficient in the treatment of N_+ necks, larger multicentre studies that comprise more patients are needed to further clarify this issue.

Conclusion

In our study, isolated level IV metastasis was not present in clinically staged N_0 or N_+ patients. The rate of level V metastasis was 0 per cent in pathologically staged N_+ patients. We suggest that it is not necessary to include level IV in elective neck dissection for clinically staged N_0 oral tongue cancer cases when pre-operative physical examination is complemented by careful radiological evaluation. Furthermore, the absence of level V metastasis in the pathologically staged N_+ patients suggests that extended supraomohyoid neck dissection with adjuvant RT could be sufficient in the treatment of selected clinically staged N_+ necks; however, further studies with more patients are needed to clarify this issue.

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