iMedPub Journals

TRANSLATIONAL BIOMEDICINE

2010
Vol.1
No. 2:4
doi: 10:3823/411

Possible correlation of plica-limbal distance with the presence of primary medial pterygium

Herman Christiaan Izaak Themen[1,2], Dennis Ricardo August Mans[3], Robbert Bipat[4], Denise Judith Doelwijt[1], Dineshpersad Jiawan[1], Annemarie Thelma Bueno de Mesquita-Voigt[1,2,]

1Department of Ophthalmology, Academic Hospital Paramaribo, Paramaribo, Suriname;
2Department of Ophthalmology, Faculty of Medical Sciences, Anton de Kom University of Suriname;
3Department of Pharmacology, Faculty of Medical Sciences, Anton de Kom University of Suriname;
4Department of Physiology, Faculty of Medical Sciences, Anton de Kom University of Suriname

Running title: Plica-limbal distance and pterygium
Key words: primary medial pterygium; plica-limbal distance; inverse correlation
Correspondence to: H. Themen, MD, Department of Ophthalmology, Academic Hospital Paramaribo, Flustraat 1, Paramaribo, Suriname. Tel: 597 442222 # 585. Fax: 597 441071. E-mail: hthemen@gmail.com

Abstract

Background: Loss of elastic properties, the introduction of tractional forces, and shortening of the plica-limbal distance (the distance between the nasal limbus and the semilunar plica bottom in full abduction) are common anatomical abnormalities in eyes of patients with primary medial pterygium. In this study, we assessed whether, and to which degree the latter phenomenon correlated with the presence of pterygium.
Methods and findings: Plica-limbal distance was measured using a slit lamp in individuals who came for routine eye examination, and was related to pterygium size, as well as to patients' gender and age. Data were expressed as means (95% CI). Eighty-three males and 118 females were enrolled in the study. There were 49 eyes from patients with unilateral pterygium, 84 from patients with bilateral pterygium, and 220 from individuals who did not suffer from either uni- or bilateral pterygium. The mean plica-limbal distance in eyes with pterygium (7.3 mm, 95% CI: 6.9 – 7.7 mm) was significantly shorter than that in eyes without pterygium (9.9 mm, 95% CI: 9.7 – 10.1 mm). Plica-limbal distance correlated inversely with pterygium size ($r2 = 0.32$, $p < 0.0001$), was not related to gender, but decreased with increasing age in both individuals with and without pterygium.
Conclusion: Our results suggest that plica-limbal distance correlated inversely with the presence of pterygium. This finding may have important consequences for the identification of individuals at risk, as well as for improvement of the treatment of this condition.

Introduction

Pterygium is a common surface lesion of the conjunctiva that often encroaches onto the cornea and is usually located medially at the limbus. The overgrowth of conjunctival tissue is presumably triggered by inflammation caused by chronic irritation. Although in general asymptomatic, it may progress to an inflammatory, invasive, and proliferative lesion, particularly after recurrent surgical excision. The result is loss of bulbar conjunctival tissue and restriction of bulbar motility [1]. For these reasons, pterygium is among the most complex and difficult-to-manage common diseases of the conjunctiva.

The exact cause of pterygium is unknown. However, long-term exposure to direct and reflected sunlight - especially ultraviolet B (UV-B) rays - as well as chronic eye irritation caused by windblown dust, sand, ice, and snow, presumably play an important role in its development [2]. This may account for the relatively high prevalence of pterygium in areas near the equator and in diverse groups such as Australian Aboriginals, Pacific Islanders, and Eskimos [3]. No incidence rates are available, but worldwide prevalence rates are between 3 and 10% [3]. Reports on the male-to-female distribution are conflicting [6-11], but elderly people seem to be more susceptible than younger individuals [6-11], with onset most common in individuals aged between 20 and 30 years [3-8].

Converging lines of evidence suggest the involvement of several anatomical and mechanical changes and the generation of tractional forces in the development of pterygium. Firstly, the

2010
Vol.1
No. 2:4
doi: 10:3823/411

formation of pterygium under the influence of UV-B is accompanied by the excessive production of matrix metalloproteinases in ocular epithelial cells [9,10]. This may promote the degradation of fibrillar collagen, which may result in loss of the elastic properties of primary pterygium tissue and the introduction of traction in the pterygium tissue. Also, subconjunctival fibrovascular tissue of pterygia contains an appreciable number of contractile myofibroblasts [11]. This has been indicated by an immunohistochemical and ultrastructural assessment of surgically removed primary and recurrent pterygia and exenterated eyes without pterygia, and may also lead to contraction, restricting eye motility even more. Furthermore, a study on the developmental relationship between semilunar temporal ectopia and primary nasal pterygia not only substantiated the presence of tractional forces in pterygium, but also that these forces were operating at both pterygium ends [12].

Notably, using a bovine eye model along with computer-assisted ray-tracing techniques to model limbal focusing, the nasal part of the conjunctiva was shown to be more exposed to light when compared to the temporal part [13]. This may provide an explanation for the location of most pterygia at the medial limbus, in the junction between the sclera and the cornea on the nasal side [13]. In addition, since the nasal part of the conjunctiva is shorter than the temporal part, it can be argued that the former may be more susceptible to traction with eye and lid movements when compared to the latter.

Together, the data mentioned above suggest that the development of pterygium is accompanied by tractional forces which may pull stronger at the nasal than at the temporal side. If true, the possibility exists that such forces may progressively shorten the distance between the nasal limbus and the semilunar plica bottom – the plica-limbal distance – during pterygium formation. In this study, we searched for indications for this hypothesis by determining distances between the nasal limbus and the semilunar plica bottom in maximum abduction in eyes with primary medial pterygium, and comparing these findings to those with eyes without pterygium. The data obtained were also related to pterygium size which can be taken as an indication for the degree of pterygium progression [14]. Because the disease may or may not have a predilection for either gender [3-8] and may manifest preferentially in older than in younger individuals [3-8], the data were also related to patients' gender and age at the time of diagnosis.

Patients and methods

Study population

This study was carried out at the Department of Ophthalmology of the Academic Hospital Paramaribo (Paramaribo, Republic of Suriname) and its auxiliary branch in Nickerie (Republic of Suriname), and at a private practice in Paramaribo, in the period between January 2004 and April 2009. Individuals who were included in the study were between 7 and 100 years of age, had presented for routine eye examination for mainly refraction anomaly, or had been diagnosed with pterygium. To certify that all pterygia studied had developed in an untroubled way and were located at the semilunar plica, only eyes with primary medial pterygium were included. Eyes with either motility restrictions, or surgical scars or visible pathologies in the plica-limbal area, were not eligible. Eyes in which the plica-semilunar temporal or bulbar fold bottom mark was not visible were also excluded. All individuals included in the study had given their oral consent after having been informed of its aims. The study design had been approved by the Ethics Committee of the Academic Hospital Paramaribo.

Determination of plica-limbal distance and pterygium size

Plica-limbal distance was determined by measuring the distance in mm from the temporal or bulbar part of the semi-lunar fold bottom mark to the limbus in full abduction (Figure 1). Pterygium size was determined by measuring the distance in mm from apex to limbus (Figure 1), as has been done in a previous study [15].

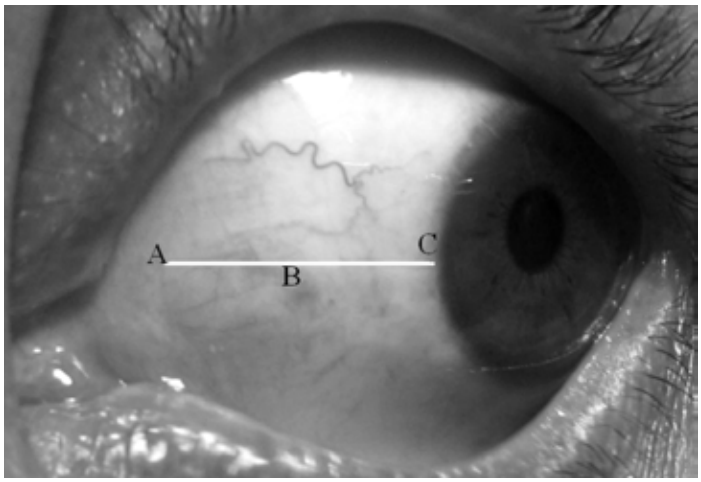

Figure 1. Measurement of the plica-limbal distance in an eye in maximum abduction. A: plica semilunaris, B: light reflection of slit lamp, C: limbus. Subject has given oral and written permission to publish photograph.

For measurements, subjects' heads were held straightforward behind a Haag-Streit 900 slit lamp (Bern, Switzerland) with minimum and maximum slit lengths of 1 and 8 mm, respectively. The margins of the slit had to be clear when reading the distances. Plica-limbal distances greater than 8 mm were determined by projecting one end of the 8-mm slit on the vertical line through the center of the temporal or bulbar plica bottom area, turning the slit perpendicular to this line, pointing perpendicular at the vertical tangent of the limbus in the horizontal meridian, searching for a marking point - usually a blood vessel in the conjunctiva - and from that point on measuring further to the limbus in the horizontal meridian. When measuring pterygium size, distances less than 1 mm were estimated at 0.25,

2010
Vol.1
No. 2:4
doi: 10:3823/411

0.50, or 0.75 mm. All measurements were performed by the same person.

Data processing

Plica-limbal distances and pterygium sizes of eyes of patients with both unilateral and bilateral pterygium were averaged, and compared to those of the means of eyes of patients who did not suffer from this condition. Comparisons were made using Student's t-test (95% CI). Differences were considered statistically significant with $p < 0.05$.

Results

Patient characteristics

In the period covered by the study, a total of 201 individuals (83 males and 118 females) presented for routine eye examination for mainly refraction anomaly. There were 49 eyes from patients with unilateral pterygium, 84 eyes from patients with bilateral pterygium, and 220 eyes from individuals who did not suffer from either uni- or bilateral pterygium. The median age of the individuals without pterygium was 37 years (range 7 – 100 years), that of those with pterygium was 52 years (range 12 – 87 years).

Plica-limbal distance of eyes with and without pterygium

The mean plica-limbal distance in the group of patients with both unilateral and bilateral pterygium was 7.3 mm (95% CI: 6.9 – 7.7 mm), that in the group of patients without pterygium 9.9 mm (95% CI: 9.7 – 10.1 mm) (Figure 2). This difference was statistically significant ($p < 0.0001$), suggesting that the average plica-limbal distance of eyes with pterygium was approximately three-quarters of that of eyes without pterygium.

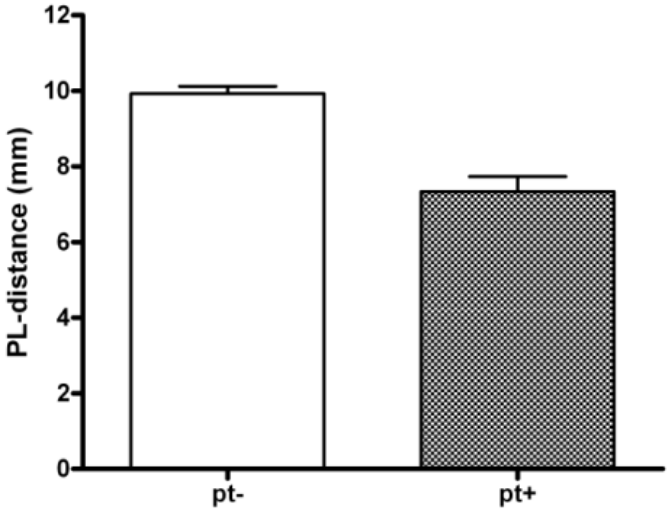

Figure 2. Mean (CI 95%) plica-limbal distance (mm) in eyes of individuals without (pt -) and in those of individuals with uni- or bilateral pterygium (pt +).

Relationship between pterygium size and plica-limbal distance

To explore to which degree plica-limbal distance was associated with pterygium size, plica-limbal distances of all eyes with pterygium were plotted against their respective size. As shown in Figure 3, linear regression of this plot generated a straight line ($r^2 = 0.32$, $p < 0.0001$), suggesting that plica-limbal distance was inversely related to pterygium size.

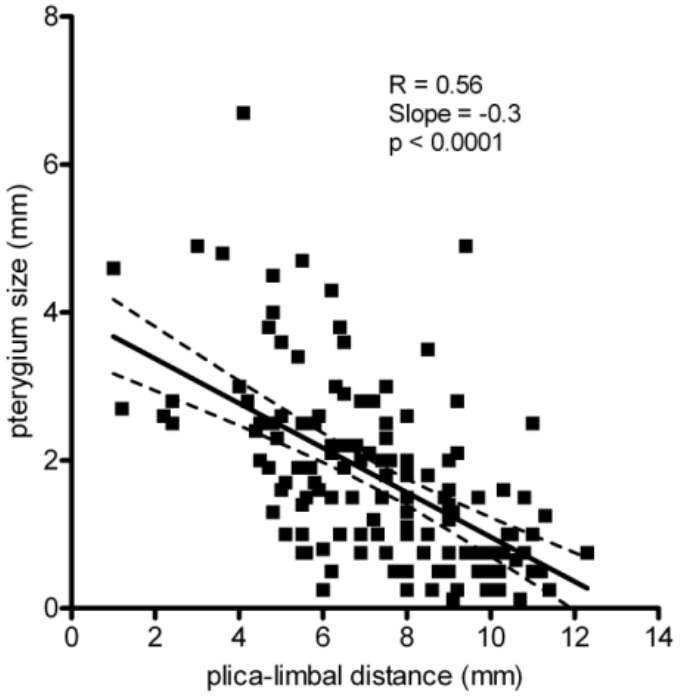

Figure 3. Relationship between plica-limbal distance (mm) and pterygium size (mm).

Plica-limbal distance and gender

There were 54 women and 38 men with uni- or bilateral pterygium. As shown in Figure 4, the mean plica-limbal distance of eyes of males with pterygium did not differ significantly from that of females suffering from the disease (7.8, CI 7.3 – 8.4, and 7.0, CI 6.5 – 7.5), respectively). The same held true for plica-limbal distances of eyes without pterygium (10.4, CI 10.1 – 10.7, and 9.6, CI 9.3 – 9.8, respectively).

Plica-limbal distance and age

Figure 5 depicts the relationship between plica-limbal distances of individuals with or without pterygium, and age. Plica-limbal distance decreased in eyes with pterygium at the same rate as in eyes with pterygium with older age (average 0.02 – 0.03 mm/year), suggesting that this phenomenon was a general age-associated phenomenon. However, plica-limbal distances in eyes with pterygium were at every age consistently shorter when compared to eyes without pterygium with a mean difference of 2.5 mm.

2010
Vol.1
No. 2:4
doi: 10:3823/411

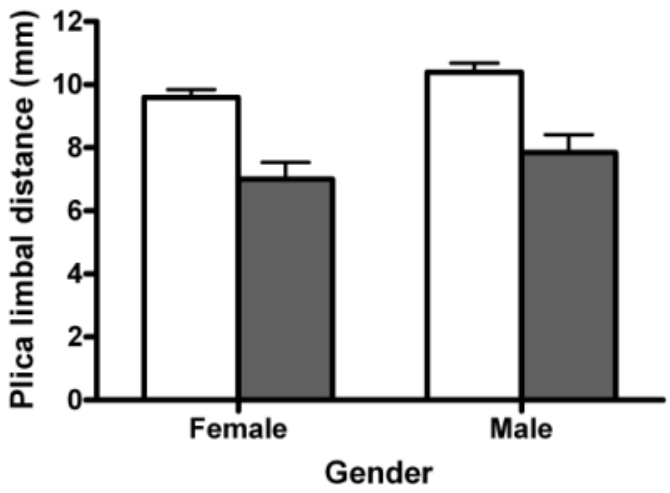

Figure 4. Mean plica limbal distance (mm) in eyes of men and women without pterygium (blank bars) and with uni- or bilateral pterygium (grey bars).

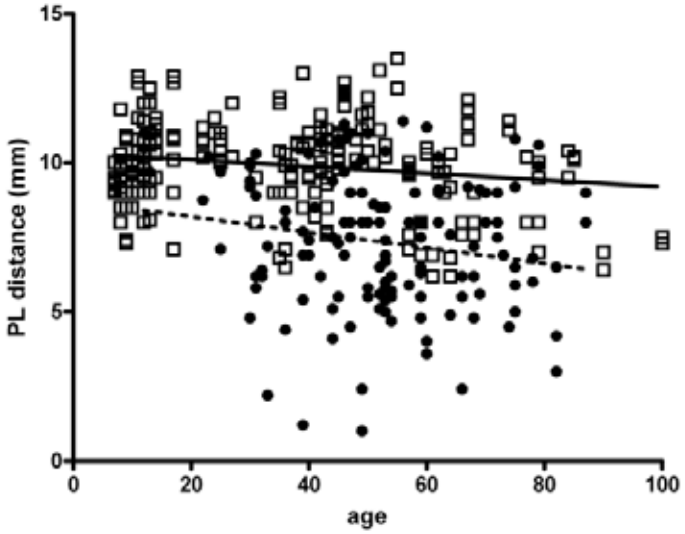

Figure 5. Relationship between plica-limbal distance (mm) and age (years) in individuals without (£) and with pterygium (ò).

Discussion

Insight into the etiology and pathogenesis of pterygium can contribute to the diagnosis and treatment of this ocular disorder. On the basis of previous data [9-13], we hypothesized that tractional forces may be active during pterygium formation, that these forces may pull stronger at the nasal than at the temporal side, and that this may lead to shortening of the plica-limbal distance. Assessing plica-libal distance in eyes without pterygium and in eyes with pterygia of a wide variety of sizes, the results from this study may support this hypothesis.

This supposition is based on two observations. Firstly, plica-limbal distances of eyes with primary medial pterygium were consistently and significantly smaller (on average approximately three-quarters) when compared to those of eyes without pterygium. This hints that a relatively small plica-limbal distance may represent a characteristic of pterygium that may help in the identification of individuals at risk for this condition. Secondly, plica-limbal distance appeared to correlate inversely with pterygium size. Assuming that the size of the lesion may correspond to the degree of development of the pterygium, this raises the possibility that plica-limbal distance shortens progressively during the formation of this lesion, possibly as a result of tractional forces reported to be operative in this process [9-13].

Support for these assumptions is provided by the observation that individuals suffering from conditions associated with fornix contraction are more susceptible to pterygium-like lesions such as acquired and congenital symblepharon as well as pseudopterygium [16]. Indeed, such conditions are often accompanied by shallowing of the conjunctival sac and shortening of the fornico-limbal distance [17] Unfortunately, this is easily overlooked if the eyelids are not averted. Pseudopterygium, for instance, is regularly attributed to corneal or limbal trauma, ignoring the possibility of a preexisting symblepharon [16,18]

Additional support for a role for plica-limbal distance in the development of pterygium is the fact that surgical procedures that accomplish the successful removal of pterygia concomitantly achieve enlargement of the plica-limbal distance. This holds true for, for instance, the placement of sound conjunctival or amniotic tissue as a barrier to the limbus following pterygium excision, and the removal of subconjunctival fibrotic tissue during pterygium excision that is accompanied by retraction of remaining pterygium or conjunctival tissue to the cantal region [19] In fact, surgical procedures that manage to totally and permanently cover the longer plica-limbal distance with epithelial tissue or basement membrane after pterygium excision have ten times less recurrence rates when compared to the bare sclera procedure [19,20]

Our results indicate furthermore that the mean plica-limbal distance in males and females did not differ significantly from each other. This observation is in line with those from several others carried out in different parts of the world [3-8], according to which pterygium manifested either not significantly or only slightly more often in males than in females. On the other hand, the results from case-control studies carried out in Australia and Jordania suggested the opposite, reporting that this condition occurred almost 2 and 6 times, respectively, more frequently in men than in women [4,5]. Thus, further investigations on the male-female distribution of pterygium are warranted

Various epidemiologic studies suggest that the incidence of pterygium is age-dependent and that older individuals run a

greater risk to develop this condition than younger ones [3,4]. Thus, if plica-limbal distance and pterygium size are indicators of anatomical and/or physiological mechanisms associated with pterygium formation, as suggested above, a shorter plica-limbal distance should occur more often in older than in younger individuals. Surprisingly, our results indicated that plica-limbal distances in eyes with pterygium decreased at a comparable rate with older age as in eyes without pterygium, but were at every age consistently shorter. This is in agreement with the data mentioned above, and suggests that the development of pterygium may be related to shortening of an already shorter plica-limbal distance rather than to merely shortening of the plica-limbal distance. Obviously, this hypothesis needs also to be verified in future studies.

Summarizing, the results from this study suggest the existence of an inverse correlation between plica-limbal distance and the presence of primary medial pterygium. This finding may help in the identification of individuals at risk to develop pterygium. In this respect, the preliminary results from follow-up studies after six years with 34 previously non-pterygium patients who had participated in the present study, indicated the development of 9 pterygia in eyes with the shortest plica-limbal distance. Our observations provide also support for procedures that increase the plica-limbal distance rather than those that merely excise the lesion. Such procedures may involve pterygium undermining and recession with autograft secured to the sclera, and may spare conjunctiva and prevent recurrences.

Reference List

1. Hill JC, Maske R (1989) Pathogenesis of pterygium. Eye 3 (Pt 2): 218-226.
2. Taylor HR (1980) Aetiology of climatic droplet keratopathy and pterygium. Br J Ophthalmol 64: 154-163.
3. Saw SM, Tan D (1999) Pterygium: prevalence, demography and risk factors. Ophthalmic Epidemiol 6: 219-228.
4. McCarty CA, Fu CL, Taylor HR (2000) Epidemiology of pterygium in Victoria, Australia. Br J Ophthalmol 84: 289-292.
5. Al-Bdour M, Al-Latayfeh MM (2004) Risk factors for pterygium in an adult Jordanian population. Acta Ophthalmol Scand 82: 64-67.
6.
Schellini SA, dos Reis Veloso CE, Lopes W, Padovani CR, Padovani CR (2005) Characteristics of patients with pterygium in the Botucatu region. Arq Bras Oftalmol 68: 291-294.
7. Paula JS, Thorn F, Cruz AAV (2005) Prevalence of pterygium and cataract in indigenous populations of the Brazilian Amazon rain forest. Eye 20: 533-536.
8. Nemesure B, Wu SY, Hennis A, Leske MC (2008) Nine-year incidence and risk factors for pterygium in the barbados eye studies. Ophthalmology 115: 2153-2158.
9. Di GN, Chui J, Coroneo MT, Wakefield D (2004) Pathogenesis of pterygia: role of cytokines, growth factors, and matrix metalloproteinases. Prog Retin Eye Res 23: 195-228.
10. Digirolamo N, Coroneo M, Wakefield D (2005) Epidermal growth factor receptor signaling is partially responsible for the increased matrix metalloproteinase-1 expression in ocular epithelial cells after UVB radiation. Am J Pathol 167: 489-503.
11. Touhami A, Di Pascuale MA, Kawatika T, Del VM, Rosa RH, Jr., et al. (2005) Characterisation of myofibroblasts in fibrovascular tissues of primary and recurrent pterygia. Br J Ophthalmol 89: 269-274.
12. Denion E, Chambaz A, Dalens PH, Petitbon J, Gerard M (2007) Plica semilunaris temporal ectopia: evidence of primary nasal pterygia traction. Cornea 26: 769-777.
13. Coroneo MT, Muller-Stolzenburg NW, Ho A (1991) Peripheral light focusing by the anterior eye and the ophthalmohelioses. Ophthalmic Surg 22: 705-711.
14. Detorakis ET, Spandidos DA (2009) Pathogenetic mechanisms and treatment options for ophthalmic pterygium: trends and perspectives (Review). Int J Mol Med 23: 439-447.
15. Bueno-Gimeno I, Montés-Micó R, España-Gregori E, Pons A (2002) Epidemiologic study of pterygium in a Saharan population. Annals of Ophthalmology 34: 43-46.
16. Shimazaki J, Shinozaki N, Tsubota K (1998) Transplantation of amniotic membrane and limbal autograft for patients with recurrent pterygium associated with symblepharon. Br J Ophthalmol 82: 235-240.
17. Memarzadeh F, Chuck RS, McCulley TJ (2006) Fornix reconstruction with conjunctival inclusion cyst marsupialization in Stevens-Johnson syndrome. Ophthal Plast Reconstr Surg 22: 475-476.
18. Gagnon MR, Dickinson PJ (2005) Ocular surface injury from a microwave superheated egg resulting in a pseudopterygium. Eye Contact Lens 31: 109-110.
19. Katircioglu YA, Altiparmak UE, Duman S (2007) Comparison of three methods for the treatment of pterygium: amniotic membrane graft, conjunctival autograft and conjunctival autograft plus mitomycin C. Orbit 26: 5-13.
20. Kenyon KR, Wagoner MD, Hettinger ME (1985) Conjunctival autograft transplantation for advanced and recurrent pterygium. Ophthalmology 92: 1461-1470.