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The Impact of Cyclosporine A on Pterygium Recurrence After Surgery: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 August 2026 and was last updated on 1 August 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review and meta-analysis is to evaluate the efficacy of topical cyclosporine A (CsA) in reducing the recurrence rate of pterygium after surgical excision, and to explore potential moderators of treatment effect, including CsA concentration, treatment duration, dosing frequency, surgical procedure, intraoperative use of anti-proliferative agents, control group medication regimens, recurrence definition, follow-up duration, and ultraviolet (UV) exposure level.

Condition being studied Pterygium is a common ocular surface disorder characterized by abnormal fibrovascular proliferation of the conjunctiva that extends onto the cornea, potentially causing visual impairment, astigmatism, and ocular discomfort. Surgical excision remains the primary treatment; however, postoperative recurrence remains a significant challenge, with rates varying widely depending on surgical technique and patient factors. Recurrence is primarily driven by postoperative inflammation, fibrovascular tissue regrowth, and environmental influences such as ultraviolet (UV) exposure. Adjuvant therapies, including immunomodulatory agents like cyclosporine A (CsA), have been explored to mitigate recurrence by modulating the local immune response and inhibiting fibroblast proliferation. This meta-analysis aims to evaluate the efficacy of topical CsA as an adjunctive treatment in preventing postoperative recurrence of pterygium, addressing key clinical variables such as CsA concentration, treatment duration, and surgical approaches.

METHODS

Search strategy ("Pterygium Of Conjunctiva And Cornea"[Title/Abstract] OR "Pterygium"[MeSH

Terms] OR "Pterygiums"[Title/Abstract]) AND ("Ciclosporin"[Title/Abstract] OR "CsA"[Title/Abstract] OR "CsANeoral"[Title/Abstract] OR "CyA"[Title/Abstract] OR "Cyclosporin"[Title/Abstract] OR "Cyclosporine"[MeSH Terms] OR "Cyclosporine"[Title/Abstract] OR "Neoral"[Title/Abstract] OR "OL 27 400"[Title/Abstract] OR "OL 27400"[Title/Abstract] OR "Restasis"[Title/Abstract] OR "Sandimmun"[Title/Abstract] OR "Sandimmune"[Title/Abstract]) AND ("Reappearance"[Title/Abstract] OR "Recrudescence"[Title/Abstract] OR "Recrudescences"[Title/Abstract] OR "Recurrence"[MeSH Terms] OR "Recurrences"[Title/Abstract] OR "Recurrent"[Title/Abstract] OR "Relapse"[Title/Abstract] OR "Relapses"[Title/Abstract] OR "Reoperation"[Title/Abstract] OR "Second occurrence"[Title/Abstract]).

Participant or population The study population includes patients diagnosed with pterygium (both primary and recurrent) who have undergone surgical excision. Participants encompass adults of any gender and age, treated in various clinical settings. Eligible studies must involve individuals who received postoperative interventions following specific surgical techniques, such as bare sclera technique (BST), pterygium excision with conjunctival autograft (PE+CA), pterygium excision with conjunctival flap rotation technique (PE+CFRT), or pterygium excision with limbal-conjunctival autograft (PE+LUCA). The analysis will focus on comparing outcomes between patients treated with topical Cyclosporine A (CsA) as an adjuvant therapy and those receiving standard postoperative medication or placebo.

Intervention Topical Cyclosporine A (CsA) eye drops administered postoperatively as an adjuvant therapy.
The intervention involves the administration of CsA eye drops following pterygium excision surgery. This encompasses various concentrations (including 0.05%, 0.1%, and 1%), administration frequencies (e.g., twice daily, four times daily, or adjusted according to epithelial healing), and treatment durations (ranging from 20 days to 6 months). The CsA treatment is typically applied in addition to standard postoperative regimens, which may include topical antibiotics and/or corticosteroids.

Comparator Standard postoperative medication, placebo, or treatment without topical Cyclosporine A (CsA).
The comparator groups include patients who underwent pterygium excision but did not receive topical CsA as an adjuvant therapy. This category encompasses:

Standard Postoperative Medications (SPM): The most common comparator, involving the use of topical antibiotics (e.g., fluoroquinolones) and corticosteroids (e.g., dexamethasone, prednisolone) to control inflammation and prevent infection.
Placebo: Inert eye drops administered in randomized controlled trials to ensure blinding.
Supportive Care: Treatments such as artificial tears, with or without standard medications.
Other Anti-proliferative Agents: In some studies, the control group may have received intraoperative or postoperative anti-metabolites (such as Mitomycin C or 5-Fluorouracil) for the prevention of recurrence, but without the addition of CsA.

Study designs to be included Study designs to be included:Randomized Controlled Trials (RCT)、Non-randomized Controlled Trials、Cohort studies and Case-control studies.

Eligibility criteria Inclusion criteria:
1. Study designs: Randomized controlled trials (RCTs), non-randomized controlled trials (Non-RCTs), cohort studies, and case-control studies.
2. Participants: Patients diagnosed with pterygium (primary or recurrent) who have undergone surgical excision.
Intervention: Administration of topical Cyclosporine A (CsA) eye drops postoperatively.
3. Comparator: Control groups receiving placebo, no CsA, standard postoperative medications (e.g., antibiotics and/or corticosteroids), or other topical treatment regimens without CsA.
4. Outcomes: Studies reporting postoperative recurrence rates. The recurrence definition should be based on the study's criteria (e.g., fibrovascular tissue crossing the limbus, specific distance thresholds, or Prabhasawat grade), with data extractable at the final follow-up or specific time points (e.g., 3, 6, 12 months).
5. Language: Studies published in Chinese or English.
Exclusion criteria:
1. Study types: Reviews, meta-analyses, case reports, conference abstracts with insufficient extractable data, animal experiments, or in vitro studies.
2. Participants: Studies involving populations not undergoing pterygium surgery, or mixed surgical populations where pterygium data cannot be extracted separately.
3. Lack of control: Studies without a control group or where data for the CsA and non-CsA groups cannot be distinguished.

4. Data availability: Studies with severe missing outcome data that cannot be obtained from the authors or derived statistically.
5. Duplicate publications: Multiple publications arising from the same study cohort; only the study with the largest sample size or most complete data will be retained.
6. Sample size: Studies with a sample size of fewer than 10 participants/eyes per group.
7. Unit of analysis issues: Studies involving bilateral eye surgeries that do not clearly define the unit of analysis, provide independent data for each eye, or employ appropriate statistical methods to handle inter-eye correlation.

Information sources Electronic databases: We will search the following databases from inception to 13 April 2026: PubMed, Embase, Web of Science, The Cochrane Library, and OpenAlex.
Additional sources: We will screen the reference lists of included studies and relevant reviews to identify additional eligible studies. No other sources (e.g., trial registries, conference proceedings) will be used.

Main outcome(s) Pterygium recurrence rate.

Quality assessment / Risk of bias analysis Quality assessment / Risk of bias analysis:
Two investigators will independently assess the methodological quality and risk of bias for all included studies. Disagreements will be resolved through discussion or consultation with a third investigator.

For Randomized Controlled Trials (RCTs):
We will use the Cochrane Risk of Bias 2 (RoB 2) tool. The assessment covers five domains:
1.Bias arising from the randomization process.
2.Bias due to deviations from intended interventions.
3.Bias due to missing outcome data.
4.Bias in measurement of the outcome.
5.Bias in selection of the reported result.
Special considerations: We will assess whether the unit of randomization (patient vs. eye) was appropriate and whether outcome assessors were blinded to the group assignment. The overall risk of bias for each study will be judged as "Low risk," "Some concerns," or "High risk."

For Non-randomized Controlled Trials:
We will use the Risk Of Bias In Non-randomized Studies of Interventions-I (ROBINS-I) tool. This tool evaluates seven domains:
1.Confounding bias.
2.Bias in selection of participants.
3.Bias in classification of interventions.
4.Bias due to deviations from intended interventions.
5.Bias due to missing data.
6.Bias in measurement of outcomes.
7.Bias in selection of the reported result.
The overall risk will be categorized as "Low," "Moderate," "Serious," or "Critical."

For Cohort Studies:
We will use the Newcastle–Ottawa Scale (NOS), which evaluates three dimensions:
1. Selection of study groups (0–4 stars).
2. Comparability of the groups (0–2 stars).
3. Assessment of outcome (0–3 stars).
A total score of 7–9 will be considered high quality, 4–6 moderate quality, and 0–3 low quality.

Strategy of data synthesis Statistical unit and effect measures:
The primary analysis unit will be the operated eye. For the dichotomous outcome of recurrence, we will calculate the Risk Ratio (RR) with its 95% Confidence Interval (CI) as the effect size. The Mantel–Haenszel method will be used to pool effect sizes.
Assessment of heterogeneity and model selection:
Statistical heterogeneity will be assessed using the Cochran's Q test (significance level $P < 0.10$) and the I^2 statistic. Heterogeneity will be categorized as low (I^2 50%).
If $I^2 < 50\%$ and the Q test $P \geq 0.10$ (low heterogeneity), a fixed-effect model will be used.
If $I^2 \geq 50\%$ or the Q test $P < 0.10$ (substantial heterogeneity), a random-effects model will be used, and potential sources of heterogeneity will be explored through subgroup analysis or sensitivity analysis.
Assessment of publication bias:
If 10 or more studies are included in the meta-analysis, funnel plots will be generated for visual inspection, and Egger's regression test will be performed to quantitatively assess potential publication bias ($P < 0.05$ indicating significant bias).

Subgroup analysis To investigate the influence of clinical and methodological variables on the effect of CsA, we plan to perform the following subgroup analyses:
1.CsA concentration: 0.05%, 0.1%, and 1%.
2.Duration of CsA therapy: (e.g., 3 months vs. 6 months).
3.Frequency of administration: (e.g., twice daily vs. four times daily).
4.Surgical procedures: Bare sclera technique (BST), pterygium excision + conjunctival autograft (PE+CA), pterygium excision + conjunctival flap rotation technique (PE+CFRT), and pterygium

excision + limbal-conjunctival autograft (PE+LUCA).
5.Intraoperative use of anti-proliferative drugs: Yes vs. No.
6.Control group medication: Standard postoperative medications, with/without artificial tears, or with anti-proliferative drugs.
7.Definition of recurrence: (e.g., Prabhasawat grade, specific distance thresholds).
8.Follow-up duration: (e.g., 3, 6, 12 months).
9.UV exposure levels: High vs. Low.

Sensitivity analysis We will conduct sensitivity analyses to assess the robustness of the results using the leave-one-out method (removing one study at a time). Additionally, we will re-analyze the data after excluding studies with a high risk of bias to determine if the overall conclusion is affected.
Assessment of publication bias.

Country(ies) involved China - Anqing Municipal Hospital.

Keywords Pterygium; Cyclosporine A; Recurrence; Meta-analysis.

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