Pterygium recurrence and corneal stabilization point after pterygium excision using the controlled partial avulsion fibrin glue technique

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Abstract

**Background:** This study aimed to evaluate the pterygium recurrence rate and corneal stabilization point after pterygium excision via the controlled partial avulsion fibrin glue technique using multiple corneal parameters. **Methods:** One hundred eyes of 100 patients who had undergone primary pterygium excision surgery via the controlled partial avulsion fibrin glue technique were retrospectively reviewed. Corneal stabilization points were determined over four follow-up sessions (i.e., the 1st, 3rd, 6th, and 12th months after surgery) based on changes in Simulated-K, corneal irregularity measurement, shape factor, and toric mean keratometry. Post-operative courses were followed for 12 months after surgery. Recurrence was defined as the regrowth of fibrovascular tissue 1 mm past the corneoscleral limbus. **Results:** No sign of pterygium recurrence and the corneal stabilization point were observed at the third month post-operation. Significance improvements in all corneal parameters were noted between the 1st and 3rd months (both $p < 0.001$); however, insignificant changes were noted at the following 6th- and 12th-month visits (both $p > 0.05$). **Conclusion:** The controlled partial avulsion fibrin glue technique may improve surgical outcomes with long-term recurrence rates equal to or lower than those previously reported. Corneal surface recovery is completed after the third month of the excision procedure.

**Keywords:** cornea, fibrin tissue adhesive, pterygium, recurrence

Introduction

A common chronic non-communicable disease in tropical countries is pterygium, which is due to prolonged exposure to ultraviolet rays. Pterygium refers to a corneal-limbal disorder characterized by the abnormal growth of fibrovascular tissue originating from bulbar conjunctiva into the cornea. In terms of histology, pterygium is composed of the head of the conjunctival epithelium and hyperproliferative vascularization along the body of the degenerated connective tissue, which signifies elastotic degeneration. Because of these distinct characteristics, pterygium was previously considered to be a degenerative disorder. However, recent studies have proven that pterygium also has proliferative histological characteristics, such as mild dysplasia, local invasiveness, and abnormal p53 gene expression, and clinical features, notably a high recurrence rate following excision. The primary treatment for pterygium is surgical excision. Indeed, over the last two decades, several new approaches in surgical techniques have been proposed and promising success rates have been obtained. Some of these novel treatment modalities include bare sclera, adjuvant therapy using antimetabolites and β-irradiation, adjuvant surgery via conjunctival autograft, amniotic membrane transplantation, and the fibrin glue adhesive method.

The exact mechanisms or causes of pterygium proliferation remain unknown. However, the tendency of a pterygium to proliferate is most prominent when it recurs after excision. Aggressive fibrovascular proliferation is more common in recurrent pterygium compared with primary pterygium. Several studies have addressed pterygium recurrence and its incidence after pterygial tissue excision and surgical results may vary greatly according to the preoperative demographics, surgical techniques, and adjunctive treatments applied. Although a number of treatment options to manage pterygium are available, the primary outcome is still the same which is to explore treatment approach that provides minimum post-operative complications for patients and shorter operating time for surgeons.

The present study aims to evaluate the pterygium recurrence rate and corneal stabilization point subsequent to pterygium excision using the controlled
partial avulsion fibrin glue technique by evaluating changes in four corneal indices, namely, simulated-K (SimK), corneal irregularity measurement (CIM), shape factor (SF), and mean toric keratometry (TKM). Best-corrected visual acuity (BCVA) and contrast sensitivity function (CSF) with emphasis on oculovisual function were also evaluated. These parameters comprehensively represent changes in the anterior corneal surface and visual performance.

Methods

Study design. One hundred primary pterygium eyes from 100 patients who voluntarily participated in this prospective cohort study and visited a university eye specialist were recruited to this study to incorporate a wide range of pterygium severities in the analysis. All participants underwent full comprehensive optometric examination by a certified optometrist (MRH) and a consultant ophthalmologist (KMK). The number of participants recruited for this study was calculated according to the mean difference in corneal astigmatism (SimK) between pre- and 3-month post-operative patients reported in a previous study using Power and Sample Size Calculation software (Version 3.1.2; PS software, Nashville, TN, USA). The calculations revealed that a minimum number of 60 participants are required to achieve the desired level of significance (power, 90%; \( p < 0.05 \)).

Inclusion and exclusion criteria. All participants in this study were selected based on specific criteria. The inclusion criteria were an established diagnosis of primary pterygium, patients of either gender with ages between 20 and 70 years, and no history of ocular trauma, ocular surgery, and contact lens wear. Patients with significant ocular surface diseases, such as recurrent pterygium, corneal irregularity, and opacity due to diseases other than pterygium, were excluded. Patients for whom corneal topography could not provide reproducible measurements due to obstruction of the central cornea by pterygium were also excluded. This study was conducted according to the principles of the Declaration of Helsinki and approved by the ethical research committee of International Islamic University Malaysia (IIUM/310/G13/4/4-125). Written consent forms were obtained from all participants after they were explained the objectives and consequences of the study.

Pterygium Classification. Pterygium was classified according to Tan’s classification, and clinical grading was based on the transulence of the growth. Tan’s classification of pterygium divides pterygium into types of atrophy, intermediate, and fleshy. Grade I (atrophy) pterygium is defined as growth in which the underlying episcleral vessels are unobscured and clearly distinguished. Grade II (intermediate) pterygium is defined as a growth in which details of the episcleral vessel are indistinct or partially obscured. Finally, Grade III pterygium (fleshy) is defined as growth in which the underlying episcleral vessels are completely obscured. In the present study, diagnosis and classification of primary pterygium were conducted by a single consultant ophthalmologist (KMK).

Study procedures. All participants underwent standard optometric examination comprising dry refraction, slit-lamp examination, and fundus examination. Then, each participant’s average central corneal curvature (SimK and CIM) and overall corneal curvature (SF and TKM) indices were objectively measured using Zeiss ATLASTM 995 corneal topographers (Zeiss Meditec, Inc., Dublin, USA). Visual performance parameters (BCVA and CSF) were measured using an M&S Technologies Smart System II instrument (SSII, Park Ridge, IL, USA). The setting of this system is similar to those described in previous studies. Three measurements were taken, and the measurement with the best image quality was taken as the final measurement value. All measurements were carried out by a single operator and performed on the same visit. Then, all participants underwent pterygium excision as described in detail below; all operations were performed by a single surgeon (KMK). All participants were then followed up for a 1-year period divided into four sessions (i.e. the 1st, 3rd, 6th, and 12th months post-operation), and all corneal indices were measured following procedures established during the pre-surgical session. The same operator performed all procedures for all sessions. Photographs were taken on each data collection session to determine pterygium recurrence, which was defined as any fibrovascular growth 1 mm past the corneoscleral limbus and into the clear cornea.

Data analysis. Statistical analysis were performed using IBM SPSS (Version 19, SPSS Inc., Chicago, IL, USA). The normality of the data was evaluated using the ratio of skewness to kurtosis; here, a ratio of \( \pm 2.50 \) was considered to indicate a normal distribution. Comparisons of the mean of each set of measurements for all parameters were performed using one-way analysis of variance (ANOVA). Repeated-measures one-way ANOVA was then employed to determine significant differences in all intended parameters between all five sessions. Bonferroni post hoc analysis was employed to determine the session with the most significant changes, and statistical significance was established at \( p < 0.05 \).

Surgical procedures. This study adopted a standardized procedure for all 100 pterygium samples, and a single surgeon (KMK) performed the operations via a standardized surgical method. All of the surgical procedures were performed as day-care operations under topical and subconjunctival anesthesia. Specifically, the
body of the pterygium was dissected 4 mm from the limbus and reflected over the cornea, a removal of the pterygium head was continued using a Beaver No. 64 surgical blade (Becton Dickenson, Waltham, Mass) via the blunt dissection technique. Excessive tenons were cleared from the bare area, and limbus regions were polished and smoothened using a 3.3 mm diamond burr (Katena ophthalmic burr (No. K2-4920), Katena diamond burr 3.3 mm diameter ball (No. K2-4923), Katena Product Inc., NJ, USA).

All eyes received a conjunctival autograft. A superficial thin free conjunctival graft was carefully dissected from the superior bulbar conjunctiva to avoid taking the underlying Tenon’s layer. Grafts were pre-measured to be oversized by 1 mm horizontally and vertically compared with the bare sclera defect. Graft margins were glued using fibrin glue (Tisseel™, Baxter AG, Vienna, Austria) at the scleral area. All patients received gutt 5 ml of 0.5% moxifloxacin (Alcon Laboratories, Fort Worth, TX, USA) qid, gutt 5 ml of 0.1% dexamethasone (Alcon Laboratories) qid, and 0.3 ml 0.18% Vismed® preservative-free artificial tear drops (TRB Chemedica International SA, Geneva, Switzerland) qid on both eyes for 3 weeks post-operation.

Results

The present analysis included 100 participants, 55% (n = 55) of whom were men. Normality testing showed that all data (i.e., SimK, CIM, SF, TKM, BCVA, and CSF) were normally distributed. Demographic data revealed that the average means for all intended parameters were within the normal range and had fairly large standard deviations (SDs). This finding could be explained by the inclusion of different grades of primary pterygium to reflect the clinical epidemiological data of the population comprehensively. ANOVA showed that the average means for all data measurements were consistent at baseline (p > 0.05). This finding confirms that all data included in the analysis are reliable. Moreover, a decreasing trend in all four corneal parameters (SimK, CIM, SF and TKM) and both visual performance (BCVA and CSF) measurements was observed from baseline (pre-surgery) to the 12th-month follow-up.

**Table 1.** Comparative analysis of corneal topographic parameters between pre- and post-surgical excision patients over 1 year of follow up (N = 100)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>1 month&lt;sup&gt;a&lt;/sup&gt;</th>
<th>3 months&lt;sup&gt;b&lt;/sup&gt;</th>
<th>6 months&lt;sup&gt;c&lt;/sup&gt;</th>
<th>12 months&lt;sup&gt;d&lt;/sup&gt;</th>
<th>p&lt;sup&gt;*&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>SimK (D)</td>
<td>4.64±4.18</td>
<td>0.63±0.43</td>
<td>0.57±0.45</td>
<td>0.57±0.45</td>
<td>0.57±0.44</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>CIM</td>
<td>4.31±5.30</td>
<td>1.87±2.32</td>
<td>0.53±0.30</td>
<td>0.53±0.30</td>
<td>0.53±0.30</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>SF</td>
<td>0.55±0.20</td>
<td>0.41±0.14</td>
<td>0.33±0.08</td>
<td>0.33±0.08</td>
<td>0.33±0.08</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>TKM (D)</td>
<td>46.95±4.47</td>
<td>46.61±4.32</td>
<td>46.51±4.27</td>
<td>46.52±4.27</td>
<td>46.49±4.28</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>BCVA (LogMAR)</td>
<td>0.44±0.30</td>
<td>0.20±0.12</td>
<td>0.12±0.04</td>
<td>0.13±0.05</td>
<td>0.12±0.05</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>CSF (%)</td>
<td>24.28±17.66</td>
<td>8.74±4.47</td>
<td>6.32±0.89</td>
<td>6.29±0.92</td>
<td>6.27±0.93</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>*</sup> Repeated measure of analysis of variance (RM-ANOVA), significance level set at 0.05 (2-tailed)
<sup>a</sup> between baseline and 1-month
<sup>b</sup> between 1-month and 3-month
<sup>c</sup> between 3-month and 6-month
<sup>d</sup> between 6-month and 12-month
Corneal parameters. RM-ANOVA indicated that all corneal parameters measured showed a significant change within the first 3 months of follow-up followed by a plateau. The mean±SD of SimK, for example, was highest at baseline (4.64±4.18 Diopters (D)) and significantly decreased to 0.63±0.43 D within the first month post-surgery (p < 0.001). SimK showed a similar decreasing trend until the third month post-surgery (0.57±0.45 D; p < 0.001). However, no significant difference in SimK between the 6th month (0.57±0.45 D) and 12th month (0.57±0.44 D) post-surgery was observed (both p > 0.05).

The other corneal indices, namely, CIM, SF, and TKM, showed trends similar to that observed in SimK; specifically, these indices significantly decreased from baseline to the first month (p < 0.001) and from the first month to the third month (p < 0.001) post-surgery. Moreover, no significant difference between the fourth (6 months) and fifth (12 months) follow-up sessions were noted for CIM, SF, and TKM (all p > 0.05).

BCVA and CSF revealed prominent improvements within the first 3 months after surgery and then tended to plateau thereafter. The average BCVA decreased from 0.44±0.30 LogMAR at baseline to 0.20±0.12 LogMAR at 1-month post-surgery and then to 0.12±0.04 at 3 months post-surgery (both p < 0.001). CSF significantly decreased from 24.28%±17.66% at baseline to 8.74%±4.47% at 1-month post-surgery and then to 6.32%±0.89% at 3 months post-surgery (both p < 0.001). Both parameters revealed no significant changes from the third month onward. All pre-and post-surgical results are summarized in Table 1.

The results of the current study suggest that the corneal stabilization point occurs at the third month post-surgery because all corneal indices returned to their original values at this timepoint, which suggests that the anterior corneal curvature had recovered. Moreover, zero recurrences of pterygium were observed after 12 months of follow-up.

Discussion

This study evaluates the pterygium recurrence rate and corneal stabilization point subsequent to pterygium excision using the controlled partial avulsion fibrin glue technique by evaluating magnitude changes in four corneal indices (i.e., SimK, CIM, SF, and TKM) and two ocularvusial parameters (i.e., BCVA and CSF). Histologically, pterygium is composed of the head of the conjunctival epithelium and hyperproliferative vascularization along the body of the degenerated connective tissue, which signifies elastotic degeneration.1-3 Because of these characteristics, pterygium was previously considered a degenerative disorder. However, recent studies have proven that pterygium also has proliferative histological characteristics,4,9 such as mild dysplasia, local invasiveness, and abnormal p53 gene expression, and clinical features, including a high recurrence rate following pterygium excision.

Pterygium is usually associated with adult cataract, which often co-occurs with the growth. Thus, determination of the appropriate time for cataract removal may be difficult because the intraocular (IOL) power calculation for cataract could be inaccurate. Inaccuracies in IOL power calculation could occur due to the anterior corneal curvature was not fully recovered, which could give rise to errors in corneal measurement. Our literature search revealed limited evidence on the minimum duration needed for corneas to recover after pterygium excision using the fibrin glue adhesive method.

Koranyi, Seregard, and Kopp first introduced the fibrin glue adhesive method based on their “cut-and-paste” approach for treating pterygium.31 This method features a conjunctival autograft attached with a fibrin glue adhesive rather than sutures. Fibrin glue is a blood-derived product consisting of fibrinogen and thrombin. Thrombin activates fibrinogen, and an adhesive fibrin network is formed.32 This method adopts a similar normal biological reaction in a wound healing process and has been proven to result in a lowest risk of pterygium recurrence (0 – 8.16%) compared with other methods.27,28 Indeed, no recurrence of pterygium was noted throughout the duration of the present study. The fibrin glue adhesive method shows promising results and several advantages. For example, this method is sutureless, which means fewer post-operative complications, less operating time, and high safety and efficiency.18,33,34

Significant reductions in SimK, CIM, SF, and TKM were noted within the first 3 months post-surgery (all p < 0.001) in this work; stabilization of these indices occurred from the third month onward. Variations in SimK, CIM, SF, and TKM signify that the anterior corneal curvature returns to its standard prolate shape and that corneal compression due to localized flattening by pterygium progression is reduced.21 Changes in SimK and CIM represent changes to the anterior apical corneal curvature, which could be associated with the acuity of central vision as pterygium covers the central 5-mm of the central cornea. Low SimKs indirectly signify minimal residual corneal astigmatism, while a higher value of, for instance, over 0.68 μm signifies an irregular corneal curvature.35 Decreasing the CIM to the normal range of 0.03–0.68 μm is crucial to ensure that the central corneal curvature returns to its original state.39 Recent work revealed a significant increment in CIM as pterygium progresses.36
Changes in SF and TKM reflect changes in the anterior apical corneal curvature, which could be associated with overall visual quality. Increments in SF and TKM indicate increases in overall corneal irregularity and corneal instability due to pterygium progression. An SF of greater than 0.47, which indicates corneal flattening at the periphery, is considered abnormal. A previous work reported similar findings. A TKM of greater than 47.3 dioptres (D) indicates an increase in average keratometry, which reflects a significant variation of the corneal curvature. TKM utilized elevation data obtained by corneal topographer and compare the toric reference to the actual cornea. This provides better toric representation of a patient's cornea and also its corneal regularity. An earlier work found that elevation data analyzed based on TKM values showed better accuracy in measurement of astigmatism in irregular cornea.

Recent research also revealed that pterygium induces higher corneal toxicity as reflected by abnormal TKM values which indicates higher elevation data obtained in pterygium cases due to increase in corneal toxicity of the anterior corneal curvature. BCVA and CSF represent the oculovisual function status, which indirectly provides information on visual quality. Changes to the corneal surface cause by the pterygium may affect visual quality. The results of this study showed significant improvements in BCVA and CSF within the first 3 months post-surgery (all $p < 0.001$) and stable values from the third month onward. This finding agrees with previous reports. Some researchers have suggested that the anterior corneal curvature stabilizes and recovers to its original state 3 months post-surgery. However, any obstruction during corneal healing process could cause corneal irregularity and reductions in visual function.

The findings suggest that corneal stabilization occurs because of two reasons: pterygium morphology and mechanical-traction on the anterior corneal surface due to pterygium progression. First, the pterygium morphology could affect the corneal stabilization as fibrovascular tissue could present as a thick pterygium tissue and this could change the curvature of the anterior corneal surface. Previous works had commented that an increase in thickness could suggest excessive proliferative disorders. The excessive proliferative growth of the pterygium could induce corneal compression, which may also lead to increases in the corneal indices and result in induced astigmatism.

Considering the mechanical traction on the anterior corneal surface due to pterygium progression, this study suggests that pterygium indirectly induces localized flattening, which could lead to corneal compression, as the growth progresses. Compression of the anterior corneal curvature could be due to two reasons. First, the tension of the fibrovascular pterygium tissue on the cornea, which stretches from the bulbar conjunctiva, may increase, thereby causing corneal flattening. Second, corneal compression may occur because of the fibrovascular tissue pressing against the corneal surface. However, our literature search revealed little information on this topic.

This study presents some limitations that must be taken into account when interpreting the results. First, this study includes primary pterygia with a wide range of corneo-pterygium total areas and multiple pterygium types, which could indirectly cause a high SD during measurement. An extremely large pterygium could also cause errors in topographic measurement because the instrument may be unable to detect the central cornea as its reference.

The current study suggests that a broader view is needed to evaluate how pterygium induces changes to the anterior corneal curvature. Previous theories mainly focusing on pterygium size, width, and length are inadequate to explain the changes that may occur over the course of pterygium progression. The results of this study indicate that the combination of a corneo-pterygium approach and a good understanding of pterygium grades based on the transulence of the growth could help predict the changes induced by pterygium on the corneal surface.

Conclusion

The controlled partial avulsion fibrin glue technique provides stable corneal and visual recovery within 3 months post-surgery with zero recurrence of pterygium. It may improve surgical outcomes with long-term recurrence rates equal to or lower than those previously reported. Corneal surface recovery is completed after the third month of the excision procedure.

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Conflict of Interest Statement

The authors report no conflicts of interest.

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