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Characterization, treatment and outcomes of salivary ductal carcinoma using the National Cancer Database

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ABSTRACT

Objectives: To analyze clinical, treatment and outcome data for patients with salivary ductal carcinoma in a large population-based sample.
Materials and methods: The National Cancer Database was queried to identify patients diagnosed with salivary ductal carcinoma between 2004 and 2013. Kaplan Meier and Cox regression analysis were used to assess overall survival (OS) and identify impact of specific variables on OS.
Results: A total of 495 patients were identified. The most common site of tumor origin was the parotid (80%). 130 patients (26.3%) presented with early stage (I-II) disease, 257 patients (51.9%) with locoregionally advanced pathologic stage (III-IVB) disease and 41 patients (8.3%) with metastatic disease. The 5 year OS for these patients was 79.5%, 40.4% and 0% respectively. At presentation, 46.6% had node positive disease. Surgery was performed in 100% of patients with early stage disease, 98.4% with advanced disease and 90.2% with metastatic disease. Radiation therapy, generally postoperative radiation, was given to 58.5% of patients with stage I-II disease, 71.6% with stage III-IVB disease and 53.7% with metastatic disease. Chemotherapy was utilized in 5.4% of patients with stage I-II disease, 35% with stage III-IVB and 70.7% with metastatic disease. On multivariable analysis, there were no significant differences in OS based on receipt of adjuvant radiotherapy, chemotherapy, or chemoradiotherapy.
Conclusion: Salivary ductal carcinoma represents an uncommon and aggressive subset of salivary tumors for which current adjuvant treatments do not have a detectable impact on overall survival.

Introduction

Of the approximately 4000 cases of salivary gland tumors in the US annually, only about 1–3% are of salivary ductal origin [1,2], Given its rarity, the published literature is limited to small retrospective studies, typically single-institution. As a result, the optimal treatment is unclear. The National Cancer Care Network guidelines currently recommend postoperative radiation for T3-4 disease with one of the following additional risk factors: close or positive margins, intermediate or high grade disease, positive lymph nodes, perineural invasion, or lymphovascular invasion, adenoid cystic pathology [3].

However, it is not clear whether salivary ductal carcinoma (SDC) is included within this recommendation. SDC was first described in 1968, with pathologic features similar to duct carcinoma of the breast [4]. It is considered to be high grade and regardless of treatment, patients are generally thought to have a poor prognosis. Lymphatic spread and distant metastasis are more common than other salivary tumor subtypes [5].

Since this is a rare disease without well-established treatment guidelines, we set out to examine the National Cancer Database (NCDB), to evaluate the practice patterns and survival outcomes for patients with salivary duct carcinoma in a large hospital-based study.

Methods

The NCDB is a hospital-based registry that is the joint project of the American Cancer Society and the Commission on Cancer of the American College of Surgeons. It is estimated that 70% of all diagnosed malignancies in the United States are captured by facilities

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participating in this registry and reported to the NCDB. The Commission on Cancer's NCDB and the hospitals participating in the NCDB are the source of the de-identified data used in this study. However, they have not verified and are not responsible for the statistical validity or conclusions derived by the authors of this study. Exemption was obtained from the New York Harbor Veterans Affairs Committee for Research and Development prior to the initiation of this study.

We identified patients of any age who were diagnosed with salivary ductal carcinoma of the parotid gland, submandibular gland, or major salivary gland not otherwise specified from 2004 to 2013. Information was collected regarding surgical procedure, if any was performed, as well as whether or not radiation and/or chemotherapy were received as part of their treatment. Staging information was collected based on the coding within the NCDB. Surgical treatment was divided into no surgical therapy, local excision, and partial/total parotidectomy. When a gland other than the parotid was involved, then this coding identified partial or total removal of the involved gland. For ease of reading, the term curative resection is used to describe partial/total parotidectomy, submandibular, sublingual or other salivary gland removal and to distinguish from local excision.

The purpose of this study was to assess the patterns of care as well as outcomes in this patient population. The primary outcome endpoint was overall survival, which was calculated from the month and year of initial diagnosis. Vital status at the date of last contact was not available for patients diagnosed in 2013. Therefore, survival analyses were performed on the 405 patients for whom there was follow up data. Kaplan Meier analysis was performed to analyze overall survival and comparisons were made via the log-rank test. Multivariable Cox Regression was performed to determine the impact of covariables on overall survival. The variables measured included age (continuous), race (White, Black, Other), gender (male, female), Charlson/Deyo score (0, 1, $\geq$2), location of tumor (parotid, submandibular, major salivary gland not otherwise specified), surgery type (none, local excision, curative resection), radiation to head and neck region (no, yes), chemotherapy (no, yes). All analyses were conducted using SPSS V 23.0 (IBM Inc, Armonk, NY, USA). A p value <0.05 was used to determine statistical significance.

Results

A total of 495 patients were identified. Of those, 41 (9.8%) were identified as having metastatic disease at diagnosis. The primary tumor as identified as in the parotid gland for 396 patients (80%), submandibular gland for 65 patients (13.1%), and major salivary gland not otherwise specified for 34 patients (6.9%). The median patient age was 65 years (interquartile range 55–75 years). Most patients (68.9%) were male and White race (85.1%). The median follow up for all patients was 32.4 months and the median follow up for living patients was 40.1 months (interquartile range 23.1–70.0 months). With regards to clinical presentation, 42.2% presented with T3-4 disease. In addition, 46.6% of patients presented with node positive disease, with N2b the most common presentation (34.1%). Most patients (87.1%) underwent curative resection, consisting of partial or total parotidectomy, or removal of gland involved if not parotid, as part of their treatment, with an additional 63.4% receiving radiation therapy to the head and neck and 29.3% receiving chemotherapy. Of the 314 patients who received radiation, 307 were identified as having received postoperative radiation therapy, 1 had preoperative radiation therapy, and for 6 the sequence was unknown. Further details regarding patient characteristics are available in Table 1.

Table 1
Patient characteristics.

	No patients (%)
Gender	
Male	341 (68.9)
Female	154 (31.1)
Race	
White	421 (85.1)
Black	46 (9.3)
Other	28 (5.7)
Tumor location	
Parotid	396 (80.0)
Submandibular	65 (13.1)
Major salivary gland not otherwise specified	34 (6.9)
Clinical stage	
Not recorded	175 (35.4)
I-II	113 (22.8)
III	56 (11.3)
IVA-B	110 (22.2)
IVC	41 (8.3)
Pathologic stage	
Not recorded	67 (13.5)
I-II	130 (26.3)
III	62 (12.5)
IVA-B	195 (39.4)
IVC	41 (8.3)
Surgery	
None	16 (3.2)
Local excision	48 (9.7)
Partial/Total Parotidectomy	431 (87.1)
Radiation therapy to head and neck	
Yes	314 (63.4)
No	181 (36.6)
Chemotherapy	
Yes	145 (29.3)
No	350 (70.7)

Patterns of care for stage pI-II

There were 130 patients with pathologic stage I-II disease, consisting of pT1-2Nx-0M0 disease. The median overall survival was 108.2 months and the 5 year overall survival was 79.5%. All patients had surgical removal of the tumor, with 113 (86.9%) recorded as receiving curative resection and 17 (13.1%) receiving local excision. The median number of lymph nodes removed was 2, and zero lymph nodes were removed for 33.8% of patients. Regarding adjuvant radiation therapy, 76 patients (58.5%) received adjuvant radiation and 7 (5.4%) received chemotherapy. For those who received radiation, the dose was recorded as between 5000 and 7400 cGy for 86.8% of patients and the median dose was 6000 cGy. The 3 year and 5 year overall survival was 89.9% and 89.9% for those not receiving radiation versus 80.6% and 70.7% for those who did receive radiation (p = 0.28) (Fig. 1).

Patterns of care for stage pIII-IVB

There were 257 patients with pathologic stage III-IVB disease, comprising of 33 (12.8%) patients with pT3N0, 29 patients (11.3%) with pT1-3N1, 18 patients (7.0%) with pT4N0, 12 patients (4.7%) with pT4N1, and 162 patients (63.0%) with T1-4N2-3 disease. The median overall survival was 45.9 months and the 5 year overall survival was 40.4%. Most patients (91.8%) underwent curative resection, with 6.6% undergoing local excision, and 4 not receiving surgery. The median number of lymph nodes removed was 21, with 5.4% of patients have no nodes removed. The median number of positive lymph nodes was 4. One hundred eighty-four patients (71.6%) received adjuvant radiation, and 90 (35%) received chemotherapy. Of the 90 who received chemotherapy, 90% received radiation as well whereas 10% had only chemotherapy. The 3 year and 5 year overall survival was 50.7% and 42.2% for those who did not receive radiation and 63.4% and 39.3% for those