Keratoplasty for Treatment of *Acanthamoeba* Keratitis

Anna S. Kitzmann, MD, Kenneth M. Goins, MD, John E. Sutphin, MD, Michael D. Wagoner, MD

Purpose: To evaluate and compare the outcomes of therapeutic keratoplasty (TKP) and optical keratoplasty (OKP) in the management of medically unresponsive *Acanthamoeba* keratitis and post-keratitis scarring, respectively.

Design: Retrospective, nonrandomized, comparative, interventional case series.

Participants: Thirty patients with *Acanthamoeba* keratitis treated at a single center.

Methods: Retrospective review of all cases of penetrating keratoplasty (PKP) or lamellar keratoplasty (LKP) performed for *Acanthamoeba* keratitis at a single center between January 1, 1980, and December 31, 2007. Inclusion criteria included histopathologic confirmation of *Acanthamoeba* organisms in the surgical specimen and at least 6 months of postoperative follow-up.

Main Outcome Measures: Postoperative complications, microbiological cure, graft survival, and visual acuity.

Results: Thirty-one eyes of 30 patients met the inclusion criteria. This included 22 eyes (22 patients) that were initially treated with TKP (20 PKP/2 LKP) and 9 eyes (8 patients) treated with OKP (8 OKP/1 LKP). Of the 22 eyes treated with TKP, multiple keratoplasties (range, 2–6) were performed in 12 eyes (55%), whereas repeat keratoplasty was performed in only 1 eye (11%) treated with OKP ($P = 0.004$). Recurrent *Acanthamoeba* keratitis, glaucoma, early and late persistent epithelial defects, and endophthalmitis were more likely to occur after TKP than after OKP. A microbiological cure was achieved in all surgical cases. Among eyes treated with TKP, this required 1 keratoplasty in 14 eyes, 2 keratoplasties in 6 eyes, and 3 keratoplasties in 2 eyes. After the initial keratoplasty, Kaplan–Meier survivals after TKP were 45.5%, 45.5%, and 37.5% at 1 year, 5 years, and 10 years, respectively, compared with 100%, 100%, and 66.7%, respectively, after OKP ($P = 0.004$). The median visual acuity was 20/40 after TKP and 20/25 after OKP. Eyes treated with TKP were less likely to obtain visual acuity of 20/40 or better and more likely to have vision of 20/200 or worse.

Conclusions: Therapeutic keratoplasty can successfully treat medically unresponsive cases of *Acanthamoeba* keratitis, although multiple grafts may be required and the visual prognosis is guarded. Optical keratoplasty performed after resolution of active keratitis is associated with an excellent prognosis for both graft survival and visual outcome.

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Acanthamoeba is a ubiquitous, free-living protozoan that can causes a painful and sight-threatening keratitis.[1–5] *Acanthamoeba* keratitis is typically associated with contact lens wear or ocular exposure to contaminated water.[6–8] Although this infection is rare,[9] it is particularly difficult to treat because this organism can exist in 2 forms: an infective trophozoite that may be responsive to treatment and a dormant cyst form that is resistant to antiprotozoal therapy and can persist for years. In addition, there are limited medications available to treat *Acanthamoeba* keratitis, and those medications that do exist can be toxic to the cornea.[1–8,10–12] Medication-resistant cases often require surgical treatment with corneal transplantation.[2,3,13–16] In other cases that are medically responsive, corneal transplantation may be necessary for permanent scarring that limits vision.

There have been few large clinical series reported to date that have evaluated the results of keratoplasty for *Acanthamoeba* keratitis. Furthermore, there are limited comparisons available of outcomes associated with keratoplasty performed to treat medically uncontrolled keratitis versus medically cured cases in which residual scarring or astigmatism has induced visual disability. The present study addresses these issues in the largest consecutive, comparative series of keratoplasties performed, to the best of our knowledge, for *Acanthamoeba* keratitis at a single institution.

Patients and Methods

After approval was obtained by the University of Iowa Institutional Review Board, a retrospective study was conducted of the medical records of all patients with a diagnosis of *Acanthamoeba* keratitis from January 1, 1980, to December 31, 2007, to identify those patients who underwent penetrating keratoplasty (PKP) or anterior lamellar keratoplasty (LKP) during their clinical course.

Criteria for inclusion in the statistical analysis included histopathologic evidence of *Acanthamoeba* organisms in the corneal button obtained at the time of keratoplasty and at least 6 months of postoperative follow-up. The patients were divided into 2 groups,

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Table 1. Preoperative Parameters before Initial Keratoplasty versus Surgical Indication

	Therapeutic Keratoplasty	Optical Keratoplasty
Eyes (n)		
Right	15	4
Left	7	5
Total	22	9
Gender (n)		
Male	9	3
Female	13	5
Age (y)		
Mean	40	30
Range	16–72	13–63
Diagnosis established by (n, %)		
Positive confocal microscopy	11 (50)	7 (78)
Positive epithelial biopsy	9 (41)	5 (56)
Positive corneal button biopsy	22 (100)	9 (100)
Onset of symptoms to initial keratoplasty (mos)		
Mean	6	19
Range	1–23	5–70
Risk factors (n, %)		
Contact lens wear	18 (82)	6 (67)
Soft contact lens	14 (64)	2 (22)
Hard contact lens	4* (18)	4 (44)
Tap water contact lens cleaning	2 (9)	2 (22)
Swimming/hot tub use	4 (18)	4 (22)
Clinical findings before initial keratoplasty (n, %)		
Epithelial defect	14 (64)	2 (22)
Ring infiltrate	18 (82)	0
Corneal thinning	9† (41)	3 (33)
Neovascularization	7 (32)	5 (56)
Hypopyon	3 (14)	0
Visual acuity at time of initial keratoplasty		
Median	CF	CF
Visual acuity ≤20/200 (n, %)	20 (65)	7 (78)

CF = counting fingers.
*Includes 1 patient wearing rigid gas permeable lens for orthokeratology.
†Includes 1 patient with a corneal perforation and 1 patient with a descemetocele.

depending on the reason for corneal transplantation. Eyes with active infection that could not be medically controlled were included in the therapeutic keratoplasty (TKP) group. Eyes without any clinical evidence of active infection or residual inflammation, but with visually significant residual corneal scarring or irregular astigmatism, were included in the optical keratoplasty (OKP) group.

Outcome measures included postoperative complications, microbiological cure, graft survival, and visual acuity. Postoperative complications that were reviewed included recurrent *Acanthamoeba* keratitis, graft rejection episodes, glaucoma, early and late-onset persistent epithelial defects, and endophthalmitis. A diagnosis of recurrent *Acanthamoeba* keratitis was accepted on the basis of histopathologic confirmation if repeat keratoplasty was performed or on the constellation of characteristic clinical findings (e.g., a new corneal infiltrate, subepithelial infiltrates, significant epithelialopathy, positive confocal microscopy, and positive epithelial biopsy) in cases successfully treated with medical management. An early persistent epithelial defect was defined as an epithelial defect that lasted longer than 14 days after surgery. A late persistent epithelial defect was defined as an epithelial defect that occurred after initial re-epithelialization was complete and lasted more than 14 days. A microbiological cure was defined as prolonged absence (>3 months) of clinical signs of active keratitis after the most recent surgical intervention. Graft failure was defined as irreversible loss of central graft clarity irrespective of the visual acuity. For eyes in which the graft remained clear, the follow-up interval was defined as the interval from surgery to the most recent visit; for eyes in which the graft did not remain clear, the follow-up interval was from surgery to graft failure. The final visual acuity was defined as the best vision obtained at the most recent visit after the most recent surgical intervention.

All data were entered into a Microsoft Excel (Microsoft Corp., Redmond, WA) spreadsheet. Graft survival curves were produced using the standard Kaplan–Meier method. The Fisher exact test was used for comparison of categoric variables, and the Wilcoxon log-rank sum test was used for continuous variables. Significance was accepted if the P value was <0.05.

Results

Thirty-one eyes of 30 patients met the inclusion criteria (Table 1). This included 22 eyes (22 patients) initially treated with TKP (20 PKP/2 LKP) and 9 eyes (8 patients) treated with OKP (8 PKP/1 LKP). Only 1 case of histopathologically confirmed *Acanthamoeba* keratitis was excluded because of inadequate follow-up. Cataract extraction and intraocular lens implantation were performed in conjunction with 2 eyes treated with OKP. The distribution of cases between 1980 and 2007 is summarized in Figure 1.

A clinical diagnosis of *Acanthamoeba* keratitis had been made in all cases on the basis of the constellation of the ophthalmic history and clinical findings. Additional confirmation of the diagnosis was made by confocal microscopy in 18 eyes and by epithelial biopsy in 14 eyes. Histopathologic confirmation of active or previously active *Acanthamoeba* keratitis was made in all 31 eyes.

Patients undergoing TKP were older than those treated with OKP (mean age, 40 vs. 30 years), were more likely to have had contact lens wear as a risk factor (82% vs. 67%), and had surgical intervention after a shorter duration of symptoms (mean interval = 6 vs. 19 months). Eyes treated with TKP were significantly more likely to have a ring infiltrate (82% vs. 0%, $P<0.001$) or epithelial defect (64% vs. 22%, $P = 0.05$) at the time of surgical intervention. Eyes treated with TKP had a higher prevalence of corneal thinning and hypopyon, whereas those treated with OKP were more likely to have peripheral neovascularization, although these differences were not statistically significant. There were no statistically significant differences in preoperative visual acuity between the 2 groups.

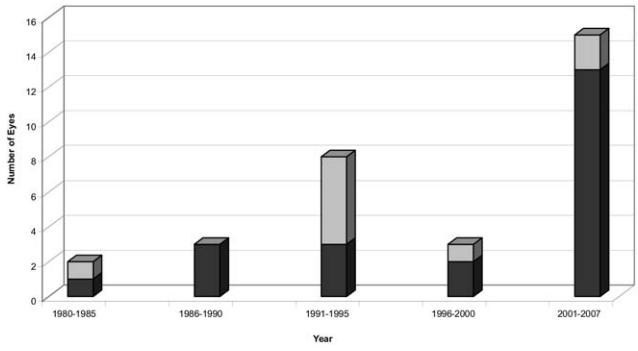

Figure 1. Number of eyes per year of diagnosis. ■, Therapeutic group; ■, optical group.