

## Autologous Conjunctival Autograft versus Intraoperative Mitomycin C In Surgery Of Primary Pterygium

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**Abstract: Purpose:** To compare the one-year outcome of primary pterygium excision using intraoperative mitomycin C (MMC) versus the results of suturing a free conjunctival autograft (CA). **Methods:** A total of 73 eyes with nasal primary pterygium of 73 patients were included in the study. After randomization into two groups, the eyes were operated on by a single surgeon. After excision of the pterygium, 35 eyes received 0.04% MMC intraoperatively on the bare sclera for 3 min and 38 eyes received a free CA sutured using 7-0 Vicryl. Postoperative follow-up was 1 year. Main outcome measures were recurrences, re-operations, surgery time, complications, visual acuity and astigmatism. **Results:** The recurrence rate was 14/35 eyes (40%) in the MMC group and 2/38 eyes (5.3%) in the CA group ( $p < 0.05$ ). The re-operation rate of the recurrences was 57.1% in the MMC group and 50% in the CA group. Average surgery time was 13 minutes (range: 6–22 min) in the MMC group and 46 min (range: 28–60 min) in the CA group ( $p < 0.01$ ). There was no significant change in best corrected visual acuity and astigmatism. The most frequently observed complication was delayed epithelial healing (40%) and mild scleral thinning (20%) in the MMC group and suture-related inflammation in the CA group (10%). **Conclusion:** Pterygium surgery including free autologous conjunctival grafting is associated with fewer recurrences, re-operations and complications than using the bare sclera technique together with single-dose intraoperative MMC.

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### 1. Introduction

In pterygium surgery a variety of surgical procedures are in use. The bare sclera technique is still common because of its simplicity. Sliding or rotational conjunctival flaps are also popular. Today, there is overwhelming evidence that the sole use of the bare sclera technique is associated with a high risk of local recurrence.<sup>1,2</sup>

Adjunctive therapies, as beta-irradiation and antimetabolic drugs, like mitomycin C (MMC) are used<sup>3,4</sup> to decrease the recurrence rate.

MMC is an antineoplastic agent which alkylates and cross-links DNA, resulting in an inhibition of the cellular proliferation for a long time.<sup>5</sup> It has proved to be safe and beneficial in glaucoma surgery.<sup>6</sup> Postoperative MMC has been reported to decrease the recurrence rate to 2.3%–39% whereas the recurrence rate after conjunctival autograft has been reported to 2%–35%. However, the risk for significant side-effects following beta-irradiation<sup>7,8</sup> and postoperative MMC<sup>9,10</sup> is substantial.

Therefore, to reduce the risk of the complications, application of a single dose intraoperative MMC after the excision of the pterygium has been advocated by some authors.<sup>11-13</sup>

On the other hand, pterygium excision combined with transplantation of a free conjunctival Autograft appears safe and effective, but was usually used only for recurrent lesions.<sup>14</sup>

With the varying published results of bare sclera with preoperative MMC and sutured conjunctival autografts in mind, we decided to compare them in this controlled, prospective, open label, randomized trial with a follow up time of 1 year.

### 2. Patients and Methods:

Primary outcome measures were recurrence rate, recurrence onset and complication rate. Secondary outcome measures were best corrected visual acuity (BCVA) and induced astigmatism.

Following informed consent, 73 consecutive patients with primary nasal pterygium were enrolled in the trial.

One eye of each patient was randomized to receive either an adjunctive MMC (n = 35) or a free conjunctival autograft (CA) (n = 38) following pterygium excision. All eyes were operated on by a single surgeon and followed up during the study together with the same trained nurse who performed the preoperative and postoperative visual tests.

Demographic factors, previous medical and surgical treatment were recorded. All patients underwent complete ophthalmological examination. Visual acuity was averaged in a logarithmic fashion. Astigmatism was noted as the spectacle correction needed for best-corrected visual acuity, and only the amount of the astigmatism was averaged. The size of the pterygium was measured, its location and type was recorded. Pterygium area was calculated as if it

was a triangle. Patients with dry eyes, ocular surface disease and systemic collagenosis or vascular disorders were excluded from the study.

The surgery was performed using a gan operating microscope. Xylocain 10 mg/ml with adrenalin 5 lg/ml was used for topical and subconjunctival. An eye speculum was placed between the eyelids. The pterygium head was detached from the cornea (figures

1-a and 2-a), and the pathologic conjunctiva with the underlying Tenon's tissue was excised with scissors.

No extended excision of the Tenon's tissue under the remaining conjunctiva was performed. The cornea was scraped clean, the sclera cleared from connective tissue and any bleeding vessels were cauterized.

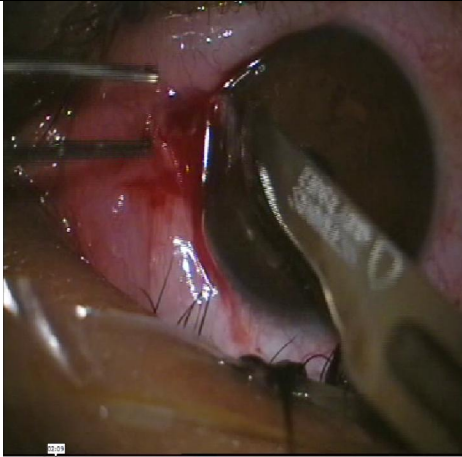


Figure 1-a: Dissection of the pterygium from the cornea (keratectomy) by a blade.



Figure 1-b: Taking the conjunctival graft with care to take conjunctival tissue only.

In the CA group, the autologous conjunctival graft was taken with care to reduce the amount of Tenon's tissue on the graft as much as possible and to be 30% larger than the pterygium site (Figure 1-b) and sutured at the pterygium site first by 4 cardinal sutures vicryl 6/0 (Figure 1-c) then other sutures to secure the rest of the graft (Figure 1-d). In the MMC group the sclera was left bare. MMC concentrations between 0.02 and 0.1% and duration between 2 and 5 min are reported. Here, we chose 0.04% and 3 min to have maximum efficacy with a reasonable safety (Figure 2-b). After 3 min, the sclera was rinsed with

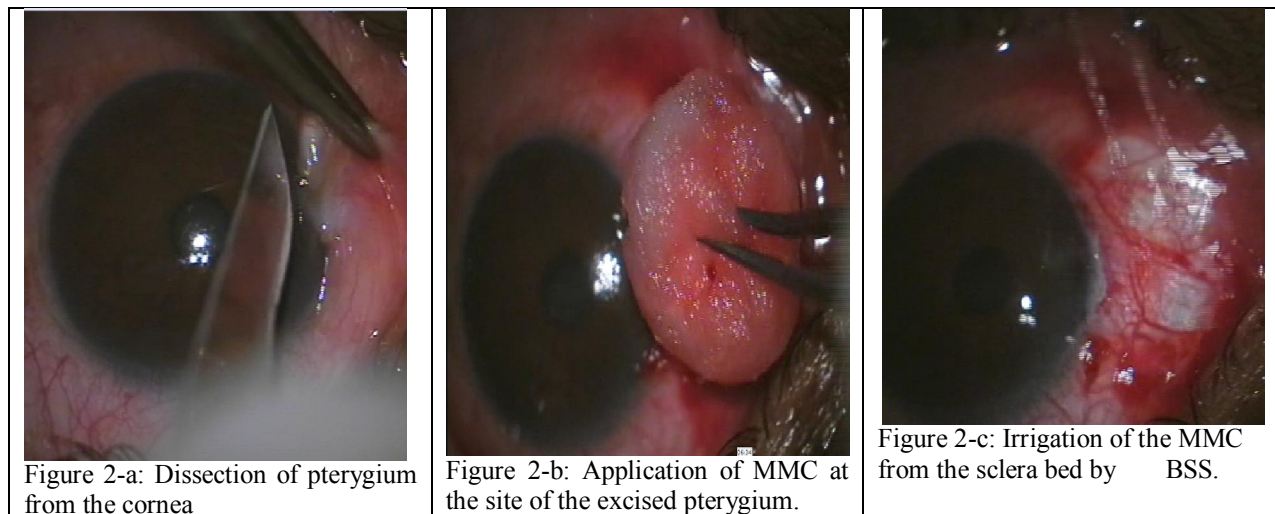
balanced salt solution (BSS; Alcon) (Figure 2-c). Postoperatively, the eyes were patched for 3 days. During the first postoperative week, dexamethason eye drops (Maxidex®; Alcon) were given six times daily together with tobramycin ointment. Dexamethason was tapered off over the next 5 weeks, and no additional antibiotics were given. The patients were examined 1 week, 1, 3, 6 and 12 months after surgery. A recurrence was defined as a lesion with more than 1 mm fibrovascular regrowth onto the cornea at the site of the surgery.



Figure 1-c: Fixation of the graft at the pterygium site by 4 cardinal sutures.



Figure 1-d: The conjunctival graft at the pterygium site.



Patients with recurrence were re-operated if the regrowth was symptomatic, aggressive or exceeded 3 mm or more onto the cornea.

### 3. Results:

There was a marked difference of the morphologic appearance of the recurrences in the two

groups: the recurrences in the MMC group were more aggressive, red and painful than those in the CA group. However, this difference was not quantified in our work.

After 1 year, the recurrence rate was 40% and 5.3% in the MMC and in the CA group, respectively ( $p < 0.05$ , chi-squared test).

**Table 1. BCVA and astigmatism before and 1 year after surgery**

	MMC	CA
Preoperative BCVA	0.8	1.0
Postoperative BCVA	0.9	1.1
Preoperative astigm (D)	0.49	0.51
Postoperative astigm (D)	0.78	0.73
No change detected	47.5%	39.6%

There was no significant difference between the preoperative and the postoperative values. CA = conjunctival autograft, MMC = mitomycin C.

**Table 2. Complications**

	MMC %	CA %
Conj fibrosis	31.4	5.3
Descemetocoele	2.5	0
Scleral thinning	20	5.3
Delayed epithelial healing	40	0
Avascular sclera	2.8	0
keratitis	5.7	2.6
symblepharon	5.7	0
Transpl necrosis	0	2.6
Suture irritation	0	10.5
Transpl over limbus	0	18.4
IOP elevation ( $\geq 30$ mmHg)	8.6	6.3

More complications occurred in the MMC group. Transplants spreading over the limbus have not caused any recurrence. CA = conjunctival autograft, MMC = mitomycin C.

The average age was  $48.3 \pm 15$  (range 22–78) in the MMC group and  $48.6 \pm 16$  (range 18–85) in the CA group. There were 40% women and 60% men in the MMC group and 39.5% women and 60.5% men in the CA group.

There was no significant difference between the treatment groups regarding gender or age. The pterygium area was measured to  $6.5 \text{ mm}^2 \pm 4.0$  (0.4–26.0) in the MMC group and  $7.5 \text{ mm}^2 \pm 5.5$  (0.4–28.0) in the CA group. No significant difference was found between the two groups.

The surgery did not significantly change the best-corrected visual acuity with LogMar calculation or the average absolute astigmatism in either group (Table 1).

Surgery time was significantly shorter in the MMC group:  $13 \pm 4$  min (range 6–22) than in the CA group:  $46 \pm 5$  min (range 28–60) ( $p < 0.01$ , Student's t-test). Re-operations were carried out if the patient experienced discomfort or the pterygium appeared to be aggressive. In the MMC group 8 of 14 (57.1%) and in the CA group 1 of 2 (50%) had to be re-operated.

Most complications were transitory and mild (Table 2). However, one graft necrosis with subsequent keratitis in the CA group. Delayed epithelialization of the cornea (more than 2 weeks) was seen in 40% ( $n = 14$ ) of the patients in the MMC group but none in the CA group. In the MMC group, 31.4% ( $n = 11$ ) of the patients healed with rough, fibrotic nasal conjunctiva. Mild scleral thinning was seen in 20% ( $n = 7$ ) and in 5.3% ( $n = 2$ ) of the patients in the MMC and in the AC group, respectively. Elevated intraocular pressure (IOP) caused by the topical steroid treatment was managed by eye drops, which could be discontinued in all cases at the 3 months visit. No patients developed glaucoma.

#### 4. Discussion

Pterygium surgery has been a challenge in the past. Our goal with this study was to implement pterygium surgery that was safe, easy to perform and with satisfactory recurrence rate. We also wanted to find out when recurrences occurred to establish proper patient follow-up. We found that pterygium excision with sutured conjunctival autograft results in a statistically significant lower recurrence rate than the bare sclera method combined with intraoperatively 0.04% mitomycin C.

Mitomycin C gained popularity as a postoperative adjunctive therapy to pterygium excision.<sup>3,4</sup> However, reports on serious side-effects such as delayed epithelial healing, scleral or corneal melting, fungal or bacterial keratitis, endophthalmitis and cataract formation were

a concern.<sup>9,10</sup> Intraoperative MMC, unlike postoperative

MMC therapy, provides the surgeon direct control regarding localization, concentration and duration.<sup>13,17</sup>

Combined with bare sclera excision it is technically simple and fast. Unlike earlier studies, where saturated sponges were used, we tried to apply the same amount of MMC on each eye by the means of standardized filter paper soaked in MMC. MMC concentrations between 0.02 and 0.1% and duration between 2 and 5 min are reported.<sup>18</sup> We choose 0.04% and 3 min to have maximum efficacy with a reasonable safety.

The recurrence rate in the group with bare sclera excision and MMC was 40% after 1 year in our study which is somewhat higher than others who advocated intraoperative over postoperative use of mitomycin.<sup>18-21</sup>

There is a considerable variation of the recurrence rates in the literature.<sup>22</sup> We think that relatively small sample sizes are an important factor causing differences in the reports.

Complications as keratitis, corneal endothelial changes, scleral thinning and melting may occur also with intraoperative MMC.<sup>23-26</sup>

In the other group, with sutured conjunctival autograft, the recurrence rate after 1 year was only 5.3%. Our results are in line with other reports on this method.<sup>22,27</sup>

Kenyon emphasized the method of using free autologous conjunctival grafts in pterygium surgery early.<sup>14</sup> This technique is considered safe, but surgically more demanding and time-consuming. In our study the average surgery time in the CA group was 26 min, twice as long as the average surgery time in the MMC group. Using absorbable 7-0 Vicryl Rapid sutures, we did not need to remove the stitches. Reports on complications are sparse. In our study no grafts were lost. Only one serious complication occurred in the CA group; the graft turned pale after 1 week, became necrotic and secondary infected. After autograft removal and antibiotic therapy the eye healed without further complications.

All recurrences after pterygium surgery appeared within a year. Hirst and co-workers showed that there is a 50% chance for a recurrence after pterygium surgery to occur within 4 months and a 97% chance within 1 year.<sup>28</sup> In another article on recurrence time<sup>29</sup> it is shown that 1-year follow-up is optimal, which also coincides with our results. Nowadays there are some very good results i.e. the perfect method<sup>30</sup> with good cosmesis and low recurrence rate. However, this surgery is extensive and hard to master. The difficulties are to harvest, suture and place the conjunctival autograft properly; hence, the procedure is more time-consuming than the simple bare sclera surgery. The first article using fibrin glue instead of sutures when securing the conjunctival autograft was published in 1993.<sup>31</sup> This issue was explored by extensive studies with long-term follow-up and



revealed easy surgery, short operation time and significantly less patient discomfort.<sup>32,33</sup> After the introduction of fibrin glue in pterygium surgery the recurrence rate using conjunctival autograft has dropped, possibly because of less post operative inflammation without sutures.<sup>34</sup> Also other techniques, as use of amniotic membrane emerged.<sup>35</sup> The initial results were not encouraging, the procedures were evolved and also long term studies were carried out with better results.<sup>36</sup> Fibrin glue and amniotic membrane have also been combined in some works with favourable results.<sup>37</sup>

At the time of this study, we wanted to find a safe surgery method with satisfactory long-term recurrence rate. In this study we found that pterygium excision with sutured conjunctival autograft results in a statistically significant lower recurrence rate than the bare sclera method combined with intraoperative 0.04% mitomycin C. Based on our results we chose the conjunctival autograft as our preferred method. Also later reports<sup>38,39</sup> confirmed the superiority of the conjunctival autografting technique over that with bare sclera and intraoperative MMC.

### Conclusion

In the present study, the conjunctival autotransplant appeared to be significantly more effective in terms of recurrence rate than bare sclera with a single intraoperative dose of MMC. The recurrences after MMC were more aggressive and demanded additional surgery at a higher rate. Also, the complications appeared to be more frequent in the latter group. There was no significant difference in change of BCVA or astigmatism.

Therefore, we recommend the transplantation of autologous conjunctiva as the preferred technique for surgery also for primary pterygia. As not any late onset recurrences appeared, we suggest that 12-month follow-up is satisfactory in future studies on pterygium surgery.

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