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ORIGINAL PAPER

Ocular surface squamous neoplasia: analysis based on the 8th American Joint Committee on Cancer classification

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Abstract

Purpose To evaluate outcomes of ocular surface squamous neoplasia (OSSN) based on American Joint Committee on Cancer (AJCC), 8th edition classification.

Methods Retrospective, non-randomized interventional case series of 127 patients (136 eyes) with OSSN.

Results On the basis of the AJCC (eighth edition), OSSN was classified as per T category as Tis (n = 14, 10%), T1 (n = 0), T2 (n = 4, 3%), T3 (n = 113, 83%), and T4 (n = 5, 4%). The following parameters increased with increasing T category: mean age at presentation at 37 years for Tis, 43 years for T2, 46 years for T3, and 55 years for T4 (p = 0.04); mean tumor basal diameter of 4 mm for Tis, not applicable (na) for T1, 6 mm for T2, 7 mm for T3, 20 mm for T4 (p = 0.001); extent of clock hours of corneal involvement (0, na, 0, 4, 8; p = 0.02), and conjunctival involvement (1, na, 2, 3, 9; p = 0.0005); involvement of adjacent structures including fornix (0%, na, 0, 9, 80%; $p < 0.001$), and caruncle (0%, na, 0, 3, 60%; $p < 0.001$) for Tis, T1, T2, T3, and T4, respectively. Overall, of the 136 eyes, 19 (14%) had tumor recurrence, and all tumor recurrences were seen in T3. Regional lymph node metastasis was noted in 4 (3%) patients. No systemic metastasis or death occurred in any patient during the mean follow-up period of 15 months (median, 11 months; range 6–55 months).

Conclusion Increasing T category based on AJCC 8th edition classification is associated with increasing severity of disease, tumor recurrence rate, and the rate of regional lymph node metastasis.

Keywords Eye · Squamous cell neoplasms · Eye neoplasms · Neoplasm staging · Local neoplasm recurrence

Introduction

American Joint Committee on Cancer Classification (AJCC) stages a tumor based on T (tumor features), N (regional node spread), and M (distant metastases) for prognosticating the cancer and providing uniformity in tumor evaluation [1]. The 8th edition of AJCC for conjunctival tumors categorizes ocular surface squamous neoplasia (OSSN) into five categories Tis, T1, T2, T3, and T4 (Table 1) [1]. OSSN, being a low-grade malignancy, rarely metastasizes or causes death but has 5–39% risk of tumor recurrence [2–7].

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Table 1 Ocular surface squamous neoplasia based on T category American Joint Cancer Committee (AJCC) classification, 8th edition *Source*: Conway et al. [1]

Primary tumor (T)	Definition	$n = 136$ n (%)
Tx	Cannot assess the tumor	0 (0)
T0	No evidence of tumor	
Tis	Carcinoma in situ	14 (10)
T1	Tumor ($\leq$ 5 mm in greatest dimension) invades through the basement membrane without invasion of adjacent structures	0 (0)
T2	Tumor ($>$ 5 mm in greatest dimension) invades through the basement membrane without invasion of adjacent structures[a]	4 (3)
T3	Tumor invades adjacent structures excluding the orbit	113 (83)
T4	Tumor invades orbit with or without further extension	5 (4)
T4a	Tumor invades orbital soft tissues without bone invasion	5 (4)
T4b	Tumor invades bone	0 (0)
T4c	Tumor invades adjacent paranasal sinuses	0 (0)
T4d	Tumor invades brain	0 (0)

[a]Adjacent structures include cornea, forniceal conjunctiva, palpebral conjunctiva, tarsal conjunctiva, intraocular compartments, caruncle, lacrimal punctum and canaliculi, plica, anterior or posterior eyelid lamellae, and/or eyelid margin

Surgical excision has been the mainstay of treatment with recent increasing trend toward conservative approach [8–11]. Galor et al. [12]analyzed 389 cases of OSSN who underwent excisional biopsy and reported 1-year recurrence of 10% and 5-year recurrence of 21% with AJCC 7th edition stage T2 and T3 associated with increased recurrence risk. Literature-based analysis of comparison between surgical versus Interferon a2b (IFN a2b) treatment concluded that excisional biopsy followed by IFN a2b for positive margins was the best modality to minimize tumor recurrence [13]. Shields et al. [8] found AJCC to be non-predictive of tumor outcome in cohort of 81 cases treated with Interferon a2b (IFN a2b), where all stages achieved 90–100% tumor control. The new 8th edition of AJCC classification for conjunctival tumors has modified categories T1 and T2, which now includes conjunctival OSSN with breach in continuity of basement membrane rather than size based differentiation alone (AJCC 7th) [1]. Herein, we evaluate a cohort of 127 patients (136 tumors) based on the new AJCC 8th edition classification of conjunctival tumors and provide outcomes in relation to patient and tumor characteristics.

Methods

The approval of Institutional Ethics Committee, L V Prasad Eye Institute, Hyderabad, India, was obtained, and the study adhered to the tenets of Declaration of Helsinki. The medical records of all patients clinically diagnosed with OSSN from January 1, 2011, to December 30, 2014, and managed at the Operation Eyesight Universal Institute for Eye Cancer were reviewed. Demographic data including age, gender, and laterality of tumor were recorded. Related factors such as smoking status, human immunodeficiency virus infection, immunocompromised status, and papillon-lefevre syndrome were recorded. Patients with less than 6 months of follow-up from the date of completion of treatment and with xeroderma pigmentosum were excluded from analysis [14].

Previous OSSN treatment(s) before referral was noted. The recorded clinical findings included best-corrected visual acuity, tissues involved (cornea, bulbar conjunctiva, forniceal conjunctiva, tarsal conjunctiva, caruncle, plica semilunaris), epicenter of tumor, number of tumors, tumor basal diameter (millimeters), quadrantic location (superior, nasal, inferior, temporal quadrants; upper tarsus, lower tarsus, upper fornix, lower fornix), number of clock hours of limbal involvement, nature of lesion

(leukoplakia, papillomatous, nodular, pigmented, placoid, gelatinous), presence of feeder or intrinsic vessels, and keratin. The details of investigative methods such as ultrasound biomicroscopy (UBM), anterior segment optical coherence tomography (ASOCT), and computed tomography of the orbit also were noted, when available. Each eye was classified according to the AJCC clinical staging of conjunctival carcinomas, 8th edition (OSSN; Table 1) [1]. Clinical photographs and large drawing documentation were reviewed to note down clinical characteristics. Treatment details were recorded. Wide excisional biopsy with a no-touch technique was performed in cases without any orbital or intraocular tumor extension. It was combined with alcohol keratoepitheliectomy when a corneal component was present. Lamellar sclerectomy was performed in cases with clinical evidence of scleral invasion. Double freeze–thaw cryotherapy to the surrounding conjunctival margins was performed in all cases. Cryotherapy to the tumor bed was performed in cases with episcleral fixity, scleral invasion on imaging, or adherence of lesion to the base during surgery. Based on the size of the surgical defect, the defect was closed either by direct closure or with amniotic membrane graft. Before excisional biopsy, topical chemotherapy (0.04% mitomycin-C [MMC] or Interferon a2b) was used in cases with diffuse tumor (occupying > 6 clock hours of ocular surface). Extended enucleation was performed in cases with intraocular extension, along with cryotherapy to the conjunctival margins. The details of use of primary or adjuvant topical chemotherapy (MMC) or immunotherapy (Interferon a2b) details were noted. Orbital exenteration was performed in cases with orbital extension of OSSN based on computed tomography scan of the orbit. Secondary treatment with plaque brachytherapy (ruthenium 106) was performed in cases with microscopic residual tumor with positive tumor base based on histopathological evaluation. Histopathological characteristics included grading into mild, moderate, severe dysplasia, carcinoma in situ and invasive squamous cell carcinoma. Involvement of resected margins and base, corneal invasion, scleral invasion, and actinic keratosis were also noted.

"Complete response" was defined as complete tumor regression with no residual tumor. "Tumor recurrence" was defined as reappearance of tumor at the previous location. This definition excluded the new tumor occurrence at a different site/eye. Treatment outcomes of tumor recurrence, locoregional lymph node metastasis, systemic metastasis, and death were recorded.

Statistical analysis

The statistical analysis was performed using the software Origin v7.0 (OriginLab Corporation, Northampton, MA, USA). Based on the AJCC 8th edition classification, each OSSN was categorized into specific subcategories (Table 1). The major categories of Tis, T1, T2, T3, or T4 were compared regarding demographic (Table 2) and clinical features (Table 3). The continuous data were checked for the normality of distribution using Shapiro–Wilk test and the equality of their variance was assessed using Levene test. One-way analysis of variance was used to compare parametric data with equal variance and Kruskal–Wallis test was used to compare parametric data with unequal variance and nonparametric data. The categorical data were compared using Chi-square test. A p value of < 0.05 was considered statistically significant. T2 was not included in analysis due to small sample size when compared for extent of clock hours of tumor involvement and duration of symptoms. Treatment outcomes (Table 4) and histopathological features (Table 5) among categories were compared using Chi-square test. Univariate analysis was conducted for features predictive of tumor recurrence, recurrent versus non-recurrent tumor across all cases and in subcategory of T3 as well (Table 6).

Results

A total of 127 patients (136 eyes) with OSSN were included in this study. Based on T category of AJCC classification, the tumors were classified as Tis ($n = 14$, 10%), T1 ($n = 0$), T2 ($n = 4$, 3%), T3 ($n = 113$, 83%), and T4 ($n = 5$, 4%) (Table 1). Based on definition by 8th edition of AJCC, none of the tumor belonged to T1 category. There was an increase in mean age at presentation (years) with increasing T category (37 for Tis, not applicable (na) for T1, 43 for T2, 46 for T3, 55 for T4; $p = 0.04$) (Table 2). Mean duration of symptoms was more in advanced stage but not statistically significant (6, na, 3, 10, 13; $p = 0.20$) (Table 2).

Table 2 Demographics of patients with ocular surface squamous neoplasia

Feature	Tis *n* = 14 *n* (%)	T2 *n* = 4 *n* (%)	T3 *n* = 113 *n* (%)	T4 *n* = 5 *n* (%)	*p* value
Age (years), Mean (median, range)	37 (34, 11–67)	43 (42, 29–60)	46 (46, 15–81)	55 (52, 37–81)	0.04[a]
Gender					
Male	10 (71)	3 (75)	82 (73)	3 (60)	0.94[b]
Female	4 (29)	1 (25)	31 (28)	2 (40)	0.94[b]
Laterality					
Unilateral	14 (100)	4 (100)	97 (92)	5 (100)	0.30[b]
Bilateral	0 (0)	0 (0)	8 (8)	0 (0)	0.63[b]
Duration of symptoms (months) Mean (median, range)	6 (3, 1–36)	3 (3, 1–6)	10 (4, < 1–60)	13 (7, 6–36)	0.20[c]

[a]T2 is not included in analysis due to small sample size; statistical test—analysis of variance

[b]Chi-square test

[c]T2 is not included in analysis due to small sample size; statistical test—Kruskal–Wallis test

The tumor features are listed in Table 3 and histopathology features are listed in Table 5. Based on primary tumor category (Tis, T1, T2, T3, and T4), the tumor features that showed significant increase with tumor category included mean tumor basal diameter (4 mm for Tis, na for T1, 6 mm for T2, 7 mm for T3, 20 mm for T4; $p = 0.001$); extent of clock hours of corneal involvement (0, na, 0, 4, 8; $p = 0.02$) and conjunctival involvement (1, na, 2, 3, 9; $p = 0.0005$); and involvement of adjacent structures including fornix (0%, na, 0, 9, 80%; $p < 0.001$) and caruncle (0%, na, 0, 3, 60%; $p < 0.001$), and orbit (0%, na, 0, 0, 100%; $p < 0.001$). Tumor multifocality was noted in T3 only ($n = 7$, 6%).

The treatment details and outcomes are listed in Table 4. Based on tumor category, wide excision biopsy was performed in all cases with Tis and T2 tumor, and in 59% ($n = 67$) cases with T3 tumor. All cases managed with surgical excision achieved complete tumor resolution. Topical chemotherapy in the form of MMC was used in 9% ($n = 10$) as adjuvant and as primary treatment in 17% ($n = 19$) cases with T3 tumor. Interferon a2b was employed as a primary mode of treatment in 9% ($n = 10$) where complete tumor regression was achieved in 7% ($n = 8$) and served as immunotherapy and as immunoreduction in 2% ($n = 2$) making them amenable to surgical excision. Ruthenium plaque brachytherapy was administered in two patients with T3 tumor with positive base on histopathology. Over a mean follow-up period of 15 months (median, 11 months; range 6–55 months), 17% ($n = 19$) cases had tumor recurrence. All recurrences were seen in T3. Regional lymph node metastasis was noted in 3% ($n = 3$) cases of T3 and 20% ($n = 1$) cases of T4 ($p < 0.001$).

Univariate analysis for outcomes is listed in Table 6. Presence of feeder vessels at presentation was a significant predictor of tumor recurrence ($p = 0.01$). Since only one factor was predictive of tumor recurrence, multivariate analysis could not be performed.

Discussion

OSSN is the most common non-pigmented ocular surface malignancy and typically severe cases are managed at an ocular oncology referral center [4]. Incidence of OSSN varies according to the latitude, with lower incidence rates observed in areas away from the equator and highest incidence noted among African population [15].

Yousef et al. evaluated 101 eyes with OSSN based on AJCC (7th edition) classification [6]. They found that 65% of cases fall under Tis and T1 category, whereas only 1% in T2 and 2% in T4 categories.

Table 3 Tumor features of ocular surface squamous neoplasia based on T category of American Joint Cancer Committee classification, 8th edition

Feature	Tis *n* = 14 *n* (%)	T2 *n* = 4 *n* (%)	T3 *n* = 113 *n* (%)	T4 *n* = 5 *n* (%)	*p* value
Quandrantic tumor location (n = 136)					
Nasal	6 (43)	2 (50)	36 (32)	1 (20)	0.66
Inferior	2 (14)	0 (0)	21 (19)	1 (20)	0.79
Temporal	6 (43)	1(25)	42 (37)	1 (20)	0.78
Superior	0 (0)	1 (25)	5 (4)	0 (0)	0.18
Diffuse	0 (0)	0 (0)	9 (8)	2 (40)	0.04
Tumor epicenter (n = 138)					
Cornea	0 (0)	0 (0)	15 (13)	0 (0)	0.33
Limbus	0 (0)	0 (0)	47 (42)	0 (0)	0.002
Bulbar conjunctiva	14 (100)	4 (100)	50 (44)	3 (60)	< 0.001
Forniceal conjunctiva	0 (0)	0 (0)	0 (0)	0 (0)	1.00
Tarsal conjunctiva	0 (0)	0 (0)	1 (1)	0 (0)	0.98
Diffuse with fungating mass	0 (0)	0 (0)	0 (0)	2 (40)	< 0.001
Extent of tumor involvement (n = 138)					
Cornea	0 (0)	0 (0)	101(85)	5 (100)	< 0.001
Bulbar conjunctiva	14 (100)	4 (100)	110(97)	5 (100)	0.89
Tarsal conjunctiva	0 (0)	0 (0)	5 (4)	3 (60)	< 0.001
Fornix	0 (0)	0 (0)	10 (9)	4 (80)	< 0.001
Caruncle	0 (0)	0 (0)	3 (3)	3 (60)	< 0.001
Orbital extension	0 (0)	0 (0)	0 (0)	5 (100)	< 0.001
Tumor pattern (n = 138)					
Leukoplakic	9 (64)	0 (0)	32 (28)	1 (20)	0.02
Gelatinous	3 (21)	1 (25)	24 (21)	1 (20)	1.00
Nodular	0 (0)	3 (75)	18 (16)	2 (40)	0.002
Papillary	0 (0)	0 (0)	18 (16)	1 (20)	0.33
Diffuse placoid	0 (0)	0 (0)	4 (4)	0 (0)	0.84
Pigmented	2 (14)	0 (0)	17 (15)	0 (0)	0.67
Tumor basal diameter (mm), mean (median, range)					
Conjunctival + corneal tumor	na	na	11 (9, 3–39)	24 (25, 16–30)	< 0.0001
Corneal tumor	na	na	5 (5, 1–14)	6 (6, 5–8)	0.91
Conjunctival tumor	4 (4, 2–9)	6 (5, 4–8)	7 (6, 1–30)	20 (20, 10–30)	0.001
Number of clock hours of involvement by tumor, mean (median, range)					
Cornea	na	na	4 (3, 1–12)	8 (9, 2–12)	0.02
Bulbar conjunctiva	1 (1, 1–2)	2 (2, 2–3)	3 (3, 1–12)	9 (9, 4–12)	0.0005
Associated features					
Keratin	9 (64)	4 (100)	83 (74)	3 (60)	0.49
Multifocality	0 (0)	0 (0)	7 (6)	0 (0)	0.68
Feeder vessels	10 (71)	3 (75)	93 (82)	5 (100)	0.52

Advanced tumor stages [T3 (34% recurrence rate) and T4 (50% recurrence rate)] were associated with higher recurrence rates. The small number of cases in the T2 and T4 cohorts was a drawback for analysis in that

Table 4 Treatment and outcome of patients with ocular surface squamous neoplasia based on T category of American Joint Cancer Committee classification, 8th edition

Feature	Tis *n* = 14 *n* (%)	T2 *n* = 4 *n* (%)	T3 *n* = 113 *n* (%)	T4 *n* = 5 *n* (%)	*p* value
Primary treatment (*n* = 136)					
Interferon a2b (Topical ± perilesional)					
Immunoreduction	0 (0)	0 (0)	2 (2)	0 (0)	0.94
Immunotherapy	0 (0)	0 (0)	8 (7)	0 (0)	0.63
Mitomycin-C (topical)					
Chemoreduction	0 (0)	0 (0)	10 (9)	0 (0)	0.53
Chemotherapy	0 (0)	0 (0)	19 (17)	0 (0)	0.21
Wide excision biopsy + cryotherapy	14 (100)	4 (100)	67 (59)	0 (0)	< 0.001
Plaque radiotherapy	0 (0)	0 (0)	2 (2)	0 (0)	0.94
Extended enucleation	0 (0)	0 (0)	1 (1)	0 (0)	0.98
Systemic chemotherapy	0 (0)	0 (0)	0 (0)	1 (20)	< 0.001
Orbital exenteration	0 (0)	0 (0)	4 (3)	4 (80)	< 0.001
Tumor recurrence (*n* = 19)[§]	0 (0)	0 (0)	19 (17)	0 (0)	0.21
Time interval between the treatment and tumor recurrence (months) Mean, median (range)	na	na	8, 6 (2–25)	na	na
Regional lymph node metastasis	0 (0)	0 (0)	3 (3)	1 (20)	< 0.001

Interferon a2b = Interferon alfa 2b; na = not applicable

Table 5 Histopathology features of ocular surface squamous neoplasia

Feature	Tis *n* = 14 *n* (%)	T2 *n* = 4 *n* (%)	T3 *n* = 94 *n* (%)	T4 *n* = 5 *n* (%)	*p* value
Tumor type (n = 117)					
Mild dysplasia	4 (29)	0 (0)	12 (13)	0 (0)	0.25
Moderate dysplasia	3 (21)	0 (0)	22 (23)	0 (0)	0.44
Severe dysplasia	1 (7)	0 (0)	3 (3)	0 (0)	0.82
Carcinoma in situ	6 (43)	0 (0)	31 (33)	0 (0)	0.17
Invasive squamous cell carcinoma	0 (0)	4 (100)	26 (28)	5 (100)	< 0.001
Associated actinic keratosis	5 (36)	0 (0)	23 (25)	0 (0)	0.27
Surgical margin involvement	0 (0)	0 (0)	19 (20)	0 (0)	0.14
Surgical base involvement	0 (0)	0 (0)	2 (2)	0 (0)	0.35

study. Similarly, Chauhan et al. [16] in their cohort of 64 patients reported advanced stages (T3, T4) to be predictor of reduced recurrence-free survival. Only 34% cases belonged to T3 and T4, whereas 67% were classified to T1 and T2. Combining stages T3 and T4 for recurrence risk analysis was the drawback for analysis in that study.

The AJCC, established in 1959, provided its most recent eighth edition of the AJCC manual in 2016 [1]. The AJCC manual includes clinical and pathological staging for eye cancers like for rest of the body [17]. The clinical staging for carcinoma of the conjunctiva is based on tumor size with Tis as carcinoma in situ; T1 and T2 as tumor less than and more than 5 mm with breach in continuity of basement membrane, respectively; T3 as tumor invasion into adjacent tissues (excluding orbit); and T4 as tumor invasion into surrounding tissues including orbit (Table 1). This 8th

Table 6 Features predicting tumor recurrence

Feature	Tumor recurrence (including all cases)					Tumor recurrence in T3 tumors				
	Yes $n = 19$ n (%)	No $n = 117$ n (%)	p value	Odds ratio	95% confidence interval	Yes $n = 19$ n (%)	No $n = 94$ n (%)	p value	Odds ratio	95% confidence interval
Univariate analysis										
Feeder vessels	13 (68%)	104 (89%)	0.03	0.27	0.09–0.84	13 (68%)	86 (92%)	0.01	0.20	0.06–0.68

edition differs from 7th edition in the definition of T1 and T2 [17]. While, in the 7th edition, the definition of T1 and T2 was based on tumor size, in the 8th edition, the additional factor included is the absence of breach in the continuity of basement membrane. AJCC classification for OSSN does not have a separate clinical and pathological classification. Though recent investigative modalities like anterior segment optical coherence tomography can give information about the basement membrane breach, the information may not be accurate or reliable compared to histopathology data in subtle cases. Thus, the classification into T1 and T2 may not be accurate unless the lesion is excised and histopathology data is available regarding the integrity of basement membrane. Majority of OSSN have their epicenter at limbus, which results in their categorization under T3 category despite being carcinoma in situ and smaller size.

In this series, based on 8th edition AJCC, OSSN were classified as Tis (10%), T1 (0%), T2 (3%), T3 (83%), and T4 (4%). No tumor belonged to T1 since we did not find any case with a small tumor ($\leq$ 5 mm) that breached the basement membrane and majority of cases belonged to T3 since most of the tumors have limbal proximity and thus have corneal involvement. Distribution of OSSN among various T category is non-uniform even with prior reports based on 7th edition of AJCC. Shields et al. [8] classified 81 cases treated with interferon as Tis (12%), T1 (16%), T2 (7%), T3 (63%), and T4 (1%) based on 7th edition AJCC. Galor et al. [12] classified post-excisional 389 OSSN cases into T1 (53%), T2 (36%), T3 (10%), and T4 (1%) based on 7th edition AJCC. This non-uniformity can be attributed to different epidemiological tumor incidences, bias due to referral centers, and inclusion of corneal OSSN in T3.

Increasing age, larger tumor size, and higher pathologic grading were associated with higher T category (T3, T4) in current series as also observed in prior studies based on 7th edition of AJCC [6, 12, 16]. The most common treatment modality of OSSN regardless of T category remains surgical excision except for diffuse cases. Recently, there is an increasing trend toward use of medical treatment with interferon alfa 2b compared to surgical excision [8, 11]. Majority of cases (63%) in our series were managed with surgical excision followed by chemotherapy or immunotherapy for positive margins. Presence of feeder vessels was found to be the predictor of higher tumor recurrence rates. Size and location of tumor were not associated with increased recurrence rates. Jakobiec et al., Galor et al., and Tabin et al. also reported no association between tumor size, and recurrence rates similar to our study [7, 12, 18].

Higher AJCC T category by AJCC 7th edition was found to be predictor of tumor recurrence by Yousef et al. 6, Chauhan et al. [12], and Galor et al. [16]. But the distribution of cases into T3 and T4 was highly variable across these studies. Galor et al. [12] found that T2 and T3 groups have increased rates of tumor recurrences and Chauhan et al. [16] found T3 and T4 to be associated with high rate of tumor recurrence. Treatment modalities employed in these studies are highly variable which could affect the recurrence rates. Similarly, in the current study based on 8th edition AJCC, higher T category was associated with higher tumor recurrence rates. There were no tumor recurrences in Tis, T2, and T4. All tumor recurrences were noted in T3. The lack of tumor recurrence in higher T category T4 could be related to complete tumor removal along with residual orbital tissue by orbital exenteration. All recurrences in T3 were post-wide excisional biopsy. Based on statistical analysis,

none of the tumor-related factors like tumor size, tumor type, or tumor extent were predictive of tumor recurrence in the current series. The only factor predictive of tumor recurrence was the presence of feeder vessels on presentation, thus indicating that higher vascularity on presentation was associated with higher recurrence rate.

Erie et al. [19] reported recurrence rate of 53% in cases with involved margins compared to 5% when margins were uninvolved irrespective of conjunctival and corneal intraepithelial neoplasia (CIN) or invasive squamous cell carcinoma (SCC). Jakobiec et al. and Tabin et al. also did not find any association between CIN/SCC and recurrence rates [7, 17]. Similarly, in our series, higher-grade lesions were not associated with increased risk of recurrence. This is in contrary to the results shown by few studies, where invasive SCC was found to be a predictor of recurrence [6, 12, 16]. We assume stringent evaluation of margins and base for positivity and use of adjuvant treatment reduces recurrence risk even in invasive SCC.

Locoregional lymph node metastasis in OSSN is low at $< 2\%$ [6]. In our series, the locoregional lymph node metastasis was detected in 3% patients. Higher T category was predictive of regional lymph node metastasis with 3% in T3 and 20% in T4 ($p < 0.001$).

Based on our observations, certain improvements can be made into existing AJCC. This newer classification cannot be accurately applied to conjunctival tumors especially Tis, T1, and T2 where pathological details are not established. A separate clinical and pathological classification of OSSN will be helpful. Tumors classified as T3 needs to be readdressed. Corneal/limbal involvement is seen more commonly with OSSN. Categorization of tumors based on size rather than invasion of adjacent structures especially cornea may be helpful.

In conclusion, based on our study, increasing T category based on AJCC 8th edition classification is associated with increasing severity of disease, tumor recurrence rate, and the rate of regional lymph node metastasis. Presence of feeder vessels at presentation was a significant predictor of tumor recurrence. Further focus upon segregating clinical and pathological classification of AJCC and redefining T3 may increase the prognostic value of AJCC classification.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Research involving human participants and/or animals This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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