Four-Year Survival Comparison of Endothelial Keratoplasty Techniques in Patients With Previous Glaucoma Surgery

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Purpose: To compare 4-year survival outcomes of Descemet membrane endothelial keratoplasty (DMEK) and Descemet-stripping automated endothelial keratoplasty (DSAEK) in eyes with previous glaucoma surgery.

Methods: This is a retrospective, comparative case series, including patients with previous trabeculectomy or glaucoma drainage device implantation, who later underwent either DMEK (n = 48) or DSAEK (n = 41). Follow-up was limited to 12 to 60 months to prevent bias. Primary outcomes were graft survival and rejection. Secondary outcomes were best spectacle-corrected visual acuity (BSCVA), detachment/rebubble, endothelial cell loss, and intraocular pressure elevations.

Results: Baseline characteristics, follow-up duration, and preexisting glaucoma parameters did not differ significantly between the groups. Graft survival probability after DMEK and DSAEK was 75% and 75% at 1 year, 63% and 50% at 2 years, 49% and 44% at 3 years, 28% and 33% at 4 years, and 28% and 29% at 5 years, respectively (P = 0.899 between the groups). Graft rejection rates were 20.8% and 19.5%, respectively (P = 1.000). Primary failure, rebubbling, endothelial cell loss, and intraocular pressure elevation did not differ significantly between the groups. Preoperative BSCVA did not differ between the groups (P = 0.821). Postoperative BSCVA was significantly better in the DMEK group at 6, 12, and 24 months ($P < 0.001$, $P = 0.022$, and $P = 0.047$, respectively). In a multivariable model ($R^2 = 0.576$), the type of surgery was the only significant factor affecting postoperative BSCVA, in favor of DMEK (coefficient value −0.518, $P = 0.002$).

Conclusions: In eyes with previous glaucoma surgery, DMEK and DSAEK had comparably low survival and comparably high rejection rates. Postoperative visual acuity might be better after DMEK in this setting.

Key Words: DMEK, DSAEK, Descemet membrane endothelial keratoplasty, Descemet-stripping automated endothelial keratoplasty, survival, glaucoma drainage device, GDD, trabeculectomy, tube

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Endothelial keratoplasty is the preferred treatment for corneal endothelial cell (EC) failure. In the setting of previous glaucoma surgery, the procedure is more challenging to perform because of altered anterior chamber anatomy and difficulty maintaining air tamponade.[1] Both Descemet membrane endothelial keratoplasty (DMEK) and Descemet-stripping automated endothelial keratoplasty (DSAEK) have been shown to have good early outcomes in the setting of previous glaucoma surgery.[2–5]

However, in the longer-term, high rates of secondary failure and rejection have been found after both DMEK and DSAEK performed in this setting.[6–9] Secondary failure might be linked to increased rejection rates, direct EC loss caused by the presence of a glaucoma drainage device (GDD), or a chronic breakdown of the blood–aqueous barrier after glaucoma surgery.[10]

Lin et al[2] have compared early outcomes of both techniques in patients with previous glaucoma surgery and found that DMEK offered faster visual recovery, better final visual acuity, and a lower rate of secondary graft failure compared with DSAEK over the first postoperative year. Because the risk for graft rejection and secondary failure is cumulative, a head-to-head comparison between the 2 techniques over the longer term can demonstrate whether they differ in rejection and survival. The purpose of this study was to compare 4-year outcomes of DMEK and DSAEK in eyes with previous glaucoma surgery, with emphasis on graft survival and rejection rates.

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METHODS

A retrospective chart review was performed for all eyes with a history of trabeculectomy and/or GDD implantation, which later underwent DMEK or DSAEK between 2007 and 2018 at Toronto Western Hospital and the Kensington Eye Institute (Toronto, Ontario, Canada) and had at least 12 months of follow-up. Patients who developed graft failure before 12 months of follow-up were also included in the study to prevent bias. Of 824 endothelial keratoplasties performed between 2007 and 2018 (DMEK: 526 procedures, DSAEK: 298 procedures), 89 eyes of 85 patients with previous glaucoma surgery were included (DMEK n = 48, DSAEK n = 41). All patients underwent surgery by a single corneal surgeon (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 adhered to the tenets of the Declaration of Helsinki. Because DSAEK has been in use for a longer period than DMEK and because follow-up length can affect survival parameters, we limited recorded follow-up of both groups to 60 months to prevent bias relating to longer follow-up in patients who underwent DSAEK.

Surgical Technique

All donor tissue used was stored in corneal storage solution (Optisol; Bausch & Lomb, Rochester, NY) and received from the Eye Bank of Canada, Ontario division. Donor characteristics of both groups are detailed in Table 1.

Descemet Membrane Endothelial Keratoplasty

Grafts were prepared as previously described.[11] Graft preparation was performed according to the modified Melles technique using an "F" marking through a scleral window.[12] Our DMEK technique has been described previously.[13] In brief, descemetorhexis size was marked on the cornea, and 2 limbal paracenteses were performed at 2 and 10 o'clock. A temporal 2.4-mm clear corneal incision was performed. An anterior chamber maintainer was inserted inferotemporally into the anterior chamber. In previously vitrectomized eyes, a pars plana infusion was used to better control anterior chamber depth.[14] A descemetorhexis was created using a reverse Sinskey hook under balanced salt solution (BSS) infusion, followed by removal of the recipient Descemet membrane. Vision Blue (D.O.R.C., Zuidland, Netherlands) was injected into the anterior chamber to ensure complete removal of Descemet membrane remnants. The graft was loaded into either a glass pipette (Geuder AG, Heidelberg, Germany) or an intraocular lens injector (Monarch D; Alcon Labs Inc, Fort Worth, TX) and injected into the anterior chamber through the clear corneal incision. The anterior chamber infusion was turned on and off as needed to keep the anterior chamber shallow but was removed after injection of the donor tissue into the anterior chamber. Tapping technique

TABLE 1. Donor Parameters, Baseline Recipient Characteristics, and Preexisting Glaucoma Parameters of the DMEK and DSAEK Groups

	DMEK (n = 48)	DSAEK (n = 41)	*P*
Donor parameters			
Donor age (yr)	66.1 ± 4.8	62.0 ± 9.4	0.048
Graft diameter (mm)	8.3 ± 0.3	8.3 ± 0.4	0.851
EC density (cells/mm^2)	2814 ± 252	2676± 258	0.073
Baseline recipient characteristics			
Recipient age (yr)	66.1 ± 4.8	62.0 ± 9.4	0.592
Sex: man	37.5%	48.8%	0.390
Laterality: right	47.9%	53.7%	0.672
Type of previous glaucoma surgery			
GDD	62.5%	61.0%	1.000
No GDD (trabeculectomy only)	37.5%	39.0%	
Lens status			
Pseudophakic	83.3%	80.5%	0.569
Phakic	10.4%	7.3%	
Aphakic	6.3%	12.2%	
Indication			
Pseudophakic bullous keratopathy	56.3%	58.5%	0.976
Previous graft failure (PKP or EK)	33.3% (PKP 18.7%, EK 14.6%)	31.7% (PKP 19.5%, EK 12.2%)	
Other (FED and ICE)	10.4%	9.8%	
Postoperative follow-up (mo)	30.0 ± 15.5	33.9 ± 22.5	0.892
Preexisting glaucoma			
Cup-to-disc ratio	0.81 ± 0.19	0.75 ± 0.19	0.211
Preoperative IOP (mm Hg)	13.0 ± 4.4	14.2 ± 5.7	0.394
No. of glaucoma medications	1.5 ± 1.6	1.5 ± 1.4	0.808

FED, Fuchs endothelial dystrophy; ICE, iridocorneal endothelial syndrome; PKP, penetrating keratoplasty.

was used to unfold and position the graft,[15] and the anterior chamber was then filled with air. BSS was injected into the anterior chamber between the air bubble and the iris to reduce the air bubble size up to a diameter slightly larger than that of the graft.

Descemet-Stripping Automated Endothelial Keratoplasty

DSAEK lenticule was prepared immediately before transplantation as previously described.[16] In brief, the donor disc was cut with the Moria ALTK microkeratome system equipped with a 300 or 350-μm head and associated artificial anterior chamber (Moria, Antony, France). After dissection and punch with a corneal trephine, the donor disc was placed on either a Busin glide or a Macaluso inserter. Descemetorhexis and removal of host Descemet membrane was performed using a reverse Sinskey hook, followed by insertion of the new donor disc into the anterior chamber using either a suture pull-through or forceps-assisted technique.[17] The anterior chamber was filled with air for 10 minutes, and then, part of the air was removed and replaced with BSS.

No peripheral iridectomies were performed. Cyclopentolate hydrochloride 1% (MINIMS Cyc 1.0; Chauvin Pharmaceuticals Ltd, United Kingdom) and phenylephrine hydrochloride 2.5% (MINIMS PHNL 2.5; Chauvin Pharmaceuticals Ltd) were instilled to prevent pupillary block. All patients remained supine for 2 hours and were then instructed to remain so as much as possible at home until the next morning. All patients were examined at 2 hours and at 1 day after surgery. Three patients in DMEK group and 1 patient in DSAEK group required air release because of either elevated intraocular pressure (IOP) or a total anterior chamber air fill. All eyes underwent pressure patching overnight. 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 1 week. Then, the antibiotic-steroid drops were discontinued and 0.1% dexamethasone sodium phosphate (Maxidex; Alcon Labs Inc) eye drops were tapered down from 4 times daily to once daily over a 3-month period and continued once daily thereafter for a prolonged period of time. Hypotensive drops were maintained as preoperatively and changed according to clinical indication. Patients were examined at 1 week, 1 month, quarterly for the first postoperative year, semiannually for the second postoperative year, and annually thereafter.

Significant graft detachment was defined as any total or partial separation of the graft from the host cornea, which required either rebubbling or repeat keratoplasty. Rebubbling was performed within 24 hours in eyes with detachment of more than one third of the DMEK graft area or in eyes with a significant DSAEK separation if no air bubble was left in the anterior chamber. Rebubbling was also performed later on if there was unresolved 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 (OptoVue, Fremont, CA) was performed to determine whether there was graft detachment. Primary graft failure was defined as persistent, nonclearing corneal edema 2 months after surgery. Secondary graft failure was defined as corneal decompensation after an initially functional graft. Endothelial graft rejection was defined as the presence of inflammation as evidenced by anterior chamber cells, keratic precipitates or endothelial rejection line, and/or the presence of corneal edema with conjunctival injection and symptoms of pain or light sensitivity.

Study Outcomes

Primary outcomes included graft survival and graft rejection rates. Secondary outcomes included rates of detachment/rebubble, visual acuity, EC loss, and the rate and management of IOP elevations.

Data Collection and Statistical Analysis

The data collected in this study included patient demographics, best spectacle-corrected visual acuity (BSCVA), associated operative procedures (including details on timing and indication for glaucoma surgeries), IOP, number of hypotensive ocular medications, intraoperative and postoperative complications, corneal donor characteristics, and EC density using a noncontact specular microscope (Robo, KSS 300; Konan Medical, Hyogo, Japan).

In eyes where graft failure occurred, follow-up data were included up to the point of graft failure. Data after graft failure were not included in EC loss and BSCVA analyses. Data were also recorded on the management of failed grafts. Because of the high failure rates, EC loss and BSCVA data sufficient for analysis were available up to 36-month follow-up only. Comparison of visual acuity between DMEK and DSAEK was performed for eyes that had no visually significant comorbidities (such as age-related macular degeneration, cystoid macular edema, end-stage glaucoma, optic atrophy, history of retinal detachment, amblyopia, stromal scarring, and irregular astigmatism). There were a total of 22 of 48 DMEK eyes (46%) and 18 of 41 DSAEK eyes (44%) with visually significant comorbidities ($P = 1.000$ between the groups).

Data were recorded in Microsoft Excel (2016) and analyzed using XLSTAT (version 2020.3.1). Continuous paired variables were compared using either Wilcoxon nonparametric test or paired t test. Continuous nonpaired variables were compared using either Mann–Whitney U test or independent t test. Categorical variables were analyzed using Fisher exact test. Graft survival was analyzed using Kaplan–Meier survival analysis and was compared between groups using log-rank test. Graft survival was compared between the DMEK and DSAEK groups and between eyes with and without a GDD. Univariate analysis was performed to evaluate factors affecting postoperative BSCVA (at 6 mo) using either Pearson correlation or Kruskal–Wallis test for continuous or categorical variables, respectively. Factors included were patients' age, sex, laterality, lens status, cup-to-disc ratio, presence of a GDD, indication for surgery, donor age, graft diameter, date of surgery, type of surgery (DMEK or DSAEK), preoperative BSCVA, preoperative EC density, and the occurrence of significant detachment postoperatively. Factors that were found to be significant or were borderline

TABLE 2. Simultaneous Procedures Performed in Combination With Keratoplasty

	DMEK (n = 48)	DSAEK (n = 41)	*P*
Tube trimming	7 (15%)	7 (17%)	0.778
Synechiolysis	5 (10%)	2 (5%)	0.445
Cataract extraction	5 (10%)	3 (7%)	0.721
IOL exchange and/or fixation	5 (10%)	4 (10%)	1.000

IOL, intraocular lens.

significant on univariate analysis were included in a multivariable model using analysis of covariance to evaluate their independent association with postoperative BSCVA. Because 4 variables were included in the model, the threshold for statistical significance in the model was calculated using Bonferroni adjustment to a *P* value of 0.0125 (=0.05/4). In all other tests, the threshold for statistical significance was defined as a *P* value <0.05.

RESULTS

Eighty-nine eyes of 85 patients (37 men, 48 women) aged 67.5 ± 17.1 years (range 18–94 yrs) were included, with 48 eyes in the DMEK group and 41 eyes in the DSAEK group. The mean follow-up time was 30.0 ± 15.5 months in the DMEK group and 33.9 ± 22.5 months in the DSAEK group ($P = 0.892$). The mean follow-up time excluding 53 eyes with graft failure was 34.2 ± 14.4 months in the DMEK group and 39.5 ± 24.3 months in the DSAEK group ($P = 0.748$). Baseline characteristics of both groups are summarized in Table 1. There were no significant differences between the groups in age, sex, laterality, type of previous glaucoma surgery, lens status, and the indication for endothelial keratoplasty. The main indications for surgery in the DMEK and DSAEK groups were pseudophakic bullous keratopathy (56.3% and 58.5%, respectively), followed by previous graft failure (33.3% and 31.7%, respectively).

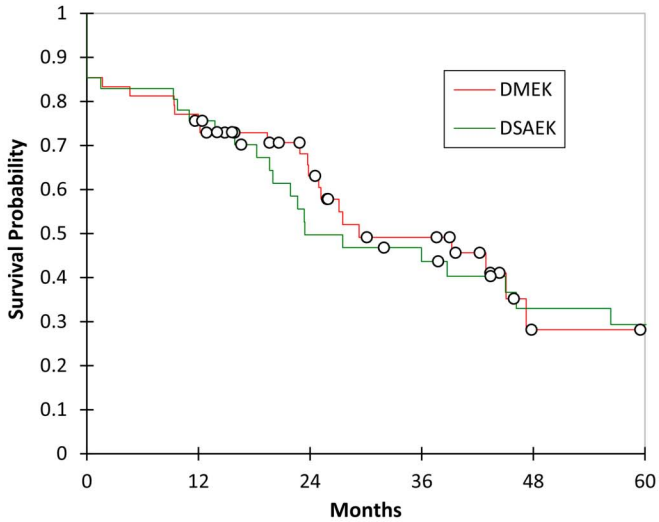
There were no significant differences between the groups in preexisting glaucoma parameters such as cup-to-disc ratio, preoperative IOP, and the number of glaucoma medications (Table 1) and in the rate of simultaneous procedures performed in combination with keratoplasty (Table 2).

Graft Survival and Rejection

Cumulative graft survival probability after DMEK and DSAEK was 75% and 75% at 1 year, 63% and 50% at 2 years, 49% and 44% at 3 years, 28% and 33% at 4 years, and 28% and 29% at 5 years (Fig. 1). Overall, survival probability did not differ significantly between DMEK and DSAEK ($P = 0.899$). The mean survival time was 33.7 ± 3.7 months after DMEK and 35.3 ± 4.5 months after DSAEK.

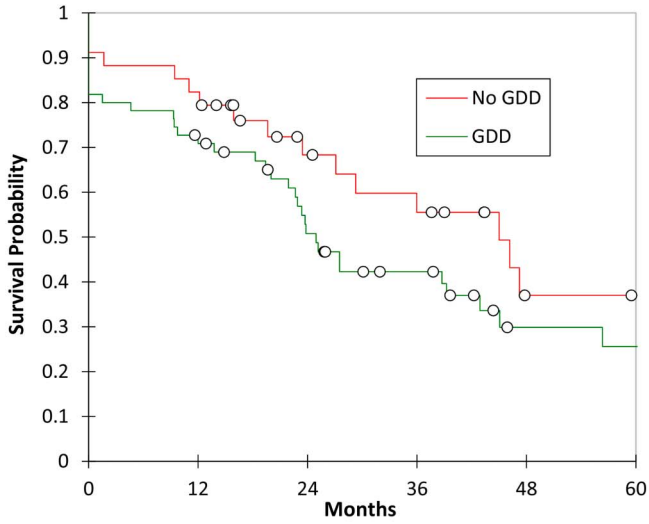
When comparing eyes with a GDD (n = 55) and eyes without a GDD (n = 34), cumulative graft survival probability was 71% and 82% at 1 year, 51% and 68% at 2 years, 42% and 55% at 3 years, 30% and 37% at 4 years, and 26% and 37% at 5 years (Fig. 2). Overall, survival probability did not differ significantly between the groups ($P = 0.193$).

Primary failure occurred in 7 eyes in the DMEK group (14.6%) and 6 eyes in the DSAEK group (14.6%, $P = 1.000$). All primary failure cases were related to graft detachment except for 1 case in the DMEK group and 2 cases in the



Cumulative survival probability	Time (Months)	12	24	36	48	60	
	DMEK (n at risk)	75% (37)	63% (26)	49% (17)	28% (4)	28% (3)	P=0.899
	DSAEK (n at risk)	75% (31)	50% (18)	44% (15)	33% (10)	29% (9)	

FIGURE 1. Kaplan–Meier survival curve demonstrating the cumulative survival probability of DMEK grafts compared with DSAEK grafts in eyes with previous glaucoma surgery. Circles represent censored observations. (The full color version of this figure is available at www.corneajrnl.com.)



	Time (Months)	12	24	36	48	60	
Cumulative survival probability	No GDD (n at risk)	82% (29)	68% (18)	55% (14)	37% (6)	37% (5)	P=0.193
	GDD (n at risk)	71% (39)	51% (26)	42% (18)	30% (8)	26% (7)	

FIGURE 2. Kaplan–Meier survival curve demonstrating the cumulative survival probability of endothelial grafts in eyes with a GDD (n = 55) compared with eyes without a GDD (n = 34). Circles represent censored observations. (The full color version of this figure is available at www.corneajrnl.com.)

DSAEK group, which had persistent corneal edema despite an attached graft. All primary failures were managed with repeat keratoplasty except for 1 case in the DMEK group and 2 cases in the DSAEK group, where no further intervention was performed in accordance with patients' requests. When comparing eyes with a GDD and eyes without a GDD, primary failure rates were 18.2% (10 of 55 eyes) and 8.8% (3 of 34 eyes, $P = 0.355$), respectively.

Graft rejection occurred in 10 eyes in the DMEK group (20.8%) and 8 eyes in the DSAEK group (19.5%, $P = 1.000$). Topical antirejection steroidal treatment was tapered down (either dose reduction or change to a less potent steroid) shortly before appearance of rejection symptoms in 7 of 10 eyes (70.0%) and 3 of 8 eyes (37.5%) in the DMEK and DSAEK groups, respectively. Six DMEK grafts (60%) and 5 DSAEK grafts (63%) failed after rejection. When comparing eyes with a GDD and eyes without a GDD, rejection rates were 21.8% (12 of 55 eyes) and 17.6% (6 of 34 eyes, $P = 0.788$), respectively.

Graft Detachment and Rebubbling

Significant graft detachment (defined as any total or partial separation of the graft from the host cornea, which required either rebubbling or repeat keratoplasty) occurred in 15 eyes in the DMEK group (31.2%) and 9 eyes in the DSAEK group (22.0%, $P = 0.349$). Rebubbling was required in 12 eyes (25.0%) and 8 eyes (19.5%, $P = 0.615$) in the DMEK and DSAEK groups, respectively. When comparing eyes with and without a GDD, significant detachment was seen in 16 of 55 eyes with a GDD (29.1%) and in 8 of 34 eyes with no GDD (23.5%, $P = 0.630$).

Visual Acuity

Preoperative BSCVA in the DMEK and DSAEK groups was 1.88 ± 0.92 logMAR (Snellen equivalent ~20/1500) and 1.79 ± 0.89 logMAR (Snellen equivalent ~20/1200), respectively ($P = 0.610$). Preoperative BSCVA excluding eyes with visually significant comorbidities was 1.57 ± 0.78 logMAR (Snellen equivalent ~20/740) and 1.67 ± 0.88 logMAR (Snellen equivalent ~20/930), respectively ($P = 0.821$). There was no significant difference between the groups in the number of eyes with visually significant comorbidities (DMEK, n = 22; DSAEK, n = 18; $P = 1.000$). Postoperative BSCVA was significantly better in the DMEK group at 6, 12, and 24 months ($P < 0.001$, $P = 0.022$, and $P = 0.047$, respectively) (Fig. 3).

Because of the difference found between the 2 groups in postoperative BSCVA, a univariate analysis was performed to evaluate factors that might have influenced postoperative BSCVA (at 6 months). These included patients' age, sex, laterality, lens status, cup-to-disc ratio, presence of a GDD, indication for surgery, donor age, graft diameter, date of surgery, type of surgery (DMEK or DSAEK), preoperative BSCVA, preoperative EC density, and the occurrence of a significant detachment postoperatively. Of those, a statistically significant or borderline significant association was found for the type of surgery (DMEK vs. DSAEK, $P = 0.001$), donor age ($r = -0.470$, $P = 0.015$), preoperative BSCVA ($r = 0.299$, $P = 0.072$), and the presence of a GDD ($P = 0.089$). In a multivariable model ($R^2 = 0.576$), the type of surgery was the only factor remaining significant, with DMEK associated with better postoperative BSCVA (coefficient value −0.518, $P = 0.002$).

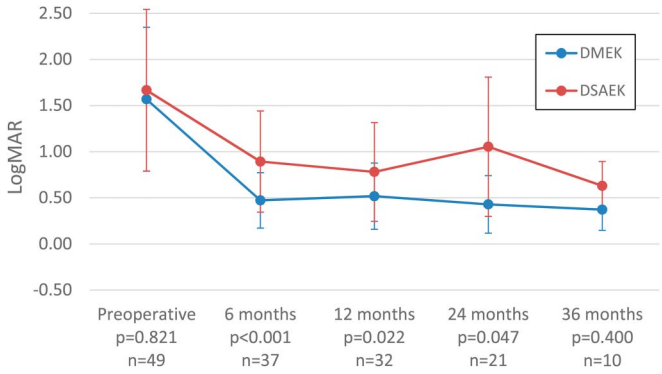


FIGURE 3. Mean logMAR BSCVA of eyes with no visually significant comorbidities in the DMEK group (n = 26) and DSAEK group (n = 23). *P* values represent comparison between the DMEK and DSAEK groups. (The full color version of this figure is available at www.corneajrnl.com.)

EC Loss

Mean donor EC densities of the DMEK and DSAEK groups were 2814 ± 252 cells/mm^2 and 2676 ± 258 cells/mm^2, respectively (P = 0.073). Cell loss rates of both groups were 48% and 53% at 12 months (P = 0.595), 55% and 60% at 24 months (P = 0.535), and 57% and 50% at 36 months (P = 0.886), respectively (Fig. 4).

Intraocular Pressure

A total of 7 of 48 DMEK eyes (14.6%) and 5 of 41 DSAEK eyes (17.1%) had IOP elevation during follow-up (elevated IOP range 22–45 mm Hg, P = 0.768 between the groups). These cases were managed medically in 5 eyes and surgically in 3 eyes. In 4 eyes, no further intervention was performed due to either patient request (2 eyes) or a blind glaucomatous eye (2 eyes).

DISCUSSION

Recent literature reports high secondary failure rates of DMEK grafts in patients with previous glaucoma surgery. Bonnet et al found 4-year secondary failure probability of 42% in this setting, which is lower than 73% reported by our group but is still considered very high compared with failure rates after standard DMEK such as in DMEK performed in virgin eyes with Fuchs dystrophy (where secondary 4-yr failure rates could be as low as 0%).[6,7] In DSAEK performed in the same setting, graft survival at 3 to 5 years has been reported in the literature to range between 25% and 69%.[8,9] Previous glaucoma surgery has been reported to be a significant independent risk factor for Descemet-stripping endothelial keratoplasty graft failure.[8] Because of the reduced reported survival of both techniques in eyes with previous glaucoma surgery, this study aimed at comparing 4-year survival outcomes of DMEK and DSAEK in such eyes to ascertain whether one technique has superior survival. The results show a comparably low graft survival probability after both techniques, reaching 28% and 33%, respectively, at 4 years.

Graft survival in the setting of previous glaucoma surgery might initially be affected by greater intraoperative challenges because of altered anterior chamber anatomy, presence of a GDD, and difficulty maintaining gas tamponade. This might be reflected in elevated early EC loss, as reported by Bonnet et al in their study, which showed increased EC loss in eyes with previous glaucoma surgery after DMEK (~55% EC loss at 1 yr) compared with DMEK performed in glaucomatous eyes that did not undergo previous glaucoma surgery and DMEK performed in nonglaucomatous eyes (~40% EC loss at 1 yr for both control groups). This is comparable with the 1-year EC loss found in this study for both DMEK (48%) and DSAEK (53%). Beyond the early postoperative period, graft survival in eyes with previous glaucoma surgery might be consistently affected by ongoing EC loss attributed to either the presence of a GDD or chronic endothelial toxicity relating to breakdown of the blood–aqueous barrier after any glaucoma surgery.[10] Our group has reported high EC loss after DMEK in eyes with previous glaucoma surgery, which was 12% to 22% higher over 4 years of follow-up compared with a control group of eyes with Fuchs dystrophy undergoing DMEK.[6] This might reflect the ongoing EC damage leading to high secondary failure in eyes with previous glaucoma surgery. Patients and physicians should be cognizant of the apparent high likelihood of graft

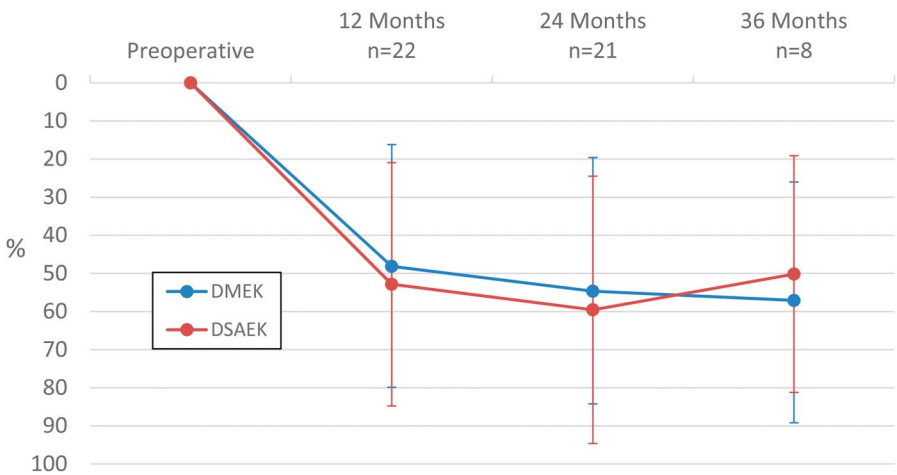


FIGURE 4. EC loss rates after DMEK and DSAEK in eyes with previous glaucoma surgery. Eyes with failed grafts were not included in the analysis beyond the failure point. The n value refers to the total number of eyes from both groups that had available EC counts at each timepoint. (The full color version of this figure is available at www.corneajrnl.com.)

failure after both endothelial keratoplasty techniques performed in this setting.

Four-year rejection rates of 16% to 20% for DMEK and 5-year rejection rates of 9% to 13% for DSAEK have been reported in eyes with previous glaucoma surgery.[6–9] This study found similar rejection rates of 21% after DMEK and 20% after DSAEK, which are much higher than rejection rates reported in standard DMEK and DSAEK.[18,19] Eyes with previous glaucoma surgery that undergo endothelial keratoplasty might be more challenging to manage postoperatively for rejection prophylaxis. On one hand, they seem more prone to graft rejection, possibly because of a chronic subclinical inflammation induced by glaucoma surgery and breakdown of the blood–aqueous barrier, indicating the need for more aggressive antirejection treatment. On the other hand, these eyes are at higher risk for steroid response and have reduced nerve fiber layer reserves, which might limit steroid use in fear of worsening glaucomatous damage.[20] In this study, steroid response rates were 15% and 17% after DMEK and DSAEK, respectively ($P = 0.768$), which are not higher than expected for any patient on long-term steroidal treatment.[20] It should also be noted that a significant portion of rejection episodes occurred shortly after a steroid taper (either dose reduction or a change to a less potent steroid). Therefore, we believe that a change in postoperative management can be considered in those patients. Future studies may determine whether a slower steroid taper, addition of steroid sparing agents such as tacrolimus or cyclosporine A, and reduction in the use of pro-inflammatory glaucoma medications such as prostaglandins, could bring rejection rates down.

One previous publication comparing early outcomes of DMEK and DSAEK in patients with previous glaucoma surgery found that DMEK offered better visual acuity during the first postoperative year.[2] In this study, we identified a similar trend toward better postoperative visual acuity in the DMEK group over the first 2 years postoperatively. Because of the significantly better visual acuity found in DMEK, we performed a univariate analysis on multiple factors that can potentially affect postoperative visual acuity and constructed a multivariable model based on univariate results. The analysis found that the type of endothelial keratoplasty performed was the only significant factor affecting postoperative visual acuity, with DMEK associated with better postoperative visual acuity. Although DMEK is known to produce better visual outcome than DSAEK in noncomplex eyes, its visual advantage in more complex eyes is still a subject of some debate.[21–23] The findings of this study support early findings of the study by Lin et al regarding visual advantage of DMEK over DSAEK in the setting of previous glaucoma surgery and should be further validated prospectively.

Although there was no statistically significant graft survival difference between eyes with and without a GDD, the survival curves (Fig. 2) suggest a trend toward reduced endothelial graft survival in eyes with a GDD. Larger-scale studies could provide more insight and potentially help corneal surgeons determine what is expected after transplantation in eyes with different types of previous glaucoma procedures. Such information might even guide glaucoma surgeons in their decision making regarding which glaucoma procedure would be most appropriate for a patient with uncontrolled glaucoma and concomitant endothelial dysfunction.

This study has several limitations, first of which is its retrospective nature. In addition, due to high failure rates and missing observations, available sample size for visual acuity and EC loss analyses beyond 3 years was limited. Nevertheless, this is the first study to compare 4-year survival outcomes of DMEK and DSAEK in eyes with previous glaucoma surgery and to compare visual outcomes of the 2 techniques in this setting beyond the first postoperative year.

In conclusion, in eyes with previous glaucoma surgery, DMEK and DSAEK had comparably low survival and comparably high rejection rates. Postoperative visual acuity might be better after DMEK in this setting.

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