Carcinoma of the buccal mucosa

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OBJECTIVE: **The goal was to analyze the outcome of surgical therapy for buccal carcinoma.**
STUDY DESIGN: **A retrospective chart review was done.**
SETTING: **The study took place in a major tertiary-care hospital.**
RESULTS: **Twenty-seven patients received first-time surgical therapy for buccal carcinoma. Treatment was surgery alone in 15 and surgery followed by radiation therapy in 6 patients. Six additional patients received surgical salvage for radiation therapy failure. Composite resection of the tumor was performed in 16 patients (59%). Five-year observed actuarial survival rates were 100%, 45%, 67%, and 78%, and locoregional recurrence rates were 0%, 27%, 44%, and 0% for stages I to IV, respectively. The 5-year actuarial survival rates were 80% after surgery and 82% after surgery and postoperative radiation therapy. Patients who underwent surgical salvage after radiation therapy failure had a 1-year survival rate of 0%.**
CONCLUSION: **Aggressive surgical treatment of buccal carcinoma may result in better survival rates.**
SIGNIFICANCE: **The article analyzes buccal carcinoma in regards to the patterns of presentation, treatments rendered, and patterns of failure.** (Otolaryngol Head Neck Surg 2000;123:566-71.)

The buccal mucosa includes all the intraoral mucosal lining of the inner surface of the cheeks and lips overlying the buccal space. It extends from the line of contact of the opposing lips anteriorly to the pterygomandibular raphe posteriorly and attaches to the mucosa of the alveolar ridges superiorly and inferiorly. Although carcinoma of the buccal mucosa is the most common form of oral cancer in southern India and among the Indian population in Southeast Asia, it is uncommon in the Western world. Tobacco and alcohol use are considered the major risk factors for buccal carcinoma in the United States. In the Asian Indian population the high incidence of buccal carcinoma is believed to stem from the highly prevalent habit of chewing betel nut.[1]

Carcinoma of the buccal mucosa gains easy access to the adjacent intraoral structures such as the alveolar ridges, retromolar trigone, lips, and buccal space because of the lack of anatomic barriers. Patients may have heterogeneous involvement of adjacent oral cavity structures that may require an equally varied approach to therapy. Surgical treatment of buccal carcinoma often leads to obvious scars and disfigurement, and there may be some tendency to avoid or perform less radical forms of surgical therapy. Current philosophy on treatment of buccal carcinoma is guided by a few retrospective reviews of institutional experiences. To examine our experience with buccal carcinoma, we performed a retrospective review of patients treated surgically for the first time at our institution. We focus on the patterns of presentation and the treatments rendered, and we analyze the outcomes and patterns of failure.

METHODS AND MATERIAL

A search was performed through the records of the University of California, Los Angeles, Department of Pathology to identify all patients with biopsy-verified carcinoma involving the buccal mucosa between the years 1970 and 1990. Each patient's medical chart was reviewed to select only those with primary buccal carcinoma. Primary buccal carcinoma was defined as a malignant neoplastic process originating from the buccal mucosa. Buccal carcinomas with involvement of the adjacent oral cavity subsites were included only if it was clear from clinical records that the tumor arose from the buccal mucosa. Other oral cavity carcinomas with secondary buccal involvement, presence of synchronous carcinomas of the upper aerodigestive tract, or prior surgical therapy were excluded. A significant number of cases were referred from outside hospitals and clinics. Patients referred for failure of the tumor to respond to a course of primary radiotherapy were included.

Analysis was thus performed in all patients with carcinoma of the buccal mucosa receiving first-time definitive surgical therapy. This cohort was restaged according to the most recent recommendations of the American Joint Committee on Cancer.[2] Adequate descriptive and clinical information was available for accurate staging in all patients. The patterns of presentation, treatments rendered, locoregional recurrence,

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Table 1. Distribution of TNM stage (n = 27)

T	N0	N1	>N1
T1	2	1	0
T2	11	4	0
T3	3	1	0
T4	3	1	1
TOTAL	19	7	1

development of second primaries, and survival data were analyzed. Any oral carcinoma that arose in an area adjacent to the primary tumor within 5 years of treatment was considered a local recurrence unless it was documented as a second primary by the treating surgeon.

The life-table method was used to calculate observed and adjusted survival data. The date surgical therapy was rendered was used as the starting time for purposes of calculating survival data. There was no significant delay from diagnosis to surgical treatment in all cases. Vital and tumor status at the end of the follow-up period was available either from patient records or from the Central Tumor Registry at the University of California, Los Angeles.

RESULTS

From the initial search of the pathology database, we encountered 138 cases of carcinoma involving the buccal mucosa. Lesions originating from adjacent intraoral structures with secondary buccal involvement were excluded. This identified 31 cases (22%) of primary buccal carcinoma. Four patients with primary buccal squamous cell carcinoma were excluded from further analysis. Two had significant cardiac disease and were medically unfit to undergo surgery, and 1 had an unresectable lesion involving the pterygoid plates. These 3 patients were referred for primary radiation therapy. The fourth patient had a synchronous T1 lesion of the buccal mucosa and T2 lesion of the lateral oral tongue. Thus 27 patients received definitive surgical therapy. TNM distribution of these cases is illustrated in Table 1.

The ages of the patients ranged from 27 to 87 years (mean 67 years), and 67% were women. A significant history of smoking and alcohol consumption was present in 70% and 26%, respectively (Table 2). Other risk factors included a prior history of radium implant for a contralateral lip lesion in 1 patient and a longstanding habit of betel nut chewing in another. Follow-up until death was available in 18 patients (67%). Follow-up intervals ranged between 9 months and 18 years in the remaining 9 patients. Of these 9 patients, only 2 (both with stage IV disease) had follow-up periods of less than 5 years (9 and 42 months, respectively).

Table 2. Patient demographics by stage

	Age (y)			
Stage	Range	Mean	Smoking (%)	Alcohol (%)
I (n = 2)	64-78	71	50	0
II (n = 11)	48-87	70	55	27
III (n = 9)	27-80	63	78	22
IV (n = 5)	61-87	70	100	20
TOTAL (n = 27)	27-87	67	70	26

The most common signs and symptoms of buccal carcinoma were mass of the buccal mucosa, pain, and mucosal ulcers (Table 3). A few patients' carcinomas were diagnosed after biopsy of a leukoplakia on routine examination, and several had more advanced signs and symptoms such as trismus, ulcerations of cheek skin, and paralysis of the marginal mandibular branch of the facial nerve. All lesions were confirmed by histopathologic examination (Table 4). Most (93%) were squamous cell carcinomas. One patient had mucoepidermoid carcinoma, and 1 had verrucous carcinoma; these 2 patients were included in the study analysis.

Stage I buccal carcinoma was treated with wide local excision. By comparison, 64%, 56%, and 80% of stage II, III, and IV patients, respectively, underwent composite resection. Additional resections included 3 partial maxillectomies and 1 superficial parotidectomy in 4 stage II patients, 3 through-and-through buccal skin excisions and 1 superficial parotidectomy in 4 stage III patients, and 4 partial maxillectomies, 2 through-and-through resection of buccal skin, 1 superficial parotidectomy, and 1 partial glossectomy in 4 stage IV patients.

Seven patients had received prior radiation therapy. One had received radiation therapy 7 years earlier for ipsilateral buccal carcinoma and was considered a new case of buccal carcinoma. Of the remaining 6 patients, 2 stage II patients and 1 stage III patient underwent surgery for residual disease after radiation therapy, and 1 patient with stage II and 1 with stage III disease underwent surgery for local recurrence after primary radiation therapy. One stage IV patient did not tolerate radiation therapy and received surgery.

A summary of treatment and reconstruction rendered is presented in Table 5. Treatment was surgery alone in 15, surgery followed by radiation therapy in 6, and surgical salvage for residual or recurrent disease after radiation therapy in 6 patients. Surgical therapy was composite resection in 16 (59%) and wide local excision in 11 (41%). Among those who underwent composite resection, bone resection was marginal mandibulectomy in 11, segmental resection in 3, and hemimandibulectomy

Table 3. Major signs and symptoms of buccal carcinoma at presentation

Stage	Mass	Leukoplakia	Pain	Mucosal ulcer	Skin ulcer	Trismus	Facial paralysis
I (n = 2)	1	1	—	—	—	—	—
II (n = 11)	4	2	4	2	—	—	—
III (n = 9)	6	—	4	5	—	2	—
IV (n = 5)	5	—	1	—	2	1	1
TOTAL (n = 27)	16	3	9	7	2	3	1

Table 4. Histopathologic distribution of buccal carcinoma (n = 27)

Carcinoma type	%
Squamous cell carcinoma (n = 25)	93.0
Well differentiated	28
Moderately differentiated	48
Poorly differentiated	4
Differentiation unknown	20
Mucoepidermoid carcinoma (n = 1)	3.5
Verrucous carcinoma (n = 1)	3.5

in 2. Both cases of hemimandibulectomy were performed in stage IV patients with T4 lesions. A tracheostomy was performed concurrently with all composite resections. Neck dissections were modified radical neck dissections sparing the accessory nerve.

A summary of neck treatment is presented in Table 6. No elective neck therapy was performed for stage I disease. Neck treatment for stage II disease was no therapy in 5, elective neck dissection in 5, and postoperative radiation therapy in 1 patient. One of the neck dissection specimens was positive for metastatic tumor, worsening the diagnosis to stage III disease. Neck treatment for the 3 stage III patients with clinically negative necks was preoperative radiation therapy in the first, elective neck dissection in the second, and elective neck dissection followed by radiation therapy in the third. A positive node was found in each of the neck dissection specimens. Neck treatment for the 6 stage III patients with clinically positive neck disease was neck dissection in 4 and neck dissection followed by radiation therapy in the other 2. Multiple positive nodes were found in 2 of the neck dissection specimens, thus worsening the diagnosis to stage IV disease. Among stage IV patients, the 3 with clinically negative necks were treated with expectant management in the first, neck dissection in the second, and neck dissection followed by radiation therapy in the third. The remaining 2 patients with clinically positive necks were treated with neck dissection in one and neck dissection followed by radiation therapy in the other. The clinical stage at presentation is used for our study analysis.

Surgical margins were negative in both stage I cases. Five-year locoregional recurrence was 0% in this group. Among stage II patients, surgical margins were negative in 8 cases and close (1-4 mm) in 3 cases. One patient who had close margins and histopathologic evidence of perineural invasion received postoperative radiation therapy. One local and 2 regional failures occurred in this group. The local recurrence occurred, despite negative surgical margins, in a patient who received surgical salvage after failed radiation therapy. This recurrence was treated unsuccessfully with chemotherapy. The first regional failure occurred in a level II node in a patient whose neck received no elective therapy. This failure was treated with neck dissection, but parotid metastases developed 4 years later, and the patient rapidly died of disease despite superficial parotidectomy and radiation therapy. The second regional failure occurred as a recurrence in a level II node after initial elective neck dissection. The neck dissection specimen had been positive for metastatic disease (N1). This failure was treated unsuccessfully with radiation therapy.

Among stage III patients, surgical margins were negative in 5 cases, close (1 mm) in 2 cases, and positive in 2 cases. Three patients (1 each with positive, close, and negative margins) received postoperative radiation therapy. There were 2 local recurrences; both were in patients with positive surgical margins. The first occurred at 5 months in a patient treated with surgery alone who underwent successful salvage with local resection. The second occurred at 4.5 years in a patient treated with surgery and postoperative radiation therapy who underwent successful salvage with cryotherapy. Regional failure occurred in 2 patients. The first occurred in the dermal lymphatics of a patient who underwent surgical salvage for recurrence after radiation therapy. This patient had received composite resection with through-and-through buccal skin excision and neck dissection. The neck specimen had been negative for metastatic disease on histopathologic examination. Chemotherapy was offered to this patient, but the patient rapidly died of disease. The second regional failure occurred in the paratracheal lymph nodes in a patient after initial neck dissection and postoperative

Table 5. Summary of treatment and reconstruction

	XRT		Surgery			Closure			
Stage	Pre-operative	Post-operative	WLE	Composite	+ Other	Primary	STSG	Local flap	PMC
I (n = 2)	0	0	2	0	0	1	1	0	0
II (n = 11)	3	1	4	7	4	1	6	3	1
III (n = 9)	2	3	4	5	4	2	2	4	1
IV (n = 5)	1	2	1	4	4	0	2	3	2
TOTAL (n = 27)	6	6	11	16	12	4	11	10	4

XRT, Radiation therapy; *WLE,* wide local excision; *+ Other,* additional structures resected (see text); *STSG,* split-thickness skin graft; *PMC,* pectoralis myocutaneous flap.

Table 6. Summary of neck treatment

Stage	Neck status	None	Pre XRT	ND	ND + Post XRT	Post XRT	Total
I	N0	2	—	—	—	—	2
II	N0	**5**	—	**5**	—	1	11
III	N0	—	1	1	1	—	3
	N+	—	—	**4**	**2**	—	6
IV	N0	1	—	1	1	—	3
	N+	—	—	1	1	—	2
TOTAL	—	8	1	12	5	1	27

There were a total of 4 neck failures, and the treatment category where each occurred is indicated by *boldface.*
Pre XRT, Preoperative radiation therapy; *ND,* neck dissection; *Post XRT,* postoperative radiation therapy.

radiotherapy. This recurrence was treated unsuccessfully with paratracheal lymph node dissection and further radiation therapy. Among stage IV patients, there were no cases of locoregional failure during a follow-up period ranging from 9 months to 8 years (median 5 years).

The overall stage-specific observed actuarial 5-year survival rates were 100%, 45%, 67%, and 78% for stages I through IV, respectively (standard errors of 0%, 15%, 16%, and 20%, respectively) (Fig 1). The observed actuarial survival rate was not significantly different between stages II and III (z test = 1, $P = 0.32$, 2 tailed). The adjusted 5-year survival rates were 100%, 64%, 67%, and 78%, respectively (Fig 2). The overall determinate 5-year survival rate for all patients was 60%. Meaningful 10-year survival data were obtained in only stage II and III patients. Observed and adjusted 10-year survival rates were 13% and 35% for stage II and 40% and 50% for stage III patients, respectively. The 6 patients who received surgical salvage after failure of radiation therapy had a 1-year survival rate of 0%. Among this group, 5 died of disease, and 1 died of cerebrovascular accident in the immediate postoperative period. The actuarial 5-year survival rates in patients undergoing surgery alone (n = 15) or surgery and postoperative radiation therapy (n = 6) were 80% and 82%, respectively.

A total of 7 (26%) locoregional failures were encountered, 6 (86%) of which occurred within 6 months after surgery. The 5-year stage-specific locoregional recurrence rates were as follows: stage I, 0%; stage II, 27%; stage III, 44%; and stage IV, 0%. Five-year neck failure rates in clinically N0 and N+ necks were 11% and 25%, respectively. Second primary cancers arose within 5 years in 4 patients (15%) and during the entire follow-up period in 10 patients (37%). Nine of these 10 cases were squamous cell carcinomas involving other oral cavity sites. One was breast adenocarcinoma. No distant metastasis was encountered.

DISCUSSION

Primary buccal carcinoma is a relatively rare oral cavity neoplasm. The 70% rate of smoking in these patients is consistent with tobacco use being a risk factor. A positive history of alcohol consumption was found in only 26% and is lower than reported elsewhere. The high proportion of women in this study may account for this difference. An increasing proportion of women with oral cavity carcinoma has been noted, along with an increasing incidence of smoking and alcohol consumption in this group.[3] The previously reported female proportion with buccal carcinoma in Europe and the United States is about 35% to 45%.[3-5]

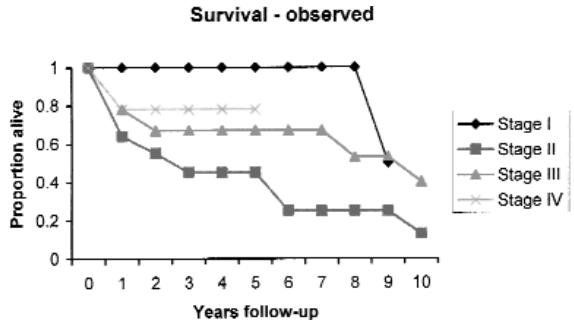

Fig 1. Observed stage-specific survival rates for patients with buccal carcinoma (life-table method).

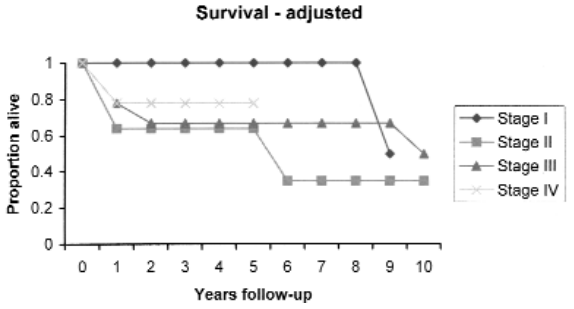

Fig 2. Adjusted stage-specific survival rates for patients with buccal carcinoma (life-table method).

However, 86% of 89 patients with buccal carcinoma reported by Urist et al[6] were female, and these authors attributed it to the high rate of snuff use among the female population in the southeastern United States.

The more common signs and symptoms of buccal carcinoma include pain and mucosal ulceration.[1] Less common signs and symptoms are trismus, skin ulceration, and facial nerve paralysis. This is associated with a growing buccal mass that patients are well aware of. A meta-analysis of this and 3 other reports where details on tumor size and clinical neck status were available (for a total of 223 cases) revealed that tumor size at presentation was as follows: T1, 12%; T2, 47%; T3, 19%; and T4, 22%.[4,7,8] The presence of clinically palpable neck nodes at presentation was 13%, 40%, 52%, and 45% for T1 to T4 lesions, respectively. In our experience, patients with T4 lesions invariably ignored or denied the growth in their buccal mucosa for 1 to 2 years.

Chemotherapeutic treatment of buccal carcinoma has been disappointing. Dhawan et al[9] randomly distributed 39 previously untreated patients into 2 groups to receive bleomycin and methotrexate or cyclophosphamide, methotrexate, and 5-fluorouracil. This cohort consisted of patients with T3 and T4 lesions. Although responses were better in the first group and partial response to therapy was seen in most, overall complete regression of the tumor was noted in only 9 (23%) patients. A vast majority needed surgical salvage. Furthermore, regression in the size of the lymph nodes was not significant in any of the patients. Other authors have reported similar findings.[10,11] However, cisplatin-based neoadjuvant chemotherapy has shown encouraging results in the treatment of advanced stage oral cavity carcinoma.[12]

Primary radiation therapy is a good therapeutic option for early buccal carcinoma. Advanced-stage tumors and tumors closer to bone fare worse with this modality alone. Nair et al[13] treated 234 patients with radical radiation therapy for cure. Delivery of radiation therapy was tailored to the cancer size and location. Overall 3-year disease-free survival rate was 42%. Three-year disease-free survival rates by stage were 85%, 63%, 41%, and 15% for stages I to IV, respectively. For all treatment types, patients with larger lesions and more advanced neck disease fared worse. For stages II through IV, primary failure was observed in 27%, 43%, and 62% and regional failure in 14%, 36%, and 42%, respectively. Patients with advanced neck disease had extremely low survival rates.

The overall determinate 5-year survival rate of 60% reported here is an improvement over other rates reported to date. In 1965 O'Brien and Catlin[14] from Memorial Sloan-Kettering Cancer Center reported an improvement of the determinate cure rate from 28% to 51% when surgery replaced radiation therapy as the preferred treatment. A 1980 report from the same institution reported a decrease in the 5-year determinate cure rate to 42%.[4] The authors noted that the presence or absence of nodal enlargement was the most significant prognostic factor. The better results obtained in this study may have resulted from the relatively lower proportion of patients with nodal disease (30%) compared with their report (59%). Our results also suggest a fairly uniform stage-specific survival rate after aggressive surgical treatment of buccal carcinoma. Others have reported lower survival rates, especially for advanced-stage disease. It should be noted that most patients in this study, including those with stage II disease, underwent aggressive composite resection. A high rate of local recurrence has been noted after wide local resection of buccal carcinoma.[5]

Although the number of patients receiving postoperative radiation therapy was small (22%), we have found similar survival rates between patients treated with surgery alone and those treated with surgery followed by radiation therapy. Others have reported the benefit of postoperative radiation therapy. Mishra et al[15] performed a prospective randomized trial comparing surgery alone versus surgery plus postoperative exter-

nal beam radiation therapy. Surgical therapy consisted of composite resection of tumor with concomitant supra-omohyoid neck dissection for clinically negative neck disease and radical neck dissection for clinically positive neck disease. The overall 3-year disease-free survival rate was 38% with surgery alone and 68% after combined therapy. Fang et al[8] reported a 3-year disease free survival rate of 62% and overall 3-year actuarial survival rate of 55% in 57 patients with stage II to IV tumors after surgery and postoperative radiation therapy.

Our experience reveals that patients treated for residual or recurrent buccal carcinoma after radiation therapy have an extremely poor prognosis. All 6 patients in this study who received surgical salvage after primary radiation therapy died within 1 year. This is noteworthy given the fact that 5 of these patients underwent radical resections consisting of composite resection and neck dissection. We encountered no reports specifically on surgical salvage after radiation therapy of buccal carcinoma.

Locoregional recurrence after definitive therapy for buccal carcinoma has invariably been reported to occur within 18 months.[7,8,11] Most (86%) locoregional recurrences in this study occurred within 6 months. The 26% rate of locoregional recurrence encountered in this study is just slightly lower than the range of 28% to 45% reported by others.[4,6,7] Neck failure did not develop in any of the 4 patients with clinically negative necks who received radiation therapy to the neck. On the other hand, regional failures occurred in 1 of 8 (13%) N0 necks treated expectantly and 1 of 7 (14%) N0 necks treated with neck dissection. Among the clinically positive necks, regional recurrence developed in 1 of 5 (20%) treated with neck dissection and 1 of 3 (33%) treated with neck dissection and radiation therapy. Pop et al[7] have also reported that neck disease did not develop in any of the clinically negative necks treated prophylactically with radiation therapy, whereas the incidence of regional failure was 21% without elective treatment. Among clinically positive necks, they reported a 27% recurrence rate after radical neck dissection and an 80% rate after radiation therapy. Ildstad et al[3] reported a 27% neck failure rate in patients with clinically N0 necks managed expectantly. Nair et al[13] reported a 7.2% neck recurrence at 3 years with expectant management.

Our study supports findings by others that oral cavity carcinomas are notorious for development of second primary neoplasms. This report found a 37% incidence during the entire follow-up period, 90% of which were squamous cell carcinomas involving the upper aerodigestive tract. Ildstad et al[3] reported a 29% incidence of metachronous or synchronous lesion; 67% occurred in the supradiaphragmatic aerodigestive tract. Strome et al[5] reported a 32% incidence, of which 56% occurred in the upper aerodigestive tract. Other reported locations for second primaries include the pancreas, stomach, lung, and thyroid. We did not encounter any distant metastases in our cases. Distant metastasis has been reported to be between 0% and 23%. Most metastases are reported to occur to the lungs and bone.[3,8]

CONCLUSION

This study found a better survival rate after aggressive surgical treatment of buccal carcinoma. The lower incidence of nodal disease and the lower locoregional recurrence rate may account for the better survival. Radiation therapy failure invariably portends poor prognosis and survival.

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