· Original article ·

Narrow versus wide inferior limbal conjunctival autograft transplants combined with Mitomycin C in primary pterygium surgery: a comparative study

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角膜缘干细胞移植术中结膜瓣的宽与窄对原发性翼状胬肉的疗效比较

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摘要

目的:对比下方角膜缘干细胞窄结膜瓣与宽结膜瓣移植联合丝裂霉素 C 治疗原发性翼状胬肉的长期效果与复发率。

方法:采用回顾性研究,共纳入 146 例(193 眼)原发性翼状胬肉患者。其中 91 例采用下方角膜缘干细胞窄结膜瓣移植联合丝裂霉素 C 治疗(NI-LCAT 组),102 例采用下方角膜缘干细胞宽结膜瓣移植联合丝裂霉素 C 治疗(WI-LCAT 组)。随访对比两组复发率、供体区、植片植床情况与相应并发症。

结果:NI-LCAT 组与 WI-LCAT 组复发率分别为 3.3%与 4.9%,两者差异无统计学意义。两组植片植床情况未见明显差别。两组供体区最常见并发症均为轻中度结膜瘢痕(NI-LCAT 组 18.6%,WI-LCAT 组 13.2%)。其他并发症包括结膜下上皮囊肿与受体区肉芽肿发生率在两组间差异无统计学意义。Kaplan-Meier 生存分析显示两组间累积手术成功率差异无统计学意义。

结论:下方角膜缘干细胞窄结膜瓣与宽结膜瓣移植联合丝裂霉素 C 治疗原发性翼状胬肉复发率相似。相比宽结膜瓣组,窄结膜瓣组对结膜供体区创伤较小,对保留上下方结膜更为有效。

关键词:结膜瓣移植;丝裂霉素 C;翼状胬肉切除术;复发

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Abstract

• AIM: To compare long-term outcomes and recurrence rates of narrow versus wide inferior limbal conjunctival autograft transplants combined with Mitomycin C in primary pterygium surgery.

• METHODS: This retrospective study included 146 consecutive patients (193 eyes) with primary pterygium. Ninety-one eyes had a narrow inferior limbal conjunctival autograft transplant (NI-LCAT) and 102 had a wide inferior limbal conjunctival autograft transplant (WI-LCAT) combined with Mitomycin C application. Outcome measures included recurrence rate, residual conjunctival bed status, and complications.

• RESULTS: The recurrence rate in the NI-LCAT and WI-LCAT group was 3.3% and 4.9%, respectively (P = 0.844). The grade of residual bed appearance in the NI-LCAT group was similar to the WI-LCAT group. Mild to moderate conjunctival scarring at the donor site was the most common complication in both groups (18.6% and 13.2% in NI-LCAT and WI-LCAT groups, respectively). There were no significant differences in the incidence of any other complications including subconjunctival epithelial cyst and granuloma at the recipient site between the two groups. Kaplan-Meier survival analysis showed that the cumulative probabilities of success between the two groups were not statistically significantly different.

• CONCLUSION: Both NI-LCAT and WI-LCAT combined with Mitomycin C in primary pterygium surgery have low recurrence rates. Compared with WI-LCAT, NI-LCAT technique is found to be less traumatic and an effective surgery in terms of preserving the superior and inferior conjunctiva.

• KEYWORDS: conjunctival autograft; Mitomycin C; pterygium excision; recurrence
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INTRODCTION

Pterygium is a common ocular surface disease that occurs most frequently in tropical equatorial areas. It comprises a wing-shaped abnormal fibrovascular tissue usually located on the nasal side. Surgical removal comprises the main treatment method of pterygium, but recurrence remains the main complication. The recurrence rate of simple excision ranges from 24% to 89%[1]. The current commonly adopted methods for reducing the recurrence rate include administration of antimetabolite adjuvants such as Mitomycin C (MMC) or 5-fluorouracil[2-3], conjunctival or limbal conjunctival autograft transplantation (LCAT)[4-5], and amniotic membrane transplantation[6-7].

Conjunctival autograft transplantation (CAT) was first reported by Kenyon as an adjunctive method after pterygium removal with a low recurrence rate of 5.3%[8]. Since then, numerous studies had demonstrated that this technique was safe and effective at reducing the recurrence rate. Furthermore, surgeons have developed various modified CAT techniques including LCAT[4], extended CAT[9], LCAT with limbal fixation suture[10], mini or narrow-strip CAT[11-13], and inferior CAT[12, 14-17].

The optimum size of the CAT and its positioning on the bare sclera after pterygium removal remains controversial. Although most reports advocated a large graft with complete coverage of the bare scleral defect[8], smaller or narrow CAT had also been advocated[7,11,13,18]. Dupps *et al*[11] described a narrow-strip CAT technique in a retrospective non-comparative study. The authors proposed that this modified method could create an intervening bare sclera area between the secured conjunctival graft and the anterior margin of the conjunctiva to prevent recurrence. To our knowledge, no study has compared the results of narrow inferior LCAT (NI-LCAT) and wide inferior LCAT (WI-LCAT) with adjunctive intraoperative low-dose MMC application, which has been demonstrated to reduce the recurrence after pterygium surgery[3].

The purpose of this study was to compare outcomes, recurrence rates, and complications between NI-LCAT and WI-LCAT combined with intraoperative low-dose MMC in the management of primary pterygium.

SUBJECTS AND METHODS

We retrospectively reviewed 193 eyes of 146 consecutive patients who underwent primary pterygium surgery at the Department of Ophthalmology, Fujian Provincial Hospital between Aug. 2011 and Jul. 2014. This study was approved by the human ethics committee of the Fujian Provincial Hospital, and informed written consent was obtained from each patient, which was conducted in accordance with the guide lines of the Helsinki Declaration (2008). All patients underwent a detailed complete ophthalmic examination, including slit-lamp biomicroscopy, noncontact tonometry, ophthalmoscopy, and measurements of the length of the pterygium invading the cornea (mm). All patients were randomized into two groups: NI-LCAT group and WI-LCAT group.

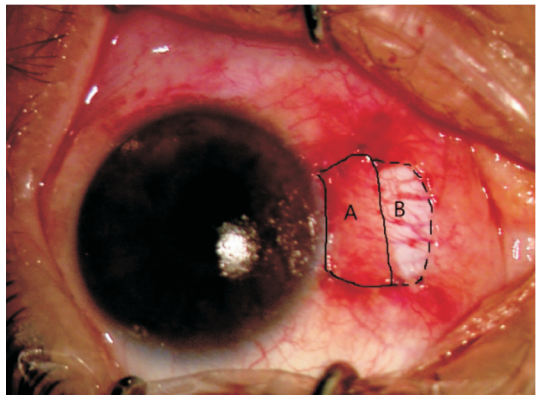

Figure 1 Schematic example of narrow inferior limbal conjunctival autograft transplant for primary pterygium A 2-3 mm wide conjunctival graft was harvested from the inferior conjunctiva and sutured to the nasal bare limbus (A), leaving a 2-3 mm zone of bare sclera between the graft and the residual conjunctival margin (B).

All surgical procedures were performed by one surgeon. Eyes were anesthetized with topical proparacaine drops and subconjunctival injection of 2% lidocaine with or without epinephrine. The pterygium head was stripped off by blunt dissection. Westcott scissors were used to incise the conjunctiva at approximately 5-6 mm posterior to the limbus to dissect the pterygium, fibrous tissue, and Tenon's capsule completely, taking care to avoid injuring the adjacent medial rectus muscle. After applying pressure or cautery hemostasis, a merocel sponge supersaturated with 0.02% (0.2 mg/mL) of MMC was applied to the bare scleral bed for 3 minutes, followed by irrigation with 200 ml balanced salt solution. A free limbal conjunctival autograft was harvested from the inferior bulbar conjunctiva with the superior margin of the graft dissected towards the cornea to include part of the superficial limbus. A limbal graft was equal in arc length to that of the nasal bare limbus.

For patients in the NI-LCAT group, an autograft 3-4 mm wide was sutured to the limbus and bare sclera, leaving a 2-3 mm zone of bare sclera between the graft and the residual conjunctival margin (Figure 1). For patients in WI-LCAT group, an autograft approximately 1 mm wider than that of the bare sclera was sutured in order to cover the defect completely. Both autografts were secured using interrupted 8-0 Vicryl sutures. In order to prevent the autograft from contracting, we sutured it from the sclera to the conjunctiva rather than from the conjunctiva to the conjunctiva. Tobradex eye drops were prescribed four times daily for 1mo when the cornea defect was healed by the epithelium 3-5 days postoperatively in both group. All patients were followed-up at postoperative days 1, 3, and 5, at postoperative weeks 1 and 2, and then monthly for 3mo, and at every 3mo for at least 1y. The patients were reminded by telephone if they did not follow their control visits.

Definition of recurrence was graded based on residual bed appearance described by Prabhasawat *et al*[19]. In brief, grade 1 was defined as the normal appearance of the operated eye;

grade 2 was defined as the presence of fine episcleral vessels without fibrous tissue in the surgical area extending to the limbus, but not beyond; grade 3 was defined as the presence of fibrovascular tissue in the surgical area, but without invasion into the cornea; and grade 4 was defined as true recurrence with fibrovascular tissue invading the cornea.

Statistical Analysis Data were analyzed using the independent-sample *t*-test, Chi-square test, Kruskal-Wallis H test, and Kaplan-Meier survival analysis with Log-rank test for estimation of success. A $P<0.05$ was considered statistically significant. SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data.

RESULTS

Patients' demographic and clinical data in both groups are presented in Table 1. In total, 91 eyes underwent NI-LCAT and 102 eyes underwent WI-LCAT. Mean patient age, men-to-women ratio, laterality, and mean length of the pterygium invading the cornea were not significantly different between the NI-LCAT and WI-LCAT groups. Figure 2 depicts the preoperative and postoperative outcomes of representative cases in NI-LCAT group. Most patients were satisfied with the cosmetic outcomes of the surgery. There were no intraoperative complications encountered in NI-LCAT group.

Mean follow-up period, recurrence rate, grade of residual bed appearance, and postoperative complications for each group are shown in Table 2. The mean follow-up time was 22.4±6.6mo (range, 10-36mo) for the NI-LCAT group and 20.4±9.6mo (range, 6-35mo) for the WI-LCAT group ($P=0.367$). The recipient bare sclera zone in the NI-LCAT group was epithelialized between day 5-15 (Figure 3). The grade of residual bed appearance in NI-LCAT was comparable to that of the WI-LCAT group. Pterygium recurred in three (3.3%) of 91 eyes in the NI-LCAT group and five(4.9%) of 102 eyes in the WI-LCAT group ($P=0.844$).

Mild to moderateconjunctival scarring at the donor site was the most common complication (Figure 4). Donor site scarring was noted in 12 patients in the NI-LCAT group (13.2%) and 19 patients in the WI-LCAT group (18.6%); However, the difference was not statistically significant ($P=0.304$). Subconjunctival epithelial cysts at the recipient site were found in two of 102 eyes (1.9%) in the WI-LCAT group and in no eyes in the NI-LCAT group. Granuloma at the recipient site occurred in two of 91 eyes (2.1%) in the NI-LCAT group and in one of 102 eyes (0.9%) in the WI-LCAT group. There was no significant difference in the incidence of these complications between the two groups. There were no severe complications, such as scleral necrosis and symblepharon formation, in either group.

Kaplan-Meier survival analysis was used to take into account differences between the follow-up periods for each group of patients. As shown in Figure 5, the cumulative probabilities of success were 96.7% and 95.1% in the NI-LACT and WI-LCAT groups, respectively. The difference between the cumulative probabilities of success between the two groups was not statistically significant ($P=0.561$).

Table 1 Demographic and clinical patient data in the NI-LCAT and WI-LCAT groups

Clinical data	NI-LCAT	WI-LCAT	*P*
No. of eyes	91	102	
Age (a)	63.1±9.8	65.8±7.9	0.875
Sex (M:F)	38:53	50:52	0.312
Laterality (OD:OS)	59:32	61:41	0.472
Mean length of pterygium invading the cornea (mm)	3.76±1.21	3.33±1.15	0.673

NI-LCAT: Narrow inferior limbal conjunctival autograft transplantation; WI-LCAT: Wide inferior limbal conjunctival autograft transplantation.

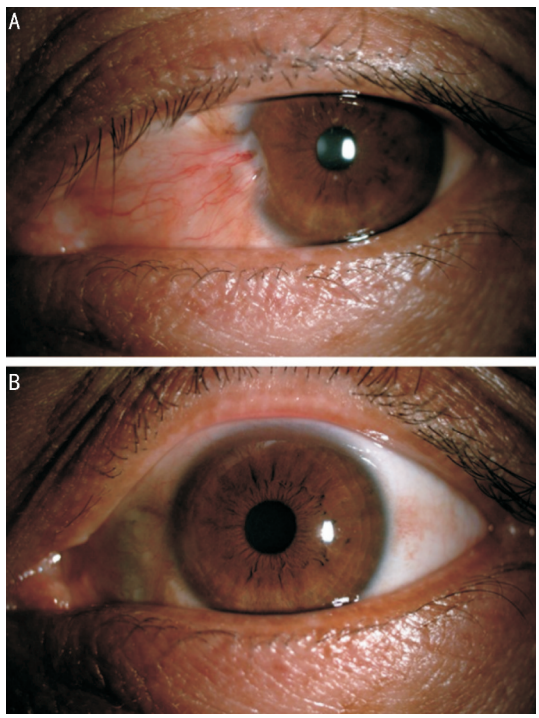

Figure 2 The preoperative and postoperative outcomes of representative cases in NI-LCAT group A: Preoperative appearance of a nasal pterygium before surgery; B: The same patient 12 months after surgery without recurrence.

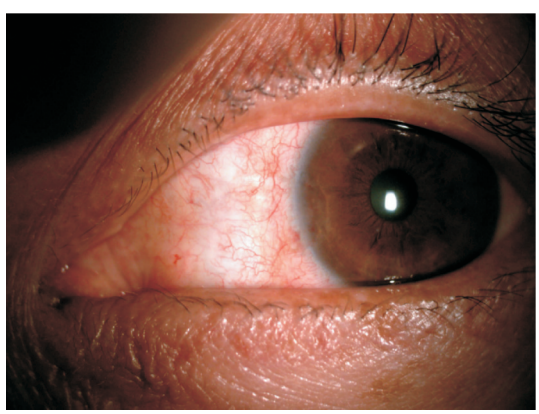

Figure 3 The recipient bare sclera zone was epithelialized in day 7 after surgery.

DISCUSSION

Although all types of conjunctival autograft techniques in primary pterygium have been shown to successfully reduce the recurrence rate to some degree, no single technique has demonstrated complete effectiveness against recurrence. Some

Table 2 Final outcomes of NI-LACT versus WI-LACT for primary pterygium

Final outcomes	NI-LCAT (n=91)	WI-LCAT (n=102)	P
Follow-up (mo)	22.4±6.6	20.4±9.6	0.367
Recurrence rate	3.3%	4.9%	0.844
Grade of residual bed appearance			0.619
1	57 (62.6%)	61 (59.8%)	
2	28 (30.7%)	35 (34.3%)	
3	3 (3.2%)	1 (0.9%)	
4	3 (3.3%)	5 (4.9%)	
Type of complication			
Conjunctival scaring at donor site	12(13.2%)	19 (18.6%)	0.304
Subconjunctival epithelial cyst at recipient site	0 (0%)	2 (1.9%)	0.500
Granuloma at recipient site	2 (2.1%)	1 (0.9%)	0.603

NI-LCAT: Narrow inferior limbal conjunctival autograft transplantation; WI-LCAT: Wide inferior limbal conjunctival autograft transplantation.

Figure 4 Mild conjunctival scarring (arrow head) in donor site after surgery.

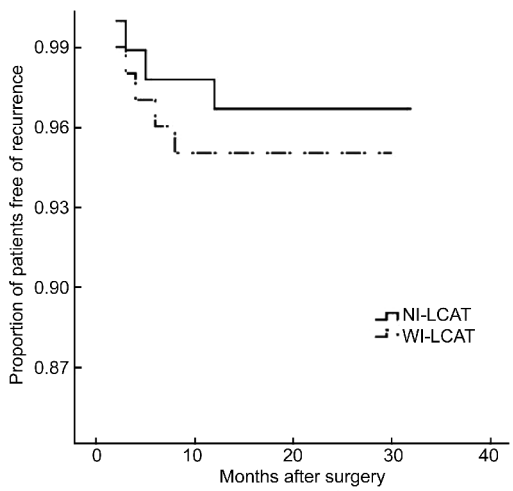

Figure 5 Kaplan-Meier survival analysis of pterygium recurrence with narrow inferior limbal conjunctival autograft transplant (solid line) and wide inferior limbal conjunctival autograft transplant (dashed line) (P = 0.561, Log-rank test).

surgeons have advocated small or narrow autografts based on the principle of minimal invasion to donor tissue, with a reported recurrence rate between 0% and 10.7% in primary pterygium[7,11-13,18]. In the present study, there were no significant differences in pterygium recurrence rate between NI-LCAT and WI-LCAT combined with intraoperative low-dose MMC. The NI-LCAT group had a low recurrence rate (3.3%) without remarkable complication comparable to the WI-LCAT group (4.9%), which is the main CAT technique performed currently[4-5,9,19-20].

The NI-LCAT technique appears to offer certain advantages over the WI-LCAT technique. Narrow autografts cause less trauma to the donor conjunctiva, reduce the risk of violating the fornix conjunctiva and rectus muscle, and reduce the incidence of conjunctival scarring or granuloma of donor site compared with large grafts. Our result that the incidence of inferior bulbar conjunctival scarring tended to occur less in NI-LCAT group supports this. On the other hand, we created a 2-3 mm thin bare sclera between the autograft margin and the nasal residual conjunctiva margin. Dupps *et al*[11] defined the bare sclera as an intervening bare sclera watershed zone, that may provide additional protection through epithelialization of bare sclera from the margin of the autograft, and thus providing a barrier to fibrovascular proliferation by enhancing epithelial-scleral adhesion and eliminating the potential subepithelial space for pterygium recurrence[11].

The utilization of the inferior bulbar conjunctiva as donor site was described by Syam *et al*[16]. It has been demonstrated to be an effective and safe technique for primary pterygium and is associated with less irritation during blinking and an absence of postoperative symblepharon formation[21]. Furthermore, inferior autografts can preserve the superior bulbar conjunctiva for future filtration surgery, and show no significant difference in recurrence rates compared with the superior autograft for pterygium surgery[14]. Another reason for the low recurrence rate may be the limbal autograft transplantation. The limbal epithelium is believed to act as a barrier between the conjunctiva and the cornea. Therefore, a deficiency in limbal epithelium may play a role in the pathogenesis of pterygium[22]. Previous reports have shown that limbal transplantation appeared to be more effective than

free conjunctival transplantation in the treatment of pterygium, especially for cases of recurrent pterygium[4,23].

In the present study, the reason for administering low-dose MMC intraoperatively in both groups was to further reduce the recurrence rate. Previous research in pterygium surgery has shown that recurrence rates with CAT combined with intraoperative application of MMC range from 0% to 12.5%[5,24-26]. However, few studies have used adjunctive MMC for surgery with LCAT. Kheirkhah *et al*[5] reported no recurrence in LCAT technique with adjunctive use of MMC. Nabawi *et al*[27] administered intraoperative MMC for 3 minutes combined with LCAT in the treatment of recurrent pterygium and reported no cases of recurrence after a period of at least 18mo. Therefore, it appears that the inhibitive and toxic effect of MMC on fibroblasts reduces pterygium recurrence[3,28-29].

Although the present study did not directly compare the recurrence rates and postoperative complications of NI-LCAT and WI-LCAT using a prospective randomized design, the extremely low recurrence rates and lack of significant complications over long-term follow-up demonstrate the effectiveness of both NI-LCAT and WI-LCAT combined with MMC in primary pterygium surgery. Furthermore, compared with WI-LCAT, NI-LCAT tended towards being less traumatic to donor site and it may therefore be an effective technique for preserving the superior and inferior conjunctiva.

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