Cystadenocarcinoma of the salivary gland is an extremely rare malignant tumor that was first described by the World Health Organization in 1991. The estimated incidence of cystadenocarcinoma is ~2–5% of all salivary gland malignancies. Diagnosis is based on pathologic findings in which there is a predominantly cystic growth pattern with intraluminal papillary proliferation. Currently, there are few reported cases related to cystadenocarcinoma of the salivary gland, and the related clinicopathological characteristics, treatment, and outcome results are limited. In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

Introduction

Cystadenocarcinoma of the salivary gland is an extremely rare malignant tumor that was first described by the World Health Organization in 1991. The estimated incidence of cystadenocarcinoma is ~2–5% of all salivary gland malignancies. Diagnosis is based on pathologic findings in which there is a predominantly cystic growth pattern with intraluminal papillary proliferation. Currently, there are few reported cases related to cystadenocarcinoma of the salivary gland, and the related clinicopathological characteristics, treatment, and outcome results are limited. In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

Patients and methods

Patients and clinicopathological characteristics

Patients with a pathologic diagnosis of cystadenocarcinoma of the salivary gland were identified using the SEER database from 1991 to 2012. Pathologic diagnoses was based on the primary site using the International Classification of Disease for Oncology, 3rd edition and the related clinicopathological characteristics, treatment, and outcome results are limited. In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

Results

A total of 46 patients were identified, of whom 63% received surgical treatment. 5 underwent lymphadenectomy, and four (16.0%) patients had nodal metastasis and did not affect survival. The estimated incidence of cystadenocarcinoma of the salivary gland is ~2–5% of all salivary gland malignancies. Diagnosis is based on pathologic findings in which there is a predominantly cystic growth pattern with intraluminal papillary proliferation. Currently, there are few reported cases related to cystadenocarcinoma of the salivary gland, and the related clinicopathological characteristics, treatment, and outcome results are limited. In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

Conclusion

Salivary gland cystadenocarcinoma is a rare disease. The estimated incidence of cystadenocarcinoma of the salivary gland is ~2–5% of all salivary gland malignancies. Diagnosis is based on pathologic findings in which there is a predominantly cystic growth pattern with intraluminal papillary proliferation. Currently, there are few reported cases related to cystadenocarcinoma of the salivary gland, and the related clinicopathological characteristics, treatment, and outcome results are limited. In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

Keywords: cystadenocarcinoma, salivary gland, SEER, treatment, survival

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3. Current treatment is based on surgical resection, with or without adjuvant radiotherapy. However, the optimal treatment remains controversial due to the rarity of the disease.
4. Patients with a pathologic diagnosis of cystadenocarcinoma of the salivary gland were identified using the SEER database from 1991 to 2012. Pathologic diagnoses was based on the primary site using the International Classification of Disease for Oncology, 3rd edition and the related clinicopathological characteristics, treatment, and outcome results are limited. In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

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Conflict of interest

The authors declare no conflicts of interest.

Ethics approval

This study was approved by the institutional review board of the First Affiliated Hospital of Sun Yat-sen University (Approval No. 2016-068). Due to the retrospective nature of the study, informed consent was not obtained from any patients.

Data availability

The data used in this study are available from the SEER database (https://seer.cancer.gov/).

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The following clinicopathological characteristics were obtained from the SEER database: year of diagnosis, race, age, tumor location, grade, SEER stage, and nodal status. Local treatment modalities including surgery, lymphadenectomy, and radiotherapy were also identified. Survival status, including cause of death, and the duration of follow-up were recorded.

Statistical analysis
Univariate and multivariate Cox regression analyses were used to analyze the risk factors for cause-specific survival (CSS) and overall survival (OS). Calculation of survival rates was plotted using the Kaplan–Meier method and compared using the log-rank testing. All data were analyzed using the SPSS software package, version 21.0 (IBM Corporation, Armonk, NY, USA). A P-value of <0.05 was considered statistically significant.

Results
Clinicopathological characteristics
A total of 16,923 patients were diagnosed with salivary gland malignant tumors from 1991 to 2012, including 65 (0.4%) patients with cystadenocarcinoma (Table 1). The median age was 62.0 years (range, 10–95 years); 90.8% of patients were diagnosed after 2000, and there was equal disease incidence in male and female patients. The most common tumor location was the parotid gland (57 patients, 87.7%), followed by the submandibular gland (four patients, 6.2%); four patients (6.2%) had no specific site records. Most of the patients (98.5%) were at localized and regional SEER stage, and only one patient (1.5%) was unstaged. Of the 47 patients with histological grade available, 42.6%, 55.3%, and 2.1% had Grade 1, Grade 2, and Grade 3 disease, respectively.

Treatment
Of the 65 patients, 64 (98.5%) received surgical treatment. Of the 61 patients with surgical procedure information available, 43 (70.5%) underwent local tumor excision or less than total parotidectomy, and 18 (29.5%) underwent total parotidectomy or radical parotidectomy. A total of 25 patients underwent lymphadenectomy, and only four patients (16.0%) had nodal metastasis. A total of 16 patients underwent adjuvant radiotherapy.

Outcomes
The median follow-up was 55 months (range, 1–204 months). A total of 13 patients died; ten patients died of noncancer disease, and three patients died of other malignant tumors; none of the patients died of salivary gland malignant-tumor-related disease. The 5- and 10-year CSS rates were 97.0% and 81.4%, respectively (Figure 1A). The 5- and 10-year OS rates were 84.6% and 60.7%, respectively (Figure 1B).

Table 1 Clinicopathological characteristics of patients (n=65)

<table>
<thead>
<tr>
<th>Characteristics</th>
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<td><strong>Age (years)</strong></td>
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| Median (range)  | 62.0 (10–95)  
| <50  | 7  
| ≥50  | 58  
| **Year of study** |  
| 1991–1995  | 2  
| 1996–2000  | 8  
| 2001–2005  | 15  
| 2006–2012  | 40  
| **Race** |  
| White  | 52  
| Black  | 5  
| Other  | 8  
| **Sex** |  
| Male  | 34  
| Female  | 31  
| **Tumor location** |  
| Parotid gland  | 57  
| Submandibular gland  | 4  
| Others  | 4  
| **Grade (n=47)** |  
| 1  | 20  
| 2  | 26  
| 3  | 1  
| **SEER stage** |  
| Localized  | 56  
| Regional  | 8  
| Unstaged  | 1  
| **Surgery** |  
| No  | 1  
| Yes  | 64  
| **Surgical procedures (n=61)** |  
| Total parotidectomy  | 18  
| Partial parotidectomy  | 43  
| **Radiotherapy** |  
| No  | 49  
| Yes  | 16  
| **Lymphadenectomy (n=64)** |  
| No  | 39  
| Yes  | 25  
| **Nodal status (n=25)** |  
| Negative  | 21  
| Positive  | 4  

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.
Influence of local treatment on survival

The effects of local treatment for cystadenocarcinoma of the salivary gland on CSS and OS were further analyzed, and the results showed that surgical procedures, lymphadenectomy, and adjuvant radiotherapy did not affect the CSS and OS (all, \(P > 0.05\)).

Discussion

Cystadenocarcinoma of the salivary gland had an excellent prognosis, but most studies currently have few patients.\(^5-10\) The study with the most patients in the literature was by Foss et al,\(^3\) which involved 57 patients; the median age was 58.8 years, and the main disease site was the parotid gland (61.4%). In our study, we used the SEER database to assess the clinicopathological characteristics, treatment, and survival outcomes of cystadenocarcinoma of the salivary gland, and our findings are similar to those of Foss et al.\(^3\) Regarding cystadenocarcinoma of the salivary gland, a high-grade malignant tumor usually leads to a relatively high risk of disease recurrence with rapid progression.\(^12,13\) However, in our study, only one patient was pathologically diagnosed with poorly differentiated disease.

Currently, the main treatment for cystadenocarcinoma of the salivary gland is radical surgery. Lymphadenectomy is recommended for patients with lymph node enlargement.\(^14\) The main site of recurrence following radical resection is the cervical lymph nodes, and there is less recurrence in the primary tumor bed.\(^3,15\) Mills et al\(^16\) reported that three of five patients (60%) with cystadenocarcinoma of the salivary gland had cervical lymph node metastases after 2–21 years. Similarly, Mukaigawa et al\(^15\) reported on four patients with cystadenocarcinoma of the salivary gland who underwent radical resection, where two patients underwent lymph node dissection, and three patients had cervical lymph node recurrence after 7, 17, and 24 months (with parotid lymph node recurrence after 43 months), respectively. Foss et al reported that one patient had regional lymph node metastasis after 55 months and three patients had lymphatic metastasis at initial diagnosis.\(^3\) In our study, 25 patients underwent lymphadenectomy, and 16.0% of patients were node positive. Due to the limitations of the SEER data, we could not clarify the lymph node status of the patients. However, based on the results of the abovementioned studies, the clinical course of follow-up for patients should also pay close attention to lymph node metastasis.

Radiotherapy is usually recommended for high-grade, recurrent disease, or for inoperable patients.\(^14\) Foss et al\(^3\) also recommended postoperative radiotherapy for patients with cervical lymph node metastasis. Our results also show that surgery is the main therapeutic method for cystadenocarcinoma of the salivary gland; other local treatment modalities such as lymphadenectomy and adjuvant radiotherapy had no effect on survival, which may be related to the excellent control rate of surgical resection.

In this study, none of the patients with cystadenocarcinoma of the salivary gland died of salivary gland malignant-tumor-related disease. Although mortality in cystadenocarcinoma of the salivary gland tends to be from other causes, long-term follow-up is essential, as some patients might relapse after a very long time, which may be associated with the slow growth and low-grade destructive features of cystadenocarcinoma of the salivary gland.\(^16\)

The current study has several limitations that need to be considered. The main limitation is the inherent biases that
exist in any retrospective study. Second, the SEER database does not record data such as systemic therapy regimen and dose, margin status, and local and regional recurrence. In addition, there is little information to guide the analysis of why lymphadenectomy and postoperative radiotherapy were or were not completed in certain patients. Furthermore, some adenocarcinomas recorded in the SEER database such as cystadenocarcinomas may be other entities that have been only recently recognized, ie, cribiform adenocarcinoma of tongue, mammary analog secretory carcinoma, and acinic cell carcinoma, which may be difficult to discriminate from cystadenocarcinoma and may require advanced techniques (immunohistochemistry and molecular pathology).

Conclusion
Cystadenocarcinoma is an extremely rare type of salivary gland malignant tumor with excellent prognosis, and surgery is the mainstay of treatment.

Disclosure
The authors report no conflicts of interest in this work.

References