Surgical management and lymph-node biopsy of rare malignant cutaneous adnexal carcinomas: a population-based analysis of 7591 patients

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Abstract

Objective—To analyze the prognosis of cutaneous adnexal malignancies, survival relative to surgical management, and utility of lymph-node biopsy.

Design—Population-based study of the SEER-18 database from 1975 to 2016.

Participants—7591 patients with sweat gland carcinoma, hidradenocarcinoma, spiradenocarcinoma, sclerosing sweat duct tumor/microcystic adnexal tumor (SSDT/MAC), porocarcinoma, eccrine adenocarcinoma, and sebaceous carcinoma

Results—Five-year OS ranged from 68.0 to 82.6%, while 5-year DSS ranged from 94.6 to 99.0%. The majority of patients were treated with narrow (42.4%) or wide local excision (16.9%). DSS at 5 years showed that patients with stage IV had significantly poorer survival (50.3%) than I, II, or III (99.3%, 97.8%, and 89.0% respectively). 5-year OS was significantly higher for narrow excision (excision with < 1 cm margin, 78.5%) than observation (65.0%), excisional biopsy (66.8%), or wide local excision (WLE, 73.2%). Lymph-node biopsy was performed in a minority of cases (8.1%) and patients showed no significant difference in survival based on nodal

status. The sensitivity and specificity of lymph-node biopsy for all malignancies were 46% and 80%, respectively. The PPV and NPV for that group were 0.46 and 0.80, respectively. Invasion of deep extradermal structures was a poor predictor of nodal positivity.

Conclusions—These malignancies have excellent DSS. Narrow excisions demonstrate better 5-year DSS and OS compared with WLE. Lymph-node biopsy is a poor predictor of survival in advanced stage disease and utility is limited.

Keywords

Adnexal carcinoma; Sweat gland carcinoma; Hidradenocarcinoma; Spiradenocarcinoma; Sclerosing sweat duct tumor; Microcystic adnexal tumor; Porocarcinoma; Eccrine adenocarcinoma; Sebaceous carcinoma; Eccrine carcinoma; Sebaceous adenocarcinoma; Adnexal neoplasm

Introduction

Cutaneous adnexal carcinomas comprise a group of rare cutaneous malignancies that are generally considered non-aggressive. Guidelines for the treatment of many of these malignancies are sparse, including guidance on surgical management [1, 2] including the utility of lymph-node biopsy [3, 4]. In addition, there has been minimal concerted effort to understand the differences in survival between the various cutaneous adnexal malignancies. Furthermore, details regarding the prognosis of these malignancies are thus far limited.

Malignant cutaneous adnexal carcinomas can fall into several categories including folliculosebaceous, eccrine, and apocrine [5]. These can develop as a result of malignant transformation of a benign adnexal neoplasm, such as transformation of a spiradenoma into a spiradenocarcinoma or a poroma into porocarcinoma, or may occur de novo, as in a sclerosing sweat duct tumor/microcystic adnexal carcinoma (SSDT/MAC) or sebaceous carcinoma [5]. Histopathology can be challenging, and some lesions have mixed features, defying standardized categorization in one of these groups [1].

In general, malignant cutaneous adnexal neoplasms are fairly indolent, although cases of metastasis, aggressive behavior, and death are represented in the literature [6]. Given a general lack of information about the prognosis of these malignancies, it can be difficult to decide how to clinically manage them, including determination of surgical margins and assessment of the utility of lymph-node biopsy. In this study, we seek to use data from the Surveillance, Epidemiology, and End Results-18 (SEER-18) database to analyze the prognosis of a number of malignant cutaneous adnexal neoplasms, survival relative to type of surgical management, and utility of lymph-node biopsy.

Methods

Data used in this analysis were found in SEER-18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2018 Sub (1975–2016) <Katrina/Rita Population Adjustment>. The SEER-18 database was searched for cases of cutaneous adnexal tumors. Malignancies with < 100 cases were excluded. Included malignancies were sweat gland carcinoma (ICD-O-3 8400/3), hidradenocarcinoma (ICD-O-3 8403/3), spiradenocarcinoma

(ICD-O-3 8404/3), sclerosing sweat duct tumor/microcystic adnexal tumor (SSDT/MAC, [ICD-O-3 8407/3]), porocarcinoma (ICD-O-3 8409/3), eccrine adenocarcinoma (ICD-O-3 8413/3), and sebaceous carcinoma (ICD-O-3 8410/3).

Incidence rates were calculated using SEER*Stat 8.3.6 (NCI/NIH, Bethesda, MD) Rate module. Cases were identified using the Case Listing module. Routine methods of categorical (Chi-squared test) and continuous (Student's *t* test and ANOVA) testing were applied, with statistical significance defined at alpha level 0.05 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC). Survival analysis was performed in SAS (Version 8). All deaths due to non-melanoma skin cancer were assumed to be due to the cutaneous adnexal neoplasm of interest. Details about nodal architecture are not included in SEER.

Derived AJCC 6th edition staging defines stage I as a tumor 2 cm or less in greatest dimension [7]. Stage II is > 2 cm in greatest dimension but without deep extradermal structure invasion. Stage III is defined as invasion of deep extradermal structures or a single positive node. Stage IV denotes any distant metastasis. Derived AJCC 6th edition staging was used as it was available for the majority of cases; in SEER, cases are listed as they are staged at the time of diagnosis and staging is not updated with the publication of new staging guidelines.

Results

Incidence and demographics

We identified 7591 patients with cutaneous adnexal carcinomas in the SEER database; subtypes with > 100 cases were included in this analysis (Table 1). We found an overall incidence of 11.2 per million person-years for all adnexal carcinomas. Incidences ranged from 0.4 per million person-years for spiradenocarcinoma to 18 per million person-years for sebaceous carcinoma. The median age at diagnosis ranged from 65 to 73, patients with hidradenocarcinoma being the youngest (65 years), and those with sebaceous carcinoma being the oldest (73 years). The vast majority of patients were white.

Survival by tumor type

Overall survival (OS) ranged from 82.4% for spiradenocarcinoma to 92.9% for SSDT/MAC at 2 years. SSDT/MAC had better 2-year OS than all other tumors ($p < 0.05$). Overall survival at 5 years ranged from 68.0% for spiradenocarcinoma to 82.6% for MAC/SSDT. SSDT/MAC had a significantly better 5-year overall survival than other neoplasms ($p < 0.05$).

Regarding disease-specific survival (DSS), at 2 years, survival ranged from 96.8% for spiradenocarcinoma to 99.6% for MAC. There were no statistically significant differences in 2-year DSS between malignancy types. 5-year DSS was lowest for hidradenocarcinoma at 94.6% and highest for SSDT/MAC at 99.0%. SSDT/MAC had significantly better survival than sweat gland carcinoma (95.4%) and hidradenocarcinoma (94.6%) ($p < 0.05$ for both).

Survival based on disease extent

Disease was categorized based on derived AJCC 6th edition staging (Table 2). Derived AJCC 6th edition staging is only recorded for tumors diagnosed between 2004 and 2015, and, thus, was only available for 1863 of 7591 patients (24.5%). The majority of cases were stage I (65.5%), with 23.6% stage II, 8.3% stage III, and 2.5% stage IV. This distribution was consistent across all adnexal neoplasm types. Exceptions included spiradenocarcinoma and hidradenocarcinoma which tended to be diagnosed at stage II rather than stage I, meaning > 2 cm rather than < 2 cm. OS at 5 years revealed that patients with stage IV disease had significantly poorer survival (17.1%) than I, III, or III (79.0%, 74.4%, and 67.4%). This distribution was roughly consistent across all adnexal neoplasm types. DSS at 5 years showed that patients with stage IV had significantly poorer survival (50.3%) than I, II, or III (99.3%, 97.8%, and 89.0%, respectively), a trend again roughly consistent across all adnexal neoplasm types.

TNM staging

Regarding size of lesions, 1109 patients had T1 disease (< 2 cm, 69.5%). T2 (2–5 cm) was found in 311 patients (14.9%). T3 disease (> 5 cm) was identified in 71 patients (4.4%). T4 disease (invasion of deep extradermal structures) was found in 80 patients (5.0%). Thus, the majority of patients present with tumors < 2 cm. Of 73 tumors invading deep extradermal structures (T4), only 4 were node positive. Distant metastases were seen with all T stages: T1 disease (< 2 cm) in 3 cases, T2 disease (2–5 cm) in 1 case, T3 disease (> 5 cm) in 4, and T4 disease (deep extradermal invasion) in 6. Eighteen cases had T stage of Tx.

Radiation and chemotherapy

Radiation and chemotherapy were used in only a small fraction of patients (Table 3). Of all patients, 5.3% received beam radiation and 1.4% received chemotherapy. Radiation was more likely to be utilized for eccrine adenocarcinoma than for other malignancies ($p <$ 0.0001). Use of chemotherapy was limited across all malignancies (0.4% for SSDT/MAC to 2.3% for sweat gland tumor). There were no significant differences in chemotherapy use between groups.

Surgical management

Several surgical management options are delineated in Table 3. The majority of lesions were treated with biopsy followed by narrow excision (42.4%), although a significant number were treated with excisional biopsy alone (26.7%). Wide local excision was performed in 16.9% of cases. Notably, a number of patients underwent observation only (12.9%).

For the group of all malignancies, patients who underwent observation were significantly younger than patients given alternative treatment [mean age of 66.8 years (range 15–104 years) for observation; 71.2 years (range 15–103 years) for excisional biopsy, 69.3 years (range 6–102) for narrow excision (< 1 cm), and 68.5 years (range 8–101) for wide local excision]. All comparisons with observation were statistically significant at $p <$ 0.002. Gender and race breakdown between groups were comparable ($p >$ 0.05).

Survival based on surgical management

Five-year OS and DSS were calculated for the overall group of all adnexal neoplasms. Five-year OS was significantly higher for narrow excision (78.5%) than no surgical intervention (65.0%), excisional biopsy (66.8%), or wide local excision (73.2%). Five-year DSS showed a small but statistically significant advantage to narrow excision (99.7%) compared to wide local excision (98.7%, $p < 0.05$). There was significantly worse survival for no surgery (90.8%) as compared to excisional biopsy (99.4%), narrow excision (99.7%), and wide local excision (98.7%, $p < 0.05$).

With the exception of sebaceous carcinoma, none of the malignancies showed any significant difference in OS or DSS based on surgical treatment. For sebaceous carcinoma, observation had a poorer OS than narrow excision or wide local excision (57.9% versus 73.8% and 71.2%, respectively). Biopsy of DSS for sebaceous carcinoma reveals that observation (96.2%) was significantly worse than excisional biopsy, narrow excision, or wide local excision (98.6%, 99.5%, and 97.0%, respectively).

Lymph node biopsy was performed in a minority of cases (578/7591, 8.1%) (Table 4). Of those cases, 138 (23.9%) were positive. Patients with sweat gland carcinoma who had a lymph node biopsied were more likely to have a metastatic lymphadenopathy in comparison to the aggregate of all other malignancies (46.4% vs. 21.8%, $p = 0.0012$).

Lymph-node positivity for adnexal malignancies

The percentage of cases in which a lymph-node biopsy was performed ranged from 7.2% for SSDT/MAC to 26.0% for hidradenocarcinoma. Factors resulting in selection of patients for lymph-node biopsy could not be assessed in this database. The proportion of lymph nodes found to be positive for malignancy ranged from 9.1% for spiradenocarcinoma to 50% for sweat gland carcinoma. Notably, there were no differences in overall survival detected between patients who had positive and negative lymph-node biopsies for any of the examined malignancies.

Assessment of lymph-node biopsy utility for adnexal malignancies

Meaningful stratification of survival by lymph-node status and stage for individual malignancies was not possible given small sample size; and survival analyses were performed for all adnexal malignancies as a group. The prevalence of death at the end of follow-up due to any cause in patients with nodal biopsy was 26% (Table 5). Accuracy of lymph-node biopsy in predicting outcome (alive vs. dead) was 71% (95% CI 65–76%). Sensitivity was 0.46 and specificity was 0.8, with PPV and NPV of 0.46 and 0.80, respectively. Stratification by stage had limited validity due to small number of cases, but overall showed similar PPV, NPV, sensitivity, and specificity.

The prevalence of death at the end of follow-up due to NMSC in patients with nodal biopsy was 6%. Accuracy of lymph-node biopsy in predicting outcome (alive vs. dead due to NMSC) was 76% (95% CI 70–81%). Sensitivity was 0.77 and specificity was 0.76, while PPV and NPV were 0.14 and 0.98, respectively. Although 24% of patients with a positive node died of NMSC, only 2% with a negative node did. Stratification by stage had limited

validity due to small number of cases, but overall showed similar PPV, NPV, sensitivity, and specificity.

Thus, although nodal biopsy has low sensitivity for both all-cause and NMSC-specific survival, the specificity and negative predictive value of a positive lymph-node biopsy suggest that it may have some utility in predicting survival.

Discussion

Cutaneous adnexal neoplasms are rare, and malignant transformation is even more uncommon. All of these malignancies have demonstrated moderate OS and excellent DSS with a few deaths due to non-melanoma skin cancer. Survival is worse for patients with regional/generalized disease as compared to localized disease. Overall, these data support an indolent disease course with a favorable natural history [6]. The consistencies in survival and disease behavior across malignancy type may offer some reassurance in cases with phenotypic overlap or challenging histopathology.

We identified no significant differences in choice of surgical management (excisional biopsy, excision with < 1 cm margins, and wide local excision) on survival metrics, suggesting that narrow excision may be as appropriate as wide local excision for these patients. The choice of surgical management appeared to be based on patient factors with the average age of those selected for observation substantially younger than those undergoing surgical management. Prior SEER-17 analysis of 3925 patients with sweat gland neoplasms demonstrated similar findings. However, that report did find a negative impact on DSS of observation (HR 2.38, 95% CI 1.09–7.23) [6]. Wide-spread use of narrow excision could significantly decrease morbidity and improve quality of life in patients diagnosed with malignant cutaneous adnexal carcinomas. Of note, the available dataset does pool patients undergoing simple narrow excision with Mohs micrographic surgery (MMS). These data do not characterize the probability of local recurrence as a function of extent of surgical excision. Further studies on other datasets will be needed to characterize the impact of well-defined surgical technique on local recurrence and survival.

The use of radiation and chemotherapy was limited, and there is minimal guidance as to which patients would benefit from these treatments. Previous reports show no survival benefit for radiation therapy (HR 1.27, 95% CI 0.99–1.63) [6]. Case reports of metastatic disease treated with combination chemotherapy are present in the literature [8, 9]. However, chemotherapy details are not specified in SEER, confounding this analysis.

There are no US or European guidelines regarding sentinel lymph node for sweat gland carcinoma, hidradenocarcinoma, porocarcinoma, or eccrine carcinoma. European guidelines for spiradenoma note that although regional LN excision is recommended with positive nodes, and SLN is acknowledged as helpful in clinically uninvolved nodes, there is no proven benefit of locoregional lymph-node dissection [10]. For MAC, US evidence-based clinical practice guidelines recommend against nodal staging in the absence of overt clinic disease [2]. Likewise, for sebaceous carcinoma, US guidelines do not recommend staging by sentinel lymph-node biopsy or elective lymphadenectomy [11]. We found that a significant

proportion of patients with each of these malignancies did undergo lymph-node biopsy, although given the small number of cases and few deaths, it is not possible to parse the data by stage in addition to diagnosis. Due to limitations of the data, we had to calculate the NPV, PPV, sensitivity, and specificity of lymph-node biopsy as a predictor of OS and DSS for all of the adnexal neoplasms as a group. For this population, we found that the overall accuracy of lymph-node biopsy was 71% for OS and 77% for DSS. Sensitivity and specificity were both poor for all stages grouped together and for each individual stage. There was increased prevalence of death in patients with higher stage disease, as expected. Overall, this suggests that lymph-node biopsy is of unclear value in evaluating these adnexal neoplasms. The calculation of a lumped estimate of the utility of lymph-node biopsies in this context is limited by the fact that this group of malignancies is very heterogeneous. Thus, the conclusions regarding lymph-node biopsies from these analyses must be considered with some circumspection. Additional work must be done to assemble well annotated cohorts of patients from which additional data on lymph-node utility can be gathered.

Because little is known about the clinical presentation of these rare adnexal neoplasms, the aggregation of stage information for a large number of tumors allows us to draw conclusions about the physical characteristics of the tumors being described. The absence of nodal positivity in the majority of adnexal tumor cases with deep extradermal invasion suggests that deep extradermal invasion is not a good predictor of nodal positivity and should not guide the decision to do a lymph-node biopsy. That decision should stem from identification of palpable adenopathy or other localizing symptom, although it is not possible to assess the sensitivity and specificity of tumor size on nodal positivity. In any case, there is no survival benefit to knowledge of nodal positivity or negativity in stage III or IV disease.

There are several variables missing in this analysis. Further studies on specific histologic characteristics as they correlate to survival are needed. Data on the use of MMS for adnexal carcinomas would also be extremely helpful [12–15]. Additional limitations include the low incidence and number of cases, which limits our ability to calculate and compare survivals, potentially obscuring inter-malignancy differences. The assumption that all deaths due to NMSC are due to the adnexal carcinomas is limiting, as patients could have potentially had another lethal keratinocytic or Merkel cell carcinoma. The inclusion of positive lymph nodes in both stags III and IV in AJCC 6th edition makes it difficult to make conclusions about survival for node-positive disease. Finally, due to the small sample size for some neoplasms and stages, it was not possible to calculate sensitivity, specificity, NPV, and PPV for each malignancy and each stage individually. In these analyses, it is important to notes that we lack significant points of information about the lymph-node analysis, including exactly how lymph nodes were assessed histopathologically (immunohistochemistry, serial sections, etc.) and what criteria were used to select patients for lymph-node biopsy.

One of the nuances in performing an analysis of adnexal neoplasms in SEER is that many of these malignancies have multiple synonyms in the literature, which can make application of results difficult. For example, sclerosing sweat duct tumor (SSDT) is also known as microcystic adnexal carcinoma (MAC). Hidradenocarcinomas are alternatively referred to as clear cell hidradenocarcinoma and malignant hidradenoma. Likewise, spiradenocarcinomas are also referred to as malignant eccrine spiradenomas. Porocarcinomas may also be called

malignant eccrine poromas or eccrine porocarcinomas. Sebaceous carcinomas may also be referred to as sebaceous gland adenocarcinoma or sebaceous carcinoma. Sweat gland carcinoma and eccrine adenocarcinoma are specific rare adnexal neoplasms, not wastebasket terms. Careful reference to histopathology may be necessary when extrapolating from these results.

Overall, these malignancies appear to be non-aggressive and present with excellent disease-specific survival. Narrow excisions have equivalent survival to WLE and may reduce patient morbidity significantly. Although lymph-node biopsy is a fairly robust predictor of improved survival when negative, given the indolence of these malignancies, the overall utility of lymph-node biopsy for these malignancies is not well validated. Additional studies examining the utility of lymph-node biopsy for individual malignancies are sorely needed to guide clinicians and patients, and although this study provides some information, its limitations prevent us from thoroughly elucidating the topic. Further studies on specific histopathologic correlates of disease, as well as the utility of radiation and chemotherapy, will be necessary.

Acknowledgments

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Table 1

Demographics and survival for patients with selected adnexal tumors

	All adnexal	Sweat gland carcinoma	Hidradenocarcinoma	Spiradenocarcinoma	Sclerosing sweat duct tumor (MAC)	Porocarcinoma	Eccrine adenocarcinoma	Sebaceous carcinoma
Incidence (per million persons, 95% CI)	11.2 (10.8–11.4)	4.0 (3.6–4.4)	2.0 (1.8–2.3)	0.4 (0.3–0.6)	2.7 (2.3–3.0)	2.2 (1.9–2.5)	1.8 (1.6–2.1)	18 (17.8–19.5)
N	7591	694	485	117	766	644	567	4325
Age [(median, range), years]	71 (6–104)	68 (11–99)	65 (8–100)	66 (22–99)	67 (6–103)	72 (20–103)	69 (15–98)	73 (9–104)
Follow-up [months, median (range)]	55 (0–501)	87 (0–501)	64 (0–435)	53 (0–280)	74 (0–377)	43 (0–204)	56 (0–251)	50 (0–454)
Gender								
Male [n (%)]	4240 (55.9)	376 (54.2)	277 (57.1)	54 (46.1)	327 (42.7)	364 (56.5)	285 (50.3)	2557 (59.1)
Female [n (%)]	3358 (44.2)	318 (45.8)	208 (42.9)	63 (53.8)	439 (57.3)	280 (43.5)	282 (49.7)	1768 (40.9)
Race								
Black [n (%)]	348 (4.6)	49 (7.1)	47 (9.7)	8 (6.8)	22 (2.9)	42 (6.5)	52 (9.2)	128 (3.0)
White [n (%)]	6467 (85.2)	586 (84.4)	399 (82.3)	97 (82.9)	685 (89.4)	533 (82.8)	460 (81.1)	3707 (85.7)
Other [n (%)]	395 (5.2)	30 (4.3)	21 (4.3)	6 (5.1)	19 (2.5)	35 (5.4)	29 (5.1)	255 (5.9)
Survival								
Alive [n, (% of total)]	446 (58.8)	321 (46.3)	273 (56.3)	65 (55.6)	562 (73.4)	414 (64.3)	389 (68.6)	2436 (56.3)
Dead [n (% of total)]	3132 (41.2)	373 (53.7)	212 (43.7)	47 (40.2)	204 (26.6)	230 (35.7)	178 (31.4)	1889 (43.7)
Dead 2/2 NMSC [n (% of total)]	162 (5.1)	36 (10.2)	21 (9.9)	5 (10.6)	7 (3.4)	10 (4.3)	11 (6.2)	72 (3.8)
2-Year OS (95% CI)	86.0 (85.1–86.8)	86.7 (84.2–89.4)	85.3 (82.1–88.6)	82.4 (75.5–90.0)	92.9 (91.1–94.9)	85.2 (82.3–88.1)	87.5 (84.7–90.4)	84.6 (83.5–85.8)
5-Year OS (95% CI)	71.1 (70.0–72.2)	73.7 (70.3–77.2)	72.0 (67.8–76.5)	68.0 (59.3–78.0)	82.6 (79.7–85.7)	69.1 (65.1–73.3)	76.4 (72.6–80.4)	68.1 (66.5–69.6)
2-Year DSS (95% CI)	98.8 (98.6–99.1)	97.0 (95.7–98.3)	98.1 (96.9–99.4)	96.8 (93.4–100)	99.4 (98.8–100)	99.6 (99.1–100)	99.0 (98.1–99.9)	99.1 (98.7–99.4)
5-Year DSS (95% CI)	97.8 (97.4–98.2)	95.4 (93.7–97.1)	94.6 (92.3–97.0)	96.8 (93.4–100)	99.0 (98.3–99.8)	98.8 (97.8–99.9)	98.2 (97.0–99.5)	98.2 (97.7–98.7)

OS overall survival, *DSS* disease-specific survival, *CI* confidence interval

Table 2

Survival based on derived AJCC stage, 6th edition for selected adnexal carcinomas

	All adnexal	Sweat gland carcinoma	Hidradenocarcinoma	Spiradenocarcinoma	Sclerosing sweat duct tumor (MAC)	Porocarcinoma	Eccrine adenocarcinoma	Sebaceous carcinoma (n, %)
Stage (derived AJCC stage group, 6th ed (2004–2015)	N = 1863	N = 70	N = 127	N = 46	N = 236	N = 229	N = 187	N = 968
I (n, %)	1221 (65.5)	40 (57.1)	56 (44.1)	14 (30.4)	150 (63.6)	140 (61.1)	103 (55.1)	718 (74.2)
II (n, %)	440 (23.6)	14 (20.0)	54 (47.5)	28 (60.9)	47 (19.9)	64 (27.9)	51 (27.3)	182 (18.8)
III (n, %)	155 (8.3)	12 (17.1)	11 (8.7)	3 (6.5)	38 (16.1)	20 (8.7)	28 (15.0)	43 (4.4)
IV (n, %)	47 (2.5)	4 (5.7)	6 (4.7)	1 (2.2)	1 (0.4)	5 (2.2)	5 (2.7)	25 (2.6)
5-Year OS based on stage								
I, OS (95% CI)	79.0 (75.6–82.0)	85.7 (61.7–95.2)	91.1 (74.5–97.1)	80.3 (69.9–85.4)	87.7 (79.2–92.9)	78.4 (67.5–86.1)	80.2 (67.9–88.1)	74.1 (69.0–78.5)
II, OS (95% CI)	74.4 (68.8–79.2)	53.5 (21.2–77.7)	80.9 (63.6–90.6)	60.3 (35.3–78.2)	85.0 (67.6–93.5)	77.4 (60.9–87.6)	72.4 (55.0–85.3)	73.3 (63.7–80.7)
III, OS (95% CI)	67.4 (56.6–76.0)	62.5 (22.9–86.1)	53.3 (17.7–79.6)	–	83.3 (61.0–93.4)	52.9 (24.3–76.3)	81.4 (52.8–93.6)	53.2 (30.3–71.7)
IV, OS (95% CI)	17.1 (4.6–26.5)	–	–	–	–	–	–	30.0 (7.1–57.8)
5-Year DSS based on stage								
I, DSS (95% CI)	99.3 (98.2–99.7)	100 (97.6–100)	96.5 (94.0–98.2)	97.9 (95.2–98.1)	96.9 (90.4–99.0)	97.4 (89.7–99.3)	98.7 (91.2–99.8)	99.0 (96.9–99.7)
II, DSS (95% CI)	97.8 (95.2–99.0)	87.5 (38.7–98.1)	94.1 (78.4–98.5)	90.3 (66.3–97.5)	93.3 (75.9–98.3)	95.2 (87.3–96.7)	93.9 (77.7–98.5)	98.3 (93.5–99.6)
III, DSS (95% CI)	89.0 (79.8–94.2)	71.4 (35.8–92.0)	70.0 (22.5–91.8)	–	83.3 (61.0–93.4)	66.1 (31.6–86.2)	–	79.8 (49.4–93.0)
IV, DSS (95% CI)	50.3 (18.5–75.7)	–	–	–	–	–	–	53.7 (13.1–82.7)

AJCC American Joint Committee on Cancer, OS overall survival, DSS disease-specific survival, CI confidence interval

Table 3

Surgical and medical management of cutaneous adnexal neoplasms

Treatment	All adnexal carcinomas	Sweat gland carcinoma	Hidradenocarcinoma	Spiradenocarcinoma	Sclerosing sweat duct tumor (MAC)	Porocarcinoma	Eccrine adenocarcinoma	Sebaceous carcinoma
Radiation								
Beam radiation [n (%)]	396 (5.3)	57 (8.3)	41 (8.6)	8 (6.9)	57 (7.4)	26 (4.1)	68 (12.1)	186 (4.3)
None/unknown [n (%)]	7109 (94.7)	632 (91.7)	438 (91.4)	108 (93.1)	710 (92.6)	611 (95.9)	494 (87.9)	4125 (95.7)
Chemotherapy								
Yes [n (%)]	106 (1.4)	16 (2.3)	6 (1.2)	1 (0.9)	3 (0.4)	8 (1.3)	9 (1.6)	63 (1.5)
No/unknown [n (%)]	7492 (98.6)	678 (97.7)	479 (98.8)	116 (99.1)	763 (99.6)	626 (98.7)	558 (98.4)	4262 (98.5)
Surgical management								
Punch/shave/incisional biopsy with no additional surgical intervention [n (%)]	951 (12.9)	41 (9.7)	38 (13.1)	9 (6.5)	102 (13.3)	81 (19.8)	57 (8.9)	623 (14.8)
Excisional biopsy as definitive treatment [n (%)]	1966 (26.7)	122 (28.8)	44 (15.2)	45 (32.6)	197 (25.6)	2 (0.5)	76 (27.4)	1122 (26.7)
Biopsy then electrocautery/cryosurgery/laser [n (%)]	23 (0.3)	1 (0.2)	4 (1.4)	2 (1.4)	1 (0.1)	2 (0.5)	1 (0.2)	15 (0.4)
Biopsy then narrow excision (< 1 cm margin) [n (%)]	3120 (42.4)	155 (36.6)	201 (69.9)	55 (39.9)	321 (41.7)	314 (76.6)	279 (43.5)	1821 (43.3)
Biopsy then wide local excision (> 1 cm margin) [n (%)]	1240 (16.9)	101 (23.8)	0 (0)	27 (19.6)	144 (18.7)	11 (2.7)	122 (19.0)	593 (14.1)
Biopsy then amputation (removal of digit, extremity, nose, ear) [n (%)]	53 (0.7)	4 (0.9)	2 (0.7)	0 (0)	4 (0.5)	0 (0)	7 (1.1)	31 (0.7)
Survival based on surgical management								
Punch/shave/incisional biopsy with no additional surgical intervention	65.0 (61.3–69.0)	77.3 (63.5–94.1)	61.4 (46.3–81.5)		85.0 (74.6–91.4)	64.5 (53.9–77.3)	69.0 (55.7–85.4)	57.9 (53.2–62.9)
Excisional biopsy as definitive treatment	66.8 (64.3–69.4)	70.5 (61.0–81.4)	66.2 (56.2–78.0)	53.4 (38.4–74.1)	79.7 (73.2–86.6)	65.2 (57.3–74.3)	74.4 (67.4–82.8)	63.2 (59.8–66.9)
Biopsy then narrow excision (< 1 cm margin)	78.5 (76.5–80.5)	74.9 (63.2–88.7)	75.3 (65.6–86.4)	74.1 (56.8–96.8)	88.8 (84.8–92.9)	69.4 (62.5–77.1)	77.9 (71.2–85.3)	73.8 (71.1–76.7)
Biopsy then wide local excision (> 1 cm margin)	73.2 (70.0–75.9)	85.1 (78.2–92.6)	79.2 (72.1–87.0)	72.5 (55.9–94.0)	78.6 (71.7–86.2)	77.7 (70.0–86.2)	81.3 (74.4–88.9)	71.2 (67.4–75.2)

Treatment	All adnexal carcinomas	Sweat gland carcinoma	Hidradenocarcinoma	Spiradenocarcinoma	Sclerosing sweat duct tumor (MAC)	Porocarcinoma	Eccrine adenocarcinoma	Sebaceous carcinoma
5-Year DSS (95% CI)								
No surgery	90.8 (88.0–93.6)	93.5 (85.2–100)	100 (100–100)	87.5 (67.3–100)	95.9 (91.5–100)	96.3 (91.3–100)	92.7 (85.1–100)	96.2 (94.1–98.4)
Excisional biopsy as definitive treatment	99.4 (99.0–99.9)	96.6 (92.9–100)	96.1 (90.7–100)	95.2 (86.6–100)		98.8 (96.6–100)	100 (100–100)	98.6 (97.6–99.6)
Biopsy then narrow excision (< 1 cm margin)	99.7 (99.4–100.0)		96.3 (91.2–100)	95.7 (87.7–100)	99.6 (98.8–100)	99.3 (97.1–100)	99.2 (97.7–100)	99.5 (99.0–99.9)
Biopsy then wide local excision (> 1 cm margin)	98.7 (98.0–99.3)	97.8 (94.8–100)	93.7 (88.8–98.8)	100 (100–100)	99.2 (97.8–100)	99.1 (97.4–100)	99.2 (97.5–100)	97.0 (95.6–98.5)

Treatment options included: punch/shave/incisional biopsy without additional surgical intervention ("observation"), excisional biopsy as definitive treatment, biopsy then electrocautery/cryosurgery/laser, biopsy then narrow excision (< 1 cm margin), biopsy then wide local excision (< 1 cm margin), biopsy then wide local excision (> 1 cm margin), and biopsy then amputation (removal of digit, extremity, nose, or ear)

Table 4

Lymph-node biopsy and survival

	All adnexal carcinomas	Sweat gland carcinoma	Hidradenocarcinoma	Spiradenocarcinoma	SSDT/MAC	Porocarcinoma	Eccrine adenocarcinoma	Sebaceouscarcinoma
Frequency of nodal biopsy								
Nodes not biopsied [*n* (%)]	6592 (91.9)	52 (74.2)	94 (74.0)	35 (76.0)	219 (92.7)	179 (78.2)	138 (73.7)	878 (90.7)
Nodes biopsied [*n* (%)]	578 (8.1)	18 (25.7)	33 (26.0)	11 (23.9)	17 (7.2)	50 (21.8)	49 (26.2)	90 (9.3)
Positive [*n* (% of cases biopsied)]	138 (23.9)	9 (50.0)	7 (21.2)	1 (9.1)	3 (17.6)	18 (36.0)	12 (24.4)	21 (23.3)
Negative [*n* (% of cases biopsied)]	440 (76.1)	9 (50.0)	26 (78.8)	10 (90.9)	14 (82.4)	32 (64.0)	37 (75.6)	69 (76.7)
5-Year survival of patients with nodes biopsied								
Positive [*n* (%)]	87.1 (76.9–94.2)	77.8 (54.9–100)	53.6 (25.7–100)	100 (no deaths)	66.7 (30.0–100)	50.4 (30.8–82.5)	64.3 (41.2–100)	60.3 (42.2–86.2)
Negative [*n* (%)]	94.1 (71.3–99.3)	53.3 (25.1–100)	95.8 (88.2–100)	64.3 (38.5–100)	70.1 (49.4–99.6)	93.8 (85.7–100)	88.4 (78.3–99.8)	78.3 (67.9–90.4)

Table 5

Sensitivity, specificity, PPV, and NPV of lymph-node biopsy based on stage for all adnexal neoplasms grouped

	Overall survival						Disease-specific survival					
	Prevalence of death in patients with nodal biopsy	Accuracy	Sensitivity	Specificity	PPV	NPV	Prevalence of death due to NMSC with examined node	Accuracy	Sensitivity	Specificity	PPV	NPV
All	0.26	0.71 (0.65–0.76)	0.46	0.80	0.46	0.80	0.04	0.76 (0.70–0.81)	0.77	0.76	0.14	0.98
I	0.16	0.83 (0.76–0.90)	0.0	1.00	–	0.83	–	–	–	–	–	–
II	0.15	0.84 (0.73–0.92)	0.00	1.00	–	0.84	0.00	0.97 (0.89–0.99)	0.00	1.00	–	0.97
III	0.44	0.43 (0.31–0.54)	0.74	0.18	0.41	0.47	0.11	0.30 (0.20–0.41)	0.89	0.23	0.12	0.94
IV	0.67	0.75 (0.42–0.94)	0.87	0.50	0.78	0.67	0.16	0.42 (0.15–0.72)	1.00	0.30	0.22	1.00