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Advanced Stage Buccal Carcinoma: Effect of Local Extension on Prognosis

Ela Cömert[1], Ümit Tunçel[2], Fatih Turan[3], Caner Kılıç[2], Pınar Atabey[2]

[1]Department of Otolaryngology, Kırıkkale University School of Medicine, Kırıkkale, Turkey
[2]Department of Otolaryngology, Ankaran Oncology Training and Research Hospital, Ankara, Turkey
[3]Department of Otolaryngology, Erzincan University School of Medicine, Erzincan, Turkey

ORCID IDs of the author: E.C. 0000-0001-7739-2717; Ü.T. 0000-0002-3289-4075; F.T. 0000-0002-1242-2353; C.K. 0000-0003-2879-2524; P.A. 0000-0002-2055-8437

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BACKGROUND/AIMS
The aim of this study was to evaluate the effects of alveolar mucosa, bone, cheek skin, and lip invasion of buccal carcinoma on locoregional recurrence and survival rates.

MATERIALS and METHODS
The study included 36 patients with T3-T4a buccal carcinoma. Both T3 and T4a tumors were divided into two subgroups: T3 tumors limited to buccal mucosa, T3 tumors with the involvement of alveolar mucosa, T4a tumors with bone invasion, and T4a tumors with skin and/or lip invasion.

RESULTS
In T3-T4a tumors, the rates of tumors limited to the buccal mucosa, tumors involving alveolar mucosa, bone of either the maxilla or mandible, and skin and/or lips were 25%, 22.2%, 33.3%, and 19.4%, respectively. The 3-year disease-free survival rate of patients with T3 and T4a tumors was 70.6% and 52.6%, respectively. The 5-year disease-free survival rate of patients with T3 and T4a tumors was 58.8% and 42.1%, respectively. Regarding the 3- and 5-year survival rates, no statistically significant difference was observed between T3 and T4a tumors and between their subgroups.

CONCLUSION
Despite the lack of statistical significance, there seemed to be a trend toward worse survival among the patients with bone invasion.

Keywords: Buccal mucosa, cancer, survival

INTRODUCTION

Carcinoma of the buccal mucosa is a rare and aggressive tumor of the oral cavity. The buccal area is defined as the mucosal lining of the cheeks and lips from the oral commissure anterior to the pterygomandibular raphe and posteriorly merging with the alveolar ridges superiorly and inferiorly. The anatomic barriers within the buccal space provide almost no resistance to tumor spread, and this feature of the buccal space was shown as the major reason why buccal carcinoma acts more aggressively than those originating in other subsites in the oral cavity (1-3).

Treatment for stage I and II buccal carcinoma has been either surgery or radiation therapy as a single modality. For advanced stage tumors, surgical excision combined with postoperative radiotherapy is the main treatment modality. Therapeutic neck dissection has been performed in early stage tumors with neck metastasis and in all advanced stage tumors. (2, 4, 5).

This study was presented at the 35th National Otolarngology and Head and Neck Surgery Congress, November 2013, Antalya, Turkey.

Corresponding Author: Ela Cömert
E-mail: drelacomert@gmail.com

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The involvement of the maxilla, mandible, cheek skin, and lips lead to varied and morbid resections and may affect the prognosis of the tumor. The aim of this study was to evaluate the effects of alveolar mucosa, bone, cheek skin, and/or lip invasion of buccal carcinoma on locoregional recurrence and survival rates.

MATERIALS and METHODS

Records of patients from 2003 to 2012 were reviewed. Thirty-six patients were categorized as having T3-T4a buccal squamous cell carcinoma. Tumors with significant extension to other portions of the oral cavity or oropharynx making the primary site unclear and tumors that were not primarily treated by surgery were excluded. The medical charts were retrospectively reviewed to determine patient's age, sex, tumor site, pathologic staging, differentiation, margin status, involvement of other subsites of the oral cavity, treatment, recurrence, and survival.

All the patients were treated through en-block resection of the primary site and unilateral selective (level I-2-3), modified radical, or radical neck dissection. If the tumor was extended to the mucosa of the alveolar process and hard palate or had invaded the mandible and/or maxilla, marginal or segmental mandibulectomy and/or partial or hemimaxillectomy was performed for adequate margins. The defects were reconstructed either with full thickness skin graft or with local flaps. Selective (level I-2-3) neck dissection was performed for a clinically N0 neck, and modified radical or radical neck dissection was performed when clinically positive neck lymph nodes were detected. Tumors were staged retrospectively according to the tumor, node, metastasis (TNM) staging system, as proposed by the seventh edition of American Joint Committee on Cancer (AJCC) (6). Tumors extending to the mucosal side of the alveolar process and hard palate without bone invasion were considered T3 tumors. Tumors involving lips, skin, and bony structures of the maxilla and mandible were considered T4a tumors. All the T3 tumors were sized >4 cm, but a group of them extended to the mucosa of the alveolar process of either maxilla or mandible. Thus, T3 tumors were divided into two groups: T3 tumors limited to the buccal area and T3 tumors involving the alveolar mucosa. All the T4a tumors included in the study had either invasion of the alveolar process of the maxilla/mandible or skin/lips and hence they were also divided into two groups: T4a tumors with bone (maxilla or mandible) invasion and T4a tumors with lips and/or skin invasion.

Postoperative radiotherapy was performed on patients with pathologic T4a tumors, positive surgical margins, multiple lymph node metastasis, and extracapsular spread. Irradiation was started within 4-6 weeks post operation. Radiation dosage ranged as 60-66 Gy. The prescribed dose was 1.8-2.0 Gy per fraction per day administered 5 days a week for 6 weeks.

The study was approved by the local institutional review board. As the study was based on the retrospective analysis of the survival, patients' consent was not required.

TABLE I. Clinical and surgical parameters of 36 patients with buccal carcinoma

Variable		n	%
Sex	Male	22	61.1
	Female	14	38.9
Location	Only buccal mucosa	9	25
	Alveolar mucosa involvement	8	22.2
	Bone invasion	12	33.3
	Lips and skin invasion	7	19.4
Tumor thickness	Mean	10.4	
	≤4 mm	7	16.6
	>4 mm	29	83.3
Histological differentiation	Well	19	52.7
	Moderate	9	25
	Poor	8	22.2
T stage	T3	17	47.2
	T4a	19	52.8
N stage	N0	18	50
	N1	8	22.2
	N2	10	27.7
Excision margins (mm)	Positive	9	25
	≤5 mm	7	16.6
	>5 mm	20	55.5

T: tumor stage; n: number of patients; p: statistical analysis of recurrence rates between T3 and T4a tumors with log-rank test

TABLE 2. Summary of pathological findings by stage

T	Well differentiated	Moderately differentiated	Poorly differentiated	Positive margins
T3 buccal mucosa I	4	2	3	
T3 alveolar mucosa involvement	3	4	1	1
T4a bone invasion	7	3	2	5
T4a lip or skin invasion	5	-	2	2
Total	19	9	8	9

T: tumor stage; p: statistical analysis of disease-free survival between subgroups with log-rank test

Univariate association with disease-free survival was evaluated using the Kaplan-Meier analysis and tested using the log-rank test. Two-tailed p values of ≤0.05 were considered statistically significant. The Statistical Package for Social Sciences, version 16.0 (SPSS Inc.; Chicago, IL, USA) program was used for statistical analysis.

RESULTS

The group studied consisted of 36 patients (T3-T4a buccal carcinoma) with a mean age of 57 years (28-75 years). The

clinical and histological parameters are summarized in Table I. Of these 36 patients, 17 (47.2%) had T3 disease and 19 (52.8%) had T4a disease. The histopathology of tumor differentiation showed that most patients (52.8%) had well-differentiated tumors. The summary of the pathologic findings by stage is provided in Table 2. The distribution of tumors according to its extension to the adjacent sides of the oral cavity and skin and their N status are presented in Table 3.

Among all the tumors included to the study, the rate of T3 tumors limited to the buccal mucosa was 25% (n=9); the rates of involvement of the alveolar mucosa, bone of maxilla or mandible, and skin and/or lips were 22.2% (n=8), 33.3% (n=12), and 19.4% (n=7), respectively. A pathologic examination of the neck dissection specimens of these groups of patients revealed metastatic lymph nodes in 44.4% (n=4), 62.5% (n=5), 50% (n=6), and 42.8% (n=3) patients, respectively. In our series, 24 patients (66.7%) required adjuvant radiotherapy in addition to surgical management.

Excision of the bony structures of the hard palate and alveolar process of the mandible and maxilla was performed in 55.5% (n=20) of our patients. In the pathological examination, invasion of the bone was observed in 60% (n=12) of the patients.

The mean follow-up time for all patients was 84 months (range, 62-152). The mean time between initial treatment and locoregional recurrence for the entire group was 21.7 months (range, 9-27 months). Locoregional recurrence developed in 18 (50%) patients during follow-up. Among them, 9 (50%) had disease recurrences only at the primary sites, 4 (22.2%) had recurrences only in the ipsilateral neck, and 5 (27.7%) had simultaneous primary and neck recurrences. Five of these patients underwent salvage surgery followed by palliative radiotherapy, and the remaining received only palliative radiotherapy.

The 3- and 5-year recurrence rates of T3 tumors were 29.4% and 41.2%, respectively. The 3- and 5-year recurrence rates of T4a tumors were 47.4% and 57.9%, respectively. With regard to 3- and 5-year recurrence rates, no statistically significant difference was observed between T3 and T4a tumors based on the log-rank test (p>0.05). The data are presented in Table 4.

The 3-year disease-free survival rate of patients with T3 and T4a tumors was 70.6% and 52.6%, respectively. The difference was not statistically significant (p=0.282 using log-rank test). The 5-year disease-free survival rate of patients with T3 and T4a tumors was 58.8% and 42.1%, respectively. The difference was not statistically significant (p=0.324).

The 3-year disease-free survival rate of patients with T3 tumors limited to the buccal mucosa and T3 tumors involving the alveolar mucosa was 66.7% and 75.0%, respectively. The 5-year disease-free survival rate of patients with T3 tumors limited to the buccal mucosa and T3 tumors involving the alveolar mucosa was 66.7% and 50%, respectively. The 3-year disease-free survival rate of patients with T4a tumors with bone invasion and T4a tumors involving skin and/or lip was 50% and 57.1%, respectively. The 5-year disease-free survival rate of patients with T4a tumors with bone invasion and T4a tumors involving skin and/or lip was 33.3% and 57.1%, respec-

TABLE 3. Distribution of T-N stage

T	N0 (%)	N1 (%)	N2 (%)	Total (%)
T3 limited to buccal mucosa	5 (55.5)	2 (22.2)	2 (22.2)	9 (25)
T3 alveolar mucosa involvement	3 (37.5)	2 (25)	3 (37.5)	8 (22.2)
T4a bone invasion	6 (50)	2 (16.7)	4 (33.3)	12 (33.3)
T4a lip or skin invasion	4 (57.1)	2 (28.5)	1 (14.3)	7 (19.4)
Total	18 (50)	8 (22.2)	10 (27.8)	36

T: tumor stage; N: nodal stage

TABLE 5. Three- and 5-year disease-free survival rates of T3 and T4a tumors

T	3-year disease-free survival %	p	5-year disease-free survival %	p
T3 buccal mucosa	66.7	0.780	66.7	0.572
T3 alveolar mucosa involvement	75		50	
T4a bone invasion	50	0.732	33.3	0.397
T4a lip or skin invasion	57.1		57.1	

T: tumor stage

TABLE 4. Three- and 5-year recurrence rates of T3 and T4a tumors

		T3		T4a		Total		
		n	%	n	%	n	%	p
Three-year recurrence	Patients without recurrence	12	% 70.6	10	% 52.6	22	% 61.1	0.270
	Patients with recurrence	5	% 29.4	9	% 47.4	14	% 38.9	
Five-year recurrence	Patients without recurrence	10	% 58.8	8	% 42.1	18	% 50.0	0.317
	Patients with recurrence	7	% 41.2	11	% 57.9	18	% 50.0	

T: tumor stage; n: number of patients

tively. With regard to survival rates, no statistically significant difference was observed between T3 and T4a tumors and between the subgroups of T3 and T4a. The data are presented in Table 5.

DISCUSSION

Buccal carcinoma is a locally aggressive tumor and is associated with a poor prognosis of the high incidence of locoregional recurrence rates of 26.5%-56%, as reported in literature (1-3, 5, 6-8). The worldwide incidence of buccal carcinoma varies according to the cultural and environmental differences. There are some differences between whites and Asians, such as incidence, presenting age, and etiologic factors (1, 4). The incidence of buccal carcinoma is much higher in Asia and Taiwan because of the high prevalence of betel quid chewing (1, 7, 8). In Turkey, the major etiologic factors are cigarette and alcohol abuse, similar to European countries. This difference in the etiology may also change the prognosis particularly in advanced stage disease, as most of the tumors in the early stages can be controlled either by primary or salvage surgery.

Most of the reports in literature include every stage of buccal carcinoma regardless of extension of the tumor (1-3, 5, 7-9); hence, it is difficult to compare our results with the existing reports. Similar with our findings, the incidence of lymph node metastasis of buccal carcinoma ranged as 0%-80% for T3 tumors and 50%-63% for T4a tumors in literature (2, 3, 8).

Patients with moderately/poorly differentiated buccal carcinoma tended to present more often with N+ disease than well-differentiated tumors and had a poor survival rate (1). In contrast with previous reports, >50% of the tumors in our study were well differentiated and presented poor prognosis.

The locoregional failure rate was reported as 39.3% for patients with T1–2N0 disease treated with surgery alone (8). In our series, the locoregional control for patients with T3-T4a disease was 50% after surgery and adjuvant radiotherapy. Most recurrences in our study occurred within 2 years of primary treatment (10 [55.5%] of 18 patients), but a remarkable number of recurrences also occurred in the third year. Compared with literature, our data are within average ranges.

The 5-year disease-specific survival ranged as 31%-69% for T3 tumors and 50%-53% for T4 tumors (1, 2, 7). We observed lower survival rates particularly for T4a tumors with bone invasion. The present study confirms yet again that local recurrence is the major cause of death in particularly advanced stage oral cancer patients treated through radical surgery. All local recurrences developed at the base and edges of the flaps, infiltrated to either the pterigopalatine fossa, mandible, or pterigoid muscles and could not be diagnosed early despite a persistent clinical or radiological suspicion. Both, the presence of local flaps and fibrosis caused by radiotherapy, were the main causes of the late diagnosis of recurrence. Most of the patients refused salvage surgery and received palliative radiotherapy. Clear surgical margins could not be achieved in patients who underwent salvage surgery.

In AJCC staging, T1-3 tumors of the oral cavity are staged according to the diameter of the tumor (6). All the tumors that extended to the adjacent sides were classified as T4 tumors, but the effect of involvement of different sides on survival has not yet been examined for buccal carcinoma. Our series challenges the assumption that the involvement of the different adjacent sides portend different prognosis in advanced carcinoma of the buccal mucosa. Secondary to the low incidence of these tumors, this study is limited by a small sample size as well as by the retrospective design. The number of patients was extremely small to allow comparison of results for the involvement of all adjacent sides. The patients were divided into four groups, which mainly presented the advanced tumors limited to the buccal mucosa, tumors with invasion of adjacent mucosal sides, tumors with bone invasion, and tumors with skin invasion.

Advanced stage buccal carcinoma, even limited to buccal mucosa, has been shown to have high recurrence and low disease-free survival rates. Despite the lack of statistical significance, there seemed to be a trend toward worse survival among the patients with bone invasion. The differences in the survival, which did not have a statistical significance, could be significant if the sample size was larger. Further studies with a large number of patients are required to define the effect of involvement of different sites on prognosis.

Ethics Committee Approval: Ethics committee approval was received for this study from Ankara Oncology Training and Research Hospital (Approval No: 03.2013).

Informed Consent: Informed consent was not necessary due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

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