Prognostic factors and occult nodal disease in mucoepidermoid carcinoma of the oral cavity and oropharynx: An analysis of the National Cancer Database

Mark A. Ellis [a], Evan M. Graboyes [a], Terry A. Day [a], David M. Neskey [a,b,*]

[a] Department of Otolaryngology-Head and Neck Surgery, Medical University of South Carolina (MUSC), Charleston, SC, United States
[b] Department of Cell and Molecu+lar Pharmacology and Experimental Therapeutics, MUSC, Charleston, SC, United States

ABSTRACT

Objectives: Mucoepidermoid carcinoma (MEC) is an uncommon malignancy that most commonly occurs in the parotid gland followed by the minor salivary glands of the upper aerodigestive tract, most notably in the oral cavity (OC) and oropharynx (OP). Because of its rarity, few studies have been performed that are specific to MEC within the OC and OP. The objective of this study is to describe the tumor characteristics and prognostic features for MEC of the OC and OP.
Materials and Methods: The National Cancer Database (NCDB) was used for this study. The primary outcome measure was 5-year overall survival (OS). The secondary outcome measure was occult nodal disease. Fischer's exact tests, chi-square tests, log-rank tests and Cox proportional hazards analyses were performed.
Results: We identified 3005 patients with MEC of the OC/OP. The 5-year overall survival for MEC of the OC and OP was 87%. Increasing age, male sex, Charlson/Deyo comorbidity score of 2+, clinical T3-4 tumors, nodal + disease, high grade tumors and positive margins were independently associated with decreased 5-year OS. Occult nodal disease occurred in 14.1% and 17.3% of high grade and clinical T3-T4 tumors respectively.
Conclusion: MEC of the OC/OP has an excellent survival as the majority of these patients have low/intermediate grade and early stage disease. Negative prognosticators include increasing age, male sex, Charlson/Deyo comorbidity score of 2+, clinical T3-4 tumors, nodal+ disease, high grade tumors and positive margins. Our findings justify strong consideration of prophylactic neck dissection for high grade and clinical T3-4 tumors.

Introduction

Salivary gland malignancies are rare and account for only 3% of head and neck cancers [1]. Despite their rarity, these neoplasms are heterogeneous and are classified into 24 different histologic subtypes by the World Health Organization [2]. Mucoepidermoid carcinoma (MEC) is the most common salivary gland malignancy and is most often located in the parotid gland followed by the minor salivary glands throughout the upper aero-digestive tract, most notably in the oral cavity (OC) and oropharynx (OP) [3,4].

Clinicopathologic characteristics, oncologic outcomes, and prognostic factors for MEC of the parotid gland have been well defined [5,6]. However, because of their scarcity, few studies have been performed that are specific to MEC of the OC and OP [7]. Instead, previous publications have grouped MEC of the OC/OP with MEC of the major salivary glands [8,9]. Other studies have focused on minor salivary gland malignancies as a conglomerate thereby grouping MEC with other histologic subtypes [10–13]. Therefore, there is limited data specific to MEC of the OC and OP and a head and neck surgical oncologist must counsel patients and make treatment decisions with evidence inferred from studies containing heterogeneous tumor subsites and/or histologies.

In the following study, we utilize the National Caner Database (NCDB), the world's largest tumor registry, to describe the clinicopathologic characteristics, survival and prognostic factors specific to MEC of the OC and OP.

* Corresponding author at: Department of Otolaryngology-Head and Neck Surgery, Medical University of South Carolina, 135 Rutledge Avenue, MSC 550, Charleston, SC 29425, United States.
E-mail address: neskey@musc.edu (D.M. Neskey).

Methods

Data source and study population

The NCDB is a hospital-based registry that is the result of a joint effort between the Commission on Cancer (COC) of the American College of Surgeons and the American Cancer Society. It captures 70% of all cancer cases in the United States and collects data from more than 1500 COC-accredited programs. The Medical University of South Carolina Institutional Review Board deemed this study exempt from review.

We reviewed the NCDB from 2004 to 2013. We selected cases using the *International Classification of Diseases for Oncology, 3rd edition (ICD-O-3)* histologic code "8430″ and topography codes for all histologically confirmed MEC of the OC and OP. A schematic illustrating the inclusion/exclusion criteria for this study is illustrated in Fig. 1. We identified 3312 patients with MEC of the minor salivary glands in the upper aerodigestive tract (UADT), the majority of which (3005) occurred within the OC/OP. Given the rarity of non OC/OP MEC and our desire to analyze a clinically homogenous data set, we decided to exclude non OC/OP MEC from analysis. Because of the challenge in distinguishing MEC of the OC from those of the OP (e.g. oral vs. base of tongue and hard vs. soft palate), we decided to analyze both OC and OP MEC.

Outcome measures

The primary outcome measure was 5-year overall survival (OS). OS was defined as the time period from the date of diagnosis to death from any cause. Neither patterns of failure nor disease-specific survival are available in the NCDB. The secondary outcome measure was rate of occult nodal disease, which was defined as the number of clinical N0 patients who were pathologic N+ divided by all clinical N0 patients with available pathologic N staging.

Study variables

Relevant demographic and clinical variables were extracted for analysis including age at diagnosis, gender, race, Charlson/Deyo comorbidity score, tumor grade, clinical (c) and pathologic (p) Tumor-Node-Metastasis stage in accordance with the American Joint Committee on Cancer classification (AJCC), treatment modality, and overall survival (OS). Comorbidity is categorized in the NCDB as 0, 1, or ≥ 2. Tumor grade was classified as low, intermediate and high grade as described previously using the NCDB [5,14].
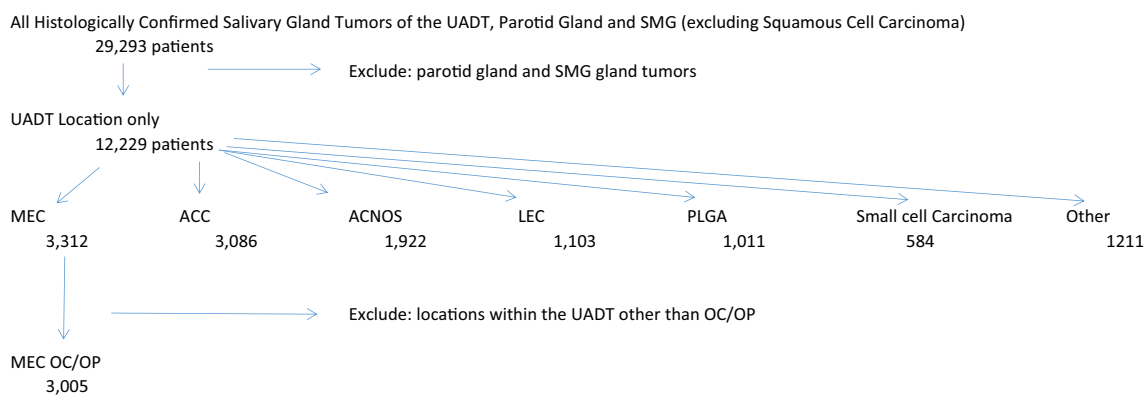
Statistical analysis

The study variables listed above were imported into the SPSS, version 23 (IBM Corp., Armonk, NY) for analysis. Patients missing overall survival data were included for clinicopathologic characteristics and occult nodal disease calculations but were excluded (307 patients) from survival analysis. Clinical and pathologic information were summarized by means of summary statistics. Comparisons were made with Fisher's exact test and chi-square test where appropriate. 5- year OS data was tabulated using the life-tables function and compared using the log-rank test. Univariate and multivariate Cox proportional hazards analyses were performed to determine factors associated with 5-year OS. Patients with known metastatic disease or unknown metastatic coding were excluded from our proportional hazard model (102 patients). Log minus log plots were performed for each categorical variable to confirm that the proportional hazards assumption was satisfied. Variables deemed clinically relevant and/or statistically significant on univariate Cox regression analysis were included in our multivariate analysis. Variables included in our multivariate analysis were age, sex, comorbidity score, tumor subsite, clinical tumor stage, clinical nodal disease, grade and surgical margins. A backwards stepwise entry method with $p > 0.1$ as exclusion criteria was used for our multivariate analysis; subsite was dropped out of the final multivariate model. All statistical tests were two-sided and a p value < 0.01 was considered significant for all tests given the large sample size.

Results

Clinical, pathologic and treatment characteristics

We identified 12,229 patients with histologically confirmed salivary gland malignancies within the UADT. MEC was the most common histology (3312, 27.1%) followed by adenoid cystic (3086, 25.3%) and adenocarcinoma not otherwise specified (1922, 15.7%). Among the 3312 MEC within the upper aero-digestive tract, 3005 (90.7%) were in the OC/OP (1813 in the OC, 699 in the OP and 493 in the OC/OP NOS). Of the 3005 MEC within the OC/OP, 1276 occurred on the palate (42.5%). Clinical, pathologic and treatment characteristics are presented in Table 1. Regarding treatment modality, 2193 patients (75.7%) received surgery alone, 422 (14.6%) received surgery and radiotherapy, 44 (1.5%) received surgery and chemoradiotherapy, 88 (3.0%) received radiotherapy alone, 48 (1.7%) received other, and 101 (3.5%) received none.

All Histologically Confirmed Salivary Gland Tumors of the UADT, Parotid Gland and SMG (excluding Squamous Cell Carcinoma)
29,293 patients
→ Exclude: parotid gland and SMG gland tumors

UADT Location only
12,229 patients

| MEC | ACC | ACNOS | LEC | PLGA | Small cell Carcinoma | Other |
| 3,312 | 3,086 | 1,922 | 1,103 | 1,011 | 584 | 1211 |

→ Exclude: locations within the UADT other than OC/OP

MEC OC/OP
3,005

Abbreviations: UADT, upper aerodigestive tract. SMG, submandibular gland. MEC, mucoepidermoid carcinoma. ACC, adenoid cystic carcinoma. ACNOS, adenocarcinoma not otherwise specified. LEC, lymphoepithelial carcinoma. PLGA, polymorphous low grade adenocarcinoma. OC, oral cavity. OP, oropharynx.

Fig. 1. Definition of study cohort.