Descemet Membrane Endothelial Keratoplasty Under Failed Penetrating Keratoplasty Without Host Descemetorhexis for the Management of Secondary Graft Failure

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Purpose: To evaluate the safety and efficacy of the treatment of secondary graft failure in penetrating keratoplasty (PK) by performing Descemet membrane endothelial keratoplasty (DMEK) without host descemetorhexis.

Methods: This is a retrospective case series study of 8 eyes from 8 patients who underwent non host Descemet membrane stripping DMEK surgery under a previously failed PK. The DMEK graft diameter was either matched or 0.25 to 0.5 mm undersized in relation to the PK diameter. Six-month postoperative data are presented. Primary outcome measures were safety and anatomical success.

Results: No intraoperative complications were registered. Postoperatively, 1 case developed a PK host–donor junction dehiscence in relation to a previous early suture removal, requiring PK resuturing and DMEK rebubbling. Only 1 additional case required DMEK rebubbling. No primary graft failure was detected, and all cases achieved full PK transparency within 2 weeks. Corrected distance visual acuity improved from a median of counting fingers (CF-0.2) to 0.57 (0.05–0.7). Median central corneal thickness improved from 650.5 (497–897) to 464 (372–597) μm. Median endothelial cell density was 1080 (581–2043) cells/mm^2. Rebubbling rate (25%) was lower than that previously reported. All patients had extensive preoperative ocular comorbidity.

Conclusions: DMEK under PK without host descemetorhexis is a feasible surgical alternative for the treatment of graft failure after PK. It is associated with equivalent levels of efficacy and safety compared with Descemet membrane stripping DMEK techniques but simplifies the surgical procedure and avoids potential intraoperative complications associated with Descemet stripping. Further studies with a larger sample and a longer follow-up are necessary to confirm our preliminary outcomes.

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Late endothelial failure is one of the leading causes of reintervention after full-thickness corneal transplant. Endothelial keratoplasty (EK) techniques have demonstrated their efficacy in restoring the clarity of full-thickness grafts with endothelial decompensation and nowadays are becoming the preferred surgical approach for this graft indication.[1,2] EK is preferred over penetrating regraft because it has a lower risk of rejection, is safer in the presence of ocular surface disease, is associated with fewer intraocular pressure rises and less glaucoma, and typically allows for faster visual recovery and more acceptable refractive outcomes.[3,4] In addition, recent results have shown prolonged graft survival in eyes that underwent EK under a failed penetrating keratoplasty (PK), compared with a PK regraft.[5,6]

In the past few years, Descemet membrane endothelial keratoplasty (DMEK) has become a popular EK procedure and has demonstrated its superiority over Descemet stripping endothelial keratoplasty (DSEK) for faster and better visual outcomes. DMEK has also been used to treat PK graft failure.[6–9] Performing DMEK under a failed PK can be more technically challenging than performing DSEK. Small Descemet membrane (DM) tags or stromal fibers dislodged by traumatic DM stripping maneuvers can disproportionally affect DMEK graft adhesion and increase the risk of its detachment as, in contrast to DSEK (which maintains a flat profile), in DMEK the force required to compress these dislodged stromal fibers is similar to that required to push the DMEK graft back into a scrolled configuration and detach it, as in DMEK grafts the interface surface is smoother and the tissue scrolls, allowing small areas of detachment to propagate more easily.[10] There is increasing evidence that it is not mandatory to perform host DM–endothelium stripping in DMEK surgery as long as these layers are anatomically intact and do not have guttae.[11–15] Given that PK failure is not typically associated with guttae, we hypothesized that non-Descemet stripping DMEK (NS-DMEK) would be an appropriate treatment for secondary PK failure.

To the best of our knowledge, no previous publications have independently reported the outcomes of DMEK for PK secondary graft failure treatment without stripping the host DM–endothelium complex. The aim of the current study is to investigate the safety and efficacy of this surgical alternative.

MATERIALS AND METHODS

The records of 8 consecutive eyes from 8 patients operated on by 2 surgeons (J.L.A.B. and M.B.) at the 2 study hospitals were analyzed retrospectively. All eyes underwent NS-DMEK surgery under a previously failed PK. As part of the surgical planning, all patients underwent preoperative anterior segment optical coherence tomography to determine the smallest posterior diameter free from irregularities. DMEK size was either matched or undersized by 0.25 to 0.5 mm depending on the posterior graft configuration to avoid the DMEK graft being positioned under the donor–host posterior corneal surface interface and step.

Local anesthesia with sedation was used for all surgeries. A standard DMEK graft was performed as previously described,[12,16] with the only variation that the DM–-endothelium complex from the recipient and previously failed penetrating graft was not excised and was left untouched. In brief, the surgeons (J.L.A.B. and M.B.) prepared the donor tissue on the day of surgery using an orientation mark.[16] The donor graft was then inserted through a 3.2-mm temporal limbal incision with the Geuder DMEK injector (Geuder, Germany), unfolded using a "no-touch" technique, and finally attached to the recipient PK endothelium with a 20% SF6 anterior chamber (AC) fill.

All patients received topical antibiotics for 1 week, and prednisolone acetate 1% eye drops were used 8 times a day for the first week, 4 times a day for the first 3 months, and then tapered by 1 drop/d every 2 months to a dose of 1 drop/d. Patients who had suffered >1 episode of graft rejection previously were considered as high risk of rejection and received additional topical (0.03%) and systemic (1 mg every 12 hours) tacrolimus (Prograf, Astellas Pharma Inc, Tokyo, Japan) for a year and oral steroids for a month.

Data were recorded up to the sixth postoperative month. Primary outcome measures were safety and anatomical success. This retrospective study was approved by the Ethical Board Committees of our institutions and followed the tenets of the Declaration of Helsinki.

RESULTS

Eight eyes of 8 patients were included in the study (4 eyes from each study hospital). Seventy-five percent were men (6 eyes), and 50% were right eyes (4 eyes). The median age at the time of DMEK was 70 years (55–84 years). A common finding among all patients was a history of an extensive ocular comorbidity and multiple ophthalmic

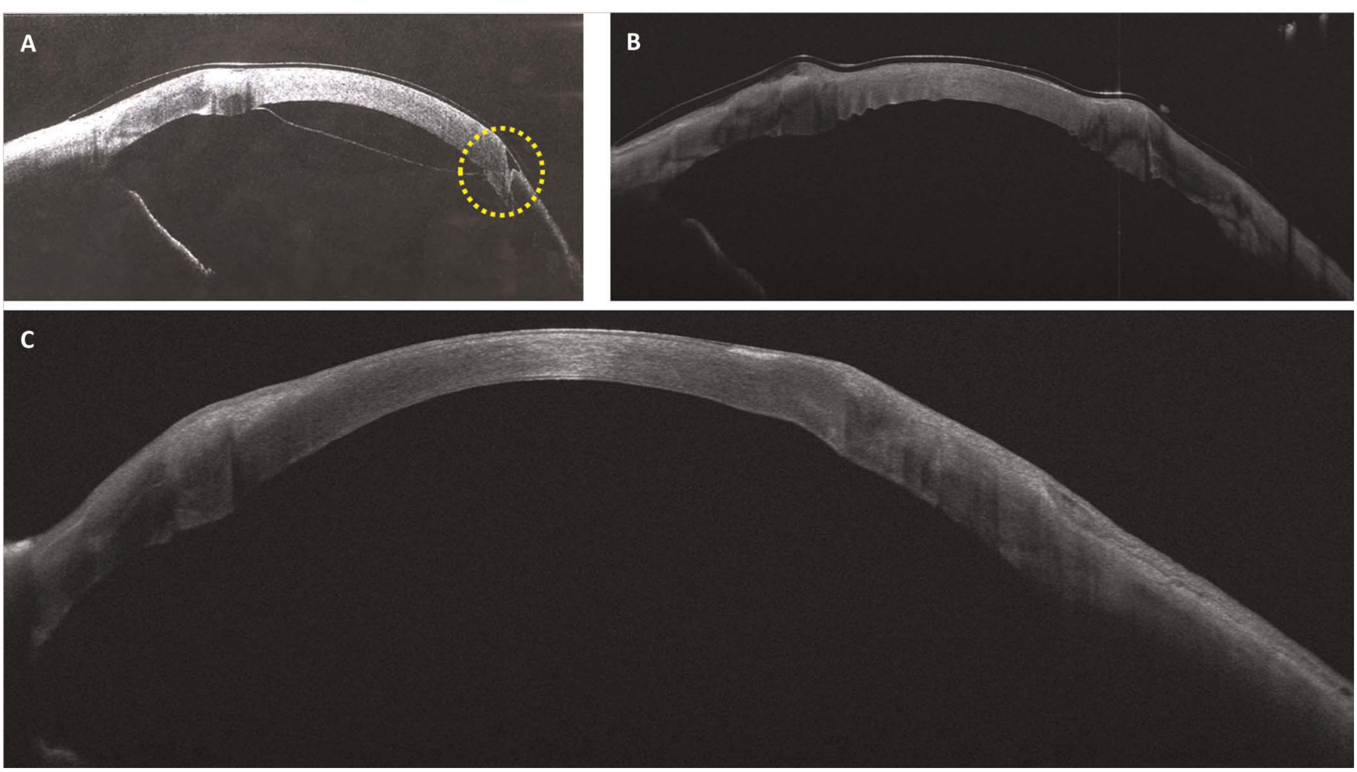

FIGURE 1. Anterior segment optical coherence tomography images (MS-39, CSO, Italy) of patient 4. Ten days after a successful DMEK procedure, the graft–host junction of the PK graft developed a severe dehiscence (dashed line) with secondary subtotal detachment of the underlying DMEK lenticule (A). PK resuturing and DMEK rebubbling achieved a resolution of the corneal edema 1 week after the reintervention (B). Six months later, the PK graft remained healthy and clear (C).

surgical procedures, with preoperative glaucoma being reported in 6 eyes (75%) with the presence of a glaucoma drainage valve in 2 eyes and trabeculectomy in 1 eye. Other reported ocular comorbidities were age-related macular degeneration (2 eyes), AC dysgenesis (1 eye), diabetic retinopathy (1 eye), macular edema (2 eyes), aphakia (1 eye), and panuveitis (1 eye). Previous surgical procedures included cataract surgery (7 eyes), complicated cataract surgery (2 eyes), pars plana vitrectomy (3 eyes), and intravitreal injection of dexamethasone (2 eyes; Ozurdex, Allergan Inc, Dublin, Ireland). The median number of penetrating keratoplasties performed per patient before the DMEK transplant was 2 (1–3). The reasons for the first corneal graft were keratoconus (2 eyes), pseudophakic bullous keratopathy (4 eyes), Fuchs endothelial dystrophy (1 eye), and corneal scarring (1 eye). The median time between the last PK graft and the DMEK graft was 6.9 years (5 months–17 years). PK endothelial failure was reported to be related to a graft rejection episode in 2 eyes and secondary to a glaucoma valve implantation in 1 eye. Before endothelial decompensation of the last PK graft, the median best documented corrected distance visual acuity (CDVA) was 0.5 (0.05–1), whereas after graft failure, the CDVA dropped to a median value of counting fingers (CF-0.2).

The median DMEK graft diameter used was 7.5 mm (7.5–8.25), whereas the median failed PK diameter was 7.75 mm (7.7–8.25). The median endothelial cell density (ECD) of the donor endothelium reported by the eye bank was 2550 cells/mm^2 (2300–2824). In 1 case, DMEK surgery was combined with phacoemulsification and intraocular lens implantation. In 1 patient, DMEK was combined with an iris reconstruction and PK resuturing for intraoperative graft–host junction dehiscence.

Postoperatively, 1 case developed a PK host–donor junction dehiscence in relation to a previous early suture removal, requiring PK resuturing and DMEK rebubbling (Fig. 1). One additional case required 2 rebubblings because of a partial detachment of the DMEK lenticule in relation to the presence of a glaucoma tube. No primary graft failure case was detected, and all cases achieved full PK transparency within 2 weeks of the transplant (Figs. 2 and 3). We did not observe any cases of graft rejection or secondary graft failure during the follow-up time.

Corrected distance visual acuity improved from a median of CF (CF-0.2) to 0.57 (0.05–0.7) 6 months postoperatively, and the unaided distance visual acuity improved from a median of (CF-0.1) to 0.26 (0.05–0.7). The median central corneal thickness improved from 650.5 (497–897) to 464 (372–597) μm. The median ECD 6 months postoperatively was 1080 (581–2043) cells/mm.^{2} Visual outcomes for all patients are summarized in Table 1.

DISCUSSION

Recently, a few publications have suggested the feasibility of performing modern EK without stripping the host DM–endothelium complex, as long as the host DM is intact without abnormalities such as guttae, scarring, or

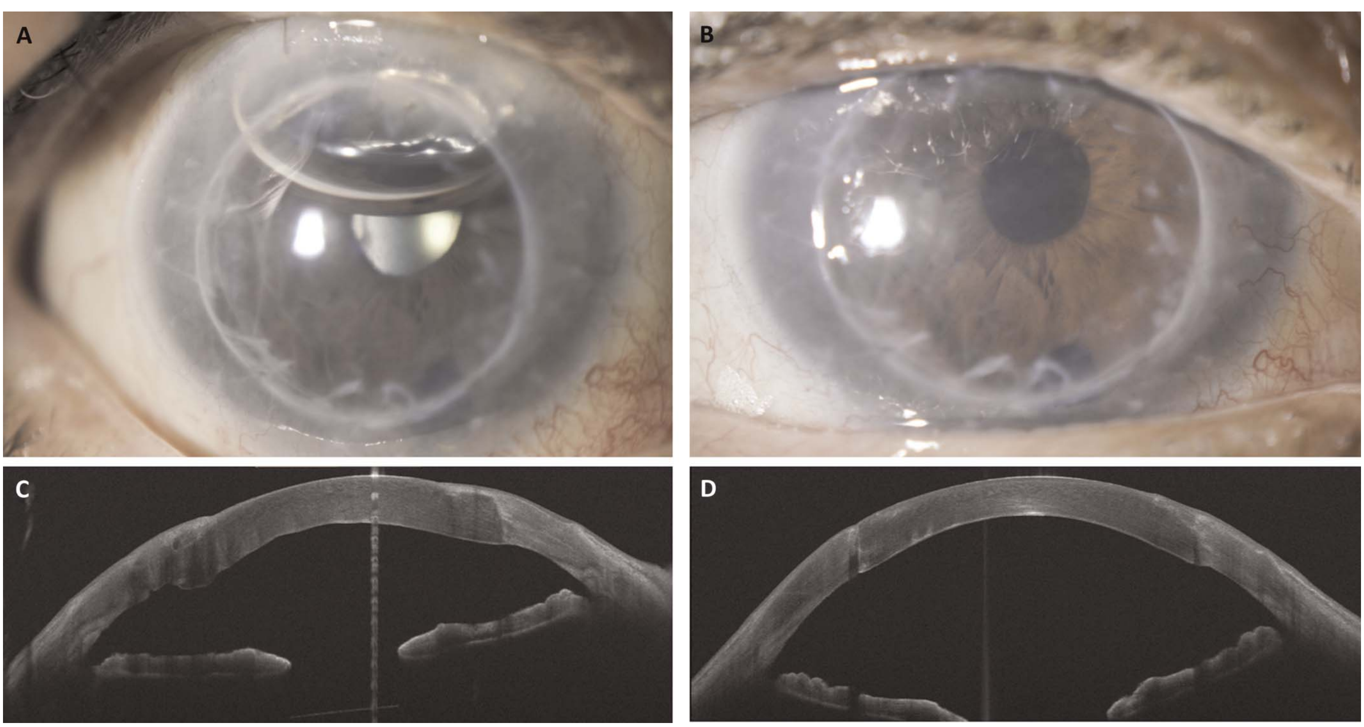

FIGURE 2. Slit-lamp images of patient 3 1 week (A) and 1 month (B) after DMEK under failed PK without host descemetorhexis for the management of secondary PK graft failure. The absence of posterior corneal haze was observed. Preoperative (C) and 1 month postoperative (D) anterior segment optical coherence tomography images showing the improvement of the PK graft edema and thickening.

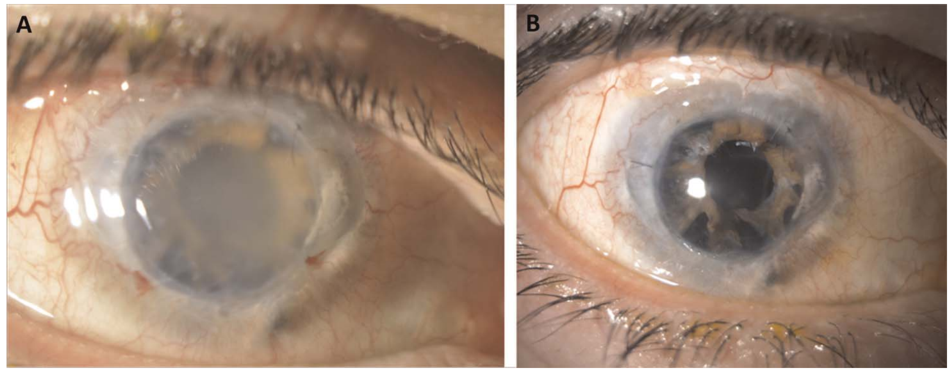

FIGURE 3. Slit-lamp images of patient 2 preoperatively (A) and 6 months postoperatively (B) after DMEK under failed PK without host descemetorhexis.

retrokeratic precipitates.[11–15] These published outcomes show comparable visual outcomes and rebubbling rates to cases performed with regular DM stripping EK. Because DMEK is a newer and more technically challenging procedure, fewer cases of DMEK after PK have been reported. Indeed, many surgeons only offer DMEK as a primary surgical procedure in uncomplicated cases. Pasari et al[6] recently reported the outcomes of 93 cases of DMEK under PK. These authors stated that they stripped the DM–endothelium complex in all their DMEK under PK cases "*except in a few early cases in the series done before the surgeons appreciated that DMEK did not adhere as well to residual Descemet membrane and the endothelium*." The authors did not provide any analysis to support this assertion. To the best of our knowledge, no previous publications have separately reported the outcomes of DMEK under PK without stripping the host DM–endothelium complex.

Despite the small study sample, our study provides the proof of concept about the safety and feasibility of performing DMEK under a failed PK graft without the host DM–endothelium removal, even in complex cases with additional anterior segment pathology.

The rate of postoperative complications remained unaffected despite the fact of avoiding this critical surgical step. Moreover, we show initial encouraging results about its efficacy in restoring the corneal clarity and visual function in such cases with previously failed PK, as previous studies have already reported with DM stripping DMEK.[6–9,17]

The main concern with performing descemetorhexis is disruption of the graft–host junction or inadvertent production of an irregular posterior surface.[10] There is always a concern that manipulation near the graft–host junction could lead to traumatic graft dehiscence. Patients undergoing repeat PK may be elderly and might have been treated with prolonged steroids to reduce the risks of PK. These factors make the graft–host interface weaker than in other patients. Actually, in 1 of our patients, the pressure of the AC infusion was sufficient to rupture the graft–host junction, necessitating the placement of addition sutures. In a second patient, a dehiscence was noted postoperatively, perhaps related to the high pressure of gas fill at the conclusion of the case. Given that disruption of the graft–host interface is a serious concern, all authors in the previous descriptions of DMEK under PK describe performing descemetorhexis well within the graft margin. These risks produce an irregular surface and, unless a significantly undersized graft is used, it will result in significant graft–descemetorhexis overlap, a phenomenon associated with graft detachment.[18] The poor visibility associated with working through an edematous, often scarred cornea increases the risk of creating a rough interface with

TABLE 1. Six-Month Postoperative Visual Outcomes (Decimal Scale) After DMEK Under Failed PK Without Host Descemetorhexis for the Management of Secondary PK Graft Failure

	No. of PK Grafts	Pre-PK Failure CDVA	Post-PK Failure CDVA	Post-DMEK CDVA	ECD (cells/mm^2)	Complications	No. of Rebubblings	Ocular Comorbidity
1	2	0.5	0.1	0.4	581	50% graft detachment	2	Glaucoma (tube), ARMD
2	2	0.8	0.1	0.7	824	None	0	Glaucoma (tube), AC dysgenesis
3	1	0.15	0.05	0.6	1080	None	0	Diabetic retinopathy, CME
4	1	0.05	CF	0.05	861	PK dehiscence + subtotal DMEK detachment	1 (+PK resuture)	Glaucoma, ARMD
5	3	0.25	CF	0.4	1641	Intraoperative graft dehiscence	0	Advanced glaucoma, aphakia
6	2	0.25	CF	0.55	2043	None	0	Glaucoma (trabeculectomy)
7	2	1	0.2	0.7	1357	None	0	Glaucoma
8	2	0.5	CF	n/a (0.17)*	n/a	None	0	Panuvetis, CME

*The last documented CDVA is shown in parenthesis, that is, 1 month after surgery.
ARMD, age-related macular degeneration; CME, cystoid macular edema; n/a, not available.

stromal fibrils or residual fragments of DM. This could prevent the correct attachment of the graft and limit the visual outcome.[19,20]

Although our case series is small, our rebubble rates compared favorably with the other reports: 25% versus 37% to 50%.[6,8,17] In both cases requiring additional gas injection, additional factors relating to graft detachment were present. In 1 case, a complete loss of the AC gas bubble by day 2 had occurred because of a quick migration of the gas through a glaucoma tube, requiring 2 consecutive rebubblings because of partial graft detachment at day 2 and day 7 postoperatively. In the second case, the initially attached DMEK graft became detached after the patient developed a wound dehiscence at day 7 postoperatively. Despite the initial success in this case, we chose to count this as a case of graft detachment. Both were successfully reattached at 1 week after rebubbling (after 2 attempts in one of the cases). This suggests that maintenance of an AC gas fill in the early postoperative period is important in DMEK after PK. We used SF6 as standard for all DMEK's, and all cases of NS-DMEK had SF6 20%. This contrasts to the other authors who primarily used air as a tamponade agent.

A restoration of corneal clarity associated with a reduction in corneal thickness was seen in all cases.

An improvement in vision was seen in all patients, although final visual acuity was limited by irregular astigmatism and a high percentage of ocular comorbidities in our cohort. It has been postulated that retaining the host DM may limit final visual acuity because of the creation of an interface.[13] We did not observe cases of interface haze or scarring in our sample. Actually, in a previous publication of our group where we examined NS-DMEK after DMEK secondary graft failure, we showed that the presence of 2 consecutive DM's does not negatively affect eye aberrations, light scatter or visual acuity potential.[12]

In 2 cases, the CDVA after the DMEK was superior to that recorded before the PK failure (Table 1). In patient 3, this was related to the fact that the PK corneal suture was removed after the DMEK graft, and in patient 6, because an improvement in media clarity after neodymium-YAG laser capsulotomy.

Our ECD loss results at 6 months were worse than those previously reported with DM stripping DMEK under PK,[6,17] with an approximately 50% ECD loss in comparison with preoperative values supplied by the eye bank. We believe this is connected to the high ocular comorbidity of our patients and the almost constant presence of previous glaucoma and filtration surgery, which has been reported to be the most important risk factor for DMEK failure and cell loss.[6]

The main limitation of this study is the small sample size, the relatively short follow-up time, and the presence of high ocular comorbidity that limited the final visual potential. However, given that our main aim was to assess the feasibility of NS-DMEK for primary graft success, we believe the data presented are valid and point to a useful surgical modification that warrants further investigation.

In conclusion, our study is the first to independently assess the outcomes of DMEK under failed PK performed without stripping the host DM–endothelium layers. Avoiding this surgical step simplifies the technique and may reduce the risk of intraoperative complications. We believe that maintaining a regular posterior surface (by not stripping DM), preventing abnormal graft draping (by measuring the minimum posterior graft diameter on optical coherence tomography and avoiding grafts overlapping the graft–host junction), and ensuring a gas fill for several days (by using SF6 and asking patients to posture), all contribute to high attachment rates in DMEK after PK. Further studies with a larger sample and follow-up are necessary to confirm the long-term outcomes and real ECD loss of this surgical alternative.

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