Systematic Review of the Prevention and Management of Postoperative Trachomatous Trichiasis

KREIS, Andréas Josef

Abstract

Among ocular infections, trachoma is the main cause of blindness. Repeated conjunctival Chlamydia trachomatis infections lead to trichiasis, corneal opacification and visual impairment. Surgery is often needed to relieve discomfort and preserve vision. However, a high recurrence rate is observed. There are many hypotheses that may explain this high failure rate. We systematically reviewed the literature on the pathogenesis and clinical features of postoperative trachomatous trichiasis (PTT) and the evidence for interventions to prevent and manage it.

Reference


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"Systematic Review of the Prevention and Management of Postoperative Trachomatous Trichiasis"

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Andréas J. KREIS

University of Geneva

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Systematic Review of the Prevention and Management of Postoperative Trachomatous Trichiasis

Andreas J Kreis, MD

1Ophthalmology Department, University Hospital of Geneva, Geneva, Switzerland
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1. Summary

Among ocular infections, trachoma is the main cause of blindness. Repeated conjunctival *Chlamydia trachomatis* infections lead to trichiasis, corneal opacification and visual impairment. Surgery is often needed to relieve discomfort and preserve vision. However, a high recurrence rate is observed. There are many hypotheses that may explain this high failure rate. This paper is a systematic review of the literature on the pathogenesis and clinical features of postoperative trachomatous trichiasis (PTT) and the evidence for interventions to prevent and manage it.

A search of PubMed was undertaken using the terms (“recurrent” OR “postoperative” OR “post-operative” OR “post-surgical” OR “postsurgical” OR “secondary”) AND “trichiasis”) with no date or language restrictions. The titles (and where available, abstracts) of each of the returned records were screened; full-text papers of records identified as potentially being relevant were obtained. Reference lists of full-text papers were hand-searched. Relevant material was extracted from all relevant papers. Prisma guidelines were adhered to. The review was registered on Prospero.

Of 197 papers screened, 142 studies were identified for inclusion. 55 studies were excluded for not being relevant.

Addressing PTT is a major challenge. Published literature on the management of postoperative trachomatous trichiasis (PTT) is sparse. To date there are no management guidelines available. Clinical studies are needed to generate evidence for optimal ways to address this problem. It is likely that the PTT patient pathway will need reconsideration.

Keywords: Postoperative Trachomatous Trichiasis, Trichiasis Surgery, Trachoma, Systematic Review
2. Introduction

Trachoma is a disease caused by particular strains of *Chlamydia trachomatis*.\[1\] A public health problem in parts of at least 44 countries,\[2\] it is concentrated in low-income communities, and within those communities, tends to affect the very poorest.\[3\] It is the main cause of blindness due to infection. About 1.3 million people are irreversibly blind due to trachoma.\[4\]

Transmission of ocular *C. trachomatis* is thought to occur relatively easily in trachoma-endemic communities, particularly amongst household contacts, and therefore to recur often. With repeated recurrence, infection-induced scarring leads to eyelash inversion (trachomatous trichiasis, TT), corneal scarring, and eventually blindness (Pic 1/Table1).\[5, 6\] In 2016, an estimated 2.8 million people had TT worldwide.\[6\] For relief of pain and preservation of remaining vision, eyelid surgery for TT is a key component of the World Health Organization (WHO)-recommended SAFE strategy (surgery, antibiotics, facial cleanliness and environmental improvement)

Picture 1: Patients with trachomatous trichiasis and concomitant corneal opacities

Numerous surgical techniques for managing TT have been described. Those most commonly used within national programmes are bilamellar tarsal rotation (BLTR) and the method of Trabut.\[7-9\] Unfortunately, the incidence of postoperative trichiasis (PTT) after either of these procedures is high, averaging 30–40% within 1 year after
The reasons for this high failure rate are unclear but probably include a combination of imperfections in surgical technique and ongoing disease-related scarring processes within affected eyelids.[9, 15, 20-22]

Here we systematically review the published literature on PTT with the aim of better understanding this condition. In particular, we ask: what is known about its pathogenesis and presentation, and what evidence is there for preventing and treating it?

Table 1. World Health Organization simplified classification of trachoma infection.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trachomatous inflammation—follicular (TF)</td>
<td>The presence of 5 or more follicles (each of at least 0.5 mm diameter) in the central part of the upper tarsal conjunctiva</td>
</tr>
<tr>
<td>Trachomatous inflammation—intense (TI)</td>
<td>Pronounced inflammatory thickening of the tarsal conjunctiva that obscures more than half of the deep normal tarsal vessels</td>
</tr>
<tr>
<td>Trachomatous scarring (TS)</td>
<td>The presence of easily visible scarring in the tarsal conjunctiva</td>
</tr>
<tr>
<td>Trachomatous trichiasis (TT)</td>
<td>At least one eyelash touches the eyeball</td>
</tr>
<tr>
<td>Corneal opacity (CO)</td>
<td>The presence of easily visible corneal opacity which obscures at least part of the pupil margin</td>
</tr>
</tbody>
</table>

TF  TI  TS  TT
3. Methods

We undertook a systematic review following PRISMA guidelines (http://www.prisma-statement.org). We prospectively registered the review on Prospero (https://www.nihr.ac.uk/) having previously searched the Prospero database (using the search terms nominated below) to prevent duplication of an existing as-yet unpublished review.

We searched PubMed (https://pubmed.ncbi.nlm.nih.gov/) with no limits on the year or language of publication. We used the search terms ("recurrent" OR "postoperative" OR "post-operative" OR "post-surgical" OR "postsurgical" OR "secondary") AND "trichiasis"). Two reviewers independently screened the titles and (where available) the abstracts of the search output. Full-text versions of papers selected by either reviewer were obtained for more detailed scrutiny. Data extraction and study quality evaluation were performed independently by the same two reviewers. Reference lists of full-text papers were hand-searched. All potentially relevant non-English publications were translated into English. The authors’ personal reference collections were also hand-searched for relevant material. Where there was a disagreement on whether or not to include a particular paper, the authors reviewed it together and reached consensus through discussion.

Due to an absence of randomized controlled trials on the management of PTT and an across-the-board very low quality of evidence within included studies, neither an assessment of risk of bias nor meta-analysis of data was applicable.
4. Results

Of 197 papers identified in the PubMed search, 142 studies were felt sufficiently likely to be relevant to warrant full-text review (Fig 1). Of the remainder, 55 papers were excluded for being in animals other than humans (3 studies), covering oculoplastics in general and/or not being related to PTT (52 studies). Of the 142 studies assessed by full text review no study was further excluded. No studies of the management of PTT were sufficiently methodologically sound to warrant formal assessment of the risk of bias. No statistical meta-analysis was performed. Instead, we subjected the 142 included studies to qualitative synthesis.

4.1 Pathophysiology and Clinical Features of PTT

Much is known about the epidemiology and pathophysiology of trachoma. Standardized population-based prevalence surveys have estimated the district-level prevalence of TF in children and TT in adults in the vast majority of suspected-trachoma-endemic districts worldwide. Where necessary, elimination programs are implementing the SAFE Strategy: surgery for TT, mass drug administration of antibiotics active against C. trachomatis, promotion of facial cleanliness, and environmental improvement. This strategy has successfully eliminated trachoma in several countries and further inroads are being made year-on-year.[23, 24] However, little has been documented about the pathophysiology of PTT. This lack of investigation is troubling, given the observed high surgical failure rate, and may reflect both the logistical difficulty in following-up and studying individuals who receive operations for TT and the (unjustified) hope that correction of TT constitutes a definitive procedure. The limited understanding of PTT’s pathophysiology is accompanied by a relative dearth of high-quality evidence on how to minimize or manage it. It has been argued that ongoing recurrent conjunctival C. trachomatis infection, with accompanying scarring as each infection resolves, might account for a proportion of failures.[25-27] Alternatively, or in addition, an inflammatory process in the absence of further chlamydial infection could promote abnormal healing, leading to
malposition of the lid and eventually recurrence of TT.[28] It has also been postulated that the location of the eyelashes touching the eye preoperatively predicts the likelihood of developing PTT, with peripheral TT being more commonly followed by PTT.[29] Amongst other possible mechanisms, this association could potentially be explained by deficiencies in surgical technique: inexperienced or apprehensive surgeons may find it difficult to extend the eyelid incision as far temporally and nasally as is required to ensure adequate external rotation of the whole eyelid margin.

In general, one could postulate that all the primary pathophysiological processes that culminate in TT in the first place could play important roles in post-surgical failure, leading to PTT.[11, 15, 29, 30] This is important considering that scarring in general can be unpredictable and the more scarred the tissue, the more difficult it is to operate on.[22] Surgery itself does nothing to ameliorate the scarring process that underlies the development of TT and may in fact augment it. Inappropriate surgery (e.g., incorrect incision height [31], or implementing an entropion correction procedure in the absence of entropion) may therefore potentially also contribute to the overall PTT load.[21, 32]

The clinical features of primary TT are well known and have been described previously.[33] The same features are found in PTT and the severity of trichiasis in PTT (Table 2) has been also been in investigated and classified by different trials like the STAR or PRET trial.[29] But additional features complicating the prior operation, including pyogenic granulomata and eyelid contour abnormalities (ECAs) (Pic 2), may also be found.[30] These additional elements may complicate the management algorithm.
### Table 2. Trichiasis severity classification by trial

<table>
<thead>
<tr>
<th>Category</th>
<th>STAR Trial</th>
<th>PRET Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>1–4 trichiatic eyelashes and no epilation OR Epilation and no trichiatic eyelashes</td>
<td>1–4 trichiatic eyelashes and no epilation OR &lt;1/3 of eyelid epilated and no trichiatic</td>
</tr>
<tr>
<td>Moderate</td>
<td>5–9 trichiatic eyelashes and no epilation OR 1–4 trichiatic eyelashes and epilation</td>
<td>5–9 trichiatic eyelashes and no epilation OR 1–4 trichiatic eyelashes and &lt;1/3 epilated</td>
</tr>
<tr>
<td>Severe</td>
<td>5–9 trichiatic eyelashes and epilation OR 10+ trichiatic eyelashes</td>
<td>5–9 trichiatic eyelashes and any epilation OR 10+ trichiatic eyelashes OR &gt;1/3 eyelid epilated</td>
</tr>
</tbody>
</table>

#### Picture 2. Eyelid contour abnormality or ECAs (A) and pyogenic granuloma (B) after trichiasis surgery for trachomatous trichiasis

![Eye with eyelid contour abnormality](imageA.jpg)

![Pyogenic granuloma](imageB.jpg)
4.2 Treatment of PTT

The aims of treatment for primary TT are (1) to prevent further corneal opacification due to trauma from the eyelashes abrading the cornea; (2) to reduce the risk of ongoing corneal trauma providing a portal of entry for secondary corneal infection from bacteria or fungi; (3) to relieve pain; and (4) to recover some vision through relief of blepharospasm and reduction in corneal oedema.[8] These aims can be realized by repositioning the eyelashes so that they no longer touch the eyeball. This is done most commonly with one of three well-established procedures: bi-lamellar tarsal rotation (BLTR/Fig 2A), Trabut’s tarsotomy (Fig 2B) or tarsal advance and rotation (Fig 2C). A range of other non-surgical and surgical treatments (Table 3) have been described for primary TT, including epilation, eyelid taping, electrolysis of involved eyelash follicles, cryotherapy to involved eyelash follicles, excision of lash-bearing tissue (through, e.g., wedge excision) or some combination of these approaches, with or without upper lid blepharoplasty.[7, 9, 22]
**Table 3. Non-Surgical and Surgical Treatments for Primary TT and PTT**

<table>
<thead>
<tr>
<th>Non-surgical treatments</th>
<th>Surgical treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>epilation (manual removal of eyelashes, usually with forceps)</td>
<td>Surgical procedures for lash ablation or removal</td>
</tr>
<tr>
<td>eyelid-taping (to force eyelashes back to correct position)</td>
<td>electrolysis (fine needle used to pass electric current to base of lash follicle)</td>
</tr>
<tr>
<td></td>
<td>cryotherapy (freezing treatment to the lash follicles)</td>
</tr>
<tr>
<td></td>
<td>excision of lash-bearing tissue</td>
</tr>
<tr>
<td><strong>Surgical options for the treatment of upper lid entropion</strong></td>
<td>Bilamellar tarsal rotation (BLTR): full-thickness incision through the eyelid, including the scarred tarsal plate, orbicularis oculi and the skin, fixation with everting sutures</td>
</tr>
<tr>
<td></td>
<td>Posterior lamellar tarsal rotation (PLTR)/Trabut: incision through the scarred tarsal plate and conjunctiva only, leaving the skin and orbicularis oculi intact, fixation with everting sutures</td>
</tr>
<tr>
<td></td>
<td>Tarsal advance and rotation: incision of the tarsal plate and rotation of the terminal portion. The upper part of the tarsus is separated from the anterior lamellar, advanced and fixed with sutures</td>
</tr>
<tr>
<td><strong>Mainly in PTT</strong></td>
<td>Either surgery combined with or without blepharoplasty and/or wedge excision</td>
</tr>
</tbody>
</table>

The choice of treatment generally depends on factors such as available resources and expertise, location (opportunity for follow up) and how advanced the disease is, as well as global and local recommendations. In most jurisdictions, eyelid surgery is delivered by trained and certified ophthalmic assistants or ophthalmic nurses as well as ophthalmologists, with ophthalmologists providing only a very small fraction of the required operations because their numbers are typically overwhelmingly insufficient to meet demand, and their skills are felt to be better deployed elsewhere. [7, 34, 35]

The published literature on the management of PTT is sparse. Guidelines are virtually non-existent. [22] Surgery of PTT to correct the eyelid deformity seems to be widely
recognized as the treatment of choice. Most cases of primary TT, and therefore also of PTT, occur in sub-Saharan Africa. As noted above, primary TT is generally treated by ophthalmic nurses with only limited surgical training.[7] PTT, a significantly more complex surgical problem, is treated in general using the same techniques and by the same personnel who undertake primary TT surgery. This may not be ideal. The World Health Organization, whilst noting the need for more research on the treatment of PTT, recommends that in the absence of specific evidence on optimal approaches, it “should be managed by the most experienced trichiasis surgeon or eye specialist available” and that “between diagnosis and review by that professional, epilation should be encouraged”. [36]

4.3 Prevention of PTT

Some published data indicate that peri-operative single-dose oral azithromycin, but not doxycycline, can help prevent PTT.[18, 37, 38] However, evidence for efficacy of azithromycin for this purpose is mixed [7, 39] This suggests that more long-term data is needed to determine the value of oral azithromycin, with the effect potentially being applicable to some but not all settings.

We found no published data demonstrating management approaches for primary TT that exclude the risk of PTT. However, numerous studies have suggested that PTT is in part related to surgical skill or performance.[11, 14, 21, 26, 31, 32] A high-quality randomized controlled trial conducted in Ethiopia suggests that the Trabut procedure is followed by a lower incidence of PTT than is BLTR.[30] Exactly which aspects of primary TT surgery most influence outcome are unclear. It is however obvious that for multiple reasons, not limited to having an effective prevention strategy for PTT, there is a need to improve surgical skills and have a reliable postoperative follow up strategies and systems.[14, 20, 22, 40, 41]
5. Discussion

Poor outcomes from TT surgery affect both the individual patient and the trachoma control program as a whole, since confidence in surgery is likely to affect community confidence in the worth of other components of the SAFE strategy. A good understanding of the factors that increase the likelihood of an adverse outcome is therefore crucial for surgeons, surgical trainers, and program planners.[30]

As noted above there are a number of factors that have been linked to poor outcomes of primary TT management. The strength of evidence for these associations is variable, and it is presently impossible to propose a way in which the incidence of PTT could be expected to be reduced to zero. There seems however to be a consensus that surgical systems to prevent people going blind from trachoma need strengthening, starting from the physical infrastructure where surgery takes place, to the skills of surgeons, to the systems that facilitate follow-up, routine audit and surgical supervision.[11, 14, 21, 22, 26, 31, 32] In Mali recently, we experienced imperfect theatre lighting, lack of cleaning services and sub-optimal operating tables, cautery devices, and so on. These conditions made surgery considerably more challenging (Pic 3).[22] From the surgeon’s viewpoint, such deficiencies add technical barriers, slow patient throughput and heighten team stress. Eyelid surgery in general is delicate work, requiring dexterity and a clear, magnified field of view; it is even more difficult in the already-operated eyelid of PTT. A lot of primary TT surgery, however, is undertaken in outreach settings with little to no fixed infrastructure. Studies reporting no difference in outcomes between surgery performed in rural villages (Pic 4) and in the hospital setting are testament to both the skill of the surgeons involved and the level of stoicism of the patient.[42] Such attributes are even more critical in PTT, where patient and provider have to deal with consequences of previous failure. To give surgery the best possible chance of success, adequate infrastructure, working theatre equipment and the availability of decent binocular magnification are necessary (but not sufficient) to facilitate good outcomes.[22]
Intra-operative patient discomfort at the time of primary surgery could lead to reluctance to return for review or reoperation if needed, and poor uptake of TT surgery by others in the community.[43, 44] Intra-operative patient discomfort at the time of surgery for PTT would make achieving good results extremely difficult. PTT by definition occurs in a pre-operated eyelid, which therefore will be scarred and may also be inflamed. The volume of local anaesthetic (LA) used must be sufficient to completely numb the tissues. Failure to do so puts both surgeon and patient under significant stress due to patient pain and movement. [22] The possible role of adjunctive hyaluronidase to improve local anaesthetic tissue penetration and/or steroids to decrease postoperative tissue inflammation in PTT has not been explored.[45-48]
Based on our review, there are no data to assist in decision-making about which surgical technique should be preferred when addressing PTT. Unlike cataract surgery where there is common agreement among surgeons on how to perform cataract surgery and the surgeon’s choice is a gold standard approach in the majority of cases, i.e., phacoemulsification,[49] in PTT surgery numerous approaches are used sometimes even combined.[22] And similar to glaucoma surgery, where there seem to be different schools with different approaches, the success rate of glaucoma surgery varies a lot too as they do in trachoma surgery.[50] It almost seems symptomatic that having numerous approaches lead to poor outcome, significant loss of resources as well as loss of patient trust and wellbeing.

Management thus is complex and will need to be addressed by highly skilled hands, regardless of the cadre of operator, which may need to be an oculoplastic surgeon, ophthalmologist or a specially trained TT nurse, depending on the local context. In the absence of evidence to the contrary and based on first principles inherent in revision surgery at any anatomical sight, it seems likely that individualized patient assessment and planning will be needed. This would mean that the patient pathway for PTT should be reconsidered and redesigned. Ideally, PTT patients would be directed to tertiary level hospitals designated as PTT centres, in which well-trained oculoplastic surgeons managed cases with support from a multidisciplinary team. Failing this, programmes may elect to choose particularly skilled TT nurses and invest in their training to generate a cohort of PTT nurse-surgeons.

In any case, the selection and training processes for TT and PTT surgeons should be clearly defined and adhered to. Structured program monitoring and evaluation as well as further clinical research will be key to decreasing the complication rate of TT surgery.[31, 51] Evaluation for uncorrected refractive error, cataracts or inadequate stereoscopic vision should be a mandatory part of the selection process for TT nurses.[52] Finally a no-fault error culture must be fostered in which it is recognized that untoward events occur despite the best efforts of all involved. This will facilitate ongoing learning, system improvement, enhanced patient safety and better outcomes.[53-55]
6. Conclusion

Addressing PTT is a major challenge. The published literature on its management is sparse. High-quality surgery with a low rate of unfavourable outcomes is likely to require enhanced surgical training of a smaller group of identified, highly skilled PTT surgeons. The PTT patient pathway needs reconsideration. Further studies are needed to define optimal interventions. A no-fault error culture should be encouraged.
7. References


8. Figure

Figure 1. Flow Chart demonstrating PubMed search selection

- Records identified through database searching (n = 197)
- Additional records identified through other sources (n = 0)
- Records after duplicates removed (n = 0)
- Records screened (n = 192) → Records excluded (n = 55)
- Full-text articles assessed for eligibility (n = 142) → Full-text articles excluded, with reasons (n = 0)
- Studies included in qualitative synthesis (n = 142)
- Studies included in quantitative synthesis (meta-analysis) (n = 142)
Figure 2A. Bilamellar tarsal rotation:

Figure 2B. Posterior lamellar tarsal rotation (Trabut)
A: Posterior lamellar incision. B: Dividing anterior and posterior lamellae.
C: Horizontal mattress sutures. D: Postoperative lid eversion
Figure 2C. Tarsal advance and rotation.
A: Posterior lamellar incision and division between posterior and anterior lamellae (arrow indicates 180 rotation of terminal tarsus). B: Rotation and suturing of terminal tarsus, inferior advancement and suturing of posterior lamella (arrow indicates inferior movement of posterior lamella).