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CLINICAL INVESTIGATION **Head and Neck**

TREATMENT OUTCOME OF COMBINED MODALITIES FOR BUCCAL CANCERS: UNILATERAL OR BILATERAL NECK RADIATION?

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Purpose: To evaluate the outcome of treatment for buccal cancers and assess the impact of unilateral vs. bilateral adjuvant neck radiation.

Methods and Materials: We retrospectively reviewed the course of 145 patients newly diagnosed with buccal squamous cell carcinoma without distant metastases who completed definitive treatment between January 1994 and December 2000. Of 145 patients, 112 (77%) had Stage III or IV disease. All underwent radical surgery with postoperative radiotherapy (median dose, 64 Gy), including unilateral neck treatment in most (n = 120, 82.8%). After 1997, cisplatin-based concomitant chemoradiotherapy was given for high-risk patients with more than two involved lymph nodes, extracapsular spread, and/or positive margins.

Results: The 5-year disease-specific survival rate for Stages I–IV was 87%, 83%, 61%, and 60%, respectively (p = 0.01). The most significant prognostic factor was N stage, with the 5-year disease-specific survival rate for N0, N1, and N2 being 79%, 65%, and 54%, respectively (p = 0.001). For patients with more than two lymph nodes or positive extracapsular spread, cisplatin-based concomitant chemoradiotherapy improved locoregional control (p = 0.02). Locoregional control did not differ between patients undergoing unilateral or bilateral neck treatments (p = 0.95). Contralateral neck failure occurred in only 2.1%.

Conclusions: In patients with buccal carcinoma after radical resection, ipsilateral neck radiation is adequate. Bilateral prophylactic neck treatment does not confer an added benefit. © 2008 Elsevier Inc.

Buccal cancer, Survival, Postoperative radiotherapy, Neck treatment, Concomitant chemoradiotherapy.

INTRODUCTION

The major risk factors for oral cavity cancers are use of tobacco and alcohol and betel quid chewing (1–5). The incidence of oral cavity cancer and the commonly involved anatomic sites may vary by ethnicity, environment, and oral habits. The most common sites reported in the Western literature are the oral tongue and the floor of the mouth (6, 7). However, buccal cancer is common in South Asia and India because of betel quid chewing (4, 8–10). Frequent use of betel quid may be associated with mutations of the *ras* oncogene and *p53* tumor suppressor gene, gene defects that portend a poor prognosis (11–14). Because of the diversity among oral cavity cancers, it has been suggested that the anatomic site (6) and local culture (15) be specified when being reported.

According to the database of tumors maintained by our hospital in Taiwan, approximately 30–40% of oral cavity cancers we have seen are of buccal origin. Three fourths of the patients chewed betel quid, and most received ipsilateral neck radiotherapy. Contralateral neck prophylactic radiotherapy was not routinely given. We designed this study to review the long-term treatment outcome of buccal cancers in patients who had undergone adjuvant radiotherapy.

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METHODS AND MATERIALS

Patients and staging workup

From October 1994 to September 2000, 145 patients were newly diagnosed with nonmetastatic buccal carcinoma and underwent definitive treatment with radical surgery and postoperative radiotherapy. They were closely followed for at least 3 years or until death. The last follow-up was recorded on the basis of the last outpatient visit, a telephone interview, or the date of death.

Pretreatment workup in all patients included chest X-ray, liver ultrasound, and bone scan to exclude metastasis, as well as baseline complete blood count and biochemistry tests. Either computed tomography (CT) or magnetic resonance imaging (MRI) were used to determine tumor extent. Clinical staging was based on clinical and image findings, whereas final staging was based on the pathology report according to the 2002 American Joint Committee on Cancer staging system.

Treatment

Surgery in all patients involved composite resection of the tumor with immediate flap reconstruction. Depending on the tumor extent, marginal mandibulectomy, segmental mandibulectomy, or inframaxillectomy was performed to achieve adequate margins. Intraoperative frozen examination was performed to ensure negative margins. The definition of an adequate margin for this study was a tumor-free margin of at least 5 mm in the final pathology report.

Patients with risk factors for recurrence (i.e., advanced T stage [T3 or T4], involved lymph nodes, or inadequate margins) were given adjuvant radiotherapy by a megavoltage linear accelerator. The irradiation field included the primary tumor bed and neck lymphatics either unilaterally or bilaterally, depending on the radiation oncologist's preference. Unilateral radiotherapy was given by three-dimensional conformal techniques. Bilateral radiotherapy was given to opposing fields bilaterally with or without lower anterior neck portals. Computed tomography simulation was performed for all patients to check the postoperative status and to contour the portals. Radiotherapy was given in fractions of 1.8–2 Gy five times per week. The prophylactic dose was 46 Gy, with a 60–66-Gy boost to high-risk areas. Cisplatin-based concomitant chemoradiotherapy was given for high-risk patients after 1997. These were patients who had more than two involved lymph nodes, extracapsular spread (ECS), or positive surgical margins.

If patients recurred or developed a second primary malignancy, salvage surgery was usually performed. Adjuvant radiotherapy with or without chemotherapy was given, depending on the pathology status. If the tumor was unresectable or surgery was otherwise contraindicated, radical concurrent chemoradiotherapy was given.

Statistical methods

Time intervals were calculated from the date of radical surgery to the event of interest. Overall survival (OS) was defined as survival until death from any cause. Disease-specific survival (DSS) was survival until death from the disease *per se*, not including a second primary malignancy. Disease-free survival (DFS) was defined as the interval until either locoregional recurrence or distant metastasis. Distant metastasis-free survival (DMFS) was the interval until distant metastases were found. The type of failure was recorded as the first site of relapse, such as local, regional, distant, or any combination thereof.

Commercial statistical software (SPSS 11.0; SPSS, Chicago, IL) was used. Variables that might affect nodal or ECS status were analyzed by an independent *t* test, chi-square test, or one way analysis of variance for univariate analysis. We used Fisher's exact test if more than 25% of cases in a subgroup whose number was less than 5. Multivariate analysis was performed by binary logistic regression. Survival curves were calculated by the Kaplan-Meier method with the log–rank test for univariate analysis and Cox regression model for multivariate analysis.

RESULTS

Patients

The median age was 46.9 years (range, 25–74 years), with significant male predominance (n = 139, 95.9%). Most patients used tobacco (n = 125, 86.2%), alcohol (n = 99, 68.3%), and betel quid (n = 123, 84.8%). Only 5.5% of patients did not have any habits of smoking, drinking, or betel quid chewing. Nine patients (6.2%) had been treated previously for benign head-and-neck lesions, such as dysplasia, hyperplasia, atypia, or papilloma. The median follow-up was 4 years (range, 0.3–13 years).

Staging

One hundred eight patients (74.5%) had CT scans, 62 (42.8%) had MRIs, and 26 (17.9%) had both. The clinical stages were recorded for 144 patients before surgery. On the basis of the 2002 American Joint Committee on Cancer staging system, the final pathologic staging distribution of Stages I–IV was 5.5%, 17.2%, 17.9%, and 59.3%, respectively. The detailed T and N stage distribution is listed in Table 1. However, discrepancies between clinical and pathologic staging were not uncommon, with a difference of 43.4% for N stage and 29.7% for T stage. Approximately two thirds of patients were clinically over-staged for T, and two thirds were under-staged for N (discrepancy in T staging, $p = 0.401$; discrepancy in N staging, $p = 0.801$). The overall incidence of discrepancy did not differ significantly whether MRI or CT was used for clinical staging.

Treatment

Eighty-eight patients had elective ipsilateral neck dissection. Fifty patients had therapeutic whole-neck dissection either ipsilaterally (n = 47) or bilaterally (n = 3), for a total of 138 patients (95%) undergoing neck dissection. The remaining 7 patients underwent wide local excision without neck dissection.

Table 1. Pathologic tumor and nodal stage distribution in 145 patients with buccal cancer

	T stage				
	1	2	3	4	Total
N stage					
0	8	25	5	26	64 (44.1)
1	6	13	2	7	28 (19.3)
2	6	17	16	14	53 (36.6)
Total	20 (13.8)	55 (37.9)	23 (15.9)	47 (32.4)	145 (100)

Values in parentheses are percentages.