

Impact of Pterygium Excision Combined with Autologous Limbal Stem Cell Transplantation on Microvascular Density, Tear Film Stability, and Corneal Wound Healing

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AIM: This study aimed to evaluate the impact of pterygium excision combined with autologous limbal stem cell transplantation on microvascular density, tear film stability, and corneal wound healing in the management of pterygium.

METHODS: A retrospective analysis was conducted on 317 patients with pterygium who underwent treatment between January 2021 and January 2024. Patients were divided into a control group (pterygium excision alone, $n = 161$) and a study group (pterygium excision combined with autologous limbal stem cell transplantation, $n = 156$) based on the surgical approach. The study compared the surgical efficacy, perioperative outcomes, and corneal healing between the two groups. Preoperative and postoperative changes in conjunctival microvascular density, tear film stability indicators, and ocular comfort scores were also assessed.

RESULTS: The effective treatment rate was significantly higher in the study group compared to the control group ($p < 0.05$). Postoperative uncorrected visual acuity, vertical corneal curvature, and horizontal corneal curvature were significantly better in the study group, whereas corneal astigmatism was lower than in the control group ($p < 0.05$). The postoperative levels of pigment epithelial derived factor (PEDF) were higher in the study group, while levels of vascular endothelial growth factor (VEGF) and microvascular density (MVD) were lower than in the control group ($p < 0.05$). Corneal healing scores on postoperative days 1, 3, and 7 were lower in the study group than in the control group, and the time resolution of corneal wound congestion and corneal epithelial coverage was significantly shorter compared to the control group ($p < 0.05$). Tear film stability, as indicated by the Schirmer I test (SIt) and tear breakup time (BUT), was improved in the study group than that in the control group ($p < 0.05$). Postoperative ocular comfort scores were lower in the study group compared to the control group ($p < 0.05$). No significant difference in postoperative complication rates was observed between the groups ($p > 0.05$).

CONCLUSIONS: Pterygium excision combined with autologous limbal stem cell transplantation effectively inhibits angiogenesis, improves visual function, enhances tear film stability, and accelerates corneal wound healing, making it a superior treatment option for pterygium.

Keywords: pterygium; pterygium excision; autologous limbal stem cell transplantation; microvascular density; tear film stability; corneal wound healing

Introduction

Pterygium is a prevalent ophthalmic disorder characterized by the invasion of fibrovascular tissue from the bulbar conjunctiva onto the cornea, leading to symptoms such as vision loss and dry eye disease [1]. Surgical excision remains the primary treatment approach. However, postoperative discomfort is a significant concern for many patients [2]. Previous study has indicated that the discomfort primarily arises from irritation to corneal and conjunctival wounds,

underscoring the need to optimize postoperative recovery for these tissues [3].

Histologically, pterygium comprises atrophic conjunctival epithelium, hyperplastic vascularized stroma, and elastotic degeneration of connective tissue. Surgical excision often damages the conjunctival tissue. Some researchers have demonstrated that combining autologous limbal stem cell transplantation with pterygium excision significantly enhances the recovery of the cornea and conjunctiva [4]. Autologous corneal limbal stem cells have the potential to differentiate into conjunctival goblet cells and corneal limbal epithelial cells after transplantation, promoting corneal epithelium regeneration during the early postoperative period.

The tear film is the primary protective barrier for the ocular surface, safeguarding against external damage while maintaining the stability, structure, and function of the corneal epithelium. However, evidence suggests that tear film dysfunction is a common feature during the development of

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pterygium, and early recovery of tear film stability postoperatively has been shown to reduce the risk of disease recurrence [5]. Pterygium formation, development, and postoperative recurrence are closely associated with neovascularization [6]. Vascular endothelial growth factor (VEGF) is a key regulator of angiogenesis, promoting endothelial cell proliferation and vascular permeability. It also facilitates extracellular matrix deposition, enabling endothelial cell migration and blood vessel formation, ultimately contributing to the maturation of new blood vessels [7]. Elevated VEGF expression has been closely correlated with the development, progression, invasion, and postoperative pterygium recurrence [8].

Conversely, pigment epithelial derived factor (PEDF), a natural angiogenesis inhibitor, suppresses endothelial cell migration and induces apoptosis. Recent study has reported that PEDF expression is significantly reduced in pterygium tissue, suggesting its potential involvement in the pathogenesis and progression of the disease. Furthermore, PEDF positively correlates with the angiogenic activity observed in retinal neovascularization [9].

Despite the advances, the clinical effects of pterygium excision combined with autologous limbal stem cell transplantation on conjunctival microvascular density remains inconclusive. This study aimed to evaluate the impact of this combined surgical approach on microvascular density, tear film stability, and corneal wound healing in the treatment of pterygium. The findings from this study provide evidence-based guidance for choosing optimal treatment options for patients with pterygium.

Materials and Methods

Clinical Data

This retrospective study analyzed clinical data from 317 patients diagnosed with pterygium and treated in the Second Affiliated Hospital of Nantong University, China, between January 2021 and January 2024. Patients were divided into a control group ($n = 161$) and a study group ($n = 156$) based on the surgical methods. The control group underwent pterygium excision alone, while the study group underwent pterygium excision combined with autologous limbal stem cell transplantation. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Nantong University, China (approval number: 2023KT122) and adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all participants in the study.

Inclusion criteria: ① Patients meeting the diagnostic criteria for primary pterygium [10]; ② Patients with unilateral pterygium; ③ Patients with complete clinical data. Exclusion criteria: ① Patients with severe organ dysfunction; ② Patients with a history of ocular trauma or surgery; ③ Patients with coexisting corneal diseases; ④ Patients with conditions affecting ocular circulation, such as glaucoma; ⑤ Patients with high myopia or amblyopia; ⑥ Patients with

cataracts; ⑦ Patients with pupil dilation disorders; ⑧ Patients allergic to pupil-dilating agents.

Methods

The same experienced surgical team performed all surgeries. Anesthesia was induced preoperatively using surface anesthesia with oxybuprocaine hydrochloride (Shandong Bausch & Lomb Freda Pharmaceutical Co., Ltd., Jinan, China, H20056587), and subconjunctival infiltration anesthesia was achieved with 20 g/L lidocaine (Shandong Yijian Pharmaceutical Co., Ltd., Weifang, China, SinopOD H20043708). The surgery was performed under a microscope.

For patients in the control group, pterygium excision was performed by incising the bulbar conjunctiva along the upper and lower margins of the pterygium. The corneal portion of the pterygium was dissected to expose the clear cornea, and the residual conjunctival edges were sutured to the superficial sclera 4 mm from the limbus. The eye was bandaged for one day postoperatively. In the study group, the surgical procedure included a pterygium incision combined with autologous limbal stem cell transplantation. After removing the pterygium, a conjunctival graft of similar size was harvested from the superior limbus of the same eye, approximately 1 mm from the limbus. The graft, with the epithelial surface facing up, was laid flat over the exposed scleral area and sutured to the superficial scleral surface using 10-0 nylon sutures. No additional treatment was required for the donor site wound.

Postoperative care for all the patients included the application of tobramycin dexamethasone eye cream. Starting the following day, loteprednol suspension eye drops were administered 4 times daily for three weeks. Sutures were removed 14 days postoperatively.

Clinical Data Collection

Patient demographic and clinical data, including gender, age, best-corrected visual acuity (BCVA) at baseline, disease course, and pterygium-related indices, were collected from medical records for analysis.

Clinical Efficacy Evaluation

Clinical outcomes were assessed based on established criteria [11], classifying results as cured, effective, or ineffective. A cured outcome was defined as complete epithelial coverage of the corneal wound, smooth conjunctiva without congestion, and no evidence of neovascularization or pterygium recurrence. An effective outcome indicated partial epithelial coverage of the corneal wound, mostly conjunctiva, with minimal congestion and no neovascularization or pterygium recurrence. An ineffective outcome was defined as failure to meet the above criteria. The total effective rate was calculated using the formula:

Total Effective Rate (%) = (Cured + Effective)/Total Cases \times 100%.

Observation Indicators

The study employed several indicators to evaluate the outcomes of surgical interventions: (1) Visual function: Uncorrected visual acuity (UCVA), corneal astigmatism (CAD), vertical corneal curvature, and horizontal corneal curvature were measured preoperatively and one month postoperatively in both groups. Measurements were obtained using a computer keratometer (KR-800, Topcon, Tokyo, Japan) and an electronic vision screening device (VS100, Welch Allyn, Skaneateles Falls, NY, USA).

(2) Microvascular-related indicators: Non-irritating tear samples (10 μ L) were collected using a capillary pipette from the lower lacrimal river and stored at -20°C for analysis. Enzyme-linked immunosorbent assay (ELISA) was used to quantify VEGF and PEDF levels in the tear samples before and one month after surgery. ELISA kits were purchased from Xcel Biotechnology (Taicang) Co., Ltd., Taicang, China (Kit IDs: 21F322, 21F471, respectively). Conjunctival microvascular density (MVD) was assessed using a Heidelberg laser confocal microscope (HRT-II, Heidelberg Co., Baden-Wurttemberg, Germany) before and one month after surgery. Microvessels were labeled with CD34 and visualized as tan or brownish-yellow structures without background staining. Tissue sections were scanned at low power to identify areas of dense microvessels and clear endothelial cell staining. Five areas with the highest microvascular density were selected for observation under $\times 400$ magnification, and the average number of vessels was calculated as the MVD value. Vessels with lumens larger than the diameter of 8 red blood cells or with a thick muscular layer were excluded. A continuous and uninterrupted branching structure was counted as a blood vessel, and distinguishable brown-stained clusters of cells or single endothelial cells were also included in the counts.

(3) Corneal healing status: Postoperative corneal healing was evaluated by comparing corneal healing scores, the resolution time of corneal wound congestion, and the time required for corneal epithelial coverage. Fluorescein sodium staining (FLS: Alcon PuertpRico, 500 mg/5 mL, Fort Worth, TX, USA) was performed on postoperative days 1, 3, and 7 to assess corneal healing scores [12]. The cornea was divided into four quadrants, each scoring from 0 to 3 (total score range: 0–12). A higher score indicated poorer corneal healing. A score of 0 was assigned for no significant staining, 1 for slight dotted staining, 2 for moderate faint fusion staining, and 3 for dense fused staining.

(4) Tear film stability: Tear film stability was evaluated preoperatively and postoperatively using the Schirmer I test (SI_t) and the tear film breakup time (BUT). For the SI_t test, a filter paper strip was placed in the lower eyelid, and the length of the strip wetted by tears was measured over five minutes; a length of <10 mm was considered abnormal. For BUT, a sterile fluorescein strip was used to determine

the time from the last blink to the appearance of a black spot on the cornea; a BUT of <10 seconds indicated dry eye symptoms or unstable tear film function.

(5) Ocular comfort: Ocular comfort was assessed seven days postoperatively using a comfort score [13]. This scale evaluated seven symptoms: photophobia, foreign body sensation, lacrimation, eye pain, itchy eye, discharge, and conjunctival injection. Each symptom was scored on a scale of 0 to 4, where 0 indicated no symptoms, and 4 represented extremely severe symptoms.

Statistical Analyses

Statistical analyses were performed using SPSS software (version 22.0, IBM Corporation, New York, NY, USA). Categorical data were expressed as frequencies and percentages [n (%)] and analyzed using the chi-square (χ^2) test to compare group differences. Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed data were expressed as mean \pm standard deviation ($\bar{x} \pm s$) and analyzed using the independent t -test to compare differences between groups. A p -value of <0.05 was considered statistically significant.

Results

Comparison of Clinical Data between the Two Groups

No significant differences were observed in the baseline clinical characteristics between the two groups ($p > 0.05$), indicating that the groups were comparable (Table 1).

Comparison of Treatment Efficacy between the Two Groups

The treatment efficacy rate in the study group was significantly higher than in the control group ($p < 0.05$) (Table 2).

Comparison of Visual Function before and after Surgery between the Two Groups

Preoperative visual function indicators, including uncorrected visual acuity (UCVA), corneal astigmatism (CAD), vertical corneal curvature, and horizontal corneal curvature, showed no significant differences between the two groups ($p > 0.05$). Postoperatively, UCVA, vertical corneal curvature, and horizontal corneal curvature improved in both groups compared to preoperative values, with the study group presenting higher values than the control group ($p < 0.05$). Conversely, corneal astigmatism decreased postoperatively in both groups compared to preoperative values, with the study group showing a more significant reduction than the control group ($p < 0.05$, Fig. 1).

Comparison of Microvascular Density and Tear-related Indicators before and after Surgery between the Two Groups

No significant differences were observed in preoperative microvascular-related indicators between the two groups ($p > 0.05$). Postoperatively, PEDF levels increased in

Table 1. Comparison of clinical data between the two groups [$\bar{x} \pm s/(n, \%)$].

Variable	Study group (n = 156)	Control group (n = 161)	t/χ^2	p-value
Gender			0.009	0.924
Male	89 (57.05)	91 (56.52)		
Female	67 (42.95)	70 (43.48)		
Age (years)	51.38 \pm 6.89	50.85 \pm 7.24	0.667	0.505
Best corrected vision	1.09 \pm 0.15	1.11 \pm 0.18	1.073	0.284
Duration of illness (years)	6.14 \pm 0.91	6.09 \pm 1.03	0.457	0.648
Pterygium length (mm)	6.30 \pm 1.08	6.21 \pm 1.15	0.718	0.473
Pterygium height (mm)	4.19 \pm 0.72	4.11 \pm 0.69	1.010	0.313
Pterygium area (mm ²)	21.26 \pm 2.76	21.13 \pm 2.92	0.407	0.684
Intraocular pressure (mmHg)	18.95 \pm 2.71	18.76 \pm 3.05	0.586	0.559
Depth of corneal invasion (mm)	3.41 \pm 0.58	3.50 \pm 0.61	1.345	0.179
Comorbid conditions				
Type 2 diabetes	39 (25.00)	43 (26.71)	0.121	0.728
Hypertension	49(31.41)	46 (28.57)	0.304	0.581
Hyperlipidemia	43(27.56)	41 (25.47)	0.179	0.672

Table 2. Comparison of treatment efficacy between the two groups (n (%)).

Group	n	Cured	Effective	Ineffective	Total effective rate (%)
Study group	156	32.69% (51/156)	60.90% (95/156)	6.41% (10/156)	93.59% (146/156)
Control group	161	27.95% (45/161)	54.04% (87/161)	18.01% (29/161)	81.99% (132/161)
χ^2					9.885
p-value					0.002

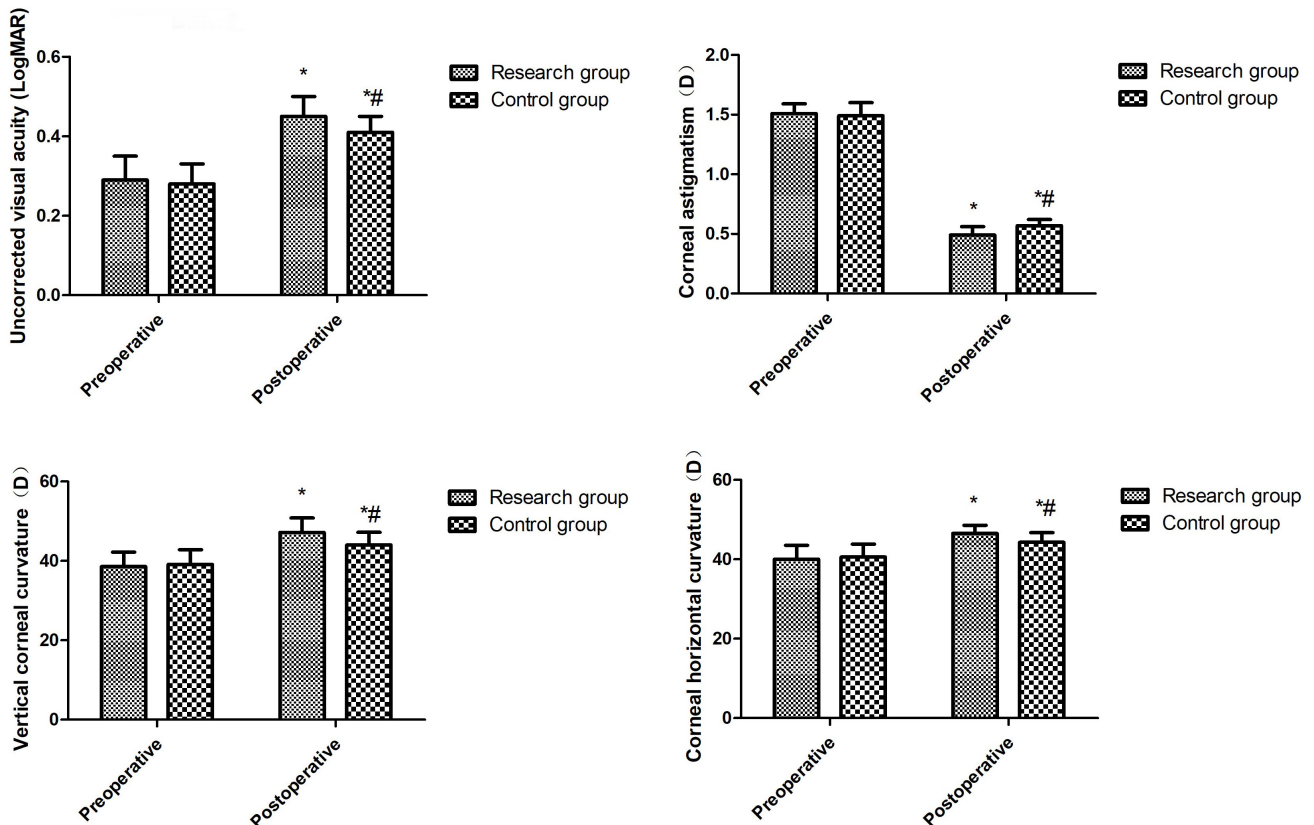
**Fig. 1. Comparison of visual function before and after surgery between the two groups ($\bar{x} \pm s$). Note: Compared to preoperative values within the same group, * $p < 0.05$; compared to the study group post-treatment, # $p < 0.05$.**

Table 3. Comparison of microvascular density-related indicators before and after surgery between the two groups ($\bar{x} \pm s$).

Group	n	PEDF ($\mu\text{g/L}$)		VEGF (ng/L)		MVD	
		Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
Study group	156	2.75 ± 0.49	$10.39 \pm 2.04^*$	296.58 ± 30.35	$192.31 \pm 28.06^*$	19.05 ± 4.36	$9.49 \pm 2.05^*$
Control group	161	2.68 ± 0.46	$8.12 \pm 1.79^*$	294.02 ± 31.33	$241.29 \pm 29.14^*$	19.38 ± 4.21	$11.12 \pm 2.25^*$
t-value		1.312	10.540	0.739	15.237	0.686	6.736
p-value		0.191	<0.001	0.461	<0.001	0.493	<0.001

Note: PEDF, pigment epithelial derived factor; VEGF, vascular endothelial growth factor; MVD, microvascular density. Postoperative values marked with * indicate significant differences compared to preoperative values within the same group ($p < 0.05$).

Table 4. Comparison of corneal wound healing between the two groups ($\bar{x} \pm s$).

Groups	n	Corneal healing score (points)			Time for corneal wound	Time for epithelial coverage
		Postoperative 1 day	Postoperative 3 days	Postoperative 7 days	congestion to subside (days)	of the corneal wound (days)
Study group	156	4.29 ± 0.49	2.41 ± 0.41	1.26 ± 0.32	4.69 ± 0.52	4.53 ± 0.50
Control group	161	4.52 ± 0.43	3.06 ± 0.58	1.71 ± 0.30	5.47 ± 0.51	5.41 ± 0.49
t-value		4.446	11.489	12.921	13.483	15.826
p-value		<0.001	<0.001	<0.001	<0.001	<0.001

both groups compared to preoperative levels, with the study group showing significantly higher levels than the control group ($p < 0.05$). VEGF levels and MVD decreased postoperatively in both groups, with the study group exhibiting a more pronounced reduction than the control group ($p < 0.05$, Table 3).

Comparison of Corneal Wound Healing between the Two Groups

The corneal healing scores at postoperative days 1, 3, and 7 were lower in the study group compared to the control group ($p < 0.05$). Additionally, the resolution time for corneal wound congestion and the time required for complete corneal epithelial coverage were shorter in the study group than in the control group ($p < 0.05$, Table 4).

Comparison of Tear Film Stability before and after Surgery between the Two Groups

Preoperative tear film stability indicators, including SIt and tear film breakup time (BUT), showed no significant differences between the two groups ($p > 0.05$). Postoperatively, SIt and BUT values increased in both groups compared to preoperative levels, with the study group showing significantly greater improvements than the control group ($p < 0.05$, Table 5).

Comparison of Ocular Comfort between the Two Groups

Ocular comfort scores were significantly lower in the study group compared to the control group, indicating better postoperative comfort ($p < 0.05$, Fig. 2).

Comparison of the Incidence of Complications between the Two Groups

There were no significant differences in the incidence of postoperative complications between the two groups ($p > 0.05$, Table 6).

Discussion

Pterygium is a prevalent ophthalmic condition characterized by the triangular fibrovascular proliferation of conjunctival tissues from the limbal region invading the cornea [5]. Surgical excision remains the primary treatment method for this condition. While recent advances in surgical techniques have improved outcomes, patients often experience postoperative discomfort, such as eye pain, photophobia, foreign body sensation, tearing, and itchiness, which can affect corneal healing. The extent and depth of corneal wound damage are directly proportional to the severity of postoperative pain and discomfort symptoms, making the promotion of corneal healing a key element in pterygium management [14]. Autologous limbal stem cell transplantation (LSCT) is a promising approach that enhances corneal healing while improving local symptoms [15,16]. Pterygium excision is the standard treatment to mitigate the effects of the disease on visual acuity. In this study, the treatment efficacy in the study group was significantly higher than in the control group. Postoperatively, patients in the study group showed improved uncorrected visual acuity (UCVA), vertical corneal curvature, and horizontal corneal curvature compared to the control group, while the corneal astigmatism was notably reduced than that in the control group. These findings suggest that adding LSCT enhances clinical efficacy and improves patient's vision. The effect can be attributed to that after autologous limbal stem cell transplantation, the survival of stem cells can promote the division and proliferation of tissue cells, promote the growth of blood vessels and conjunctival epithelium into the cornea, improve the matrix microenvironment of limbal stem cells in pterygium, and achieve the purpose of cure [17,18].

When the pterygium does not extend to the pupil area, its primary visual effect is corneal astigmatism. Pterygium-

Table 5. Comparison of tear film stability before and after surgery in the two groups ($\bar{x} \pm s$).

Group	n	SIt (mm/5 min)		BUT (s)	
		Preoperative	Postoperative	Preoperative	Postoperative
Study group	156	9.51 \pm 1.38	13.43 \pm 1.16*	9.35 \pm 0.86	12.07 \pm 1.52*
Control group	161	9.68 \pm 1.50	12.19 \pm 1.42*	9.29 \pm 0.89	10.75 \pm 1.56*
<i>t</i> -value		1.049	8.500	0.610	7.627
<i>p</i> -value		0.295	<0.001	0.542	<0.001

Note: SIt, Schirmer I test; BUT, breakup time. Postoperative values marked with * indicate significant differences compared to preoperative values within the same group ($p < 0.05$).

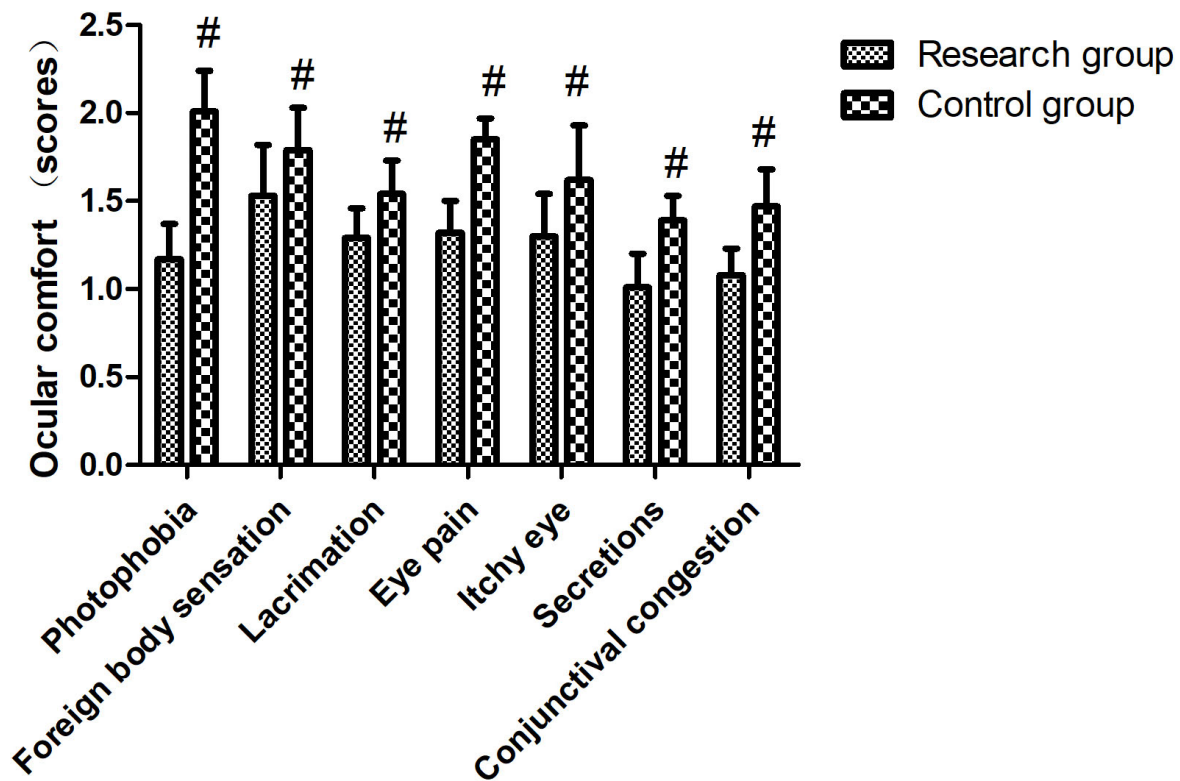


Fig. 2. Comparison of ocular comfort scores between the two groups ($\bar{x} \pm s$). Note: Compared to the research group, # $p < 0.05$.

induced astigmatism, typically axial hypermetropic astigmatism, results from the invasive nature of the pterygium at the corneal edge, leading to corneal traction and compression. The corneal mechanical disruption flattens the local corneal contour, resulting in reduced corneal refractive power and altered optical reflection. In this study, combined surgical treatment significantly reduced corneal astigmatism. The underlying mechanism likely involves the ability of limbal stem cell transplantation (LSCT) to restore corneal shape and elasticity. Post-transplantation, the proliferative and centripetal behavior of the limbal stem cells helps regenerate the damaged limbal area and corneal epithelial defects, facilitating corneal remodeling and reducing corneal astigmatism.

Neovascularization is critical in pterygium formation, progression, and recurrence [6]. This study showed that postoperative levels of PEDF were significantly higher in the study group than in the control group, while VEGF

and MVD were markedly lower than those in the control group. These findings suggest that the combined approach of pterygium excision and LSCT inhibits angiogenesis. The inhibition can be attributed to the role of limbal stem cells in cell renewal and tissue regeneration. Autologous LSCT is more suitable for the anatomical structure and physiological environment of the patient's own ocular surface tissue. Therefore, it can promote epithelial regeneration, inhibit inflammation, scar and neovascularization, effectively prevent shallow neovascularization and abnormal tissue invasion, and greatly help rebuild limbal barrier function, thus inhibiting angiogenesis [19].

Additionally, the study revealed the corneal healing scores at 1 day, 3 days, and 1 week were significantly lower in the study group than in the control group, indicating faster recovery. The shorter time to resolve corneal wound congestion and complete epithelial coverage in the study group further underscores the benefits of the combined treatment.

Table 6. Comparison of the incidence of complications between the two groups (n (%)).

Group	n	Delayed healing of the corneal epithelium	Corneal epithelial edema	Corneal ulcer	Overall incidence rate (%)
Study group	156	2 (1.28)	2 (1.28)	0 (0.00)	4 (2.56%)
Control group	161	5 (3.11)	3 (1.86)	1 (0.62)	9 (5.59%)
χ^2					1.845
<i>p</i> -value					0.174

LSCT enhances corneal epithelial regeneration, isolates the conjunctiva from the cornea, and inhibits neovascularization and pterygium invasion into the cornea, collectively accelerating wound healing and corneal recovery [20].

The tear film is the first line of defense of the ocular surface, protecting it from external damage while maintaining the normal structure and function of the corneal epithelium. However, disruptions in the tear film function may lead to various ocular conditions. Postoperative tear film instability is a documented phenomenon that can cause ocular discomfort, increase the risk of dry eye syndrome, and lead to corneal lesions and other ocular surface disorders [21]. In recent years, the coexistence of abnormal tear film function and pterygium has garnered significant attention among ophthalmologists [22]. Research suggests that tear film dysfunction plays an important role in the onset and progression of pterygium; therefore, the state of the tear film after pterygium surgery is a critical determinant of disease recurrence [23].

Tear film stability is commonly evaluated using the BUT, which reflects functional stability and, the SIt, which assesses aqueous tear secretion. In this study, the SIt and BUT values in the study group were significantly higher than in the control group, indicating that the combined treatment of pterygium excision with autologous limbal stem cell transplantation (LSCT) improves tear film stability. This improvement is primarily attributable to the ability of LSCT to reconstruct and repair the corneal limbus, promote local tissue regeneration, and restore corneal elasticity. These processes facilitate the recovery of ocular surface function, leading to enhanced tear film stability. Additionally, our study showed that ocular comfort scores in the study group were significantly lower than in the control group, indicating that the combined surgical treatment reduces postoperative ocular discomfort. This effect is mainly due to the combined treatment capacity to improve tear film function and accelerate wound healing.

Despite these promising results, the study has several limitations. The relatively small sample size may introduce bias into the results, necessitating caution when interpreting the outcomes. Future studies with larger sample sizes are required to validate these findings and enable a more robust analysis.

Conclusions

In summary, pterygium excision combined with autologous limbal stem cell transplantation for the treatment of pterygium can inhibit angiogenesis, improve visual function, enhance tear film stability, and promote the healing of corneal wounds.

Availability of Data and Materials

The data analyzed are available on the request for the corresponding author.

Author Contributions

MXH and NL designed the research study. MXH and JIL performed the research. NL and XBH analyzed the data, and XBH provided help and advice on the experiments. MXH analyzed the data and drafted the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Nantong University, China (approval number: 2023KT122) and adhered to the Declaration of Helsinki. Informed consent was obtained from all participants in the study.

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Conflict of Interest

The authors declare no conflict of interest.

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