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ARTICLE

# Sebaceous gland carcinoma: analysis based on the 8th edition of American Joint Cancer Committee classification

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**PURPOSE:** To assess the prognostic value of T category of the 8th edition of American Joint Committee on Cancer (AJCC) classification in periocular sebaceous gland carcinoma (SGC).
**METHODS:** Retrospective interventional case series of 119 cases.
**RESULTS:** Based on the T category of 8th edition of AJCC classification, 119 periocular SGCs were classified into T1 ($n = 33$, 28%), T2 ($n = 37$, 31%) T3 ($n = 17$, 14%) and T4 ($n = 32$, 27%). There were no statistically significant differences in the rate of tumour recurrence based on T category. The outcome measures that showed significant increase with increase in T category included regional lymph node metastasis (3% for T1, 3% for T2, 12% for T3, and 44% for T4; $p < 0.0001$), systemic metastasis (0% for T1, 0% for T2, 12% for T3, and 25% for T4; $p = 0.002$) and death due to metastasis (0% for T1, 0% for T2, 12% for T3, and 22% for T4; $p = 0.005$). The 5-year Kaplan-Meier estimate rate for regional lymph node metastasis, systemic metastasis and metastasis-related death were all higher for the T4 category tumours (42%, $p = 0.005$; 34%, $p = 0.0002$; and 43%, $p = 0.0001$ respectively) compared to T1 (9%, 0%, and 0%), T2 (5%, 0%, and 0%) and T3 (10%, 17 and 8%) tumours.
**CONCLUSION:** Primary tumour (T) category of the 8th edition AJCC classification predicts the prognosis of patients with periocular SGC. The rates of lymph node metastasis, systemic metastasis, and death is much higher in T4 tumours compared to T1, T2, and T3 tumours. There was no association between T category and tumour recurrence.

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## INTRODUCTION

The American Joint Committee on Cancer (AJCC) Classification is currently in its 8th edition and is widely used to prognosticate various ocular and periocular tumours. The AJCC staging and/or its T category has been shown to correlate with specific outcomes of metastasis and survival in patients with eyelid basal cell carcinoma, squamous cell carcinoma, sebaceous gland carcinoma (SGC) as well as other rare eyelid carcinomas [1–4].

The AJCC (8th edition) has classified eyelid tumours based on the primary tumour (T), status of locoregional lymph nodes (N), and distant metastasis (M). It has also introduced modifications in the T and N staging criteria. The T staging places more emphasis on tumour size while doing away with subjective descriptions like 'need for enucleation or exenteration' found in the 7th edition to define T3/T4 categories [4, 5]. Furthermore, 'perineural invasion' has been eliminated as an automatic upstaging to T3a [5]. It has been reported that the application of the 8th edition of the classification may also predict regional lymph node metastasis with greater accuracy [6].

A previous in-house publication has outlined the prognosis of patients with SGC based on the tumour (T) category of the 7th AJCC classification [7]. In this study, we discuss the correlation between the clinical presentation and assess the prognosis of 119 cases of primary SGC based on the T category of the 8th AJCC classification.

## METHODS

This is a retrospective study and the Institutional Ethics Committee of L V Prasad Eye Institute, Hyderabad, India approved the study. The study adhered to the tenets of Declaration of Helsinki. Informed consent was obtained from all patients included in this study. Medical records of all patients with histopathologically proven primary eyelid SGC examined at the Operation Eyesight Universal Institute for Eye Cancer, L V Prasad Eye Institute, Hyderabad, India between June 1995 and September 2016 were included in the study. Those with inadequate data to classify the tumour, lack of histopathological confirmation of diagnosis of SGC, and those with prior interventions were excluded from this study.

The data retrieved from the patient records included patient demographics, referral diagnosis, history and type of prior intervention, laterality, presenting complaints, and duration of symptoms. Best-corrected visual acuity was recorded. The tumour details recorded included tumour location, tumour size, status of the eyelid margin, gland of tumour origin based on tumour location (meibomian gland, Glands of Zeiss, sebaceous glands of caruncle or ectopic), lesion morphology, and associated ocular features. Documentation by large drawings and external photography was done. Computed tomography (CT) of the orbit was performed in those cases with clinical suspicion of orbital tumour extension. Locoregional lymph node examination was performed routinely in all cases. In those patients with palpable lymph nodes, fine needle aspiration cytology was performed to rule out locoregional metastatic spread of tumour. Systemic metastatic workup included a chest x-ray, ultrasound of the abdomen, and liver function tests every year. All tumours were retrospectively classified based on the primary tumour category of the 8th edition of AJCC

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classification [4] as T1, T2, T3 or T4 based on documented tumour details, clinical photographs, and CT orbit.

The treatment details were recorded. T1 to T3 tumours underwent 4 mm clear margin wide excisional biopsy under frozen section control followed by appropriate eyelid reconstruction, T4 tumours were treated either with neoadjuvant chemotherapy or orbital exenteration. Wide excisional biopsy was rarely performed for T4 tumours when patient is not agreeable/suitable to chemotherapy or orbital exenteration, and the lesions are suitable for excision. Neoadjuvant chemotherapy (3 weekly 5-Fluoro Uracil and Cisplatin/carboplatin) was preferred in patients with T4 tumour having a good vision potential and suitable for chemotherapy, while the remaining T4 tumours were treated with orbital exenteration. All patients who underwent neoadjuvant chemotherapy subsequently underwent wide excision of the residual tumour or orbital exenteration based on response to treatment. Surgery was followed by adjuvant chemotherapy in these patients. Radical neck dissection followed by adjuvant chemotherapy and radiotherapy was advised for all patients with regional lymph node metastasis at presentation. Orbital external beam radiotherapy was advised in patients with microscopic tumour residue in the orbit post-orbital exenteration. Histopathology features such as pagetoid spread, growth pattern, rate of mitosis, degree of tumour differentiation and perineural and/or perivascular invasion were noted. Any incidence of locoregional metastasis, systemic metastasis, or death (including specified cause) were recorded. The time interval to metastasis was recorded. In case of deceased patients, the time interval to metastasis-related death as indicated by the family was noted.

### Statistical analysis

The statistical analysis was performed using the software Origin v7.0 (OriginLab Corporation, Northampton, MA, USA) and STATA v14.2 (StataCorp, College Station, TX, USA). The continuous data were checked for the normality of distribution by Shapiro–Wilk test and for the equality of variance by Levene test. The comparisons among stages T1 to T4 were performed by analysis of variance for continuous parametric data with equal variance, Kruskal–Wallis test for continuous non-parametric data or continuous parametric data with unequal variance and Chi-square test for categorical data. Multiple pair-wise comparisons between different T categories were performed by t-test for continuous parametric data with equal variance, Mann–Whitney test for continuous non-parametric data or continuous parametric data with unequal variance and Chi-square test or Fisher-Exact test for categorical data. Kaplan-Meier survival analysis was performed to estimate the rates of locoregional lymph node metastasis, distant metastasis and metastasis-related death over the time and Cox proportional hazards regression model was used to evaluate the effect of T staging and hazard ratio was estimated. A $p$-value of <0.05 was considered statistically significant. For multiple pair-wise comparisons, Bonferroni correction was applied and a $p$-value <0.017 was considered statistically significant.

## RESULTS

Based on the inclusion criteria, a total of 119 cases were included in this study. Based on the T category, they were classified into T1 ($n$ = 33, 28%), T2 ($n$ = 37, 31%) T3 ($n$ = 17, 14%) and T4 ($n$ = 32, 27%) (Table 1). Slight female preponderance was noted in all four T categories. The tumour epicentre was in the upper eyelid in a greater proportion of cases regardless of T category compared to the lower eyelid or caruncle. Based on the definition of T category, the tumour features that showed significant increase with increasing tumour category included mean tumour basal diameter (7 mm for T1, 13 mm for T2, 22 mm for T3, and 27 mm for T4; $p < 0.0001$) and extension of tumour to the orbit (0% for T1, T2, and T3, and 53% for T4; $p < 0.0001$). All other clinical features were not significantly different among different T categories. The demographic and clinical features of each T category are outlined in Table 1.

The histopathological features and their comparison are outlined in Table 1. No significant differences were noted in the gland of origin, growth pattern, degree of differentiation, mitotic activity, and an incidence of pagetoid spread, and perivascular and perineural invasions based on T category.

Comparison of treatment outcomes per T category is outlined in Table 2. The rate of wide excisional biopsy decreased with progressive increase in T category (100% for T1, 97% for T2, 82% for T3, and 19% for T4; $p = 0.003$). The rate of orbital exenteration as primary treatment increased with increasing T category (0% for T1, 0% for T2, 12% for T3, and 47% for T4; $p < 0.0001$). Primary neoadjuvant chemotherapy was used in T4 category tumours alone ($n = 7$, 22%; $p < 0.001$). Over a mean follow-up period of 2 years (median, 1 year; range, <1 to 10 years), the rate of primary/secondary orbital exenteration increased with increasing T category (3% for T1, 3% for T2, 8% for T3, and 63% for T4; $p <$ 0.0001). The rate of tumour recurrence was highest in T2 category but the difference was not statistically significant (3% for T1,14% for T2, 6% for T3, and 9% for T4; $p = 0.52$). The outcome measures that showed significant increase with increase in T category included regional lymph node metastasis (3% for T1, 3% for T2, 12% for T3, and 44% for T4; $p < 0.0001$), systemic metastasis (0% for T1, 0% for T2, 12% for T3, and 25% for T4, $p = 0.002$) and metastasis-related death (0% for T1, 0% for T2, 12% for T3, and 22% for T4; $p = 0.005$). In these 3 parameters, T4 tumours were significantly different from T1 and T2 tumours.

Kaplan–Meier estimates of regional lymph node metastasis at 1 and 5 years, respectively, were 0 and 9% for T1, 5 and 5% for T2, 10 and 10% for T3, and 11 and 42% for T4 ($p = 0.005$; hazard ratio 2.38; Fig. 1). Kaplan–Meier estimates of systemic metastasis at 1 and 5 years, respectively, were 0 and 0% for T1, 0 and 0% for T2, 17 and 17% for T3, and 12 and 34% for T4 ($p = 0.0002$; hazard ratio 4.30; Fig. 1). Kaplan–Meier estimates of death due to metastasis at 1 and 5 years, respectively, were 0 and 0% for T1, 0 and 0% for T2, 8 and 8% for T3, and 8 and 43% for T4 ($p = 0.0001$; hazard ratio 6.62; Fig. 1). The Kaplan–Meier analysis of outcomes is outlined in Table 3.

## DISCUSSION

The AJCC classification system was established in 1959 to develop a uniform classification system and common language for cancer staging worldwide. Categorization of eyelid carcinomas with the AJCC TNM classification allows risk stratification to provide guidelines for management in terms of both survival and local tumour control [4]. Application of the 8$^{th}$ edition results in recategorization of tumours (previously assigned based on the 7th AJCC edition) into new T categories [5, 6, 8–10]. The major differences between 7$^{th}$ and 8$^{th}$ editions of AJCC classification of periocular SGC is the definition of T1 (tumours size 10 mm or less in 8$^{th}$ edition vs 5 mm or less in 7$^{th}$ edition) resulting in down staging of the disease when classified using 8$^{th}$ edition of AJCC. Also, all T categories in the 8$^{th}$ edition are classified based on clinical features including tumour size and extent of ocular/periocular invasion without any consideration of histopathology features or type of surgical treatment [5, 6, 8–10].

In our study cohort based on 8$^{th}$ edition of AJCC, T2 category tumours formed the largest group ($n$ = 37; 31%). A study of SGC in an ethnic Chinese cohort also reported highest numbers in the T2 category ($n$ = 26; 41%) [8]. In comparison, studies from Caucasian cohort reported T1 tumours as the largest category (39 to 45%) [5, 9]. Another study reported higher proportion of T3 tumours (36%) [10]. Variation in the distribution of tumour size could point to ethnic differences in clinical presentation of SGC or a referral bias, which may also impact outcomes.

Our cohort reflected a preponderance of SGC in elderly female patients ($n$ = 69; 58%) with the mean age at diagnosis being 57 years (range, 21 to 100). This observation has been supported by other studies in both Caucasian and Asian cohorts [3, 9–13]. There was no significant correlation between T category with patient age or sex in our study population. Similar to other studies, the upper eyelid was the tumour epicentre in 63% of cases in our study.

In our study, an increase in T category also revealed a shift from wide excision biopsy as a primary treatment modality towards orbital exenteration for a greater proportion of T4 category

**Table 1.** Sebaceous gland carcinoma based on T classification of American Joint Committee on Cancer: Demographics, clinical features, and histopathology features.

| Feature | All cases ($n = 119$) *n* (%) | T1 ($n = 33$) *n* (%) | T2 ($n = 37$) *n* (%) | T3 ($n = 17$) *n* (%) | T4 ($n = 32$) *n* (%) | *p*-value |
|---|---|---|---|---|---|---|
| Age (years); mean (median; range) | 59 (60; 21–100) | 57 (59; 35–83) | 60 (60, 26–90) | 58 (59, 21–82) | 61 (60, 30–100) | 0.83 |
| Gender | | | | | | |
| Male | 50 (42) | 15 (45) | 15 (40) | 6 (35) | 14(44) | 0.91 |
| Female | 69 (58) | 18 (54) | 22 (60) | 11 (65) | 18 (56) | |
| Referral Diagnosis | | | | | | |
| Sebaceous gland carcinoma | 16 (13) | 8 (24) | 4 (11) | 1 (6) | 3 (10) | 0.32 |
| Squamous cell carcinoma | 11 (9) | 2 (6) | 5 (14) | 2 (12) | 2 (6) | 0.71 |
| Basal cell carcinoma | 10 (8) | 3 (9) | 4 (11) | 1 (6) | 2 (6) | 0.91 |
| Stye | 1 (1) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0.54 |
| Chalazion | 1 (1) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0.54 |
| Blepharoconjunctivitis | 2 (2) | 0 (0) | 0 (0) | 1 (6) | 1 (3) | 0.36 |
| Eyelid mass | 5 (4) | 1 (3) | 0 (0) | 2 (12) | 2 (6) | 0.26 |
| Duration of symptoms (months) mean, (median; range) | 11, (7; 1–53) | 8, (6; 2–26) | 12, (6; 1–48) | 12, (12; 1–36) | 14, (7; 1–53) | 0.55 |
| Tumour Epicentre | | | | | | |
| Upper eyelid | 75 (63) | 20 (61) | 21 (57) | 15 (88) | 19 (60) | 0.77 |
| Lower eyelid | 41 (34) | 11 (33) | 15 (40) | 2 (12) | 13 (40) | 0.42 |
| Caruncle | 3 (2) | 2 (6) | 1 (3) | 0 (0) | 0 (0) | 0.43 |
| Tumor Basal Dimension (mm) mean, (median; range) | 16, (12; 3–80) | 7, (7; 3–10) | 13, (12; 6–20) | 22, (20; 8–30) | 27, (26; 6–80) | <0.0001[a] |
| Gland of origin based on tumor location | | | | | | |
| Meibomian glands | 109 (92) | 26 (79) | 35 (94) | 17 (100) | 31 (97) | 0.93 |
| Glands of Zeiss | 7 (6) | 5 (14) | 1 (3) | 0 (0) | 1 (3) | 0.10 |
| Caruncle | 3 (2) | 2 (6) | 1 (3) | 0 (0) | 0 (0) | 0.43 |
| Extent of Tumor Involvement | | | | | | |
| Orbital extension | 17 (14) | 0 (0) | 0 (0) | 0 (0) | 17 (53) | <0.0001[b] |
| Paranasal sinus extension | 3 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (10) | 0.054 |
| Lacrimal system | 1 (1) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0.45 |
| Intracranial extension | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | N/A |
| Histopathology features | | | | | | |
| Tumor differentiation ($n = 111$) | | | | | | |
| Well differentiated | 17 (15) | 6 (19) | 5 (14) | 3 (19) | 3 (11) | 0.87 |
| Moderately differentiated | 76 (68) | 23 (74) | 26 (70) | 10 (63) | 17 (63) | 0.99 |
| Poorly differentiated | 18 (16) | 2 (6) | 6 (16) | 3 (19) | 7 (26) | 0.39 |
| Growth pattern ($n = 117$) | | | | | | |
| Lobular | 57 (49) | 19 (56) | 16 (43) | 8 (50) | 14 (45) | 0.91 |
| Comedo | 9 (8) | 2 (6) | 2 (5) | 2 (13) | 3 (10) | 0.82 |
| Papillary | 6 (7) | 2 (6) | 4 (11) | 0 (0) | 0 (0) | 0.21 |
| Mixed | 45 (38) | 10 (30) | 15 (41) | 6 (38) | 14 (45) | 0.87 |
| Mitotic activity ($n = 112$) | | | | | | |
| High | 70 (63) | 19 (63) | 22 (59) | 9 (60) | 20 (67) | 0.99 |
| Moderate | 28 (25) | 8 (27) | 9 (24) | 5 (33) | 6 (20) | 0.90 |
| Low | 14 (13) | 3 (10) | 6 (16) | 1 (7) | 4 (13) | 0.83 |
| Pagetoid involvement of the conjunctiva detected by map biopsy | 59 (50) | 12 (36) | 20 (54) | 8 (47) | 19 (59) | 0.72 |
| Perivascular invasion | 9 (8) | 3 (9) | 1 (3) | 0 (0) | 5 (16) | 0.18 |
| Perineural invasion | 3 (3) | 1 (3) | 1 (3) | 0 (0) | 1 (3) | 0.92 |

[a]Post-hoc analysis showed that all pair-wise comparisons were significantly different (all $p < 0.0001$) except for T3 vs T4 ($p = 0.25$).
[b]Post-hoc analysis showed that only T4 was significantly different from T1 ($p < 0.0001$), T2 ($p < 0.0001$) and T3 ($p = 0.005$).

tumours. This reflects the increased incidence of invasion into surrounding anatomic structures and a need for more radical surgery to provide local tumour control as the T category increases. Only 1 case of a T1 category tumour (3%) underwent orbital exenteration while 63% ($n = 20$) of the T4 category tumours required orbital exenteration at some stage in the management. Radical surgery in advanced cases may achieve local tumour control but may not influence the final outcome. In our study, T4 tumours were associated with poor outcomes inspite of radical surgery.

**Table 2.** Sebaceous gland carcinoma based on T classification of American Joint Committee on Cancer: Treatment outcomes.

| Feature | All cases $n = 119$ | T1 ($n = 33$) | T2 ($n = 37$) | T3 ($n = 17$) | T4 ($n = 32$) | *p*-value |
|---|---|---|---|---|---|---|
| Primary Treatment | | | | | | |
| Wide excision biopsy | 89 (75) | 33 (100) | 36 (97) | 14 (82) | 6 (19) | 0.003[a] |
| Orbital exenteration | 17 (14) | 0 (0) | 0 (0) | 2 (12) | 15 (47) | <0.0001[b] |
| Neoadjuvant systemic chemotherapy | 7 (6) | 0 (0) | 0 (0) | 0 (0) | 7 (22) | 0.001[c] |
| Lost to follow-up | 6 (5) | 0 (0) | 1 (3) | 1 (6) | 4 (13) | 0.16 |
| Adjuvant Treatment | | | | | | |
| External beam radiotherapy | 8 (7) | 0 (0) | 2 (5) | 1 (6) | 5 (16) | 0.13 |
| Systemic chemotherapy | 8 (7) | 0 (0) | 0 (0) | 2 (12) | 3 (9) | 0.08 |
| Radical neck dissection | 4 (3) | 0 (0) | 1 (3) | 1 (6) | 2 (6) | 0.53 |
| Primary/Secondary orbital exenteration | 25 (21) | 1 (3) | 1 (3) | 3 (18) | 20 (63) | <0.0001[d] |
| Tumor recurrence | 10 (8) | 1 (3) | 5 (14) | 1 (6) | 3 (9) | 0.52 |
| Final outcome at last follow-up | | | | | | |
| Regional lymph node metastasis | 18 (15) | 1 (3) | 1 (3) | 2 (12) | 14 (44) | <0.0001[e] |
| Systemic metastasis | 10 (8) | 0 (0) | 0 (0) | 2 (12) | 8 (25) | 0.002[f] |
| Death due to metastasis | 9 (8) | 0 (0) | 0 (0) | 2 (12) | 7 (22) | 0.005[g] |

[a]Post-hoc analysis showed that only T4 was significantly different from T1 ($p = 0.001$), T2 ($p = 0.001$) and T3 ($p = 0.007$).
[b]Post-hoc analysis showed that only T4 was significantly different from T1 ($p < 0.0001$) and T2 ($p < 0.0001$).
[c]Post-hoc analysis showed that only T4 was significantly different from T1 ($p = 0.01$) and T2 ($p = 0.007$).
[d]Post-hoc analysis showed that only T4 was significantly different from T1 ($p < 0.0001$) and T2 ($p < 0.0001$).
[e]Post-hoc analysis showed that only T4 was significantly different from T1 ($p = 0.002$) and T2 ($p = 0.001$).
[f]Post-hoc analysis showed that only T4 was significantly different from T1 ($p = 0.006$) and T2 ($p = 0.004$).
[g]Post-hoc analysis showed that only T4 was significantly different from T1 (p = 0.01) and T2 ($p = 0.007$).

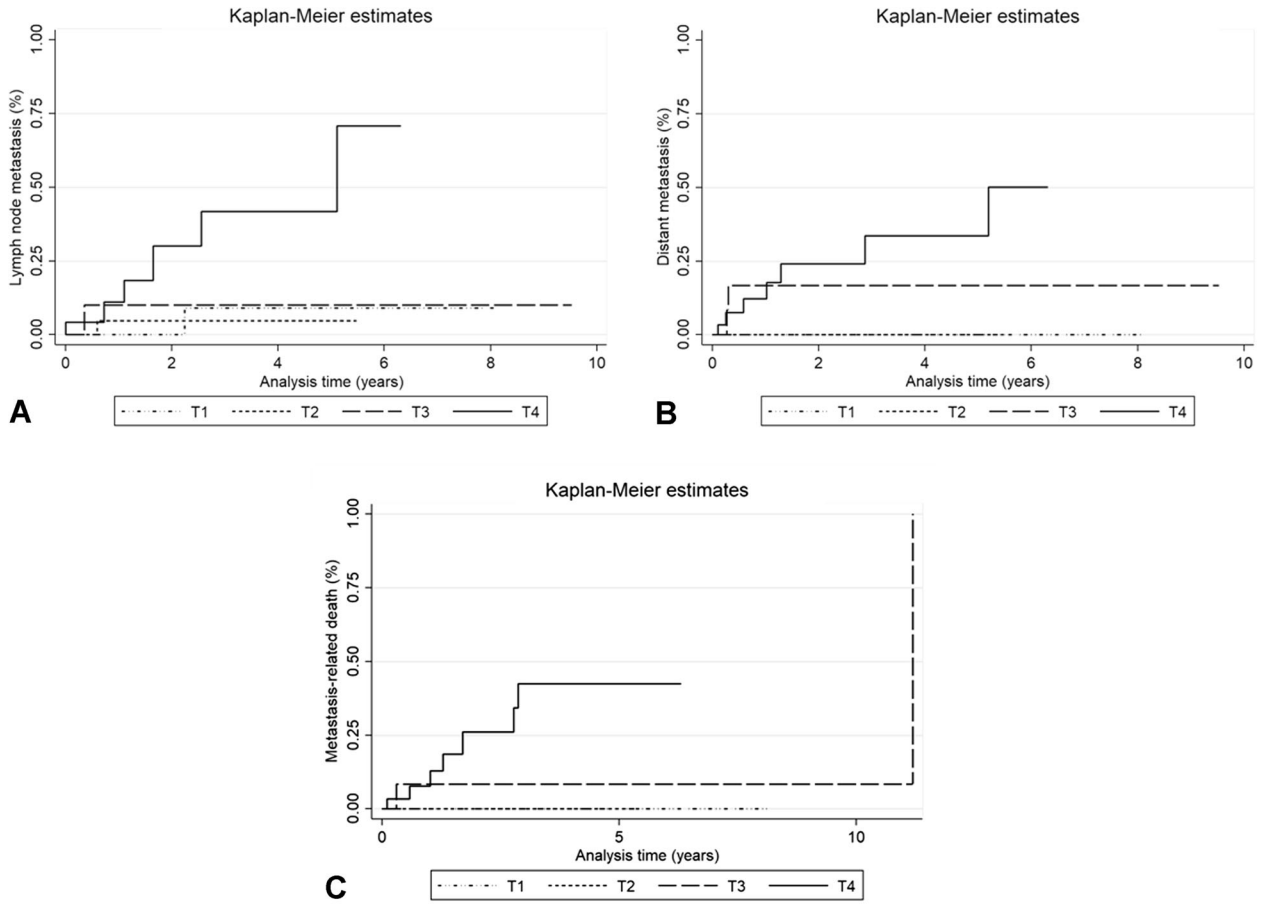


**Fig. 1 Kaplan–Meier estimates.** Kaplan–Meier estimate of **A** regional lymph node metastasis, **B** distant metastasis, and **C** metastasis-related death.

**Table 3.** Kaplan–Meier analysis of the outcomes.

| Kaplan–Meier analysis | All cases $n = 119$ % estimate ± SE | T1 $n = 33$ % estimate ± SE | T2 $n = 37$ % estimate ± SE | T3 $n = 17$ % estimate ± SE | T4 $n = 32$ % estimate ± SE | *p*-value |
|---|---|---|---|---|---|---|
| Locoregional lymph node metastasis | | | | | | 0.005; HR = 2.38 ± 0.83 (95% CI, 1.20–4.72) |
| 1 year | 5.4% ± 2.7% | 0% ± 0% | 4.8% ± 4.7% | 10% ± 9.5% | 11.0% ± 7.6% | |
| 3 years | 15.5% ± 5.4% | 9.1% ± 8.7% | 4.8% ± 4.7% | 10% ± 9.5% | 41.7% ± 15.6% | |
| 5 years | 15.5% ± 5.4% | 9.1% ± 8.7% | 4.8% ± 4.7% | 10% ± 9.5% | 41.7% ± 15.6% | |
| Distant metastasis | | | | | | 0.0002; HR = 4.30 ± 2.49 (95% CI, 1.38–13.40) |
| 1 year | 5.8% ± 2.5% | 0% ± 0% | 0% ± 0% | 16.7% ± 10.8% | 12.3% ± 6.7% | |
| 3 years | 12.7% ± 4.8% | 0% ± 0% | 0% ± 0% | 16.7% ± 10.8% | 33.6% ± 12.3% | |
| 5 years | 12.7% ± 4.8% | 0% ± 0% | 0% ± 0% | 16.7% ± 10.8% | 33.6% ± 12.3% | |
| Metastasis-related death | | | | | | 0.0001; HR = 6.62 ± 5.66 (95% CI, 1.24–35.34) |
| 1 year | 3.5% ± 2.0% | 0% ± 0% | 0% ± 0% | 8.3% ± 8.0% | 7.7% ± 5.3% | |
| 3 years | 15.1% ± 5.4% | 0% ± 0% | 0% ± 0% | 8.3% ± 8.0% | 42.5% ± 13.1% | |
| 5 years | 15.1% ± 5.4% | 0% ± 0% | 0% ± 0% | 8.3% ± 8.0% | 42.5% ± 13.1% | |

*CI*: confidence interval; *HR* = Hazard ratio; *SE* = Standard error.

Sa et al showed that there is correlation between 8th edition AJCC and tumour recurrence [10]. In their study of 100 patients with periocular SGC, there was correlation between T3b or worse and tumour recurrence [10]. Hsia et al found an association of local recurrence with aggressive histopathological patterns and extent of tumour invasion into surrounding tissues, but not with tumour size [8]. AlHammad et al did not note a significant correlation between tumour recurrence and advanced disease in their cohort [6]. In our study, tumour recurrence was higher in T2 tumours but there was no statistically significant correlation between T category and tumour recurrence.

The 8th edition of AJCC classification gives relevance not only to the size of the tumour but also to local tumour invasion into the eyelid margin/tarsus or full thickness invasion. Both these factors in conjunction may contribute to improved accuracy in predicting regional lymph node metastasis. Studies report that patients who developed nodal metastasis had greater tumour size and also showed features such as eyelid margin or tarsal plate invasion beyond the tumour nidus [6]. In our study, a correlation between T category and nodal metastasis was noted with T4 category tumours showing the highest rate of metastasis. Hsia et al. and Sa et al. noted that T categories at T2c or higher have greater incidence of nodal metastasis [8, 10], while AlHammad et al noted the highest risk of regional lymph node metastasis in T4 tumours [6], similar to our study. Sa et al performed sentinel lymph node biopsy for detection of lymph node metastasis [10], which could have resulted in early detection of nodal metastasis even before it was clinically apparent. In our study, sentinel lymph node biopsy was not performed which could have resulted in under-diagnoses of few cases. This underscores the importance of sentinel lymph node biopsy in patients with SGC.

The T category of the 8th AJCC classification may more accurately predict the occurrence of tumour-related death. Hsia et al and Sa et al found increased incidence of tumour-related death in category T3b or worse [8]. Our cohort study revealed a significant association between T staging of tumours and systemic metastasis as well as death due to metastasis with T4 tumours accounting for the highest rates. Our analysis also noted that the prognostic indicators such as poor tumour differentiation and perivascular invasion were found in a greater proportion of T4 tumours than in lesser T categories, though this was not statistically significant. In contrast, AlHammad et al reported no significant correlation between T category and tumour-related deaths but noted that poor tumour differentiation and papillary pattern were associated with T3/T4 categories [6]. Periodic systemic review of all patients with SGC is important regardless of T category [6].

Limitations of the study include retrospective nature of the study and lack of routine colour doppler ultrasound or magnetic resonance imaging of head and neck or sentinel lymph node biopsy for accurate diagnosis of regional lymph node metastasis. However, the strength of the study is large cohort size of this relatively rare eyelid malignancy from a single centre with uniform treatment and follow-up protocol.

In conclusion, the 8th edition of AJCC staging system when applied to our cohort, reflected greater association of regional lymph node metastasis, systemic metastasis and tumour-related death for the T4 category tumours. The survival of patients in earlier stages of T should be better than that of patients in advanced stages/greater T in a good prognostic system [8]. This trend was observed in our study suggesting that the 8th edition of AJCC is a good predictor for patient outcomes. However, there was no association between T category and its predictive value in tumour recurrence. The current AJCC staging system could benefit from improvement of the monotonicity of its parameters between categories and include histopathological factors, which could further improve its accuracy in predicting outcomes.

## Summary

What was known before

- American Joint Committee on Cancer classification has prognostic value

What this study adds

- 8th edition of AJCC can predict metastasis and metastasis-related death in cases of periocular sebaceous gland carcinoma However, it is not useful in predicting tumour recurrence rates

## DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are not publicly available due to protection of patient privacy but are available from the corresponding author on reasonable request.

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## AUTHOR CONTRIBUTIONS

AM was responsible for data acquisition and drafting the manuscript; AMd was responsible for statistical analysis, data interpretation and revision of the manuscript; AK and SDJ were responsible for data acquisition and revision of the manuscript; and SK was responsible for conception of the study, data analysis, and critical revision of the manuscript. SK is accountable for all aspects of the work.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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