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Title: Penetrating Keratoplasty for Trachomatous Corneal Scarring

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Abstract: Purpose: To evaluate graft survival and visual outcome after penetrating keratoplasty (PKP) for trachomatous corneal scarring.

Methods: A retrospective review was conducted on all cases of PKP performed at King Khaled Eye Specialist Hospital between January 1, 1997, and December 31, 2001, for trachomatous corneal scarring.

Results: This study included 127 eyes. The mean age at the time of surgery was 64.7 years (range, 40-90 years). The mean follow-up was 1266 days (range, 91-3423 days). At the most recent visit, 102 (80.2%) grafts were clear, and 25 (19.7%) had failed. Kaplan-Meier graft survival was 98.3% at 1 year, 85.9% at 2 years, 83.2% at 3 years, 80.2% at 4 years, and 76.6% at 5 years. Major postoperative complications included glaucoma escalation (27.6%), endothelial rejection (17.3%), and bacterial keratitis (8.7%). Visual acuity improved in 107 (84.3%) eyes, remained the same in 12 (9.5%) eyes, and worsened in 8 (6.3%) eyes. Final visual acuity of 20/160 or better was obtained in 67 (56.7%) eyes.

Conclusion: Treating trachomatous corneal scarring with PKP can be associated with a good prognosis for graft survival and improved vision in carefully selected cases with mild or well-controlled ocular surface disease, and absent or previously surgically corrected eyelid abnormalities.

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15 August 2007

R. Doyle Stulting, MD, PhD  
Editor in Chief  
Cornea

Dear Dr. Stulting:

RE: CORNEA-D-07-00251, entitled "Penetrating Keratoplasty for Trachomatous Corneal Scarring"

I would like to thank the reviewers for their kind comments and useful suggestions that contributed to further improvement of the manuscript. Their concerns have been addressed as follows:

**Reviewer #1:** An excellent manuscript, and a model on which others should be judged.

*Response:* Thank you.

A few grammatical issues:

"glaucoma escalation" should be "worsening of glaucoma"

*Response:* The expression "glaucoma escalation" has been changed to "worsening of glaucoma in the 3 places that it occurs in the manuscript (Abstract, results, line 6; Results, paragraph 3, line 4-5; Discussion, paragraph 4, line 3)

"the Saudis" should be "Saudis"

*Response:* This expression "the Saudis" has been changed to "Saudis" in the 2 places that it occurs in the manuscript (Introduction, paragraph 2, sentences 2 and 3).

"6 million" should be "six million"

*Response:* This has been changed as requested (Introduction, first paragraph, line 9)

Delete the word "Logically"... and begin with "Judiciously..."

*Response:* Done (Introduction, paragraph 3, line 7).

**Reviewer #2:**

**Abstract:** The authors conclude that in carefully selected cases the patients do well with corneal transplantation. They should include in the abstract what comprises careful selection.

*Response:* The conclusion now includes the following language, "... in carefully selected cases with mild or well-controlled ocular surface disease, and absent or previously surgically corrected eyelid abnormalities."

*Methods:* How long did it take or what was the average time for patients to reepithelialize their transplant and was a tarsorrhaphy and/or a thermal punctal occlusion used to help any of these patients epithelium heal?

*Response:* The information about re-epithelialization that was requested has been included in the results section, rather than in the methods. It can be found in Results, paragraph 1. Basically, "re-epithelialization occurred in less than 14 days in 119 (93.7%) eyes, and in the remainder in less than 21 days, without the need for tarsorrhaphy in any cases." The data was collected as either complete or incomplete re-epithelialization at 14 days or 21 days, so the exact average time cannot be given.

In the same paragraph, do the authors believe discontinuing the topical steroids may have contributed to the rejection of the transplants?

*Response:* There was no statistically significant difference in graft survival rates among eyes in which the postoperative steroids were stopped at 6 months vs. 12 months. This is specifically stated in the Results, paragraph 2, last sentence.

On the last page, were bacterial ulcers associated with epithelial defects?

*Response:* Neither early or late postoperative persistent epithelial defects were associated with any cases of secondary microbial keratitis. This is specifically stated in the Discussion, paragraph 2, last sentence.

The tables are copious and useful.

*Response:* Thank you.

I hope these revisions are satisfactory to you and the expert reviewers. Please do not hesitate to contact me if further changes are necessary to help insure publication of this article in your outstanding journal.

Sincerely,

Michael D. Wagoner, MD  
Corresponding Author



## **Penetrating Keratoplasty for Trachomatous Corneal Scarring**

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The authors do not have any proprietary interests or conflict of interest with respect to any equipment or products mentioned in this manuscript.

## **Abstract**

**Purpose:** To evaluate graft survival and visual outcome after penetrating keratoplasty (PKP) for trachomatous corneal scarring.

**Methods:** A retrospective review was conducted on all cases of PKP performed at King Khaled Eye Specialist Hospital between January 1, 1997, and December 31, 2001, for trachomatous corneal scarring.

**Results:** This study included 127 eyes. The mean age at the time of surgery was 64.7 years (range, 40-90 years). The mean follow-up was 1266 days (range, 91-3423 days). At the most recent visit, 102 (80.2%) grafts were clear, and 25 (19.7%) had failed. Kaplan-Meier graft survival was 98.3% at 1 year, 85.9% at 2 years, 83.2% at 3 years, 80.2% at 4 years, and 76.6% at 5 years. Major postoperative complications included worsening of glaucoma (27.6%), endothelial rejection (17.3%), and bacterial keratitis (8.7%). Visual acuity improved in 107 (84.3%) eyes, remained the same in 12 (9.5%) eyes, and worsened in 8 (6.3%) eyes. Final visual acuity of 20/160 or better was obtained in 67 (56.7%) eyes.

**Conclusion:** Treating trachomatous corneal scarring with PKP can be associated with a good prognosis for graft survival and improved vision in carefully selected cases with mild or well-controlled ocular surface disease, and absent or previously surgically corrected eyelid abnormalities.

**Key words:** graft survival, penetrating keratoplasty, trachoma

Trachoma continues to be the leading infectious cause of blindness worldwide.<sup>1-3</sup> While trachoma has lost much of its importance as a cause of corneal blindness in Western countries, it is still prevalent in large regions of Africa, the Middle East, southwestern Asia, the Indian subcontinent, aboriginal communities in Australia, and in parts of Central and South America.<sup>1-3</sup> Chronic conjunctivitis, caused by repeated infection with *C trachomatis*, affects as many as 500 million people with preferential involvement in women and children.<sup>3</sup> Late sequelae of conjunctival scarring and shrinkage, with subsequent eyelid entropion and trichiasis, and progressive corneal scarring and vascularization, are responsible for up to six million cases of blindness in the world.

For many years, active trachoma was a serious ophthalmic problem in the Kingdom of Saudi Arabia.<sup>4-6</sup> In 1984, 6.2% of the Saudi population had evidence of active trachoma and 22.2% of Saudis had evidence of active or inactive trachoma.<sup>4</sup> Up to 1.5% of Saudis had trichiasis or entropion due to previous infection.<sup>4</sup> By 1994, only 2.6% of the Saudi population had active trachoma, and those with evidence of active or inactive disease had fallen to 10.7%.<sup>4</sup> Entropion or trichiasis from healed trachoma affected only 0.2% of the population.<sup>4</sup> The contribution of trachoma as a cause of corneal blindness and visual impairment also declined with the shrinking burden of eyes with entropion and trichiasis, and corneal scarring that resulted in many of these cases.<sup>5,6</sup> In the Eastern province, the prevalence of vision impairment attributed to trachoma declined significantly from 2.1% in 1984 to 0.3% in 1990.<sup>5</sup> In a survey conducted in the Southwest in 1995, visual impairment from trachoma was 0.95%.<sup>6</sup> The remarkable socioeconomic progress in Saudi Arabia in the second half of the 20<sup>th</sup> century has virtually eliminated active trachoma as a public health concern. In the absence of new cases, continued aging and death of elderly individuals will eventually eliminate trachoma-related visual disability

from the population. In the interim, the need to provide visual rehabilitation for patients with trachomatous corneal scarring remains a public health issue.

Trachoma has traditionally been considered to have a poor prognosis for successful penetrating keratoplasty (PKP). It is important to recognize, however, that the spectrum of post-trachoma sequelae range from mild corneal scarring, without severe eyelid and ocular surface disease, to end-stage corneal scarring and vascularization associated with ankyloblepharon and advanced symblepharon, and not to forget that the prognosis for PKP should also reflect a commensurate prognostic spectrum ranging from good to hopeless. Judicious selection of milder cases, combined with strict attention to correction of eyelid abnormalities, such as trichiasis and entropion, and aggressive management of ocular surface disease, such as dry eye syndrome and meibomitis, should allow PKP to be performed with a reasonable prognosis for graft survival and good visual outcome for many patients with corneal blindness attributed to chronic trachoma. Kocak-Midillioglu and associates<sup>8</sup> reported a small series of 16 eyes with trachomatous corneal scarring that underwent PKP after dry eye, meibomian gland dysfunction, and eyelid abnormalities had been carefully identified and aggressively managed. After a mean follow-up period of 26.1 months, 14 (87.5%) eyes had clear grafts, and 13 (81.3%) eyes achieved vision of 20/200 or better.

In the present study, we retrospectively reviewed a larger series of consecutive PKP procedures performed over a 5-year period at our hospital to treat post- trachomatous scarring.

## **Patients and Methods**

After obtaining approval from the Institutional Review Board, the medical records of every patient who underwent PKP at King Khaled Eye Specialist Hospital (KKESH) between January 1, 1997, and December 31, 2001, for trichomatous corneal scarring were reviewed retrospectively. The criteria for the diagnosis of trichomatous corneal scarring were based on ocular findings consistent with evidence of healed trachoma (e.g. conjunctival fibrosis, Herbert's pits) and the absence of other explanations for corneal opacification (e.g., previous bacterial keratitis). Patients with less than 3 months of postoperative follow-up were excluded from the statistical analysis.

All surgeries were performed as inpatients by members of the Anterior Segment Division of the Department of Ophthalmology at KKESH. Topical corticosteroids and antibiotics were administered in tapering dosages after surgery. Patients were evaluated daily until reepithelialization was complete and then discharged from the hospital. They were then seen 1 week after discharge; after 1, 3, 6, 9, 12, 18, and 24 months; and then yearly thereafter. Topical antibiotics were discontinued after approximately 2 to 4 weeks, but topical steroid treatment continued for at least the first 6 months. The protocol for suture removal varied between ophthalmologists, with some physicians removing all sutures after 12 to 36 months and others only selectively removing loosened sutures or tight sutures that induced unacceptable astigmatism.

Data extracted included preoperative best-corrected visual acuity (BCVA); demographic and clinical features; intraoperative and postoperative complications; previous, concomitant, and subsequent surgical procedures; graft clarity; and postoperative visual acuity. Postoperative visual acuity was recorded as best recorded visual acuity after

surgery, as well as at the most recent follow-up examination. Graft failure was strictly defined as irreversible loss of central graft clarity, irrespective of the level of vision. The time of graft failure was defined as the visit at which irreversible loss of graft clarity was first documented. The follow-up interval was defined as the interval to the most recent visit for eyes in which the graft remained clear, and the interval from surgery to graft failure for those eyes in which the graft did not remain clear.

All data were entered onto a Microsoft (Redmond, WA, USA) Excel spreadsheet. The Fisher's exact test was used for all comparisons, and the term *significance* was accepted if the *P* value was less than 0.05. Graft survival curves were produced using the standard Kaplan-Meier method and the life table method.

## **Results**

This study included 127 eyes of 61 (48.0%) men and 66 (52.0%) women (Table 1). Two eyes were excluded due to insufficient follow-up. The mean age at the time of surgery was 64.7 years (range, 40-90 years). Re-epithelialization occurred in less than 14 days in 119 (93.7%) eyes, and in the remainder in less than 21 days, without the need for tarsorrhaphy in any cases. The mean period of follow-up was 1266 days (range, 91-3423 days).

At the most recent visit, 102 (80.2%) grafts were clear, and 25 (19.7%) had failed (Table 2). Kaplan-Meier graft survival was 98.3% at 1 year, 85.9% at 2 years, 83.2% at 3 years, 80.2% at 4 years, and 76.6% at 5 years. There were no statistically significant gender

differences in graft survival. There was no statistically significant correlation between the duration of postoperative corticosteroid use and graft survival.

Postoperative complications occurred in 71 (55.9%) eyes (Table 3). Although graft survival was lower in eyes with serious postoperative complications compared to eyes without complications (76.1% vs. 85.6%, respectively), this difference was not statistically significant ( $P = 0.18$ ). Postoperative complications included worsening of glaucoma (27.6%), endothelial rejection (17.3%), bacterial keratitis (8.7%), persistent epithelial defect in the early postoperative period (6.3%), traumatic wound dehiscence (5.5%), late-onset persistent epithelial defect (3.9%), retinal detachment (2.4%), and endophthalmitis (2.4%).

Patient visual outcomes are summarized in Table 4. Visual acuity improved in 107 (84.3%) eyes, remained the same in 12 (9.5%) eyes, and worsened in 8 (6.3%) eyes. Final visual acuity of 20/160 or better was obtained in 56.7% eyes and 20/800 or better in 74.0% of eyes.

## **Discussion**

In the present study, very gratifying results were obtained with penetrating keratoplasty performed in eyes with trachomatous corneal scarring. Overall graft survival was 80.3% after a mean follow-up time of 42.1 months. Kaplan-Meier survival was 98.3% at 1 year and 76.6% at 5 years. Gender did not significantly affect graft survival, with comparable graft survival occurring in male and female patients. The visual results in the present series were highly satisfactory: 56.7% of eyes maintained a final best-corrected visual

acuity of 20/160 or better compared to only 9.4% with this level of preoperative vision. In addition, 74.0% of eyes were 20/800 or better, compared to only 17.3% preoperatively.

As in the previous smaller series by Kocak-Midillioglu and associates,<sup>8</sup> patient selection was probably the principal reason for the unexpectedly good results. The encouraging results in this series were most likely because of the careful selection of patients without significant conjunctival shrinkage, as suggested by absence of the need for ocular surface reconstruction prior to PKP. While many eyes had received mechanical removal or cryoablation for trichiasis, only 7 (5.6%) eyes required eyelid surgery for trichiasis prior to or at the same time as PKP, and no patients had subsequent need for eyelid procedures. The relatively low prevalence of early and late persistent epithelial defects (6.3% and 3.9%, respectively) supports the hypothesis that ocular surface disease was well controlled in these eyes prior to surgery. Neither early or late persistent epithelial defects were associated with the development of secondary microbial keratitis.

There was a general tendency to select patients with longstanding corneal scars who experienced recent visual deterioration caused by the progression of senile cataracts. Cataract surgery was performed during the clinical course in 117 (92.1%) eyes, of which the vast majority of procedures were done at the same time as PKP. Most of these patients did not have significant intraocular co-morbidity, with only 7 (5.6%) eyes requiring glaucoma surgery and only 4 (3.1%) eyes requiring vitreoretinal procedures during the clinical course. The performance of intraocular surgery in the same eye (before, during, or after PKP) or the presence of a previous PKP in the contralateral eye did not significantly reduce the prognosis for graft survival.

Despite careful patient selection, serious postoperative complications occurred in more than half of the cases, although they did not significantly reduce the likelihood of graft survival. The two most common complications, worsening of glaucoma and endothelial rejection, were associated only with very slightly reduced graft survival. The complication with the greatest adverse impact on graft survival was traumatic wound dehiscence, followed by early postoperative epithelial defect, bacterial keratitis, retinal detachment, and endophthalmitis.

In conclusion, PKP can be performed in carefully selected cases of trachomatous scarring with a good prognosis for graft survival and improved vision.

**The King Khaled Eye Specialist Hospital Cornea Transplant Study Group**

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**Table 1. Penetrating Keratoplasty for Trachomatous Corneal Scarring:  
Demographic and Clinical Features**

	<b>N</b>	<b>%</b>
Eyes	127	
Patients		
Male	61	48.0
Female	66	52.0
Age at time of surgery, years		
Mean	64.7	
Range	40-90	
Follow-up, days		
Mean	1266	
Range	91-3423	
Previous surgery		
Any	16	12.5
Cataract	7	5.5
Intraocular lens	6	4.7
Eyelid surgery	5	3.9
Glaucoma	4	3.1
Concomitant surgery		
Any	103	81.1
Cataract	102	80.3
Intraocular lens	100	78.7

Eyelid surgery	2	1.6
Glaucoma	1	0.8
Vitreoretinal	1	0.8
Subsequent surgery		
Any	19	15.0
Cataract	8	6.3
Intraocular lens	8	6.3
Repair wound dehiscence	6	4.7
Vitreoretinal	3	2.4
Glaucoma	2	1.6

**Table 2. Penetrating Keratoplasty for Trachomatous Corneal Scarring: Graft Survival**

	All	Men	Women
Eyes	127	61	66
Follow-up (days)			
Mean	1266	1243	1287
Range	91-3423	91-3200	97-3423
Clear grafts			
N	102	48	54
%	80.3	78.7	81.2
K-M survival (95% CI)			
1 year	98.3 (93.3, 99.6)	96.4 (86.5, 99.1)	100.0
2 years	85.9 (77.7, 91.3)	84.5 (71.3, 92.0)	87.3 (75.1, 93.7)
3 years	83.2 (74.2, 89.3)	81.6 (67.2, 90.1)	87.3 (73.2, 99.3)
4 years	80.2 (70.4, 87.1)	81.6 (67.2, 90.1)	79.1 (64.0, 88.4)
5 years	76.6 (65.7, 84.4)	77.9 (61.8, 87.8)	75.8 (59.7, 86.1)

K-M = Kaplan Meier; CI = confidence interval.

No significant difference between men versus women ( $P = 0.86$ )

**Table 3. Penetrating Keratoplasty for Trachomatous Corneal Scarring:  
Complications vs. Graft Survival**

<b>Risk factor</b>	<b>N</b>	<b>%</b>	<b>Graft survival (%)</b>	<b>P-value<sup>1</sup></b>
<b>Complications (any)<sup>2</sup></b>				
Yes	71	55.9	76.1	0.18
No	56	44.1	85.6	
<b>Glaucoma escalation<sup>3</sup></b>				
Yes	35	27.6	80.0	1.0
No	92	72.4	80.4	
<b>Endothelial rejection</b>				
Yes	22	17.3	77.3	0.77
No	105	82.7	80.9	
<b>Bacterial keratitis</b>				
Yes	11	8.7	63.6	0.24
No	116	91.3	82.0	
<b>Persistent epithelial defect (early)<sup>4</sup></b>				
Yes	8	6.3	62.5	0.19
No	119	93.7	81.5	
<b>Trauma<sup>5</sup></b>				
Yes	7	5.5	57.1	0.14
No	120	94.5	81.7	

Persistent epithelial defect (late) <sup>6</sup>				
Yes	5	3.9	80.0	1.0
No	122	96.1	80.3	
Retinal detachment				
Yes	3	2.4	66.7	0.48
No	124	97.6	80.6	
Endophthalmitis				
Yes	3	2.4	66.7	0.48
No	124	97.6	80.6	

<sup>1</sup> Fisher's exact test.

<sup>2</sup> Some eyes had more than one complication.

<sup>3</sup> Thirty-two cases required increased medication only; 3 required surgical intervention.

<sup>4</sup> Lasting > 14 days in the immediate postoperative period.

<sup>5</sup> Five cases were associated with dehiscence only; 2 associated with intraocular injury.

<sup>6</sup> Recurrent epithelial defect lasting > 14 days after the initial postoperative period.

**Table 4. Penetrating Keratoplasty for Trachomatous Corneal Scarring: Visual Outcome**

Visual Acuity	Preoperative		Best		Final	
	N	Cum. %	N	Cum.%	N	Cum.%
20/40 or better	0	0	18	14.2	5	3.9
20/50 to 20/160	12	9.4	74	72.4	67	56.7
20/200- 20/800	10	17.3	21	89.0	22	74.0
CF	55	60.6	11	97.6	16	86.6
HM	39	91.3	2	99.2	12	96.1
LP	11	100.0	1	100.0	3	98.4
NLP	0	100.0	0	100.0	2	100.0
Total	127		127			

Cum. % = cumulative percentage; CF = counting fingers; HM = hand motions; LP = light perception; NLP = no light perception