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Mucoepidermoid carcinoma of the parotid gland: A National Cancer Database study

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ABSTRACT

Objective: To describe the demographics, tumor characteristics, and prognostic features of mucoepidermoid carcinoma of the parotid gland.

Materials and methods: A retrospective study of the National Cancer Database was reviewed for all mucoepidermoid carcinomas of the parotid gland between 2004 and 2012). Patient demographics and tumor characteristics were abstracted and analyzed. Univariate and multivariate Cox multivariate regression models were used to identify predictors of survival.

Results: A total of 4431 patients met inclusion criteria. Average age at diagnosis was 57 years (median 62, SD 19), with no overall sex preference (52% female), and majority white (78%). The 1-year overall survival was 92.9% (95% CI [92.1–93.6]) and 5-year overall survival was 75.2% (95% CI [73.8–76.7%]). Median overall survival was not reached at 5 years. Factors associated with decreased survival were increasing age, comorbidities, high tumor grade, advanced pathologic group stage, and positive surgical margins. Female sex was the only factor associated with improved survival. Controlling for either histopathologic grade or pathologic stage to determine how patient demographics and tumor characteristics affected overall survival yielded similar results. Of note, intermediate grade tumors, although not independently associated with worse survival, when seen in conjunction with tumors ≥T2 and/or ≥N2, a negative impact on overall survival was seen.

Conclusion: Although mucoepidermoid carcinoma of the parotid gland is the most common parotid gland malignancy, it is still a rare tumor with a lack of large population-based studies. Advanced stage and high-grade tumors are significant predictors of decreased survival. Females have improved survival compared to males.

1. Introduction

Salivary gland malignancies account for < 5% of all head and neck cancers, of which 70% are parotid gland malignancies [1]. Mucoepidermoid carcinoma (MEC) is the most common histologic subtype, comprising 50% of all parotid malignancies [2].

The diagnosis of MEC is based on the identification of three cell types, which occur in varying proportions: epidermoid, mucinous, and intermediate cells. This heterogeneity of tumor cell composition leads to a wide variation in pathologic and clinical behavior. Surgery represents the mainstay treatment for MEC of the parotid gland, followed by adjuvant radiation therapy when indicated [3].

In an effort to better understand its behavior, several studies have attempted to describe the epidemiology of MEC and determine independent prognostic factors for survival. The majority of studies of MEC have been single institution series which, due to its rarity, lead to relatively small sample sizes. Furthermore, for statistical purposes, these studies had to evaluate MEC of all the major salivary glands together, or sometimes, combine it with minor salivary glands [4–10].

The National Cancer Database (NCDB) is the largest cancer registry in the world. It is an excellent resource for studying rare cancers, capturing about 70% of all new cancer diagnoses in the United States [11]. The objective of this study was to use this database to describe the demographics, tumor characteristics and prognostic features of MEC of the parotid gland.

2. Material and methods

Data was abstracted from the NCDB on March 4th, 2016 for patients with tumors of the head and neck diagnosed between 2004 and 2012.

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The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. The database was established in 1989, containing comprehensive clinical surveillance oncologic data from > 1500 commission-accredited cancer programs in the United States [12]. This study was determined to be exempt by the Institutional Review Board of the Hospital of the University of Pennsylvania.

The NCDB was queried using the ICD-O-3 (International Classification of Diseases for Oncology, Third Edition) topography code for cancers of the parotid gland (C079), with a histology of mucoepidermoid carcinoma (8430). Only cases that were recorded as being a malignant neoplasm or presumed to be a primary malignancy (behavior code of 3) were included. Patients were excluded if they did not have values for either follow up or vital status. They were also excluded if they had surgery to a distant site in order to avoid confounding of different surgical procedures.

The demographic variables analyzed included age at diagnosis, sex, race and comorbid conditions (Charlson/Deyo score). Race was categorized into white, black, and other. The Charlson/Deyo score is a cumulative weighted point value given for the following comorbidities: myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, liver disease, diabetes, hemiplegia or paraplegia, renal disease, and AIDS. Since there is such a small proportion of cases with a Charlson/Deyo score that exceeds 2, the NCDB truncated the data to 0, 1 and 2 –the later representing > 1 [13,14].

The tumor variables analyzed included histologic grade, pathologic TNM stage in accordance with the American Joint Committee on Cancer classification, and surgical margin status. The NCDB lists the tumor grades as I - well differentiated, II - moderately differentiated, III - poorly differentiated, and IV - anaplastic. However, since mucoepidermoid carcinoma is typically graded as low, intermediate and high, we classified grade I into low, II into intermediate, and III and IV into high. Grade III and IV were grouped into high because they both represent high grade pathologic features. The pathologic stage group was categorized as early (stages I and II) and advanced (stages III and IV). Surgical margin status was categorized into negative (no residual), positive (residual NOS, microscopic residual or macroscopic residual) and unknown (not evaluable, no surgery, or unknown). Type of treatment and treatment sequence with regards to surgery, radiation and/or chemotherapy were also included.

Univariate analysis testing for association with overall survival was performed using Pearson chi-squared for categorical variables. Unadjusted Kaplan-Meier estimates and log-rank tests were used for univariate comparison of overall survival outcomes, and multivariable Cox proportional hazard models were generated for multivariable comparisons. All data processing and analysis was performed with Microsoft Open R v. 3.3.2 (https://mran.microsoft.com/open/) via RStudio v. 1.1.23 (RStudio, Boston, MA, USA).

3. Results

A total of 4431 cases of MEC were identified in the NCDB. The demographics are characterized in Table 1. Notable findings include a mean age of 57 years (median age 62), no overall sex preference (52% female), and a majority of white patients (78%).

Tumor characteristics are also described in Table 1. Low tumor grade was the most common (34%) histologic subtype. Most malignancies were diagnosed at an early pathologic stage group (41%), with pathologic T1 (41%) and N0 (58%) being most common. Sixty-six percent of patients had negative margins and 47% of these patients had surgery alone without adjuvant therapy.

The 1-year overall survival was 92.9% (95% CI [92.1–93.6]) and 5-year overall survival was 75.2% (95% CI [73.8–76.7%]). Overall median survival was not reached in 5 years, (i.e., more than half the patients were alive at 5 years). The remaining survival characteristics by demographics, tumor characteristics and treatment modality are listed in Table 2. Patients who were 54 years or younger, female, non-white and had no comorbidities by Charlson/Deyo score had a better survival rate than their cohorts. Tumors that were low grade, T1, N0, early stage, and had negative surgical margins also had a better overall survival.

Table 1
Demographics and tumor characteristics of all patients.

Average age at diagnosis (mean (SD))	56.67 (18.78)
Sex	
Male	2121 (47.9%)
Female	2310 (52.1%)
Race	
White	3466 (78.2%)
Black	637 (14.4%)
Other	195 (4.4%)
Unknown	133 (3.0%)
Comorbidities (Charlson/Deyo score)	
0	3656 (82.5%)
1	626 (14.1%)
2	149 (3.4%)
Grade	
Low	1496 (33.8%)
Intermediate	1245 (28.1%)
High	1155 (26.0%)
Unknown	535 (12.1%)
Pathologic T stage	
T0	7 (0.2%)
T1	1813 (40.9%)
T2	943 (21.3%)
T3	532 (12.0%)
T4	394 (8.9%)
Unknown	742 (16.7%)
Pathologic N stage	
N0	2556 (57.7%)
N1	305 (6.9%)
N2	388 (8.8%)
N3	2 (0.0%)
Unknown	1180 (26.6%)
Pathologic M stage	
0	2863 (64.6%)
1	27 (0.6%)
Unknown	1541 (34.8%)
Pathologic stage group	
Early	2157 (48.7%)
Advanced	1160 (26.2%)
Unknown	1114 (25.1%)
Surgical margins	
Negative	2947 (66.5%)
Positive	1093 (24.7%)
Unknown	391 (8.8%)
Treatment sequence	
Surgery alone	2081 (47.0%)
Surgery and radiation	1660 (37.5%)
Surgery, chemotherapy & radiation	200 (4.5%)
Radiation alone	75 (1.7%)
Concurrent chemo and radiation alone	36 (0.8%)
No treatment	83 (1.9%)
Other	296 (6.6%)

To determine which factors were independently associated with survival, a Cox regression analysis was performed (Table 3). This demonstrated that age, female sex, comorbidities, pathologic tumor grade, T stage, N stage and stage group and surgical margins were factors predictive of survival ($p < 0.05$). Specifically, factors associated with decreased survival were increasing age, increasing number of comorbidities, high tumor grade, pathologic T3, T4, N2 and N3 tumors, and positive surgical margins. Female sex was the only factor associated with improved survival (HR 0.83, 95% CI [0.72–0.95], $p = 0.008$).

Patient survival was also categorized by histopathologic grade and pathologic group stage (Table 4). Low grade and early stage were the most common (21.4%), and had the best survival. High grade and