Survival and Prognosis for Malignant Tumors of Odontogenic Origin

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Abstract

Objective. Determine survival and factors affecting survival for patients with malignant tumors of odontogenic origin.

Study Design. Retrospective analysis of the National Cancer Institute’s SEER database (Surveillance, Epidemiology, and End Results).

Setting. Tertiary medical center.

Subjects and Methods. All cases of malignant tumors of odontogenic origin were extracted from the SEER database for the period of 1973 to 2011. Demographic, tumor-specific, and survival data were tabulated and Kaplan-Meier survival analysis conducted according to histopathologic results. Cox regression analysis stratified for histopathology was conducted to determine factors that influenced survival.

Results. A total of 308 cases of malignant tumors with odontogenic origin were analyzed. Malignant ameloblastoma accounted for 59.7% of cases, followed by malignant odontogenic tumor (35.4%; including odontogenic carcinoma, odontogenic sarcoma, primary intraosseous carcinoma, and ameloblastic carcinoma) and ameloblastic fibrosarcoma (2.9%). The overall mean and median were 229 and 227 months, respectively, while the 5-year survival rate was 81% for the entire cohort. Malignant ameloblastoma exhibited the best mean survival (237 months), whereas malignant odontogenic tumor (139 months) and ameloblastic fibrosarcoma (42 months) had lower mean survival rates. Younger age, surgery with adjuvant radiation, and smaller tumor size were found to improve survival.

Conclusions. Significantly different survival can be expected depending on individual tumor histopathology, tumor size, age at diagnosis, and treatment modality.

Keywords

malignant odontogenic tumor, malignant ameloblastoma, ameloblastic fibrosarcoma

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Odontogenic tumors are a heterogeneous group of tumors that arise from tooth-forming tissues in the mandible and maxilla. Odontogenic tumors consist of lesions with varying biological presentations, including hamartomas and malignant tumors. Odontogenic tumors constitute about 1% of all jaw tumors, and their geographic distribution is variable.

In 1971, the World Health Organization released a classification system for odontogenic tumors; this system was updated in 1992 and subsequently 2005. However, due to the diverse nature of odontogenic tumors, controversies remain regarding their classification, terminology, and diagnosis. Specifically, the literature reports a wide range in the diagnosis of malignant tumors of odontogenic origin, composing 0% to 6.1% of all odontogenic tumors. Malignant tumors of odontogenic origin often present with similar histopathology to benign lesions, which can result in a delayed diagnosis or misdiagnosis.

Several studies have described the presentation of odontogenic tumors with attention to their clinical manifestation and histopathologic features. However, these studies are case studies or single-institution reviews resulting in region-specific outcomes and lacking meaningful consensus. This study uses the SEER database (Surveillance, Epidemiology, and End Results) to investigate the demographic and oncologic characteristics of malignant tumors of odontogenic origin in patients in the United States from 1973 to 2011.

Methods

This study examined the SEER database for the period of 1973 to 2011. Institutional Review Board approval was not required per the standing policy of the University of Cincinnati College of Medicine, as SEER does not disclose sensitive patient information. For this period, all cases of tumors of odontogenic origin with ICD-O-3 codes 9270 to
9342 with malignant behavior were included. Fields extracted from the database included demographic information, such as year of diagnosis, age at diagnosis, sex, and race. Clinical variables pertaining to the malignancy were also extracted, including histopathology, primary site, and size of the primary tumor. Treatment variables that were extracted included type of cancer-directed surgery and application of radiation therapy. The selected group of patients was then further restricted to those without evidence of distant metastatic disease.

Data were then imported into SPSS (IBM, Chicago, Illinois) for statistical analysis. Standard demographic information was computed. Kaplan-Meier survival analysis for each tumor histopathology was conducted. Mean, median, and 5-year survival values were determined. Cox regression analysis for overall survival was performed for age, sex, race, histopathology, primary site, surgery, radiation, radiation sequence, and tumor size.

### Results

For the period under examination, a total of 308 cases of malignant tumors of odontogenic origin were identified. Malignant ameloblastoma accounted for 59.7% of cases, followed by "malignant odontogenic tumor" (35.4%; including odontogenic carcinoma, odontogenic sarcoma, primary intraosseous carcinoma, and ameloblastic carcinoma) and ameloblastic fibrosarcoma (2.9%). The complete distribution of histopathology is depicted in Table 1.

Thirteen cases (4%) presented with distant metastatic disease and were excluded from subsequent survival analysis.

After exclusion of cases with <8 patients per histopathology, 290 cases remained for survival analysis. The median age interval at diagnosis was 50 to 54 years with a slight male predominance (62%). The average size of the primary tumor was 4.4 cm; 86.9% of patients underwent cancer-directed surgery; and 62.1% of patients received postoperative radiation therapy. The results of the Kaplan-Meier survival analysis are shown in Table 2.

No statistically significant survival difference was noted among the various histopathologies. Survival rates for malignant ameloblastoma trended toward being better than both malignant odontogenic tumors and ameloblastic fibrosarcoma. The Kaplan-Meier survival curves according to histopathology are displayed in Figure 1.

Beyond 1983, tumor size data were maintained in the SEER database, and 158 cases had this information documented. Patients with tumors from 0 to 20 mm had a better survival rate than patients with tumors 21 to 40 mm. The lowest survival rate was found for patients with tumors ≥41 mm. The Kaplan-Meier curves demonstrating survival based on tumor size are shown in Figure 2.

The results of the Cox regression analysis are given in Table 3.

### Discussion

The diagnosis of a malignant odontogenic tumor is complicated because of its rare presentation, limited clinical information, and low index of suspicion. The majority of retrospective studies on malignant odontogenic tumors have been conducted in Asia, United States, Africa, and Europe in the form of single-institution studies or case reports. Our study benefits from the nationally representative SEER database to describe the incidence of malignant odontogenic tumors in the United States from 1973 to 2011.

A total of 308 patients were isolated in this study, which represents the largest collection of malignant odontogenic tumor patients reported in the United States. This analysis demonstrates a threefold increase in the annual number of malignant odontogenic tumors diagnosed after 1992 as compared with that before. This increase in diagnoses coincides with the update of the World Health Organization classification for odontogenic tumors in 1992.

Studies suggest that the selection of the type of treatment should consider the clinical type of tumor, patient age, location of tumor, and tumor size. Increasing age at diagnosis, lack of radiation treatment after surgery, increasing

### Table 1. Distribution of Histopathology for Malignant Tumors of Odontogenic Origin.

<table>
<thead>
<tr>
<th>ICD-O-3 Histology</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>9270/3: Odontogenic tumor, malignant</td>
<td>109</td>
<td>35.4</td>
</tr>
<tr>
<td>9282/3: Complex odontosarcoma</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>9290/3: Ameloblastic odontosarcoma</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>9310/3: Ameloblastoma, malignant</td>
<td>184</td>
<td>59.7</td>
</tr>
<tr>
<td>9312/3: Squamous odontogenic tumor, malignant</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>9321/3: Central odontogenic fibrosarcoma</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>9330/3: Ameloblastic fibrosarcoma</td>
<td>9</td>
<td>2.9</td>
</tr>
<tr>
<td>9342/3: Odontogenic carcinosarcoma</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

### Table 2. Histopathologic Results of the Kaplan-Meier Survival Analysis for Each Tumor and the Overall Cohort.

<table>
<thead>
<tr>
<th>Survival time, mo</th>
<th>Entire Cohort</th>
<th>Malignant Odontogenic Tumor</th>
<th>Malignant Ameloblastoma</th>
<th>Ameloblastic Fibrosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>229</td>
<td>139</td>
<td>237</td>
<td>42</td>
</tr>
<tr>
<td>Median</td>
<td>227</td>
<td>179</td>
<td>234</td>
<td>52</td>
</tr>
<tr>
<td>5-y survival rate</td>
<td>80.6</td>
<td>72.8</td>
<td>86.5</td>
<td>44.4</td>
</tr>
</tbody>
</table>
tumor size, and ameloblastic fibrosarcoma histopathology were each found to exert a statistically significant negative impact on survival. However, our analysis showed that primary site, sex, and race did not statistically influence survival. Our analysis with the Cox regression model shows a significant difference in the mortality among different age groups. Patients ≥75 years of age at the time of diagnosis are 11 times more likely to die. This is relevant given that of 343 reported malignant odontogenic tumors, more than one-third of these cases presented in patients ≥60 years old.1

The results of the analysis support a multimodality approach to treatment. Only 1 patient received radiation prior to surgery. Of the 44 patients who received radiation, 36 (81.8%) had prior surgery. Patients who were not treated with radiation were almost 20 times more likely to die. Oral cavity malignancies are typically treated with surgery followed by radiation therapy. Not enough patients were treated with neoadjuvant radiation or radiation alone to draw a conclusion about this therapeutic approach; however, the addition of adjuvant radiation therapy to surgical resection was beneficial.

Patients diagnosed with malignant ameloblastoma had a better survival rate than patients with malignant odontogenic tumors or ameloblastic fibrosarcoma. Ameloblastic fibrosarcoma had the lowest 5-year survival rate of 44.4%. The persistent nature of these tumors depicted in the survival curves supports the need for follow-up >10 years. To date, <80 cases of ameloblastic fibrosarcoma have been published in the literature.15,16

Tumor size was found to be associated with survival. Patients with tumors ≥41 mm in size were more than twice as likely to die than patients with smaller tumors, after controlling all other covariates in the model.

Many of the limitations of this study stem from the relatively small number of cases spanning a long period. Over the last 30 years, SEER has adapted reported variables such as extent of disease, size, and other features, which resulted in a heterogeneous data set with limited common features to analyze. Lack of information regarding resection margins, for example, leaves room for further investigation in future case reports. Furthermore, our analysis on patient survival is limited because the majority of our patient sample was diagnosed after 1992. Although we were able to assess 5-year survival of patients with malignant odontogenic tumor, it will be important to obtain long-term follow-up to determine the survival of these patients over a period of 25 years.

Rizzitelli et al also analyzed patients with malignant ameloblastoma from the SEER database and reported that an overall incidence rate of 1.79 per 10 million persons per year. Our study considers all malignant tumors of odontogenic origin and reports the largest such series in the literature. Additionally, our study is unique from that of Rizzitelli et al in that it analyzes the relationship between tumor size and overall patient survival.17

In conclusion, we have reviewed information from the SEER database to identify important characteristics of
patients with malignant odontogenic tumors and to conduct a Kaplan-Meier survival analysis of demographic, tumor-specific, and survival data. Its individualized risk assessment may assist in patient counseling on prognosis and can help to identify factors that influence survival in these patients.

Author Contributions
Sunil Agarwal, collected data, wrote article, revised article;
Jonathan Mark, collected data, wrote article, revised article;
Changchun Xie, analyzed data, wrote article; Enas Ghulam, analyzed data, wrote article; Yash Patil, designed study, revised article.

Disclosures
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References