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Cryopreserved Amniotic Membrane Using the TissueTuck Technique: A Sutureless Approach for Pterygium Surgery

Neel R. Desai, MD, and Bryan Adams, MS3

Purpose: The purpose of this study was to evaluate the clinical outcomes of the TissueTuck technique in the management of pterygium.

Methods: This was a single-center, retrospective review of patients with primary or recurrent pterygium that underwent surgical excision followed by application of cryopreserved amniotic membrane (AM) using the TissueTuck technique. All patients underwent surgery between January 2012 and May 2019. Patient profile, surgical time, complications, and rates of pterygium recurrence were analyzed.

Results: A total of 582 eyes of 453 patients (328 female patients; 65.1 ± 13.9 years) were included for analysis and initially presented with primary (92%) pterygium. The average duration of pterygium excision surgery was 14.7 ± 5.2 minutes (median: 14, range: 4–39 minutes) with mitomycin C administration in 257 (45%) eyes. At the last follow-up of 30.2 ± 22.2 months (median: 24.5, range: 3–94 months), BCVA significantly improved from logMAR 0.23 at baseline to logMAR 0.19 ($P < 0.0001$). Recurrence rate was 2.3% but only 0.7% (2/274) in those cases with primary, single-headed pterygium without mitomycin C treatment. Other postoperative complications in that cohort included granuloma (7.9%), scarring (3.8%), and diplopia in extreme lateral gaze (2.5%). The AM remained secured to the ocular surface throughout the postoperative period.

Conclusions: The TissueTuck surgical technique with cryopreserved AM can be performed in minimal time and result in a low recurrence and complication rate after pterygium surgery.

Key Words: amniotic membrane, pterygium

(*Cornea* 2023;42:181–185)

Pterygium is a common ocular surface disease characterized by abnormal fibrovascular tissue of the conjunctiva that commonly encroaches onto the cornea and causes visual impairment.[1–6] Surgical excision is the only treatment option; however, persistent inflammation and inadequate removal of fibrovascular tissue are believed to contribute to pterygium recurrence.[7–10] Consequently, many techniques have been devised over the years to mitigate recurrence and achieve better postoperative outcomes. Mitomycin C (MMC) is one such modality that has been used intraoperatively to suppress fibroblast proliferation and prevent recurrence.[11,12] Furthermore, transplantation of amniotic membrane (AM) or conjunctival autograft with or without limbal tissue has been used to reduce recurrence rates to under 10%.[13–15] The use of cryopreserved AM can be advantageous because it has shown to reduce inflammation, scarring, and angiogenesis;[16–18] promote conjunctival epithelialization;[19,20] and aid in limbal epithelial stem cell expansion.[21] Although cryopreserved AM is effective, its success is dependent on the application method and surgical technique as demonstrated by the wide range of recurrence rates.[21–25]

After pterygium bare scleral excision, a gap is created between the remaining conjunctiva and Tenon capsule (Fig. 1B; gap denoted by “”). This gap, which is more evident and open in the caruncle area, can allow infiltration of fibrovascular tissue and cause pterygia to recur.[26] Sealing the gap with sutures or fibrin glue along with subsequent AM transplantation (AMT) creates a strong barrier against re-entry and has been shown to reduce pterygium recurrence to ≤6.3%.[26–29] In this article, we describe a reproducible technique of AMT termed TissueTuck, which uses cautery to seal the Tenon capsule and fibrovascular tissue to prevent advancement of fibrovascular tissue followed by the placement of oversized cryopreserved AM that is tucked deep inside the gap. Therefore, the principal goals of this surgical technique are to remove the abnormal fibrovascular tissue and seal the gap using cauterization and AMT to prevent recurrence and improve cosmesis without complications.

MATERIALS AND METHODS

On the IRB approval, we retrospectively reviewed the medical records of all patients who underwent pterygium excision using AMT by the same surgeon (N.D.) at The Eye Institute of West Florida (Largo, FL) between January 2012 and May 2019 and had completed at least 3 months of follow-up.

TissueTuck Surgical Technique

Topical anesthesia with tetracaine was applied. A 7-0 Vicryl (Ethicon; Raritan, NJ) corneal traction suture was then placed to achieve adequate exposure and put the medial rectus

Received for publication November 1, 2021; revision received June 2, 2022; accepted June 11, 2022. Published online ahead of print September 16, 2022.

From the The Eye Institute of West Florida, Largo, FL.

The authors have no funding or conflicts of interest to disclose.

Correspondence: Neel R. Desai, MD, The Eye Institute of West Florida, 1225 W Bay Dr, Largo, FL 33770 (e-mail: desaivision2020@gmail.com).

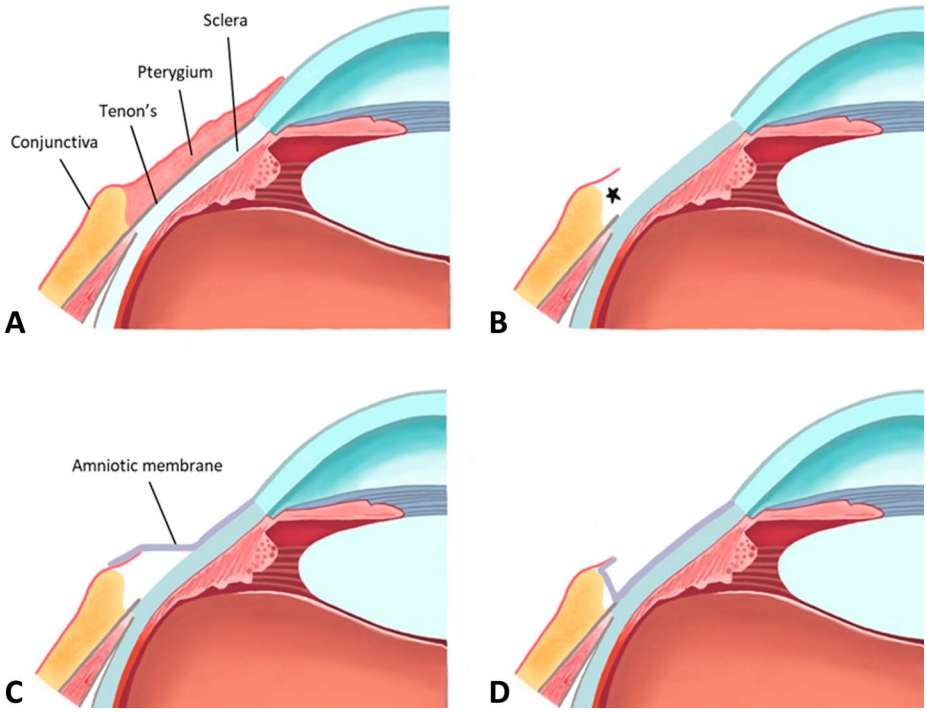

FIGURE 1. Representative surgical steps of the TissueTuck technique. Fibrovascular tissue growth between the conjunctiva and the Tenon fascia displaces the semilunar fold, causing recurrent pterygium (A). After meticulous dissection of all fibrovascular tissue and Tenon fascia, a gap () is invariably created (B). After application of thrombin and fibrinogen, an oversized piece of amniotic membrane is slid over the scleral bed and placed 3 to 4 mm past the edge of the posterior conjunctival rim (C). The graft is then swept and tucked under the conjunctival rim and pinched to the edge of the conjunctiva to create a wide margin of contact, which further seals the gap and helps to barricade fibrovascular growth (D).

muscle under tension against the globe. Subconjunctival injection of 2% lidocaine with epinephrine was performed to separate tissue planes. Pterygium head was excised from the cornea and lifted away from the scleral surface to allow for blunt dissection of fibrovascular tissue and abnormal Tenon. Relaxing incisions through conjunctiva and Tenon along the planned superior and inferior wound margins were created. The fibrovascular tissue, Tenon, and conjunctiva were resected along the leading border of where the new semilunar fold would be recreated. Tenon and remaining fibrovascular tissue were then pulled anteriorly and excised until they naturally recessed at least 2 to 3 mm to allow the conjunctiva to lay flat against bare sclera. Conjunctival tissue was recessed and not resected in recurrent cases. Next, angled bipolar cautery with angled McPhersons forceps was used to cauterize the leading edge of Tenon capsule and fibrovascular tissue to seal the conjunctival–Tenon gap. This creates the first barrier to prevent advancement of fibrovascular tissue and produces a well-defined rim for reconstruction of the semilunar fold. In cases of aggressive or recurrent pterygia, sponges were soaked in 0.02% MMC and applied to the gap covering the fornix region 10 to 20 seconds, avoiding unnecessary contact with the bare sclera. The eye was then thoroughly rinsed with balanced salt solution to avoid prolonged exposure, necrosis, or stromalysis.

Cryopreserved AM (AmnioGraft; Bio-Tissue, Miami, FL) was trimmed to the general shape of the exposed bed, oversizing the graft by at least 2 to 3 mm in width and 3 to 4 mm in length. Using 2 curved tying forceps, the AM was temporarily placed with the sticky stromal side down on the cornea. Next, 3 drops of the thrombin were dripped at the limbus and allowed to spread over the scleral bed. Excess pooled thrombin was blotted away. Next, 3 drops of fibrinogen were applied, and the AM was slid over the scleral bed using curved tying forceps, coating the stromal side with glue, and placed 3 to 4 mm past the edge of the posterior conjunctival rim. The AM was then tucked under the conjunctival rim and into the gap (Fig. 1) exposing the stromal side of the graft to the stromal side of the conjunctival rim. Forceps were then used to pinch the edge of the conjunctiva to the AM, and the glue was "squeegeed" in an anterior direction so that glue is not sequestered posteriorly in the gap. This creates the second barrier to recurrence. The superior and inferior conjunctival margins were inspected, and if a raised transition was observed, the conjunctiva was again raised, additional Tenon was removed, and the conjunctiva reglued smoothly down. Any excess glue or AM was removed, traction suture was removed, and bandage contact lens (BCL) was placed.

Postoperative Management and Follow-up

Postoperative treatment included antibiotics and difluprednate 0.05% (Durezol, Alcon) 4 times a day for the first week, the latter of which was tapered over 4 weeks. The BCL was removed 1 week after surgery. Patients who were observed to have conjunctival injection at the operative site or any apparent fibrovascular tissue regrowth in the area of the gap or reconstructed semilunar fold postoperatively were administered ~0.3 cc triamcinolone acetonide (Kenalog) injection, which was performed after concentrating the triamcinolone acetonide solution by allowing the 40 mg particulate in 1 cc to settle out of solution and decanting off the diluent. For patients noted to have granuloma in the postoperative period, the granuloma was excised and triamcinolone was injected. Recurrence was the primary

outcome measured and was defined as postoperative fibrovascular regrowth on the conjunctiva or growth that extended to the cornea across the limbus. Recurrence was only reported for those patients with a follow-up duration of 6 months or greater. Complications such as pyogenic granuloma, inclusion cysts, dellen formation, and epithelial defects were also recorded.

Statistical Analysis

All statistical analyses were performed using SPSS v20.0 (IBM SPSS Statistics, Chicago, IL). A P value <0.05 was used to determine statistical significance. Kaplan-Meier survival analysis and the log-rank test were used to compare the time to recurrence by stratifying primary and recurrent pterygia. The influence of risk factors such as age, sex, and ethnicity on the relation with time to recurrence was evaluated by Cox proportional hazards survival regression. Binary logistic regression was used to determine the influence of age, sex, race, smoking status, comorbidities, surgical history, surgical duration (obtained from anesthesia records), and use of MMC on developing complications.

RESULTS

A total of 746 eyes of 590 patients underwent pterygium excision with AM using the TissueTuck technique from January 2012 and May 2019 by a single surgeon. Of these, 164 eyes (137 patients) had less than 3 months of follow-up and were excluded. Thus, 582 eyes of 453 patients (328 female patients and 254 male patients; 65.1 ± 13.9 years) were included for analysis. Pterygium was primary in 524 (90%) eyes. Nearly all patients presented with single-head pterygium (96%). Eighty-five (15%) patients had undergone prior ocular surgeries such as pterygium or neoplasia excision (9%), keratoplasty (3%), and ocular surface reconstruction (1%). Patient characteristics are presented in Table 1.

The average duration of pterygium excision surgery was 14.7 ± 5.2 minutes (median: 14, range: 4–39 minutes), 22.4 ± 8.0 minutes for recurrent cases and 14.0 ± 4.4 minutes for primary pterygium ($P < 0.0001$). MMC was administered in 257 (45%) eyes. Baseline characteristics are compared by intraoperative treatment regimen in Table 1. Surgery was uneventful in all cases, and the AM remained secured to the ocular surface postoperatively (Fig. 2).

Postoperatively, Kenalog injection was administered in 79 (14%) patients at 3.3 ± 2.7 months (median: 2, range: 1–12 months). Of these eyes, 82% had experienced postoperative complications including granuloma (63.3%), diplopia (7.6%), and scarring (6.3%). Notably, no eyes that underwent injection experienced pterygium recurrence and these eyes demonstrated a trend for improved visual acuity compared with eyes without injection, although not statistically significant (logMAR 0.13 vs. logMAR 0.20; $P = 0.12$). Significant predictors of receiving Kenalog injection included male patients, age, history of shingles, and history of conjunctival cysts.

At the last follow-up of 30.2 ± 22.2 months (median: 24.5, range: 3–94 months), BCVA significantly improved from logMAR 0.23 at baseline to logMAR 0.19 ($P < 0.0001$). For eyes that had at least 6 months follow-up (n = 529), recurrence occurred in 12 (2.3%) patients at an average follow-up of 15.7 ± 10.7 months. The recurrence rate was 0.4% (2/529) at 6 months, 1.7% (7/420) at 1 year, 3.1% (9/294) at 2 years, and 5.7% (12/211) at 3 years. Overall recurrence was higher in cases that were recurrent (4.2%) versus primary (2.1%), double-head (9.1%) versus single-head (2.0%), and treated with MMC (3.2%) versus AM alone (1.3%) ($P > 0.05$). The recurrence rate was only 0.7% (2/274) in those cases with primary, single-headed, AM alone without MMC application. Other postoperative complications are listed in Table 2, which included granuloma (11.9%), scarring (5.7%), and diplopia (4.0%). Diplopia, when noted, was only reported in extreme lateral gaze because no cases of diplopia affecting primary gaze were

TABLE 1. Demographics and Characteristics of Pterygium Cases

	AM (n = 315)	AM-MMC (n = 257)	*P*
Age (yr)	69.9 ± 12.3	59.4 ± 12.8	<0.0001*
	72 (18, 93)	60 (22, 86)	
Sex, n (%)			
Female	215 (66%)	109 (34%)	<0.0001*
Male	100 (40%)	148 (60%)	
Race/Ethnicity, n (%)			
White	265 (62%)	163 (38%)	<0.0001*
Hispanic	22 (31%)	48 (69%)	
Black or African American	16 (41%)	23 (59%)	
Asian	10 (44%)	13 (57%)	
Smoker, n (%)			
Yes	10 (32%)	21 (68%)	0.008*
No	302 (57%)	231 (43%)	
Pterygium type, n (%)			
Primary	299 (96%)	225 (88%)	0.001*
Recurrent	12 (4%)	31 (12%)	
Morphological features, n (%)			
Single-head	308 (57%)	237 (43%)	0.0001*
Double-head	4 (17%)	20 (83%)	
Comorbidities, n (%)			
Conjunctivochalasis	153 (91%)	15 (9%)	<0.0001*
Thyroid disease	84 (77%)	25 (23%)	<0.0001*
Ocular rosacea	32 (84%)	6 (16%)	0.0002*
Dry eye disease	154 (74%)	55 (26%)	<0.0001*
Rheumatoid Arthritis	28 (90%)	3 (10%)	<0.0001*
Glaucoma	21 (55%)	17 (45%)	0.98
Preoperative BCVA (logMAR)	0.28 ± 0.46	0.17 ± 0.25	0.0004*
	0.1 (0, 3)	0.1 (0, 2.3)	
Postoperative BCVA	0.24 ± 0.42	0.13 ± 0.22	<0.0001*
	0.1 (0, 3)	0.1 (0, 2.3)	
Surgical time (min)	13.9 ± 4.3	15.6 ± 6.0	<0.0001*
	13 (4, 30)	14 (7, 39)	
Follow-up (mo)	35.3 ± 22.7	23.5 ± 19.7	<0.0001*
	34 (3, 94)	16.7 (3, 82)	

*Statistically significant. BCVA, best corrected visual acuity; logMAR, logarithm of the minimum angle of resolution.

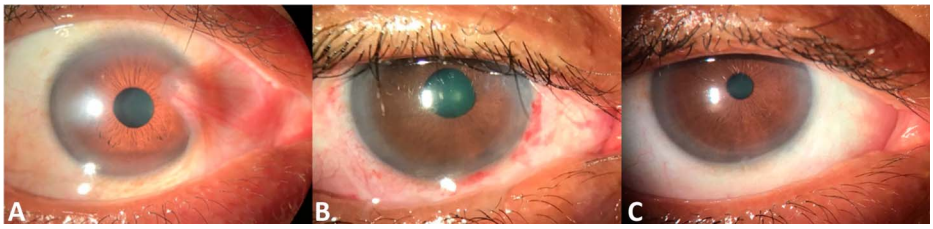

FIGURE 2. Representative case. Preoperative pterygium with moderate vascularity and anteriorly displaced semilunar fold with poor anatomic definition (A). Postoperative day 1 after TissueTuck technique with AMT, without MMC (B). Postoperative day 21 shows excellent cosmesis and restored anatomic integrity of the reconstructed semilunar fold (C).

noted. Further statistical correlative analysis showed that the aforementioned complications occurred more frequently in cases that received MMC than those who did not (34.6% vs. 20.0%, $P < 0.0001$). Postoperative granuloma (16.7% vs. 7.9%, $P = 0.002$), scarring (8.2% vs. 3.8%, $P = 0.03$), and diplopia (5.8% vs. 2.5%, $P = 0.055$) occurred more frequently in eyes treated with MMC compared with those who received AM alone.

DISCUSSION

Pterygium recurrence rates after bare scleral excision and AMT have been reported from 0% to 41% for primary cases[22–24] and 0% to 53% for recurrent cases.[25,30] Although many factors likely contribute to recurrence, the surgical technique is presumably the single most important factor. Sealing the gap between the conjunctiva and the Tenon capsule after pterygium excision is one technique that has been shown to reduce pterygium recurrence to ~6%.[26,28] Over 27.5 ± 20.5 months (range: 3–86 months), Liu et al[26] noted recurrence in only 2 cases (6.25%) after sealing the gap for multirecurrent pterygia. Although 3 different approaches (anchoring suture, fibrin glue, and running suture) were used in that study, they found a running suture most effectively sealed the gap. In another study of 556 eyes, Rosen[28] modified the surgical technique by using cauterization to seal the gap, followed by 0.02% MMC and AMT with fibrin glue to achieve a recurrence rate of 5.8% over 17.3 ± 0.8 months (range 6–74 months). In this study, cauterization was also used to seal the gap, followed by MMC application in only 45% of eyes, and AMT with fibrin glue in all eyes, resulting in an overall recurrence rate of 2.3% and only 0.7% in cases of primary, single-headed, AM alone (no MMC). Notably, this is one of the lowest recurrence rates reported thus far in a study of this size, and there was no graft dislodgement or displacement during the postoperative period.

TABLE 2. Postoperative Complications

	AM (n = 315)	AM-MMC (n = 257)	Total
Recurrence	4 (1.3%)	8 (3.2%)	12 (2.1%)
Granuloma	25 (7.9%)	43 (16.7%)	68 (11.9%)
Scar	12 (3.8%)	21 (8.2%)	33 (5.7%)
Diplopia (in extreme lateral gaze)	8 (2.5%)	15 (5.8%)	23 (4.0%)
Symblepharon	1 (0.3%)	1 (0.4%)	2 (0.3%)
Minor subconjunctival hemorrhage	—	1 (0.4%)	1 (0.2%)
Mild conjunctival necrosis	—	1 (0.4%)	1 (0.2%)
Inferior corneal infiltrates	—	1 (0.4%)	1 (0.2%)
Band keratopathy	1 (0.3%)	—	1 (0.2%)
Neovascularization	1 (0.3%)	4 (1.6%)	5 (0.9%)
Recurrent corneal lesion	—	1 (0.4%)	1 (0.2%)
Scleromalacia	—	2 (0.8%)	2 (0.3%)
Conjunctival cyst	4 (1.3%)	—	4 (0.7%)
Cicatrization of cornea	1 (0.3%)	—	1 (0.2%)
Epithelial defect	2 (0.6%)	2 (0.8%)	4 (0.7%)
Residual conjunctivochalasis	3 (1.0%)	1 (0.4%)	4 (0.7%)
SPK/diffuse keratitis	1 (0.3%)	1 (0.4%)	2 (0.3%)
Wound dehiscence	1 (0.3%)	—	1 (0.2%)
Conjunctival lesion	2 (0.6%)	1 (0.4%)	3 (0.5%)
Corneal melt	2 (0.6%)	—	2 (0.3%)
Corneal edema	2 (0.6%)	—	2 (0.3%)

SPK, superficial punctate keratitis.

Contrary to what has been reported in the literature, cases that received MMC had a slightly higher rate of recurrence (3.2% vs. 1.3%) in this study. This may also be why Rosen reported a slightly increased recurrence rate because MMC was used in all cases as opposed to only 45% of eyes in this study. MMC was selectively used in our cases for more aggressive pterygium cases that were recurrent, double-headed or for high-risk patients (Table 1). Thus, these cases already had a worse prognosis and were at a higher risk for developing recurrence as well as more postoperative complications. In fact, complications were more frequently observed in the MMC cases, which are likely attributed to the higher-risk profile. Pyogenic granuloma was a most frequently noted complication in this study, appearing in nearly 12% of cases (Table 2). Nevertheless, pyogenic granuloma is well recognized as an easily treatable complication after pterygium excision, with incidences reported from 24% to 40%[31] with intraoperative MMC and 1% to 16%[32,33] when accompanied by AMT. Hence, the use of the TissueTuck technique with or without MMC may mitigate recurrence and complications compared with the use of MMC alone.[31]

Aside from sealing the gap, this surgical technique offers several other advantages. The operative procedure takes less than 15 minutes on average, which is significantly shorter than the 30 to 60 minutes procedures that use

conjunctival autografts.[34,35] This surgery also preserves the conjunctiva in case of future glaucoma surgery and has innate biological properties known to reduce inflammation, scarring, and angiogenesis;[16–18] promote conjunctival epithelialization;[19,20] and aid in the expansion of limbal epithelial stem cells. These advantages, along with the low complication rate, suggest the TissueTuck technique with cryopreserved AM is beneficial treatment for addressing pterygium.

ACKNOWLEDGMENTS

The authors would like to thank TissueTech for awarding an investigator-initiated grant for this project and assisting in the drafting of the manuscript. Dr. Desai is a speaker, consultant, and stockholder for Bio-Tissue, Inc.

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