Sequential Therapy of Advanced Buccal Mucosa Squamous Cell Carcinoma: Three-Year Outcome

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Purpose: Squamous cell carcinoma (SCC) of the buccal mucosa is aggressive and requires multimodal treatment. The objective of this study was to evaluate the outcome of sequential therapy (neoadjuvant therapy plus surgery plus radiotherapy) in advanced buccal SCC and explore the prognostic factors.

Patients and Methods: In this retrospective cohort study, patients with advanced buccal cancer who received neoadjuvant chemotherapy (cisplatin, docetaxel, and 5-fluorouracil) followed by surgery and radiotherapy in the authors' department were reviewed. The outcomes of chemotherapy and surgery were analyzed. Overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan-Meier method. The prognostic values of age, gender, histologic grade, lymph node status, tumor stage, pathologic response, and adverse pathologic features were explored using the log-rank test and the Cox regression model.

Results: From 2008 to 2011, data from 22 patients were analyzed. The overall response rate of chemotherapy was 72.7%. The pathologic complete or partial response rate was 40.9%. The median follow-up was 36 months. The 2-year DFS and OS rates were 63.3% and 67.2%, respectively. Male and younger patients showed an association with poor outcome. Multivariate analysis showed that gender was a predictive factor with respect to DFS and OS (P = .023 and .014, respectively).

Conclusion: Sequential therapy (neoadjuvant therapy plus surgery plus radiotherapy) tends to be effective for advanced buccal cancer. Female patients have better survival.

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Squamous cell carcinoma (SCC) of the head and neck region often originates in the oral cavity, where the tongue and buccal mucosa are the most frequently affected sites. According to the database of tumors in the authors' department, SCC of the buccal mucosa represents approximately 20% of oral SCCs. Tobacco, alcohol, and betel chewing are considered major risk factors.[1,2] There are several management options for patients with buccal mucosa SCC, such as surgery and radiotherapy. However, many patients show an association with a high frequency of recurrence or metastasis, especially those at an advanced stage. Recently, some studies have reported that in advanced cases, multimodal treatment (surgery plus radiotherapy or radio-chemotherapy) yield better outcomes than surgery alone or radiotherapy alone; thus, these investigators recommended multimodal treatment for patients with advanced cancer.[1,3-5] In

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recent years, the authors have been interested in performing neoadjuvant chemotherapy before surgery and radiotherapy in advanced oral cancer, to facilitate local therapy and eliminate potential micrometastasis. The purpose of this study was to evaluate the outcome of sequential therapy (neoadjuvant chemotherapy plus surgery plus postoperative radiotherapy) for advanced buccal mucosa SCC. The authors hypothesized that advanced buccal mucosa SCC would be responsive to neoadjuvant chemotherapy and that the outcome of sequential therapy would be good. The specific aim of the study was to explore prognostic factors.

Patients and Methods

PATIENTS

Owing to the retrospective nature of this study, it was granted an exemption from informed consent in writing by the institutional review board of Shanghai Jiao Tong University (Shanghai, China). To address the research purpose, the authors designed and implemented a retrospective cohort study. The authors reviewed the records of all patients with advanced buccal mucosa SCC who were treated with sequential therapy (chemotherapy using docetaxel, cisplatin, and 5-fluorouracil [5-FU; altogether, TPF] followed by surgery and radiotherapy) in their department from May 2008 through April 2011. Evaluation of stage (according to the American Joint Committee on Cancer staging system) was based on computed tomography or magnetic resonance imaging and chest radiography.

TREATMENTS

Before local therapy, all patients received neoadjuvant chemotherapy (TPF regimen), which consisted of docetaxel (75 mg/m^2 administered intravenously on day 1), cisplatin (75 mg/m^2 administered intravenously on day 1), and 5-FU (750 mg/m^2 per day using a continuous intravenous infusion on days 1 to 5). Neoadjuvant chemotherapy was provided every 3 weeks for 2 cycles. Radical surgery was performed 2 to 3 weeks after completion of the second cycle. All patients underwent extended excision of the primary tumor and neck dissection with appropriate reconstruction. Radiotherapy was initiated 4 to 6 weeks after surgery using standard conformal or intensity-modulated radiotherapy (total dose range, 54 to 66 Gy).

STATISTICAL METHODS

Descriptive statistics were used to describe the patients' demographic, pathologic, and clinical characteristics. The primary outcome variables were disease-free survival (DFS) and overall survival (OS). OS was measured from the date of initial diagnosis to death of any cause. DFS was measured from the completion of surgery to recurrence or metastasis. OS and DFS were analyzed using the Kaplan-Meier method. The prognostic values of age, gender, histologic grade, lymph node status, tumor stage, pathologic response, and adverse pathologic features were investigated. The log-rank test was performed to test the difference in survival between subgroups. Multivariate analysis was performed using the Cox regression model. All tests were 2-sided, and a P value equal to .05 was set as the level of statistical significance. All statistical analyses were performed using SPSS 13 (SPSS, Inc, Chicago, IL).

Results

RESPONSE TO NEOADJUVANT CHEMOTHERAPY

In total, 22 patients were analyzed. All patients had stage III or IVa buccal mucosa SCC. No patients had received prior radiotherapy, chemotherapy, or surgery (except diagnostic biopsy). The patients' characteristics are listed in Table 1. Common adverse reactions included alopecia, nausea, hematologic toxicity, and altered liver function, but serious adverse effects or death did not occur. Assessment of clinical response to neoadjuvant chemotherapy by clinical examination and imaging scans was performed 2 weeks after the completion of chemotherapy. The response was characterized according to RECIST 1.0.[6] In 22 patients, the overall response rate was 72.7% (complete response [CR], 4.5%; partial response, 68.2%; stable disease,

Table 1. PATIENTS' CHARACTERISTICS (N = 22)

Characteristics	n (%)
Age (yr), median (range)	55.4 (37-75)
Gender	
Male	9 (40.9%)
Female	13 (59.1%)
Stage at time of diagnosis	
III	4 (18.2%)
IVa	18 (81.8%)
Tumor size	
T1-2	2 (9.1%)
T3	4 (18.2%)
T4	16 (72.7%)
Nodal status	
N0	4 (18.2%)
N1	13 (59.1%)
N2	5 (22.7%)
Histologic grade (biopsy)	
I	4 (18.2%)
II	17 (77.3%)
III	1 (4.5%)

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