Cervical Lymph Node Metastatic Status and Adjuvant Therapy Predict the Prognosis of Salivary Duct Carcinoma

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Purpose: Salivary duct carcinoma (SDC) is an aggressive malignancy that is not yet fully understood. We designed the present retrospective study to investigate the factors affecting the prognosis of SDC and the effects of adjuvant therapies on the clinical outcomes of patients.

Materials and Methods: Patients with SDC treated surgically from 2006 to 2016 were enrolled in the present retrospective cohort study. The demographic data, clinical pathologic characteristics, and follow-up results were recorded. The prognostic indicators of overall survival (OS), locoregional failure-free survival (LRFFS), and distant metastasis-free survival (DMFS) were analyzed using the Kaplan-Meier method and the Cox proportional hazard model.

Results: The study sample included 66 patients, most of whom were male (81.8%). The 5-year OS, LRFFS, and DMFS for all patients was 52.5%, 63.9%, and 51.3%, respectively. Univariate analysis showed that stage N2-N3, lymph node involvement of levels IV and V, 8 or more positive lymph nodes, and extranodal extension were all negative prognostic indicators for OS. The only significant indicator on multivariate analysis was the number of positive lymph nodes. Multivariate analysis revealed that extracapsular invasion and no adjuvant radiotherapy were risk factors for LRFFS. In contrast, lesions involving both glands and 8 or more positive lymph nodes were prognostic factors for DMFS. Further subgroup analysis showed that radiotherapy was only useful for patients with locally advanced lesions for local control.

Conclusions: Cervical lymph node metastatic status is an important factor in predicting the prognosis of SDC patients. Adjuvant radiotherapy is useful for local control, especially for patients with stage T4 disease but does not benefit OS and DMFS.

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Salivary duct carcinoma (SDC), first described by Kleinsasser et al[1] in 1968, is an aggressive malignancy with a tendency toward early distant metastases and a poor prognosis, accounting for approximately 1 to 3% of all salivary gland tumors.[2,3] The major organs affected by SDC are the parotid gland and submandibular gland. However, a small number of cases occurring in the minor salivary glands, oral cavity, or larynx have also been reported.[4,5]

SDC mainly occurs in aging men,[6] with no specific clinical presentation or laboratory diagnosis available. Most patients first come to the hospital because of a painless mass in their face or neck.[2,7] In addition, a substantial number of patients will visit a doctor

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because of facial paralysis.[8] At present, surgery remains the main clinical treatment. However, SDCs are prone to metastasize at an early stage and have a high recurrence rate[9]; thus, multimodal treatments are expected to prolong survival time. Therefore, individually tailored combined therapy, usually consisting of surgery and radiotherapy, has gradually become the standard plan for SDC.[10,11] Because of the low incidence, the effectiveness of multimodal treatment of SDC remains to be determined. In addition, the predictive factors influencing prognosis are not yet completely understood.

Therefore, the purpose of the present study was to identify the prognostic factors for SDC. We hypothesized that additional unrecognized factors might affect the course of SCD. The specific aims of the present study were to investigate whether cervical lymph node metastatic status was closely related to the prognosis and whether adjuvant therapies were effective in improving the clinical outcomes of patients with SDC.

Materials and Methods

STUDY DESIGN AND SAMPLING

To address the research goals, we designed and implemented a retrospective cohort study. The study population was composed of all patients with major SDC treated at Fudan University Shanghai Cancer Center from April 2006 to November 2016. To be included in the study sample, patients had to have undergone surgery. Some patients also received adjuvant therapy, including radiotherapy and chemotherapy. Patients who did not undergo surgery and those with distant metastasis at initial treatment were excluded from the present study.

VARIABLES

A set of predictor variables was recorded for each patient included in the present study. The primary predictor variables, including demographic data (eg, age, gender, smoking history), initial symptoms and signs (eg, pain, facial paralysis), and clinical and pathologic characteristics (eg, tumor site, size, TNM stage, tumor invasion, cervical lymph node metastatic status, adjuvant therapies), were obtained from the medical records. The primary outcome variables were overall survival (OS), locoregional-free survival (LRFFS), and distant metastasis-free survival (DMFS). All survival outcomes were defined as the duration from the end of disease treatment to event occurrence (ie, death, locoregional recurrence, and distant metastasis).

DATA COLLECTION

All patients underwent parotidectomy (partial or total), or submandibular gland excision and neck dissection (supraomohyoid neck dissection or radical neck dissection) was performed routinely. In some cases, only periparotid lymph node dissection or submandibular triangle dissection was performed because the preoperative and intraoperative diagnosis was not a high-grade tumor and because no lymph node lesions were identified clinically. Of these study patients, 8 underwent parotid lymph node dissection or submandibular triangle dissection, 25 underwent submandibular triangle dissection, and 33 underwent radical neck dissection. Facial nerve resections were performed if significantly invaded by tumor tissue.

Adjuvant radiotherapy was routinely recommended after surgery for each patient with pathologically confirmed SDC. Of the 66 patients, 48 received postoperative radiotherapy and 18 did not. The 48 patients received adjuvant 3-dimensional conformal radiotherapy or intensity-modulated radiotherapy. The median prescribed dose for these patients ranged from 54 to 70 Gy. Whether chemotherapy was necessary was determined by the medical oncologists. Of the 13 patients who underwent chemotherapy, 2 received neoadjuvant chemotherapy and 11 received postoperative chemotherapy.

After treatment completion, the patients were required to visit their doctor every 3 months for the first 2 years, followed by every 6 months for the next 3 years, and annually thereafter. The locoregional treatment response was evaluated using physical examination, neck ultrasonography, and magnetic resonance imaging. Chest computed tomography and abdominal ultrasound examinations were performed routinely to identify distant metastases. Positron emission tomography and isotope bone scanning were performed during the follow-up period, if indicated.

STATISTICAL ANALYSIS

All clinical and pathologic statistical variables obtained in the present study were analyzed using SPSS, version 22.0 (IBM, Armonk, NY). The OS, LRFS, and DMFS rates were calculated using the Kaplan-Meier method, and univariate analyses of the prognostic values were performed using log-rank tests. Cox proportional hazards regression models were used to assess the predictors of OS, LRFFS, and DMFS on multivariate analysis, and only the variables yielding a P value < .05 were subsequently included in the Cox model analyses. P values < .05 were considered statistically significant.

ETHICS

All participants or their guardians provided written informed consent, and the institutional ethics