

Risk factors for relapse of middle-stage squamous cell carcinoma of the submandibular region and floor of mouth: the importance of en bloc resection

Zhien Feng, Qiao Shi Xu, Li Zheng Qin, Hua Li, Jin Zhong Li, Ming Su, Zhengxue Han*

Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, Capital Medical University, Beijing 100050, China

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Abstract

Our aim was to investigate retrospectively the rate of recurrence in the intervening region for middle-stage squamous cell carcinoma (SCC) of the tongue and identify the factors that predict relapse and prognosis. A total of 204 patients were included, 96 in the en bloc group and 108 in the control group. The groups were comparable. Two patients in the en bloc group (2%) and 12 in the control group (11%) developed recurrences in the intervening region. Kaplan-Meier analysis showed a reduction in the 5-year disease-specific survival once a recurrence had developed after the primary operation (77% compared with 14%, $p < 0.001$). The en bloc group developed significantly fewer recurrences (2%) than the control group (11%) during the five years; $p = 0.037$, and also had better 5-year disease-specific survival (80% compared with 66%, $p = 0.04$). Cox's multivariate regression indicated that the pathological nodal status ($p = 0.016$) and surgical technique ($p = 0.037$) were independent predictive factors for the 5-year recurrence rate, as well as of 5-year disease-specific survival ($p = 0.001$ and $p = 0.050$, respectively). Recurrence in the intervening region is a negative prognostic factor for these patients, and we recommend en bloc resection as the management of choice for middle-stage SCC of the tongue.

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Keywords: Tongue; Sublingual node; Squamous cell carcinoma; En bloc; Lymph node metastasis; Prognosis

Introduction

The tongue is the most common site of oral squamous cell carcinoma (SCC), which is liable to metastasise to the lymph nodes even in the early stages.¹ We have previously studied the best indications for neck dissection and the prognostic factors of oral SCC,^{2–8} and the results showed that middle-late oral SCC (T2–4N0–3M0) is an indication for simultaneous neck dissection, even in patients whose nodes are clear.^{2–5} However, few studies have focused on the

outcomes of treatment after different surgical approaches such as en bloc resection and discontinuous resection, or considered the importance of continuity of neck dissection with these primary tumours.⁹

En bloc dissection requires continuity between the tumour and the level I neck nodes, and involves removal of the sublingual gland and the mylohyoid muscle, together with the associated sublingual nodes.¹⁰ In a prospective study, Lee-mans et al.¹¹ found a significantly reduced recurrence rate in the submandibular area when they compared an en bloc group with a discontinuous dissection group (2/34 (6%) compared with 5/27 (19%), respectively) for stage T2 carcinomas of the tongue.

Other authors have recommended in-continuity resection of the primary site and lymph nodes, even for elective excision of oral SCC, to remove the cancer cells from the oral

* Corresponding author at: Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, Capital Medical University, No. 4 Tian Tan Xi Li, Dongcheng District, Beijing 100050, P.R. China. Tel.: +86-10-57099150; fax: +86-10-57099150.

E-mail address: hanf1989@hotmail.com (Z. Han).

cavity and along the lymphatic channels into the neck.¹² However, some authors think that en bloc resection often results in greater morbidity than discontinuous dissection. The removal of tissues from the floor of the mouth that separates the oral cavity from the neck creates an increased risk of formation of a fistula and infection, and free or pedicled flaps must be used to reconstruct the normal tissue barrier. In addition, the procedure can delay both the time to oral feeding and to postoperative radiotherapy. Removal of the intervening structures can also impair the mobility of the tongue and swallowing. To reduce the morbidity of discontinuity dissection, some authors have studied discontinuous neck dissections together with transoral partial glossectomies in patients with oral SCC, and they found no adverse effects on survival.^{9,13}

The selection of the best surgical treatment for patients with oral SCC is one that balances the cure rate and the preservation of function, and that identifies the risk factors for recurrence in the intervening area. From January 2000 to January 2010, patients with SCC of the tongue were enrolled at random into two wards in our department (ward I for the en bloc group and ward II for the discontinuous resection group) to compare the results of treatment between the two.

The purposes of this retrospective study were to evaluate the recurrence rate in the intervening region (the submandibular area and floor of mouth) and to identify the predictive factors for relapse in that region. Based on a better understanding gleaned from the results of different management options, a more strategic treatment policy may be adopted in the future.

Patients and methods

This research was conducted in full accordance with ethical principles, including the World Medical Association's Declaration of Helsinki (2002 version), and with the approval of the Institutional Review Board of the Beijing Stomatological Hospital of Capital Medical University. In addition, written informed consent was obtained from each participant.

The medical records of all the patients who were treated by primary resection of SCC of the tongue between January 2000 and January 2010 were reviewed at the Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, Capital Medical University. We reviewed the records, and then restaged the tumours according to the 2002 version of the UICC/AJCC classification, based on the initial clinical description. All primary cancers of the tongue at clinical stages T2-3N0M0 that had complete clinicopathological data were included in the study, and all the tumours were unilateral (they did not cross the midline). Patients who had had previous treatment, whose cancer involved the floor of the mouth, and who had not had a neck dissection, were excluded.

Management

In the en bloc group the mandible was split and swung, and primary tumours, sublingual gland, mylohyoid muscle, sublingual and neck nodes were resected in continuity.

In the control group (discontinuous resection): the primary tumours were removed transorally, followed by neck dissection.

If necessary the defects were reconstructed using free or pedicled flaps, the procedure being selected by the surgeons depending on local practice.

Patients who had pathologically-invaded nodes in the neck, pT3 disease, perineural infiltration, vascular emboli, and extracapsular spread, were treated with radiotherapy within 4–8 weeks. The prescribed dose was 1–2 Gy/fraction/day for 5 days/week. The total radiation dose was 66 Gy for patients with multiple invaded lymph nodes, and 60 Gy for the remainder.

Follow-up

The frequency of follow-up was explained in our previous study.² The patients had annual chest radiographs and other imaging examinations (ultrasonography, computed tomography, magnetic resonance imaging, or positron emission tomography, or a combination) were planned as necessary. Patients who had clinical signs or symptoms of discomfort could return for a visit at any time.

Statistical analysis

The follow-up study continued until 31 January 2015, and the median duration of follow-up was 82 (range 60–176) months for the survivors. We used SPSS (version 17.0, SPSS Inc, Chicago, Ill, USA) for all statistical analyses. The descriptive statistics were summarised using frequencies, percentages, and mean (SD). The baseline demographic data were compared using the chi square test for categorical variables and Student's *t* test for continuous variables. The primary outcome variable was the 5-year relapse rate of recurrence in the intervening region, the secondary outcome variable was the 5-year disease-specific survival, and the significance of differences was assessed by the log-rank test. Univariate and multivariate analyses were used to identify the independent predictors of recurrence during the five years, and the 5-year disease specific survival. Independent prognosticators were identified by Cox's multivariate regression analysis using the forward selection method. All the tests were two-tailed, and probabilities of less than 0.05 were accepted as significant.

Results

Between January 2000 and January 2010, 229 consecutive patients with previously untreated unilateral SCC of

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