Comparison of Manual and Femtosecond Laser–Assisted Descemet Membrane Endothelial Keratoplasty for Failed Penetrating Keratoplasty

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• PURPOSE: To compare outcomes of manual Descemet membrane endothelial keratoplasty (M-DMEK) and femtosecond laser–assisted Descemet membrane endothelial keratoplasty (F-DMEK) in treatment of penetrating keratoplasty (PK) graft failure.

• METHODS: SETTING: Retrospective, interventional comparative case series. PATIENT POPULATION: Included were all patients with a failed PK graft who underwent either F-DMEK (10 eyes of 10 patients) or M-DMEK (29 eyes of 29 patients) at Toronto Western Hospital and the Kensington Eye Institute between 2014 and 2019, and had 6 months of postoperative follow-up. OUTCOME MEASURES: Rates of graft detachment, rebubbling, rejection and failure, best spectacle-corrected visual acuity (BSCVA), and endothelial cell (EC) density.

• RESULTS: Rate of significant graft detachment (detachment requiring either rebubble or repeat keratoplasty) was 10.0% in F-DMEK and 65.5% in M-DMEK (P = .003). Rebubble rate was 10.0% in F-DMEK and 58.6% in M-DMEK (P = .011). Primary failure rate was 0% in F-DMEK and 27.6% in M-DMEK (P = .086). Rates of rejection and secondary failure did not differ between the groups (P = 1.000 for both). In a multivariable analysis, F-DMEK was found to be the only independent factor significantly associated with reduced postoperative detachment. Postoperative BSCVA at 6 months returned to prefailure levels in both groups, with no significant difference between the groups at any time point. EC loss rates were 43.8% in F-DMEK and 38.0% in M-DMEK at 6 months (P = .453).

• CONCLUSIONS: F-DMEK is a safe and effective procedure in failed PK patients, with outcomes comparable to M-DMEK, and with reduced detachment and rebubble rates. A trend towards reduced primary failure should be further studied. (Am J Ophthalmol 2020;214:1–8. © 2019 Elsevier Inc. All rights reserved.)

ENDOTHELIAL DECOMPENSATION AND FAILURE OF A penetrating keratoplasty (PK) graft is not uncommon, with decompensation risk increasing with aging of the graft. Historically, endothelial failure of a PK graft could only be managed by a repeat PK procedure. The emergence of endothelial keratoplasty enables restoration of PK endothelial function by selectively replacing the decompensated endothelium with an endothelial graft, obviating a full-thickness transplant. This reduces the risk of rejection, improves the visual outcome, induces minimal refractive changes, and avoids risks associated with "open-sky" surgery.[1-6]

Recent literature shows that Descemet membrane endothelial keratoplasty (DMEK) is a viable option in the management of endothelial PK graft failure with acceptable outcomes, although possibly less successful than primary DMEK. Performing DMEK in this scenario is associated with a high rate of postoperative graft detachment and rebubbling, ranging between 26% and 100%.[3-7]

In recent years, the femtosecond laser has been suggested as a novel tool for performing precise descemetorrhexis in DMEK surgery.[8,9] We previously reported good DMEK outcomes using femtosecond laser–enabled DMEK (F-DMEK) in Fuchs dystrophy, showing similar efficacy to manual DMEK (M-DMEK) with significantly lower postoperative graft detachment and cell loss rates.[9,10] We also recently reported good outcomes of F-DMEK performed in a series of eyes with a failed PK graft.[11] However, there are no data comparing outcomes of F-DMEK and M-DMEK in the treatment of failed PK. In this study, we compare outcomes of F-DMEK and M-DMEK in patients with a failed PK graft.

METHODS

A RETROSPECTIVE MEDICAL CHART REVIEW WAS performed on all patients with a failed PK graft who underwent either F-DMEK or M-DMEK at Toronto Western

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Hospital and the Kensington Eye Institute (Toronto, Ontario, Canada) between 2014 and 2019, and had at least 6 months of postoperative follow-up. The cohort was divided into 2 groups: F-DMEK group and M-DMEK group. F-DMEK and M-DMEK procedures were performed over the same time period. The choice between F-DMEK and M-DMEK was random, based on availability of a femtosecond laser technician on the day of surgery. All procedures were performed by a single experienced corneal surgeon (D.S.R.) or were directly supervised by him. All eyes included in the study were not among the first 100 DMEK surgeries performed by D.S.R. This retrospective interventional case series received Research Ethics Board approval by the University Health Network (Toronto Western Hospital, Toronto, Ontario, Canada) and was conducted in compliance with the tenets of the Declaration of Helsinki and all provincial and federal laws.

The data collected in this study included demographic characteristics, host and donor characteristics, intraoperative and postoperative complications, best spectacle-corrected visual acuity (BSCVA), endothelial cell (EC) density obtained using a noncontact specular microscope (Robo, KSS 300; Konan Medical, Hyogo, Japan), and data on graft detachment, rebubbling, rejection, and failure. Eyes with either visually significant comorbidities or early graft failure were excluded from visual acuity analysis (18 eyes in the M-DMEK group). Data on manual descemetorrhexis diameter were only partially available, and were therefore not included.

• **SURGICAL TECHNIQUE:** Patients with a failed PK were suitable for DMEK surgery if there was no significant stromal or subepithelial scarring and the patient possessed suitable anterior chamber anatomy. All donor tissues used were stored in corneal storage solution (Optisol; Bausch & Lomb, Rochester, New York, USA) and were received from the Eye Bank of Canada, Ontario division. DMEK grafts were prepared using a modification of the original Melles technique.[12,13] After preparation, the donor Descemet membrane was loaded into either a glass cartridge (Geuder Medical, Heidelberg, Germany) or an intraocular lens cartridge (Monarch, Alcon, Fort Worth, TX). The size of the PK graft was measured, and the size of the donor DMEK graft and the descemetorrhexis were chosen accordingly. In all patients, the descemetorrhexis was at least 0.25 mm smaller than the PK graft to avoid manipulation of the PK graft-host junction. Table 1 summarizes DMEK surgery characteristics of the F-DMEK and M-DMEK groups. The rate of surgeries where a cornea fellow was the main surgeon was 30% in F-DMEK and 16% in M-DMEK. This was not significantly different between the groups ($P = .163$).

Our DMEK surgical technique under a failed PK graft has been previously described.[7,11] Briefly, a temporal 2.4 mm incision and 3 paracenteses were performed in the host peripheral corneal rim without penetrating the PK graft, to prevent potential graft-host wound dehiscence. In the F-DMEK group, the Intralase iFS femtosecond platform (Johnson & Johnson Vision, Jacksonville, Florida, USA) was used to create a vertical ring cut whose depth extended from 100 μm above the thinnest measured corneal depth to 100 μm below the thickest measured corneal depth. Centration of the femtosecond laser's suction ring and applanation cone was guided by 8 surgical pen markings placed circumferentially at a diameter that was 1 mm larger than that of the planned descemetorrhexis incision.

TABLE 1. Descemet Membrane Endothelial Keratoplasty Surgery Characteristics of the Femtosecond-Enabled and Manual Descemet Membrane Endothelial Keratoplasty Groups

	F-DMEK (N = 10)	M-DMEK (N = 29)	*P* Value
Donor age (years)	64.1 ± 6.7	64.1 ± 5.7	.984
Endothelial cell density (cells/mm^2)	2810 ± 210	2724 ± 194	.267
DMEK graft diameter (mm)	7.9 ± 0.2	8.0 ± 0.4	.082
PK graft diameter (mm) (n = 35)[a]	7.5 ± 0.3	7.7 ± 0.5	.363
Ratio of DMEK and PK diameter (n = 35)[a]			
DMEK > PK (DMEK oversized)	70%	56%	.519
DMEK < PK (DMEK undersized)	20%	16%	
DMEK = PK (DMEK same-sized)	10%	28%	
Main surgeon			
Corneal surgeon	70%	84%	.163
Cornea fellow supervised by corneal surgeon	30%	16%	

DMEK = Descemet membrane endothelial keratoplasty; F-DMEK = femtosecond-enabled Descemet membrane endothelial keratoplasty; M-DMEK = manual Descemet membrane endothelial keratoplasty; PK = penetrating keratoplasty.

[a]Data on diameter of PK were unavailable in 4 eyes.

Corneal depth was measured prior to femtosecond planning using a Palmscan P2000U pachymeter (MicroMedical Devices, Calabasas, California, USA) at 8 points along the intended descemetorrhexis incision.[9,10] Following the femtosecond incision, Descemet membrane was dissected from the stroma using a reverse Sinskey hook. In the M-DMEK group, 360-degree scoring of Descemet membrane using a reverse Sinskey hook was performed, followed by manual scraping and removal of the recipient's Descemet membrane. Care was taken to avoid deep dissection into stromal tissue. The remainder of the procedure was identical in the F-DMEK and M-DMEK group and similar to our previously described technique.[14]

All patients stayed strictly supine for 2 hours and then "as much as possible" at home until the next morning. All patients were examined 2 hours after surgery and, if necessary, some of the air was released if the bubble was completely filling the anterior chamber and pupillary block was deemed to be likely. The following day, 0.1% dexamethasone sodium phosphate and 0.3% tobramycin antibiotic (Tobradex; Alcon, Mississauga, Ontario, Canada) eye drops were administered 4 times daily for a week. Then, antibiotic drops were discontinued and 0.1% dexamethasone sodium phosphate (Maxidex; Alcon) eye drops were tapered down to once daily during a 3-month period.

Significant graft detachment was defined as a detachment that required either rebubbling or repeat keratoplasty. Rebubbling was performed within 24 hours in eyes with Descemet membrane detachment of more than one-third of the DMEK graft if no air bubble was left in the anterior chamber. Rebubbling was also performed 7-60 days postoperatively if there was unresolved Descemet membrane detachment that was causing persistent corneal edema either limiting rapid visual recovery or causing significant ocular surface discomfort. In cases of uncertainty, anterior segment optical coherence tomography (Spectralis; Heidelberg Engineering GmbH, Heidelberg, Germany) was performed to determine whether there was graft detachment.

• **STATISTICAL ANALYSIS:** Data were recorded in Microsoft Excel (Microsoft Corp, Redmond, Washington, USA; 2016) and analyzed using XLSTAT (version 2019.1.2) (Addinsoft, Paris, France). BSCVA results were converted to logarithm of the minimum angle of resolution (logMAR). Comparisons were made either between the F-DMEK and M-DMEK groups or between the detachment and no-detachment groups. Continuous variables were compared between independent samples using the Mann-Whitney *U* test. Continuous variables comparing dependent samples (such as preoperative and postoperative BSCVA) were compared within groups using the Wilcoxon signed rank test or paired *t* test. Categorical variables were compared using Fisher exact test. A multivariable analysis for graft detachment was performed using logistic regression, for factors that differed significantly between F-DMEK and M-DMEK in univariate analyses. Regression coefficients of statistically significant independent factors in the logistic regression model are presented as odds ratios for graft detachment. All tests were 2-tailed, and the threshold for statistical significance was defined as a P value $<.05$. Bonferroni correction was used to control for multiple comparisons performed in the logistic regression model (3 independent variables where included in the model), with an adjusted P value threshold of $.05/3 = .017$. A post hoc power analysis was performed to determine the study's power in determining graft detachment rate differences between the F-DMEK (n = 10, 10%) and M-DMEK (n = 29, 65.5%) groups. The statistical power was found to be 93.5%.

RESULTS

THIRTY-NINE EYES OF 39 PATIENTS WERE INCLUDED, WITH 10 eyes of 10 patients in the F-DMEK group and 29 eyes of 29 patients in the M-DMEK group. Figure 1 shows a clinical postoperative photograph of F-DMEK under a PK graft. There were 30 pseudophakic eyes and 9 phakic eyes. Demographic and baseline data of each group are shown in Table 2. There were no significant intraoperative complications, and no issues with the creation of femtosecond descemetorrhexis (in F-DMEK)—all descemetorrhexis cuts were complete.

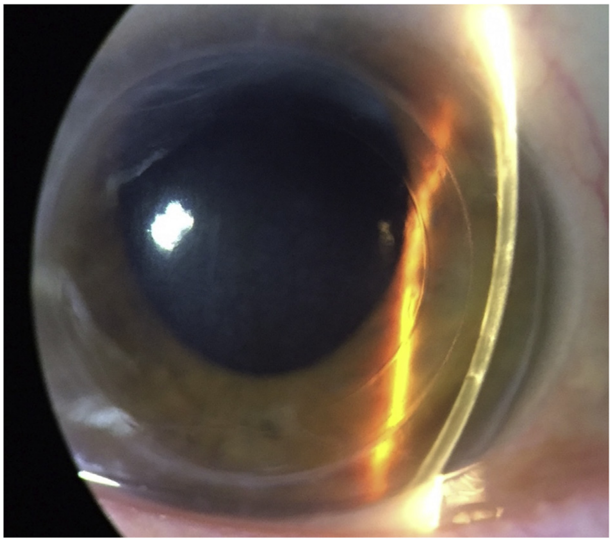

FIGURE 1. Postoperative slit-lamp photograph of a patient with a femtosecond Descemet membrane endothelial keratoplasty (DMEK) graft performed under a failed penetrating keratoplasty (PK), showing a fully attached DMEK graft and a compact cornea. The larger-diameter circle represents the PK graft edge, and the smaller-diameter circle represents the femtosecond descemetorrhexis and DMEK graft diameters.

TABLE 2. Demographics and Baseline Data of the Femtosecond-Enabled and Manual Descemet Membrane Endothelial Keratoplasty Groups

	F-DMEK (N = 10)	M-DMEK (N = 29)	*P* Value
Age (years)	61.3 ±14.7	65.5 ± 18.2	.342
Sex – male	70.0%	51.7%	.412
Laterality – right	30.0%	62.1%	.229
Presence of filtering bleb or GDD	10.0%	31.0%	.406
Presence of visual comorbidities	0%	34.5%	.040
Lens status			
Pseudophakic	60.0%	82.8%	.393
Phakic	40.0%	17.2%	
Indication for PK			
Previous graft failure	10.0%	51.7%	.037
Keratoconus	50.0%	17.2%	.053
Fuchs dystrophy	20.0%	3.4%	–
Scarred ulcer	10.0%	3.4%	–
Chemical burn	10.0%	–	–
Trauma	–	6.9%	–
Pseudophakic bullous keratopathy	–	3.4%	–
Stromal dystrophy	–	3.4%	–
Herpetic scar	–	3.4%	–
Unknown	–	6.9%	–
Number of previous PKs	1.3 ± 0.7	1.6 ± 0.7	.226
Time between PK and DMEK (years)	16.2 ± 10.8	11.0 ± 7.9	.211

DMEK = Descemet membrane endothelial keratoplasty; F-DMEK = femtosecond-enabled Descemet membrane endothelial keratoplasty; GDD = glaucoma drainage device; M-DMEK = manual Descemet membrane endothelial keratoplasty; PK = penetrating keratoplasty.

TABLE 3. Presence of Factors That May Influence Detachment in Eyes That Had a Significant Detachment and Eyes That Did Not Have a Significant Detachment

	Eyes With Significant Detachment (N = 20)	Eyes With No Significant Detachment (N = 19)	*P* Value
F-DMEK surgery	5.0%	47.4%	.003
Presence of filtering bleb or GDD	45.0%	26.3%	.320
Presence of visual comorbidities	40.0%	26.3%	.501
Main surgeon – clinical fellow			
Corneal surgeon	80.0%	74.2%	.412
Cornea fellow supervised by corneal surgeon	20.0%	25.8%	
Ratio of DMEK and PK diameter (n = 35)[a]			
DMEK > PK (DMEK oversized)	58.8%	61.0%	.991
DMEK < PK (DMEK undersized)	17.7%	16.7%	
DMEK = PK (DMEK same-sized)	23.5%	22.2%	
Indication for PK (n = 37)[b]			
Previous graft failure	47.4%	38.9%	.700
Keratoconus	21.0%	33.3%	
Other	31.6%	27.8%	
Donor age (years)	65.8 ± 5.6	62.3 ± 5.8	.819

DMEK = Descemet membrane endothelial keratoplasty; F-DMEK = femtosecond-enabled Descemet membrane endothelial keratoplasty; GDD = glaucoma drainage device; PK = penetrating keratoplasty.

[a]Data on diameter of PK were unavailable in 4 eyes.

[b]Data on indication for PK were unavailable in 2 eyes.

• **GRAFT DETACHMENT, REBUBBLE, REJECTION, AND FAILURE:** Significant graft detachment that required either rebubbling or repeat keratoplasty was seen in 1 of 10 eyes (10.0%) in the F-DMEK group and in 19 of 29 eyes (65.5%) in the M-DMEK group (P = .003). In the F-DMEK group, the single eye that had significant detachment was rebubbled successfully, with complete attachment of the graft. In the M-DMEK group, 11 of 19 eyes with a significant detachment were rebubbled successfully, 6 of 19 eyes had unsuccessful rebubbling (persistent graft detachment or persistent corneal edema following rebubbling), and 2 of 19 eyes had total detachments precluding rebubble. The difference in rebubble rate between F-DMEK (1 of 10 eyes, 10.0%) and M-DMEK (17 of 29 eyes, 58.6%) was statistically significant (P = .011). A multivariable analysis ($r^2 = 0.357$) for significant graft detachment was performed to control for baseline variables that differed significantly between the F-DMEK and M-DMEK groups. Factors included presence of visual comorbidities, PK graft indication, and type of DMEK (F-DMEK/M-DMEK). The type of DMEK was found to be the only statistically significant factor independently associated with graft detachment (P = .008, odds ratio 0.340). Presence of visual comorbidities (P = .645) and PK graft indication (P = .797) were not significantly associated with graft detachment.

A comparison was also made between eyes that had significant detachment and eyes that did not have a significant detachment. The comparison included factors that may affect graft attachment, including type of DMEK surgery (either F-DMEK or M-DMEK), presence of a filtering bleb or a glaucoma drainage device, presence of visual comorbidities, ratio of DMEK graft diameter to PK diameter (DMEK > PK, DMEK < PK, or DMEK = PK), type of surgeon (either a corneal surgeon or a clinical fellow), surgical indication for the PK (previous graft failure, keratoconus, or "other"), and the age of the donor tissue (Table 3). The type of DMEK surgery was found to be the only factor that was significantly different between eyes with detachment and those without detachment, with the rate of eyes that underwent F-DMEK being 5.0% among eyes with a significant detachment vs 47.4% among eyes with no significant detachment (P = .003).

Primary failure was seen in 8 of 29 eyes (27.6%) in the M-DMEK group (6 eyes with unsuccessful rebubble and 2 eyes with total detachment) and in 0 of 10 eyes (0%) in the F-DMEK group (P = .086). Primary failures in the M-DMEK group were managed with repeat DMEK in 4 eyes, repeat PK in 3 eyes, and monitoring only in 1 eye owing to the patient's request not to perform repeat surgery.

Rejection rates in the F-DMEK and M-DMEK groups were 1 of 10 eyes (10.0%) and 2 of 29 eyes (6.9%), respectively (P = 1.000). Secondary failure rate was 0 of 10 eyes (0%) and 2 of 29 eyes (6.9%), respectively (P = 1.000).

• **VISUAL OUTCOME:** BSCVA prior to PK graft failure in the F-DMEK and M-DMEK groups was 0.58 ± 0.42 logMAR (Snellen equivalent ~20/75) and 0.46 ± 0.31 logMAR (Snellen equivalent ~20/60), respectively (P = .711 between the groups). Following PK graft failure, BSCVA worsened significantly to 1.32 ± 0.81 logMAR (P = .016, Snellen equivalent ~20/420) in F-DMEK and 0.97 ± 0.51 logMAR (P = .017, Snellen equivalent ~20/185) in M-DMEK (P = .503 between the groups). Postoperative BSCVA at 6 months improved significantly to 0.35 ± 0.13 logMAR (P = .003, Snellen equivalent ~20/45) in F-DMEK and 0.51 ± 0.35 logMAR (P = .004, Snellen equivalent ~20/65) in M-DMEK (P = .246 between the groups). Figure 2 summarizes BSCVA changes in both groups.

• **ENDOTHELIAL CELL DENSITY:** Mean donor preoperative EC density in the F-DMEK and M-DMEK groups were 2810 ± 210 and 2724 ± 194 cells/mm^2, respectively (P = .267). Cell-loss rates were 43.8% and 38.0% at 6 months, respectively. The cell loss difference of 5.8% between the groups was not statistically significant (P = .453).

DISCUSSION

CURRENT LITERATURE SHOWS THAT DMEK IS AN ESTABlished tool for management of PK graft endothelial failure. Nevertheless, rates of detachment and rebubbling in this setting remain high compared with primary DMEK. Recent reports show DMEK rebubbling rates to be between 26% and 100% in the setting of a failed PK.[3-7] Although these rates seem to be decreasing as we learn more about performing DMEK in this setting, they still remain higher than in primary DMEK. Increased detachment rates are potentially associated with increased primary failure rates.[7] Although performed frequently, rebubbling should still be considered an intraocular procedure and is not

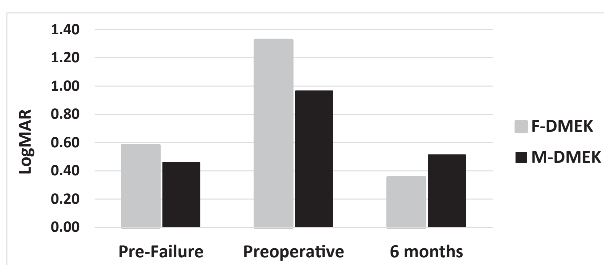

FIGURE 2. Mean best spectacle-corrected visual acuity in logMAR before graft failure, preoperatively, and 6 months postoperatively. F-DMEK = femtosecond Descemet membrane endothelial keratoplasty; M-DMEK = manual Descemet membrane endothelial keratoplasty.

without risks and discomfort. For these reasons, the aim is to minimize detachment and rebubble rates.

In this study, rates of significant detachment were substantially low in F-DMEK compared with M-DMEK, and in fact, to the best of our knowledge, the 10% detachment rate seen in the F-DMEK group is the lowest reported detachment rate to date in DMEK performed under a failed PK. Even when analyzing all variables that can potentially affect graft attachment, F-DMEK was the only independent factor significantly associated with graft attachment in our cohort. Primary failure rate was 0% in F-DMEK and 27.6% in M-DMEK. Although primary failure rate difference between the groups was not statistically significant ($P = .086$), this trend should be further studied in larger cohorts.

The reduced F-DMEK detachment and rebubble rates found in this study are consistent with reduced F-DMEK detachment and rebubble rates found in Fuchs dystrophy patients.[9,15] The reason for the reduced detachment rates in F-DMEK is unclear. One suggested mechanism is that F-DMEK enables complete removal of the host's Descemet membrane within the descemetorrhexis area, with less remnant Descemet tags and islands, owing to the precise and deep ring cut performed by the femtosecond laser. In addition to a potential reduction in the number of Descemet remnants inside the descemetorrhexis area, the clean nontraumatic incision performed by the laser also does not disturb Descemet which lies peripheral to the femtosecond incision. A DMEK graft can occasionally overlap host Descemet. Many times, this overlap is seen with no detachment of the graft. We believe that an important factor determining if host Descemet located under a DMEK graft will influence adherence is whether it was lifted off the stroma during Descemet scoring, becoming a spatial interference. The femtosecond incision constitutes a barrier that prevents disturbance of host Descemet located beyond the incision. This may reduce manipulation of host Descemet adjacent to the descemetorrhexis area and reduce spatial interference at the border of host Descemet. Since descemetorrhexis size in eyes with a PK graft is limited by the PK graft-host junction, often there is significant overlap between the DMEK graft and host Descemet. The majority of the eyes in each of our study groups had a DMEK graft larger than the PK graft, which signifies a significant overlap. Pasari and associates have shown that oversizing the DMEK in failed PK cases increases the detachment rate.[16] In our study, the F-DMEK group had a low detachment rate despite the fact that 70% of the eyes had DMEK/PK oversizing. This may indicate that evenness of the descemetorrhexis with less host Descemet that is disturbed and lifted off the surface may be an important factor in DMEK adherence under a PK graft. Another possible mechanism for reduced detachment could be femtosecond-induced inflammation, which may promote tissue adherence. Future studies on anatomy and histology of F-DMEK and M-DMEK could provide more insight into these topics.

Postoperative BSCVA did not differ significantly between F-DMEK and M-DMEK, and both were effective in restoring PK functionality (in eyes that did not have primary graft failure). Six-month EC loss rates (43.8% in F-DMEK and 38.0% in M-DMEK) were comparable to similar cohorts (of DMEK under failed PK) in published literature (6-month EC loss ranging between 31% and 41%).[7,16,17] This also seems comparable to previously reported 6-month EC loss in primary DMEK, averaging at 33% (range, 25%-47%).[18] F-DMEK performed in Fuchs dystrophy patients was found to have reduced EC loss compared with M-DMEK.[15] This was not apparent in our cohort of failed PK patients. We believe that the main causes for the reduced EC loss following F-DMEK in Fuchs dystrophy patients are the fact that F-DMEK descemetorrhexis diameter can be same-sized with DMEK graft diameter owing to F-DMEK's reduced postoperative detachment rates, and also the fact that there is no excess removal of host Descemet membrane in F-DMEK (as happens occasionally with manual descemetorrhexis that accidentally "runs out" more peripherally). These facts reduce excess removal of host Descemet and endothelium, thereby preserving more host endothelium and reducing the bare stromal area that needs to be repopulated by ECs. In failed PK patients, however, descemetorrhexis size is limited by PK graft size, and excess removal of Descemet beyond the graft-host junction is less likely. Therefore, the abovementioned advantages of F-DMEK do no manifest themselves.

One eye in the F-DMEK group had glaucoma and a glaucoma drainage device. The F-DMEK procedure in this patient was uneventful, with no issues surrounding femtosecond suction ring placement and maintenance of suction during femtosecond activation. Nevertheless, special attention should be given to glaucoma patients undergoing a femtosecond procedure such as F-DMEK. The first consideration is for potential suction ring placement issues owing to mechanical interference by either a filtering bleb, tube, valve, or irregular conjunctiva. The second consideration is for potential mechanical bleb damage caused by the suction ring. Third, although published literature showed no short-term effects of femtosecond-related intraocular pressure spikes in glaucoma patients,[19,20] it may still be recommended to have a low threshold for conversion to M-DMEK in such patients, to avoid damage from repeat femtosecond suction ring placement attempts.

The degree of corneal opacity affects visibility of the anterior chamber and could influence ease of surgery. An opaque cornea could, for example, lead to a prolonged graft unfolding time, which could affect the surgical outcome. Owing to the retrospective nature of the study, we could not specifically adjust the analysis for the degree of corneal opacity. However, the choice between F-DMEK and M-DMEK was random, as it was dependent on the availability of a femtosecond technician on the day of surgery. This will have reduced procedure choice bias relating to preoperative corneal opacity. Another factor that may potentially affect graft adherence in DMEK performed under a PK graft is the original relationship between the PK graft and host cornea diameters. Greater oversizing of the original PK graft might have produced a steeper posterior corneal surface, which could make DMEK graft attachment more difficult to achieve.

Performing multiple PKs can increase the irregularity of the posterior corneal surface, either owing to manipulation of an old PK graft-host junction or by addition of a new PK graft-host junction at a different location. Increased irregularity of the posterior corneal surface can interfere with DMEK graft adherence. Therefore, the number of previous PKs performed per eye is a factor that should be considered when comparing cohorts of DMEK performed under a previous PK. In our study, the number of PKs performed per eye did not differ significantly between the F-DMEK and M-DMEK groups (Table 2). Although the rate of failed graft PK indication differed significantly between the F-DMEK (10.0%) and M-DMEK (51.7%) groups, it was not found in our analysis to be an independent factor associated with graft detachment. Future prospective trials in larger cohorts could provide more insight into these topics.

This study is limited by its retrospective nature and cohort sizes. Nevertheless, to the best of our knowledge, it is the first study comparing F-DMEK and M-DMEK in eyes with a failed PK.

In conclusion, F-DMEK is a safe and effective procedure in failed PK patients, with outcomes comparable to M-DMEK, and with reduced detachment and rebubble rates. A trend toward reduced primary failure in F-DMEK should be further studied.

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