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Abstract

OBJECTIVES/HYPOTHESIS:

Analyze Sinonasal ACC versus Major Salivary ACC in regards to presentation, survival, and treatment.

METHODS:

In this retrospective case review of the Surveillance, Epidemiology, and End-Results (SEER) database from 1988-2011, 1,295 major salivary and 368 sinonasal ACC patients were identified. Data on race, age, sex, radiation treatment, surgical treatment, and tumor stage were extracted. Kaplan-Meier survival functions were used to calculate disease-specific survival curves. Significant contributors to survival were incorporated into a cox proportional hazards model to identify independent predictors of survival.

RESULTS:

Sinonasal tumors have a significantly have a more advance T stage ($P<0.001$), but lower rate of regional metastasis ($P<0.001$) compared to major salivary ACC. They also tended to be treated less aggressively with higher rates of radiation and lower rates of surgery/combined treatment modalities ($P<0.001$). A Cox Proportional Hazards Model demonstrated that the sinonasal site was a predictor of poor prognosis (HR=1.62 [CI=1.34-2.01, $P<0.001$]) independent of treatment modality, stage, race, age, and sex.

CONCLUSIONS:

Sinonasal ACC's poor prognosis compared to major salivary ACC has been attributed to higher tumor stage at diagnosis. However, this study finds that the relative poor prognosis is independent of tumor stage and treatment modality, and that surgery appears to offer significant benefit to survival, while radiation therapy does not. This study is limited by the retrospective nature of the data, and therefore more research is needed.

Introduction

Adenoid Cystic Carcinoma (ACC) is a slow growing indolent cancer with relentless clinical course. It has a high rate of local and distant recurrence, that can present up to 15 years after treatment. The overall survival at 15 years is ~40%¹. The most common single site is the parotid gland (25%), however it does frequently presents in minor salivary glands (60%)². ACC is commonly regarded as a neurotrophic tumor with perineural spread common. When found at difficult to access anatomical sites, surgery may be morbid and result in significant functional loss. As a result it often requires extensive and morbid surgical resection to obtain clear surgical margins. This leads many to seek possible adjuvant therapy for positive surgical margin or "un-resectable" cases

Sinonasal ACC has received considerable attention due to its proximity to the skull base. Sinonasal ACC is thought to arise primary from minor salivary glands within the nasal mucosa. Sinonasal ACC has been shown to have a worse prognosis than major salivary ACC, primarily due to its later stage at presentation and proximity to the skull base¹. Study of this disease is limited due to rare nature and indolent course, require 15+ years to differentiate survival rates.

Our aim to use the SEER database (a national cancer database) to better characterize Sinonasal ACC in relation to Major Salivary ACC, and to assess the effectiveness of general modalities of treatment across the two groups.

Methods and Materials

We pulled patient records from the SEER database from 1988-2011.

- 1,295 patients with Major Salivary ACC, and 368 patients with Sinonasal ACC were found.
- Data on race, age, sex, radiation treatment, and surgical treatment was obtained
- Staging was obtained by using site specific codes and recoded into Early (T1 & T2), Intermediate (T3), and Late Stage (T4). This was due to the high percentage of late stage ACC, particular in the sinonasal region.

Kaplan-Meier survival functions were used to calculate disease-specific survival curves.

Significant contributors to survival were incorporated into a cox proportional hazards model to identify independent predictors of survival.

	Major Salivary ACC	Sinonasal ACC	P Value
Age			P=0.024
10-44	27.26%	24.46%	
45-54	23.78%	20.11%	
55-64	19.54%	19.02%	
65-74	18.38%	19.29%	
74+	11.04%	17.12%	
Sex			P=0.01
Female	59.92%	52.45%	
Male	40.08%	47.55%	
T Stage			P<0.001
Early (T1/T2)	37.53%	16.58%	
Intermediate (T3)	19.54%	16.58%	
Late (T4)	42.93%	66.85%	
Regional Metastasis			P=0.430
No	90.97%	98.37%	
Yes	9.03%	1.63%	
Distant Metastasis			P=0.139
No	97.37%	98.1%	
Yes	2.63%	1.9%	
Total	1,295	368	
Treatment	Major Salivary ACC	Sinonasal ACC	
None	2%	2%	
Surgery	28%	19%	
Radiation	26%	12%	

Table 1. Demographics

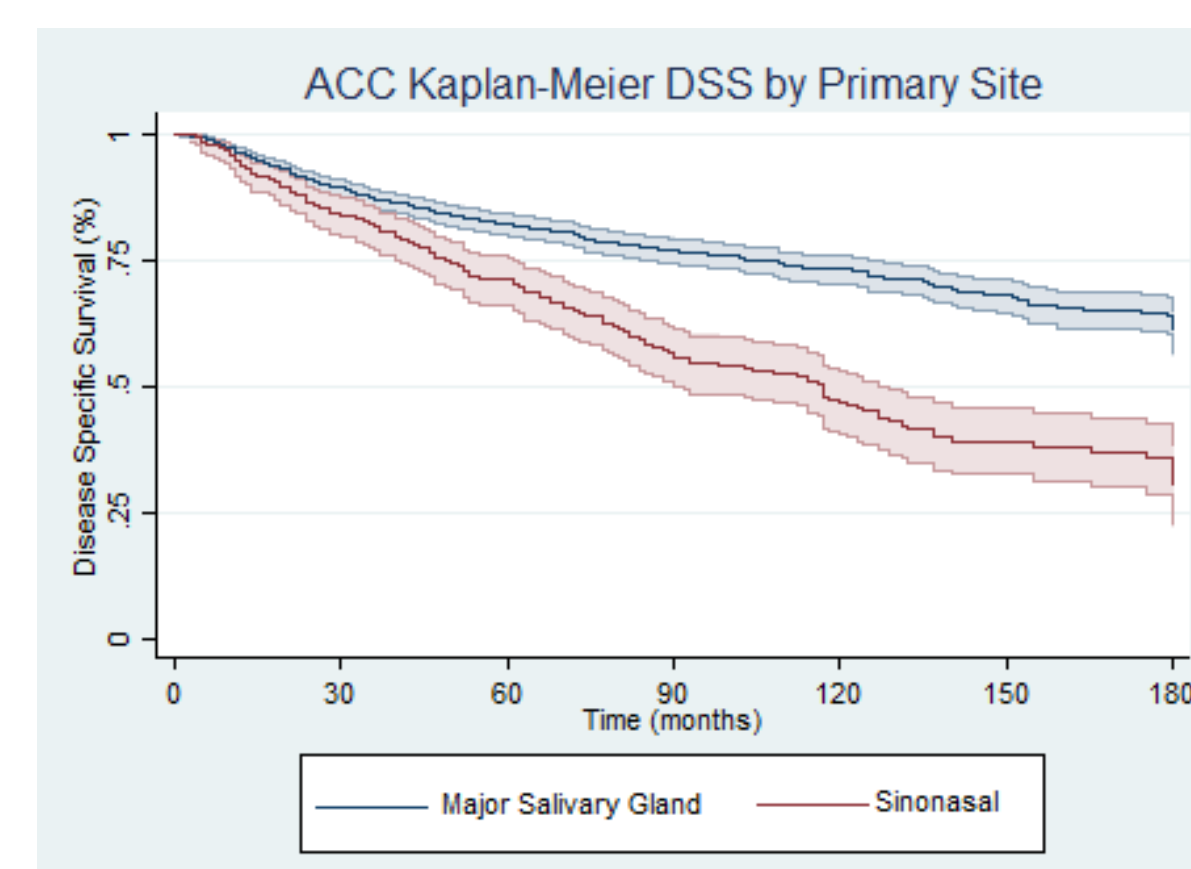


Figure 1. Adenoid Cystic Carcinoma Kaplan-Meier Disease Specific Survival by Site of Primary. ($p<0.001$)

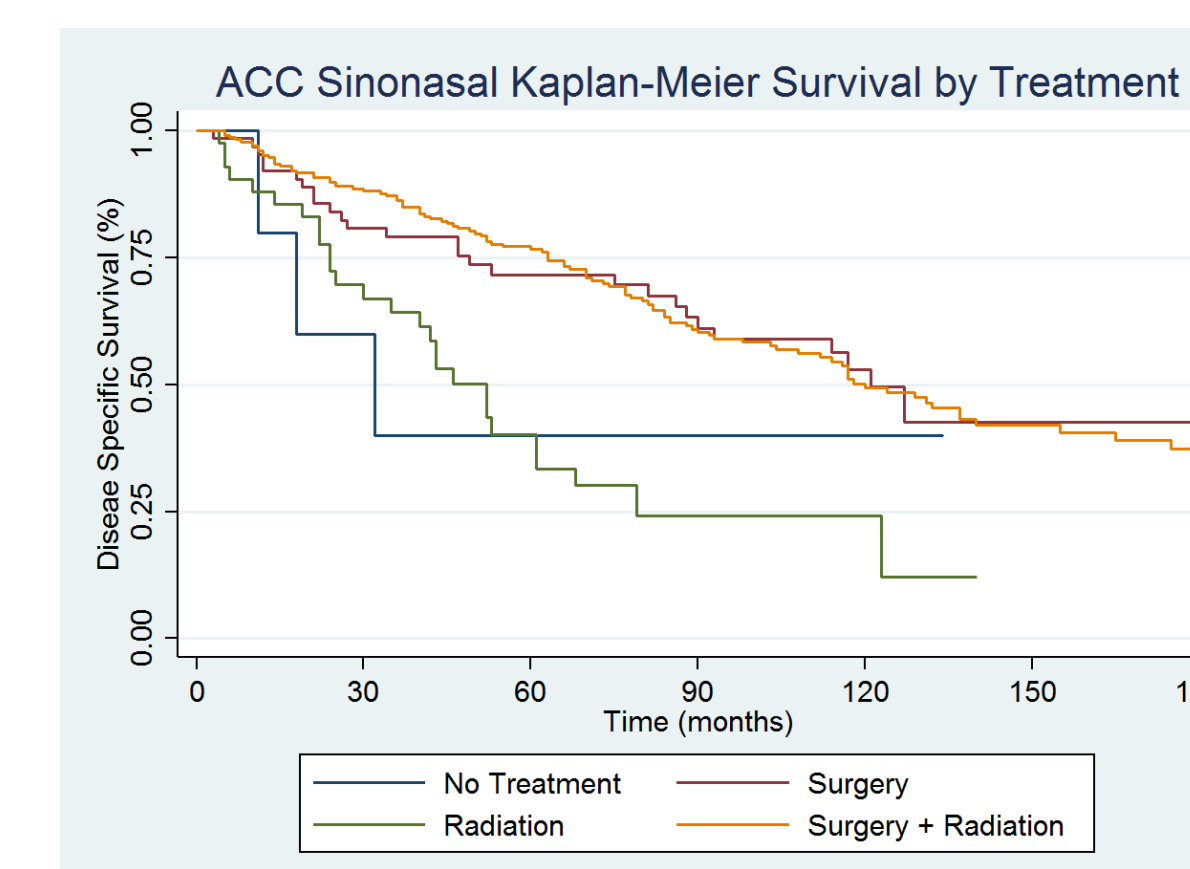


Figure 2. Sinonasal ACC Survival by Treatment Modality

Results

Demographics: Sinonasal ACC patients present at an older age and have a higher proportion of male patients than their major salivary ACC counterparts ($P<0.001$). In addition, sinonasal ACC present at a high T stage, but have a lower rate of regional metastasis ($P<0.001$). In spite of its high T stage, treatment was less aggressive with higher rates of radiation and lower rates of surgery ($P<0.001$).

Results

The 5 year disease specific survival (DSS) was significantly worse in the sinonasal ACC patients compared to the major salivary ACC patients. A cox proportional hazard model confirmed a worse prognosis for the sinonasal ACC patients despite controlling for T stage, age, treatment modality, and gender.

Site specific analysis of sinonasal ACC found a trend with surgery appearing to offer a significant survival advantage when compared to radiation therapy alone. This trend was confirmed in a cox proportional hazard regression which demonstrated a survival advantage for the groups that had surgery compared to those that did not (Figure 2).

Cox Multiple Hazard Regression Major Salivary ACC				
		HR	Lower 95% CI	Upper 95% CI
Treatment	Nothing	1		
	Surgery	0.31	0.17	0.56
	Radiation	1.24	0.61	2.52
Both		0.37	0.21	0.66
	T Stage			
	Late (T4)	1		
	Intermediate (T3)	0.77	0.59	1.02
	Early (T1/T2)	0.27	0.2	0.37
Age	10-44	1		
	45-54	1.42	1.02	1.96
	55-64	1.69	1.21	2.37
	65-74	1.95	1.39	2.73
75+		2.76	1.88	4.07
	Sex			
	Female	1		
	Male	1.34	1.08	1.67

Table 2: Cox Multiple Hazard Regression of Sinonasal ACC

Discussion

Our study demonstrates sinonasal ACC has a significantly worse survival than major salivary ACC independent of tumor stage and overall treatment modality. Sinonasal ACC does have several surgical limitations. Namely, the proximity to the cranial vault and use of surgical endoscopic techniques makes en bloc resection difficult to achieve and potentially result in patient morbidity. Traditional surgical dictum has taught that this can lead to tumor seeding and higher rates of local recurrence. However, multiple endoscopic reviews have demonstrated comparable survival rates to en bloc resection³. More likely, the survival difference noted in our study is due to ACC's relatively moderate response to radiation and chemotherapy, as well as its neurotrophic nature and close proximity to the skull base that makes clear surgical margins difficult to obtain. A major limitation of the SEER database is that there is no record of surgical margin status or other treatment specifics and therefore we were unable to assess this important questions.

In regards to treatment, radiation therapy appears to have little impact on sinonasal ACC survival rates. These results were confirmed in a similar SEER study by Unsal et al⁴. A Retrospective Case Control study by Ramakrishna et al. of 51 patients did demonstrate an overall survival advantage on univariate analysis for adjuvant radiation therapy, however this variable did not maintain significance after controlling for age, gender, and T stage. The surgical margin status was the primary predictor of survival in this model¹.

In conclusion, sinonasal ACC has a worse survival than its major salivary counterpart despite differences in T stage and overall treatment modalities. ACC is a locally and distantly aggressive disease with high rates of recurrence, but a slow growing nature. Surgery appears to be the primary effective treatment modality for ACC with a questionable benefit of radiotherapy on survival.

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References

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