

# Limbal-conjunctival Autograft Transplantation Versus Conjunctival Autograft Transplantation In The Treatment Of Pterygium: A Self-control Study

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## Research article

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# Abstract

**Background :** Pterygium is a common ocular growth, which affects vision, ocular surface function, and aesthetics of the eye. Although various surgical methods are used for treating pterygium, there has been no consensus on the most suitable method. Therefore, it is important to choose the most appropriate and effective surgical method for the treatment of pterygium. The aim of this study was to compare the characteristics and efficacy of limbal-conjunctival autograft transplantation and conjunctival autograft transplantation for the treatment of pterygium.

**Methods :** From August 2015 to December 2016, 80 patients with bilateral primary pterygium in Minhang Hospital affiliated to Fudan University were treated with limbal-conjunctival autograft transplantation in one eye (group A) and conjunctival autograft transplantation in the fellow eye (group B). The operative times of the two surgical methods were compared. The corneal epithelial healing times and recurrence rates for the two methods were observed and recorded after two years of follow-up.

**Results :** Eight patients dropped out of the study and 72 patients participated in the final evaluation. The average operative time for group A and group B was 27.56 ± 1.48 minutes and 26.91 ± 1.39 minutes, respectively. There was no significant difference between the operative times for the two groups ( $t = 1.93$ ,  $P = 0.058$ ). The average corneal epithelial healing time for groups A and B was 2.56 ± 0.34 days and 4.85 ± 0.49 days, respectively ( $t=25.26$ ,  $P < 0.001$ ). Two years after the surgery, pterygium recurred in two eyes (2.78%) in group A and in nine eyes (14.29%) in group B. The difference between the two groups was statistically significant ( $\chi^2=4.82$ ,  $P=0.028$ ).

**Conclusion :** In primary pterygium surgery, the healing time of the corneal epithelium after limbal-conjunctival autograft transplantation is shorter than that after conjunctival autograft transplantation, and the pterygium recurrence rate after limbal-conjunctival autograft transplantation is lower than that after autologous conjunctival transplantation. Although both limbal-conjunctival autograft transplantation and conjunctival autograft transplantation can achieve good clinical results, limbal-conjunctival autograft transplantation is superior to conjunctival autograft transplantation in terms of the corneal epithelial healing time and recurrence rate of pterygium after surgery.

## Background

Pterygium is a common ocular growth that resembles insect wings. It is mainly characterized by tissue proliferation of the nasal bulbar conjunctiva in the palpebral fissure, which usually invades the cornea. It slowly enlarges and encroaches the pupil area in a triangular shape. It is most commonly observed among outdoor workers. Further, the etiology of pterygium is complex. There is currently no authoritative literature on the specific pathogenesis of pterygium. Factors such as ultraviolet radiation, smoke, wind, and dust can cause the formation of pterygium; this is because stimulation by sunlight causes the integrity of the corneal limbus and its barrier function to deteriorate. Pterygium affects vision, ocular surface function, and the aesthetics of the eye. Surgery is the only recognized and effective treatment for

pterygium. However, although there are various surgical methods for the treatment of pterygium, there has been no consensus yet on which surgical method is the best choice[1–3]. The recurrence rate of pterygium is the main challenge for ophthalmologists[4, 5]; therefore, it is important to choose the most appropriate and effective surgical method for the treatment of pterygium[6, 7]. Common surgical techniques include simple pterygium excision, conjunctival autograft transplantation, pterygium transposition, pterygium excision combined with amniotic membrane transplantation, limbal-conjunctival autograft transplantation, and adjunctive therapies such as use of mitomycin C, anti-VEGFs, or anti-fibrotics.[8–11]. Pterygium transposition can change the direction of pterygium growth, but it affects the facial beauty of patients. Conjunctival autograft transplantation, limbal-conjunctival autograft transplantation, and pterygium excision combined with amniotic membrane transplantation are the methods most commonly used in the hospital. Simple pterygium excision may not remove the pterygium tissue completely, and the recurrence rate ranges from 24% to 89%[2]. Studies have shown that for patients with primary pterygium, the recurrence rate after amniotic membrane transplantation is between 6.4% and 42.3%[12], the recurrence rate after conjunctival autograft transplantation is between 5% and 30%[13, 14], and the recurrence rate after limbal-conjunctival autograft transplantation is between 0% and 15%[15, 16]. Limbal-conjunctival autograft transplantation and conjunctival autograft transplantation can effectively reduce the rate of pterygium recurrence[1, 16, 17]. In terms of recurrence rate, limbal-conjunctival autograft transplantation seems to be superior to conjunctival autograft transplantation. The aim of this study was to compare the operative times, corneal epithelial healing times, and recurrence rates after surgery for limbal-conjunctival autograft transplantation and conjunctival autograft transplantation and to provide clinical basis for the treatment of primary pterygium.

## Methods

This study aimed to compare the characteristics of limbal-conjunctival autograft transplantation and conjunctival autograft transplantation and compare the efficacy of each technique for the treatment of pterygium. From August 2015 to July 2017, 80 patients with bilateral primary pterygium were admitted to the department of ophthalmology in Minhang Hospital affiliated to Fudan University. The pterygia in both eyes were located on the nasal side and had invaded 2 mm–4 mm of the cornea. The affected eyes were divided into two groups by using the random number table method, with 40 eyes of 40 cases in each group.

The patients enrolled in the study met the following inclusion criteria: (1) bilateral pterygia located at the nasal side and invading more than 2 mm of the cornea; and (2) good compliance and willingness to follow up regularly. Patients with ocular diseases such as dry eyes, conjunctivitis, keratitis, and iridocyclitis, which may affect the outcome of surgery, and patients with severe systemic diseases were excluded from the study

All procedures in this study were conducted ethically in accordance with the tenets of the World Medical Association Declaration of Helsinki. All the patients gave written informed consent, and the study

protocol was approved by the ethic committee of Minhang Hospital, Fudan University on human research.

## Surgical procedure

After admission, the patient signed the consent form for the surgery. Before the surgery, the patient was trained on proper eye movement and rotation. Surgery was scheduled only after basic ocular examinations such as measurement of visual acuity, measurement of intraocular pressure, and funduscopy showed no special abnormalities. All the surgeries were microsurgeries; 5 ml lidocaine mixed with an 0.4 ml epinephrine was used for subconjunctival anesthesia. The cervical part of the pterygium was cut along the corneal limbus with a microscissors, and then, the conjunctiva and the pterygium tissue were bluntly separated to avoid damaging the blood vessels and the surrounding normal tissues. The pterygium was separated up to the plica semilunaris and care was taken to protect the lacrimal caruncle and the plica semilunaris. Minor bleeding was managed mainly by proper compression with a cotton ball; electric coagulation and cauterization was used less frequently for hemostasis. The pterygium tissue was then cut off. Afterwards, the corneal tissue was dissected shallowly about 0.5 mm around the head of the pterygium with a scalpel blade, and the pterygium tissue on the surface of the cornea was grasped with toothed forceps. The pterygium head tissue was pulled out in the opposite direction to ensure that the pterygium could be completely torn off the surface of the cornea, so that there was no residual pterygium tissue on the cornea surface. Excessive scratches were avoided to reduce the occurrence of complications. After this step, patients were randomly assigned to the limbal-conjunctival autograft transplantation group (group A) or the conjunctival autograft transplantation (group B) using a random number table. The superotemporal conjunctiva was exposed in group A. The thin onion-like conjunctival flap was grasped with a microscissors and pulled forward to preserve the epithelial layer; when pulling forward, the Vogt area of the corneal limbus was included to ensure that the conjunctival flap contains limbal tissue (1 mm). The conjunctival flap was then properly attached to the exposed area of the sclera after pterygium excision. Care was taken to avoid effusion and hemorrhage beneath the conjunctival flap. The corneal margins of the conjunctival flap were sutured with an 8-0 suture through the shallow sclera, and then, the remaining two corners of the conjunctival flap were sutured as well; finally, the four sides of the conjunctival valve were sutured and fixed properly. The main difference between the two surgical methods was that the conjunctival flap in group A contained limbal stem cell tissue, whereas that in group B did not. At the end of the surgery, an anti-inflammatory eye ointment was applied to the conjunctival sac.

On the first postoperative day, routine dressing was performed, and tobramycin and dexamethasone eye drops, levofloxacin eye drops, and sodium hyaluronate eye drops were administered four times a day. Tobramycin and dexamethasone eye drops were instilled three times a day in the second week, twice a day in the third week, and once a day in the fourth week. Levofloxacin eye drops and sodium hyaluronate eye drops were administered for two weeks, during which intraocular pressure was monitored. Sutures were removed two weeks after the surgery and medications were discontinued after a month.

## Postoperative management

The patients were examined and observed using slit lamp biomicroscopy and fluorescein staining, and the evaluation criteria were as follows: (1) cure: no conjunctival congestion, with smooth and transparent corneal surface showing no new blood vessels; and (2) recurrence: bulbar conjunctival hyperplasia, congestion, fibrovascular tissue invasion of corneal limbus, and invasion range > 1 mm.

## Statistical analysis

The data generated from this study were analyzed with SPSS 18.0 statistical software. Quantitative data were presented as mean  $\pm$  standard deviation. Two independent samples t-test was used to assess the difference test between groups. Counting data were compared with the  $\chi^2$  test, and  $P < 0.05$  was considered statistically significant.

## Results

### Patient follow-up

The patients were followed up every day in the first week, once a week in the first month, once every three months in the first year, and once every six months in the second year. Both groups had a certain degree of foreign body sensation after operation, accompanied with occasional tingling and tearing. These symptoms were most obvious on the second postoperative day, after which they gradually reduced.

### Operative time and corneal epithelial healing time

The operative time was measured from anesthetic administration for local infiltration to conjunctival flap suture. The average operative time for group A was  $27.56 \pm 1.48$  minutes, whereas that of group B was  $26.91 \pm 1.39$  points. The average operative time for group A was longer than that of group B. There was no significant difference between the two groups ( $t = 1.93$ ,  $P = 0.058$ ).

The average healing time of corneal epithelial defects was  $2.56 \pm 0.34$  days in group A and  $4.85 \pm 0.49$  days in group B. The healing time of corneal epithelial defects in group A was shorter than that in group B. There was a significant difference between the two groups ( $t = 25.26$ ,  $P < 0.001$ ).

### Comparison of recurrence rate

Two groups of patients were followed up for 24 months. Eight patients dropped out of the study during follow-up for various reasons; 72 patients participated in the final evaluation. Two cases showed recurrence in group A (recurrence rate - 2.78%); there were nine cases of recurrence after surgery in group

B (recurrence rate - 14.29%). The recurrence rate in group A was significantly lower than that in group B ( $\chi^2 = 4.82, P < 0.05$ ).

## Complications

In group B, there were two cases of conjunctival granuloma. No infectious keratitis, corneal ulcers, medial rectus muscle injuries, conjunctival flap exfoliations, scleral dissolutions, eyelid adhesions, or other complications were observed in both groups.

## Discussion

Due to the lack of effective therapeutic drugs, surgical excision is currently the only option for effective treatment of pterygium. With the increasing use of microsurgical techniques, patients' expectations of improved visual and cosmetic outcomes are increasing. There are several surgical methods available for the treatment of pterygium. At present, no surgical method can absolutely prevent the recurrence of pterygium. The recurrence of pterygium usually occurs within one year after surgery, which is a major challenge for ophthalmologists. Limbal-conjunctival autograft transplantation is currently considered one of the most effective surgical procedures for treating pterygium[18, 19]. Based on the results of the present study, limbal-conjunctival autograft transplantation is superior to conjunctival autograft transplantation in terms of recurrence rate and corneal epithelial healing time. Limbal stem cells are present in the Vogt barrier structure of the corneal basal layer. They repair corneal injuries and maintain epithelial homeostasis; in addition, they can increase the number of corneal epithelial cells by differentiation and proliferation and inhibit the migration of conjunctival epithelial cells. Furthermore, they are indispensable for enabling the corneal tissue to maintain transparency[19, 20]. In conjunctival autograft transplantation, limbal stem cells are derived from the patient's own tissues, and no immune rejection occurs. Conjunctival flaps with limbal stem cells shorten corneal epithelial healing time and reduce the recurrence rate of pterygium. The possible reason for this is that conjunctival flaps provide healthy limbal stem cells for the defect area, which restore the barrier function of the corneal conjunctival margin to a certain extent. In contrast, without limbal stem cells, neovascularization and abnormal tissue can invade the cornea easily, leading to an increased possibility of recurrence. Although there are many surgical methods for the treatment of pterygium, each has its advantages and disadvantages. Therefore, in clinical practice, ophthalmologists should make individualized treatment plans according to the patient's condition and hospital setting. Limbal-conjunctival autograft transplantation and conjunctival autograft transplantation have little difference in operative time, but in terms of reducing corneal epithelial healing time and recurrence rate, limbal-conjunctival autograft transplantation seems to be superior to conjunctival autograft transplantation.

The main strength of this study is that it was a self-control study. The limitation of the study is that the sample size was not large enough. Owing to the insufficiency of samples, there logically comes a

limitation as the result. Further studies on the clinical feature of pterygium surgery involving larger samples, prospective study designs are needed to verify the findings of the present study.

## **Conclusion**

This study showed that limbal-conjunctival autograft transplantation has the advantages of faster corneal epithelial healing time and lower recurrence rate compared with conjunctival autograft transplantation in the treatment of primary pterygium. The surgical technique is relatively simple and incurs less injury. Therefore, limbal-conjunctival autograft transplantation is an easy method that is seemingly better for the treatment of primary pterygium at present.

## **Declarations**

### **Ethics approval and consent to participate**

the informed consent obtained from study participants was written and the ethic committee of Minhang Hospital, Fudan University [issue: medical ethics committee (2015) No(32)] approved this procedure.

### **Consent for publication**

not applicable.

### **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests

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### **Authors' contributions**

TY W: data analysis and interpretation and write the article

YF G: collection and assembly of data

Y Z: perform surgeries

L P: research concept and design

All authors read and approved the final manuscript.”

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## Tables

**table 1 Surgical time and corneal epithelial healing time in two groups [±s]**

group	Eye number	Surgical time	corneal healing time
group A	72	27.561.48	2.560.34
group B	72	26.911.39	4.850.49
t		1.93	25.26
P		0.058	<0.001

group A: Limbal-conjunctival autograft transplantation

group B: conjunctival autograft transplantation

**table 2 Comparison of recurrence rate between two groups after operation (24 months)**

	recurrence	No recurrence
group A	2[2.78%]	70[97.22%]
group B	9[14.29%]	63[85.71%]
$\chi^2$		4.82
P		0.028

group A: Limbal-conjunctival autograft transplantation

group B: conjunctival autograft transplantation