



Original research

# Comparison of free conjunctival autograft versus amniotic membrane transplantation for pterygium surgery

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Received 19 April 2017; revised 9 July 2017; accepted 1 August 2017

Available online 18 August 2017

## Abstract

**Purpose:** To compare the recurrence rate and surgical outcomes of amniotic membrane transplantation (AMT) and free conjunctival autograft (CAT) for pterygium surgery.

**Methods:** In this prospective study, 60 patients with primary pterygium were randomly assigned to two groups of CAT or AMT and were compared in terms of recurrence rate, mean healing time of corneal epithelial defects, the mean level of inflammation, and complications.

**Results:** The mean  $\pm$  SD age of patients was  $48.98 \pm 9.8$  years (range, 27–71 years). 73.3% were men, and 26.7% were women. The groups did not differ with respect to demographic characteristics ( $P > 0.05$ ). Patients were followed for an average of  $12.6 \pm 1.3$  months. The recurrence rates were 6.7% and 3.3% in the AMT and CAT groups, respectively ( $P > 0.05$ ). Comparison of mean inflammation score showed higher inflammation in the AMT group in the first, third, and sixth postoperative month ( $P < 0.05$ ). Mean healing times of corneal epithelial defects were  $2.5 \pm 0.572$  and  $2.67 \pm 0.479$  days in the CAT and AMT groups, respectively ( $P = 0.173$ ).

**Conclusions:** No significant complication was observed during or after both surgical methods. No statistically significant difference was seen in visual acuity changes and epithelial healing in CAT and AMT groups, but more inflammation and recurrence rate were seen in AMT group. Copyright © 2017, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Keywords:** Pterygium surgery; Conjunctival autograft; Amniotic membrane transplantation

## Introduction

Pterygium is a common ocular surface disease that is a wing-shaped fibrovascular growth from the conjunctiva onto the cornea and can affect one or both eyes on one or both (nasal/temporal) sides of the eye.<sup>1</sup> Ultraviolet light, which is believed to cause pterygium may induce chronic inflammatory cells in the conjunctiva or damage limbal stem cells. Chronic inflammatory cells were shown to be present in pterygium samples, thus chronic inflammation may contribute to pterygium occurrence.<sup>2</sup>

The incidence of pterygium is twice in men compared to women, and its incidence increases with age.<sup>1</sup> It may impair visual acuity, thus, surgical procedure has been suggested since 1940 as the treatment of choice for pterygium.<sup>3</sup> but the high recurrence rate remains the major problem of pterygium surgery,<sup>4</sup> which may be provoked by inflammation that may activate the remaining pterygial body fibroblasts and evolve into an invasive phenotype of the disease.<sup>5–7</sup>

Different surgical approaches have been suggested for treatment of pterygium since the primary technique (bare sclera technique) is associated with a recurrence rate of 37–90%.<sup>8</sup> Intraoperative administration of 0.02% mitomycin C (MMC) is suggested as an efficient method to reduce the recurrence rate but is associated with several post-surgical complications.<sup>9</sup> Several adjunctive measures have also been

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Peer review under responsibility of the Iranian Society of Ophthalmology.

suggested for the closure of the defect, caused by the excision of pterygium. Free conjunctival autograft (CAT) is a quick and safe procedure, where the resected conjunctiva is transplanted to the excised area,<sup>10</sup> it has gained attention in recent decades and is established to have a low recurrence rate.<sup>11</sup> Amniotic membrane transplantation (AMT) is another suggested procedure with improved surgical results, including reduced scarring, inflammation, and vascularization, resulting from its biological properties.<sup>12,13</sup> Also, AMT is suggested to cause rapid pain relief that is regarded as an important benefit for it.<sup>13</sup>

Several studies have compared the recurrence rate of AMT with CAT and most of them have reported a higher recurrence rate in AMT than CAT,<sup>14–16</sup> whereas other studies have reported equal recurrence rates for the two procedures.<sup>17–20</sup> Thus, it is still required that further studies investigate the different aspects of pterygium surgery in order to suggest one procedure as the method of choice. Accordingly, we aimed to compare the recurrence rate and surgical outcomes of CAT and AMT.

## Methods

In this prospective study, patients with primary pterygium (>3 mm on a horizontal axis of the cornea) who referred for surgery to Amir-Al-Momenin Hospital, Rasht, Guilan province, Iran, from August 2014 until September 2015 were recruited. Recurrent cases of pterygium and pseudo-ptyerygium were not included into the study.

The protocol of the study was approved by the Ethics Committee of Guilan University of Medical Sciences, Rasht, Guilan, Iran. Before recruitment, the design and objectives of the study were explained to them, and written informed consent was obtained. Principles of the Declaration of Helsinki were met throughout each step of the study.

In this consecutive case series, the patients referred to the Cornea Clinic were recruited into the study during a 6-month period ( $N = 60$ ) and were randomly assigned (simple randomization, according to random number table) to two surgical methods: CAT or AMT. The diagnosis and surgical procedures were performed by one ophthalmologist (M.A).

For AMT, the speculum was used to expose the surgical field. Local anesthesia was performed by 2% lidocaine. The pterygium was disconnected from cornea by the blade and pterygium's body, the surrounding tenon capsule and 0.5–1 mm of the free side of the pterygium was separated from the conjunctiva and uncovered sclera, and the bleeding was controlled with light cautery. An applicator containing 0.02% MMC was kept in connection with the tissue for 90 s. Cornea and limbus were observed not to be in contact with MMC. Then the eye surface was rinsed with 100 mL saline. The amniotic graft was used as a basement membrane side up in the defect site, which was sutured by Nylon 10.0 to episclera, and the surrounding conjunctival tissue continuously. In addition, fibrin glue was not used in this study.

For CAT, the speculum was used to expose the surgical field. Local anesthesia was performed by 2% lidocaine, and

the pterygium was disconnected from the cornea by the blade and pterygium's body, the surrounding tenon capsule, and 0.5–1 mm of the free side of the pterygium was separated from the conjunctiva and uncovered sclera. The bleeding was controlled with light cautery. An applicator containing 0.02% MMC was kept in connection with the tissue for 90 s. Cornea and limbus were observed not to be in contact with MMC. Then the eye surface was rinsed with 100 mL saline. Lidocaine 2% was used to disconnect conjunctiva from the surrounding tenon capsule at 12 o'clock. The free graft was placed in the scleral bed and sutured with Nylon 10.0 to episclera and the surrounding conjunctival tissue.

The day after surgery, all patients received topical steroid, betamethasone 0.1% (Betasonate, Sina Darou, Tehran, Iran) and antibiotic, chloramphenicol 0.5% (Chlobiotic, Sina Darou, Tehran, Iran) that were prescribed to be used for two weeks. Then fluorometholone 0.1% (Fluocort, Sina Darou, Tehran, Iran) was used and tapered in 3 months.

In addition to demographic characteristics (age and sex) before surgery, the best corrected visual acuity (BCVA), slit-lamp examination and the size of pterygium were recorded. Follow-up visits were performed on day one, every day till one week, every week till one month, and the 3rd, 6th, 9th, and 12th months after surgery. In each visit, BCVA and slit-lamp examination was done. Inflammation at months 1, 3, and 6 months after surgery was recorded. Required healing time for the corneal epithelial defect, recurrence, size and time of recurrence, and possible complications including granulation tissue, tenon cyst, graft necrosis, Dellen formation, and scleral thinning were also recorded and compared between groups.

The inflammation was clinically graded according to hyperemia in the site of pterygium excision zone as follows: 0 = none, 1 = mild, 2 = moderate, and 3 = severe.<sup>18</sup> Recurrence of pterygium was defined as an encroachment of fibrovascular connective tissue across the limbus and onto the cornea for any distance in the position of the previous lesion during the follow-up period. BCVA was calculated by logarithm of the minimum angle of resolution (logMAR) using the Snellen chart.

## Statistical analysis

For the statistical analysis, the statistical software SPSS version 17.0 for Windows was used. Descriptive analysis included mean  $\pm$  standard deviation (SD) for quantitative variables and frequency (percentage) for categorical variables. The normality of data distribution was tested by Kolmogorov–Smirnov test. Quantitative binary variables between the groups were compared using Independent Samples *T*-test or Mann–Whitney-*U* test, according to the normality of data distribution. Qualitative variables were, on the other hand, compared using chi-square test or Fisher's exact test. Mean inflammations in different postoperative months were compared using repeated measures ANOVA. *P* values less than 0.05 were considered statistically significant. Power analysis was done with PASS software.

**Results**

The mean age of patients was  $48.98 \pm 9.8$  years (range, 27–71 years); 73.3% were men and 26.7% women. The demographic characteristics of the groups are shown in Table 1. As shown, the two groups were not significantly different regarding age or sex ( $P > 0.05$ ). Patients were followed for an average of  $12.6 \pm 1.3$  months (min = 11, max = 16 months).

Comparison of the mean logMAR of BCVA before and after surgery showed significant differences between groups in pre-surgical BCVA ( $P = 0.007$ ), but post-surgical BCVA, as well as logMAR differences, were similar between groups ( $P = 0.479$ , and  $0.417$ , respectively) (Table 2).

Comparison of mean inflammation score showed higher inflammation in AMT than CAT in the first ( $P = 0.006$ ), third ( $P = 0.013$ ), and sixth postoperative month ( $P = 0.048$ ) (Table 3). Although the inflammation decreased in both groups in the sixth months ( $P < 0.0001$ ) compared with the first month, comparison of AMT and CAT groups using repeated measures

**Table 1**  
Comparison of demographic characteristics and pre-surgical values between amniotic membrane transplantation (AMT) and free conjunctival autograft (CAT) groups.

Variable	AMT	CAT	P-value	
Age category	<50 years, no. (%)	17 (56.7%)	15 (50%)	0.605
	>50 years, no. (%)	14 (43.3%)	15 (50%)	
	Mean $\pm$ SD	$46.27 \pm 9.16$	$51.70 \pm 9.71$	
Sex, no. (%)	Male	21 (70%)	23 (76.7%)	0.559
	Female	9 (30%)	7 (23.3%)	

AMT: Amniotic membrane transplantation; CAT: Free conjunctival autograft.

**Table 2**  
Comparison of mean logMAR of best corrected visual acuity (BCVA) before and after surgery between the study groups.

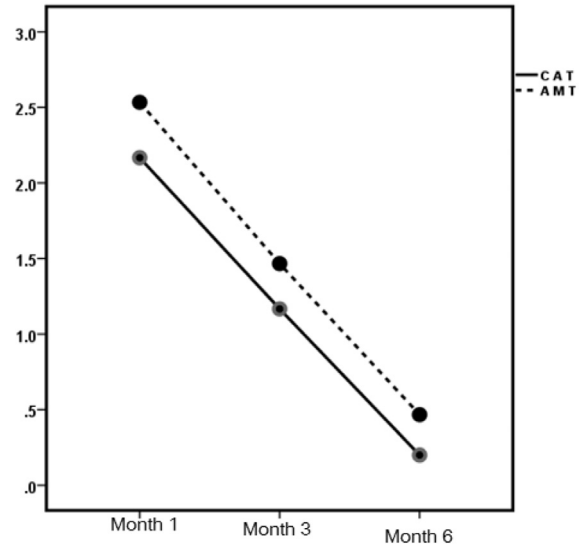
Variable	AMT	CAT	P-value
BCVA before surgery, mean $\pm$ SD logMAR	$0.234 \pm 0.08$	$0.312 \pm 0.12$	0.007
BCVA after surgery, mean $\pm$ SD logMAR	$0.148 \pm 0.23$	$0.191 \pm 0.23$	0.479
Difference in mean $\pm$ SD of logMAR (BCVA)	$0.642 \pm 0.17$	$0.610 \pm 0.13$	0.417

AMT: Amniotic membrane transplantation; CAT: Free conjunctival autograft; BCVA: Best corrected visual acuity; logMAR: Logarithm of the minimum angle of resolution.

**Table 3**  
Comparison of inflammation one, three, and six month(s) after surgery between groups.

Inflammation score	Total	AMT	CAT	P-value
After one month	Mean $\pm$ SD	$2.35 \pm 0.515$	$2.53 \pm 0.507$	0.006
	Mean rank	35.73	25.27	
After three months	Mean $\pm$ SD	$1.32 \pm 0.469$	$1.47 \pm 0.507$	0.013
	Mean rank	35.00	26.00	
After six months	Mean $\pm$ SD	$0.33 \pm 0.510$	$0.47 \pm 0.571$	0.048
	Mean rank	34.10	26.90	

AMT: Amniotic membrane transplantation; CAT: Free conjunctival autograft.



AMT: Amniotic membrane transplantation  
CAT: Free conjunctival autograft

**Fig. 1.** The trend in the mean inflammation score from the first until the sixth month after surgery.

ANOVA showed no statistically significant difference between the groups ( $P = 0.536$ , Fig. 1). Mean recurrence time was  $6.50 \pm 0.707$  (min = 6, and max = 7) months with a mean size of  $2.50 \pm 0.707$  (range, 2–3) mm in AMT group and  $6 \pm 0$  (6) months with a  $2 \pm 0$  (2) mm in CAT group.

The recurrence rate was 6.7% (two patients) in the AMT group and 3.3% (one patient) in the CAT group ( $P = 0.5$ , Fisher's exact test). Also, the recurrence rate was not statistically different between the two study groups in terms of patients' age, sex, or pterygium's size ( $P > 0.05$ , Table 4).

Mean healing time of corneal epithelial defects size in AMT group was  $2.5 \pm 0.572$  days (mean rank = 27.83) and  $2.67 \pm 0.479$  days in CAT group (mean rank = 33.17), but the difference was not statistically significant between the groups, based on Mann–Whitney *U* test ( $P = 0.173$ ). No significant complications were observed during or after surgery in any of the groups.

**Discussion**

While the recurrence rate in AMT group was almost twice, (6.7%) in AMT vs. 3.3% in CAT group, but we found no

**Table 4**  
Comparison of recurrence rate between the study groups, in terms of age, sex, and pterygium's size.

Variable	AMT	CAT	P-value	
Age	<50 years, no. (%)	1/17 (5.9%)	0/15	0.340
	>50 years, no. (%)	1/13 (7.7%)	1/15 (6.7%)	
Sex	Male	1/21 (4.8%)	1/23 (4.3%)	0.950
	Female	1/9 (11.1%)	0/7	
Pterygium's size	3 mm	0/6	0/1	–
	4 mm	1/11 (9.1%)	0/17	
	5 mm	1/13 (7.7%)	1/12 (8.3%)	

AMT: Amniotic membrane transplantation; CAT: Free conjunctival autograft.

statistically significant difference in the recurrence rate between the groups. Also mean inflammation score was higher in the AMT group in the first, third, and sixth postoperative month ( $P < 0.05$ ) with a decreasing trend in both groups.

Many studies have been published with conflicting results for the recurrence rate of these two techniques. Kheirkhah and colleagues reported a recurrence rate of 10.5% in AMT group and 10% in CAT group one month after surgery, with no statistically significant difference between groups.<sup>18</sup> The recurrence rate in their study was much higher than the present study. In another study, a much higher recurrence rate was reported 35% in AMT group and 25% in CAT group over a 6-month period follow-up.<sup>19</sup> However, they also found no significant difference in the recurrence rate between AMT and CAT, which is consistent with the results of the present study. As mentioned above, the recurrence rate in the present study was much lower than similar Iranian studies, even after one year of follow-up in our cases. The recurrence rate reported in the present study resembles other studies, performed in other countries.<sup>17,21</sup> In addition, the success rate depends greatly on various factors, such as differences in the surgical procedures performed.<sup>22</sup> Moreover, the characteristics of the study population (such as sex distribution and mean age of participants) can justify the different recurrence rates reported, as well.<sup>10,23</sup> Nevertheless, several studies have reported higher recurrence rate in AMT than CAT.<sup>14–16,24</sup> This difference among the studies can be due to the differences in the definition of recurrence, as Chen and colleagues have identified no differences between groups in grade D recurrence, while they established higher recurrence in grades A, B, and C in AMT vs. CAT group.<sup>25</sup> Moreover, the differences in the surgical procedures performed can play a significant role in such a discrepancy among studies,<sup>22</sup> as different applications in each surgical method have been suggested, such as the use of fibrin glue,<sup>26</sup> and sutureless procedures.<sup>27</sup> Also, a meta-analysis reported no difference in the recurrence rate at three postoperative months but a higher recurrence rate in cases undergoing AMT compared to CAT in six-month follow-up.<sup>11</sup> Therefore, the diverse conditions of the studies might be the main reason for this discrepancy.

Moreover, we found no association between recurrence rate and pterygium size, patient age or sex, which is in line with previous studies,<sup>28</sup> although some other studies reported different recurrence rates according to patients' age.<sup>10,23</sup> Also, the mean recurrence time was  $6.33 \pm 0.57$  months in the present study, which is in line with studies reporting the recurrences 4–6 months after surgery.<sup>23</sup> Although only 3 cases were complicated with a recurrence of pterygium in one-year follow-up in the present study.

In this study we used the same dose and same duration for application of MMC for all patients in both groups to achieve a more comparable result and to limit the influence of factors implicated in pterygium recurrence. It is possible that using sutures versus fibrin glue to fix the tissue graft over the location of pterygium removal may have an effect on the risk of recurrence.<sup>29</sup> Our techniques included the only suture without fibrin glue.

An unexpected finding of the present study was higher inflammation in AMT than CAT group, as the biological properties of AMT suggest anti-scarring, and anti-inflammatory properties for AMT,<sup>12,13</sup> so these conditions need to be further explored. The degree of conjunctival inflammation might affect the outcome of pterygium surgery. More inflammation in the site of pterygium surgery may induce more recurrence in AMT group. Previous studies reported persistent conjunctival inflammation around the surgical site after pterygium surgery in 31.5–40.7% of eyes that received an AMT,<sup>26</sup> as in AMT group in our study, and therefore the recurrence rate was twice in this group.

Another important finding of the present study was similar healing time and post-surgical BCVA, which has been suggested by previous studies. For instance, Katircioglu et al have reported no statistically significant difference in postoperative visual acuity, change in visual acuity, and epithelial defect healing time between AMT and CAT,<sup>20</sup> which is consistent with the results of the current study. Similarly, in the study by Chen and colleagues, the healing time was not different between groups,<sup>25</sup> which confirms the results of the present study.

Both surgical procedures appear to be safe. We found no adverse events in both CAT and AMT groups. Adverse events specific to the surgeries evaluated in this study are granulation tissue, tenon cyst, graft necrosis, Dellen formation, and scleral thinning, ulceration or necrosis, which is similar to previous studies,<sup>17,19,30</sup> while several studies have reported various complications, such as retraction,<sup>31</sup> granuloma, scleral thinning, and glaucoma,<sup>18,22</sup> but, as suggested, complications of AMT and CAT are minor and do not threaten the visual acuity,<sup>32</sup> which, in line with the present study, confirms the safety of both procedures.

The present study had several strengths, including following the patients for at least one year which gives a better perspective towards long-term recurrence rate. However, a longer follow-up period is needed to observe the late complications of MMC, which can include scleral necrosis. Moreover, the groups were comparable, as patients were randomly allocated to the surgical method and had similar demographics. This study had some limitations, including a relatively small sample size with an estimation of low statistical power (33%) and a disregard of the stages of pterygium which could have an impact on the results. The result of our studies may be influenced by populations selection (north of Iran), the indication for surgery, the definition of recurrence, and postoperative care. Moreover, despite the statistical result, this study showed a higher recurrence rate in AMT. Because the sample size affects statistical power, more patients should be enrolled in order to compare the two treatments in future studies.

In conclusion, the results of the present study indicated similar visual acuity changes and epithelial healing in CAT and AMT groups, but more inflammation and recurrence rate were seen in the AMT group. Therefore, it seems that CAT is the preferred method of pterygium surgery. We can also consider AMT because of the acceptable recurrence rate. It may be

particularly advantageous for patients with glaucoma who require intact conjunctiva for future glaucoma procedures.

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