symblepharon

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Huixiang Ma*^(D), Jiahui Shen*^(D), Xuhao Chen^(D), Xianfeng Ye^(D), Shuxia Xu^(D) and Zongduan Zhang^(D)

Abstract

Background: Managing recurrent pterygium combined with symblepharon presents significant challenges in ophthalmology. Clinicians aim to reconstruct the ocular surface, alleviate eye movement restrictions, and minimize recurrence risks.

The efficacy and safety of continuous blanket

suture for severe recurrent pterygium with

Objective: Evaluation of efficacy and safety of continuous blanket sutures (CBS) for fixation of large autologous conjunctival grafts in patients with severe recurrent pterygium with symblepharon.

Methods: Retrospective, observational case series. Thirty-nine patients (40 eyes) were included, all with severe recurrent pterygium with symblepharon. During surgery, CBS was employed to affix large autologous conjunctival grafts to the exposed sclera, aiming to restore the ocular surface to smoothness as much as possible. All patients were followed up for more than one year. Main outcome measures include the rate of recurrence, improvement of eye movement, and intraoperative and postoperative complications.

Results: Nearly all patients exhibited a smooth ocular surface and largely restored physiological structures during the follow-up period. There were no graft loss or contraction cases until the last follow-up, with only three eyes experiencing a pterygium recurrence (recurrence rate 7.5%, 3/40). Preoperative eye movement limitations improved significantly from 2.10 ± 0.71 (range 1–3) to 0.33 ± 0.53 (range 0–2; p < 0.001) post-surgery. Other postoperative complications included varying degrees of corneal scarring and a single instance of conjunctival granulomatous hyperplasia (1 eye, 2.5%).

Conclusion: When addressing severe recurrent pterygium with Symblepharon, using CBS to secure large autologous conjunctival grafts during surgery can achieve favorable postoperative outcomes. This surgical method is safe and feasible and effectively rebuilds a smooth ocular surface, improves the appearance of the ocular surface, and reduces the recurrence rate of pterygium after excision.

Keywords: continuous blanket suture, conjunctival autograft, recurrent pterygium, surgical technique, symblepharon

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Introduction

A pterygium is a wing-shaped fibrovascular proliferation of the conjunctiva that progressively encroaches upon the corneal surface.¹ The occurrence of pterygium is generally associated with environmental and lifestyle factors. Previous studies have indicated that advanced age, being male, outdoor occupations, and living in rural areas are the primary risk factors for pterygium.^{2,3} Pterygium recurrence mostly occurs within the first 12 months after surgery, characterized by fibrovascular infiltration and inflammation.^{1,4} This condition often leads to recurrent episodes, marked by subconjunctival fibrosis and corneal thinning, which are further complicated by the development of corneal scars. Additionally,

Correspondence to: Zongduan Zhang

National Clinical Research Center for Ocular Diseases, EyeHospital, Wenzhou Medical University, 270 Xueyuan Road, Wenzhou, Zhejiang 325027, China zzduan@yeah.net

Huixiang Ma

Xuhao Chen Xianfeng Ye Shuxia Xu

National Clinical Research Center for Ocular Diseases, EyeHospital, Wenzhou Medical University, Wenzhou, China

Jiahui Shen

National Clinical Research Center for Ocular Diseases, EyeHospital, Wenzhou Medical University, Wenzhou, China Department of Optometry, Wenzhou Eye Valley Super Eye Hospital, Wenzhou, Zhejiang, China

*These contributed equally to this study as the first authors

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recurrent pterygium is frequently compounded by symblepharon, a condition typically arising from associated scarring, which presents a spectrum of clinical complications. Mild symblepharon near the lacrimal punctum may obstruct tear flow, potentially leading to dry eye syndrome. In contrast, more extensive symblepharon in the inferior fornix can deplete the tear reservoir, disrupting the effective distribution of tears across the tear meniscus and ocular surface.^{5,6} Such recurrences with symblepharon pose significant treatment challenges due to alterations in the conjunctival fornix length, the extension of scar tissue into the rectus muscles, and more rapid corneal involvement.^{7–9}

Previously, surgeons have explored ocular surface reconstruction using substitutes such as conjunctival tissue and amniotic membranes following symblepharon release.^{10–13} Despite these efforts, the recurrence rate remains high.^{5–11} These complexities necessitate sophisticated management strategies to address the multifaceted impact of recurrent pterygium and associated symblepharon on ocular health.¹⁴ Additionally, aside from recurrence, issues such as graft loss, conjunctival fragility, and poor extensibility resulting from previous surgeries must also be addressed.

In previous studies, our research team has identified the advantages of the Continuous Blanket Suture (CBS) technique in ocular surface surgeries, particularly in pterygium excision.¹⁵ This suturing method effectively disperses the tensile forces exerted on the graft and has been demonstrated to address complications such as the loss or contraction of large grafts and the issue of recurrence. It is considered by surgeons for application in patients with recurrent pterygium combined with symblepharon, potentially achieving desirable outcomes with fewer grafts. In this retrospective study, we analyzed cases where the CBS technique was employed during surgery in patients with recurrent ptervgium with symblepharon.

Methods

This retrospective analysis was performed on 40 eyes from 39 patients diagnosed with recurrent pterygium and concurrent symblepharon, utilizing the CBS technique during surgical interventions from March 1, 2014, to June 30, 2017. This research was conducted under the auspices of the

ethics committee and adhered to the principles outlined in the Declaration of Helsinki. All subjects or their legal guardian gave written informed consent to participate.

Inclusion criteria: (1) Patients diagnosed with recurrent pterygium and concurrent symblepharon; (2) patients who have undergone one or more pterygium excision surgeries previously; (3) patients meeting the clinical indications for surgery; and (4) patients able to adhere to a 1-year postoperative follow-up regimen.

Exclusion criteria: (1) Patients with active ocular inflammation or infection; (2) patients with severe ocular diseases, such as glaucoma or retinal disorders; (3) patients with systemic diseases that could affect surgical outcomes or postoperative recovery, such as severe diabetes or hyperthyroidism; and (4) patients allergic to surgical or anesthetic agents.

These patients received pterygium surgical interventions conducted by the same seasoned ophthalmologist. The preoperative data collected included patient demographics, the number of previous pterygium excision surgeries, anterior segment photography, and the degree of ocular limited abduction.

The assessment method for ocular limited abduction is as follows: limited abduction was estimated using a slit-lamp microscope. Based on the 9-point scale mentioned in the chapter 'Diagrammatic Recording of Ocular Motility' of *Clinical Orthoptics* and considering that all patients in this study presented with limited abduction, the method for recording movement restrictions was simplified. A horizontal slit lamp light band was adjusted to estimate the degree of abduction.¹⁶ A ratio of approximately 0–1/4 was 1 (normal); 1/4-2/4 was 2 (mild); 2/4-3/4 was 3 (moderate); and 3/4-1 was 4 (severe).

The surgical procedure utilized the CBS technique, with detailed descriptions of the methodology provided in subsequent sections. Sutures were removed on the 10th day postoperatively, coinciding with the initial follow-up. Additional follow-up assessments were scheduled at 1 month, 6 months, and annually post-surgery, during which the postoperative status of the ocular surface and any complications were systematically documented and evaluated.

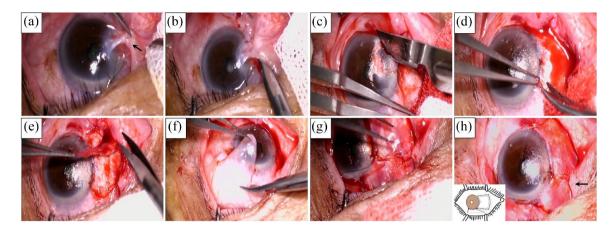


Figure 1. Key surgical steps. (1) Observation of Affected Region: The left eye exhibited involvement of the superior lacrimal point, indicated by an arrow, alongside severe restrictions in motility (a); (2) Preparation of Surgical Site: Healthy conjunctival tissue was carefully dissected on either side of the pterygium neck, followed by blunt dissection of the fascia tissue (b); (3) Removal of Pterygium from Cornea: The pterygium tissue adhering to the cornea was meticulously excised, and the corneal surface was subsequently scraped to ensure smoothness (c); (4) Excision of Pterygium and Subconjunctival Fibrosis: Using scissors, both the pterygium tissue and subconjunctival fibrosis were excised from the limbus to the posterior edge, revealing a smoothly bare scleral surface (d); (5) Extensive Removal of Tenon's Capsule: The subconjunctival Tenon's capsule was extensively removed to prevent recurrence (e); (6) Graft Harvesting: A graft was harvested from the superior nasal bulbar conjunctiva (f); (7) Graft Placement and Suturing: The conjunctival graft was accurately positioned on the bare sclera and secured with CBS. The fornix was reconstructed near the lacrimal point, indicated by an arrow. A schematic representation of the CBS technique at the recipient site is displayed in the lower left corner (g); (8) Post-surgical Assessment: Following graft fixation, the corneal surface appeared smooth and free of significant motility limitations (h).

Surgery process

Fully informed surgical consent was obtained from all patients before surgery. After disinfecting the ocular surface and administering topical anesthesia, an appropriate amount of 2% lidocaine hydrochloride was injected subconjunctivally at the site of the ptervgium. Initial accurate identification of the pterygium boundaries was essential. The superior and inferior edges of the ptervgium were incised using ophthalmic scissors. The pterygium head was carefully detached from the cornea with toothed forceps, and the body of the pterygium, along with the underlying hyperplastic tissues, was transected. At this stage, the surgeon carefully distinguished and removed scar tissue on the scleral surface until after the attachment point of the internal rectus muscle, further separating and eliminating the scar tissue beneath the conjunctiva of the retracted fornix. The surgeon must preserve the normal conjunctival epithelial tissue as much as possible for subsequent manipulation. Subsequently, the retracted conjunctiva was repositioned to the superior and inferior fornices, aiming to restore a smooth and continuous structure at the inner canthus and fornices much as possible, thus preparing for as

the subsequent grafting. Residual tissues were meticulously excised using a circular scalpel to refine the corneal surface. Throughout this process, the extensively exposed sclera was consistently shielded with sterile gauze to ensure protection.

A trapezoid conjunctival graft of similar size to the prepared site was harvested from the infratemporal or supertemporal bulbar conjunctiva. Before harvest, a local anesthetic (lidocaine hydrochloride, 2%) was administered at the donor site, and the bulbar conjunctiva was simultaneously separated from Tenon's capsule. The residual conjunctiva from the donor side was drawn toward the corneal limbus and intermittently sutured with two stitches using a 10-0 nylon thread between the limbus and the sclera, ensuring complete coverage of the exposed sclera (Figure 1).

The free auto-conjunctival graft was transplanted onto the bare sclera using the CBS technique, previously described by the surgeon ZZD.¹⁵ This technique involved placing continuous stitches around the graft, excluding the limbus. The distal ends of the sutures were not knotted but threaded **Table 1.** Patient characteristics (preoperative and postoperative).

Parameters	Data
Number of eyes (right/left)	16/24
Sex (M/F)	25/14
Age (mean \pm SD, years)	61.00 ± 7.76
No. previous operations (mean ± SD)	1.68 ± 0.83
Recurrence rate	7.5% (3/40)
Ocular motility restriction	
Preoperative	2.10 ± 0.71
Postoperative	0.33 ± 0.53
<i>p</i> Value	p<0.001*
Complications	
Corneal nebula	31 (77.5%)
Corneal macula	4 (10.0%)
Leucoma	2 (5.0%)
Granulomatous hyperplasia	1 (2.5%)

*Chi-square test, p < 0.05 was considered statistically significant.

through the tail of the preceding knot. The final knot was secured with the tail of the initial knot. All sutures were arranged radially, perpendicular to the edge of the graft, and were passed through the episclera. Additionally, at the corneal limbus, supplementary interrupted sutures were considered to ensure precise apposition of the limbal conjunctiva, particularly if the alignment was suboptimal.

Postoperative treatment included applying ofloxacin eve ointment (Singi Pharmaceutical, Shenvang, China) thrice daily for 4weeks, in conjunction with tobramycin/dexamethasone eve drops (Alcon-Couvreur, Puurs, Belgium) four times daily, which were then gradually tapered until discontinued. The initial follow-up occurred 10 days post-surgery, at which the point sutures were removed. Following the cessation of the topical tobramycin/dexamethasone, treatment with 0.1% fluorometholone eye drops (Santen Pharmaceutical Co., Osaka, Japan) was initiated, then tapered and discontinued within 1 month. Recurrence was

identified by the emergence of fibrovascular proliferative tissue crossing the limbus. Patients were advised to seek immediate hospital care in the event of any acute complications, including but not limited to graft detachment, suture loosening, and significant subconjunctival hemorrhage. Notably, no patients in this study experienced such acute postoperative complications.

Statistic

The data in our study are presented as mean \pm SD and were analyzed by SPSS statistical software (version 24.0; SPSS Inc., Chicago, IL, USA). Change in ocular limited abduction before and after surgery was compared using the paired Student's *t*-test. Categorical variables between groups were analyzed using the Chisquare test. P < 0.05 was considered statistically significant.

Results

During the follow-up period (mean, 32.65 ± 9.47 months; range, 13.10-56.27 months), a total of 40 eyes of 39 patients (25 males and 14 females, age 61.00 ± 7.76 years) were included in our study. The characteristics data and the clinical outcomes of patients are given in Table 1.

There were different degrees of restricted ocular motility in each of the 40 eyes preoperatively. The mean preoperative ocular limited abduction was 2.10 ± 0.71 , significantly improving to 0.33 ± 0.53 postoperatively (p < 0.001). The recurrence rate was 7.5% (3/40).

Postoperative follow-up results indicated that the smoothness of the corneal anterior surface was satisfactorily restored, and the physiological structure of the ocular surface was largely regained. Rough scarring was observed between the edge of the graft and the lacrimal caruncle in almost all eyes but was unnoticeable to the naked eye. However, residual corneal scarring of varying degrees was inevitable, including corneal opacity in 31 eyes (77.5%), corneal nebula in 4 eyes (10.0%), and leukoma in 2 eyes (5.0%). There was 1 patient with postoperative conjunctival granuloma hyperplasia (2.5%). This was later excised, and no recurrence was found during follow-up. None of the patients reported severe discomfort, pain, or a foreign body sensation. No additional postoperative complications were noticed during long-term follow-up.



Figure 2. Representative cases. The lacrimal points (indicated by arrows) adhere to the eyeball preoperatively and were reconstructed after surgery. Despite varying degrees of corneal scarring in most cases, the cosmetic outcomes were satisfactory.

Discussion

In this study, we addressed the challenge of treating recurrent pterygium combined with symblepharon bv employing an autologous conjunctival transplant secured with CBS. This technique minimized the stretching of the surrounding tissues and effectively restored the smoothness and physiological structure of the ocular surface (Figure 2). Notably, our approach vielded a low recurrence rate during a follow-up period exceeding 13.10 months, providing sufficient time to conclusively identify any recurrences.17,18

In our study, we employed an advanced suture technique that integrates CBS with scleral tacking to secure conjunctival grafts firmly to the ocular surface, ensuring minimal graft mobility. This method utilizes a single knot configuration in the CBS, which markedly diminishes the sensations of foreign bodies and reduces irritation, compared to traditional interrupted sutures.15 Extensive removal of recurrent pterygium and the transplantation of a large graft necessitate an increased number of knots at the recipient bed when using the traditional interrupted suture technique. However, excessive suture ties can elevate discomfort and inflammation, potentially inducing a granulomatous foreign body reaction and contributing to the formation and progression of pterygium.¹⁹ This problem will be solved when applying CBS.

Research has shown that applying primary pterygium surgical techniques to recurrent cases increases the risk of secondary recurrence.20 Consequently, surgeons are investigating more aggressive or novel techniques, either standalone or in combination, to improve outcomes despite the increased procedural complexity and associated costs. Specifically, Mitomycin C (MMC) is applied directly to the exposed sclera in the postexcision phase of pterygium to reduce recurrence which often leads to a higher incidence of severe postoperative complications, including uveitis, glaucoma, and scleral melting.^{11,21} Alternatively, some researchers suggest that injecting 5-FU into the lesion after surgery can prevent the progression of potential or existing recurrent pterygium. According to their findings, this method has a success rate of over 75%. However, it can also cause complications such as scleral thinning, corneal toxicity, and graft-related issues. The optimal dosage and injection frequency have not vet been established.²² In this study, we successfully mitigated these significant risks by opting for CBS without any associated risks or the need for longterm monitoring. The study confirmed that for patients with recurrent pterygium combined with symblepharon, optimal clinical outcomes can be achieved by strategically planning the conjunctival graft area in conjunction with the CBS suturing technique. This approach is associated with low costs and minimal risks and does not require additional medications during the procedure, thereby eliminating concerns regarding potential side effects.

Our surgical strategy emphasized the complete removal of scar tissue, extensive excision of

Tenon's capsule, and the use of a large graft to isolate the cornea from the conjunctiva. Expanding the excision and enlarging the graft, as suggested by Hirst, can achieve a recurrence rate near zero.^{20,23} These findings are corroborated by other studies, suggesting that extensive removal of Tenon's capsule is pivotal in achieving low recurrence rates.^{24,25} In our study, the surgeon excised Tenon's capsule approximately 5-10 mm beyond the edge of the conjunctival defect and 3-5 mm beyond the superonasal and inferonasal half-edges of the pterygium folds. The primary rationale for this approach was to smooth the graft's edge, ensure a precise fit to the conjunctival edge around the entire perimeter, and minimize conjunctival scarring.

The anatomical importance of the conjunctival fornix in maintaining a tear reservoir crucial for ocular surface health cannot be overstated. The presence of pterygium with symblepharon disrupts this integrity, necessitating the restoration of the deep fornix and tear meniscus as prerequisites for successful limbal stem cell transplantation.¹³ Our technique involved the surgical release of symblepharon, a fundamental step in reconstructing the fornix in patients with fornix contracture or symblepharon.

The presence of symblepharon typically extends the duration of surgery and is associated with suboptimal recovery of ocular surface functionality, as well as potential postoperative visual impairment and pain.¹² Few studies have recorded the operating time of their technique for managing recurrent pterygium. Mashhoor Al Fayez⁷ reported 39.12 min in limbal-cunjuctival autograft (LCAG) and 37.58 min in cunjuctival autograft CAG. The P.E.R.F.E.C.T method used by Hirst required 1.5–2h.²³ Although operating time is related to case complexity, the surgeon's proficiency, and the technique used, the time necessary in our study, less than 20 min, was significantly reduced when compared with other studies.

We have examined the literature on the outlook for repeat pterygium surgery over the past decade, as presented in Table 2. Certain surgical approaches have displayed favorable outcomes, with a relatively low incidence of recurrence. Nonetheless, the patient's age and the criteria used to define recurrent pterygium after surgery have a significant influence on estimating the rate of postoperative recurrence. To facilitate comparative research, we have identified key factors that should be considered in future investigations, including surgery, age, and definition of recurrence.

Table 2 Literature	on the curaical a	nnroachae far raeurra	nt ntorvaium ovo	r the nact decade
	on the surgical a	pproaches for recurre	ni pierygiuni ove	i lile past decade.

Year	Author (s)	Surgery	Age (years)	Number of eyes	Recurrence rate (%)	Mean follow-up periods (months)	Definition of recurrence
2012	Bekibele, Charles O et al.	CAG with 5-FU	49.8 ± 13.8	46	8.7	8.8±7.3 (over all)	Over limbus
		CAG with MMC	51.9 ± 12.1	34	11.8		
2012	Zaky, Khaled S, and Yasser M Khalifa	Preoperative injection of mitomycin + bare sclera pterygium excision surgery	55.1 ± 10.1	25	4	12	Over limbus
		intraoperative application of mitomycin + bare sclera pterygium excision surgery	57.5 ± 9.9	25	8	12	Over limbus
2013	Mashhoor Al Fayez,	CAG	36.9 ± 3.5	100	10	63 (36–96)	Over limbus
		LCAG	36.1±3.2	105	1	61 (36–96)	Over limbus

(Continued)

Table 2. (Continued)

Year	Author (s)	Surgery	Age (years)	Number of eyes	Recurrence rate (%)	Mean follow-up periods (months)	Definition of recurrence
2013	Narsani, Ashok Kumar et al.	CAG with MMC	43.26 ± 12.81	65	4.6	6	Over limubs>1mm
2013	Ozgurhan, Engin B et al.	CAG + topical Bevacizumab drop for 2 months	48.4±11.3	22	0	6	Over limbus
		CAG	50.5±17.8	22	9.1	6	
2014	Huchzermeyer, C et al.	Combined ipsilateral autologous limbus and homologous amniotic membrane transplantation	63 (50–72)	4	25%	39 ± 4	NA
2014	Akhter, Waseem et al.	CAG	60 (51.50– 63.00)	26	7.96	6	Over limubs>1mm
		CRFG	57 (45.00- 60.00)	31	9.76	6	Over limubs>1mm
2014	Katırcıoglu, Yasemin Arslan et al.	Amniotic Membrane Transplantation(AMT) with MMC	59.1 ± 12.1	25	8	28.8 ± 15.7	Over limbus
		CAG with MMC	55.4±12.9	30	13.3	25.9 ± 24.4	Over limbus
2016	Ono, Takashi et al.	preserved limbal autograft and amniotic membrane	67.0±8.9	84	11.9	73.0±38.1 (12–154)	Over limbus
2016	Toker, Ebru, and Muhsin Eraslan	CAG with Fibrin Glue	52.0 ± 13.7	37	5.4	12	Over limbus
		AMT with Fibrin Glue	49.8 ± 14.1	36	13.8	12	
2017	José Bonifácio Barbosa, et al.	AMT with narrow-strip conjunctival autograft	52.1±11.7	39	9.75	12	Over limbus
		CAG	45.8 ± 12.9	41	17.9	12	Over limbus
2017	Chen, Rongxin, et al. ²⁶	LCAG with MMC	53.10 ± 12.18	47	2.1	12	Over limbus
		AMT with MMC	55.77 ± 11.87	46	10.9	12	Over limbus
2017	Lee, Jun Seok et al.	LCAG	56.5 ± 10.2	126	4	17.7±17.6	Over limbus
2018	Monden, Yu et al.	MMC, double amniotic membrane transplantation, and a large conjunctival flap	68.2±11.3	31	3.2	43.2±34.8 (6-127)	Over limbus
2018	Rosen, Ronald	AMT with MMC	51.9 ± 13	556	5.8	17.3 ± 0.8	Over limbus
2019	Kam, Ka Wai, and Alvin L Young	LCAU	54.3 ± 10.7 (over all)	17	5.9	189.6±6 (over all)	over limbus>1.5mm
		MMC		15	0		Over limbus>1.5mm

(Continued)

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Table 2. (Continued)

Year	Author (s)	Surgery	Age (years)	Number of eyes	Recurrence rate (%)	Mean follow-up periods (months)	Definition of recurrence
		LCAU with MMC		8	0		Over limbus>1.5mm
2019	Chen, Di et al.	Excimer laser Phototherapeutic Keratectomy + LCAG	55.1 ± 10.1	39	10.34	50.4 ± 38.1 (over all)	Over limbus
		LCAG	57.5 ± 9.9	60	13.3		
2020	Monden, Yu et al.	MMC, Double Amniotic Membrane Transplantation, Cryopreserved Limbal Allograft, and a Conjunctival Flap	73.8±6.1	10	0	36.0 ± 22.8 (12-80)	Over limbus
2021	Lee, Jong Soo et al.	Double-sliding flaps procedure	59.5±11.3	53	7.5	8.3±13.0 (6-48)	Over limbus
2021	Trinh, Tanya et al.	Ipsilateral simple limbal epithelial transplantation (SLET), MMC, tenonectomy, and AMT	60.70 6 ± 18.4	10	10	15.2±10.0	Over limbus>1mm
2021	Wagdy, Faried M et al.	CAG with MMC	41.8 ± 15.98	32	0	24	Over limbus>1mm
		CAG with Ologen implantation	46.2±12.77	31	8	24	Over limbus>1mm
2022	Sharma, Vikas et al.	Sutureless and glue-free limbal- conjunctival autograft	32.52 ± 6.49	25	8	12	Over limbus
2022	Kim, Yonwook Justin et al.	CAG + MMC	51.9 ± 13.8 (over all)	8	0	22.5 ± 23.7 (over all)	NA
		CAG		17	17.7		
		AMG + MMC		11	45.5		
		AMG		5	80		
2022	Allam, Waleed A et al.	Extended conjunctival transplant	41.2 ± 10.3	33	0	25.64 ± 9.24	Over limbus

In this study, all cases included a different degree of symblepharon, which may be labeled C3 (the caruncle was flattened) as described by Jingbo Liu et al.²⁷ We used a self-developed method to evaluate the degree of symblepharon. Although grade 1 is considered to be a mild restriction, considering the age of the patients, some may have been within a normal range. Even so,

postoperative improvements in eye movement were significant in both groups. Furthermore, we achieved a low recurrence of three eyes, few patients had postoperative complications, and none had severe postoperative complications such as severe pain, granuloma, or scleral melting. These results were comparable with those of previous studies. Due to the flattened caruncle and symblepharon, postoperative scars at the bulbar conjunctiva were inevitable. Because of accelerated corneal involvement, corneal nebula was seen in almost all cases. However, the bulbar conjunctiva and cornea scars were invisible to the naked eye. We therefore achieved satisfying cosmetic results, following a previous study by Hirst et al.²³

A limitation of this study is that we did not perform preoperative and postoperative comparisons of ocular surface function. The surgeon released the symblepharons during the procedure to restore the smooth ocular surface and physiological structures as much as possible. However, we did not conduct assessments of ocular surface function, such as tear film break-up time. Additionally, it is impossible to compare this surgical method with other effective procedures concurrently to better evaluate its advantages and disadvantages, no control group was established. In conclusion, our study showed that CBS used for large conjunctival autograft fixation is an effective and easy technique for the management of severe recurrent ptervgium and symblepharon. This technique is worthy of clinical promotion and adoption.

Declarations

Ethics approval and consent to participate

This research was conducted under the auspices of the Ethics Committee of the Affiliated Optometry Hospital of Wenzhou Medical University (2020-170-K-155) and adhered to the principles outlined in the Declaration of Helsinki.

Consent for publication

Consent for publication was obtained from the participants.

Author contributions

Huixiang Ma: Investigation; Writing – original draft; Writing – review & editing.

Jiahui Shen: Data curation; Investigation; Writing – original draft; Writing – review & editing.

Xuhao Chen: Data curation; Writing – original draft.

Xianfeng Ye: Data curation.

Shuxia Xu: Data curation; Formal analysis; Writing – original draft.

Zongduan Zhang: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing – original draft; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data supporting this study's findings are available from the corresponding author upon reasonable request.

ORCID iDs

Huixiang Ma (D) 6428-0062	https://orcid.org/0009-0000-
Jiahui Shen 🝺 4881-5838	https://orcid.org/0009-0008-
Xuhao Chen 🕩 3611-817X	https://orcid.org/0000-0002-
Xianfeng Ye D 6755-752X	https://orcid.org/0009-0001-
Shuxia Xu 🕩 https 8380	://orcid.org/0009-0009-7413-
Zongduan Zhang 0002-9509-231X	bttps://orcid.org/0000-

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