Clinicopathological Analysis of Local Spread of Carcinoma of the Tongue

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BACKGROUND: The aims of the study are three-dimensional analysis of mode and distance of local spread of oral tongue carcinoma.

METHODS: The glossectomy specimens were examined in the coronal plane in 3 mm thickness section.

RESULTS: There were 50 glossectomy specimens. The maximum spread was 1.8 cm. Ninety-six percent of specimens had local spread within 1.2 cm. The distance of spread was not correlated with tumor size, including the diameter, depth, and volume. The incidence of local recurrence was 27% with positive histological margin. Perineural infiltration was the most important prognostic factor for local recurrence and survival.

CONCLUSIONS: A minimum of 1.5-cm surgical resection margin is recommended. A smaller margin is not recommended as it has significant risk of local recurrence. A maximum of 2-cm surgical resection margin is recommended; larger margins will increase the surgical morbidity without a significant advantage of local control. *Am J Surg.* 1998;175:242–244. © 1998 by Excerpta Medica, Inc.

Carcinoma of the oral tongue is well known for its high propensity for regional metastasis and poor prognosis. Although regional failure is the most common site of recurrence after surgical treatment, local recurrence is also an important cause of treatment failure after surgery.[1–8] Local recurrence can be attributed to tumor seeding during dissection, but the main cause of local recurrence is probably inadequate resection.

Irrespective to the techniques of glossectomy, the aim of surgical resection is to achieve reasonably clear resection. An optimal resection should not compromise local control from inadequate resection or cause unnecessary functional morbidity from too much resection. The aims of the present study are evaluation of the three-dimensional tumor size and local spread by using serial sectioning of glossectomy specimens of oral tongue carcinoma. The results are useful in the understanding of tumor progression and planning of surgical management of patients.

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METHODS

A total of 50 glossectomy specimens of squamous cell carcinoma of oral tongue were included for whole-organ serial sectioning from the Department of Surgery, the University of Hong Kong, Queen Mary Hospital, Hong Kong, from January 1989 to February 1995.

The glossectomy specimens were fixed on a foam board by pins during the process of formalin fixation to prevent shrinkage of tissue. The specimens were then sectioned in coronal plane into blocks of 3 mm thickness. Sections were cut from these blocks for hematoxylin and eosin stain. The slides were examined under the light microscope, and the tumors were outlined by color ink on the glass slides. The tumor width, depth, and area on each glass slide was traced and analyzed by computer (Houston Instrument Hipad Plus and Qikdraw version 3.22 Unitec Technology Ltd., Houston, Texas). The total tumor volume was calculated by adding the tumor volume of each block, which was measured by multiplying the tumor area and the thickness of the block. The distance of tumor spread and resection margin were marked under the microscope on the slides and were measured.

RESULTS

All 50 patients had squamous cell carcinoma of oral tongue. There were 28 male and 22 female patients. The median age was 56 years (range 16 to 86, SD 19). Forty-five patients received primary surgical treatment and the other 5 patients had prior radiotherapy failures with surgical salvage for local recurrence. The preoperative clinical stages were 13 T1 (12 N0, 1 N2), 28 T2 (25 N0, 3 N1), and 9 T3 (6 N0, 2 N1, 1 N2). There were 28 well-differentiated, 21 moderately differentiated, and 1 poorly differentiated squamous cell carcinomas. Of those patients who were alive without disease at the last follow-up, the mean follow-up was 31 months.

The modes and distance of local spread were analyzed in all 50 specimens and are summarized in **Table I.** The maximum distance of spread was 1.8 cm (mean 0.3 cm, 96% within 1.2 cm). There were no significant correlations between distance of local spread to tumor diameter (Pearson correlation coefficient = 0.18, $P = 0.196$), depth (Pearson correlation coefficient = 0.15, $P = 0.293$), and volume (Spearman correlation coefficient = 0.21, $P = 0.142$). The distance of spread was also not related to the pathological T stage by analysis of variance (ANOVA, $F = 1.099$, $P = 0.342$), and histological differentiation (ANOVA, $F = 0.564$, $P = 0.573$).

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TABLE I
Mode and Distance of Local Spread

Mode of Local Spread	Incidence	Maximum Distance of Spread (cm)
Submucosal direct spread	5 (10%)	0.6 cm
Intramuscular direct spread	19 (38%)	1.5 cm
Intramuscular perineural spread	6 (12%)	0.5 cm
Submucosal microsatellite spread	8 (16%)	1.2 cm
Intramuscular microsatellite spread	11 (22%)	1.8 cm

TABLE II
Resection Margin and Local Recurrence

Resection Margin (mm)	Patient Number	Local Recurrence
0	7	2 (29%)
1	8	2 (25%)
2	8	1 (13%)
3	7	0
4	7	1 (14%)
5	8	1 (13%)
6	1	0
8	1	0
10	2	1 (50%)
Total	49	8 (16%)

Of all 50 patients, 1 died of chest infection within 30 days of operation and was excluded from subsequent analysis of risk factors of local recurrence. Fifteen (30%) patients developed tumor recurrences, including 6 local, 6 nodal, 2 local and nodal, and 1 distant metastasis.

Eight (16%) patients developed local recurrence (2 local and 6 locoregional). The local recurrence rate with respect to the different resection margin is shown in **Table II.** There is a trend toward higher local recurrence rate with close histological resection margin of less than 2 mm (odds ratio = 2.27, 95% CI 0.46 to 16.47). The other risk factors of local recurrence were analyzed including T stage, tumor diameter, tumor depth, tumor area, tumor volume, differentiation, lymphatic permeation, perineural infiltration, lingual gland infiltration, sublingual gland infiltration, microsatellite spread, and tumor edge (smooth or infiltrative). Perineural infiltration was found to be the only significant risk factor for local recurrence; the local recurrence rate was 4% without perineural infiltration and increased to 30% with the presence of perineural infiltration (Fisher's test, $P = 0.018$).

At the last follow-up, 1 patient died of operative complication, 13 died of carcinoma of the tongue, 1 died of a second primary, 2 died of other causes, 2 are alive with a second primary, 31 are alive free of tumor. The overall 5-year actuarial survival rate was 71%. Perineural infiltration was found to be the only poor risk factor for survival; and the 5-year actuarial survival rates were 86% without perineural infiltration compared with 53% with presence of perineural infiltration (Wilcoxon, $P = 0.01$). Other factors including gender, age, differentiation, stage, tumor diameter, tumor depth, tumor volume, lymphatic permeation, lingual gland infiltration, sublingual gland infiltration were not significant risk factor for survival (Wilcoxon, all factors with $P > 0.05$).

COMMENTS

Tumors are three-dimensional structures. When the three-dimensional tumor size is not accurately documented, surgical resection may not be adequate, and this factor may account for the positive resection margin and local recurrence. When the tumor size is overestimated, it may result in unnecessary excess resection of normal tissue and gives rise to more surgical morbidity. There are reports on the more accurate T-staging of oral carcinoma by using ultrasound, computed tomography, and magnetic resonance imaging.[9,10] With the continuous improvement of radiological imaging facilities, three-dimensional assessment of tumor size may be more accurate in the future. These imaging modalities are, therefore, recommended for accurate staging and guidance of the distance of the resection margin from the tumor margin.

It is well documented that the incidence of local recurrence is higher with positive histological resection margin compared with negative histological resection margin in head and neck cancer. The reported incidences of local recurrence rate in positive margin ranged from 29% to 70% and were 4% to 38% for negative resection margin.[1–6] The distance of histological resection margin cannot be accurately measured unless a whole-organ serial sectioning method is employed. With the present serial sectioning method, less than a 2-mm histological margin should be considered inadequate margin, and the risk of local recurrence was high (27%). While there are reports showing no significant benefit of radiotherapy for positive margin,[1,4,6] of those reports showing benefit of reduction of local recurrence, the local recurrence rates were still higher than those patients with negative margin.[5] It is therefore important to note that postoperative adjuvant radiotherapy cannot replace the clear resection in the prevention of local recurrence. Of those patients who have histologically positive resection margin, postoperative adjuvant radiotherapy is still recommended despite the controversy of its efficacy in the literature.

Local recurrence could still occur in patients with histologically clear resection margins, and it might be due to failure of the detection of tumor histologically at the margin, skip micrometastasis to beyond the resection margin, or tumor implantation during surgery. The diagnosis of local recurrence is sometimes questionable because of the problem of the field cancerization phenomenon and of second primary tumors. The local recurrence rate of negative resection margin was 12% in the present study. Postoperative radiotherapy is not necessary with clear resection margin unless there are other reasons for the adjuvant therapy. Although we can never be certain about the completeness of surgical resection because of histological sampling error, skip micrometastasis, or tumor implantation during surgical treatment, a clear histological resection margin should be an achievable target of surgical treatment.

Although hemiglossectomy has been the standard glossectomy technique for early oral tongue carcinoma. There were, however, no anatomical features of barrier of spread found in the midline of the oral tongue in the present

study. Hemiglossectomy is therefore not recommended. In fact, hemiglossectomy irrespective to the size, depth, and site of the tumor may compromise the resection margin in large tumors or cause more morbidity with the unnecessary resection of normal tissue in small tumors. The maximum distance of local spread was 1.8 cm in 1 patient, and another patient had maximum distance of spread of 1.5 cm. All other 48 patients (96%) had maximum distance of spread of 1.2 cm or less. There were no correlations between the distance of spread with the tumor size and differentiation. Local spread of up to 1.2 cm could be found in small tumors. A surgical resection margin of less than 1.5 cm is not recommended as it will compromise the prognosis of local recurrence. On the other hand, more radical resection of more than 2-cm surgical resection margins could further increase the confidence of histological clear resection margins; the benefit of the radical resection, however, should be judged against the price of the surgical morbidity. Therefore, glossectomy with an optimal 1.5-cm to 2-cm resection margin is recommended with an over 95% confidence of clear histological resection margin.

Perineural infiltration has been reported to be a poor prognostic histological feature in head and neck cancer.[7,8] The incidence of local recurrence increases significantly with the presence of the histological feature of perineural infiltration. Perineural infiltration was found to be a more reliable prognostic factor than tumor stage, three-dimensional size, and other histological factors in the prediction of local recurrence. Perineural infiltration was also a poor prognostic factor for survival owing to the high incidence of local recurrence. Postoperative adjuvant radiotherapy may be considered in these patients. Its efficacy, however, requires further prospective study.

In conclusion, three-dimensional assessment of tumor size is important in the management of oral tongue carcinoma. A minimum of a 1.5-cm surgical resection margin is recommended; a smaller resection margin will increase the risk of local recurrence. A maximum of a 2-cm surgical resection margin is recommended, with a larger resection margin increasing the surgical morbidity without a significant advantage for local control.

REFERENCES

1. Loree TR, Strong EW. Significance of positive margins in oral cavity squamous cell carcinoma. *Am J Surg*. 1990;260:410–414.
2. van Es RJJ, van Nieuw Amerongen N, Slootweg PJ, Egyedi P. Resection margin as a predictor of recurrence at the primary site for T1 and T2 oral cancers. *Arch Otorhinolaryngol Head Neck Surg*. 1996;122:521–525.
3. Chen TY, Emrich LJ, Driscoll DL. The clinical significance of pathological findings in surgically resected margins of the primary tumor in head and neck carcinoma. *Int J Radiat Oncol Biol Phys*. 1987;13:833–837.
4. Scholl P, Byers RM, Batsakis JG, et al. Microscopic cut-through of cancer in the surgical treatment of squamous carcinoma of the tongue. *Am J Surg*. 1986;152:354–360.
5. Sadeghi A, Kuisk H, Tran LM, et al. The role of radiation therapy in squamous cell carcinoma of the upper aerodigestive tract with positive surgical margin. *Am J Clin Oncol*. 1986;9:500–503.
6. Zieske LA, Johnson JT, Myers EN, Theale PB. Squamous cell carcinoma with positive margins. *Arch Otolaryngol Head Neck Surg*. 1986;112:863–866.
7. Carter RL, Tanner NSB, Clifford P, Shaw HJ. Perineural spread in squamous cell carcinomas of the head and neck: a clinicopathological study. *Clin Otolaryngol*. 1979;4:271–281.
8. Maddox WA, Urist MM. Histopathological prognostic factors of certain primary oral cavity cancers. *Oncology*. 1990;4:39–42.
9. Campbell RSD, Baker E, Chippendale AJ, et al. MRI T staging of squamous cell carcinoma of the oral cavity: radiology-pathological correlation. *Clin Radiol*. 1995;50:533–540.
10. Fruehwald FX. Clinical examination, CT, US in tongue cancer staging. *Eur J Radiol*. 1988;8:236–241.