

Close Resection Margins Do Not Influence Local Recurrence in Patients With Oral Squamous Cell Carcinoma: A Prospective Cohort Study

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Purpose: This study investigated the clinical relevance of the distance between the resection margin and tumor cells of the primary sites for oral squamous cell carcinoma, with particular attention to local recurrence rate.

Patients and Methods: All patients diagnosed with oral squamous cell carcinoma from 1995 to 2006 and treated primarily with surgery formed the initial cohort of the study. Patient with various degrees of dysplasia in the margin, patients who received radiotherapy, and patients who died of causes other than oral cancer were excluded. Margins 1 to 5 mm were considered close. A margin of at least 5 mm was considered free of disease (clear). Local recurrence was defined as tumor development at the site of the primary tumor during the follow-up period (≥ 5 yr). The Fisher exact test was used to determine the relevance of the differences between the studied groups (free vs close margins) in relation to local recurrence.

Results: Histologic analysis of the specimens was performed. Of the 53 patients, 32 had free margins and 3 of the 32 had a local recurrence. In addition, 21 patients had close margins and 3 of the 21 had a local recurrence. The difference between the 2 groups was not statistically relevant.

Conclusions: The authors advocate that the strategy of using close resection margins as a generic indicator for local recurrence and adverse prognosis might have to be reassessed. The histopathologic evidence of tumor cells within a distance less than 0.5 cm from the surgical margins does not necessarily seem to offer a certain indication for additional treatment. Other prognostic factors, such as involvement of cervical lymph nodes and tumor depth, must be considered in the decision making for further treatment.

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Surgery is the preferred and most important treatment modality for patients with oral squamous cell carcinoma (SCC). The status of the surgical margin is a prognostic factor of paramount importance that has been well reported to influence the survival rate of patients with head and neck cancer.¹⁻⁴ Surgical margins involved with tumor cells not only result in a higher risk of local recurrence but also have a negative

effect on survival.^{5,6} Achieving cancer clearance at the primary site can often become a challenge because of anatomic restrictions and tumor biological characteristics.

Despite the universally recognized importance of obtaining clear margins, the precise safe distance seems to be a matter of dispute and ambiguity. A review of the recent literature showed that the most

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widely accepted definition of a “positive” margin was evidence of microscopic tumor within 5 mm,⁷ but other studies have stated that a 3-mm⁸ or 2-mm⁹ margin should be considered a cutoff point. The presence of dysplasia or carcinoma in situ has been reported as an “involved” margin by other studies.⁴ According to guidelines from the Royal College of Pathologists in the United Kingdom, the status of surgical margins is divided into 3 groups: a margin of at least 5 mm is clear, a margin of 1 to 5 mm is close, and a margin smaller than 1 mm is involved.¹⁰

In this study, the authors used a consistent protocol in the management of patients presenting with histologically proved SCC in which surgery was offered as the primary treatment modality, with most patients undergoing wide resection of the primary tumor and simultaneous selective neck dissection. The oncologic defects were mainly reconstructed with vascularized free tissue transfer.

The purpose of this study was to investigate the clinical relevance of the distance between the resection margin and tumor cells of the primary sites for oral SCC, with particular attention to the local recurrence rate.

Patients and Methods

All patients diagnosed with oral SCC from 1995 to 2006 and treated primarily with surgery had their details entered prospectively into a computerized database. The data were meticulously collected by the senior surgeon of the unit who also had responsibility for tumor resection and overall patient care. Then, the data were analyzed retrospectively. The follow-up ranged from 5 to 11 years after initial treatment and consisted of monthly clinical visits in the first year, bimonthly visits in the second year, visits every 3 months in the third year, visits every 4 months in the fourth year, and visits twice per year in the fifth year and every year onward. The institutional review board advised that “the study is not required to be ethically reviewed under the terms of the governance arrangements for NHS Ethics committee.”⁵

The preferred method of treatment consisted of elective tracheostomy for the early postoperative period for cases in which serious edema was expected, radical resection of the primary tumor aiming for a 1-cm margin when possible, preservation of mandibular continuity by marginal mandibulectomy when suitable, and a low threshold for pull-through or lip-split and mandibulotomy techniques for access when needed. Supraomohyoid neck dissection (levels I, II, and III) was used routinely for patients with T2N0 status. Patients with SCC of the oral tongue and floor of the mouth underwent extended supraomohyoid neck dissection (levels I to IV).⁵ The TNM classification of

the Union for International Cancer Control was used for tumor staging.¹¹

This treatment protocol is in accordance with the head and neck cancer multidisciplinary team guidelines in the United Kingdom.¹² All patients were presented and discussed at a multidisciplinary tumor board composed of surgeons, radiation oncologists, medical oncologists, and other allied health care professionals dedicated to the overall treatment and prevention of head and neck cancer. Routine intraoperative frozen sections of the resection margins and an effort to deliver the specimen in continuity were the preferred techniques.

The surgical specimens were pinned out on a cork board before fixation in 10% buffered formalin. The specimens were examined in the laboratory 1 to 2 days after fixation. All histologically assessed sections were stained with hematoxylin and eosin. A margin positive for the presence of invasive SCC was considered involved. A margin with carcinoma in situ was considered involved. Margins 1 to 5 mm were considered close. A margin of at least 5 mm was considered free of disease (clear).⁵ All patients with various degrees of dysplasia at the surgical margin were excluded. Patients were offered postoperative radiotherapy dependent on the histologic outcome. Factors influencing postoperative therapy included involved margins and bone, perineural, or vascular invasion at the primary site. All patients who received radiotherapy were excluded from the study.

Local recurrence was defined as tumor development at the site of the primary tumor during the follow-up period (≥ 5 yr). All patients who died of causes other than cancer during the follow-up period were excluded. The Fisher exact test was used to determine the relevance of the differences between the studied groups (free vs close margins) in relation to local recurrence. A *P* value less than .05 was selected as the level of statistical significance.

Results

During the period studied, 178 patients (107 men and 71 women) were prospectively enlisted. The patients' mean age was 56.3 years and the most frequent age range was 70 to 79 years. Sixty-seven patients who received radiotherapy and 31 who died of causes other than oral cancer were excluded from the study. Twenty-seven patients had various degrees of epithelial dysplasia in the resection margins and were excluded. As a result, the studied cohort included 53 patients. Table 1 presents the site distribution of the tumors included in the study. Histologic analysis of the specimens was performed. Of the 53 patients, 32 had free margins and 3 of the 32 had a local

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