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Survival in patients with submandibular gland carcinoma — Results of a multi-institutional retrospective study

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ABSTRACT

Objective: Clinical studies demonstrating the prognostic factors in submandibular gland carcinoma are limited because the tumor is relatively rare. The aim of this study was to identify clinical outcomes and prognostic factors in submandibular gland carcinoma.
Methods: The study included 65 patients with submandibular gland carcinoma who underwent initial surgical treatment at the Kyoto University and its affiliated hospitals.
Results: The 3-year overall survival (OS), disease specific survival, locoregional control (LRC), and no distant metastasis (NDM) rates were 74.2%, 74.2%, 90.0%, and 64.8%, respectively. In the current follow-up study, 16 patients died of the disease, 5 patients were alive with recurrence, 43 patients were alive without disease, and 1 patient died of unrelated disease without recurrence. All patients who died of the disease had developed distant metastasis. Based on univariate analysis, tumor grade (high grade) and lymph node metastases (≥N2) were significant prognostic factors for OS and LRC. It also revealed tumor grade (high grade), T classification (≥T3), and lymph node metastases (≥N2) were significant for distant metastasis. Multivariate analysis showed the following significant prognostic factors: lymph node metastases (≥N2) for OS, LRC, and NDM, and high tumor grade for NDM.
Conclusion: Our study suggested death of submandibular gland carcinoma occurred mainly due to distant metastasis. The significant predictors of distant metastasis were lymph node metastases (≥N2) and tumor grade (high grade).

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1. Introduction

Salivary glands comprise the parotid, submandibular, sublingual, and minor glands. The 2005 World Health Organization classification included 24 malignant salivary gland tumors with many subtypes [dataset] [1]. Submandibular gland carcinoma is relatively rare; 7–11% of all primary epithelial salivary gland tumors occur in the submandibular glands, and 41–45% of submandibular gland tumors are malignant [dataset] [1]. Because of the rarity of the tumors, the literature is consequently limited and the information provided to patients is not sufficient. A better understanding of the tumor, including the patient, tumor, and treatment characteristics remains to be established. Although several studies [dataset] [2–8] have been conducted to reveal the clinical outcomes and prognostic factors of submandibular gland carcinoma, there are only a few reports [dataset] [2–6] so far that involve more than 50 patients. A multi-institutional study enables us to analyze a relatively large number of patients. The aim of this retrospective study was to update the clinical outcomes and prognostic factors of submandibular gland carcinoma, based on data from multiple centers.

2. Patients and methods

This study involved 65 patients with previously untreated submandibular gland carcinoma who underwent curative surgery at the Kyoto University and its affiliated hospitals between 2006 and 2015. These included 12 medical centers in Japan: the Kyoto University Graduate School of Medicine, Japanese Red Cross Wakayama Medical Center, Kurashiki Central Hospital, Japanese Red Cross Osaka Hospital, Kobe City Medical Center General Hospital, Kitano Hospital, Tenri Hospital, Shizuoka General Hospital, National Hospital Organization Kyoto Medical Center, Kokura Memorial Hospital, Hyogo Prefectural Amagasaki General Medical Center, and Japanese Red Cross Otsu Hospital. We excluded patients who did not undergo surgery or had distant metastasis at the time of initial surgery. This study was approved by the ethics committee of the respective hospital.

All clinical information was extracted from the electronic medical records. Preoperative diagnosis of malignancy and preoperative stages evaluation consisted of physical examination, fine-needle aspiration cytology (FNAC), magnetic resonance imaging (MRI), computed tomography (CT), and/or positron emission tomography (PET)/CT. The patients underwent surgery either by local excision alone or with the neck dissection (in the form of therapeutic [levels 1–5] or prophylactic neck dissection [typically levels 1–3]). In principle, patients with preoperatively diagnosed malignancy received either therapeutic or prophylactic neck dissection. Postoperative radiotherapy (PORT) was mainly administered to patients with stage IV or high-grade carcinoma. Pathological TNM classification was determined according to the 2009 International Union Against Cancer (UICC) guidelines [dataset] [9].

In this study, the main outcome measures were overall survival (OS), disease-specific survival (DSS), locoregional control (LRC), and no distant metastasis (NDM). We investigated factors associated with OS, LRC, and NDM.

The Kaplan–Meier method and log-rank test were used for the analysis of time-dependent variables. A p value <0.05 was regarded as significant. Variables that were significant at univariate analysis were included in the Cox proportional hazard regression model to determine the independent prognostic factors.

All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics [dataset] [10].

Table 1
Patient, tumor, and treatment characteristics.

Characteristic	Total (n = 65)	
	No.	%
Age, y		
<60	27	42
≥60	38	58
Sex		
Males	34	52
Females	31	48
Tumor grade		
High	38	58
Intermediate	18	28
Low	8	12
Unknown	1	2
pT stage		
T1	6	9
T2	20	31
T3	34	52
T4	5	8
pN stage		
N0	42	65
N1	7	11
N2a	0	0
N2b	15	23
N3	1	2
M stage		
M0	65	100
Stage		
Stage I	5	8
Stage II	16	25
Stage III	25	38
Stage IV	19	29
Nueral/perineural invasion		
Present	24	37
Absent	26	40
Unknown	15	23
Lymphatic/vascular invasion		
Present	16	25
Absent	35	54
Unknown	14	22
Adjuvant therapy		
PORT+	33	51
PORT−	32	49

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