

Predictive Value of the Seventh Edition American Joint Committee on Cancer Staging System for Conjunctival Melanoma

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Objective: To evaluate the predictive value of the seventh edition American Joint Committee on Cancer (AJCC) staging system for conjunctival melanoma.

Methods: Retrospective, observational case series of 42 eyes of 42 patients with conjunctival melanoma studied by reviewing medical records, pathology reports, and color photographs. The main evaluated outcomes were demographic information, laterality, tumor size, thickness, pathologic diagnosis, seventh edition AJCC stage (clinical and pathologic), recurrence, metastasis, and duration of follow-up.

Results: There was no sex preference, and the median age was 61 years. Recurrent disease was noted in 33% of patients (n=14 of 42), with 64% occurring at a median of 2.5 years (range, 1-5 years) after primary treatment. Metastasis was noted in 19% of patients. The significant predictive factors for high risk of tumor recurrence were tumors involving more than 1 quadrant ($P=.02$), tu-

mors thicker than 0.5 mm ($P=.04$), and tumor multifocality ($P=.04$). The significant predictive factors for high risk of tumor metastasis were tumors thicker than 0.5 mm ($P=.005$), tumor invasiveness ($P=.04$), pathologic diagnosis of conjunctival melanoma rather than melanoma in situ ($P=.04$), and tumor recurrence ($P<.001$). Similarly, increasing AJCC T stages (clinical and pathologic) were associated with unfavorable outcomes. For example, clinical stage-related recurrence rates were 19% (Tis), 27% (T1), 33% (T2), and 75% (T3). Clinical stage-related lymphatic and distant metastasis rates were 0% (Tis), 20% (T1), 0% (T2), and 63% (T3).

Conclusions: Advanced AJCC T-stage (clinical and pathologic) tumors were at higher risk for recurrence and metastasis. In this study, the seventh edition AJCC staging system was predictive of local control and systemic spread of conjunctival melanoma.

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CONJUNCTIVAL MELANOMAS are rare.¹⁻⁵ Ten-year melanoma-related mortality has been reported to be 25% to 30%. Risk factors include involvement of nonbulbar conjunctiva, local tumor recurrence, multifocal tumors, increased tumor thickness, a high mitotic rate, epithelioid cells, and lymphatic invasion.⁶⁻⁸ Reports of 12% to 50% recurrence rates after treatment and an overall 26% incidence of metastasis highlight the need for improved treatment options.^{5,9}

Local therapeutic success is reported to depend on the size, location, and number of tumors present when initiating treatment.¹⁰⁻¹² For example, in the treatment of small- or medium-sized epibulbar tumors, local excision followed by double-freeze cryotherapy has been reported to offer an 88% local control rate.^{1,12} However, the management of large, diffuse, and multifocal tumors has been reported to be more

complex and less effective.⁹ Multimodality therapy (eg, excision and cryotherapy or excision and radiotherapy) showed up to 77% success rates.^{9,10} It is reasonable to assume that the visually pigmented tumor seems to offer a poor definition of the tumor's "edge."¹³ Therapeutic options have included local surgical removal, cryotherapy, radiotherapy, topical chemotherapy, and exenteration.¹⁴⁻¹⁹

Conjunctival melanoma has been reported to arise from preexisting nevi de novo or in the context of antecedent primary acquired melanosis with atypia.^{1,18,20} In 2009, the seventh edition American Joint Committee on Cancer (AJCC) universal staging system defined primary acquired melanosis with atypia as "conjunctival melanoma in situ."^{21,22} In this study, we will follow that convention. The aim of this study was to examine the predictive value of the seventh edition AJCC staging system for conjunctival melanoma (local control and metastasis).²²

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Table 1. Malignant Melanoma of the Conjunctiva: Seventh Edition AJCC Staging System

Clinical Primary Tumor		Pathologic Primary Tumor	
TX	Primary tumor cannot be assessed	TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor	T0	No evidence of primary tumor
Tis	Melanoma confined to the conjunctival epithelium	Tis	Melanoma confined to the conjunctival epithelium ^a
Malignant Conjunctival Melanoma of the Bulbar Conjunctiva			
T1		pT1	
T1a	≤1 quadrant ^b	pT1a	Melanoma ≤ 0.5 mm thick, with invasion of the substantia propria
T1b	>1 to 2 quadrants	pT1b	Melanoma >0.5 mm to 1.5 mm thick, with invasion of the substantia propria
T1c	>2 to 3 quadrants	pT1c	Melanoma >1.5 mm thick, with invasion of the substantia propria
T1d	>3 quadrants		
Malignant Conjunctival Melanoma of the Nonbulbar (Palpebral, Fornical, Caruncular)			
T2		pT2	
T2a	Noncaruncular, ≤1 quadrant	pT2a	Melanoma ≤0.5 mm thick, with invasion of the substantia propria
T2b	Noncaruncular, >1 quadrant	pT2b	Melanoma >0.5 to 1.5 mm thick, with invasion of the substantia propria
T2c	Any caruncular, ≤1 quadrant	pT2c	Melanoma >1.5 mm thick, with invasion of the substantia propria
T2d	Any caruncular, >1 quadrant		
Any Malignant Conjunctival Melanoma With Local Invasion			
T3		pT3	Melanoma invades the eye, eyelid, nasolacrimal system, sinuses, or orbit
T3a	Globe		
T3b	Eyelid		
T3c	Orbit		
T3d	Sinus		
T4	Tumor invades the central nervous system	pT4	Melanoma invades the central nervous system
Clinical Regional Lymph Nodes		Clinical Distant Metastasis	
NX	Regional lymph nodes cannot be assessed	M0	No distant metastasis (no pathologic M0; use clinical M to complete stage group)
N0a (biopsy)	No regional lymph node metastasis, biopsy performed		
N0b (no biopsy)	No regional lymph node metastasis, biopsy not performed		
N1	Regional lymph node metastasis	M1	Distant metastasis

Abbreviation: AJCC, American Joint Committee on Cancer.

^apT(is) melanoma in situ (includes the term *primary acquired melanosis*) with atypia replacing greater than 75% of the normal epithelial thickness, with cytologic features of epithelioid cells, including abundant cytoplasm, vesicular nuclei or prominent nucleoli, or the presence of intraepithelial nests of atypical cells.

^bQuadrants are defined by clock hour, starting at the limbus (eg, 6, 9, 12, and 3 o'clock) and extending from the central cornea to and beyond the eyelid margins. This will bisect the caruncle.

METHODS

This study adhered to the tenets of the Declaration of Helsinki of 1975, as revised in 2000, and the Health Insurance Portability and Accountability Act of 1996. The institutional review board of The New York Eye Cancer Center approved the study.

This study is a retrospective case review concerning 42 eyes of 42 patients with pathologically diagnosed conjunctival melanoma or conjunctival melanoma in situ. Selection also required that we have access to the patient's medical records, pathology reports, and color photographs (photographs taken when first seen at The New York Eye Cancer Center or by the primary treating ophthalmologist). Data included the patient's age, sex, laterality, visual acuity, tumor location, clinical appearance, tumor invasiveness (eg, corneal, scleral, uveal, orbital, lymphatic, and distant metastasis), and pathologic and clinical seventh edition AJCC stage for each tumor. We recorded the pathologic diagnosis, primary and secondary treatment modalities, recurrence rates, and durations of follow-up. Recurrence was recorded if there was clinical evidence of tumor after at least a 6-month disease-free period after the end of the planned treatment.

FOCUSED OPHTHALMIC EXAMINATION

When first seen, all the patients underwent slitlamp examination of all the conjunctival surfaces (including eversion of the upper eyelid and tarsus). At each visit, slitlamp photography was used to record all these same conjunctival surfaces. Intraocular invasion was evaluated by gonioscopy, gonioscopy, and ultrasound imaging. Adherence to

the sclera was evaluated by proparacaine-assisted Q-tip palpation under the slitlamp observation. Only tumors found adherent to the eye wall were selected for high-frequency ultrasound imaging.²³ Corneal tumor extension was clinically photographed and histopathologically confirmed. Orbital invasion was defined as tumor tissue detected in the orbit posterior to the conjunctiva by surgical evaluation, orbital computed tomography, or magnetic resonance imaging. Palpation was used to examine the preauricular and submandibular lymph nodes. Analysis of those tests was used to stage the tumors at presentation according to the seventh edition AJCC staging system (**Table 1**).²²

TREATMENT MODALITIES

Local treatments for conjunctival tumors include primary excision, excision with cryotherapy, topical chemotherapy (interferon and mitomycin), irradiation, and exenteration.^{14,17,24-26} These surgical and chemotherapy techniques are widely used and represent those available in the ophthalmic oncology community.

CLINICAL FEATURES AND STAGING

Multifocal tumors were defined as having at least 2 tumors separated by 5 mm of normal-appearing tissue (**Figure 1**). According to clinical appearance, tumors were classified into focal tumors (thickened focal lesions with well-defined margins) and spreading tumors (flat lesions with diffuse, ill-defined margins) (**Figure 1**). As seen in **Table 1**, according to the seventh



Figure 1. Tumor characteristics. A, Eye with unifocal localized conjunctival melanoma. B, Diffuse multifocal tumor of the bulbar conjunctiva separated by more than 5 mm of tumor-free tissue. C, Another superior palpebral conjunctival melanoma in the same eye.

edition AJCC staging system, tumor sizes were divided into 4 subgroups: (1) tumors less than or equal to 1 quadrant, (2) tumors more than 1 but less than or equal to 2 quadrants, (3) tumors more than 2 but less than or equal to 3 quadrants, and (4) tumors greater than 3 quadrants (**Figure 2** and **Figure 3**). Furthermore, tumor location according to the seventh edition AJCC staging system was divided into 2 groups: (1) melanoma of the bulbar conjunctiva and (2) melanoma of the non-bulbar conjunctiva (palpebral, forniceal, and caruncular) (Figure 3); tumors involving more than 1 location (eg, bulbar conjunctiva, caruncle, and eyelid) were graded according to the highest grade.

PATHOLOGIC FEATURES AND STAGING

Conjunctival melanomas were evaluated according to the seventh edition AJCC pathologic staging system. Tumors were divided into 4 groups: (1) melanoma of the conjunctiva confined to the epithelium; (2) melanoma of the conjunctiva not more than 0.5 mm thick, with invasion of the substantia propria; (3) melanoma of the conjunctiva more than 0.5 to 1.5 mm thick, with invasion of the substantia propria; and (4) melanoma of the conjunctiva greater than 1.5 mm thick, with invasion of the substantia propria. The pathologic features used to stage tumors at presentation were defined by the seventh edition AJCC pathologic staging system (Table 1).²²

Statistical analyses of conjunctival melanoma (clinical and pathologic) seventh edition AJCC stages were correlated with the recurrence and metastatic rates of the tumor. The *P* values and statistical significance were measured using the Fisher exact test.

RESULTS

Forty-two eyes from 42 patients aged 9 to 90 years (median, 61 years) were studied. Half of the patients were male. Melanoma was present on the right eye in 45% of patients (n=19). Analysis of tumor focality showed that 31% (n=13) were multifocal and 69% (n=29) were unifocal. In terms of clinical appearance, 52% of the tumors (n=22) were diffuse and 48% (n=20) were localized. Melanomas were limited to the bulbar conjunctiva in 62% of patients (n=26). Additional extrabulbar sites included the palpebral conjunctiva in 24% of patients (n=10), the forniceal conjunctiva in 29% (n=12), and the caruncle in 21% (n=9). Overall, the tumors were localized to the conjunctiva in 76% of patients (n=32), invaded the eyelid alone in 12% (n=5), invaded the orbit alone in 2% (n=1), invaded both the eyelid and the orbit in 5% (n=2), invaded the sinus alone in 2% (n=1), and involved the eyelid, orbit, nasolacrimal drainage sys-

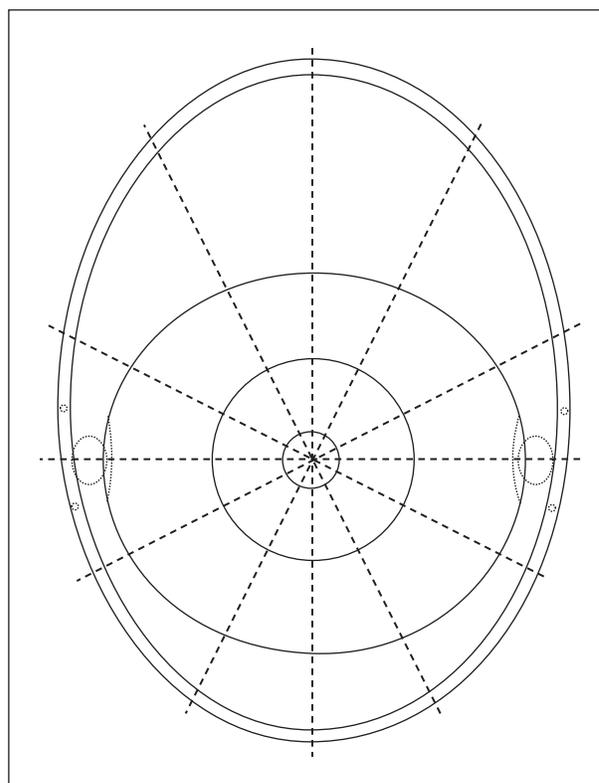


Figure 2. Graphic demonstration guide. The conjunctival and corneal surfaces are divided into quadrants to stage conjunctival melanoma according to the seventh edition American Joint Committee on Cancer staging system. Image courtesy of Bertil Damato, MD.²¹

tem, and sinuses in 2% (n=1). No patient had intraocular invasion.

INITIAL AJCC STAGING

AJCC T Staging (Clinical)

Thirty-eight percent of the 42 tumors (n=16) were staged as T(is) according to the pathologic diagnosis of conjunctival melanoma in situ, 36% (n=15) were staged T1 (bulbar lesions), and 7% (n=3) were staged T2 (being palpebral, forniceal, or caruncular lesions). Further subdivisions of the T1 and T2 groups according to tumor size are seen in Table 1. Nineteen percent of the tumors (n=8) were T3 due to eyelid, orbit, or nasolacrimal invasion. No tumors demonstrated central nervous system invasion (0% were T4).

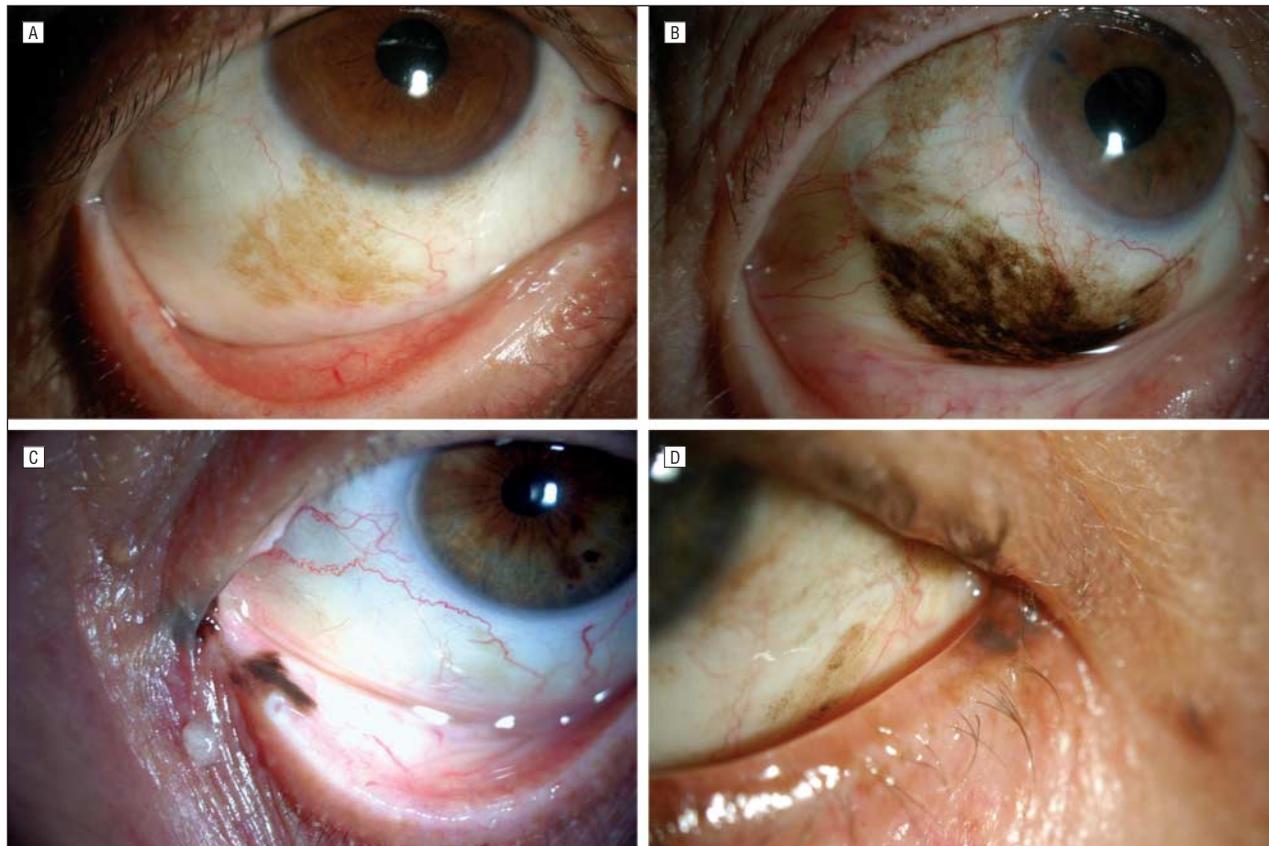


Figure 3. Tumor American Joint Committee on Cancer stage. A, T1a-staged conjunctival tumor (bulbar tumor involving <1 quadrant). B, T1d-staged conjunctival tumor (bulbar tumor involving >3 quadrants). C, T2c-staged conjunctival tumor (caruncular tumor involving <1 quadrant). D, T3b-staged conjunctival tumor (involving the eyelid margin).

AJCC T Staging (Pathologic)

Thirty-eight percent of the 42 tumors (n=16) were AJCC staged as pT(is), 31% (n=13) as pT1 (bulbar lesions), and 12% (n=5) as pT2 (being palpebral, forniceal, or caruncular lesions). Further subdivisions of the pT1 and pT2 groups were according to tumor thickness (Table 1). Nineteen percent of the tumors (n=8) were staged pT3 due to eyelid, orbit, nasolacrimal duct, or sinus invasion. No tumors demonstrated central nervous system invasion (0% were T4).

ANALYSIS OF AJCC STAGING AND OUTCOMES

AJCC TNM Staging and Regional and Systemic Metastases

Overall, of the 42 tumors, metastasis was seen in 19% of patients (n=8), lymph node metastasis (N1) was found in 10% (n=4), and 90% (n=38) were non-biopsy-proven extranodal (N0b). In terms of extranodal (distant) metastasis, 17% (n=7 of 42) were M1; of those, 43% (n=3 of 7) involved the parotid gland, 29% (n=2 of 7) had lung metastases, and 29% (n=2 of 7) had liver metastases. Last, 1 patient with liver involvement also had bone metastasis.

AJCC Clinical T Staging and Tumor Recurrence

Higher clinical AJCC-staged tumors trended toward being more likely to recur (**Table 2**). For example, by clinical stage, the recurrence rate was 19% (n=3 of 16) for Tis, 27% (n=4 of 15) for T1, 33% (n=1 of 3) for T2, and 75% (n=6 of 8) for T3. However, this trend was not significant ($P=.34$). Furthermore, the AJCC clinical staging system subdivides T1 and T2 according to the number of conjunctival quadrants affected by melanoma (Table 1). Accordingly, the recurrence rates were 0% (n=0 of 6) for T1a tumors and 44% (n=4 of 9) and 50% (n=1 of 2) for T1b and T2b tumors, respectively (no tumors in this series were staged as T1c, T1d, T2a, or T2c). The solitary T2d tumor did not recur. When analyzed by quadrants affected, the recurrence rate for tumors affecting more than 1 quadrant was 48% (n=14 of 29), and no tumors involving less than 1 quadrant recurred ($P=.02$). According to the AJCC, T3 tumors were also subdivided according to local invasion (Table 1). Accordingly, the recurrence rate was 50% (n=1 of 2) for T3b (tumors invading the eyelid alone), 80% (n=4 of 5) for T3c (tumors invading the orbit), and 100% (n=1 of 1) for T3d (tumors invading the sinuses). Last, no patients in this series had T3a or T4 tumors.

Table 2. AJCC Classification (Clinical and Pathologic) for 42 Patients With Conjunctival Melanoma

Classification	Patients, No. (%)	Recurrence, No. (%)	Metastasis, No. (%)
T stage^a			
Tis	16 (38)	3 (19)	0
T1	15 (36)	4 (27)	3 (20)
T1a	6 (14)	0	0
T1b	9 (21)	4 (44)	3 (33)
T1c	0	0	0
T1d	0	0	0
T2	3 (7)	1 (33)	0
T2a	0	0	0
T2b	2 (4.8)	1 (50)	0
T2c	0	0	0
T2d	1 (2.4)	0	0
T3	8 (19)	6 (75)	5 (63)
T3a	0	0	0
T3b	2 (5)	1 (50)	0
T3c	5 (12)	4 (80)	4 (80)
T3d	1 (2)	1 (100)	1 (100)
T4	0	0	0
P stage^b			
pTis	16 (38)	3 (19)	0
pT1	13 (31)	4 (31)	2 (15)
pT1a	7 (17)	0	0
pT1b	4 (10)	3 (75)	1 (25)
pT1c	2 (5)	1 (50)	1 (50)
pT2	5 (12)	1 (20)	1 (20)
pT2a	4 (10)	1 (25)	1 (25)
pT2b	0	0	0
pT2c	1 (2)	0	0
pT3	8 (19)	6 (75)	5 (63)
pT4	0	0	0
N stage			
N0	37 (90)	0	0
N1	4 (10)	0	0
M stage			
M0	35 (83)	0	0
M1	7 (17)	0	0

Abbreviation: AJCC, seventh edition American Joint Committee on Cancer staging system for conjunctival melanoma.

^aT stage is the initial clinical stage of the tumor.

^bpT stage is the pathologic stage of the tumor.

AJCC Pathologic pT Staging and Local Tumor Recurrence

Tumor recurrence was seen in 19% of tumors (n=3 of 16) for pTis, 31% (n=4 of 13) for pT1, 20% (n=1 of 5) for pT2, and 75% (n=6 of 8) for pT3, local recurrence increased with pT stage. The pathologic AJCC staging system further subdivides the pT1 and pT2 groups according to the thickness of the conjunctival melanoma (Table 1). Accordingly, the recurrence rates were 0% (n=0 of 7) for pT1a tumors, 75% (n=3 of 4) for pT1b tumors, 50% (n=1 of 2) for pT1c tumors, and 25% (n=1 of 4) for pT2a tumors. There were no tumors in this series with pT2b and 1 tumor staged pT2c that did not recur.

Recurrence Over Time

Local recurrence was seen in 33% of patients (n=14 of 42). Subgroup analysis of these patients revealed that at 6

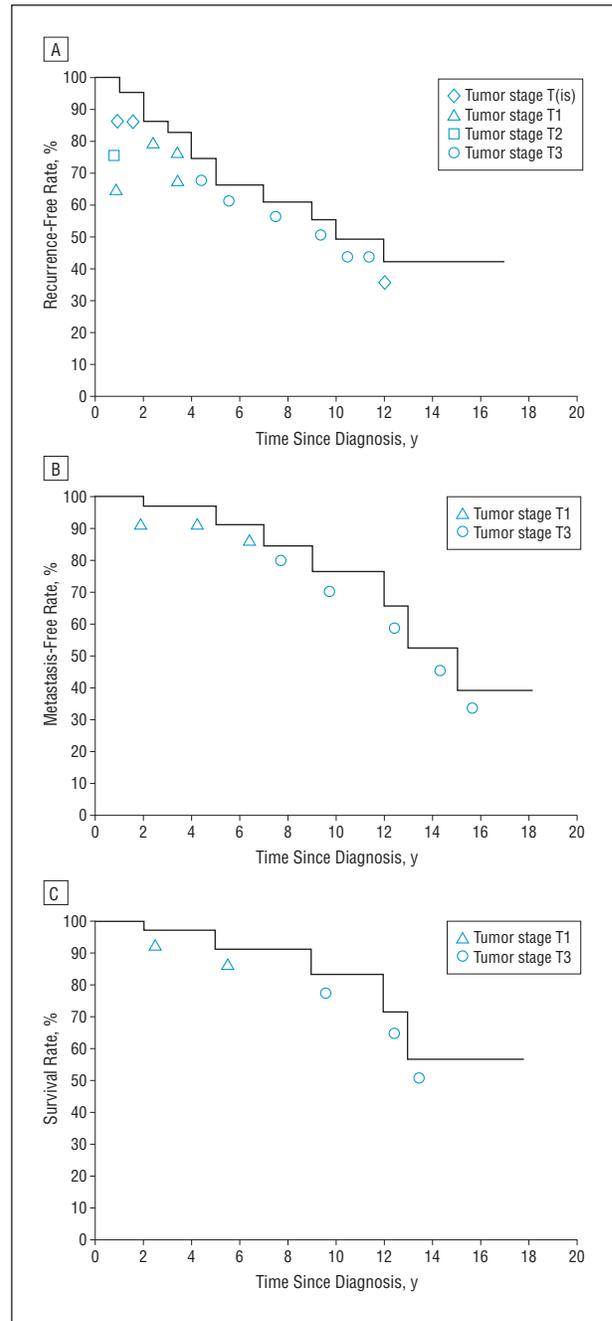


Figure 4. Kaplan-Meier curves showing the recurrence-free rate (A), metastasis-free rate (B), and survival rate (C) in relation to time since diagnosis. The curves also show the relationship between the clinical T stage of each tumor and the duration of time between initial diagnosis and the development of recurrence, metastasis, or death.

months, 1 (7%) had recurred. Most recurrences (64% [n=9 of 14]) occurred during 1 to 5 years of follow-up (median, 2.5 years). The remaining recurrences (29% [n=4 of 14]) occurred between 6 and 12 years of follow-up (median, 10 years). The Kaplan-Meier analysis of recurrence rates correlated with AJCC T stage is presented in **Figure 4A**.

AJCC Staging and Tumor Thickness

Alternatively, we analyzed recurrence rates by tumor thickness. Conjunctival melanomas histopathologically

measured to be less than 0.5 mm thick were noted to have a 13% recurrence rate (n=3 of 23); those greater than 0.5 mm thick demonstrated 58% recurrence (n=11 of 19). Statistical analysis revealed that tumors thicker than 0.5 mm were at significantly higher risk for recurrence than were tumors less than 0.5 mm thick ($P=.04$). Further analysis demonstrated recurrence rates of 43% (n=3 of 7) for tumors larger than 1.5 mm and 67% (n=8 of 12) for tumors 0.5 to 1.5 mm thick. This difference in recurrence rates between tumor sizes was not significant ($P=.70$).

The AJCC staging system did not code for biopsy or attempted cure before referral. However, this history was analyzed as an independent risk factor for recurrence. Overall, 33% of patients (14 of 42) were first seen after being primarily treated by excision with or without cryotherapy at another medical center. Subgroup analysis of the 14 failures of local control noted in this series showed that 71% (n=10 of 14) occurred in previously biopsied or treated tumors. In contrast, patients treated primarily at The New York Eye Cancer Center showed a recurrence rate of 14% (n=4 of 28). Therefore, treatment before referral was noted to be a significant risk factor for recurrence ($P=.03$).

AJCC Staging Does Not Evaluate Multifocality

In this series, 69% of multifocal tumors (n=9 of 13) recurred, whereas only 17% of unifocal tumors (n=5 of 29) recurred. Therefore, multifocality was found to be significant as a risk factor for failure of local control ($P=.04$). In this series, overall median follow-up was 30 months (range, 6-216 months).

In summary, significant features associated with a high risk of local recurrence were tumors involving more than 1 quadrant ($P=.02$), tumors greater than 0.5 mm thick ($P=.04$), tumor multifocality ($P=.04$), and previous treatment before referral ($P=.03$). Tumor invasiveness, clinical appearance, location, sex, and laterality were not significantly associated with tumor recurrence (Table 2 and **Table 3**).

AJCC Staging as Related to Metastasis

In general, the higher the AJCC stage, the more likely the occurrence of lymphatic or distant metastasis (Table 2). For example, the metastatic rate was 0% (n=0 of 16) for Tis, 20% (n=3 of 15) for T1, 0% (n=0 of 3) for T2, and 62% (n=5 of 8) for T3. This was also seen with histopathologic staging, where the metastatic rate was 0% (n=0 of 16) for pTis, 15% (n=2 of 13) for pT1, 20% (n=1 of 5) for pT2, and 62% (n=5 of 8) for pT3. Note that the metastatic rate in T2 tumors is less than that in T1 tumors. This can be due to the low number of patients in this group (only 3 patients). All the patients were primarily treated by an ocular oncologist at first presentation and, thus, avoided the risk of inadequate primary treatment. Local tumor invasiveness (eyelid, orbit, or sinuses) was not significantly associated with a high risk of local recurrence ($P=.19$), but this may be due to the low number of patients with these findings. Overall, melanoma invasiveness was significantly associated with

higher risk of systemic metastasis compared with tumors limited to conjunctiva ($P=.04$).

Local Tumor Control and Metastasis

Local control was highly correlated with the occurrence of lymphatic and distant metastases. In this series, 14 patients experienced local recurrence; of those, 57% (n=8 of 14) developed lymphatic or distant metastasis (AJCC stage N1 or M1). Therefore, all cases of metastatic melanoma occurred after tumor recurrence. None of the 28 patients without a history of recurrence developed metastasis. Although there was no statistically significant difference in recurrence rates between conjunctival melanoma and conjunctival melanoma in situ ($P=.34$), there was a significant difference in systemic spread. No patients with melanoma in situ developed lymph node or distant metastasis ($P=.04$). Metastasis was seen 1 to 15 years after primary treatment (median, 48 months) (Figure 4B).

Survival and Vision Outcomes

At the most recent follow-up, 86% of patients (n=36 of 42) were alive, 12% (n=5 of 42) had died of metastatic disease, and 2% (n=1 of 42) had died of myocardial infarction (Figure 4C). At the most recent follow-up, 10% of patients (n=4 of 42) had visual acuity worse than 20/200, including 2 patients who underwent orbital exenteration, 1 with a central retinal vein occlusion and 1 with age-related macular degeneration. Seventy-four percent of patients (n=31 of 42) had visual acuity better than or equal to 20/25, and 17% (n=7 of 42) had visual acuity of 20/200 to 20/25.

COMMENT

The seventh edition AJCC staging system for conjunctival melanoma can be used to predict local recurrence and lymphatic and distant metastases. For example, conjunctival melanomas with advanced AJCC stage when first seen were found to be at higher risk for recurrence and metastasis. Significant predictive factors of recurrence were tumors involving more than 1 quadrant ($P=.02$), tumors greater than 0.5 mm thick ($P=.04$), tumor multifocality ($P=.04$), and history of treatment before referral to The New York Eye Cancer Center ($P=.03$). The significant predictive factors for tumor metastasis were tumors greater than 0.5 mm thick ($P=.005$), tumor invasiveness ($P=.04$), pathologic diagnosis of conjunctival melanoma vs melanoma in situ ($P=.04$), and tumor recurrence ($P<.001$).

The present results are similar to those of other medical centers. Although published recurrence rates are 34% to 62% at a mean follow-up of 30 months,^{2,5,8,27-30} the present recurrence rate was 33%. Whereas Savar et al³⁰ reported nodal and distant metastases in 15% of patients, the present study showed metastasis in 19% (n=8 of 42). Furthermore, the seventh edition AJCC staging system upstages melanomas involving palpebral, forniceal, plica, and caruncle compared with bulbar conjunc-

Table 3. Correlations Among Tumor Features, Recurrence, and Metastatic Rate

Feature	Patients, No. (%)	Recurrence, No. (%)	P Value	Metastasis, No. (%)	P Value		
Sex							
Male	21 (50)	7 (33)	>.99	4 (19)	>.99		
Female	21 (50)	7 (33)		4 (19)			
Visual acuity							
OD	19 (45)	8 (42)	.54	4 (21)	>.99		
OS	23 (55)	6 (26)		4 (17)			
Size, quadrant							
≤1	13 (31)	0	.02	0	.09		
>1 to 2	18 (43)	7 (39)		3 (17)			
>2 to 3	7 (17)	4 (57)		2 (29)			
>3	4 (9)	3 (75)		3 (75)			
Thickness, mm							
<0.5	23 (55)	3 (13)	.04	0	.005		
≥0.5	19 (45)	11 (58)		8 (42)			
Focality							
Monofocal	29 (69)	5 (17)	.05	3 (10)	.12		
Multifocal	13 (31)	9 (69)		5 (38)			
Morphology							
Focal	20 (48)	6 (30)	>.99	4 (20)	>.99		
Spreading	22 (52)	8 (36)		4 (18)			
Location(s)							
Bulbar alone	26 (62)	6 (23)	.23	4 (15)	.70		
Tarsus or fornix	6 (14)	4 (67)		2 (33)			
Caruncle alone	2 (5)	0		0			
Caruncle + (tarsus/fornix)	7 (17)	4 (57)		2 (29)			
Invasion							
Conjunctival	32 (76)	8 (25)	.19	3 (9)	.04		
Globe	0						
Lid	5 (12)	2 (40)		1 (20)			
Orbit	1 (2.4)	1 (100)		1 (100)			
Sinus	1 (2.4)	1 (100)		1 (100)			
Eyelid + orbit	2 (4.8)	1 (50)		1 (50)			
Eyelid + orbit + sinus	1 (2.4)	1 (100)		1 (100)			
AJCC pathologic stage							
pTis	16 (38)	3 (19)		.34		0	.04
pT1	13 (30)	4 (31)	2 (15)				
pT2	5 (12)	1 (20)	1 (20)				
pT3	8 (19)	6 (75)	5 (63)				
AJCC clinical stage							
Tis	16 (38)	3 (19)	.34	0	.04		
T1	15 (36)	4 (27)		3 (20)			
T2	3 (7)	1 (33)		0			
T3	8 (19)	6 (75)		5 (63)			
T4	0						
Recurrence							
Yes	14 (33)			8 (50)	<.001		
No	28 (77)			0			
NM stage							
N1	4 (10)	4 (100)	.10				
N0	38 (90)	4 (11)					
M1	7 (17)	7 (100)		<.001			
M0	35 (83)	1 (3)					

Abbreviations: AJCC, American Joint Committee on Cancer staging system for conjunctival melanoma (for subgroups, see Table 1); TNM, tumor, node, and metastasis.

tival tumors.^{22,31} Similarly, the review by Paridaens et al²⁸ of 256 cases supports these site-specific stages by identifying palpebral, forniceal, plica, caruncle, and lid margin sites as unfavorable. Similarly, the present clinical recurrence rates were 27%, 33%, and 75% for T1, T2, and T3 tumors, respectively.

The seventh edition AJCC pathologic staging system upstages conjunctival melanomas as they become thicker

(Table 1).²² This decision is supported by the research of Tuomaala and Kivelä,²⁷ Stefani,³² and Savar et al.³⁰ In the present study, we divided thickness into 3 subgroups and found that 75% of patients (3 of 4) with lymph node involvement had a tumor thickness greater than 1.5 mm, 25% (1 of 4) had a tumor thickness of 0.5 to 1.5 mm, and no tumors less than 0.5 mm thick developed nodal or distant metastasis. This finding supports the con-

vention used by the seventh edition AJCC staging criteria in which a thickness greater than 0.5 mm is considered to have predictive value for the risk of metastasis.

Regarding local recurrence, 19% of Tis and 39% of invasive conjunctival melanomas recurred, and no Tis cases developed nodal or distant metastasis. However, 29% of invasive conjunctival melanomas (8 of 28) metastasized. The better outcomes of Tis vs higher-stage tumors supports the seventh edition AJCC staging system in separating tumors into Tis vs T1, T2, and T3 tumors according to their histopathologic diagnosis.²²

We evaluated the seventh edition AJCC staging system, which was written by 45 ophthalmic oncologists from 11 countries.²² Its site-specific subclassifications have proved to offer predictive value for local recurrence and systemic metastasis of conjunctival melanoma. It allowed for standardized collection of information regarding histopathologic diagnosis, tumor size, local invasion, recurrence, lymph node involvement, and distant metastasis. Use of universal staging allows the present information to be added to that derived from other centers using the AJCC classification. A major drawback of AJCC staging is its inability to discriminate between tumors according to focality (multifocal vs unifocal). In the present series, multifocal tumors showed a significantly high risk of recurrence.

Herein, we examined the predictive value of AJCC staging for conjunctival melanoma. Although this is unique work, we realize that it is retrospective and of limited size. Therefore, a larger, more comprehensive, multicenter validation study should be performed to better analyze and improve the predictive power of AJCC staging for conjunctival melanoma.

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