Descemet Membrane Endothelial Keratoplasty as a Secondary Approach After Failure of Penetrating Keratoplasty

Enken Gundlach, Anna-Karina B. Maier, Aline Isabel Riechardt, Tobias Brockmann, Eckart Bertelmann, Antonia Joussen, Necip Torun

Abstract

Objectives: To investigate visual outcome and postoperative complications in patients undergoing Descemet membrane endothelial keratoplasty with graft failure after penetrating keratoplasty.

Materials and Methods: A retrospective analysis was performed with 5 patients who underwent Descemet membrane endothelial keratoplasty after failed penetrating keratoplasty. Intraoperative and postoperative complications were recorded. Visual acuity, rehabilitation phase, refraction stability, central corneal thickness, endothelial cell count, possible immunologic reactions, and optical coherence tomography of the anterior eye segment were evaluated. A subjective questionnaire was used to evaluate patient satisfaction.

Results: There were no intraoperative complications. All patients had graft detachment, which made air injection necessary. In all cases, visual acuity significantly increased (medium visual acuity [logarithm of the minimum angle of resolution]: 0.68 ± 0.31 logarithm of the minimum angle of resolution after 4 weeks and 0.35 ± 0.37 after 6 months; \( P = .043 \)), refraction was stable, corneal thickness was reduced (average, 514 ± 11 μm), and endothelial cell count was reduced (average, 1398 ± 510 cells/mm\(^2\)) after 6 months, which corresponds with a medium loss 40%.

In the questionnaire, visual outcome, estimated time for recovery, and rehabilitation and patient satisfaction were better after Descemet membrane endothelial keratoplasty than penetrating keratoplasty. No postoperative elevation of pressure, development of pupillary block, or graft rejection, and no peripheral anterior synechiae or other abnormalities were observed with optical coherence tomography during the first 6 postoperative months.

Conclusions: Descemet membrane endothelial keratoplasty is a suitable technique for the treatment of graft failure after penetrating keratoplasty and helped our patients rapidly achieve good visual acuity, with reduction of postoperative complications, but the visual outcome might be limited.

Key words: Penetrating keratoplasty, Cornea, Graft failure

Introduction

The diagnosis of graft failure as an indication for keratoplasty has increased in the past several years.\(^1\) The most common cause of graft failure is dysfunction of the corneal endothelium.\(^2\) In most cases, a second penetrating keratoplasty (PKP) is needed to enable good visual acuity. However, this surgical technique has disadvantages. Intraoperative problems like severe bleeding, suture associated problems, moderate vision rehabilitation, and graft rejection may occur. In addition, visual rehabilitation takes longer with a stable refraction at a later time.\(^3-7\) Furthermore, there is a delayed possibility of adjusting contact lenses or eyeglasses, and adjusting visual aids frequently is more complicated due to high astigmatism. Therefore, these medically
complicated patients may benefit from our newly gained knowledge of lamellar surgical techniques.

In recent years, new technologies in posterior lamellar keratoplasty have improved the treatment of malfunction of the corneal endothelium.8-10 Initially, indications were limited to Fuchs endothelial dystrophy or bullous keratopathy. However, with more operative experience, indications were broadened.

In 2007, Covert and Koenig published a research study that showed good results with Descemet stripping automated endothelial keratoplasty (DSAEK) after PKP.11 Further studies confirmed this impression.12-14 However, Descemet membrane endothelial keratoplasty (DMEK) brings better final visual acuity than DSAEK.9 Therefore, investigation of DMEK after failed PKP was justified.

The aim of the present study was to analyze intra- and postoperative complications, gain in visual acuity, rehabilitation phase, refraction stability, corneal thickness, endothelial cell count, possible immunologic reactions, and optical coherence tomography of the anterior eye segment in eyes that were treated with DMEK after failed PKP. In addition, a subjective questionnaire was used to evaluate patient satisfaction.

Materials and Methods

This study followed the ethical standards of the Declaration of Helsinki. The patients gave informed consent for the treatment and participation in the study. Institutional ethical approval was obtained by the Ethics Committee of the Charité Universitätsmedizin Berlin. All DMEKs were performed between July 2012 and February 2013 by the same surgeon (NT). The demographic data of our patients are listed in Table 1.

In this study, we retrospectively analyzed 5 eyes in 5 patients who had endothelial failure after perforating PKP that were treated with DMEK. There were 2 of the 5 patients who needed 3 PKPs because of graft failure. Stripping of the endothelial Descemet membrane from the donor corneal stroma was performed immediately before transplant in a standardized manner described in detail by Melles and associates.1,15,16 The corneal scleral transplant was mounted endothelial side up on a holder (Barron corneal punch, Katena Products, Inc., Denville, NJ, USA). Stripping was started peripherally by separation of the Descemet membrane and stroma and continued to the middle. After the separation of half of the cornea, trephination of the lamella was performed. The lamella was excised completely and stored in organ culture medium until surgery. There was no tissue wastage during preparation of the grafts. The diameter of the graft was 8.0 mm. Clear corneal incisions (2.75 mm) without sutures were used in all cases, and the descemetorhexis was done with a diameter between 8.5 and 9.0 mm. The graft lamella was stained with trypan blue before injection.

After injection, the lamella was unfolded using a glass injector. As soon as the graft lamella was completely unfolded, the complete anterior chamber was filled with air to attach the graft lamella. After 1 hour, part of the air was released and exchanged with BSS (Alcon, Freiburg im Breisgau, Germany), so the anterior chamber was half-filled with air.

### Table 1. Characteristics of All Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>5</td>
</tr>
<tr>
<td>Age (y)</td>
<td>Range 68-81 (median 78)</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>3/2</td>
</tr>
<tr>
<td>Indication for DMEK</td>
<td>Failure of endothelium, 5</td>
</tr>
<tr>
<td>Time after PKP (mo)</td>
<td>Range 24-107 (median 57)</td>
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<tr>
<td>Indication for PKP</td>
<td>Fuchs endothelial dystrophy, 2</td>
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<tr>
<td></td>
<td>Keratoconus, 1</td>
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</tbody>
</table>

**Abbreviations:** DMEK, descemet membrane endothelial keratoplasty; PKP, penetrating keratoplasty

### Table 2. Results Preoperative and 6 Months Postoperative

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preoperative</th>
<th>Postoperative (6 mo)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>5</td>
<td>5</td>
<td>.</td>
</tr>
<tr>
<td>BCVA (LogMAR)</td>
<td>1.16 ± 0.38</td>
<td>0.35 ± 0.37</td>
<td>.043</td>
</tr>
<tr>
<td>Central corneal thickness (μm)</td>
<td>756.75 ± 58.42</td>
<td>514.00 ± 11.31</td>
<td>.068</td>
</tr>
<tr>
<td>Endothelial cell density (cells/mm²)</td>
<td>2348.00 ± 231.78</td>
<td>1398.00 ± 510.36</td>
<td>.043</td>
</tr>
<tr>
<td>Manifest SE (D)</td>
<td>-3.80 ± 2.49</td>
<td>-4.88 ± 1.40</td>
<td>.225</td>
</tr>
<tr>
<td>Manifest cylinder (D)</td>
<td>3.85 ± 1.82</td>
<td>3.20 ± 1.41</td>
<td>.500</td>
</tr>
</tbody>
</table>

**Abbreviations:** BCVA, best-corrected visual acuity; D, diopter; LogMAR, logarithm of the minimum angle of resolution; SE, spherical equivalent

Corneal grafts were provided by the Cornea Bank Berlin. All grafts had a minimal endothelial cell count of 2000/mm². Postoperative therapy included daily local application of steroid and antibiotic eye drops and artificial tear substitute. Although the antibiotic drops were gradually phased out within 2 weeks, steroids were reduced monthly drop by drop.

In all patients, an ophthalmologic examination was performed with anamnesis, refraction, best-corrected visual acuity, Goldmann tonometry (Haag-Streit, Bern, Switzerland), slit-lamp examination, and funduscopy. Distance visual acuity was assessed.
with Snellen charts and expressed as Snellen decimal notations. For analysis, logarithm of the minimum angle of resolution (LogMAR) values were used, as previously described.17

Graft alignment and anterior chamber anatomy were investigated using an optical coherence tomography device with an anterior chamber module (Spectrals optical coherence tomography, Heidelberg Engineering GmbH, Heidelberg, Germany) and software (Heidelberg engineering Family acquisition Module 5.3.3.0, Heidelberg engineering Viewing Module 5.3.2.0, and Heidelberg Eye explorer 1.6.4.0) (Heidelberg Engineering GmbH, Heidelberg, Germany). Endothelial cell counts were determined using a specular microscope (Noncon ROBO CA, Konan Medical Inc., Nishinomiya, Japan). These examinations were performed preoperatively at 2 weeks, 1 month, 3 months, and 6 months postoperatively. Intra- and postoperative processes were documented. At the last follow-up, the patients answered a questionnaire grading their symptoms and overall satisfaction with the surgery on a scale of 1 to 6. (How is your vision? Grade 1-6: 1, very bad; 2, bad; 3, fine; 4, good; 5, very good; 6, excellent.)

Statistical analyses
The statistical evaluation of the collected data was carried out using software (IBM SPSS, Version 19, IBM Corp. Armonk, NY, USA). Normality was tested for all outcome measures, and none of the measures followed a normal distribution. Therefore, non-parametric tests (Kruskal-Wallis and Wilcoxon signed rank test) were used for analysis. Descriptive statistics were expressed as median and range or mean ± standard deviation (SD). Differences were considered statistically significant when \( P < .05 \).

Results
Intraoperative complications were not observed in any of the cases. However, all operations were classified as technically demanding by the surgeon. Intraoperative flattening and attachment of the flap were difficult due to the irregularity of the corneal posterior cell layer. All patients had graft detachment requiring air injection in the anterior chamber during initial follow-up. In 3 of the 5 patients air injections were performed 3 times, in 1 of the 5 patients two times and in 1 of the 5 patients 1 time. The time of graft detachment ranged from postoperative day 1 to 7 (median, day 4). There was no observed postoperative elevation of pressure, development of pupillary block, peripheral anterior synechiae, or rejection.

In all cases, visual acuity increased with a medium visual acuity from preoperative 1.16 ± 0.38 LogMAR to 0.68 ± 0.31 LogMAR after 4 weeks and 0.35 ± 0.37 LogMAR after 6 months (Figure 1, Figure 2). All patients had significantly better visual acuity at the last follow-up than preoperatively (\( P = .043 \)). There was no loss of best-corrected visual acuity in any of the patients. The mean refractive spherical equivalent was -3.80 ± 2.49 D preoperatively and -4.88 ± 1.40 D after 6 months (\( P = .225 \)). The refractive cylinder was 3.85 ± 1.82 D preoperatively and 3.2 ± 1.41 D after 6 months. There was no significant difference between preoperatively and postoperative values (\( P = .500 \)).

In all patients, corneal thickness was reduced. The central corneal thickness was measured 756 ± 58 μm preoperatively and 514 ± 11 μm postoperatively after 6 months (\( P = .068 \)) and was therefore in a normal range.

A steady decline in number of postoperative endothelial cells was noted. Mean endothelial cell count/mm² was 2348 ± 232/mm² preoperatively and 1398 ± 510/mm² six months postoperatively, corresponding to a medium loss of 40% (\( P = .043 \)).

In the questionnaire, all patients subjectively evaluated their visual outcome after surgery DMEK as being better than after PKP, and the estimated time for recovery and rehabilitation was shorter after
DMEK. There were 2 patients who noted lack of improvement in visual acuity. When asked about the preferred surgical procedure, all patients preferred DMEK. There were 2 of 5 patients who stated that DMEK was more painful than PKP.

Discussion

Within a short time, DMEK has revolutionized the treatment of endothelial dysfunction and has become the standard method for treatment of Fuchs endothelial dystrophy. Due to excellent clinical results, the range of indications for DMEK has been extended in recent years. In this study, we retrospectively analyzed the data of 5 eyes in 5 patients who had endothelial failure after PKP and who were treated with DMEK. The DMEK procedure was possible after PKP and was performed successfully in the 5 patients. In all cases, the operating surgeon agreed with Anshu and associates, who also performed DMEK after PKP, that the operation was technically demanding. Due to the usually bad insight and especially the irregularity of the corneal posterior cell layer, it was difficult to apply the flap intraoperatively. Therefore, it is advisable to have an experienced DMEK surgeon in such cases.

In all patients, air injections were performed postoperatively because of graft detachments. The high and early air injection rate was due to the irregularity of the corneal posterior cell layer on which it is harder for the flap to apply on. Similar findings were described by Anshu and associates and by Clements and coworkers on DSAEK after PKP, in which a delocalization of the graft was observed frequently. However, attachment of the flap was achievable, despite the necessity of more extensive early postoperative follow-up.

All patients had significantly increased visual acuity ($P = .043$). Nevertheless, final postoperative visual acuity in these cases of secondary DMEK was lower than with primary uncomplicated DMEK. In our opinion, this had 2 main causes. First, this study included eyes with stromal opacities, which also were located in the central optical axis; most stromal opacities resolved within 4 weeks after surgery, but they may have caused opacities in the refracting media and impaired final visual acuity results. Second, most patients refused fitting of contact lenses required to equalize the preexisting astigmatism after PKP. They justified their critical position with their advanced age and preferred an adjustment of eyeglasses despite lower corrected visual acuity. The 1 patient who had adjusted a contact lens had full visual recovery. Therefore, we concluded that the final visual acuity results would be better if the astigmatism was optimally treated. Furthermore, all eyes had previous surgery, including 2 patients who had 3 PKPs. With this background, a complete visual recovery cannot always be expected.

Within the first 3 months, average loss of endothelial cells was 40%, which was higher than with our other DMEK patients (data not shown). We assume that a higher loss of endothelial cells may be explained by a higher air injection rate.

Aside from the good technical results, we also observed more benefits with DMEK than repeat PKP. First, there were no postoperative complications that may occur after repeat PKP, such as suture associated problems. Second, fast visual rehabilitation was achieved, and all patients had significant improvement of visual acuity within 4 weeks. The rapid visual rehabilitation was favorable to our patients compared with the prolonged visual rehabilitation after PKP, as noted in the analysis of the questionnaires.
The refraction was stable, and this initially allowed our patients to continue using their old eyeglasses. This may be helpful when visual acuity is restricted in the opposite eye. In addition, the fitting of new eyeglasses or contact lenses may be performed within the first 3 months because refraction was stable. This is early compared with PKP, after which the refraction may change until all sutures are removed.

Local therapy was phased out within 6 months, but lifelong local therapy after PKP may be necessary. This is not only pleasant for our patients, since some of them are depended of a nursing service or relatives for applying eye drops, but it also reduces the rate of accompanied complications. Therefore, none of our patients had high intraocular pressure or epithelial healing dysfunction, which are common complications after PKP.

Although steroids were phased out quickly after DMEK compared with PKP, and despite the high risk of rejection, no rejection was observed within 6 months after DMEK. These findings are consistent with previous studies, which described rejection after DMEK as rare cases. Therefore, DMEK instead of revision PKP may be suitable for patients who have increased risk of rejection, but further studies with prolonged follow-up are necessary.

The DMEK after previous PKP is a suitable technique that helps achieve fast and good recovery of visual acuity and reduces postoperative complications. The DMEK might be very promising, especially for patients who have a high risk for graft rejection. From our point of view dense central stromal opacities and high astigmatism are contraindications for DMEK after PKP. Nevertheless, even in the presence of these factors, DMEK may be the best option for some patients (older or disabled patients) when the advantages of DMEK, such as fast rehabilitation of visual acuity, stable refraction, decreased postoperative problems, and fast healing, outweigh the reduced prognosis of visual acuity.

This study was limited by the small number of patients and short follow-up (6 mo). Therefore, further studies with more patients and longer follow-up are required to confirm these findings.

References