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Repeat Descemet Membrane Endothelial Keratoplasty

Secondary Grafts with Early Intervention Are Comparable with Fellow-Eye Primary Grafts

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Purpose: To evaluate the outcomes of secondary Descemet membrane endothelial keratoplasty (DMEK) after failed primary DMEK.

Design: Retrospective, interventional case series.

Participants: Fifty-five DMEK recipients 42 to 89 years of age.

Methods: An initial consecutive series of 1655 DMEK surgeries was reviewed to identify cases of secondary DMEK after failed primary DMEK (n = 55). A paired fellow-eye analysis was performed with a subgroup of 29 patients who underwent secondary DMEK in 1 eye and successful primary DMEK in the fellow eye.

Main Outcome Measures: Corrected distance visual acuity (CDVA), central corneal thickness, and 1-year endothelial cell loss.

Results: The median follow-up after DMEK regraft was 18 months (range, 3–61 months). All 55 regrafts cleared, 8 (15%) had air reinjected to promote attachment, 1 eye (2%) with trabeculectomy and progressive synechiae demonstrated late endothelial failure, and no rejection episodes occurred (0%). In the paired analysis, the median duration of endothelial decompensation before the regraft was 21 days (range, 2–133 days). At 1, 3, 6, or 12 months, CDVA did not differ between the primary and secondary grafts in fellow eyes (mean difference, ≤2 Snellen letters; $P > 0.05$ at all examinations). At 1 year, the visual acuity was ≥20/20 in 61%, ≥20/25 in 81%, and ≥20/40 in 100% of the secondary grafts in the paired analysis, excluding 1 eye with retinal problems. Vision differed by ≤1 line between fellow eyes in all but the 1 patient with the longest time to regraft (133 days), who demonstrated central haze and irregular astigmatism from anterior stromal scarring during that period. At 1 year, CDVA associated with the scarring was 20/40 versus 20/20 for the fellow-eye primary graft. The central corneal thickness was comparable between fellow-eye primary and secondary grafts at 3, 6, and 12 months (mean difference at 1 year, 2 μm; $P = 0.57$). The 1-year endothelial cell loss was comparable in primary and secondary grafts (27% vs. 31%, respectively; $P = 0.58$).

Conclusions: In patients who received prompt intervention to minimize the duration of central corneal decompensation, the visual outcomes with secondary DMEK matched the fellow-eye visual outcomes with primary DMEK. *Ophthalmology 2015;122:1639-1644 © 2015 by the American Academy of Ophthalmology.*

Endothelial keratoplasty (EK) has become the preferred treatment for endothelial dysfunction[1] because it is safer, provides faster visual recovery, and allows patients to resume daily activities sooner than penetrating keratoplasty (PK).[2] The EK iteration known as Descemet membrane EK (DMEK) provides the quickest visual rehabilitation with the lowest risk of immunologic rejection.[3–5] However, DMEK is more challenging to perform and somewhat more prone to partial detachment with delayed or incomplete corneal clearing, or both, than the popular Descemet stripping automated endothelial keratoplasty technique.[6] Delayed corneal clearing has been described in some cases,[7] so the optimal time to intervene by reinjecting air or replacing the graft has not been determined definitively.

Several centers that take a conservative approach of waiting and watching for a number of months before performing a regraft have reported that secondary DMEK results in poorer visual outcomes than primary DMEK.[8,9] Our usual practice is to intervene promptly so that patients do not have to contend with poor vision, symptomatic bullae, and restricted activities for any extended period. The hypothesis of this study was that visual results after secondary DMEK are comparable with those after primary DMEK if the secondary DMEK is performed promptly to minimize the duration of corneal edema. When available, fellow eyes with primary DMEK served as the standard against which to compare the secondary DMEK visual outcomes.

Methods

Data collected prospectively at a single center from an initial consecutive series of 1655 DMEK procedures performed by 11

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surgeons between March 2008 and October 2014 was reviewed retrospectively to identify patients who underwent secondary DMEK after failed primary DMEK with at least 3 months of follow-up. The first DMEK surgeries for all surgeons were included. A subgroup of patients who underwent secondary DMEK in one eye and successful primary DMEK in the fellow eye also was identified for a paired fellow-eye analysis. The study adhered to the tenets of the Declaration of Helsinki and complied with the Health Insurance Portability and Accountability Act. Independent review board approval was obtained. All patients read and signed an informed consent document for the research as well as for the surgical procedures.

Surgical Technique

The surgical technique was described previously.[10] In brief, a surgeon prepared the donor tissue at the surgical facility on the day of surgery or up to 2 days beforehand using the submerged cornea and a background away technique to isolate the endothelium and Descemet membrane. Patients received topical anesthesia with monitored intravenous sedation. The recipient epithelium was marked lightly with a trephine to indicate the planned graft diameter and location. The host endothelium and Descemet membrane were stripped from the marked area. A surgical inferior iridotomy was performed. The prepared donor tissue was stained with trypan blue (Vision Blue; DORC, Nuidland, The Netherlands) and was inserted into the eye through a 2.8-mm corneal incision with an intraocular lens injector (Viscoject; Medicel AG [Wolfhalden, Switzerland], Carl Zeiss Meditec [Jena, Germany], or Staar Surgical [Monrovia, CA]).[10] As soon as the graft was determined to be in the proper orientation using a handheld slit beam,[11] the graft was uncurled with a no-touch technique[12] using short bursts of balanced salt solution. The graft was pressed against the posterior host cornea with an intracameral air bubble. Patients remained supine for 1 hour and then were examined with a slit lamp. If the intraocular pressure (IOP) was elevated or an air meniscus was occluding the iridotomy, some air was released using a 30-gauge needle on a 1-ml syringe inserted through the cornea. If the anterior chamber did not re-form spontaneously, balanced salt solution was injected to achieve physiologic pressure by palpation. The IOP was measured and patency of the peripheral iridotomy was confirmed at the slit lamp before the patient was released. In some cases, DMEK was combined with cataract extraction and intraocular lens implantation, as described previously.[10]

After surgery, patients used topical antibiotics for 1 week. Prednisolone acetate 1% eye drops were used 4 times daily for the first 3 to 4 months, then tapered by 1 drop daily each month to once-daily dosing, which was continued through 1 year to prevent immunologic rejection.

Rebubbling

Examinations were performed at 1 day, 2 days, and 1 week after surgery to assess graft adherence. Air was reinjected to promote graft attachment if an area of detachment obscured the visual axis, continued to increase, or was large enough that it could lead to a complete detachment after air absorption. The procedure was performed in a minor operating room, as described previously.[10]

Regraft Timing and Technique

Corneal clarity was assessed by slit-lamp examination. When a graft failed to clear initially and the surgeon suspected significant iatrogenic endothelial damage (e.g., difficult preparation, insertion, or positioning), the graft often was replaced within 1 week. When a graft failed to clear initially after routine surgery, the graft typically was monitored for several weeks before diagnosing primary graft failure, because DMEK sometimes exhibits delayed spontaneous clearing.[6] The regraft timing took into consideration individual patient circumstances. Generally, we believe it is prudent to regraft promptly whenever bullae or microcystic edema are present over the pupillary area to ensure optimal visual outcomes.

When a regraft was required, the primary DMEK graft was removed carefully from the host posterior stroma with a reverse Sinskey hook while the anterior chamber was filled with air. A new DMEK graft was inserted and positioned, as described above.

Outcome Measures

Corrected distance visual acuity (CDVA) was measured with Snellen projector charts, and data were converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis. Central corneal thickness was assessed with ultrasonic pachymetry. The postoperative central endothelial cell density (ECD) was assessed by specular microscopy (manual centers method using the Noncon Robo [Konan Medical, Inc., Hyogo, Japan] or automated analysis using the EM-3500 [Tomey Corp., Nagoya Japan]).[13] The baseline donor ECD was measured by the provider eye bank (usually Indiana Lions Eye and Tissue Transplant Bank, Indianapolis, IN) with specular microscopy (KeratoAnalyser; Konan, Hyogo, Japan). Endothelial cell loss was calculated by subtracting the 1-year postoperative ECD from the baseline donor ECD, dividing by the baseline donor ECD, and multiplying by 100. In cases of late endothelial failure, the duration of corneal decompensation was defined as the interval between the regraft and the examination when corneal edema was documented first or the interval between the regraft and the date the patient first noted decreased vision, whichever was longer. Postoperative complications, including air reinjection, immunologic rejection, IOP elevation, and graft failure, were documented.

Statistical Analysis

The paired Student *t* test was used for the fellow-eye analysis. The CDVA was converted from Snellen to logMAR units for the analysis, which was performed using Statistical Analysis Software version 9.3 (SAS Inc, Cary, NC). The tests were 2-tailed, and *P* values less than 0.05 were considered statistically significant.

Results

Demographics

Fifty-five patients (55 eyes) met the study inclusion criteria. Most had Fuchs' endothelial dystrophy, and the median age was 69 years (range, 42−89 years; Table 1). Secondary DMEK was performed as a single procedure in the 55 eyes. After surgery, the youngest patient was phakic and the remaining 54 patients were pseudophakic (Table 1). The median duration of follow-up was 18 months (range, 3−61 months).

A subgroup of 29 patients who underwent secondary DMEK in one eye and successful primary DMEK in the fellow eye met the criteria for the paired analysis; all had Fuchs' endothelial dystrophy (Table 1). The eye that required a secondary graft was the first treated eye in 11 patients (38%) and the second treated eye in 18 patients (62%). The median interval between the primary grafts in the fellow eyes was 18 weeks (range, 2 weeks to 2 years).

Reasons for Replacement of the Original Graft and Timing

The reasons for the 55 regrafts included unsuitable donor tissue (n = 5),[14−16] surgical complications (n = 21), early failure to clear