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Squamous cell carcinoma of the oral tongue: histopathological parameters associated with outcome

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Abstract. The purpose of this study was to investigate the applicability of the histological risk assessment model proposed by Brandwein-Gensler et al. in a cohort of oral tongue squamous cell carcinoma (OTSCC) patients treated with definitive surgery. We also examined the impact of additional histopathological features on disease acceleration. The cases of 49 OTSCC patients attending our institution between 1995 and 2009, who underwent definitive surgical resection followed by adjunct chemoradiotherapy when indicated, were reviewed retrospectively. Surgical resection specimens and complete clinical and demographic data were available for these patients; follow-up was at least 6 months. In this cohort we only identified a correlation between gender and the histopathological risk model score ($P < 0.001$). With regard to clinical and demographic data, histopathological parameters, and disease status at last follow-up, we identified significant correlations between disease status and (1) grade of differentiation ($P = 0.0086$), and (2) keratin score ($P = 0.026$). We found no significant correlations between the histopathological risk assessment model and disease progression or outcomes, with the exception of gender ($P < 0.0001$). Grade of differentiation, keratin score, and the lymphocytic host response significantly impacted disease acceleration. For OTSCC, it appears that clinical characteristics of the tumour as well as histopathological markers play an important role in the outcome. Efforts towards identifying predictive markers should be continued, especially by sub-site of the oral cavity.

Keywords: squamous cell carcinoma; oral tongue; histopathological markers; outcomes.

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Squamous cell carcinoma (SCC) is the most common malignancy in the head and neck region and specifically in the oral cavity. The incidence varies significantly worldwide, with a global incidence estimated at 275,000 new cases per year. It was estimated that there would be 42,440 new oral cavity/oropharynx cases and 8390 related deaths in the USA in 2014.[1] Despite current advances in diagnosis and treatment, the 5-year survival remains poor at

62.7% in the USA and below 50% in other countries.

Over the years, multiple grading systems and histopathological findings have been explored as predictors of the outcome in head and neck SCC. Thus far none of these have been universally adopted.[2–5] In 2005, Brandwein-Gensler et al. introduced a histological risk assessment model to predict the prognosis and survival.[6] This histological risk assessment model has been validated by the same group and by others, yet subsequent studies have not shown the same predictive value in oral cavity tumors.[7–12] The model is based on the evaluation of the surgical specimen for three histopathological parameters: worst pattern of invasion (WPOI), lymphocytic host response (LHR), and perineural invasion (PNI). It has been shown that this model is able to identify patients with head and neck cancers at high risk of local regional recurrence and poor survival.

The purpose of the study was to investigate the applicability of the histological risk assessment model proposed by Brandwein-Gensler et al. in a cohort of oral tongue (OT) SCC patients treated with definitive surgery. In addition we examined the impact of additional histopathological features originally described by Brandwein-Gensler et al.[6] in disease acceleration.

Materials and methods

This was a retrospective review of OTSCC patients treated with definitive surgery in our institution between 1995 and 2009. The oral tongue is defined as the portion that comprises the dorsal, lateral, and ventral two-thirds, anterior to the circumvallate papillae. Forty-nine patients with a diagnosis of OTSCC who underwent definitive surgical resection, followed by adjunct chemoradiotherapy when indicated, were included in this review. Additional inclusion criteria were the availability of surgical resection specimens for examination, complete clinical and demographic data, and follow-up of at least 6 months. The institutional review board for human subject research reviewed and approved the study.

Patients

The electronic medical records were retrieved by one of the authors (TS). Demographic and clinical data were collected from the electronic medical records by the same author and included age, gender, ethnicity, social history as related to alcohol and tobacco use, final pathological TNM classification, disease status at last follow-up, and survival.

Histopathological parameters

The surgical specimens were retrieved and reviewed independently by two pathologists (DC and SP) for the following: WPOI, LHR, PNI, keratin, grade, foreign body reaction, eosinophilia, and lymphovascular invasion. Point assignment was calculated and each case was designated as 'low', 'intermediate', or 'high' risk according to the Brandwein-Gensler et al. histological risk assessment model.[6] The two pathologists were calibrated for examination of the specimens for the specific histopathological criteria and point assignment prior to reviewing the cases. When there was disagreement between the two reviewers (2/49 cases) the worst designation was chosen for analysis. The final histopathological staging after tumour resection was used for staging purposes.

Statistical analysis

Correlations between the histopathological risk model prediction and actual outcomes were assessed by cross-tabulation and χ^2. For the statistical analysis the 'intermediate' and 'high' risk groups were combined and compared to 'low' risk for all disease stages (I–IV).

The Weibull accelerated failure time model was used to fit the data for the 49 patients, of whom 31 were right-censored. The covariates for the model were selected by individually fitting each covariate against survival time in months and selecting covariates with P-values less than 0.25 for at least one category. All calculations were done using SAS 9.2 (SAS Institute, Cary, NC, USA).

Results

Of the cohort of 49 OTSCC patients, 33 were men and 16 were women. They were aged between 18 and 80 years (mean age 55 years). With regard to ethnicity, 27 were Caucasian, 17 Black, four Hispanic, and one was of another race. Thirty-nine were smokers, 25 of whom were also consumers of alcohol. The stage distribution of the cancers was as follows: 14 stage I, 10 stage II, 7 stage III, and 18 stage IV (Table 1). Follow-up ranged from 6 to 84 months with a mean follow-up of 63 months. Status at last follow-up was reported as either 'free of disease' or 'disease progression'. Eighteen patients (36.7%) were reported to have disease progression at last follow-up and all died of disease within the first 24 months after treatment. The remaining 31 patients (63.3%) were reported to be free of disease.

The histological risk assessment model score of Brandwein-Gensler et al. assigned to the tumours in each stage were as follows: stage I: low risk $n = 1$, intermediate risk $n = 5$, high risk $n = 8$; stage II: low risk $n = 1$, intermediate risk $n = 2$, high risk $n = 7$; stage III: low risk $n = 2$, intermediate risk $n = 2$, high risk $n = 3$; stage IV: low risk $n = 3$, intermediate risk $n = 5$, high risk $n = 10$ (Table 2).

Correlations between the histological risk assessment model scores and clinical

Table 1. Demographic and clinical data.

Sex	
Male	33 (67.3%)
Female	16 (32.7%)
Ethnicity	
Caucasian	27 (55.1%)
Black	17 (34.7%)
Hispanic	4 (8.2%)
Other race	1 (2.0%)
Alcohol and tobacco use	
Tobacco	39 (79.6%)
Tobacco and alcohol	25 (51.0%)
Disease stage	
I	14 (28.6%)
II	10 (20.4%)
III	7 (14.3%)
IV	18 (36.7%)

Table 2. The Brandwein-Gensler et al. histological risk assessment model score assignment per stage and status at last follow-up.

	Stage I	Stage II	Stage III	Stage IV
Risk model assignment				
Low risk	1	1	2	3
Intermediate risk	5	2	2	5
High risk	8	7	3	10
Status at last follow-up				
Disease-free	11	8	3	9
Disease progression	3	2	4	9