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Prognostic factors and survival for malignant conjunctival melanoma and squamous cell carcinoma over four decades

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ABSTRACT

Purpose: To determine the epidemiology and survival of primary conjunctival malignant neoplasms.
Methods: Retrospective analysis of primary malignant conjunctival neoplasms using Surveillance, Epidemiology, and End Results database from 1973 to 2012.
Results: Of 1661 cases, the most common neoplasms are squamous cell carcinoma (SCC) at 54.8% and melanoma at 38.8%. Mean diagnostic age for melanoma was 62.1 compared to 65.5 years for SCC ($p = 0.002$). 52.2% of melanoma are male versus 77.4% of SCC ($p < 0.001$). For SCC only age (HR: 1.09, 95% CI:1.04–1.14) is a predictor of survival. For melanoma, age (HR: 1.07, 95% CI: 1.05–1.10), male sex (HR: 2.04, 95% CI: 1.16–3.60), T4 tumors (HR: 3.38, 95% CI: 1.17–9.80) and N1 status (HR: 8.69, 95% CI: 2.75–27.42) are all survival predictors. The 5 and 10-year overall survival (OS) estimates are not significantly different between SCC and melanoma, with 70% and 50% respectively for SCC, and 71% and 50% respectively for melanoma. Median survival time is worse for blacks (52 months) compared to whites (118 months) and Asians/Native Americans/Pacific Islanders (145 months), however race was not found to be a significant prognostic factor in multivariate analysis. Five-year survival are similar between decades 1973–1982 (66.2%), 1983–1992 (69.2%), 1993–2002 (71.3%) and 2003–2012 (70.2%).
Conclusion: Age at diagnosis is a determinant of survival for both conjunctival SCC and melanoma. Male sex, T4 and N1 staging are also important prognostic factors for melanoma. With respect to overall survival, SCC and melanoma did not differ significantly.

1. Introduction

Malignant neoplasms of the conjunctiva are uncommon. They can originate from the squamous epithelium, melanocytes and lymphocytic resident cells of the conjunctival stroma.

Squamous cell carcinoma (SCC) is the most common conjunctival malignancy [1] with incidence from 0.02 to 3.5 per 100,000 depending on geographical location [2]. Conjunctival melanoma is less common than SCC with an incidence of 0.24 to 0.53 per 1,000,000 [3]. SCC and melanoma have overlapping risk factors, including white race, older age, history of prolonged sunlight exposure [4,5]. In addition, risk factors for SCC also encompass male sex, xeroderma pigmentosum, AIDS and conjunctival infection by HPV 16 and 18 [5–7]. Both neoplasms are commonly found at the limbus in the sun-exposed interpalpebral fissure [4].

Conjunctival SCC and melanoma have high local recurrences after treatment, 30–41% [8] and 50–70% [9,10] respectively, however, melanoma is more likely to metastasize [4,8]. Surgical excision is the mainstay treatment for these neoplasms [4], but treatment paradigm have shifted over the past 20 years for SCC with topical therapy such as mitomycin C, 5-fluorouracil, and interferon alpha-2 being used as primary and adjunctive therapy [11]. The purpose of this study was to determine survival of patients with conjunctival SCC and melanoma and factors affecting survival after diagnosis. Recent survival data for conjunctival SCC and melanoma have not been examined with a population based approach.

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Table 1
Baseline characteristics for all malignant conjunctival neoplasm patients.

	Total	Melanoma	Squamous cell carcinoma	P-value
n	1661	644	911	
Age (mean [SD])	64.2 (17.1)	62.1 (18.1)	65.5 (16.2)	0.002
Sex (Male [%])	1113 (67.0)	336 (52.2)	705 (77.4)	< 0.001
Race (%)				0.01
White	1491 (89.8)	594 (92.2)	799 (87.7)	
Black	47 (2.8)	12 (1.9)	33 (3.6)	
Other	62 (3.7)	24 (3.7)	33 (3.6)	
Unknown	61 (3.7)	14 (2.2)	46 (5.1)	
Martial status (%)				0.23
Single	216 (13.0)	84 (13.0)	119 (13.1)	
Married	878 (52.9)	331 (51.4)	491 (53.9)	
Divorced	74 (4.5)	28 (4.4)	43 (4.7)	
Separated	5 (0.3)	2 (0.3)	2 (0.2)	
Widowed	197 (11.9)	96 (14.9)	89 (9.8)	
Unknown	291 (17.5)	103 (16.0)	167 (18.3)	
T stage (%)				< 0.001
1	114 (6.9)	35 (5.4)	77 (8.5)	
2	195 (11.7)	141 (21.9)	46 (5.1)	
3	128 (7.7)	86 (13.4)	37 (4.1)	
4	47 (2.8)	30 (4.7)	13 (1.4)	
TX	1117 (70.9)	352 (54.7)	738 (81.0)	
N stage (%)				0.11
0	715 (43.1)	283 (43.9)	382 (41.9)	
1	9 (0.5)	9 (1.1)	2 (0.2)	
NX	937 (56.4)	354 (55.0)	527 (57.9)	
Grade (%)				< 0.001
Well differentiated; Grade I	267 (16.1)	3 (0.5)	254 (27.9)	
Moderately differentiated; Grade II	163 (9.8)	3 (0.5)	153 (16.8)	
Poorly differentiated; Grade III	65 (3.9)	10 (1.6)	45 (4.9)	
Undifferentiated, anaplastic; Grade IV	8 (0.5)	2 (0.3)	4 (0.4)	
Unknown	1158 (69.7)	626 (97.2)	455 (50.0)	
Survival time (months, mean (SD))	75.4 (64.9)	77.2 (64.5)	75.4 (65.7)	0.54
Follow-up (years, mean (SD))	6.3 (5.4)	6.4 (5.4)	6.3 (5.5)	0.60

2. Methods

2.1. Patients and data source

All conjunctival neoplasm patients were acquired from the 1973 to 2012 Surveillance, Epidemiology, and End Results Program (SEER) databases using the primary site (*C69.0-Conjunctiva)*. All tumor types were identified by histologic type and included. Categories were made specifically for histologically confirmed melanoma and squamous cell carcinoma. Patients with and without surgery and/or radiation were included. SEER currently has 18 United States regional registries managed by the National Cancer Institute and is the most authoritative source for cancer epidemiologic characteristics in the United States. The use of the SEER database allows for analysis of rare malignant neoplasms such as conjunctival SCC and melanoma. The cancer incidence and survival data available through SEER-18 comprises 27.8% of the entire US population. The Johns Hopkins Institutional Review Board approved SEER use and analysis.

2.2. Survival

Overall survival (OS) was the primary outcome. OS was analyzed as a continuous variable in months. All patients were followed from conjunctival neoplastic diagnosis until study conclusion in 2012.

2.3. Covariates

Age was determined by age at diagnosis in years and analyzed as a continuous variable. Sex was analyzed with female as the reference group. Race was categorized as white, black, and Asian/American Indian/Pacific Islander. Marital status was grouped as single, married, divorced, separated, and widowed. Tumor grades were defined as grade I (well differentiated), grade II (moderately differentiated), grade III (poorly differentiated), and grade IV (undifferentiated, anaplastic). American Joint Committee on Cancer (AJCC) staging is not presently recommended for either conjunctival melanoma or SCC, and therefore was not recorded in the dataset. However, tumor size and nodal status were available. T and N stages were defined according to the AJCC 7th Edition Cancer Staging.

2.4. Analysis

The study population was described with general summary statistics. Group comparisons were made using the *t*-test and Wilcoxon rank-sum test for continuous variables, dependent on distribution, or the chi-squared test for categorical variables, as appropriate [Table 1]. Fisher's exact test was used for radiation sequence distribution due to small sample sizes. Survival analyses were conducted for overall survival using Kaplan-Meier (KM) method with log-rank statistic. One, five, and ten-year estimates were also performed with the KM method. Cox proportional hazard modeling was used for multivariable analyses. Statistical significance was set at $p < 0.05$. Data were retrieved using SEER*Stat Version 8.3.2 following the April 14, 2016 release (National Cancer Institute). All analyses were performed using STATA/SE 13.0 (StataCorp LP, College Station, TX).

3. Results

A total of 1661 cases of primary malignant conjunctival neoplasms were identified from 1973 to 2012. The most common histologic type was squamous cell carcinoma (SCC) at 54.8% (911 patients), followed by malignant melanoma at 38.8% (644 patients). Less common were sebaceous adenocarcinoma (1.3%) and mucoepidermoid carcinoma (1.1%). Mean diagnostic age for melanoma was 62.1 ± 18.1 years compared to 65.5 ± 16.2 years for SCC ($p = 0.002$). Males consisted of 52.2% of melanoma versus 77.4% of SCC ($p < 0.001$).

Table 2
Multivariate cox proportional hazard model of survival for 1661 malignant conjunctival neoplasm patients.

	Hazard ratio	Lower 95% CI	Upper 95% CI	P-value
Age	1.08	1.06	1.10	< **0.001**
Male sex	1.57	0.98	2.52	0.06
Marital status				
Single	Reference	–	–	–
Married	1.96	0.80	4.81	0.14
Divorced	1.12	0.21	5.85	0.90
Separated	1	–	–	1.00
Widowed	2.25	0.88	5.75	0.09
Race				
White	Reference	–	–	–
Black	0.42	0.05	3.57	0.43
Asian, American Indian, Pacific Islander	0.79	0.23	2.79	0.72
T stage				
T1	Reference	–	–	–
T2	1.00	0.52	1.94	0.99
T3	1.62	0.80	3.27	0.18
T4	2.94	1.37	6.32	**0.006**
N stage				
N0	Reference	–	–	–
N1	8.69	2.75	27.42	< **0.001**
Tumor grade				
Grade I, well differentiated	Reference	–	–	–
Grade II, moderately differentiated	0.81	0.29	2.27	0.68
Grade III, poorly differentiated	1.72	0.59	4.97	0.32
Grade IV, undifferentiated, anaplastic	1.00	–	–	1.00
Tumor type				
Melanoma	Reference	–	–	–
Squamous cell carcinoma	0.75	0.40	1.41	0.37

Bold indicates significance.
All decade cohorts compared to 1973–1982 elicited a HR of 1 and were omitted.

Table 3
Multivariate cox proportional hazard model of survival for conjunctival squamous cell carcinoma.

	Hazard ratio	Lower 95% CI	Upper 95% CI	P-value
Age	1.09	1.04	1.14	< **0.001**
Male sex	1.29	0.47	3.57	0.62
Marital status				
Single	Reference	–	–	–
Married	1.43	0.29	6.98	0.66
Divorced	–	–	–	–
Separated	–	–	–	–
Widowed	1.60	0.30	8.46	0.58
Race				
White	Reference	–	–	–
Black	0.88	0.09	9.09	0.92
Asian, American Indian, Pacific Islander	2.01	0.42	9.59	0.38
T stage				
T1	Reference	–	–	–
T2	0.58	0.20	1.67	0.31
T3	1.81	0.67	4.85	0.24
T4	3.31	0.71	15.47	0.13
N stage				
N0	Reference	–	–	–
N1	–	–	–	–
Tumor grade				
Grade I, well differentiated	Reference	–	–	–
Grade II, moderately differentiated	0.63	0.20	2.04	0.45
Grade III, poorly differentiated	1.37	0.30	6.19	0.69
Grade IV, undifferentiated, anaplastic	–	–	–	–

Table 4
Multivariate cox proportional hazard model of survival for conjunctival melanoma.

	Hazard ratio	Lower 95% CI	Upper 95% CI	P-value
Age	1.07	1.05	1.10	< **0.001**
Male sex	2.04	1.16	3.60	**0.01**
Marital status				
Single	Reference	–	–	–
Married	2.35	0.78	7.10	0.13
Divorced	2.37	0.35	15.93	0.38
Separated	–	–	–	–
Widowed	2.56	0.78	8.34	0.12
Race				
White	Reference	–	–	–
Black	–	–	–	–
Asian, American Indian, Pacific Islander	0.62	0.08	4.88	0.65
T stage				
T1	Reference	–	–	–
T2	1.30	0.48	3.55	0.61
T3	1.41	0.48	4.13	0.53
T4	3.38	1.17	9.80	**0.025**
N stage				
N0	Reference	–	–	–
N1	8.69	2.75	27.42	< **0.001**
Tumor grade				
Grade I, well differentiated	Reference	–	–	–
Grade II, moderately differentiated	–	–	–	–
Grade III, poorly differentiated	–	–	–	–
Grade IV, undifferentiated, anaplastic	–	–	–	–

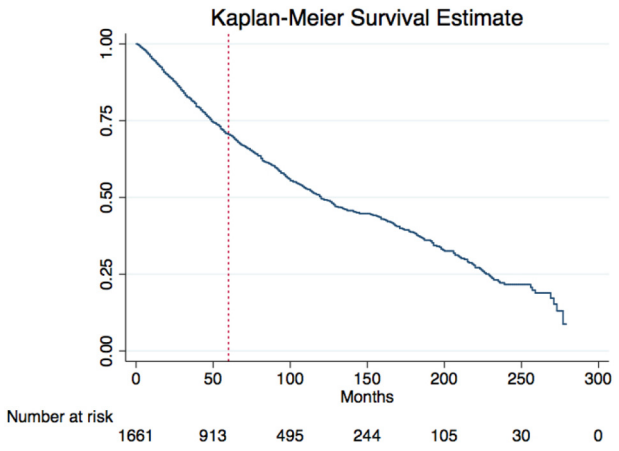

Fig. 1. Kaplan-Meier overall survival estimate for all conjunctival neoplasm patients
Dashed red line indicates 5-year survival. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Surgical treatment was performed in 1453 (87.5%) of all conjunctival neoplasm patients. By tumor type, 569 (88.4%) melanoma patients underwent surgery versus 805 (88.4%) SCC patients (p = 0.902). A majority of patients did not receive radiation therapy (1620 [97.5%]). For melanoma patients, 15 (2.3%) received adjuvant radiation, 1 (0.2%) received neoadjuvant radiation, and 1 (0.2%) received both neoadjuvant and adjuvant radiation. An additional patient also received intraoperative radiation therapy. This did not significantly differ from radiation therapy given to SCC patients (p = 0.493). For SCC patients, sixteen (1.8%) received adjuvant radiation while two (0.2%) underwent neoadjuvant radiation.

T stages were defined for 484 (29.1%) patients. Of those, 114

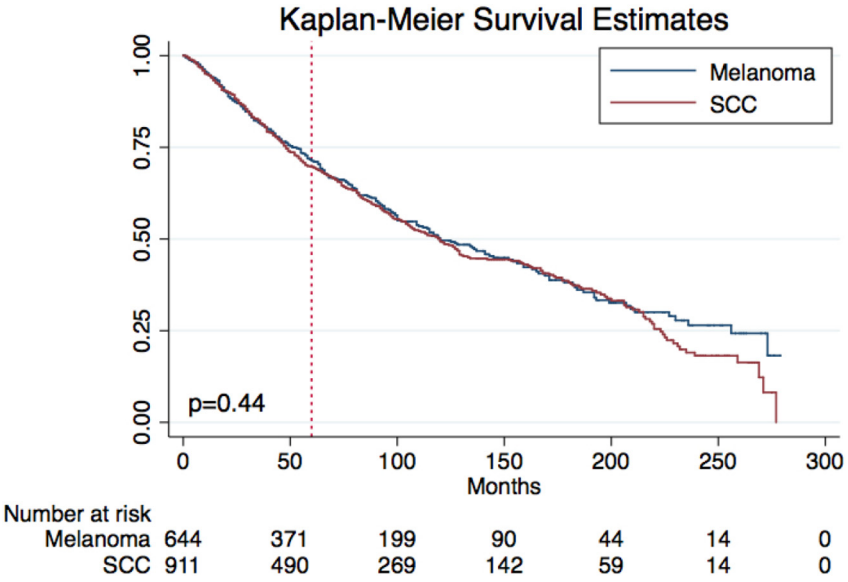

Fig. 2. Kaplan-Meier overall survival estimate for conjunctival melanoma versus squamous cell carcinoma
Dashed red line indicates 5-year survival. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

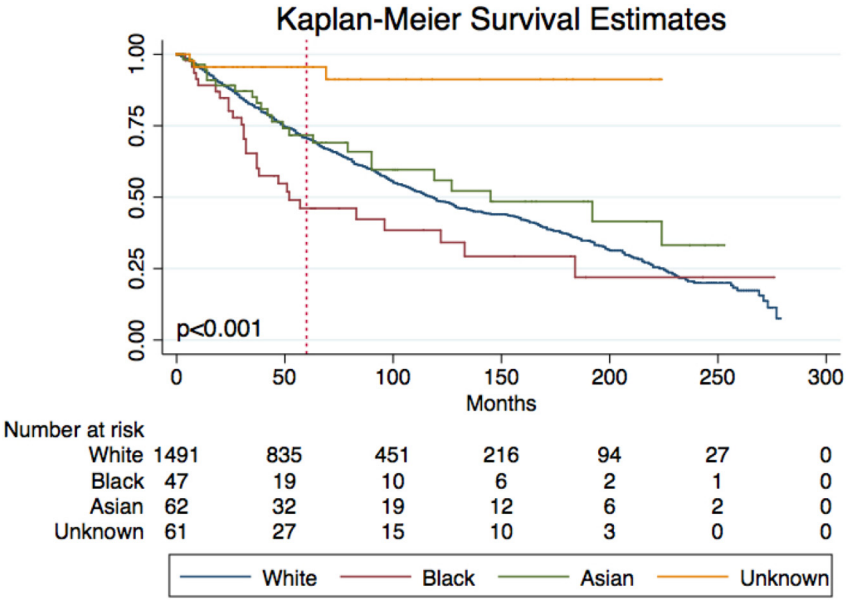

Fig. 3. Kaplan-Meier overall survival estimate by race
Dashed red line indicates 5-year survival. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

(23.6%) were T1, 195 (40.3%) were T2, 128 (26.5%) were T3, and 47 (9.7%) were T4. Seven hundred and twenty four (43.6%) had N stage information. Seven hundred and fifteen (98.8%) were N0 while 9 (1.2%) were N1. Stage grouping for either conjunctival melanoma or SCC is not presently recommended by the AJCC.

Survival predictors for all malignant conjunctival neoplasms were identified using multivariable cox proportional hazard regression [Table 2]. Age demonstrated poorer overall survival with a HR of 1.08 ($p < 0.001$) per year. Other statistically significant predictors of decreased survival included T4 tumors compared to T1 (HR: 2.94, 95% CI: 1.37–6.32) and N1 status (HR: 8.69, 95% CI: 2.75–27.42). Male sex, marital status, race, T2 or T3, and tumor grade were not significant in terms of survival. Statistical significance was not achieved comparing melanoma and squamous cell carcinoma with respect to overall survival (HR: 0.75, 95% CI: 0.40–1.41). Specifically for SCC [Table 3], only age (HR: 1.09, 95% CI:1.04–1.14) is a predictor. In comparison to melanoma [Table 4], age (HR: 1.07, 95% CI: 1.05–1.10), male sex (HR: 2.04, 95% CI: 1.16–3.60), T4 tumors (HR: 3.38, 95% CI: 1.17–9.80) and N1 status (HR: 8.69, 95% CI: 2.75–27.42) were all survival predictors.

The Kaplan-Meier overall survival estimate for all malignant conjunctival neoplasm patients can be seen in Fig. 1. The median survival time was 120 months with a standard deviation of 6.32 months (95% CI: 110–131). The 1, 5, and 10-year survival estimates were 94.4%, 70.5%, and 49.6%, respectively. The Kaplan-Meier overall survival estimate for conjunctival melanoma versus SCC was not statistically different ($p = 0.44$) [Fig. 2]. Median survival times were 120 months for both melanoma (SD: 10.7, 95% CI: 109–145 months) and SCC (SD: 6.5, 95% CI: 105–129 months). The 1, 5, and 10-year survival estimates for melanoma were 94.6%, 71.3%, and 49.6%, respectively. The 1, 5, and 10-year survival estimates for SCC were 94.6%, 69.7%, and 49.3%, respectively.

Kaplan-Meier survival estimates were generated for race [Fig. 3]

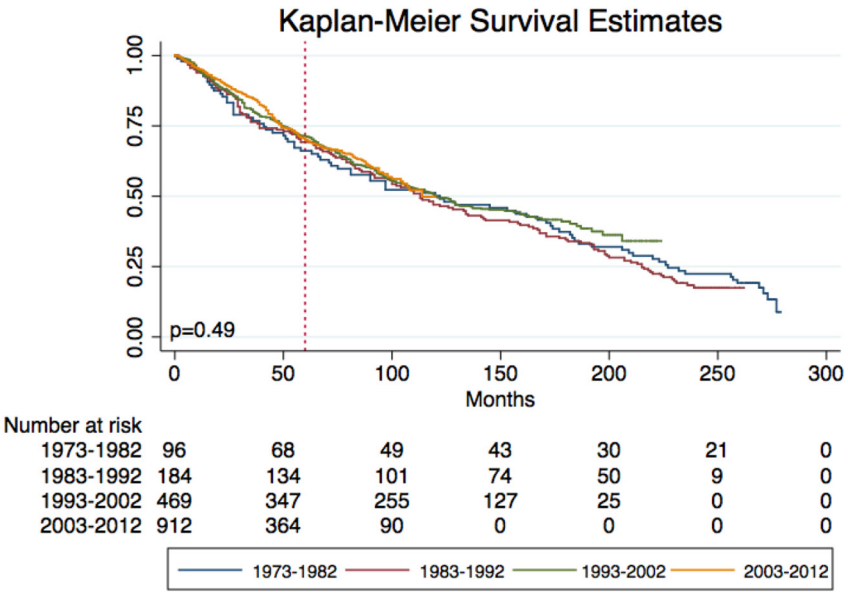

Fig. 4. Kaplan-Meier overall survival estimate by decade cohorts
Dashed red line indicates 5-year survival. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

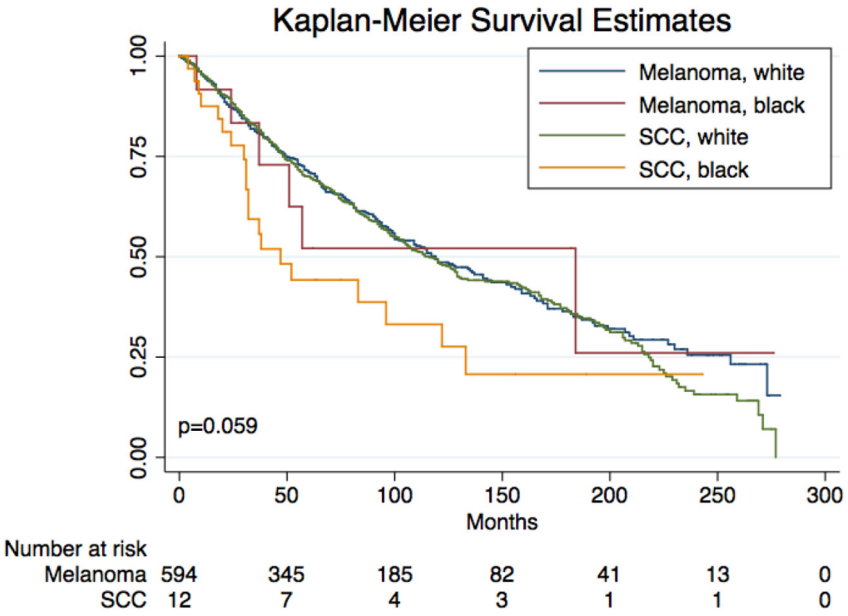

Fig. 5. Kaplan-Meier overall survival estimate by cancer type and race.

and decade cohort [Fig. 4]. Median survival times for whites, blacks, Asians/Native Americans/Pacific Islanders were 118, 52, and 145 months, respectively. These were statistically significantly different ($p < 0.001$). The 1, 5, and 10-year survival estimates by race were: whites (94.5%, 70.6%, 48.7%), blacks (89.1%, 46.1%, 38.4%), and Asians/Native Americans/Pacific Islanders (96.4%, 71.7%, 55.9%). The Kaplan-Meier overall survival estimate by decade was not statistically different ($p = 0.49$). Median survival times for decades 1973–1982, 1983–1992, 1993–2002, and 2003–2012 were 122, 113, 120, and 114 months, respectively. Five-year survival was also not statistically different at 66.2%, 69.2%, 71.3%, and 70.2%, respectively. Additionally, race and cancer type were analyzed together with groups of white melanoma, black melanoma, white SCC, and black SCC, without statistically different Kaplan-Meier overall survival estimates ($p = 0.059$) [Fig. 5]. Median survival times were 119, 184, 116, and 47 months, respectively.

4. Discussion

Our study reinforced the finding that SCC is the most common malignant conjunctival neoplasm. In this series, 55% were SCC while melanoma represented 39% of primary malignant conjunctival neoplasms. Other notable histological subtypes included sebaceous adenocarcinoma (1.3%) and mucoepidermoid carcinoma (1.1%). Due to the low statistical power of these two rare histological subtypes, majority of our analysis focused on malignant conjunctival neoplasm as an entirety and on SCC and melanoma. Mean age of diagnosis for melanoma was 62 years, which was significantly earlier than the diagnostic age for SCC (at 65 years). This is comparable to other studies that found mean age of detection for melanoma to be 55 to 65 years [12] while average age at presentation for SCC is 71 years [13]. Conjunctival melanoma in blacks is very rare, the incidence ratio of white to black is 1.4 to 4.1:1 [3,14,15], and our study found a similar ratio of 4.9:1 after

adjusting for the racial ratio of 10:1 (white to black) in the United States.

Multivariate analysis of all malignant conjunctival tumors demonstrated that age at diagnosis, T and N stage at presentation are important determinants of overall survival (OS). SCC predictive factors for prognosis have not been clearly identified other than delay in seeking medical attention [16]. Specifically for SCC, increased age is the only survival predictor with a hazard ratio of 1.09. Studies have found advanced AJCC-TNM T category to have higher risk of recurrence [17,18]. Chauhan et al. [8] found T3 and T4 stage to have independent prognostic effect on survival pattern of SCC, which were not observed by our study. This may in part due to low percentage (19%) of SCC with known T staging in our series. Regional nodal metastasis to preauricular, submandibular, and cervical lymph nodes may occur but in < 1% of cases [19]. Nodal metastasis occurred in 0.5% of our cases with known N staging, and there was not enough statistical power to examine its significance in survival. Marital status is an important factor in cancer survival analysis. It has been shown that unmarried individual are more likely to present with metastatic disease, have undertreatment, and die from their cancer [20]. However, we did not find marital status to be a significant survival predictor for conjunctival SCC.

In addition to age as a survival predictor shown in SCC, multivariate analysis of conjunctival melanoma also found male sex, T4 stage and N1 stage to be independent predictors of OS. These are similar to factors predictive of poor survival for cutaneous melanoma which includes advanced stage, increased age, male sex, nonwhite race, lower income, tumor of nodular or acral lentiginous subtype [10]. Some of the risk factors for recurrence such as orbital invasion and older patient age [9] are also the same factors predictive of survival found by this study. Study by Shields et al. [21], revealed conjunctival melanoma related death in 5% of T1, 20% T2, 23% of T3, and T2 and T3 stage were found to be factors predictive of melanoma-related death, which differs from results of our study where we found T4 but not T2 nor T3 to be survival factors. The caveat to the Shields' study is that it did not have any cases of T4 staged melanoma. Moreover, in contrast to a series of 256 cases by Paridaens et al. [22], we found both age and male sex to be prognostic factors.

Survival analysis using Kaplan-Meier curve showed no difference in OS between conjunctival SCC and melanoma. This is surprising given that melanoma has a higher likelihood of metastasis reported at approximately 25% at 10 years [9] versus SCC with a rate of < 1% for nodal metastasis [19]. The 5 and 10-year OS estimates are 70% and 50% respectively for SCC, and 71% and 50% for melanoma. For melanoma, other authors have reported a 5-year survival of 80–87% and a 10-year survival of 70–76% [22–27]. For all malignant conjunctival neoplasms, Kaplan-Meier curve revealed a difference in survival between the races with Blacks having the worst outcome when compared to Whites and Asians/Native Americans/pacific islanders, however race was not found to be a prognostic factor in multivariate analysis. Although the incidence of SCC and melanoma are on the rise [28,29] and treatment paradigm have shifted for SCC[11] in the recent times, the overall survival estimate by decade was not different between 1973 and 1982, 1983–1992, 1993–2002 and 2003–2012.

Limitations of this study include the lack of information on patient comorbidities, surgical margin status, metastasis status of the tumor and specific treatment modality from the database. As a result, these factors were not examined in this study and can be investigated in future studies. Also, data for disease specific survival was not available, as such, cause of mortality cannot be fully attributed to malignant conjunctival neoplasms.

5. Conclusions

In conclusion, this is the first study to the best of our knowledge that examined prognostic factors and survival for both conjunctival SCC and melanoma at the population level. Our study found age at diagnosis to be a determinant of survival for both conjunctival SCC and melanoma. Male sex, T4 and N1 staging are also important prognostic factors for melanoma.

Declaration of Competing Interest

The authors have not received financial assistance related to this manuscript.

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References

[1] Karp CL, Scott IU, Chang TS, Pflugfelder SC. Conjunctival intraepithelial neoplasia. A possible marker for human immunodeficiency virus infection? Arch Ophthalmol (Chicago, Ill 1960) 1996;114(3):257–61.
[2] Yang J, Foster CS. Squamous cell carcinoma of the conjunctiva. Int Ophthalmol Clin 1997;37(4):73–85.
[3] Hu DN, Yu G, McCormick SA, Finger PT. Population-based incidence of conjunctival melanoma in various races and ethnic groups and comparison with other melanomas. Am J Ophthalmol 2008;145(3):10–7.
[4] Augsburger James J, Corrêa ZM. Tumors of conjunctiva and cornea. Ophthalmology. 4th ed.Elsevier Inc.; 2014. p. 196–202.
[5] Sun EC, Fears TR, Goedert JJ. Epidemiology of squamous cell conjunctival cancer. Cancer Epidemiol Biomarkers Prev 1997;6(2):73–7.
[6] Lee GA, Williams G, Hirst LW, Green AC. Risk factors in the development of ocular surface epithelial dysplasia. Ophthalmology 1994;101(2):360–4.
[7] Lee GA, Hirst LW. Ocular surface squamous neoplasia. Surv Ophthalmol. 39(6):429–450.
[8] Chauhan S, Sen S, Sharma A, et al. American joint committee on Cancer staging and clinicopathological high-risk predictors of ocular surface squamous neoplasia: a study from a tertiary eye center in India. Arch Pathol Lab Med 2014;138(11):1488–94.
[9] Shields CL, Shields JA, Gündüz K, et al. Conjunctival melanoma: risk factors for recurrence, exenteration, metastasis, and death in 150 consecutive patients. Arch Ophthalmol (Chicago, Ill 1960) 2000;118(11):1497–507.
[10] Shields CL, Markowitz JS, Belinsky I, et al. Conjunctival melanoma: outcomes based on tumor origin in 382 consecutive cases. Ophthalmology 2011;118(2):389–95. [e1-e2].
[11] Shields CL, Shields JA. Ocular surface squamous neoplasia: from blue skies to blue dyes–we still need our ophthalmic pathologists. JAMA Ophthalmol 2015;133(11):1321–2.
[12] Larsen A-C. Conjunctival malignant melanoma in Denmark. Epidemiology, treatment and prognosis with special emphasis on tumorigenesis and genetic profile. Acta Ophthalmol 2016;94(8):842.
[13] Miller CV, Wolf A, Klingenstein A, et al. Clinical outcome of advanced squamous cell carcinoma of the conjunctiva. Eye 2014;28(8):962–7.
[14] Liesegang TJ, Campbell RJ. Mayo Clinic experience with conjunctival melanomas. Arch Ophthalmol (Chicago, Ill 1960) 1980;98(8):1385–9.
[15] Grossniklaus HE, Green WR, Luckenbach M, Chan CC. Conjunctival lesions in adults. A clinical and histopathologic review. Cornea 1987;6(2):78–116.
[16] Mckelvie PA, Daniell M, Mcnab A, Loughnan M, Mckelvie P. Squamous cell carcinoma of the conjunctiva: a series of 26 cases. Br J Ophthalmol 2002;86:168–73.
[17] Galor A, Karp CL, Oellers P, et al. Predictors of ocular surface squamous neoplasia recurrence after excisional surgery. Ophthalmology 2012;119(10):1974–81.
[18] Yousef YA, Finger PT. Squamous carcinoma and dysplasia of the conjunctiva and cornea. Ophthalmology 2012;119(2):233–40.
[19] Tunc M, Char DH, Crawford B, Miller T. Intraepithelial and invasive squamous cell carcinoma of the conjunctiva: analysis of 60 cases. Br J Ophthalmol 1999;83(1):98–103.
[20] Aizer AA, Chen M-H, McCarthy EP, et al. Marital status and survival in patients with Cancer. J Clin Oncol 2013;31(31):3869–76.
[21] Shields CL, Kaliki S, Al-Dahmash SA, Lally SE, Shields JA. American joint committee on Cancer (AJCC) clinical classification predicts conjunctival melanoma outcomes. Ophthal Plast Reconstr Surg 2012;28(5):313–23.
[22] Paridaens AD, Minassian DC, McCartney AC, Hungerford JL. Prognostic factors in primary malignant melanoma of the conjunctiva: a clinicopathological study of 256 cases. Br J Ophthalmol 1994;78(4):252–9.
[23] De Potter P, Shields CL, Shields JA, Menduke H. Clinical predictive factors for development of recurrence and metastasis in conjunctival melanoma: a review of 68 cases. Br J Ophthalmol 1993;77(10):624–30.
[24] Folberg R, McLean IW, Zimmerman LE. Malignant melanoma of the conjunctiva. Hum Pathol 1985;16(2):136–43.
[25] Jay B. Naevi and melanomata of the conjunctiva. Br J Ophthalmol 1965;49:169–204.
[26] Seregard S, Kock E. Conjunctival malignant melanoma in Sweden 1969-91. Acta Ophthalmol 1992;70(3):289–96.
[27] Lommatzsch PK, Lommatzsch RE, Kirsch I, Fuhrmann P. Therapeutic outcome of patients suffering from malignant melanomas of the conjunctiva. Br J Ophthalmol 1990;74(10):615–9.
[28] Dandala PP, Malladi P. Kavitha. Ocular surface squamous neoplasia (OSSN): a retrospective study. J Clin Diagn Res 2015;9(11):NC10–3.
[29] Yu G-P, Hu D-N, McCormick S, Finger PT. Conjunctival melanoma: is it increasing in the United States? Am J Ophthalmol 2003;135(6):800–6.