Pterygium Recurrence Rates in the Hispanic Population in the Northeastern United States

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Abstract

Purpose: To determine the rate and factors affecting pterygium recurrence in the Hispanic population of the Northeastern United States, based on patient demographic information.

Methods: In this retrospective cross-sectional study, data were collected on ethnically Hispanic patients from 2013 to 2018 who had primary single-headed pterygia excision and conjunctival autograft, with the minimum of 4-month follow-up time. This study was conducted in an academic institution in the Northeastern United States, with all patients being from the surrounding community.

Results: In 168 Hispanic patients with confirmed primary single-headed pterygium, most pterygia occurred nasally (161/168). The average age of presentation was 46.3 ± 12.0 years (range, 23–77 years). There were 22 recurrences (13.1%), occurring at an average of 3.0 ± 1.6 months (1–8 months). This cohort demonstrated a unimodal recurrence distribution. Age is significantly inversely correlated with the incidence of recurrence ($r = -0.219$, $P = 0.004$), but not with the size of the recurrent pterygia ($r = -0.112$, $P = 0.621$). There was no significant difference between recurrence based on gender ($P = 0.265$), location ($P = 0.824$), or laterality (right or left eye) ($P = 0.213$). Mean corrected visual acuity improved from 20/40 to 20/32 after pterygium excision ($P < 0.001$). Cox regression analysis for age groups shows the risk of recurrence for patients aged 20–29 is 11.4-time that of patients aged 50 and above ($P < 0.001$).

Conclusions: Recurrence occurred unimodally at around 3 months postoperatively. Younger patients are significantly more susceptible to recurrence. Future studies may seek to determine the incidence of pterygia and their recurrence patterns in relation to occupations and sun exposure time in a geographic area.

Keywords: Autograft, Excision, Hispanic, Pterygium, Recurrence

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Introduction

Pterygia are found in patients worldwide, and their prevalence varies widely depending on the region of the world.[1] There is an increased prevalence in a region referred to as the "pterygium belt" which includes the portion of the population living 30° north and south of the equator.[2,3] Previous studies have shown the prevalence to vary among different ethnicities even within the same region.[4,5] In Hispanic patients, the prevalence is notably elevated. This may be a result of various geographic, lifestyle, and genetic factors which may predispose Hispanic patients to pterygium formation.[6]

Surgical excision of pterygia is indicated when these benign growths of fibrovascular tissue impair the patient's vision by causing high regular or irregular astigmatism, blocking the visual axis, or causing restricted ocular motility. This disease may pose esthetic concern for the patient or cause

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chronic irritation, which may also be indication for surgery. According to one study, Hispanic populations have a higher tendency towards recurrence in comparison to Caucasian groups.[7] Current literature reports the incidence of recurrence to be between 5% and 15% worldwide.[8] The primary method of surgical management involves pterygium excision with conjunctival autograft (PECG). Physicians may use fibrin glue, autologous blood, or sutures to secure the conjunctival autograft. Other common methods of management following excision include using amniotic membrane as an alternative to conjunctiva as grafting material, or bare sclera surgery with or without chemotherapeutic agents such as mitomycin-C.[9-11] Due to the high recurrence rate of pterygia, there have been long-standing efforts to minimize recurrence and determine which method is least likely to lead to recurrence. Currently, conjunctival autograft is the gold standard.[12,13] In other countries, alternate methods of pterygium excision are still used, however, these methods are associated with increased recurrence.[14,15]

Herein, we present a retrospective study assessing the recurrence rate of single-headed pterygia in the Hispanic population, following primary PECG.

Methods

This was a retrospective cross-sectional study of 168 patients approved by the Institutional Review Board and Ethics Committee of Rutgers New Jersey Medical School between 2013 and 2018. The study was conducted in adherence to the tenets of the Declaration of Helsinki and the United States of America Health Insurance Portability and Accountability Act of 1996. All patients had primary single-headed pterygia that were excised and followed with conjunctival autografting at our academic institution. Exclusion criteria for this study were follow-up time <4 months, double-headed pterygia, recurrent pterygia, and nonHispanic race.

Surgical technique

All surgeries were performed by a postgraduate year-4 ophthalmology resident physician under the supervision of an attending physician (M.H.D.). Recent studies have shown that with regard to surgeon experience, there is no statistically significant difference in postoperative complications or recurrence rates.[16] For the surgical technique, we followed the technique described by Starck *et al*.[17] Briefly, after instillation of topical proparacaine and a vasoconstrictor agent (either phenylephrine 2.5% or brimonidine 0.2%), the body of the pterygium was outlined using a surgical marking pen. Lidocaine 1% with epinephrine was injected into the pterygium head. The pterygium head was then carefully dissected from the cornea taking care to follow the surgical plane of the pterygium using a surgical blade (No. 15) or a 23-gauge needle. Blunt and sharp dissection was performed to separate the pterygium from the underlying sclera and surrounding conjunctiva, and the body of the pterygium was then excised along the marking area. The area of the bare sclera was measured, and the corresponding area on the ipsilateral superior bulbar conjunctiva was marked to outline an oversized graft with an additional 1.0 mm relative to the dimensions of the graft bed. Then the entire area of the graft was inked to mark the epithelial side as well as to facilitate the plane of dissection. Lidocaine 1% with epinephrine was injected into the donor conjunctiva to balloon out the area of the graft and separate it from the underlying Tenon's capsule. The marked conjunctiva was then carefully dissected away from the Tenon's capsule. Care was taken not to include Tenon's tissue and prevent buttonholes when preparing the graft. Then the free conjunctival graft was laid into place stromal side down to cover the area of bare sclera and carefully secured in position with fibrin sealant (Tisseel, Baxter, Westlake Village, CA). Care was taken to maintain proper spatial orientation with the epithelial side facing upwards, the limbal edge facing towards the limbus, and the sides of the graft opposed to the edges of the recipient conjunctiva. At the conclusion of the procedure, a plano bandage contact lens with an 8.4 mm base curve and 14-mm diameter (Acuvue Oasys, Vistakon Inc., Jacksonville, FL, USA) was placed over the cornea. Moxifloxacin and prednisolone acetate 1% eye drops were applied 4 times daily for 1 week. The bandage contact lens was removed after 3–5 days; antibiotic eye drop discontinued after a week, and prednisolone acetate 1% eye drop tapered over 3 more weeks.

Patients included in the study required a minimum of 4 months of follow-up. The primary outcome measured was pterygium recurrence, defined as any regrowth of fibrovascular tissue past limbus onto clear cornea in the region of previous pterygium removal. Clinical examination was used to determine morphological characteristics of the pterygia to aid in grading. Additional features collected include location on the eye, single or double-headedness, and which eye it occurred in. Recurrence of pterygia was graded as either Grade 1 (pterygium head is less than halfway between the limbus and the pupillary margin), Grade 2 (pterygium head is more than halfway between the limbus and the pupillary margin), or Grade 3 (pterygium head crosses pupillary margin).

Statistical analysis

Continuous variables were described using mean, standard deviation, median, and range. Categorical variables were described using frequencies and proportions. Normally distributed data were analyzed using student's paired, while nonnormally distributed data were analyzed using Wilcoxon signed-rank test. Chi-square test was used to determine the association of two categorical variables, while analysis of variance was used to determine the association of more than two categorical variables. The relationship between continuous parameters was assessed by Pearson's correlation coefficient. Cumulative proportion of nonrecurrence estimates at different intervals were tabulated to generate Kaplan–Meier plots. Cox regression analysis for age groups (A = 20–29 years; B = 30–39; C = 40–49, D = 50+) was performed to determine the comparative risk of recurrence between age groups. Statistical significance was set at $P < 0.05$. All statistical analysis was performed using a statistical software package (SPSS for Windows, version 23.0; IBM-SPSS, Chicago, IL, USA). Graphs were created using R (R Core Team, 2018) and the ggplot2 package (Wickham *et al*., 2020).

Results

One-hundred and sixty-eight eyes of 168 patients with single-head pterygia were included in this study. The mean age at presentation was 46.3 ± 12.0 years standard deviation (46 median, 23–77 range). The average time of postoperative follow-up was 7.1 ± 4.2 months (10, 4–51). The majority of participants were female (89/168, 53%), and all patients were of Hispanic origin or descent. Most pterygia occurred in the left eyes of the cohort (90/168, 53.6%). The vast majority of patients presented with nasal pterygia (161/168, 95.8%), with the remainder presenting with temporally located pterygia (7/168, 4.2%). Patient demographics, as well as clinical and statistical data, are summarized in Table 1.

Following pterygium excision and conjunctival autograft, a majority of patients did not experience complications (164/168, 97.6%). However, the complications that did occur in the cohort include pyogenic granuloma (2/168, 1.2%), heme under the autograft (1/168, 0.6%), and corneal Dellen (1/168, 0.6%). In addition, there were no incidences of wound dehiscence or graft displacement in any patients. Of the patients that experienced complications, none experienced recurrence.

Visual acuity was collected for all patients and converted to logMAR scaling. The mean corrected visual acuity of patients before treatment was 0.3 ± 0.3 logMAR (median 0.2, range − 0.1–1.9) equal to Snellen chart equivalent of 20/40. At the latest follow-up, the average logMAR visual acuity was 0.2 ± 0.3 logMAR (median 0.1, range −0.1–1.9) equal to Snellen chart equivalent of 20/32. The change in

Table 1: Patient demographics, clinical information, and recurrence analysis

Patient demographics and information	Mean±SD (median, range)	*P*
Enrolled patients	168	
Incidence of recurrence, *n* (%)	22 (13.1)	
Age at presentation (years)	46±12 (46, 23-77)	**0.016***
Age at recurrence (years)	39±13 (37, 23-77)	
Correlation of age with recurrence		*r*=−0.219 **0.004****
Follow-up duration after excision (months)	7±4 (10, 4-51)	
Time to recurrence (months)	3±2 (3, 1-8)	
Gender, *n* (%)		
Male	79 (47)	
Female	89 (53)	
Male recurrence	13/79 (16.5)	0.224*
Female recurrence	9/89 (10.1)	
Pterygium features, *n* (%)		
Location in eye		
Nasal	161 (95.8)	
Temporal	7 (4.2)	
Nasal recurrence	21/161 (13%)	0.824*
Temporal recurrence	1/7 (14.3%)	
Recurrence grade		
Grade 1	19/22 (86.4)	
Grade 2	2/22 (9.1)	
Grade 3	1/22 (4.6)	
Correlation of recurrence grade and age		*r*=−0.112 0.621**
Correlation of recurrence grade and time to recurrence		*r*=0.133 0.555**
LogMAR visual acuity: Mean±SD (median, range)		
Preoperatively	0.26±0.31 (0.20, −0.10-1.90)	**<0.001*****
Postoperatively	0.21±0.28 (0.10, −0.10-1.90)	
Postoperative complications, *n* (%)		
Pyogenic granuloma	2 (1.2)	
Heme under graft	1 (0.6)	
Corneal dellen	1 (0.6)	

*Wilcoxon signed rank test, **Pearson's Correlation test, ***Student's *t*-test. Boldface is $P<0.05$. SD: Standard deviation visual acuity before and following PECG was statistically significant ($P < 0.001$).

Recurrence occurred in 22 patients of the cohort (13.1%), and recurrence occurred at an average 3.0 ± 1.6 months (3, 1–8) following PECG. Finally, recurrence most commonly occurred as a Grade 1 pterygium (19/22, 86.4%), followed by Grade 2 (2/22, 9.1%), followed by Grade 3 (1/22, 4.6%).

In this cohort, recurrence occurred more frequently in men (13/79, 16.5%) than it did in women (9/89, 10.1%), though this difference was not statistically significant ($P = 0.224$). The time to recurrence for men was an average 3.2 ± 1.9 months (3, 1–8) while the time to recurrence for women was an average 2.6 ± 0.7 months (2, 2–4). Recurrence of pterygia occurred more frequently in the left eye (13/90, 14.4%) than in the right eye (9/78, 11.5%) ($P = 0.625$). Of the pterygia that occurred nasally, 13% recurred (13/161). The recurrence rate of pterygia that occurred temporally was very similar at 14.3% (1/7). The location of the pterygium head on the eye was not significantly associated with recurrence ($P = 0.824$).

The average age at which recurrence occurred was 39.6 ± 13.1 years (37, 23–77) which is significantly lower than the average age of the total population at presentation, 46.3 ± 12.0 years (46, 23–77) ($P = 0.016$). In addition, age is significantly inversely correlated with the incidence of recurrence ($r = -0.219$, $P = 0.004$). However, age was not significantly correlated with the size of the recurrent pterygia ($r = -0.112$, $P = 0.621$). Finally, the time to recurrence was not significantly correlated with the size of the recurrence ($r = 0.133$, $P = 0.555$). A Kaplan–Meier curve and analysis [Figure 1] was conducted to demonstrate the role of age on the recurrence of the pterygium, which revealed an overall $P < 0.001$, suggesting that age is one of the more reliable risk factors in the prediction of whether a patient will experience recurrence or not. Patients in Group A were ages 20–29, those in Group B were ages 30–39, Group C were ages 40–49, and Group D were patients 50 and older. Cox-regression analysis for the age groups showed the risk of recurrence in Group A that is 11.4-time higher than that in Group D ($P < 0.001$).

The frequency of patients' time to recurrence was plotted to determine recurrence patterns postexcision. A histogram was produced, demonstrating a unimodal recurrence distribution around the cohort's average 3 months' time to recurrence: 3.0 ± 1.6 months (3, 1–8) [Figure 2]. Subgroup analysis was then performed on patients with minimum of 12-month follow-up (54/168, 32.1%) to determine the frequency of recurrence times in that subgroup. No patients that experienced recurrence were lost in this subgroup analysis, resulting in an identical frequency distribution of recurrence. The recurrence distribution pattern, therefore, remained unimodal with peak frequency of time to recurrence at 3 months.

Discussion

Although the pathophysiology of pterygium is not clearly understood, ultraviolet (UV) light is identified as the most important risk factor for primary pterygia. The contribution of UV radiation and pterygia pathogenesis has been supported by epidemiological data, immunohistochemical studies, and cell culture models.[18-20] UV light forms free radicals that induce damage in DNA, RNA, and the extracellular matrix of cells. Furthermore, UV-B induces the expression of cytokines and growth factors in pterygial epithelial cells.[21]

Similarly, factors of recurrence following excision are not fully understood, yet likely depend on a multitude of patient-related, environmental, clinical, and/or surgical factors. We hypothesize that the Hispanic population is at greater risk of recurrence due to increased sun exposure, as well as other exposure-related factors. Our study found an overall recurrence rate of 13.1% in the Hispanic population of Newark, New

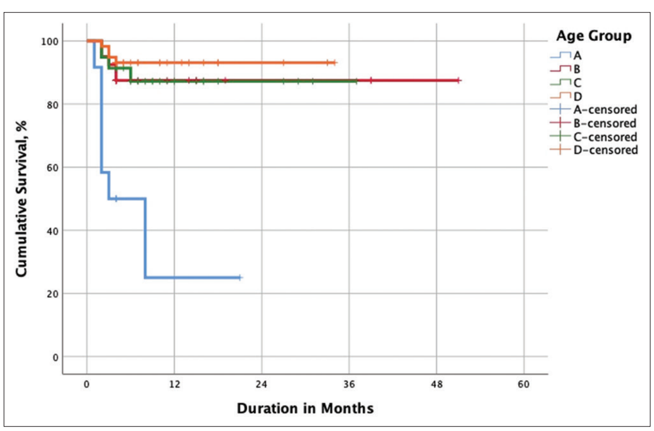

Figure 1: Kaplan–Meier analysis of pterygium recurrence. Kaplan–Meier curves showing the role of age and its association with pterygium recurrence. A = 20–29 years; B = 30–39 years ($P < 0.001$; log-rank, Mantel-Cox); C = 40–49 years ($P < 0.001$; log-rank, Mantel-Cox); D = 50+ years ($P < 0.001$; log-rank, Mantel Cox)

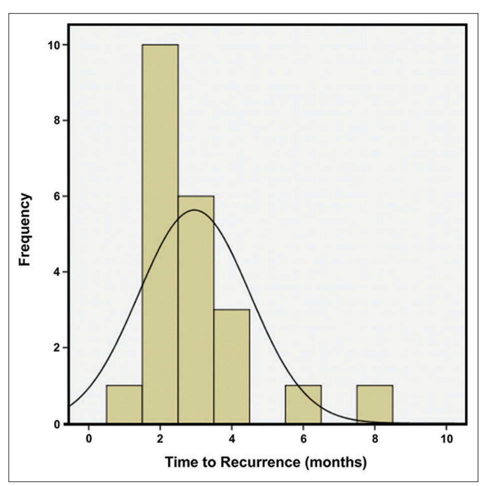

Figure 2: Time to recurrence frequency distribution. Histogram frequency graph representing the time at which patients experienced recurrence. A superimposed distribution curve demonstrates the unimodal pattern of recurrence observed in this cohort at around 3 months postoperatively

Jersey, United States. Of note, however, this recurrence rate is significantly lower than those reported in Hispanic populations by Kandavel *et al*. (40%) and Campagna *et al*. (28%).[7,22] Our lower rate of recurrence may be attributed to differences in the cohort's geographical proximity to the equator.[23] Our subset of patients is primarily from the Northeastern United States (New Jersey) which may predispose them to recurrence less so than the Hispanic population of the Southwestern United States (Southern California) in Kandavel *et al*.'s study, or Southern United States in Campagna *et al*.'s study (Texas). In addition, socioeconomic status and occupations, such as construction work and farming, may play a role in exposure to UV radiation postoperatively. This may likewise explain the higher recurrence rate in our male patients (16.5%) than our female patients (10.1%), as males in this cohort are more likely to work outdoor jobs than females. However, the difference between recurrence in males and females was not statistically significant in our cohort ($P = 0.224$).

The average age of patients at presentation with pterygia was 46 years. However, the average age of patients that experienced recurrence following excision was significantly lower at 39 years ($P < 0.001$). Although some studies suggest that younger subjects have lower recurrence rates, our study suggests that pterygium is a disease of increased age, but that increased age provides a protective effect against recurrence.[24] Furthermore, the present study demonstrated a significant negative correlation trend of age with recurrence ($r = -0.219$, $P = 0.004$). This result is consistent with numerous reports in the literature and may in part be due to environmental factors such as increased UV exposure in younger patients, as well as the possible role of a more robust inflammatory and wound healing process postexcision in younger patients, which may contribute to recurrence.[25-28] Finally, the Kaplan–Meier curve of Figure 1 shows that patients ages 20–29 are 11.4-time more likely to have recurrence than patients 50 years or older. The implication of this finding may guide physician expectations of significantly higher recurrence rates after pterygium surgery in younger patients. These patients should be encouraged to avoid sun exposure or apply more aggressive anti-inflammatory treatment postexcision.

Recurrence in this cohort had a unimodal distribution pattern with peak recurrence occurring at 3 months postexcision. Additionally, subgroup analysis was performed on patients who had minimum 12 months of follow-up time. This was done to determine the presence of any bimodal recurrence pattern that may not have been visible when patients with less follow-up were included. However, the subgroup recurrence distribution pattern remained unimodal with peak recurrence at 3 months. This is consistent with a majority of literature on recurrence patterns in Hispanic populations.[7,22,26] Few reports in the literature demonstrate bimodal recurrence patterns which interestingly occur in Chinese and Ghanaian populations.[29,30] This may therefore suggest either geographic or intraracial differences in mechanisms of recurrence, as well as interracial differences. Future studies should attempt to determine possible genetic factors accounting for variances in frequencies of recurrence interracially and intercontinentally.

The novelty of the present study is in the cohort recruited. To our knowledge, this is the largest cohort of Hispanic patients evaluated for PECG and recurrence rates in the North American continent, producing valuable data on the recurrence patterns in this geographic location and in this population. As we have shown through comparative data, there are lower recurrence rates in the Northeastern United States than in southern regions of the United States, suggesting that from all possible etiologies of pterygium recurrence, including genetic, biochemical, vascular, or alternative causes, UV radiation is still likely the most strongly implicated and modifiable risk factor following PECG. Furthermore, this study demonstrated a strongly unimodal recurrence pattern at 3-month postexcision. These pieces of information together should guide physicians in recommending that their patients should be especially cognizant of UV protection, such as by wearing sunglasses for several months following treatment. According to one study, even medium-framed sunglasses block about 75% of UV radiation to the ocular surface on cloudless summer days.[31]

A limitation of this study was that patients' types of astigmatism were not recorded and would have been helpful. However, this study demonstrated a significant improvement in visual acuity following excision and conjunctival autograft ($P < 0.001$). This improvement may be partly due to the resolution of visual obstruction by the pterygium but is more likely primarily due to improvement of astigmatism following excision.

In conclusion, this study demonstrated a high recurrence rate of pterygia postexcision and conjunctival autograft in the Hispanic population of the Northeastern United States. Increasing age was protective against recurrence and is likely due to a number of mechanisms including interracial, biologic, genetic, epigenetic, and geographic influences. Recurrence primarily occurs at around 3 months postexcision, but follow-up is important and should be emphasized to identify recurrence which occurs at a later time postexcision.

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Conflicts of interest
There are no conflicts of interest.

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