

Predictors of neck metastasis in early stage oral cavity cancer

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Abstract

Objective: To identify the effects of clinical and histopathological parameters on neck metastasis in early-stage oral cavity cancers.

Methods: The medical records of 92 patients who underwent primary surgical resection and concurrent neck dissection due to early-stage oral cavity squamous cell cancer at İzmir Atatürk Training and Research Hospital between June 2001 and June 2010 were retrospectively reviewed. The associations of clinical and histological parameters with neck metastasis were assessed. Based on the histological data, the histological sections of the operative tissue were obtained via the measurement of tumor width and tumor depth. Using an optical micrometer, the maximum width at the horizontal plane and the maximum depth at the vertical plane were measured and the maximum depth was recorded as tumor thickness.

Results: The association between neck metastasis and tumor localization, T stage, degree of differentiation, tumor thickness, perineural invasion, vascular invasion and perilymphatic invasion in early-stage oral cavity cancers was found statistically significant ($p < 0.05$). The value of critical tumor thickness for the neck metastasis was found to be 5.6 mm.

Conclusion: On the basis of our results, a tumor thickness of 5.6 mm is the critical value for the development of neck metastasis in oral cavity cancers. The neck metastasis risk showed a significant increase in cases where the tumor thickness exceeded this threshold value. In oral cavity cancers with a high risk of occult metastasis, the tumor thickness may be identified pre-operatively or intra-operatively and, a decision can be taken to perform neck dissection when they exceed critical values.

Keywords: Neck metastasis, oral cavity cancer, tumor thickness.

Özet: Erken evre oral kavite kanserlerinde boyun metastazının ön belirteçleri

Amaç: Erken evre oral kavite kanserlerinde klinik ve histopatolojik parametrelerin boyun metastazına olan etkilerini saptamak.

Yöntem: Erken evre oral kavite karsinomu nedeniyle İzmir Atatürk Eğitim ve Araştırma Hastanesinde Haziran 2001 ile Haziran 2010 tarihleri arasında primer cerrahi rezeksiyon ve eş zamanlı boyun diseksiyonu yapılan 92 hastanın medikal kayıtları retrospektif olarak incelendi. Klinik ve histopatolojik parametrelerin boyun metastazı ile olan ilişkileri değerlendirildi. Histolojik verilerden, tümör genişliği ve tümör derinliğinin ölçümü operatif dokunun histolojik kesitleri ile elde edildi. Optik mikrometre ile horizontal planda maksimum genişlik ve vertikal planda maksimum derinlik ölçüldü ve maksimum derinlik tümör kalınlığı olarak kayıt edildi.

Bulgular: Oral kavite kanserlerinde, tümör lokalizasyonu, T evresi, diferansiyasyon derecesi, tümör kalınlığı, perinöral invazyon, vasküler invazyon ve perilenfatik invazyon ile boyun metastazı arasındaki ilişki istatistiksel olarak anlamlı bulundu ($p < 0.05$). Boyun metastazı için kritik tümör kalınlığı değeri 5.6 mm olarak bulundu.

Sonuç: Bu çalışmanın sonuçlarına göre, oral kavite kanserlerinde boyun metastazı gelişiminde 5.6 mm tümör kalınlığı kritik değerdir. Bu değeri aşan hastalarda boyun metastazı riski belirgin olarak artmaktadır. Gizli metastaz riski yüksek olan oral kavite kanserlerinde tümör kalınlığı preoperatif ya da peroperatif olarak saptanabilir ve kritik değerleri aştığında elektif boyun diseksiyonuna karar verilebilir.

Anahtar sözcükler: Boyun metastazı, oral kavite kanseri, tümör kalınlığı.

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Squamous cell carcinoma of the oral cavity is among the most common malignant tumors of the head and neck following laryngeal cancers. Tumors of the lip, tongue, mouth floor, cheek, hard palate, retromolar trigone and gingiva demonstrate different biological behaviors due to their anatomic locations and different histological characteristics. The incidence rates differs along with the tumor site and, their geographical distribution may also show striking differences.^[1]

In spite of therapeutic developments and new protocols using advanced treatment modalities, the prognosis for patients is still poor.^[2] Early diagnosis is the most important factor for an effective treatment, which enables esthetically and functionally successful results.^[3]

The most important factor that determines prognosis in oral cavity cancers is neck metastasis. However, oral cavity cancers result in neck metastasis at a high rate in early stages. Although 'wait and see strategy' may be preferred by various authors due to potential complications of neck dissection, elective neck dissection is usually recommended for early-stage oral cavity cancers. Therefore, understanding of the clinical and histological parameters associated with neck metastasis is valuable in the management of neck in oral cavity cancer. To date, various entities including tumor site, T stage, differentiation of the tumor, tumor thickness, perineural invasion, vascular invasion, and perilymphatic invasion are associated with neck metastasis.^[4-6]

The aim of this retrospective study was to identify the clinical and histopathological parameters that influence neck metastasis in our oral cavity cancer series.

Materials and Methods

Patients

The medical records of 92 patients who underwent primary surgical resection and neck dissection due to early-stage oral cavity cancer between June 2001 and June 2010 at Izmir Atatürk Training and Research Hospital were reviewed retrospectively. Patients with recurrent tumor, previous radiotherapy or chemotherapy and previous neck dissection were excluded from the study. The patients who did not undergo neck dissection were also excluded from the study.

The demographic, treatment and clinico-pathological data of patients were retrospectively collected and reviewed.

Histological examination

The T stages, differentiation of tumor, tumor width, tumor thickness, perineural invasion, vascular invasion and lym-

phatic invasion were reviewed individually for each patient and their associations with neck metastasis were evaluated. Based on the histological data, the histological sections of the operative tissue were obtained via the measurement of tumor width and tumor depth. Using an optical micrometer, the maximum width at the horizontal plane and the maximum depth at the vertical plane were measured and the maximum depth was recorded as tumor thickness. The patients were divided into 3 groups as follows on the basis of their tumor thickness: 1: ≤ 3 mm, 2: >3 mm and ≤ 9 mm, 3: >9 mm. They were divided into 2 groups as follows on the basis of their tumor width: 1: <2 cm, 2: >2 cm and <4 cm.

Statistical analysis

The data obtained were statistically evaluated at a computer running on the Microsoft Windows XP operating system by using the SPSS package software (SPSS 18.0 for Windows; SPSS Inc., Chicago, IL, USA). Cross-charts were created in categorical variables. The analysis was performed using the chi-square test and Fisher's exact test. The normal distribution test for numerical variables was conducted using the Shapiro-Wilk test. The analysis for data with no normal distribution in numerical variables was performed using the Mann-Whitney U test. A value of $p < 0.05$ was accepted as statistically significant.

Results

The study included 92 patients who were treated with primary tumor resection and reconstruction as well as neck dissection operations due to early-stage oral cavity squamous cell cancer between the years 2001 and 2010 at the Ear-Nose-Throat Diseases and Head-and-Neck Surgery Clinic of Izmir Atatürk Training and Research Hospital.

The patients included 71 males (77.2%) and 21 females (22.8%) with a mean age of 59.50 ± 6.98 (ranged 28 to 83). The demographic and clinical characteristics of the patients were illustrated in Table 1.

In total, 141 neck dissections were performed; 49 of 92 (53.2%) patients underwent bilateral and 43 (46.8%) unilateral neck dissection. Neck metastasis was identified in 25 (27.2%) of the patients. Twenty (21.7%) patients had unilateral neck metastasis whereas 5 (5.4%) had bilateral. Neck metastasis according to primary tumor site and T stage was illustrated in Table 1. The association between tumor localization and neck metastasis was found statistically significant ($p < 0.05$). It was also determined that neck metastasis was directly proportional with the T stage. Neck metastasis was ($p < 0.05$).

Table 1. Demographic and clinical characteristics of patients.

Parameters		pN- n (%)	pN+ n (%)	Total
Sex	Male	54 (76.1)	17 (23.9)	71
	Female	13 (61.9)	8 (38.1)	21
Age	≤60	27 (62.8)	16 (37.2)	43
	>60	40 (81.6)	9 (8.4)	49
Smoking	No	15 (71.4)	6 (28.6)	21
	Yes	52 (73.2)	19 (26.8)	71
Alcohol	No	58 (74.4)	20 (25.6)	78
	Yes	9 (63.3)	5 (35.7)	14
Tumor localization	Lip	38 (88.4)	5 (11.6)	43
	Tongue	20 (60.6)	13 (39.4)	33
	Floor of mouth	4 (50.0)	4 (50.0)	8
	Retromolar trigon	2 (66.7)	1 (33.3)	3
	Buccal mucosa	1 (33.3)	2 (66.7)	3
	Alveolar arch	2 (100.0)	0 (0.00)	2
T staging	T1	33 (84.6)	6 (15.4)	39
	T2	34 (64.2)	19 (35.8)	53

pN-: no neck metastasis, pN+: presence of neck metastasis.

Histopathological parameters associated with neck metastasis were illustrated in Table 2. Tumor thickness ranged between 2 mm and 30 mm. The median tumor thickness was identified as 5 mm. The critical tumor thickness for neck metastasis was identified as 5.6 mm. Neck metastasis was not identified in any of the 24 patients (%0.00) with a tumor thickness ≤3 mm. Neck metastasis was identified in 15 (29.4%) out of 51 patients with a tumor thickness >3 mm and ≤9 mm and in 10 (58.8%) out of 17 patients with a tumor thickness >9mm. It was detected that the neck metas-

tasis was directly proportional with tumor thickness. The association between tumor thickness and neck metastasis was found statistically significant ($p<0.05$) (Table 2).

Differentiation of tumor, perineural invasion, vascular invasion, and perilymphatic invasion were also found to be statistically significant for neck metastasis.

Discussion

In this study, we assessed the clinico-pathological features of 92 oral cavity squamous cell carcinomas retrospectively and

Table 2. Histopathological parameters associated with neck metastasis.

Parameters		pN- n (%)	pN+ n (%)	Total	p value
Differentiation	Well	43 (91.5)	4 (8.5)	47	p=0.001
	Moderate	24 (61.5)	15 (38.5)	39	
	Poor	0 (0.00)	6 (100.0)	6	
Tumor thickness	≤3 mm	24 (100.0)	0 (0.00)	24	p=0.001
	>3 mm and ≤9 mm	36 (70.6)	15 (29.4)	51	
	>9 mm	7 (41.2)	10 (58.8)	17	
Perineural invasion	No	58 (77.3)	17 (22.7)	75	p=0.041
	Yes	9 (52.9)	8 (47.1)	17	
Vascular invasion	No	65 (76.5)	20 (23.5)	85	p=0.006
	Yes	2 (28.6)	5 (71.4)	7	
Perilymphatic invasion	No	67 (78.8)	18 (21.2)	85	p=0.001
	Yes	0 (0.00)	7 (100.0)	7	

pN-: no neck metastasis, pN+: presence of neck metastasis.

we found that neck metastasis was associated with various histopathological parameters.

In oral cavity cancers, tumor width is the only indicator for determining the T stage in all T staging efforts (T1–3) other than stage T4. Since cancer may spread to several different sites, the largest diameter of tumor per se does not indicate tumor aggressiveness. Several studies suggested that T staging fell short of showing nodal metastasis, local recurrence and lifetime expectancy.^[7–13] Tumor thickness is a much more significant histological marker in predicting lymph node metastasis, local recurrence and prognosis.^[7,14] Several studies revealed that there was a significant association between primary tumor thickness and clinical or sub-clinical neck metastasis.^[14–18] Our study also similarly found that tumor thickness was a better indicator in reflecting neck metastasis as compared to tumor width.

Larsen et al. assessed 144 patients with oral cavity cancers and reported that in their study tumor thickness ranged between 0.7 mm and 36 mm and median tumor thickness was 5.5 mm.^[4] In our study, tumor thickness ranged between 2 mm and 30 mm. The median tumor thickness was identified as 5 mm. The critical tumor thickness for predicting elective neck dissection in oral cavity cancers ranges between 2 mm and 10 mm according to various studies.^[18–21] The critical tumor thickness was found to be 5.6 mm in our study for neck metastasis. Considering the studies conducted on early-stage tongue cancers, tumor thickness was again found to be associated with increased neck metastasis. However, the T stage and degree of differentiation in these studies were not associated with neck metastasis.^[14,22] Similarly, tumor thickness in early-stage mouth floor cancers was found to pose an increased risk for neck metastasis while the association between T stage and neck metastasis was not found significant.^[7] These findings show that tumor thickness is more valuable in predicting tumor aggressiveness in early-stage oral cavity cancers as compared to the T stage.

The association of other histopathological parameters including perineural invasion, perivascular invasion and differentiation of tumor with neck metastasis were evaluated in great numbers of studies. While the association between perineural invasion and neck metastasis was found significant in several studies on oral cavity cancers,^[5,6,23,24] no significant associations were identified in certain studies.^[14] In the current study, perineural invasion had a significant association with increased neck metastasis. The association between perivascular invasion and neck metastasis was not found significant in a study conducted by Yuan et al.^[14]

whereas it was found significant in some other studies.^[22,24] Our study also found that the association between perivascular invasion and neck metastasis was significant in away similar to the study conducted by Suzuki et al.^[24] The study conducted by O-charoentrat et al.^[22] which included 50 patients with early-stage oral tongue squamous cancer cells, the association between degree of differentiation and neck metastasis was not identified to be significant while our study identified a significant difference.

On the basis of our results, we can propose that when a primary tumor resection is performed, the tumor thickness can be identified using a frozen sample so that a decision can be taken about whether a neck dissection can be made or not. The primary tumor thickness may be also determined via computerized tomography, magnetic resonance and ultrasound before surgery and an idea can be obtained about whether elective neck resection is required or not in addition to primary tumor resection. The primary tumor thickness that is significantly correlated with neck metastasis in oral cavity squamous cell cancers can be considered to be 4–6 mm. Elective neck dissection may be brought to the agenda in oral tongue squamous cell cancers by taking this critical tumor thickness into account.

Conclusion

According to our results, a tumor thickness of 5.6 mm is the critical value for the development of neck metastasis in oral cavity cancers. The neck metastasis risk showed a significant increase in cases where the tumor thickness exceeded this threshold value. Therefore, measurement of tumor thickness using preoperative imaging workup or postoperative histopathological examination is valuable for making decision on elective neck dissection.

Conflict of Interest: No conflicts declared.

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