Outcomes of Repeat Keratoplasty for Failed Therapeutic Keratoplasty

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• PURPOSE: To analyze clinical outcomes of repeat optical penetrating (PK) or endothelial keratoplasty (EK) after failed therapeutic keratoplasty (TPK).
• DESIGN: Retrospective consecutive, comparative, interventional case series.
• METHODS: SETTING: LV Prasad Eye Institute, Hyderabad, India. STUDY POPULATION: Patients aged >18 years who underwent a repeat PK or EK following a failed TPK with a follow-up of at least 1 year were included. Patients with culture-negative ulcers, viral etiology, coexistent ocular surface disease, and multiple grafts were excluded from the study. INTERVENTION: PK or EK for failed TPK. MAIN OUTCOME MEASURE: Corrected distance visual acuity at 1 year follow-up. SECONDARY OUTCOME MEASURE: Graft clarity.
• RESULTS: One hundred twelve eyes (67 PK, 45 EK) were included in the study. The PK group had a significantly higher number of cases with high-risk features prior to regraft. Improvement in visual acuity in each of the types of grafts was statistically significant ($P < .01$), but there was no difference between the 2 groups at 1 year postoperatively. A statistically significant proportion of grafts regained graft clarity after regrafting in the PK group ($P < .01$) but not in the EK group ($P = .205$) at 1 year postoperatively. Endothelial rejection rates were higher in the PK group. Subgroup analysis showed that eyes that had PK or EK for failed TPK conducted for *Aspergillus* keratitis showed better outcomes in terms of graft clarity. Kaplan-Maier (KM) survival analysis for graft clarity showed cumulative survival of 50% at 5 years. The survival using the KM curve was not statistically different between the 2 groups ($P = .33$).
• CONCLUSION: This study shows that visual rehabilitation with relatively good functional outcomes can be achieved by performing repeat PK or EK in patients after failed TPK. (Am J Ophthalmol 2016;162:83–88.

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INFECTIOUS KERATITIS IS A COMMON CAUSE OF corneal blindness in developing countries.[1] A large number of keratitis-related ulcers do not respond to medical therapy and require a therapeutic keratoplasty. Although eradication of infection and achieving anatomic success in terms of maintaining globe integrity are achieved in 70%–100% of eyes following therapeutic penetrating keratoplasty, functional success (providing useful visual acuity) achieved ranges from as low as 5% in the developing world to about 60% in certain centers across the globe.[1–5]

Visual rehabilitation of such patients with failed therapeutic grafts is of prime importance. The regrafts in failed therapeutic grafts can be more challenging than in failed optical grafts owing to the altered architecture of the anterior segment. Recently, encouraging results have been reported for rehabilitation of failed optical penetrating grafts with Descemet stripping automated endothelial keratoplasty (DSAEK).[6–13] Chaurasia and associates had reported reasonable success of DSAEK in failed therapeutic grafts.[12]

The paucity of studies on repeat keratoplasty for failed therapeutic keratoplasty prompted us to evaluate the outcomes of repeat keratoplasty, both penetrating (PK) and endothelial keratoplasty (EK), in failed therapeutic penetrating keratoplasty (TPK) at a tertiary eye care referral center in southern India.

METHODS

THIS WAS A RETROSPECTIVE INTERVENTIONAL CASE SERIES of patients who underwent optical penetrating or endothelial keratoplasty for failed primary TPK from January 1, 2000 to July 31, 2012 at L.V. Prasad Eye Institute, Hyderabad, India. All eligible patients with a minimum postoperative follow-up of at least 1 year were included. Pediatric grafts and patients who had more than 2 grafts, culture-negative ulcers, ulcers of viral etiology, or coexistent ocular surface disease such as Stevens-Johnson syndrome or ocular cicatricial pemphigoid were excluded from the study. The study was approved by the Institutional Review Board of the Hyderabad Eye Research Institute and was conducted according to the tenets of the Declaration of Helsinki.

• DATA COLLECTION: The data collected for analysis included the size of the corneal ulcer, causative organism,

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duration of infection, indication for TPK, size of therapeutic graft, and cause of failure of the therapeutic graft. Length of time between the primary graft and the regraft was recorded. High-risk characteristics from the previous graft (TPK), including the extent of deep vessels, number of quadrants of peripheral anterior synechiae, and the presence of coexistent glaucoma that could affect the outcome of the subsequent graft, were noted. Postoperative visual acuity, refraction, and graft clarity at every annual visit were also recorded.

All the corneal tissues were obtained from the Ramayamma International Eye Bank, Hyderabad, India. During TPK 1 mm of clear margin surrounding the infection was taken. A minimum period of 3 months was given between the first therapeutic graft and the subsequent optical graft to allow the inflammation to settle down. The patients could not be randomized into PK or EK groups because of the retrospective nature of the study. The size of the PK grafts was 7.5–8.5 mm, and grafts were centered on the pupil and secured with 16 interrupted 10/0 monofilament nylon sutures. In eyes that underwent EK, the donor lenticule was prepared by microkeratome dissection by trained technicians at the eye bank. Descemet stripping was done only in cases where a dense retrocorneal membrane was noted. A 4.5 mm scleral or clear corneal incision was made depending on the size of the original graft. Using a Sheet's glide (BD Medical-Ophthalmic Systems, Franklin Lakes, NJ), the push-in technique was used to insert the donor lenticule. A 10-minute complete air fill was given at the end of the procedure and partial fluid-air exchange was carried out. Venting incisions (2–4) were made at the discretion of the operating surgeon.

Postoperative treatment comprised 6–8 times daily of prednisolone acetate (1%) eye drops, which was tapered to 4 times daily for 1 month, followed by 3 times a day for 6 months, 2 times a day for 12 months and on maintenance dose on one time daily. Moxifloxacin (0.5%) eye drops were started 4 times a day for 1 week. Patients were followed up at 1 week, 1 month, 3 months, and then every 6 monthly thereafter. Immediate and late postoperative complications were recorded with emphasis on episodes of graft rejection and graft infiltrate.

• **OUTCOME MEASURES:** Primary outcome measure was corrected distance visual acuity (CDVA) at 1 year follow-up after PK or EK. Secondary outcome measure was graft clarity (central graft over the visual axis being clear) at 1 year follow-up and complications.

• **STATISTICAL ANALYSIS:** All statistical analyses were performed using R software (version 2.12). Baseline characteristics were compared using Fisher exact test for count data and *t* test or Mann-Whitney test was performed for continuous data. A Wilcoxon signed rank test was performed to compare pre- and postoperative CDVA for different organisms and for different types of regrafts. We used a cumulative Logit model for ordinal variables to test the trend. A multivariate regression model with stepwise elimination using Akaike information criteria were used to assess the association of graft clarity and logMAR CDVA with preoperative characteristics. The baseline risk characteristics were constructed and hazard ratios calculated using Cox multivariate regression analysis.

TABLE 1. Repeat Keratoplasty for Failed Therapeutic Keratoplasty: Baseline Characteristics comparing Repeat Penetrating Keratoplasty and Endothelial Keratoplasty Following Failed Therapeutic Keratoplasty

Characteristic	PK	EK	*P* Value
Number	67	45	
Mean age (y)	40	39	.96
Sex (male:female)	43:24	35:10	.18
Mean duration between TPK and regraft (IQR)	10 (6.5–15.5) months	7 (6–9.84) months	.09
Extent of PAS			<.01
None	12	19	
<3 clock hours	19	15	
3–6 clock hours	25	7	
>6 clock hours	11	4	
Deep vessels			.04
None	13	23	
1 quadrant	17	11	
2 quadrants	23	10	
3 or more quadrants	14	1	
No. of intact sutures at time of regraft	10	11	.45
Size of regraft			
<8 mm	29	36	<.01
>8 mm	38	9	<.01
Mean (SD) endothelial count of donor tissue for regraft, cells/mm^2	2726 (190)	2751 (199)	.54

EK = endothelial keratoplasty; IQR = interquartile range; PAS = peripheral anterior synechiae; PK = penetrating keratoplasty; TPK = therapeutic keratoplasty.

Wilcoxon rank sum test, *t* test, and Fisher exact test used as appropriate.

RESULTS

ONE HUNDRED AND TWELVE EYES OF 112 PATIENTS WERE included in the study (67 eyes underwent PK and 45 eyes underwent EK). Baseline characteristics of age, sex, time interval between the 2 grafts, age of donor, and endothelial cell counts of donor tissue were comparable between the 2 groups. Preoperative high-risk characteristics including deep vessels in greater than 2 quadrants ($P = .04$) and the extent of peripheral anterior synechiae (greater than