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Review Article

Comparison of postoperative recovery of primary pterygium excision combined with either limbal stem cell transplantation or amniotic membrane transplantation: a randomized controlled trial-based meta-analysis

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Abstract: Objective: To compare the postoperative recovery of primary pterygium excision combined with either limbal stem cell transplantation (LSCT) or amniotic membrane transplantation (AMT). Methods: All relevant studies on the primary pterygium excision combined with either LSCT or AMT conducted before August 2022 were extracted from PubMed, EMBASE, Web of Science, and Cochrane Library databases. The main outcomes compared were tear film stability at 1, 3, and 6 months after surgery, postoperative corneal epithelial healing time, recurrence rate, and complications. Results: Sixteen randomized controlled trials (RCTs) with 1390 eye cases were included in this meta-analysis. We found that patients of the AMT group improved significantly in the results of the tear break-up time (BUT) and Schirmer I test at 1 month after surgery (BUT: MD=-0.37, 95% CI: -0.62, -0.12, $P<0.05$; Schirmer I test: MD=-0.32, 95% CI: -0.57, -0.07, $P<0.05$) compared with those of the LSCT group, suggesting that the early stage of tear film stability after primary pterygium excision combined with AMT was superior to the LSCT combination. However, according to the Schirmer I test result, the patients in the LSCT group showed increased tear production compared to the AMT group at 3 and 6 months after surgery (3 months: MD=0.36, 95% CI: 0.08, 0.64, $P<0.05$; 6 months: MD=0.33, 95% CI: 0.07, 0.60, $P<0.05$), suggesting that the LSCT combination was superior to the AMT combination in long-term postoperative tear film stability. As for postoperative corneal epithelial healing time, the LSCT group exhibited shorter time than the AMT group (MD=-1.17, 95% CI: -2.15, -0.19, $P<0.05$). Furthermore, the recurrence rate was lower in the LSCT group than in the AMT group (RR=0.42, 95% CI: 0.30, 0.59, $P<0.05$). Lastly, there was no statistical difference in BUT and complication rate at 3 and 6 months after surgery between the LSCT and AMT groups. Conclusions: Our analysis suggests that primary pterygium excision combined with LSCT may be a better choice compared to the combination with AMT in postoperative recovery.

Keywords: Pterygium, tear film, corneal epithelial healing time, recurrence rate, complication rate, meta-analysis

Introduction

Pterygium is a wing-shaped fibrovascular growth of the conjunctiva that extends across the limbus and invades the cornea [1]. Although it is a common ocular surface disease worldwide [2], the pathogenesis of the injury is complex and remains to be completely understood. Multiple risk factors have been found to be associated with pterygium, including ultraviolet light, age, hereditary factors, chronic inflammation, microtrauma, and heat [3]. Pterygia can affect the vision of patients as well as cause redness, foreign body sensation, and decreased tear film stability in patients; as a result, some patients develop symptoms of dry eye disease (DED) [4].

The only effective treatment method for pterygium is surgery [5]. Currently, many surgical methods for pterygium have been applied, each of which has pros and cons; hence, there is no gold standard for pterygium surgery. The most commonly used surgical method for pterygium

is surgical resection of the involved area, followed by its coverage using conjunctiva with limbal stem cells, named limbal stem cell transplantation (LSCT) or using an amniotic membrane, named amniotic membrane transplantation (AMT) [6]. Limbal stem cells are located in the limbal epithelial layer and are the ultimate source of the transparent corneal epithelium [7, 8]. Nevertheless, AMT has been increasingly used in ophthalmic surgery. It can resist adhesions and is effective in promoting epithelialization as well as inhibiting inflammation and neovascularization [9]. Another advantage of AMT is that the amniotic membrane is an avascular tissue which can effectively inhibit neovascularization during corneal surface reconstruction [10]. Both LSCT and AMT can be used in pterygium surgery.

A stable anterior tear film is essential in preserving healthy ocular, as it creates a protective and lubricated environment for the tissues of the palpebral bulbar surfaces [11]. Recent studies have demonstrated that pterygium is closely related to tear film stability. Although decreased tear film stability has been reported as one of the risk factors for pterygium formation, pterygium itself also contributes to ocular surface instability [12]. Pathological conjunctival, corneal, or eyelid changes in pterygium can decrease tear film stability. Patients with pterygium have disturbances in both tear quality and quantity, as well as the reduction of the conjunctival goblet cell population [3]. One study has shown that the excision of pterygium can improve tear film stability [13]. However, thorough meta-analyses of the effect of different pterygium methods on postoperative tear film stability have not been reported.

In addition to tear film stability, the postoperative recurrence rate and the complications associated with pterygium surgery should also be evaluated. Recurrence of pterygium refers to the reinvading of fibrovascular tissue into the clear cornea across the limbus after surgery. The recurrence rate of pterygium varies widely, which depends on the experience of the surgeon and the surgical approach [14], and is with a 97% of recurrences occurring within the first year after resection [15]. It should be noted that the recurrence rate after resection alone without adjuvant therapy can be over 80%; however, the risk of recurrence is lower with pterygium excision combined with tissue grafting, e.g., LSCT or AMT [2]. Previous meta-analyses have compared the recurrence rates between the LSCT combination and the AMT combination, but the results are varied [5, 16, 17]. Another outcome of pterygium surgery is the postoperative complications which include Dellen, subgrant hematoma, graft infection, graft retraction/graft loss, and granuloma [18]. Similarly, the incidence of postoperative complications of pterygium is also influenced by the different surgical approaches.

In this study, we compared the postoperative recovery of primary pterygium excision combined with either LSCT or AMT based on meta-analyses of available data. Our findings may provide information to guide the surgeon in selecting a more appropriate surgical approach for pterygium treatment.

Materials and methods

Search strategy

We searched all publications deposited in PubMed, EMBASE, Web of Science, and Cochrane Library databases before August 2022 on the comparison of postoperative recovery of primary pterygium excision combined with either LSCT or AMT. The search queries were as follows: ("Pterygium") AND ("Limbal" OR "Limbus") AND ("Amnion" OR "Amniotic Membrane") AND ("Tear film" OR "Recurrence"). The study workflow is shown in **Figure 1**.

Selection criteria

The inclusion criteria of published studies were: (1) Type of studies: Randomized controlled trials (RCTs); (2) Type of participants: Patients with primary pterygium; (3) Interventions: Pterygium excision combined with either LSCT or AMT; (4) Acquisition of at least one of the outcome measures: Postoperative Tear break-up time (BUT), Schirmer test without anesthesia (Schirmer I test), corneal epithelial healing time, and the recurrence and complication rate of pterygium. Studies that did not meet the inclusion criteria were strictly excluded. Studies on both LSCT and AMT groups were comparable in outcome measures. At the end, 16 RCTs were selected.

Quality assessment

Each investigator individually reviewed the potential biases in selection, performance, detection, attributions, and reporting in every

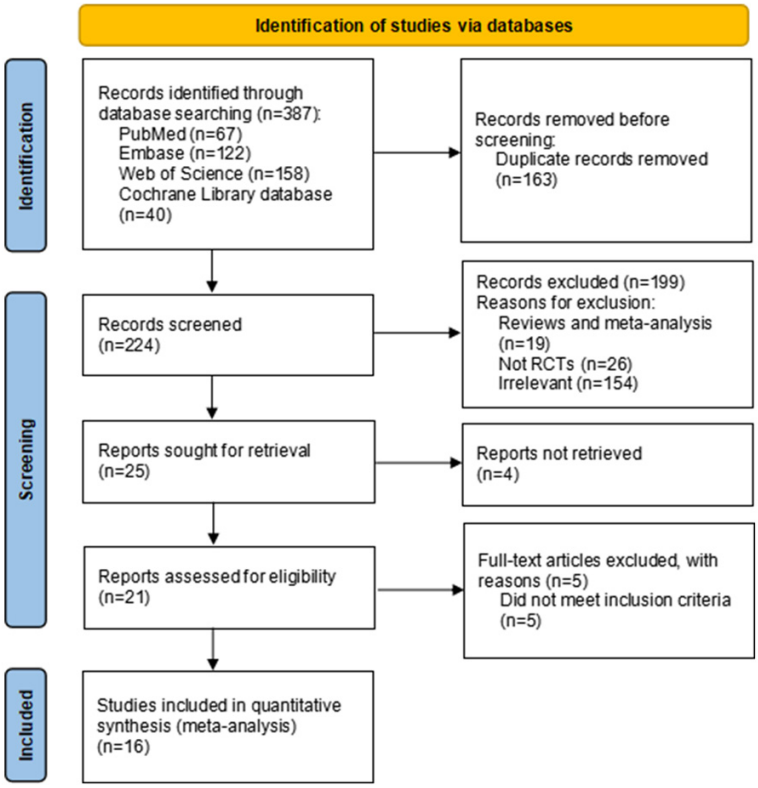

Figure 1. Study flow diagram.

RCT included in this study using the Cochrane Risk of Bias Tool. Disagreements were resolved by discussion. The bias risk of the 16 RCTs was classified as low, high, or unclear.

Data extraction

The following information was extracted from the selected 16 RCTs: the first author's surname, year of publication, country, group, sample size, BUT, Schirmer I test, corneal epithelial healing time, and the number of recurrences and complications. Continuous data were presented as mean and standard deviation (SD).

Statistical analysis

Dichotomous variables used relative risk (RR) as an effective indicator, while continuous variables were expressed as mean difference (MD) and 95% confidence interval (CI). Heterogeneity was estimated using the Cochrane I square (I^2) and Q statistics. The fixed effect model was employed for low heterogeneity (I^2<50%, P>0.1). The sensitivity analysis was performed when significant heterogeneity (I^2>50%, P<0.1) was detected. The random effect model was adopted if heterogeneity could not be eliminated. Publication bias was estimated using Begg's and Egger's tests. A P-value of less than 0.05 was considered statistically significant. All analyses were performed with RevMan version 5.3 and Stata version 15.1 software.

Results

Search results

A total of 387 relevant records were identified through the initial electronic search from PubMed, EMBASE, Web of Science, and Cochrane Library databases. After a hierarchical screening, sixteen RCT studies were selected for our meta-analysis [19-34]. The flowchart of our selection process is shown in **Figure 1**.

Characteristics of included trials

These 16 RCT studies were published between 2004 and 2022, containing a large sample size of 1390 eye cases. Twelve studies were conducted in China, while three in Turkey, and one in Thailand. These RCTs included at least one of the following outcome measures: BUT, Schirmer I test, corneal epithelial healing time, and the number of recurrences and complications. The detailed information of these 16 RCTs are shown in **Table 1**.

Quality assessment

All studies were performed with randomization, and five of them described the randomization method [21, 22, 24, 30, 31]. However, all of them lacked a full description of allocation concealment. The study by Tang et al. [30] referred to the blind method. Nevertheless, we observed a low risk of bias in both incomplete outcome data and selective reporting in all 16 RCTs. A summary of the bias risk assessment is shown in **Figure 2**.

Table 1. The detailed information of 16 RCTs selected in this study

First Author	Year	Country	Group	Sample size (n)	BUT (s)			Schirmer I test (mm/5 min)			Corneal epithelial healing time (d)	Recurrence (n)	Complication (n)
					1 month	3 months	6 months	1 month	3 months	6 months			
Chen	2012	China	LSCT	45	-	-	-	-	-	-	6.50±1.20	3	5
			AMT	45	-	-	-	-	-	-	8.10±1.40	6	6
Jiang	2008	China	LSCT	35	-	-	-	-	-	-	4.67±1.21	1	-
			AMT	30	-	-	-	-	-	-	6.48±1.25	7	-
Jiang	2021	China	LSCT	48	6.79±0.72	7.78±0.79	8.74±0.89	6.84±0.72	7.54±0.78	7.67±0.76	2.87±0.29	3	5
			AMT	48	7.15±0.73	7.42±0.77	7.89±0.82	7.18±0.73	7.21±0.74	7.34±0.75	5.34±0.56	10	8
Jiang	2022	China	LSCT	51	-	11.02±3.24	-	-	15.34±3.15	-	4.14±1.35	4	-
			AMT	51	-	11.58±3.57	-	-	13.82±3.24	-	4.72±1.37	7	-
Keklikci	2007	Turkey	LSCT	32	-	-	-	-	-	-	-	4	0
			AMT	30	-	-	-	-	-	-	-	2	1
Küçükerdönmez	2007	Turkey	LSCT	28	-	-	-	-	-	-	-	1	-
			AMT	27	-	-	-	-	-	-	-	1	-
Li	2005	China	LSCT	14	-	-	-	-	-	-	-	2	-
			AMT	16	-	-	-	-	-	-	-	3	-
Li	2007	China	LSCT	18	-	-	-	-	-	-	6.22±1.90	1	-
			AMT	22	-	-	-	-	-	-	8.36±2.61	2	-
Ma	2010	China	LSCT	45	-	-	-	-	-	-	-	0	-
			AMT	40	-	-	-	-	-	-	-	2	-
Ozer	2009	Turkey	LSCT	63	-	-	-	-	-	-	4.33±0.91	11	-
			AMT	52	-	-	-	-	-	-	4.79±1.39	12	-
Tananuvat	2004	Thailand	LSCT	42	-	-	-	-	-	-	-	2	4
			AMT	44	-	-	-	-	-	-	-	18	6
Tang	2013	China	LSCT	60	-	-	-	-	-	-	2.80±1.70	5	0
			AMT	68	-	-	-	-	-	-	2.10±1.50	11	5
Wang	2021	China	LSCT	64	11.63±2.44	-	12.86±2.67	13.96±1.45	-	14.51±1.60	-	-	-
			AMT	60	11.75±2.01	-	11.99±2.22	14.28±1.72	-	14.16±1.67	-	-	-
Xu	2014	China	LSCT	54	11.50±1.80	11.70±1.20	12.30±1.50	-	-	-	-	4	-
			AMT	49	12.00±1.50	12.00±1.60	12.50±1.60	-	-	-	-	11	-
Yue	2012	China	LSCT	46	10.80±3.50	11.80±3.20	-	12.68±1.67	12.24±1.67	-	-	-	-
			AMT	44	11.60±3.20	12.30±4.20	-	12.84±2.20	12.15±2.32	-	-	-	-
Zheng	2005	China	LSCT	66	-	-	-	-	-	-	-	3	-
			AMT	53	-	-	-	-	-	-	-	8	-

Note: The dashes represent not described. Abbreviations: RCT: Randomized Controlled Trial; LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation; BUT: Tear Break-Up Time.

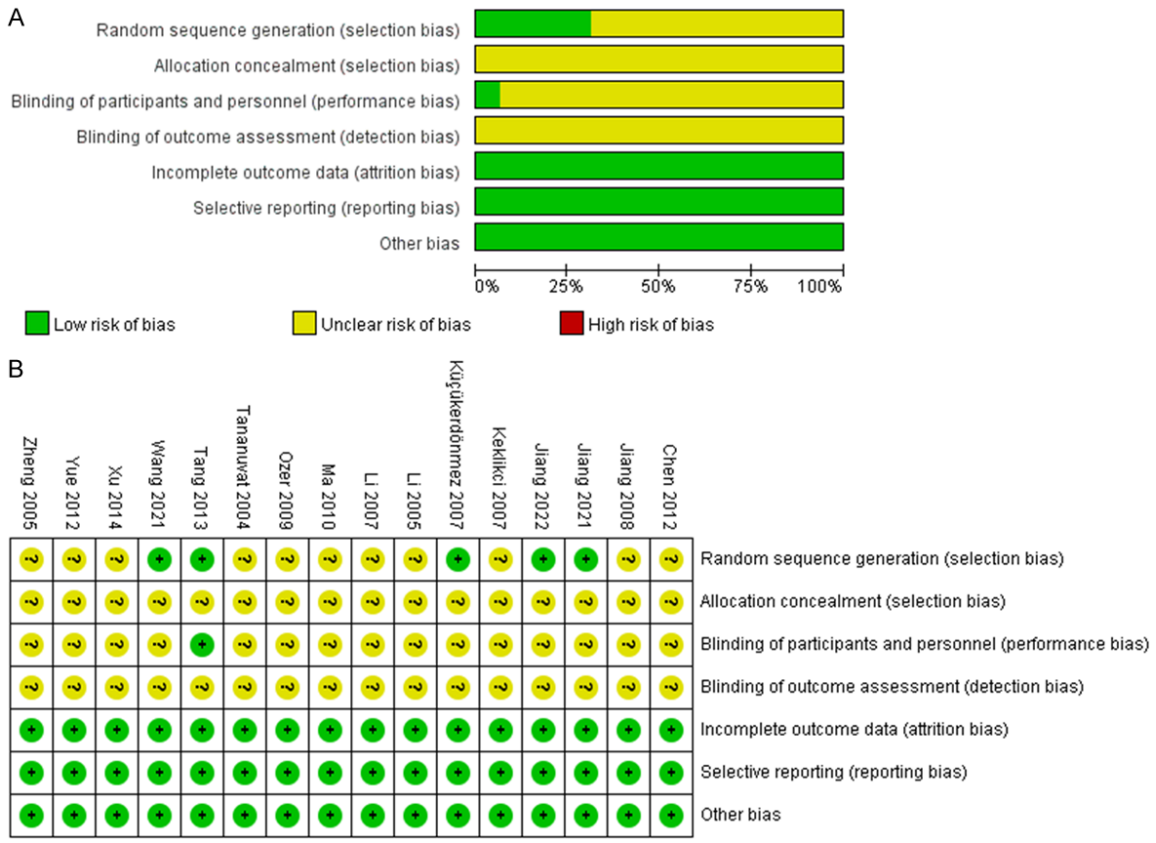

Figure 2. Cochrane risk of bias analysis. A: The graph of risk of bias: authors' assessment on the risk of bias presented as percentages across all 16 studies; B: The summary of risk of bias: authors' assessment on the risk of bias in each included study.

Quantitative analysis

BUT at 1 month after surgery: Four studies on BUT at 1 month after surgery were included in this meta-analysis [21, 31-33] with 212 eye cases in the LSCT group and 201 cases in the AMT group. Compared with that in the LSCT group, BUT in the AMT group was significantly increased (pooled MD=-0.37, 95% CI: -0.62, -0.12, $P<0.05$, fixed effect) with low heterogeneity ($I^2=0\%$, $P=0.82$) (**Figure 3A**).

BUT at 3 months after surgery: The data of BUT at 3 months after surgery were also available in 4 studies [21, 22, 32, 33]. There were 199 cases in the LSCT group and 192 in the AMT group. Heterogeneity was detected among these 4 studies by heterogeneity test ($I^2=51\%$, $P=0.11$). When a sensitivity analysis was conducted for these 4 studies, we found that the study of Jiang 2021 [21] had a significant effect on the heterogeneity since the pooled effect of the meta-analysis varied considerably (Supplementary Figure 1). Therefore, we removed the study of Jiang, performed the heterogeneity test again and found a low heterogeneity among the remaining 3 studies ($I^2=0\%$, $P=0.92$, fixed effect) (**Figure 3B**). Finally, we conducted the fixed effect model analysis, but the difference was not statistically significant (pooled MD=-0.35, 95% CI: -0.84, 0.13, $P=0.82$, fixed effect).

BUT at 6 months after surgery: Data on BUT at 6 months after surgery were available in 3 RCTs [21, 31, 32]. There were 166 cases in the LSCT group and 157 in the AMT group. The heterogeneity test results showed significant heterogeneity across these 3 studies ($I^2=78\%$, $P=0.01$). Then, a sensitivity analysis was conducted for these 3 studies, and the results revealed that the heterogeneity resulted from the study of Jiang 2021 [21] (Supplementary Figure 2). Hence, the heterogeneity test was performed again after removing the study of Jiang 2021. However, the remaining 2 studies still had high

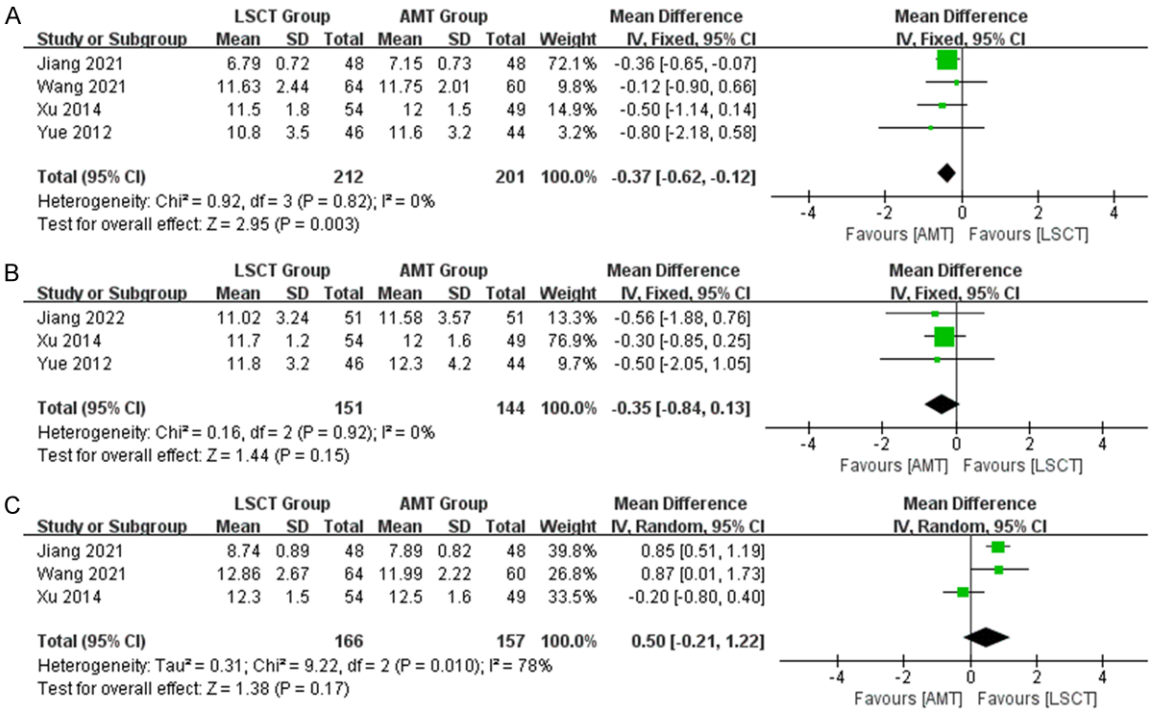

Figure 3. Forest plot of postoperative BUT between the LSCT and the AMT groups. Results of BUT 1 month (A), 3 months (B), and 6 months (C) post-surgery. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation; BUT: Tear Break-Up Time.

heterogeneity (I^2=75%, *P*=0.05). To circumvent this problem, the random effect model was adopted, and the values of BUT were increased in the LSCT group compared to the AMT group, although the difference was not statistically significant (pooled MD=0.50, 95% CI: -0.21, 1.22, *P*=0.17, random effect) (**Figure 3C**).

Schirmer I test at 1 month after surgery: The data on Schirmer I test 1 month postoperatively were obtained from 3 RCTs [21, 31, 33] with 158 cases in the LSCT group and 152 cases in the AMT group, which was summarized by a forest plot (**Figure 4A**). Heterogeneity test demonstrated an overall low heterogeneity across these 3 studies (I^2=0%, *P*=0.92). We found that the wetting length of test strips for the Schirmer I test was significantly increased in the AMT group compared with the LSCT group (pooled MD=-0.32, 95% CI: -0.57, -0.07, *P*<0.05, fixed effect).

Schirmer I test at 3 months after surgery: The data of the Schirmer I test 3 months postoperatively were available in 3 RCTs [21, 22, 33] with 145 cases in the LSCT group and 143 cases in the AMT group, which was summarized by a forest plot (**Figure 4B**). Heterogeneity test indicated that there was no significant heterogeneity among the 3 studies (I^2=47%, *P*=0.15). Opposite to the data of 1-month after surgery, the length of wetting Schirmer strip was significantly increased in the LSCT group compared to the AMT group (pooled MD=0.36, 95% CI: 0.08, 0.64, *P*<0.05, fixed effect).

Schirmer I test at 6 months after surgery: Only two RCTs on the Schirmer I test 6 months postoperatively were available for the meta-analysis [21, 31] with 112 cases in the LSCT group and 108 in the AMT group. Consistent to the results of 3 months post-surgery, the length of wetting Schirmer paper strip was significantly increased in the LSCT group compared with that in the AMT group (pooled MD=0.33, 95% CI: 0.07, 0.60, *P*<0.05, fixed effect) (**Figure 4C**).

Postoperative corneal epithelial healing time: The data on postoperative corneal epithelial healing time were obtained from 7 RCTs [19-22, 26, 28, 30] with a total of 320 cases in the LSCT group and a total of 316 cases in the AMT group. Heterogeneity test indicated an overall high heterogeneity among these 7 studies (I^2=97%, *P*<0.1). Further sensitivity analysis suggested that the study of Jiang 2021 [21]

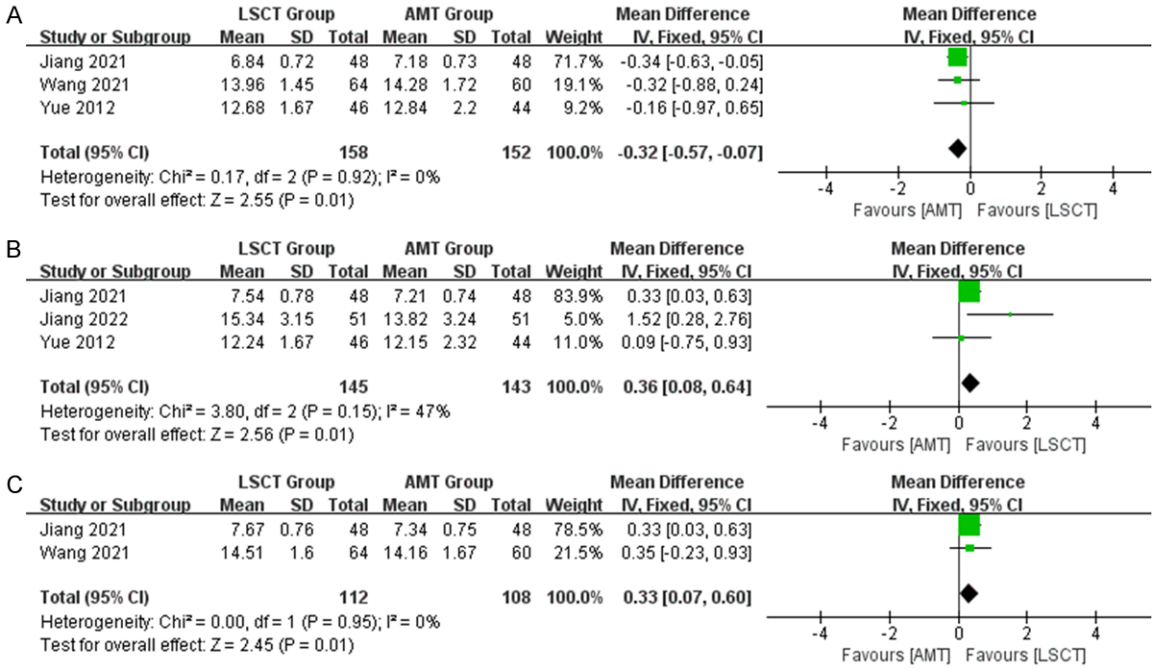

Figure 4. Forest plot of postoperative Schirmer I test between the LSCT and the AMT groups. Results of Schirmer I test 1 month (A), 3 months (B), and 6 months (C) post-surgery. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.

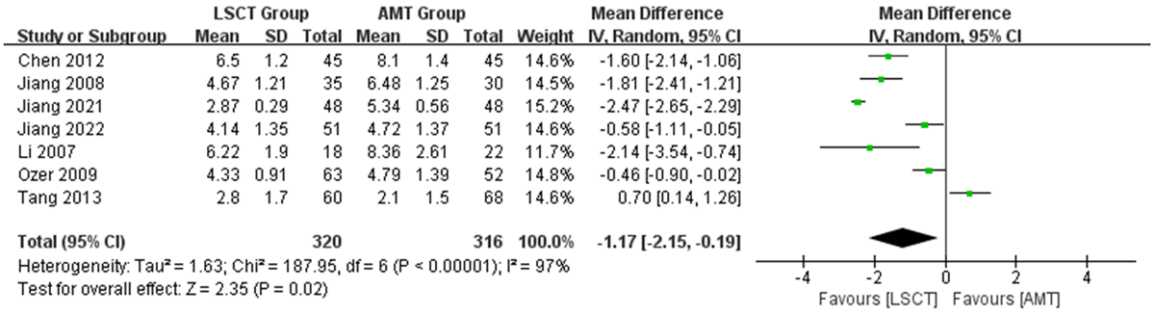

Figure 5. Forest plot of postoperative corneal epithelial healing time between the LSCT and the AMT groups. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.

had a significant impact on the heterogeneity (Supplementary Figure 3). However, when the study of Jiang 2021 was removed, the heterogeneity was still high among the remaining 6 studies (I^2=91%, P<0.1). Therefore, we chose the random effect model for the study, and the results showed that the corneal epithelial healing time was significantly shorter in the LSCT group than in the AMT group (pooled MD=-1.17, 95% CI: -2.15, -0.19, P<0.05, random effect) (**Figure 5**).

Postoperative recurrence rate: The data on the postoperative recurrence rate were obtained from 14 RCTs [19-30, 32, 34] with a total of 601 cases in the LSCT group and a total of 575 cases in the AMT group. The forest plot demonstrated that the postoperative recurrence rate was significantly lower in the LSCT group than in the AMT group (pooled RR=0.42, 95% CI: 0.30, 0.59, P<0.05, fixed effect) with low heterogeneity among all studies (I^2=0%, P=0.46) (**Figure 6**).

Postoperative complication rate: The data on the postoperative complication rate were available in 5 RCTs [19, 21, 23, 29, 30] with 227 cases in the LSCT group and 235 cases in the

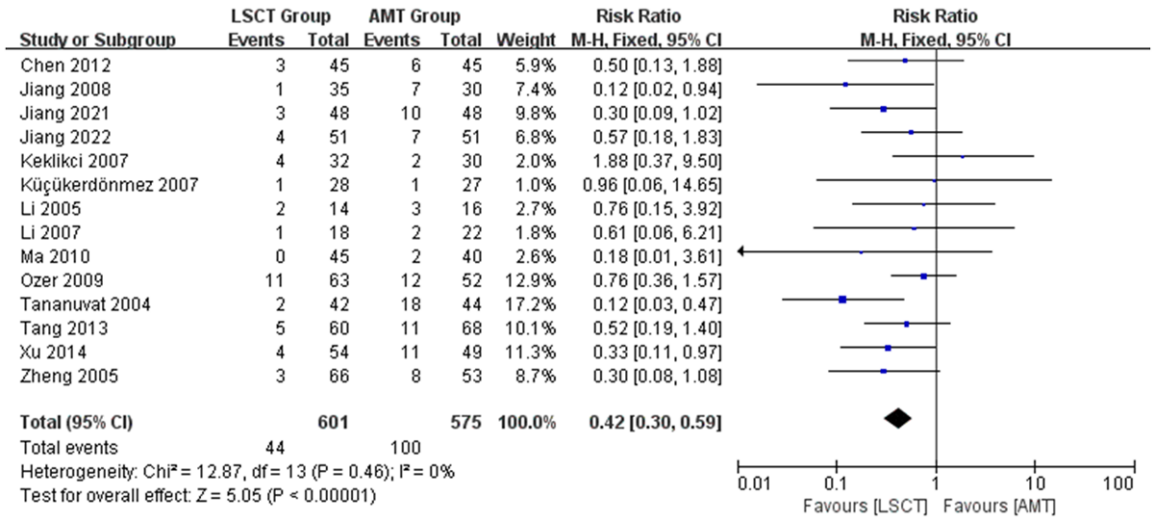

Figure 6. Forest plot of recurrence rate between the LSCT and the AMT groups. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.

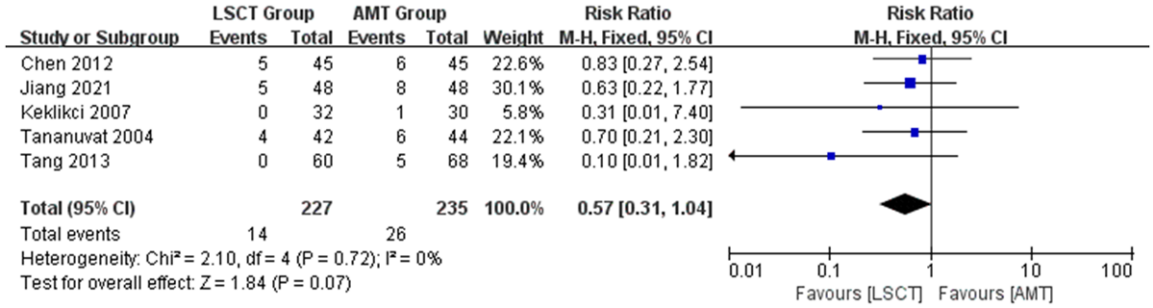

Figure 7. Forest plot of postoperative complication rate between the LSCT and the AMT groups. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.

AMT group, which is summarized by forest plot (**Figure 7**). There was no significant heterogeneity among the 5 studies as determined by heterogeneity test (I^2=0%, *P*=0.72). Similar to the results of postoperative recurrence rate, the postoperative complication rate was lower in the LSCT group than in the AMT group, although the difference was not statistically significant (pooled RR=0.57, 95% CI: 0.31, 1.04, *P*=0.07, fixed effect).

Publication bias

The shape of the funnel plot revealed that the data of each outcome measure were symmetrical (**Figure 8**), which was confirmed by Begg's and Egger's tests (all *P*>0.05), indicating that the results of each outcome measure in our meta-analysis did not have a publication bias.

Discussion

Pterygium is a common ocular surface disease with a global prevalence of 12% [35]. Although it is known that pterygium is a multifactorial degenerative disease [1], the etiopathology of pterygium remains unclear. One of the primary risk factors of pterygium is exposure to ultraviolet light, and the most effective treatment method is surgery. Furthermore, LSCT and AMT are commonly used for pterygium surgery. In recent years, the recovery of the ocular surface after pterygium surgery, such as tear film stability, corneal epithelial healing time, recurrence rate, and complications, has received increasing attention. A previous study has shown that regardless of the surgical approach, the tear film stability of patients after pterygium surgery has been improved to certain extent [13].

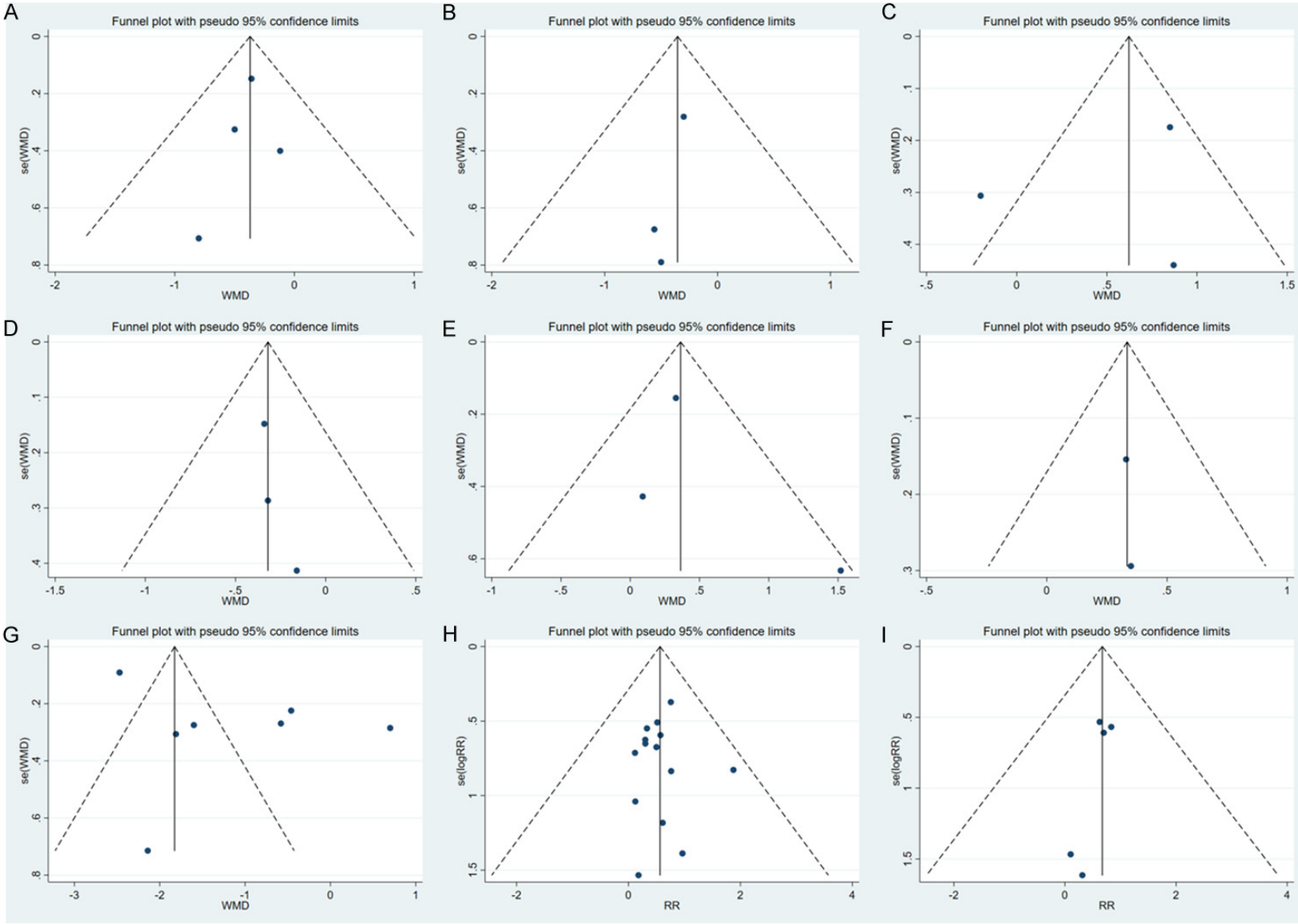

Figure 8. Funnel plot of each outcome measure between the LSCT and the AMT groups. Results of BUT 1 month (A), 3 months (B), and 6 months (C) post-surgery; Results of Schirmer I test 1 month (D) 3 months (E), and 6 months (F) post-surgery; (G) Results of postoperative corneal epithelial healing time; (H) Results of recurrence rate; (I) Results of postoperative complication rate. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation; BUT: Tear Break-Up Time.

However, there are conflicting results about the degree of improvement in tear film stability and in recurrence rates post-surgery between LSCT and AMT [5, 16, 17, 21, 22, 31-33]; hence, we conducted this meta-analysis to provide a more robust and accurate assessment on the efficacy of LSCT and AMT.

Although the Schirmer I test is also applied, the BUT is the most used clinical diagnostic test for tear film stability [36]. It measures the time interval between the complete blink and the appearance of the first break in the tear film [37]. In contrast, the Schirmer I test is a commonly used method for measuring tear production [37]. Tear osmolarity is a function of tear secretion and tear evaporation [12]. A study has shown that lower tear production can lead to higher tear osmolarity levels [38]. And there is an interconnection between hyperosmolarity and tear instability [39]. Therefore, the Schirmer I test can be used as an indirect indicator for measuring the tear film stability.

In this study, we found that patients in the AMT group presented significantly better results of the BUT and Schirmer I test at 1 month after surgery than those in the LSCT group. Nevertheless, there was no statistical difference in BUT at 3 and 6 months after surgery between the LSCT and AMT groups. However, the LSCT group showed a significantly increased tear production (based on the Schirmer I test) at 3 and 6 months after surgery compared to the AMT group, suggesting that AMT is better for the early stage of tear film stability, but LSCT seems superior in long-term postoperative tear film stability. The LSCT is the transplantation of conjunctival tissue with limbal stem cells above or below into the location following pterygium excision. Compared with the AMT, the LSCT has more damage to the conjunctival and corneal tissues in the early postoperative period, with a reduced conjunctival goblet cell population; therefore, the ocular surface integrity is more compromised. As a result, tear film stability is better in the early postoperative period in AMT than in LSCT. As the wound heals, LSCT provides normal growing conjunctival and corneal epithelial cells, accelerating the ocular surface reconstruction, thereby leading to a long-term postoperative tear film stability.

The shortened corneal epithelial healing time after pterygium surgery reflects the effective control of ocular surface inflammation which can reduce patient discomfort [40]. In contrast to the amniotic membrane, limbal stem cells not only have the ability of histiocyte renewal and regeneration, but also can continuously divide and proliferate to supplement the corneal epithelium scraped during surgery, and thus accelerating its healing. Therefore, postoperative corneal epithelial healing is theoretically faster with LSCT. Our study confirmed this notion, showing that corneal epithelial healing time was shorter in the LSCT group than in the AMT group after primary pterygium surgery, and the difference was statistically significant.

Compared with simple excision of pterygium, both LSCT and AMT are effective in reducing the postoperative recurrence rate [1]. Limbal epithelium acts as a barrier between conjunctiva and cornea, and the stem cells derived from LSCT can restore the barrier and prevent fibrous connective tissue proliferation and neovascular ingrowth, thereby inhibiting the recurrence of pterygium [17]. Hence, it is conceivable that the LSCT has the advantage in reducing postoperative pterygium recurrence. Although the studies by Zheng and Clearfield showed no statistical difference between the LSCT and the AMT in the postoperative recurrence rate, both meta-analyses suggested a lower recurrence rate in the LSCT group [5, 17]. In line with this, the study by Li indicated that the postoperative recurrence rate was significantly lower in the LSCT group than in the AMT [16], which was further supported by our findings. After pooling the postoperative complications from multiple original studies, we found that the LSCT group had a lower incidence of postoperative complications than that in the AMT group, although the difference was not statistically significant.

In this meta-analysis, we compared the tear film stability between the LSCT and the AMT. We also comprehensively analyzed the postoperative corneal epithelial healing time, recurrence rate, and complication rate using data from larger number of RCT studies. The LSCT appears to be a better option for primary pterygium, although the AMT has its own advantages. Patients can benefit from the AMT with ocular surface reconstruction, such as extensive conjunctival scarring and chemical injury, or when future glaucoma surgery is required [1, 10]. Nevertheless, it should be noted that our

study has some limitations. First, only publications written in English or Chinese were included; thus, those in non-English or non-Chinese were missing. Second, some studies had a relatively small sample size, which needs further validation.

In conclusion, our analysis showed that AMT was superior to LSCT for the early stage of tear film stability after primary pterygium excision, while LSCT was more effective than AMT in long-term postoperative tear film stability. The LSCT had a shorter postoperative corneal epithelial healing time than AMT. Furthermore, the postoperative recurrence rate of primary pterygium excision was lower in the LSCT than in the AMT. Taken together, we suggest that the postoperative recovery of primary pterygium excision combined with LSCT may be better than AMT. Further studies with larger sample sizes, well-designed RCTs, and longer follow-ups are needed to confirm our conclusion.

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Disclosure of conflict of interest

None.

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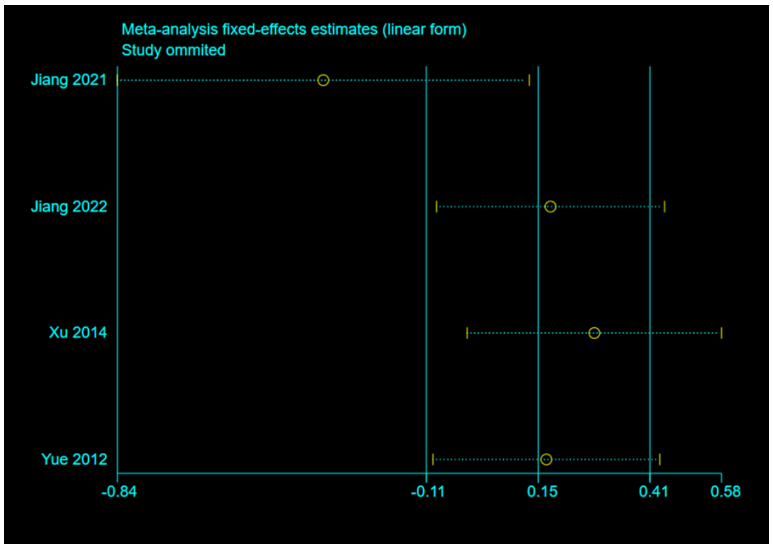
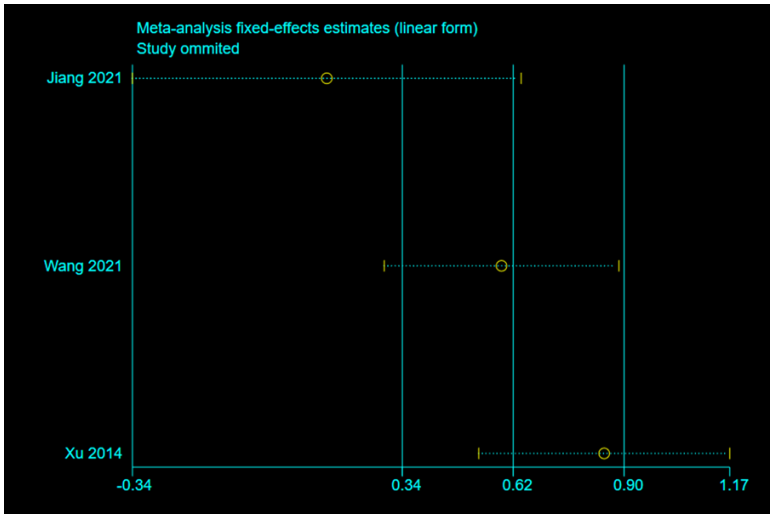
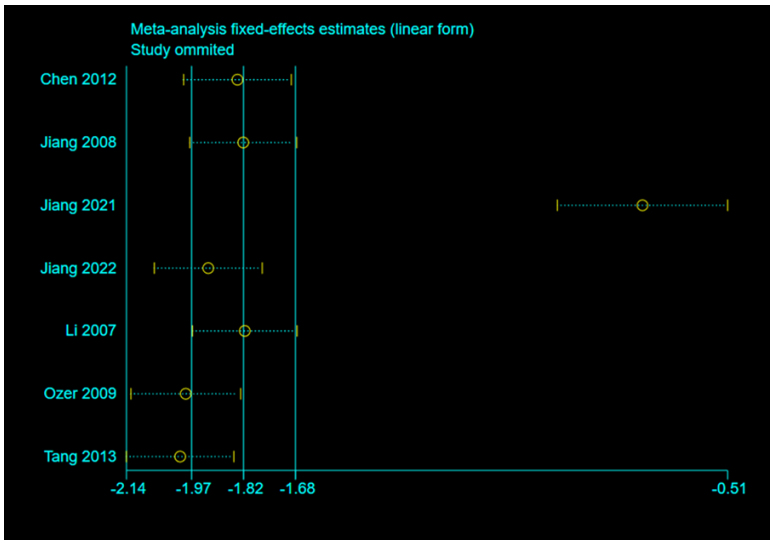


Supplementary Figure 1. The sensitivity analysis of BUT 3 months post-surgery between the LSCT and the AMT groups. Abbreviations: BUT: Tear Break-Up Time; LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.



Supplementary Figure 2. The sensitivity analysis of BUT 6 months post-surgery between the LSCT and the AMT groups. Abbreviations: BUT: Tear Break-Up Time; LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.



Supplementary Figure 3. The sensitivity analysis of postoperative corneal epithelial healing time between the LSCT and the AMT groups. Abbreviations: LSCT: Limbal Stem Cell Transplantation; AMT: Amniotic Membrane Transplantation.