Nodal Stage: Is It a Prognostic Factor for Submandibular Gland Cancer?

Q5 *Yanbin Liu, DDS, PhD,* * *Lizheng Qin, DDS, PhD,* † *RunTao Zhuang, DDS,* ‡ *Xin Huang, DDS, PhD,* § *Ming Su, DDS,* ‖ *and Zhengxue Han, DDS, PhD* ¶

Purpose: Submandibular gland cancer is relatively rare. The purpose of this study was to estimate 5-year overall survival (OS) and disease-free survival (DFS) and to identify prognostic factors associated with OS and DFS for submandibular cancer.

Materials and Methods: The authors implemented a retrospective cohort study and enrolled a sample of patients with submandibular gland cancer. The predictor variables were age, gender, tumor stage, nodal stage, margin status, and extracapsular spread. The outcome variables were 5-year OS and 5-year DFS. Kaplan-Meier methods were used to estimate survival and Cox hazards models were used to identify prognostic variables.

Results: The sample was composed of 52 patients with submandibular gland cancer (mean age, 47.4 yr; 51.9% men). The median follow-up was 81 months (range, 11 to 159 months). The 5-year OS and DFS rates were 76.9 and 67.3%, respectively. Fixed mass, positive neck node, and positive margin status were relevant predictors of OS and DFS. Nodal stage was the relevant independent predictor affecting the disease outcome of submandibular gland cancer.

Conclusion: These results identified several important prognostic factors associated with survival rate in patients with submandibular gland cancer. These prognostic variables include symptoms at presentation, pathologic nodal status, and margin status. These outcomes suggest that heightening vigilance of clinical characteristics for this disease might provide the impetus for improving the survival rate.

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Neoplasms of the submandibular gland account for an estimated 8 to 12% of salivary gland tumors, and 50% of them are malignant.[1-4] Adenoid cystic carcinoma (ACC) and mucoepidermoid carcinoma (MEC) are the most common histopathologic types, followed by adenocarcinoma and carcinoma ex mixed tumors.[3,5] Clinically, the most common presenting symptom for patients with submandibular gland

*Attending Physician, Department of Oral and Maxillofacial–Head and Neck Oncology, Beijing Stomatological Hospital, School of Stomatology, Capital Medical University, Beijing, China.

†Professor, Department of Oral and Maxillofacial–Head and Neck Oncology, Beijing Stomatological Hospital, School of Stomatology, Capital Medical University, Beijing, China.

‡Associate Chief Physician, Department of Stomatology, Beijing Jiaotong University Community Health Center, Beijing, China.

§Professor, Department of Oral and Maxillofacial–Head and Neck Oncology, Beijing Stomatological Hospital, School of Stomatology, Capital Medical University, Beijing, China.

‖Attending Physician, Department of Oral and Maxillofacial–Head and Neck Oncology, Beijing Stomatological Hospital, School of Stomatology, Capital Medical University, Beijing, China.

¶Professor, Department of Oral and Maxillofacial–Head and Neck Oncology, Beijing Stomatological Hospital, School of Stomatology, Capital Medical University, Beijing, China.

Yanbin Liu and Lizheng Qin contributed equally to this work.

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Address correspondence and reprint requests to Dr Han: Department of Oral and Maxillofacial-Head and Neck Oncology, Beijing Stomatological Hospital, School of Stomatology, Capital Medical University, No 4 Tiantanxili, Dongcheng District, Beijing 100050, People's Republic of China; e-mail: hanf1989@hotmail.com

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tumors is a painless mass in the submandibular triangle. Distinguishing malignant from benign submandibular tumors based only on history and clinical examination is difficult. The rarity of carcinoma in this gland and the frequent occurrence of sialoliths or sialadenitis can result in delayed diagnosis in patients with submandibular gland malignancies.[6-9]

Few single-institution studies have comprehensively assessed the prognostic factors for submandibular gland malignancies because of the rarity of this disease. Published retrospective studies have shown that tumor grade, lymph node metastasis, perineural invasion, extraglandular soft tissue extension, and treatment type are relevant prognostic factors for survival.[3,5,10] The present study investigated the prognostic factors that might be associated with the survival of patients with submandibular gland malignancies. The authors hypothesized that there would be at least 1 factor associated with survival that could be manipulated by the clinician to enhance outcomes. The present study retrospectively investigated the clinicopathologic features of patients with submandibular gland cancer at the Beijing Stomatological Hospital at the Capital Medical University (Beijing China) over a 14-year period to identify the risk factors and prognoses for 5-year overall survival (OS) and disease-free survival (DFS).

Materials and Methods

STUDY DESIGN AND DATA COLLECTION

To address the research objective, the authors designed and implemented a retrospective outcome analysis study. The study samples were derived from patients who presented to the Department of Oral and Maxillofacial–Head and Neck Oncology at the Beijing Stomatological Hospital for treatment of a mass in the submandibular region from January 1, 1998 through December 31, 2011. After approval from the institutional review board of the Capital Medical University, the records of all patients treated for submandibular gland cancer were retrieved. To be included in the study sample, patients had to meet these inclusion criteria: *1)* the patient had a histologically proved malignant submandibular gland neoplasm assessed by 2 pathologists without prior knowledge of the original diagnosis, *2)* the patient had detailed clinicopathologic data with sufficient follow-up, *3)* the patient did not undergo radiotherapy or chemotherapy before surgery, and *4)* the patient had no history of tumors. Patients were excluded as study subjects if they were treated for recurrent disease only and metastasis in the submandibular triangle.

VARIABLES

In this study, predictor variables involving demographics (age and gender), habits (smoking and drinking), symptoms (pain and fixed mass), TNM staging (tumor stage and nodal stage), and histopathologic characteristics (margin status and extracapsular spread) were analyzed. The outcome variables were 5-year OS and 5-year DFS.

DATA ANALYSES

The Kaplan-Meier method was used to generate curves for OS and DFS. Statistical relevance was discerned using the log-rank test. Univariate and multivariate hazard ratios (HRs) were determined through the Cox regression model to assess the impact of the prognostic factors on OS and DFS. The factors that were associated with the outcome with a P value less than .05 in the univariate analysis were considered for the multivariable Cox proportional hazard model. The following factors were included in the evaluation: age, gender, cigarette smoking, alcohol use, pain, fixed mass, tumor classification, nodal classification, margin status, and extracapsular spread. All statistical tests were performed using SPSS 19.0 (SPSS, Inc, Chicago, IL). Results were considered significant at a P value less than .05.

Results

Fifty-two patients with submandibular gland cancer were reviewed. The demographic and prognostic factors are presented in Table 1. The study group was composed of 27 men and 25 women. The median age was 47.4 years (minimum, 22 yr; maximum, 81 yr). The mean follow-up time was 81 months (minimum, 11 months; maximum, 159 months). Twelve patients were older than 60 years and 40 patients were no older than 60 years. The 5-year OS and DFS rates were 76.9 and 67.3%, respectively. ACC was the most common malignant tumor in the submandibular gland (71.2%), followed by MEC (11.5%), salivary duct carcinoma (7.7%), adenocarcinoma (5.8%), and carcinoma ex pleomorphic adenoma (3.8%). Fourteen patients were treated by surgery alone. Thirty-five patients underwent surgical resection and radiotherapy. Two patients underwent surgical resection, radiotherapy, and chemotherapy. One patient underwent surgical resection and chemotherapy. Indications for adjuvant radiotherapy included tumor larger than 4 cm, stage T4 disease, high-grade tumor, positive margins, and positive lymph node involvement.

In the univariate analysis (Table 2), a fixed mass was significantly associated with OS (P = .033). The 5-year OS estimate was 62% for a fixed mass. Patients with positive neck nodes had lower 5-year OS and DFS than those with negative neck nodes (P < .0001 and