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Systematic Review: The Effects of Pterygium and Pingueculum on The Ocular Surface and the Efficacy of Surgical Excision

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Abstract

Purpose: This systematic review examines the specific effects of pingueculum/pterygium on the ocular surface and evaluates the efficacy of surgical excision in reversing those effects.

Methods: A systematic review was performed according to the Preferred Reporting Items for the Systematic Review and Meta-Analyses (PRISMA) Statement and included 59 articles studying the effects of pingueculum/pterygium on the ocular surface as measured by tear break-up time (TBUT), Schirmer Testing, tear osmolarity, Ocular Surface Disease Index (OSDI), and the effects of surgical removal on these ocular surface parameters.

Results: In the majority of studies, eyes with a pterygium as compared to control eyes had a statistically significantly lower TBUT (average 3.72 s), lower Schirmer I without anesthesia (average 3.01 mm), lower Schirmer II (average 4.10 mm), higher tear osmolarity (average 12.33 mOsm/L), and higher OSDI (average 6.82 points). Moreover, excision of the pterygium/pingueculum led to a statistically significantly higher TBUT (average 3.15s higher at one month post-excision), lower tear osmolarity (average 3.10 mOsm/L lower at three months post-excision) and lower OSDI score (average 2.86 points lower one month post-excision) in a majority of the studies. The effect of excision on Schirmer test scores were equivocal, as a majority of studies did not reach significance.

Conclusions: Our data confirms the relationship between pterygium/pingueculum, abnormal tear function and symptoms of DED. Further, the data suggests that tear film parameters may improve after surgical removal of a pterygium/pingueculum. Future studies would be helpful in exploring the potential role of pterygium/pingueculum excision in the management of DED.

Keywords

Pterygium; Pingueculum; Dry Eye Disease; Excision; TBUT

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INTRODUCTION

Pingueculum and pterygium are diseases of the ocular surface. A pingueculum is characterized by fibro-fatty degenerative change in the bulbar conjunctiva within the palpebral aperture. In contrast, a pterygium is characterized by the proliferation and invasion of fibrovascular tissue from the bulbar conjunctiva onto the cornea. Complications of pingueculum/pterygium include chronic discomfort, changes to the tear film, astigmatism and decreased vision from involvement of the visual axis.

Certain environmental factors are thought to increase the risk of developing pingueculum/pterygium. Excessive exposure to sunlight and ultraviolet (UV) radiation are thought to increase the risk of developing these conditions, with pterygium having a stronger association.[(1)] One proposed mechanism is that UV irradiation causes a mutation in the p53 tumor suppressor gene, leading to the activation of transcription factors such as activator protein 1 (AP-1) and nuclear factor kappa B (nF-kB) that promote the formation of pterygium.[(2)] In addition, there is an association of pingueculum/pterygium with other ocular diseases. For example, there is evidence that pterygium is more prevalent in patients with dry eye disease (DED). One study found that a patient with a pterygium was more than three times more likely to have dry eye than a patient without a pterygium.[(3)]

Whether tear dysfunction causes pingueculum/pterygium growth or vice versa is unclear. The fact that the medial conjunctiva of the eye is more frequently affected by pingueculum/pterygium than the temporal conjunctiva lends support to the theory that tear dysfunction plays a pathogenic role in pingueculum/pterygium formation.[(4, 5)] It has been proposed that since the conjunctiva temporal to the cornea is situated below the lacrimal gland, it is less prone to drying, hence the relative rarity of pingueculum/pterygium in the temporal position.[(6)] Moreover, the components of tears, especially lactoferrin, which has antibacterial effects and is involved in the protection of the ocular surface, may prevent pingueculum/pterygium formation related to UV irradiation. Tear insufficiency in dry eye patients may lead to reduced protection against UV irradiation due to the deficiency of lactoferrin.[(7)] The formation of a pingueculum/pterygium may then lead to further dryness through altering tear dynamics and distribution across the ocular surface.

Many tests have been developed to assess for DED as well as general ocular surface health. For the purpose of this review, the authors chose to focus on tear break-up time (TBUT), Schirmer Testing, Tear Osmolarity and the Ocular Surface Disease Index (OSDI) due to the availability of literature studying these tear parameters in patients with pingueculum/pterygium. In addition, with the exception of tear osmolarity, these variables are frequently utilized in clinic due to their ease of use.

Tear break-up time is a measure of tear film stability and is performed via two variations. In the traditional TBUT assessment, the clinician instills a drop of fluorescein dye onto the surface of the patient’s eye and, under cobalt blue light, measures the time from the last blink to when the tear film first breaks up on the cornea. The longer the time, the more stable the tear film. During the assessment of non-invasive TBUT (NITBUT), tear film stability is measured automatically using a keratograph with software that detects the tear break-up of an image reflected from the ocular surface and the instillation of fluorescein is not used.

The Schirmer Test is a measure of tear volume and can be performed via multiple variations. The Schirmer I Test involves placing filter paper into the inferior temporal fornix of the eyelid. It can be further divided into two types – Schirmer I without topical anesthesia and Schirmer I with topical anesthesia. The Schirmer I Test without anesthesia measures basal tear secretion and reflex tear secretion together. In contrast, the Schirmer I Test with anesthesia measures only basal tear secretion. To reduce confusion, this study will refer to Schirmer I with anesthesia as the Basic Secretion Test. The Schirmer II Test is performed by using a cotton-tipped applicator to irritate the nasal mucosa and theoretically measures only reflex tear secretion of the main lacrimal gland.[(8)] For all of these variations, lower Schirmer Test values indicate smaller tear volumes.

Tear osmolarity is considered by some to be a proxy for ocular surface health and can be measured either directly via the TearLab osmometer (TearLab, San Diego, CA, USA) or indirectly via mucus fern testing. The TearLab osmometer is placed in the lower tear meniscus to obtain a direct reading of tear osmolarity. In mucus fern testing, tears are collected from the patient's eye and assessed under the microscope. The tear is allowed to dry, producing a characteristic crystallization pattern, described as a "tear fern". The patterns of crystallization are classified into four groups (I-IV) according to the criteria established by Rolando et al.[(9)] Hyperosmolar tears, which have an increased ratio of salts and macromolecules within the tear film, are categorized into groups III and IV. Regardless of testing modality, higher tear osmolarity is associated with dry eyes.

The OSDI is a survey that quantifies the severity of DED symptoms and their impact on vision-related functioning. It is made up of a 12-item questionnaire that is assessed on a scale of 0-100, with higher scores representing more severe disability from DED. This survey is being increasingly incorporated into studies examining efficacy of medical or surgical interventions on the symptoms of DED, as it has been shown to be a valid and reliable instrument for measuring the severity of symptoms in dry eye patients.[(10)]

Several studies have examined DED in patients with pingueculum/pterygium, but the results have been conflicting. In addition, few studies have evaluated the effects of pingueculum/pterygium excision on reversing the ocular surface effects associated with their growth. The purpose of this study is to review the available literature on pingueculum/pterygium and DED, with a focus on examining the specific effects of pingueculum/pterygium on tear function and evaluating the efficacy of surgical excision in reversing those effects. Furthermore, as the majority of studies found in the literature focused on pterygium, we will refer to pterygium throughout the paper and specify in the results section which studies included pingueculum in their analysis.

MATERIALS AND METHODS

This systematic review was performed according to the Preferred Reporting Items for the Systematic Review and Meta-Analyses (PRISMA) Statement.[(11)] The inclusion criteria for article selection were that the abstracts must mention a patient or patient population with pterygium or pterygium excision as well as TBUT, Schirmer Test, tear osmolarity or OSDI. Full text articles were then reviewed and excluded if the article included: a) studies of patients with pterygium that did not include a non-pterygium control group (either fellow non-involved eye or healthy patient), b) studies that did not compare the TBUT, Schirmer test, or tear osmolarity of patients with pterygium vs. controls, c) studies that did not compare the TBUT, Schirmer test, or tear osmolarity between patients with pterygium pre-excision vs. post-excision, and d) studies that were not available in English; specifically, a majority of the papers excluded were written in Chinese and published in International Eye Science. This search strategy was used to identify appropriate abstracts and subsequent articles from Pubmed, EMBase, Cochrane Library and Google Scholar. Candidate abstracts were identified using the keywords "pterygium," "pterygia" "pingueculum," "pinguecula," "dry eye disease," "Schirmer," "tear break-up time," "TBUT," "surgery," "excision," and "osmolarity." No date or language restrictions were applied to the database search. Two authors (T.L. and D.C.) performed the search and evaluated abstracts independently.

Of a total search of 2274 abstracts, 119 abstracts were selected as being relevant to our topic of interest. From the 119 total abstracts collected, 60 papers were excluded based on the above criteria. Of note, while there are several different surgical approaches, all studies looking at pingueculum/pterygium excision and DED were included in this review.

RESULTS

Pterygium vs. Control: Tear Break-up Time (TBUT)

Out of the 28 studies that examined TBUT in patients with pterygium vs. controls (Table 1) [3, 6, 7, 12–36], 21 were statistically significant, reporting a TBUT on average 3.72 s (30.27%) lower in patients with pterygium vs. controls (range 0.93 – 6.10 s, 8.74 – 51.33%). Seven studies did not find a statistically significant difference in TBUT between patients with pterygium vs. controls.

All studies were structured using a case-control format. The control group differed among studies in terms of whether the contralateral non-pterygium eye was used as control vs. eyes from healthy volunteers vs. a mix of contralateral eyes and healthy volunteers. With regards to how TBUT was measured, three studies used the OCULUS Keratograph® 5M (Oculus Optikgeräte GmbH, Wetzlar, Germany) device to measure an average NIBUT (NIBUTav) [15, 17, 22] while 23 studies used the traditional assessment of TBUT using fluorescein instillation with measurement after the last blink.

As detailed in Table 1, a majority of the studies used at least two or more measurements to record an average TBUT. The type of fluorescein strip used to instill fluorescein differed between the studies, ranging between 0.5%-2% for the five studies that specified this information.

Pterygium vs. Control: Schirmer Test

Twenty-eight studies compared tear secretion values between pterygium and control. Because tear secretion can be assessed in different ways, the studies were categorized by the method used: Schirmer I Test, Basic Secretion Test, Schirmer II Test (Table 2).[3, 7, 12–14, 16–27, 29–39] Some studies appear in more than one category if they conducted multiple types of tear tests.

Out of the 19 studies assessing Schirmer I Test values, 18 studies showed that average Schirmer I values were lower in pterygium eyes than in control eyes. However, only eight of these 18 studies (44%) achieved statistical significance, reporting Schirmer I values on average to be 3.42 mm (20.95%) lower in patients with pterygium vs. controls (range 1.40 – 6.00 mm, 8.64 – 34.09%). One of the 19 studies looking at Schirmer I values found that pterygium eyes had a higher average Schirmer I value compared to control eyes, but statistical significance was not achieved.

Out of the eight studies looking at the Basic Secretion Test, seven studies showed that average Basic Secretion values were lower in pterygium eyes than in control eyes. Five of the eight studies (62.5%) looking at Basic Secretion demonstrated statistical significance, reporting Basal Secretion values to be on average 3.01 mm (22.99%) lower in patients with pterygium vs. controls (range 2.08 – 3.70 mm, 17.06 – 26.81%). Interestingly, one of the eight studies found that pterygium eyes had higher average Basic Secretion values compared to control eyes, but no statistical significance was met.

Finally, out of the six studies assessing Schirmer II Test values, all six showed average Schirmer II values were lower in pterygium eyes than in control eyes. Four of the six studies (66%) were statistically significant, reporting Schirmer II values of, on average, 4.10 mm (27.58%) lower in patients with pterygium vs. controls (range 0.80 – 6.00 mm, 6.45 – 37.67%).

Pterygium vs. Control: Tear Osmolarity

Five studies were found that looked at tear osmolarity in patients with pterygium vs. controls, with one study evaluating with both the TearLab osmometer and mucus fern tests (Table 3).[14, 23, 27, 32, 33] Out of these six evaluations, five (83%) demonstrated that the presence of a pterygium is associated with increased tear osmolarity compared to control eyes, with all five evaluations achieving statistical significance. Of the three studies that used the TearLab osmometer, tear osmolarity was on average 12.33 mOsm/L (4.12%) higher in patients with pterygium vs. controls (range 7.00 – 17.00 mOsm/L, 2.34 – 5.56%). Of note, the study finding no significant difference in tear osmolarity between pterygium eyes and controls used the mucus fern pattern method and also found no statistically significant difference in TBUT between patients with pterygium vs controls.[32]

Pterygium vs. Control: OSDI

Four studies were found that analyzed the OSDI index in patients with pterygium vs. controls (Table 4).[17, 19, 22, 26] All four studies (100%) found that patients with pterygium had OSDI scores statistically significantly higher by an average of 6.82 points (59.37%) compared to control eyes.

Pterygium Pre- vs. Post-excision: TBUT, Schirmer Test, Tear Osmolarity, OSDI

Sixteen studies (Tables 5, 6, 7) were found that measured tear parameters before and at varying time points after surgical excision of pterygium. While a variety of surgical techniques can be utilized for pterygium removal including bare sclera, conjunctival autograft, and amniotic membrane graft, this paper does not delve into the differences in surgical techniques and the rates of pterygium recurrence with each technique.

There were 15 studies that analyzed TBUT pre- and post-pterygium excision. Out of the 15 studies, 13 studies demonstrated that TBUT increased after surgical excision as early as four weeks after surgery (Table 5).[5, 12, 13, 17, 40–50] Eight of these studies reached statistical significance (61.5%), reporting post-excision TBUT values at one month to be on average 3.15s (37.57%) higher compared to pre-excision (range 1.26 – 7.3 s, 16.20 – 137.74%). The trend in subsequent measurements demonstrated diminishing improvement relative to baseline TBUT values with a plateau at 12 months post-excision (3m (months): average 2.21 s (26.39%) higher, 12m and 18m: average 1.50 s (17.92%) higher). In two studies, no improvement in post-excision TBUT was seen; in one study, no difference was seen between pre-excision and post-excision TBUT.

Fourteen studies analyzed tear secretion via Schirmer testing pre- and post-excision (Table 6).[5, 12, 13, 17, 40–42, 44, 45, 47–51] Out of the 10 studies assessing Schirmer I Test values pre- and post-pterygium excision, eight studies showed average Schirmer I values were improved in post-excision eyes. One of the eight studies achieved statistical significance (12.5%), reporting average Schirmer I value to be 0.73 mm (12.03%) higher at one month and 1.2 mm (19.77%) higher at three months post-excision. Interestingly, one study found that the Schirmer I value worsened after pterygium excision, though this finding was not statistically significant. Additionally, one study reported no difference in Schirmer I values at three months post-excision, and improvement at 12 months post-excision, though this also did not meet statistical significance.

There were two studies that analyzed the Basic Secretion Test. One study showed that average Basic Secretion values were 0.80 mm (7.11%) higher at one month post-excision, which met statistical significance. The other study showed that average Basic Secretion values were 0.90 mm (6.77%) lower at one month post excision, but 2.00 mm (17.78%) higher at six months post excision; these findings were not statistically significant.

There were two studies assessing Schirmer II Test values. One study reported improvement in Schirmer II values post-excision, with the other reporting no difference in Schirmer II values at all measurement points post-excision; both studies did not achieve statistical significance.

There were four studies that analyzed tear osmolarity. Three of the four studies showed that tear osmolarity was statistically significantly lower in eyes after pterygium excision (Table 7).[42, 45, 47, 49] Two of these three studies were found to achieve statistical significance at all time points post-excision. The third study demonstrated that in patients with no pterygium recurrence, average tear osmolarity was statistically significantly improved at all time points post-excision (3.10 mOsm/L (1.02%) lower at three months, 4.90 mOsm/L (1.61%) lower at

12 months, and 4.80 mOsm/L (1.57%) lower at 18 months). This same study also demonstrated that in patients with pterygium recurrence, average tear osmolarity were statistically significantly lower at three months post-excision (2.40 mOsm/L (0.79%) lower), but did not improve significantly at 12 months (1.00 mOsm/L (0.33%) higher) and 18 months (2.70 mOsm/L (0.89%) higher) post excision. There was one study that reported no difference in tear osmolarity post-pterygium excision, which did not achieve statistical significance.

Only one study, Li et al., analyzed OSDI pre- and post-pterygium excision; this study found a statistically significant improvement in OSDI score post-excision of pterygium by 2.86 points (14.22%).[(17)]

DISCUSSION

Pterygium vs Control: Tear Film Stability (TBUT), Tear Secretion (Schirmer Tests), Tear Osmolarity, OSDI

Tear Film Stability (TBUT)—Overall, the majority of the studies (75%) suggest that the presence of pterygium is associated with statistically significantly decreased tear film stability of the affected eye by an average of 3.72 s (30.27% lower) compared to control eyes.

As various methodologies exist in carrying out TBUT measurements including designating of controls, number of measurements averaged, and invasive vs. non-invasive measurements, the authors reviewed the papers to identify any possible elements that may have led a study to conclude pterygium was associated with a lower TBUT or normal TBUT compared to control eyes. There were 28 total studies that evaluated TBUT. Seven of the 28 studies used the contralateral, non-pterygium eye as the control, with all seven (100%) reporting TBUT to be statistically significantly lower in pterygium eyes compared to fellow eyes. Fifteen of the 28 studies used healthy age and sex -matched controls, with 11 of the 15 studies (73%) reporting TBUT to be statistically significantly lower in pterygium eyes compared to fellow eyes. The remaining six studies had control groups as follows: two studies used a mix of healthy controls and fellow eyes as the control, with only one of these studies meeting statistical significance; four studies did not specify the nature of their control groups. This data suggests that while age and sex were appropriately matched between the cases and controls in the majority of these studies, other unaccounted factors may have served as confounding variables leading to only 73% of these studies achieving statistical significance compared to 100% of studies that used fellow eyes as controls. Hence, using a control group that consists of contralateral fellow eyes may be preferred. With regards to other variables such as number of measurements averaged or invasive vs. NITBUT testing, there was no clear pattern that suggested they may have impacted the TBUT results.

One mechanism by which pterygium may affect TBUT is through the presence of increased inflammatory factors that can infiltrate meibomian glands, ultimately leading to gland dysfunction; another hypothesis is that presence of pterygium can cause meibomian gland dysfunction by physically compressing the palpebral conjunctiva over long periods of time.

[22] Presence of pterygium may affect TBUT via disruption of the ocular surface by decreasing goblet cell density/mucin production as well.[49]

Tear Secretion (Schirmer I Test, Basic Secretion Test, Schirmer II Test)—With regards to tear secretion, the data is equivocal in terms of whether pterygium is associated with decreased tear production in comparison to normal eyes. The authors tried to isolate the various aspects of tear production by grouping the studies into Schirmer I (basal and reflex tear production), Basic Secretion Test (basal tear production), and Schirmer II (reflex tear production). Even when stratifying the studies into these aspects of tear production, the results were mixed whether pterygium impacted tear secretion or not. One might argue that consensus was highest in the studies looking at reflex tear production (Schirmer II Test), as 66% of the studies looking at Schirmer II showed statistically significantly decreased tear volume in pterygium eyes compared to control eyes by an average of 4.10 mm (27.58%). Comparatively, 62.5% of studies looking at basic secretion showed statistically significantly decreased tear volume in pterygium eyes compared to control eyes by an average of 3.01 mm (22.99%). However, at such low sample sizes of six and eight respectively, the data may not be robust enough to make any meaningful conclusions. It could be said that the least reliable Schirmer method is Schirmer I, whereby only 44% of studies looking at Schirmer I showed statistically significant decreased tear volume in pterygium eyes compared to control eyes by an average of 3.42 mm (20.95%).

The equivocal data regarding tear secretion can lead one to either conclude that there is no significant difference in tear secretion between pterygium and non-pterygium involved eyes, or that tear secretion tests such as Schirmer testing are poorly reproducible and unreliable. Prior studies have shown Schirmer tests to have generally poor reproducibility in accurately detecting aqueous tear deficiency, with one study showing a reproducibility of only 41.9%.[52–54] Additionally, wide variability existed in the methodologies described by the studies included in this literature review, including type of anesthesia used, whether the examiner allowed the patient to keep his/her eyes open or closed, what type of filter paper was used, and what part of the inferior fornix the filter paper was placed. Furthermore, many papers did not describe their methodology in detail, making it difficult to meaningfully analyze the studies for underlying variables that may be associated with decreased or increased tear secretion. When looking at the available parameters, one study demonstrated that eyelid position drastically affects Schirmer values.[55] However, together with the other studies in this review, eyes being closed/open did not seem to affect the outcome of whether pterygium was associated with decreased or normal tear production.

Tear Osmolarity—Tear osmolarity is a function of tear secretion and tear evaporation. Higher tear osmolarity is associated with ocular surface disease because hyperosmotic stress is thought to increase cell shrinkage, denature proteins, and alter cell functions. From our review, four of the five studies that looked at tear osmolarity demonstrated statistically significantly higher tear osmolarity in patients with pterygium vs. controls. For those using the TearLab osmometer, it was found that tear osmolarity was on average 12.33 mOsm/L (4.12%) higher in patients with pterygium vs. controls. These findings may support Julio et. al. who posited that pterygium causes decreased goblet cell density, leading to a hyperosmolar environment with subsequent inflammation of the ocular surface, leading to abnormal tear stability but normal tear volume.[27] The findings in this review could also support that pterygium eyes have more evaporative loss of the aqueous component of tears, leaving behind a higher osmolarity solution. However, it is difficult to draw any meaningful conclusions from this data given tear ferning is no longer commonly used in practice and only three studies evaluated tear osmolarity with the TearLab osmometer.

OSDI—The OSDI has been proven to be a valid and reliable method of quantifying the severity of DED in the clinical setting. Though there were only four studies that incorporated this metric for analysis in this review, it is telling that all four reported the OSDI to be statistically significantly higher in pterygium eyes compared to control eyes. This further supports that presence of pterygium is associated with DED and its corresponding symptoms.

Effects of Surgery on the Tear Film

The latter half of this review looked at studies evaluating the ocular surface pre and post-excision of pterygium. With regards to TBUT, eight out of the 15 studies (53%) indicated that TBUT increased significantly after pterygium excision by an average of 3.15 s (37.57%) as early as four weeks after surgery. This improvement diminished over time with a plateau with average improvement in TBUT of 1.50 s (14.00%) at 12 months post-excision. These findings suggest that the presence of pterygium leads to decreased TBUT, while also demonstrating improvement in TBUT after pterygium excision. Again, while the mechanism by which this occurs is currently unclear, it may involve improvement in meibomian gland function due to decreased inflammatory milieu affecting the meibomian glands, lack of compression by the excised pterygium, improvement in goblet cell density and mucin production, less evaporation of the aqueous portion of tear film, or simply, more even spreading of tear film across the corneal surface.

As tear stability and tear osmolarity seem to be correlated in function, it is unsurprising that tear osmolarity improved with excision of pterygium, as seen by an average decrease in tear osmolarity of 2.75 mOsm/L (0.90%) at three months after pterygium excision in the statistically significant studies. By the theory posited by Julio et al., excision of pterygium can lead to an improved osmolar environment with subsequent normalization of goblet cell density.[27] With recovery of goblet cells, markers of tear stability such as TBUT would improve as well.

With regards to tear secretion, the majority of the studies did not show any statistically significant difference in tear production pre- and post-excision. Even when stratifying assessment of tear secretion into basal tear production, reflex tear production, or the combination of the two, there is no clear effect of presence of pterygium on tear secretion. This finding lends support towards the idea that presence of pterygium does not affect actual tear production itself.

Finally, while there was only one study that examined OSDI in pre- and post-pterygium excision patients, it demonstrated a statistically significant improvement in OSDI after pterygium excision. While only one study, this data indicates that the symptoms of DED may be directly related to the presence of pterygium, and indicates the quantifiable clinical improvement in DED symptoms that could be seen in patients after pterygium excision.

In summary, these studies demonstrate that surgical excision, regardless of method, may improve ocular surface parameters, specifically tear stability and ocular surface osmolarity caused by pterygium as early as four weeks post-excision as long as the pterygium did not recur. On a broader scale, these studies imply that the tear film changes associated with pterygium are secondary to the growth of the pterygium rather than due to tear dysfunction causing pterygium growth.(17) This information coupled with the improvement in OSDI after pterygium excision in Li et al. is in support of the improvement in both tear stability and clinical dry eye symptoms seen after pterygium excision; this is akin to the improvement of tear stability and clinical dry eye symptoms seen after surgical removal of conjunctivochalasis.(56) The data suggests that removal of pterygium may be advantageous in patients suffering from symptoms of DED, even in those patients not experiencing changes in visual acuity or reporting cosmesis complaints. In such patients, severity of DED should be determined pre-excision by TBUT, Schirmer Tests, tear inflammatory markers and OSDI, with those experiencing severe disease undergoing pterygium removal as a possible way to improve their DED. Such measurements should also be recorded after pterygium excision to track tear film stability and clinical symptoms of DED over time.

Future Studies

Future studies that look at pterygium and tear function should attempt to utilize a homogeneous group of controls consisting of only contralateral eyes of patients with unilateral pterygium or age- and sex-matched controls. TBUT should be carried out with modified fluorescein strips, which have shown to be more reproducible.(57) TBUT should be measured three times, reporting an average of the three values, as studies have confirmed that taking the average of multiple TBUT readings improves reproducibility of the test.(58) Additionally, the investigator should note any corneal pathology such as scars or nodules as these may affect TBUT measurements. The use of FD-OCT to analyze the tear film, which has good reproducibility, may be preferable to using the Schirmer Test.(59) If utilizing the Schirmer Test, the following is recommended: studies should utilize the Schirmer I Test, and perform the test both with and without anesthesia to elucidate any differences between basal and reflex tearing. Patients should be instructed to keep their eyes closed during the Schirmer Test to minimize potential differences attributed to testing environment. Schirmer strips should be placed in both the infero-temporal and infero-nasal fornices to determine how proximity to pterygium affects results. While tear osmolarity could be helpful with the development of the TearLab osmometer, the measurements often are wide in variability. It may be more advantageous to measure inflammatory mediators such as cytokines and matrix metalloproteinases within the tear film, as it could provide a method of quantifying the amount of inflammation present in relation to the level of meibomian gland dysfunction as represented by symptoms of DED.

While the studies reviewed in this paper looked at pterygium's effect on the ocular surface and the effect of surgery on improving tear film parameters, it would be clinically useful for future studies to confirm on a broader scale that surgery reduces symptoms of tear dysfunction in patients. Including the OSDI score in future analyses can help to quantify the amount of symptomatic benefit one can realistically expect to gain after pterygium excision, and would be useful information to include for clinicians evaluating patients with pterygium pre- and post-surgery.

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Table 1.

TBUT in Eyes with Pterygium vs. Normal Controls.

TBUT was found to be significantly lower in patients with pterygium vs. controls in 21 of 28 studies. Eighteen studies reported TBUT as an average of three measurements, three studies reported TBUT as an average of less than three measurements, and seven studies did not specify the number of measurements used to determine TBUT.

Year	Author	n = No. patients, No. eyes	Results	No. measurements
2020	Zhao et al.[12]	n = 35, 40	4.02 s lower in pterygium[†]	2
2020	Patkar et al.[13]	n = 100, 200	0.93 s lower in pterygium[†]	1
2019	Safarzadeh et al.[14]	n = 95, 190	4.50 s lower in pterygium[†]	3
2019	Wanzeler et al.[15]	n = 83, 83	0.73 s lower in pterygium[N]	Not reported
2019	Gupta et al.[16]	n = 50, 100	2.08 s lower in pterygium[†]	3
2019	Li et al.[17]	n = 108, 108	3.03 s lower in pterygium[†N]	Not reported
2018	Küçük et al.[18]	n = 64, 96	5.40 s lower in pterygium[†1]	3
2017	Ye et al.[19]	n = 80, 80	3.90 s lower in pterygium[†]	3
2017	Manhas et al.[20]	n = 270, 270	4.34 s lower in pterygium[†]	3
2017	Antony et al.[21]	n = 100, 200	3.60 s lower in pterygium[†]	Not reported
2017	Wu et al.[22]	n = 99, 99	2.90 s lower in pterygium[†N]	Not reported
2014	Ozsutcu et al.[23]	n = 65, 130	2.00 s lower in pterygium[†]	3
2014	Kampitak et al.[24]	n = 92, 184	5.80 s lower in pterygium[†]	Not reported
2014	Gonnermann et al.[25]	n = 40, 40	6.10 s lower in pterygium[†]	1
2014	Hashemi et al.[26]	n = 1008, 1008	Lower in pterygium[2]	3
2013	Roka et al.[3]	n = 228, 228	5.96 s lower in pterygium[†]	3
2013	Rajab et al.[28]	n = 110, 110	3.60 s lower in pterygium[†3]	3
2012	Julio et al.[27]	n = 60, 60	No difference	3
2010	Bandyopadhyay et al.[29]	n = 100, 100	Lower in pterygium[†2]	Not reported
2009	Lu et al.[30]	n = 2112, 2112	Lower in pterygium[†2]	3
2006	Lekhanont et al.[31]	n = 550, 550	Lower in pterygium[†2]	3
2005	Balogun et al.[6]	n = 221, 221	1.96 s lower in pterygium[†4]	3
2001	Ishioka et al.[7]	n = 20, 40	3.30 s lower in pterygium[†]	1
2001	Ergin et al.[32]	n = 129, 202	1.38 s lower in pterygium	3
1998	Kadayifçilar et al.[33]	n = 140, 140	3.57 s lower in pterygium[†]	3
1991	Rajiv et al.[34]	n = 106, 106	4.80 s lower in pterygium[5]	Not reported

Year	Author	n = No. patients, No. eyes	Results	No. measurements
1984	Pandey et al.(35)	n = 1400, 1763	No difference[6,2]	3
1980	Taylor et al.(36)	n = 30, 54	Lower in pterygium[2]	3

[†] Statistically significant

[N] Average non-invasive tear break up time (NIBUTav)

[1] Study included pingueculum only

[2] Absolute values not reported

[3] Study included pterygium and pingueculum; 3.60 s lower in pterygium, 3.90 s lower in pingueculum

[4] Study included pterygium and pingueculum; 1.96 s lower in pterygium, 0.90 s higher in pingueculum

[5] Statistical values not reported

[6] Abnormal TBUT defined as < 30 s

Table 2.

Schirmer Test in Eyes with Pterygium vs. Controls.

Schirmer I Test was found to be significantly lower in patients with pterygium vs. controls in eight of 19 studies. Basic secretion test was found to be significantly lower in patients with pterygium vs control in five of eight studies. Schirmer II test was found to be significantly lower in patients with pterygium vs controls in four of six studies. The majority of the above studies used industry standard Schirmer tear test filter paper. Eyelid position, when specified, was either open with blinking as necessary or closed for the entire test without blinking.

	Year	Author	n = No. patients, No. eyes	Result	Eyelid position
Schirmer I Test					
	2020	Zhao et al.[12]	n = 35, 40	2.40 mm lower in pterygium[†]	O
	2020	Patkar et al.[13]	n = 100, 200	1.54 mm lower in pterygium[†]	O
	2019	Safarzadeh et al.[14]	n = 95, 190	4.60 mm lower in pterygium[†]	U
	2019	Gupta et al.[16]	n = 50, 100	1.98 mm lower in pterygium[†1]	U
	2019	Li et al.[17]	n = 108, 108	0.41 mm lower in pterygium	C
	2017	Ye et al.[19]	n = 80, 80	1.40 mm higher in pterygium	U
	2017	Manhas et al.[20]	n = 270, 270	3.23 mm lower in pterygium[†]	O
	2017	Antony et al.[21]	n = 100, 200	4.60 mm lower in pterygium[†]	U
	2017	Wu et al.[22]	n = 99, 99	1.82 mm lower in pterygium	C
	2014	Ozsutcu et al.[23]	n = 65, 130	1.40 mm lower in pterygium[†]	U
	2014	Gonnermann et al.[25]	n = 40, 40	0.20 mm lower in pterygium	U
	2013	Roka et al.[3]	n = 228, 228	4.03 mm lower in pterygium	U
	2012	Julio et al.[27]	n = 60, 60	1.00 mm lower in pterygium	C
	2010	Bandyopadhyay et al.[29]	n = 100, 100	Lower in pterygium[†2]	U
	2006	Lekhanont et al.[31]	n = 550, 550	Lower in pterygium[2]	U
	2001	Ishioka et al.[7]	n = 20, 40	0.80 mm lower in pterygium	U
	1998	Kadayifçilar et al.[33]	n = 140, 140	2.76 mm lower in pterygium	O
	1991	Rajiv et al.[34]	n = 106, 106	7.40 mm lower in pterygium[3]	U
	1980	Taylor et al.[36]	n = 30, 54	Lower in pterygium[2]	O
Basic Secretion Test					
	2017	Manhas et al.[20]	n = 270, 270	2.08 mm lower in pterygium[†]	O
	2014	Hashemi et al.[26]	n = 1008, 1008	Higher in pterygium[2]	U
	2013	Roka et al.[3]	n = 228, 228	3.24 mm lower in pterygium[†]	U
	2009	Lu et al.[30]	n = 2112, 2112	Lower in pterygium[†2]	C
	2006	Lekhanont et al.[31]	n = 550, 550	Lower in pterygium[†2]	U

	Year	Author	n = No. patients, No. eyes	Result	Eyelid position
	2001	Ishioka et al.[7]	n = 20,40	3.70 mm lower in pterygium†	U
	2001	Ergin et al.[32]	n = 129, 202	2.41 mm lower in pterygium	O
	1978	Biedner et al.[37]	n = 60, 120	0.32 mm lower in pterygium	U
Schirmer II Test					
	2020	Patkar et al.[13]	n = 100, 200	0.59 mm lower in pterygium	O
	2018	Küçük et al.[18]	n = 64, 96	6.00 mm lower in pterygium†4	O
	2017	Antony et al.[21]	n = 100, 200	5.50 mm lower in pterygium†	U
	2014	Gonnermann et al.[25]	n = 40, 40	2.11 mm lower in pterygium	U
	2010	Bandyopadhyay et al.[29]	n = 100, 100	Lower in pterygium†2	U
	2003	Chaidaroon et al.[38]	n = 30, 60	0.80 mm lower in pterygium†	O
Unspecified					
	2014	Kampitak et al.[24]	n = 92, 184	0.20 mm lower in pterygium	U
	1984	Pandey et al.[35]	n = 1400, 1763	6.61 mm lower in pterygium†	U
	1983	Pandey et al.[39]	n = 1200, 1400	10.11 mm lower in pterygium†	U

O = open, C = closed, U = unspecified

†Statistically significant

1Significant for pterygium ≥ 2 mm, but not significant for pterygium < 1 mm or 1-2 mm

2Absolute values not reported

3Significance unspecified

4Study included pingueculum only

Table 3:
Tear Osmolarity in Eyes with Pterygium vs. Controls.

Two studies used the TearLab osmometer, two studies used mucus fern testing, and one study used both the TearLab osmometer and Mucus Fern testing. Tear osmolarity was found to be statistically significantly higher in patients with pterygium vs. controls in five of the six evaluations. One study reported finding no difference in tear osmolarity between patients with pterygium vs. controls.

Year	Author	n = No. patients, No. eyes	Method	Results
2019	Safarzadeh et al.(14)	n = 95, 190	TearLab osmometer	Higher in pterygium†
2014	Ozsutcu et al.(23)	n = 65, 65	TearLab osmometer	Higher in pterygium†
2012	Julio et al.(27)	n = 30, 30	TearLab osmometer	Higher in pterygium†
2012	Julio et al.(27)	n = 30, 30	Mucus Fern	Higher in pterygium†
2001	Ergin et al.(32)	n = 84, 112	Mucus Fern	No difference
1998	Kadayifçilar et al.(33)	n = 70, 70	Mucus Fern	Higher in pterygium†

†Statistically significant

Table 4.

OSDI in Eyes with Pterygium vs. Controls.

All four studies reported an OSDI that was statistically significantly higher in pterygium eyes vs. controls.

Year	Author	n = No. patients, No. eyes	Results
2019	Li et al.[17]	n = 108, 108	Higher in pterygium †
2017	Ye et al.[19]	n = 80, 80	Higher in pterygium †
2017	Wu et al.[22]	n = 99, 99	Higher in pterygium †
2014	Hashemi et al.[26]	n = 1008, 1008	Higher in pterygium †

†Statistically significant

Table 5.

TBUT in Eyes with Pterygium Pre-excision vs. Post-excision.

The majority of studies found that TBUT improved after pterygium removal in the affected eye. Improvement was seen across varying surgical techniques as seen above. Improvement in TBUT was seen earliest at the four week mark status-post pterygium removal.

Year	Author	n = No. patients, No. eyes	Surgical Technique	Follow-up Period (m)	Results post-surgery
2020	Zhao et al.[12]	n = 35, 40	Limbal-conjunctival autograft	1, 3	Improvement
2020	Patkar et al.[13]	n = 100, 200	Limbal-conjunctival autograft	10d, 1, 2	Improvement
2019	Li et al.[17]	n = 108, 108	Limbal-conjunctival autograft	1, 3, 6	Improvement[†]
2019	Jeong et al.[5]	n = 30, 30	Conjunctival autograft	1, 3	Improvement[†]
2017	Drvmvrvprasadarao et al.[40]	n = 80, 80	Conjunctival autograft	3, 12, 18	Improvement[†1]
2017	Mittal et al.[41]	n = 43, 43	Conjunctival autograft	6	Improvement
2016	Julio et al.[42]	n = 32, 32	Limbal-conjunctival autograft	1	No difference
2015	Yu et al. [43]	n = 57, 83	Conjunctival graft w/ scleral fixation	3	Improvement[†2]
2015	Kampitak et al.[44]	n = 40, 40	Amniotic membrane graft	1	Improvement
2013	Türkyılmaz et al.[45]	n = 74, 74	Dissociated edges of conjunctiva sutured together	3, 12, 18	Improvement[†1]
2013	Yang et al.[46]	n = 38, 38	Limbal-conjunctival autograft	6w, 6, 12, 24	No Improvement
2013	Yang et al. [46]	n = 38, 38	Bare-sclera	6w, 6, 12, 24	No Improvement
2011	Wang et al.[47]	n = 60, 60	Limbal-conjunctival autograft	1	Improvement[†]
2009	Dong et al.[48]	n = 12, 12	Not Reported	1	Improvement[†3]
2007	Li et al.[49]	n = 70, 70	Bare-sclera	1	Improvement[†]
2006	Kiliç et al.[50]	n = 14, 14	Limbal-conjunctival autograft	1, 6	Improvement

m = months, d = days, w = weeks

[†] Statistically significant

[1] Significant for no recurrence of pterygium, not significant for recurrence of pterygium

[2] Patients with pterygium complicated with conjunctivochalasis

[3] Study included pingueculum only

Table 6.

Schirmer Test in Eyes with Pterygium Pre-excision vs. Post-excision.

The majority of studies demonstrated improvement in Schirmer values after pterygium excision. However, only two studies found this improvement to be statistically significant. The results seemed to be independent of surgical technique. Additionally, the majority of studies did not specify eyelid position during the tests.

	Year	Author	n = No. patients, No. eyes	Surgical Technique	Follow-up Period (m)	Results post-surgery	Eyelid position
Schirmer I Test							
	2020	Zhao et al.[12]	n = 35, 40	Limbal-conjunctival autograft	1, 3	Improvement	O
	2020	Patkar et al.[13]	n = 100, 200	Limbal-conjunctival autograft	10d, 1, 2	Improvement	O
	2019	Li et al.[17]	n = 108, 108	Limbal-conjunctival autograft	1, 3, 6	Improvement	C
	2019	Jeong et al.[5]	n = 30, 30	Conjunctival autograft	1, 3	Improvement[†]	U
	2017	Drvmvrvprasadarao et al.[40]	n = 80, 80	Conjunctival autograft	3, 12, 18	Improvement[1]	U
	2017	Mittal et al.[41]	n = 43, 43	Conjunctival autograft	6	Improvement	U
	2016	Julio et al.[42]	n = 32, 32	Limbal-conjunctival autograft	1	No Improvement	U
	2013	Türkyılmaz et al.[45]	n = 74, 74	Dissociated edges of conjunctiva sutured together	3, 12, 18	Improvement[1]	U
	2009	Dong et al.[48]	n = 12, 12	Not Reported	1	Improvement[2]	U
	2007	Li et al.[49]	n = 70, 70	Bare-sclera	1	Not Reported	U
Basic Secretion Test							
	2015	Kampitak et al.[44]	n = 40, 40	Amniotic membrane graft	1	Improvement[†]	U
	2006	Kiliç et al.[50]	n = 14, 14	Limbal-conjunctival autograft	1, 6	Improvement[3]	U
Schirmer II Test							
	2020	Patkar et al.[13]	n = 100, 200	Limbal-conjunctival autograft	10d, 1, 2	Improvement	O
	2017	Mittal et al.[41]	n = 43, 43	Conjunctival autograft	6	Improvement	U
Unspecified							
	2017	Wang et al.[51]	n = 56, 56	Conjunctival autograft	1d, 1w, 1, 6	Improvement	U
	2011	Wang et al.[47]	n = 60, 60	Limbal-conjunctival autograft	1	No difference	U

m = months, d = days, w = weeks, O = open, C = closed, U = unspecified

[†]Statistically significant

[1]Not significant for both no recurrence of pterygium and recurrence of pterygium

[2]Study included pingueculum only

[3]1m: No improvement, 6m: Improvement

Table 7.

Tear Osmolarity in Eyes with Pterygium Pre-excision vs. Post-excision.

The majority of studies demonstrated statistically significant improvement in tear osmolarity post-excision of pterygium. Only one study demonstrated no difference, which was found to not be statistically significant. The results seemed to be independent of surgical technique.

Year	Author	n = No. patients, No. eyes	Surgical Technique	Follow-up Period (m)	Results post-surgery
2016	Julio et al.[42]	n = 32, 32	Limbal-conjunctival autograft	1	No difference
2013	Türkyılmaz et al.[45]	n = 74, 74	Dissociated edges of conjunctiva sutured together	3, 12, 18	Improvement[†1]
2011	Wang et al.[47]	n = 60, 60	Limbal-conjunctival autograft	1	Improvement[†]
2007	Li et al.[49]	n = 70, 70	Bare-sclera	1	Improvement[†]

m = months

[†] Statistically significant

[1] Significant for no recurrence of pterygium at three, 12 and 18 months; significant for recurrence of pterygium at three months post-excision; not significant for recurrence of pterygium at 12 or 18 months post-excision