

Evicel versus Tisseel versus Sutures for Attaching Conjunctival Autograft in Pterygium Surgery

A Prospective Comparative Clinical Study

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Purpose: To evaluate the outcome of pterygium surgery with conjunctival autograft using Vicryl sutures (Ethicon, NJ), Evicel fibrin glue (Omrix Biopharmaceuticals Ltd, Ramat-Gan, Israel), or Tisseel fibrin glue (Baxter Corp., Deerfield, IL).

Design: Prospective, randomized study.

Participants: Eighty-nine adult patients with primary pterygium.

Methods: Patients undergoing pterygium surgery with conjunctival autografting were randomized into groups receiving 10-0 Vicryl sutures, Evicel fibrin glue, or Tisseel fibrin glue.

Main Outcome Measures: Duration of surgery, level of patient discomfort, visual acuity (VA), surgically induced refractive change (SIRC), complications, and pterygium recurrence.

Results: Eighty-nine patients participated: 25 in the Vicryl group, 29 in the Evicel group, and 35 in the Tisseel group. The patients' preoperative characteristics were similar in all groups. Fashioning and repositioning of the conjunctival autograft (flap time) was significantly shorter in the fibrin glue groups compared with the Vicryl group: 5.46 minutes for Evicel, 3.6 minutes for Tisseel, and 16.72 minutes for sutures ($P < 0.0001$). The patient discomfort level during the first postoperative day was significantly lower in the fibrin glue groups compared with the suture group ($P = 0.047$). There were no significant group differences in the change in logarithm of the minimum angle of resolution VA before surgery and 3 months after surgery ($P = 0.7$). There were also no significant group differences in the SIRC ($P = 0.108$). The recurrence rate was 17.24% in the sutures group, 4.17% in the Evicel group, and 0% in the Tisseel group ($P = 0.027$ sutures vs. fibrin glue groups). Complications included 5 cases of conjunctival graft dislocation in the Evicel group, 1 case of pyogenic granuloma in the Tisseel group, and no complications in the sutures group ($P = 0.019$ sutures vs. fibrin glue groups).

Conclusions: Tisseel fibrin glue for the repositioning of conjunctival autografts in pterygium surgery was associated with a similar functional outcome as that of Vicryl sutures in terms of VA and SIRC. Pterygium recurrence, patient discomfort level, and surgery time were reduced markedly, as were flap dislocation and pterygium recurrence with Tisseel fibrin glue compared with Evicel fibrin glue. *Ophthalmology* 2017;124:61-65 © 2016 by the American Academy of Ophthalmology



Supplemental video is available at www.aaojournal.org.

Pterygium (Latin for “little wing”) is an abnormal fibrovascular proliferative tissue extending to the cornea in the interpalpebral area. It is usually located on the nasal side, but sometimes it can be on the nasal and temporal side and rarely only on the temporal side. The cause of pterygium is unknown; however, genetic predisposition, immune mechanism, and chronic environmental irritations, including ultraviolet radiation, wind, and dust particles, are all considered risk factors.¹ Surgical removal is the treatment of choice. The prime challenge of pterygium surgery is the prevention of recurrence. Reports in the literature show that bare sclera excision alone has high recurrence rates (30%–70%).² Adjunctive postoperative therapies, such as β -irradiation or 5-fluorouracil and mitomycin C, reportedly

have reduced the recurrence rate to 4%–43%.^{3,4} Autologous conjunctival grafting seems to be the best method, yielding both a low recurrence rate and fewer side effects.^{5,6}

In an autologous limbal conjunctival autograft technique, the bulbar conjunctiva, including limbal tissue, is attached to the exposed scleral bed either by sutures or fibrin glue after the pterygium is excised.⁷ Fibrin glue is a blood-derived product that imitates the final stage of the coagulation cascade.⁸ It has been used for more than 20 years as an adhesive or sealant agent in a broad variety of surgical specialties,^{9–11} including various ophthalmic indications.¹² Today, there are a number of types of fibrin glue that are different in their composition. Tisseel (Baxter Corp., Deerfield, IL) and Evicel (Omrix Biopharmaceuticals Ltd, Ramat-Gan, Israel) are 2 of

the most common fibrin glues in clinical use worldwide. Evicel contains 3 components, human fibrinogen and human thrombin mixed with calcium chloride, whereas Tisseel contains 5 components, fibrinogen mixed with coagulation factor 13 and aprotinin, and thrombin mixed with calcium chloride.

Some earlier studies compared the use of Evicel with sutures in pterygium surgeries,^{13–15} whereas others compared the use of Tisseel with sutures.^{16–18} Those studies found that the advantages of fibrin glues over sutures included less surgery time and less pain after surgery, whereas the advantage of sutures over fibrin glue included more clinical experience.

The advantages of fibrin glues over sutures have led to their increasingly widespread use in pterygium surgery. To the best of our knowledge, differences in postoperative refraction and surgical outcomes between the 2 glues and between them and sutures have not been examined before. Therefore, the purpose of the current study was to compare clinical, economic, and surgical aspects of the use of Vicryl sutures (Ethicon) versus Evicel fibrin glue versus Tisseel fibrin glue in pterygium surgery.

Methods

Patient Selection and Data Collection

This was a prospective, randomized study. Adult patients with primary pterygium and for whom surgery was advised participated in the study. They were assigned randomly to 1 of 3 groups: Evicel fibrin glue, Tisseel fibrin glue, or 10-0 polyglactin (Vicryl) sutures. The patients and the surgeon were aware of group assignment. All operations were performed by a single surgeon (G.J.B.S.).

The following data were collected and analyzed: age, gender, best-corrected visual acuity (VA) before surgery and at 3 months after surgery, automatic refraction before the procedure and 3 months afterward, flap time (the time from fashioning the conjunctival autograft until attachment of the autograft to the bare sclera), patient discomfort on the first postoperative day (patients graded their pain from 1 = least amount of discomfort to 10 = most amount of discomfort), complications up to 3 months after the surgery, and recurrence rates up to 3 months after the surgery. Snellen VA was converted to logarithm of the minimum angle of resolution (logMAR) values. The differences between the preoperative and the 3-month postoperative logMAR values were calculated and compared among the 3 groups.

The study was approved by the local institutional review board of the Sheba Medical Center. The surgical procedure complied with the tenets of the Declaration of Helsinki, and the participants provided informed consent.

Surgical Technique

After instillation of topical lidocaine (Bausch & Lomb UK Ltd., Surrey, UK), the involved eye underwent standard ophthalmologic sterile preparation and draping, after which it was exposed for surgery by means of a lid speculum. Lidocaine was injected into the pterygium head and the upper conjunctiva. The pterygium was separated from the underlying sclera and surrounding conjunctiva by blunt dissection. The pterygium head was excised and the sclera was exposed. A limbal conjunctival autograft was formed from the superior limbus and placed on top of the cornea and kept moist. The graft was sutured to the bare sclera area with continuous

Table 1. Demographics Characteristics

Group	Vicryl	Evicel	Tisseel	P Value
Patients (no.)	25	29	35	
Age (yrs)	52.4	59.59	60.79	0.088
Gender (male:female)	16:09	16:13	22:13	0.445
Eye (right:left)	10:15	14:15	18:17	0.667

sutures by a 10-0 Vicryl suture, or a drop of fibrinogen solution together with a drop of thrombin solution were placed on the bare sclera in the Evicel and Tisseel groups. Then the graft was flipped over immediately and spread out onto the bare sclera coated with fibrinogen solution. Neomycin sulfate/polymyxin B sulfate/dexamethasone ointment (Maxitrol ointment; Alcon Laboratories, Fort Worth, TX) was applied to the operated eye and a pressure patch and an eye shield were kept in place for 24 hours (Video 1, available at www.aojournal.org).

Surgically Induced Refractive Change

To evaluate the surgically induced refractive changes (SIRCs) between the preoperative and the 3-month postoperative examinations, the difference between each postoperative refraction and the respective preoperative refraction was calculated for both eyes using double-angle mathematical methods for subtraction of refractions, as described by Holladay et al.¹⁹

Statistical Analysis

The statistical analysis was performed by an analysis of variance (ANOVA) test to compare the differences among the 3 groups with regard to epidemiologic factors, flap time, patient discomfort on the first postoperative day, logMAR VA values, SIRCs, and recurrence rates. The *t* test was used to calculate differences in variables between 2 groups. Chi-square analyses were used to calculate proportional difference among the groups. The overall significance level was set to an α value of 0.05. The statistical analysis was carried out using Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA) and SPSS software version 13.0 (SPSS, Inc., Chicago, IL).

Results

Demographics

Eighty-nine patients participated in the study. The Vicryl suture group consisted of 25 patients (16 men) with a mean age \pm SD of 52.4 ± 15.31 years (range, 25–76 years). The Evicel fibrin glue group consisted of 29 patients (16 men) with a mean age \pm SD of 59.59 ± 14.00 years (range, 31–84 years). The Tisseel fibrin glue group consisted of 25 patients (22 men) with a mean age \pm SD of 60.79 ± 14.76 years (range, 26–90 years). There were no significant group differences in age or gender. The demographics of the study population are summarized in Table 1.

Surgical Technique

There was no significant group difference in laterality of the operated eye (Table 1). The flap time in the Tisseel group was significantly shorter than the flap time in the other 2 groups (Tisseel vs. sutures, $P < 0.001$, ANOVA; Tisseel vs. Evicel, $P = 0.0165$, ANOVA). The mean flap times were: 16.72 minutes in the Vicryl group, 5.46 minutes in the Evicel group, and 3.60 minutes in the Tisseel group.

Table 2. Vision and Refraction Prognosis

	Vicryl	Evicel	Tisseel	P Value (ANOVA)	P Value (t test)
Preoperative logMAR	0.245	0.227	0.150	0.334	Vicryl vs. Tisseel, 0.175
3-Month postoperative logMAR	0.142	0.126	0.119	0.928	Vicryl vs. Tisseel, 0.706
Differences in logMAR (no. of patients)	0.095 (21)	0.088 (26)	0.057 (28)	0.703	Vicryl vs. Tisseel, 0.435
SIRC	1.52	1.33	2.35	0.108	Evicel vs. Tisseel, 0.049

logMAR = logarithm of the minimum angle of resolution; SIRC = surgically induced refractive change.

Vision and Refraction

There were no significant group differences in the mean logMAR VA values before surgery and those measured at 3 months after surgery (Table 2). The changes between the preoperative logMAR VA and the postoperative logMAR VA were: 0.095, 0.088, and 0.057 for the Vicryl, Evicel, and Tisseel groups, respectively. Those changes did not reach a level of significance ($P = 0.703$, ANOVA). The SIRCs for the Vicryl, Evicel, and Tisseel groups were: 1.52, 1.33, and 2.35, respectively ($P = 0.108$, ANOVA).

Short-Term and Long-Term Surgical Outcome

The patients graded the level of ocular discomfort on the first postoperative day as 3.42 in the Vicryl group, 1.73 in the Evicel group, and 1.83 in the Tisseel group. The differences between the level of discomfort between the Vicryl group and the Evicel group and between the Vicryl group and the Tisseel group were significant ($P = 0.031$ and $P = 0.028$, respectively, *t* test). However, the difference in the level of postoperative discomfort between the Evicel group and the Tisseel group was not significant ($P = 0.851$, *t* test).

There was no evidence of recurrence in the Tisseel group at 3 months after surgery, whereas the recurrence rate was 4.17% in the Evicel group and 17.24% in the Vicryl group ($P = 0.027$, ANOVA; Tisseel vs. Evicel, $P = 0.015$, ANOVA; Fig 1). Complications at 3 months after surgery included 5 cases of dislocated graft in the Evicel group, 1 case of pyogenic granuloma in the Tisseel group (which was removed surgically), and none in the Vicryl group ($P = 0.019$ for the fibrin groups vs. the suture group, ANOVA).

Discussion

Pterygium is a relatively common problem in the general population and more common among people in equatorial regions, probably because of the damaging effects of ultraviolet radiation.⁷ During the past decade, it was generally agreed that the best method for avoiding recurrence of pterygium is to attach an autograft to the bare sclera.⁴ However, the debate over the best approach

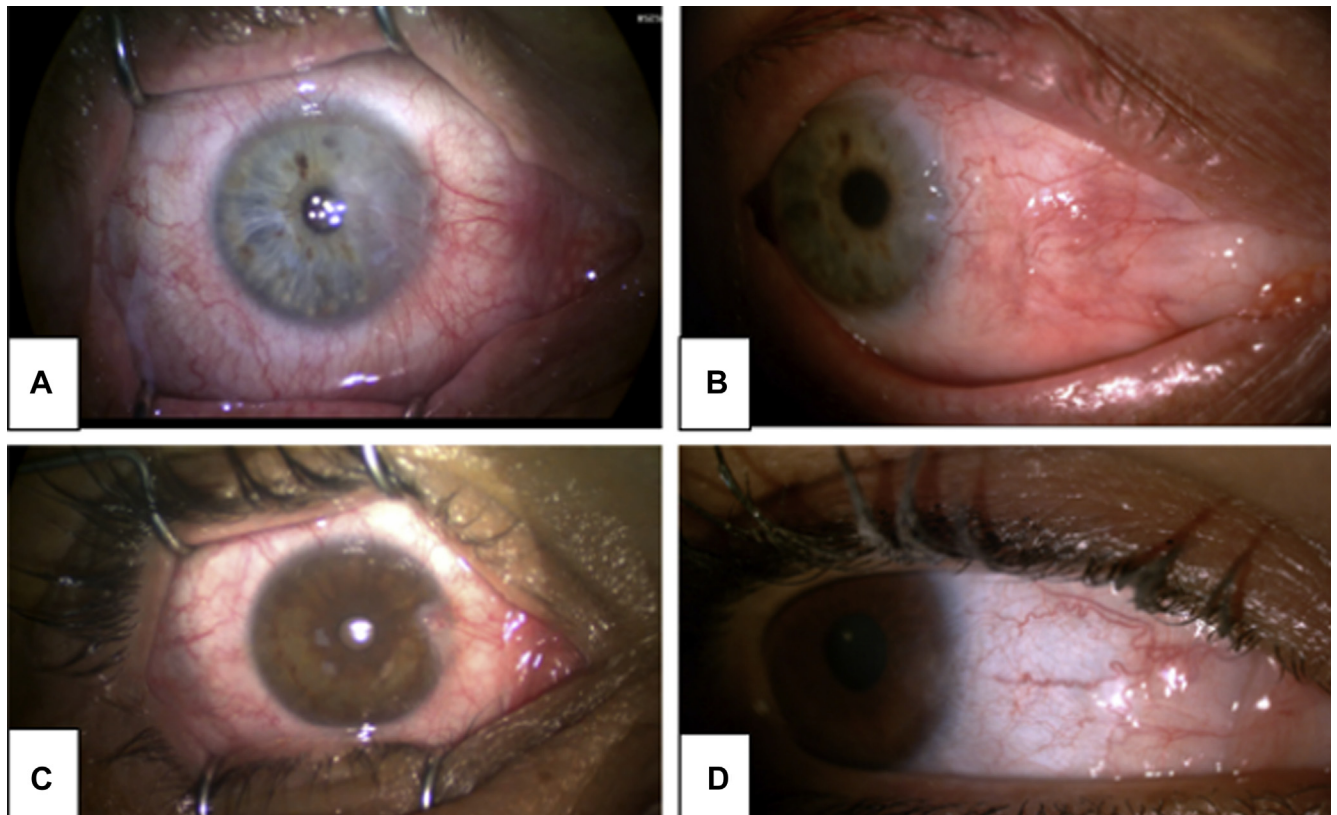


Figure 1. Preoperative and postoperative pterygium surgery with Tisseel fibrin glue. A, C, Before pterygium surgery. The pterygium tissue covers one half of the cornea. B, D, Three months after surgery. There has been no recurrence and the cosmetic results are good.

to attach the autograft has centered on whether surgeons should use sutures or fibrin glue.^{14,18} To the best of our knowledge, the question as to which is the best fibrin glue for this procedure has not been examined previously, nor have the differences in SIRC between the different methods. This study was designed to address those issues in a prospective, randomized trial of similar groups of patients.

We found that the use of fibrin glue shortened the time of surgery and lowered the level of patient discomfort on the first postoperative day. The Tisseel fibrin group had the lowest recurrence rate and no cases of dislocated graft. Our results showed that there were no group differences in changes in logMAR VA and SIRC at 3 months after surgery. Flap time was 5 times shorter in the Tisseel group and 3 times shorter in the Evicel group compared with the Vicryl group. These findings regarding flap time are of utmost importance in terms of operating theater time and shorter duration of local anesthesia.

One Vicryl suture costs US\$36 in Israel, whereas Evicel costs US\$795 and Tisseel costs US\$268. Each box of fibrin glue is used for 6 to 7 surgeries. Therefore, the cost of Vicryl is almost the same as that for 6 to 7 surgeries using Tisseel. Given that the operating theater time was much shorter in the Tisseel group, it seems that Tisseel is more cost effective than sutures and Evicel.

As expected, the patients reported less discomfort with the fibrin glues than with the sutures on the first postoperative day. Moreover, patients who also underwent pterygium surgery with a different approach on the contralateral eye reported a clear-cut difference in discomfort on the first postoperative day in favor of fibrin glue.

The VA of patients with pterygium is probably influenced by the size and location of the pterygium, the presence of astigmatism before surgery, and other characteristics, such as other ocular diseases. Therefore, it is not surprising that the choice of fixation method of the graft did not have any influence on the change in logMAR VA among the current study patients.

It is reasonable to consider that the SIRC will be higher in the sutures group than in the fibrin glues groups. However, our study results did not support such differences. We contend that it is the removal of the pterygium tissue in each method that causes changes in refraction, and not the method itself. Given that the sutures are in the conjunctiva and not on the cornea, they would not be expected to be associated with a big difference in the SIRC caused by them and the SIRC caused by the fibrin glues. However, we were surprised to find differences in SIRC between the Evicel and Tisseel groups. We think that those differences are related to the relatively small number of patients in each group, rather than to the product used for graft attachment.

There is no agreement in the literature regarding the differences in recurrence rates between fibrin glue and sutures. Some authors found both methods to have the same recurrence rates, whereas others found fewer recurrences with the fibrin glue method.^{20,21} Our findings showed no case of recurrence in the Tisseel group, some cases of recurrence in the Evicel group, and a high recurrence rate in the Vicryl group. Moreover, there were 5 cases of dislocated

graft in the Evicel group compared with none in the Tisseel group. We believe that those differences were caused by the differences in adhesive strength between the glues. Aprotinin and factor 13 are components of Tisseel fibrin glue, but not of Evicel fibrin glue. Aprotinin is a synthetic component used as a polyvalent protease inhibitor that prevents premature degradation of fibrin. Factor 13, which also exists in the human coagulation cascade, is a fibrin-stabilizing factor that cross-links the fibrin. We believe that those components strengthen the fibrin clot created by Tisseel and make it stronger than the fibrin clot created by Evicel.

In conclusion, we found that the use of fibrin glue permits shorter operative time and less postoperative discomfort compared with sutures in pterygium surgery. Tisseel fibrin glue is superior to Evicel fibrin glue in terms of lower price and shorter duration of surgery, and it is more effective because of lower recurrence rates and fewer dislocated grafts. Finally, there were no differences in the changes in logMAR VA and SIRC among the 3 study groups.

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Footnotes and Financial Disclosures

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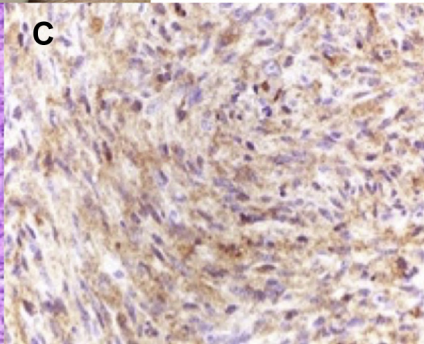
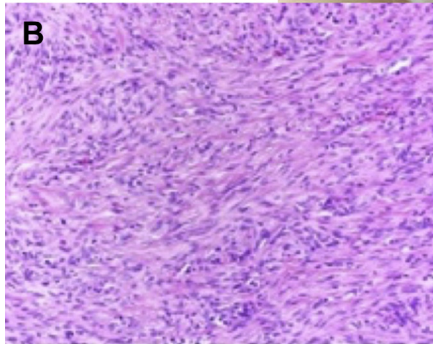
Abbreviations and Acronyms:

ANOVA = analysis of variance; **logMAR** = logarithm of the minimum angle of resolution; **MAR** = minimum angle of resolution; **SIRC** = surgically induced refractive change; **VA** = visual acuity.

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Pictures & Perspectives



Leiomyoma of the Palpebral Conjunctiva

A 58-year-old woman presented with a 6-week history of foreign body sensation from a growing left lower eyelid lesion. Physical examination showed a 1.0×0.8-cm, well-circumscribed, smooth, soft tissue mass of the medial left inferior palpebral conjunctiva distinct from the caruncle (Fig 1A). Excisional biopsy revealed intersecting eosinophilic fascicles of bland spindle cells showing blunt-ended and elongated nuclei with fine chromatin and indistinct nucleoli without mitotic activity, atypia, or pleomorphism (Fig 1B). Immunohistochemistry showed positivity to muscle specific actin (Fig 1C) and negativity to desmin, CD34, and S100 stains confirming a diagnosis of conjunctival leiomyoma.

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