SKIN

# RESEARCH LETTER

## Epidemiology and Mortality Risk Factors of Sebaceous Carcinoma: A SEER – Based Population Study

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### ABSTRACT

**Background:** Sebaceous carcinoma is a rare and potentially aggressive cutaneous malignancy. It is derived from the adnexal epithelium of sebaceous glands and tends to hold a diverse clinical presentation. Although it is often reported in the periocular region, it can manifest from any sebaceous unit in the skin. Due to the rarity of this condition, prognostic and demographic factors are largely indeterminate. Hence, we sought to assess the prognostic impact of demographic and socioeconomic factors on the outcome of patients with sebaceous carcinoma.
**Methods:** A retrospective analysis was performed utilizing data from the Surveillance, Epidemiology, and End Results (SEER) database. From the registries, cases of sebaceous carcinoma from the years 2000 to 2018 were analyzed. Univariate and multivariate cox regression analyses were used to analyze the significance of socioeconomic and demographic factors on the survival of sebaceous carcinoma. Tumor grade and extent were included in the multivariate cox regression to minimize confounding.
**Results:** A total of 4154 cases of sebaceous carcinoma were analyzed within this study. Socioeconomic and demographic factors analyzed includes age, sex, race, and income. On multivariate analysis including tumor grade, tumor extent, age, sex, race and income, African American race was a significant risk indicator for survival (hazard ratio [HR], 1.9; P=.007). Increased age of 70+ were also identified as a significant risk indicator for survival (HR, 5.86; P<0.001). Female sex was identified as a protective indicator for survival (HR, 0.82; P=0.03). Income status did not significantly influence the survival outcome of sebaceous carcinoma.
**Conclusion:** Although income status did not show any significant influence on the survival outcome of sebaceous carcinoma, sex, race, and age characteristics did. The etiology behind these prognostic factors is unclear but may be related to access to medical care or lack of social support.

### INTRODUCTION

Sebaceous carcinoma (SC) is a rare and potentially aggressive cutaneous malignancy most commonly derived from the sebaceous glands, the glands of Zeis, or meibomian glands. The current literature search does not report which demographic and socioeconomic factors are associated with increased mortality risk.[1] Our article aims to build upon the limited prognostic research by

evaluating current data from 2000-2018 with a more extensive case number. Our analysis reports the associated SC mortality risk of race, age, sex, and income.

## METHODS

Patients diagnosed with SC from 2000 to 2018 were identified in SEER 18 registry using SEER Rare Cancer classification variable “40.2 Sebaceous adenocarcinoma”. The following data were extracted: age, year of diagnosis, race, vital status, site, combined summary stage, grade (degree of differentiation), extension, metastasis at diagnosis, tumor size, lymph nodes, and median household income inflation adjusted to 2019. Survival was measured in months from time of diagnosis to loss of follow up which included all-cause mortality. Multivariate Cox regression model was conducted using covariates deemed clinically significant or with P value of less than 0.25 in univariate analysis to include all potential factors. Age categories, sex, race, grade, tumor extent, and income were included in the final model.[2-4]

## RESULTS

A total of 4154 patients with primary SC were identified. Patient demographics and tumor characteristics are summarized in **Table 1**. The majority of patients diagnosed were over 70 years of age, with a male predominance (61.7%). 85.8% of the patients were white. Median and mean months of follow-up were 50 and 64.

The results from the multivariate Cox Regression model are shown in **Table 2**. Older age at diagnosis is associated with lower survival, with highest mortality among those 70 and older (HR = 5.86 [95% confidence interval (CI) 3.62 - 9.51]). Female sex is a protective prognostic predictor, with 18% reduction in mortality compared to their male counterparts (HR = 0.82 [95% CI 0.69 - 0.98]). Black individuals with primary SC have lower survival than white individuals (HR = 1.9 [95% CI 1.19 - 3.03]). Other variables such as income, location, and tumor extent do not have statistically significant association with survival in this model.

## DISCUSSION

We corroborate previous literature describing a higher incidence of SC in white individuals. Our results demonstrated a statistically significant HR of 1.9 in individuals identifying as black, implying a higher mortality risk despite having a lower overall incidence of SC. Various factors discussed by Shao et al. regarding other skin cancers, such as Acral Lentiginous Melanoma, could similarly explain the higher mortality in SCC. For instance, reduced access to care leads to decreased early skin examination/detection rates, less awareness of melanoma, and misdiagnosis from varied clinical presentation.[5] Geographical differences may also play a role leading to increased UV radiation exposure.[6] Furthermore, age >70 had a significant HR of 5.86, and those 50-69 had a HR of 2.09. Advanced age is a recognized risk factor for cutaneous malignancies and could be related to impaired immunologic and DNA repair mechanisms that decline with age. Interestingly, we could not conclude an association between socioeconomic status and mortality. Possibly, the rarity of the condition requires a larger sample size to fully assess the association. Finally, our study described a predominance in male sex. However, females had a hazard ratio of 0.82 which suggests a lower risk of mortality. This

**Table 1.** Patient demographics and tumor characteristics.

| Characteristic | Number (Percent) |
|---|---|
| **Sex** | |
| Female | 1592 (38.3%) |
| Male | 2562 (61.7%) |
| **Age** | |
| 0-49 | 300 (7.2%) |
| 50-69 | 1459 (35.1%) |
| >70 | 2395 (57.7%) |
| **Race** | |
| White | 3566 (85.8%) |
| African American | 115 (2.8%) |
| Asian/Pacific Islander | 213 (5.1%) |
| American Indian/Alaska Native | 29 (0.7%) |
| Unknown | 231 (5.6%) |
| **Tumor extent** | |
| Localized | 2651 (63.8%) |
| Distant | 141 (3.4%) |
| Regional | 128 (3.1%) |
| Unknown | 1234 (29.7%) |
| **Site** | |
| Lip | 38 (0.9%) |
| Eyelid | 924 (22.2%) |
| External ear | 154 (3.7%) |
| Face | 1414 (34.0%) |
| Scalp and neck | 506 (12.2%) |
| Trunk | 728 (17.5%) |
| Upper limb and shoulder | 262 (6.3%) |
| Lower limb and hip | 87 (2.1%) |
| Overlapping lesion | 6 (0.1%) |
| Skin, NOS | 25 (0.6%) |
| Scrotum | 10 (0.2%) |
| **Grade** | |
| I | 515 (12.4%) |
| II | 240 (5.8%) |
| III | 340 (8.2%) |
| IV | 39 (0.9%) |
| Unknown | 3020 (72.7%) |
| **Metastasis** | |
| Metastasized | 129 (3.1%) |
| Not Metastasized | 2978 (71.7%) |

| | |
|---|---|
| Unknown | 1047 (25.2%) |
| **Income** | |
| < $35,000 | 48 (1.2%) |
| $35,000 - 39, 999 | 70 (1.7%) |
| $40,000 - 44, 999 | 148 (3.6%) |
| $45,000 - 49, 999 | 236 (5.7%) |
| $50,000 - 54, 999 | 267 (6.4%) |
| $55,000 - 59, 999 | 275 (6.6%) |
| $60,000 - 64, 999 | 770 (18.5%) |
| $65,000 - 69, 999 | 549 (13.2%) |
| $70,000 - 74, 999 | 354 (8.5%) |
| $75,000+ | 1434 (34.5%) |

**Table 2.** Cox regression multivariate analysis of overall survival of sebaceous carcinoma.

| Characteristics | HR (95% CI) |
|---|---|
| **Age** | |
| 0-49 | 1 |
| 50-69 | 2.09 (1.26-3.45) |
| >70 | 5.86 (3.62-9.51) |
| **Sex** | |
| Male | 1 |
| Female | 0.82 (0.69-0.98) |
| **Race** | |
| White | 1 |
| African American | 1.9 (1.19-3.03) |
| Asian/ Pacific Islander | 0.66 (0.43-1.02) |
| American Indian/ Alaska Native | 1.21 (0.49-2.97) |
| **Grade** | |
| Well differentiated | 1 |
| Moderately differentiated | 0.8 (0.63-1.02) |
| Poorly differentiated | 1.21 (0.99-1.48) |
| Undifferentiated | 1.26 (0.83-1.92) |
| **Tumor Extent** | |
| Localized | 1 |
| Regional | 1.21 (0.80-1.83) |
| Distant | 1.35 (0.93-1.96) |
| **Income** | |
| < $35,000 | 1 |
| $35,000 - 39, 999 | 2.15 (0.74-6.23) |
| $40,000 - 44, 999 | 1.01 (0.37-2.77) |
| $45,000 - 49, 999 | 0.88 (0.34-2.31) |
| $50,000 - 54, 999 | 1.58 (0.62-4.0) |
| $55,000 - 59, 999 | 1.12 (0.44-2.87) |
| $60,000 - 64, 999 | 1.24 (0.50-3.05) |
| $65,000 - 69, 999 | 1.16 (0.47-2.88) |
| $70,000 - 74, 999 | 0.91 (0.36-2.32) |
| $75,000+ | 1.19 (0.49-2.91) |
| HR: Hazard Ratio; CI: Confident Interval; * indicates statistically significant P value (<0.05) | |

finding could be explained by the influence of estrogen, behavioral differences, or other confounders.[7] Of note, limitations in our interpretation arise from constraints in the SEER database as recorded mortality includes deaths from any cause and losses to follow-up. Thus, these factors could cause selection bias and skewing of our analysis.

Overall, increased data collection can lead to better clinical understanding and policy changes for SC patients. A systematic analysis incorporating several multi-regional studies could paint a more accurate picture of the influence of demographic and socioeconomic factors on SC.

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