

# Prognostic Factors in Malignant Sublingual Salivary Gland Tumors

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**Purpose:** The present study identified the prognostic factors and outcomes for malignant sublingual salivary gland tumors, which are rare.

**Materials and Methods:** A retrospective cohort study of patients treated for malignant sublingual salivary gland tumors from 1997 to 2011 was performed. The predictor variables, including age, gender, tumor stage, nodal stage, perineural invasion, margin status, and lymphovascular invasion, were analyzed. The Cox regression model was used to determine the prognostic factors for locoregional recurrence, distant metastasis, and survival.

**Results:** Of the 38 patients, 16 (42.1%) were men. Their mean age was 53 years (range 36 to 75). A total of 11 patients (28.9%) had T3-T4 tumors, and 6 (15.8%) had positive neck lymph nodes. The recurrence rate at 5 years was 18.4%. The distant metastasis rate at 5 years was 23.7%. Multivariable analysis confirmed the independent prognostic importance of patient age, N stage, and limited tongue mobility in locoregional recurrence and mortality at 5 years.

**Conclusions:** Our results suggest that patient age, N stage, and limited tongue mobility are useful as independent predictors of locoregional recurrence and mortality in patients with malignant sublingual salivary gland tumors.

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Malignant salivary glands are estimated to comprise 3 to 10% of all head and neck cancers.<sup>1</sup> Brunshwig<sup>2</sup> reported a case of a 60-year-old woman with a malignant mixed tumor on the right sublingual gland in 1930, which was the first reported case of a malignant tumor of the sublingual gland. Sublingual salivary gland neoplasms are extremely rare, representing 0.3 to 5.2% of all epithelial salivary tumors and approximately 1.5% of all major salivary gland carcinomas.<sup>3,4</sup>

Despite their rarity, most sublingual tumors are malignant, and adenoid cystic carcinoma (ACC) and mucoepidermoid carcinoma (MEC) are the most common histopathologic types.<sup>5,6</sup> Investigators have reported rare tumors, including acinic cell carcinoma, polymorphous low-grade adenocarcinoma, basal cell carcinoma, salivary duct carcinoma, malignant lymphoma, and squamous cell carcinoma.<sup>7-12</sup> Clinically, sublingual salivary gland tumors

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will only be recognized at an advanced stage, mainly owing to the concealed anatomical site and mild symptoms.<sup>13,14</sup>

Given its low incidence and varied biologic behavior (heterogeneity of the histologic types), the prognostic factors for sublingual salivary tumors have been difficult to determine. The present study investigated the prognostic factors for submandibular gland tumors that might be associated with patient survival. We hypothesized that 1 or more variables might be associated with survival, in particular, in relation to the pretreatment risk factors, stage, and pathologic features. Some of these factors could be clinically modified to improve survival. The present study retrospectively investigated the clinicopathologic features of patients with sublingual salivary gland tumors treated at Beijing Stomatological Hospital, Capital Medical University, during a 14-year period. We identified the risk factors and prognoses for locoregional recurrence, distant metastasis, and survival.

## Materials and Methods

### STUDY DESIGN AND DATA COLLECTION

In the present retrospective cohort study, the study population included patients undergoing evaluation and management of malignant sublingual salivary gland tumors from January 1, 1997 to December 31, 2011. The patients who had undergone treatment of sublingual salivary tumors were reviewed after approval of the institutional review board of Capital Medical University. All the patients provided written informed consent. We applied the following inclusion criteria: 1) pathologic verification of a malignant sublingual salivary gland tumor according to the World Health Organization classification of salivary gland malignancies<sup>15</sup>; 2) all available histologic materials had been reexamined by 2 pathologists without previous knowledge of the original diagnosis or clinical data; 3) detailed clinicopathologic data with sufficient follow-up data available; 4) no radiotherapy or chemotherapy had been performed before surgery; and 5) the patient had no history of tumor. Duplicate patient records were removed. Patients were excluded if they had been treated for recurrent disease only or metastasis in the submandibular region. We maintained contact with the patients and their relatives through telephone interviews, e-mail, and letters. Thirty-eight patients were eventually included in the present study.

In the present retrospective cohort study, the primary predictor variables involving the TNM stage (tumor and nodal stage) and histopathologic characteristics (margins, perineural invasion, lymphovascular invasion, and surgical margins) were analyzed. The secondary

predictor variables were the demographic data (age and gender), habits (drinking and smoking), and symptoms (pain, fixed mass, rapid growth, tongue numbness, and limited tongue mobility). The primary outcome variable was mortality at 5 years.

### STATISTICAL ANALYSIS

The Kaplan-Meier method was used to determine the prognostic factors for locoregional recurrence, distant metastasis, and mortality after 5 years. Statistical significance was discerned using the log-rank test and 2-tailed Fisher exact test. For multivariable survival analysis, all variables were analyzed using the Cox proportional hazards regression model. The following factors were included in the evaluation: age, gender, cigarette smoking, alcohol use, pain, fixed mass, rapid growth, tongue numbness, limited tongue mobility, T stage, N stage, surgical margin status, perineural invasion, and lymphovascular invasion. All statistical tests were performed using SPSS, version 19.0 (IBM Corp, Armonk, NY), and the results were considered significant at  $P < .05$ .

**Table 1. CLINICAL CHARACTERISTICS**

Characteristic	Patients
Gender	
Male	16 (42.1)
Female	22 (57.9)
Age >60 yr	
No	29 (76.3)
Yes	9 (23.7)
Smoking >40 pack-years	
No	28 (73.7)
Yes	10 (26.3)
Alcohol use	
No	30 (78.9)
Yes	8 (21.1)
Pain	
No	19 (50)
Yes	19 (50)
Fixed mass	
No	12 (31.6)
Yes	26 (68.4)
Rapid growth	
No	27 (71.1)
Yes	11 (28.9)
Tongue numbness	
No	31 (81.6)
Yes	7 (18.4)
Limited tongue mobility	
No	33 (86.8)
Yes	5 (13.2)

Data presented as n (%).

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