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Descemet Membrane Endothelial Keratoplasty versus Descemet Stripping Automated Endothelial Keratoplasty in Complicated Vitrectomized Eyes

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ABSTRACT

Purpose: Vitrectomized eyes pose a technical challenge when performing endothelial keratoplasty (EK). The aim of the study was to compare outcomes of Descemet membrane endothelial keratoplasty (DMEK) and Descemet stripping automated endothelial keratoplasty (DSAEK) in complex eyes undergoing pars plana vitrectomy (PPV) prior to or during surgery.

Methods: This retrospective study included consecutive eyes that underwent pars plana infusion-assisted DMEK or pull-through DSAEK which underwent PPV prior to or during the EK at a tertiary center. Included were eyes with at least 1-year follow-up. The main outcome measures were best-corrected visual acuity (BCVA) and serious adverse events.

Results: Fifty-two eyes (n = 52) with a mean follow-up time of 24.6 ± 7.4 months were included. Both groups were similar in terms of baseline characteristics although the DMEK group had a significantly larger proportion of Fuchs' patients ($p = .009$). There was no significant difference in postoperative logMAR BCVA between groups at each visit ($p > .05$ for all). There was a significantly higher proportion of overall serious adverse events (50.0% versus 15.4%, $p = .02$), retinal detachments (19.2% versus 0.0%, $p = .05$) and cystoid macular edema (23.1% versus 0.0%, $p = .02$) following DMEK. Graft detachment occurred more often following DMEK (53.9% versus 11.5%, $p = .001$) with no significant difference in rebubbling rates (23.1% versus 11.5%, $p = .27$).

Conclusions: A significant and similar improvement in BCVA was achieved following DMEK and DSAEK in complex vitrectomized eyes. Patients should be advised regarding the higher rates of potential serious complications associated with a pars plana infusion DMEK in this situation.

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Introduction

Corneal endothelial decompensation is one of the leading indications for keratoplasty.[1,2] In the first world, the most popular procedures for the treatment of endothelial decompensation are currently Descemet membrane endothelial keratoplasty (DMEK) and Descemet stripping automated endothelial keratoplasty (DSAEK).[3] It has been reported that DMEK leads to superior visual outcomes and lower rejection rates when compared to DSAEK.[4]

Many studies comparing DSAEK and DMEK have included otherwise healthy eyes with the main indications being Fuchs' endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK).[3,4] Few studies have compared between the two techniques for more complex eyes. Recently, our group has reported on outcomes following previous PKP[5] and glaucoma surgery.[6] Additional situations where a DMEK may pose a technical challenge include limited visibility, aniridia, aphakia, high myopia and vitrectomized eyes.[7] The latter two situations are complex mostly because of the difficulty to shallow the anterior chamber in order to unfold the DMEK graft. The feasibility of DMEK and its long-term outcomes in vitrectomized eyes have previously been reported by us[8,9] and by others.[10–14]

Considering the complex nature of performing DMEK in vitrectomized eyes, it is of interest to assess and compare outcomes of DMEK versus DSAEK in such cases. To the best of our knowledge, no previous study has compared between these two procedures in vitrectomized eyes. Therefore, the purpose of the current study is to compare long-term outcomes of DMEK and DSAEK in complex vitrectomized eyes.

Methods

This study was conducted in compliance with the tenets of the Declaration of Helsinki and received Research Ethics Board approval from University Health Network (Toronto Western Hospital, Toronto, Canada). Data management application was not required, and all data were collected in an anonymized fashion.

Study participants

This is a retrospective study conducted by means of a chart review of consecutive eyes that underwent DMEK or DSAEK from January 2012 to December 2018 that underwent pars plana vitrectomy (PPV) prior to or during the endothelial

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keratoplasty. Only patients with at least 1 year of follow-up were included.

Data collection

Preoperative demographics that were recorded included gender, age at the time of surgery, and laterality. Additional preoperative data included the indication for surgery, concomitant eye conditions, preoperative lens status, and visual acuity. Operative data included donor endothelial cell density (ECD), graft size, combination procedures alongside the DMEK or DSAEK, status of the vitreous, and any intraoperative complications. Data from the postoperative period included best-corrected visual acuity (BCVA), ECD, the presence of graft detachment, need for rebubbling, rejection episodes, graft failures, and any other postoperative complications. Eyes with early graft failure were excluded from visual acuity analysis.

Surgical technique

Corneal donors

Corneal donors were provided by the Eye Bank of Canada, Ontario Division. All corneas were preserved in storage solution (Optisol; Bausch and Lomb, Rochester, NY). The corneal graft was prepared before the patient was brought into the operating room by the surgeon. All surgeries were performed by one of two experienced endothelial keratoplasty surgeons (n > 500). Surgeon #1 routinely performed DSAEK in vitrectomized eyes throughout the entire study period. Surgeon #2 routinely performed DSAEK from 2012 to 2014 and DMEK from 2014 to 2018 in vitrectomized eyes. None of these surgeries was performed in vitrectomized eyes while the surgeons were during their learning curve of the procedure (n > 100) and they both had over 5 years of experience with performing the procedure. In all cases, neuroleptic anesthesia was used and the use of intracameral, sub-tenon or retrobulbar anesthesia was at the discretion of the surgeon.

DMEK technique

A similar DMEK technique involving the use of pars plana infusion was routinely performed in all DMEK cases with either a history of vitrectomy or vitrectomy performed simultaneously with DMEK as previously published by us.[8,9] Briefly, Descemet membrane and endothelium were peeled using the modified Melles technique[15] with an "F" mark used for graft orientation applied through a stromal window (7.5- to 8.5--mm).[16,17] An iridectomy was not performed as our group has previously demonstrated satisfactory results in noniridectomized eyes.[18] A 23-gauge posterior infusion line was inserted into the vitreous via a trocar placed 3.0 mm from the limbus. Ink-marked calipers were used to mark the corneal diameter of the descemetorhexis. Descemetorhexis was performed under a cohesive viscoelastic with a reverse Sinskey hook. Vision Blue (D.O.R.C., Zuidland, The Netherlands) was used to ensure that no remnant Descemet tags remained in the eye. The DMEK graft was injected into the eye with the use of a glass pipette (Geuder AG, Heidelberg, Germany) or an intraocular lens (IOL) injector (Monarch D Cartridge, Alcon Inc.). The pars plana infusion was turned on and off with the foot pedal as needed to pressurize the eye and to encourage anterior chamber shallowing to facilitate graft unfolding and positioning. A tapping technique was used for unfolding. Once the graft was unrolled in the intended location, the pars plana infusion was stopped and the eye was filled with either air or SF6 (20%). Balanced salt solution was used to pressurize the eye as needed and to hydrate the wounds. The trocar was then removed from the eye and 10–0 nylon or 7–0 vicryl was used as needed for any leaking corneal incisions or sclerotomy sites, respectively (Ethicon Inc, Somerville, NJ).

DSAEK technique

A similar technique was performed in all DSAEK cases as previously published by us.[19] The DSAEK grafts were prepared using an artificial anterior chamber and a Moria ALTK microkeratome (Moria, Antony, France) using a 300 to 350-mm head. The partial thickness graft was then cut with a punch trephine (8- to 8.5-mm). A 4.0-mm limbal incision was created and Descemetorhexis performed in the same manner as in the DMEK surgery. The grafts were inserted into the eye using either a Macaluso or Busin glide under the continuous flow of an anterior chamber maintainer. After unfolding and centration of the graft the anterior chamber maintainer was removed, and a single 10–0 nylon suture was used to suture the main wound and any other leaking wounds. The anterior chamber was then completely filled with either air or SF6 (20%) for 10 minutes, and residual interface fluid was removed with surface sweeping. After 10 minutes, if necessary, some of the air was removed from the anterior chamber in order to avoid the pupillary block.

Perioperative treatment for DSAEK and DMEK

Phenylephrine hydrochloride 2.5% and cyclopentolate hydrochloride 1% (Minims; Chauvin Pharmaceuticals Ltd, United Kingdom) one drop each was instilled before patching. Patients remained in the supine position for 2 hours following surgery in the recovery unit. Patients were then examined at a slit lamp to ensure graft attachment and that the bubble was of adequate size. They were examined the following day and started on 0.1% dexamethasone sodium phosphate and 0.3% tobramycin (Tobradex; Alcon, Mississauga, ON, Canada) 4 times daily. This was discontinued at 1 week, and 0.1% dexamethasone sodium phosphate (Maxidex; Alcon) drops were tapered from 4 times daily to once daily over the course of 4 months or shorter if raises in intraocular pressure were noted and attributed to the treatment. Patients were instructed to remain in a supine position "as much as possible" over the first 3 days in both the DMEK and DSAEK groups.

Study outcomes

Primary outcomes included BCVA and serious adverse events. Secondary outcomes included rates of detachment and rebubbling. Serious adverse events included rhegmatogenous retinal detachment (RRD), cystoid macular edema (CME), graft failure and uncontrolled glaucoma requiring a glaucoma drainage device (GDD). A sub-analysis was performed on patients without significant visual comorbidities limiting potential for vision

such as severe amblyopia, end-stage glaucoma, prior retinal detachment, macular dystrophy, and macular edema.

Graft detachment

Rebubbling criteria were: (1) Descemet membrane detachment spanning >1/3 of the DMEK graft area, noted during the first postoperative day, with no bubble in the anterior chamber. (2) Unresolved Descemet membrane detachment with persistent corneal edema that either limited normal visual recovery or caused significant discomfort secondary to an abnormal ocular surface. (3) The area of detachment was inferred/estimated through slit-lamp examination and optical coherence tomography (Optovue, Optovue Inc., Fremont, CA, USA or Visante, Carl Zeiss Meditec, Jena, Germany) visualization. Automatic location and quantification of the detached area as demonstrated by Heslinga et al.[20] were not performed.

Statistical analysis

Data were analyzed with the Minitab Software, version 17 (Minitab Inc, State College, PA). For the analysis of continuous data Student's t-test was used for normally distributed variables and Kruskal–Wallis for non-parametric variables. For the analysis of categorical variables, Chi-Square or Fishers' exact test was used. Bonferroni adjustment was applied when comparing multiple groups. A two-sided P value <.05 was considered statistically significant. All presented means are accompanied by their respective standard deviations.

Results

Fifty-two eyes of 52 patients with a mean age of 71.5 ± 15.1 years (range 30–90 years) of which 56% (n = 29) were of male gender were included in this study. The mean follow-up time was 24.6 ± 7.4 months (range 12–48 months). All patients were consecutive, and none were lost to follow-up.

Baseline characteristics of both groups

Table 1 depicts a comparison between eyes that underwent DMEK versus DSAEK. There were no significant differences between both groups in terms of age, gender, preoperative BCVA, visually significant comorbidities, preoperative lens status, proportion of complicated anterior segments, donor age, whether or not they were combined with an IOL exchange or suturing, and whether they underwent a pars plana vitrectomy before or during endothelial keratoplasty. The DMEK group had a significantly larger proportion of FED patients (23.1% versus 0.0%, p = .009) and used SF6 gas for endotamponade in a larger proportion of cases (46.2% versus 7.7%, p = .002).

Table 1. Comparison of baseline variables between the DMEK and DSAEK groups.

Parameter	DMEK (n = 26)	DSAEK (n = 26)	*P-Value
Age (years)	73.4 ± 14.7	69.7 ± 15.6	0.38
Gender (%male)	57.7%	53.9%	0.78
Eye (%right)	42.3%	50.0%	0.58
Preoperative BCVA (logMAR)	1.71 ± 0.96	1.78 ± 0.63	0.77
Visual comorbidities	61.5%	57.7%	0.78
Indication			0.03
%Fuchs	23.1%	0%	0.009
%PBK	57.7%	76.9%	0.14
%Failed PKP	3.8%	15.4%	0.16
%Failed EK	15.4%	7.7%	0.39
Lens status			0.99
%Pseudophakia	76.9%	84.6%	0.48
%Phakia	3.9%	0.0%	1.00
%Aphakia	19.2%	15.4%	0.71
%Overall complicated anterior segment	50.0%	73.1%	0.09
%Glaucoma drainage device	23.1%	15.4%	0.48
%ACIOL	7.7%	26.9%	0.07
%PAS	7.7%	11.5%	0.64
%aphakia	11.5%	15.4%	0.69
%subluxated IOL	11.5%	15.4%	0.69
%aniridia	3.9%	7.7%	0.55
Prior PPV	50.0%	73.1%	0.09
Combined w IOL exchange or sutured IOL	30.8%	15.4%	0.19
Endotamponade (%SF6)	46.2%	7.7%	0.002

BCVA: best-corrected visual acuity, PBK: pseudophakic bullous keratopathy, PKP: penetrating keratoplasty, EK: endothelial keratoplasty, ACIOL: anterior chamber intraocular lens, PAS: peripheral anterior synechia, IOL: intraocular lens, PPV: pars plana vitrectomy.
*Student t-test was used for continuous variables and chi-square for categorical variables.

Visual outcomes

Following endothelial keratoplasty, at 1 year, there was a significant improvement in the entire cohort logMAR BCVA (1.69 ± 0.72 to 1.05 ± 0.90, p < .001) and in eyes with no visual comorbidities (n = 21) as well (1.63 ± 0.75 to 0.65 ± 0.69, p < .001). When comparing the results of DMEK versus DSAEK, there was no significant difference in logMAR BCVA at 6 months, 1 year and 2 years following surgery in both the entire cohort (p > .05 for all) and in eyes with no visual comorbidities (p > .05 for all) (Table 2). When assessing the entire cohort, stratification according to indication for surgery showed that DMEK and DSAEK had similar preoperative and postoperative outcomes for eyes with PBK while eyes with previous failed grafts had better preoperative and postoperative vision in the DSAEK group (p < .05 for all) (Figure 1). Eyes with FED that underwent DMEK had a better preoperative and postoperative BCVA (compared to other groups) demonstrating a significant improvement from 0.84 ± 0.42 to 0.42 ± 0.27 (p = .03). For FED, no comparison could be made as there were no FED eyes in the DSAEK group. Similar findings and patterns were identified when assessing patients without significant visual comorbidities (Figure 2) with a better appreciated improvement in vision for all indications (p < .05 for all). Table 2 depicts a comparison of all other outcomes between the DMEK and DSAEK groups.

Graft detachment and rebubbling rates

Graft detachment occurred more often in the DMEK group (53.9% versus 11.5%, p = .001) with many DMEK graft detachments resolving spontaneously leading to no significant difference in rebubbling rates (23.1% versus 11.5%, p = .27). In both groups, there was a single case of persistent detachment despite rebubbling which led to primary graft failure.

Table 2. Comparison of outcomes between the DMEK and DSAEK groups.

Outcome	DMEK	DSAEK	*P-Value
Graft detachment			0.001
Attached	46.1%	88.5%	
%<1/3rd	38.5%	0.0%	
%>1/3rd	11.5%	0.0%	
Fully detached	3.9%	11.5%	
Rebubbling (%)	23.1%	11.5%	0.27
Rebubbling timing (days)	10.8 ± 11.2	5.3 ± 3.8	0.28
BCVA (logMAR)			
Entire cohort			
Six months	1.05 ± 0.92 (20/224)	1.13 ± 0.76 (20/270)	0.74
One year	1.05 ± 1.03 (20/224)	1.06 ± 0.79 (20/230)	0.96
Two years	1.25 ± 1.10 (20/356)	1.12 ± 0.84 (20/264)	0.68
No visual comorbidities			
Six months	0.65 ± 0.98 (20/89)	0.88 ± 0.42 (20/152)	0.91
One year	0.65 ± 0.97 (20/89)	0.65 ± 0.26 (20/89)	0.44
Two years	1.00 ± 1.04 (20/200)	0.58 ± 0.29 (20/76)	0.10
Follow-up time	23.4 ± 5.3	25.8 ± 9.1	0.27
Repeat keratoplasty performed	7.7%	7.7%	1.00

BCVA: best-corrected visual acuity.
*Student t-test was used for continuous variables and chi-square for categorical variables.

Serious adverse events

Overall, there was a significantly higher proportion of serious adverse events in the DMEK group (50.0% versus 15.4%, $p = .02$) (Table 3). Specifically, there was a significantly higher proportion of RRD in the DMEK group (19.2% versus 0.0%, $p = .05$) as well as diagnosed CME (23.1% versus 0.0%, $p = .02$). There was no significant difference in retinal detachment rates between eyes with prior PPV or eyes that had combined PPV and endothelial keratoplasty surgery (9.4% versus 10.0%, respectively, $p = .94$). Survival curves of graft failure over the study period are depicted in Figure 3.

Discussion

This study compared long-term outcomes of DMEK versus DSAEK in complex post-vitrectomy eyes. Both groups were comparable in terms of baseline characteristics with the exception of the DMEK group having a significantly larger proportion of FED patients (23.1% versus 0.0%, $p = .009$). At 6 months, 1 year and 2 years there were no significant differences in BCVA between the DMEK and DSAEK groups. Overall, there was a higher rate of serious complications in the DMEK group, specifically CME and RRD. To the best of our knowledge, this is the first study to report the results of DMEK versus DSAEK in complex vitrectomized eyes.

An overwhelming majority of studies comparing outcomes of DMEK and DSAEK have focused on Fuchs' endothelial dystrophy and pseudophakic bullous keratopathy as these are indeed the leading causes of endothelial decompensation and there seems to be a clear consensus that DMEK leads to superior visual outcomes in these cases.[3,4,21] A recent meta-analysis by Marques et al. reported that at 12 months BCVA was better with DMEK compared to DSAEK (0.16 logMAR versus 0.30 logMAR, $p < .001$) in patients diagnosed with Fuchs' endothelial dystrophy.[4] Few studies have compared visual outcomes in more complicated eyes. However, recent reports are beginning to shed light on these complex situations. Lin et al. reported that in complex eyes with prior glaucoma surgery, DMEK offered faster visual recovery with better final visual acuity.[6] Our group recently reported that eyes with endothelial

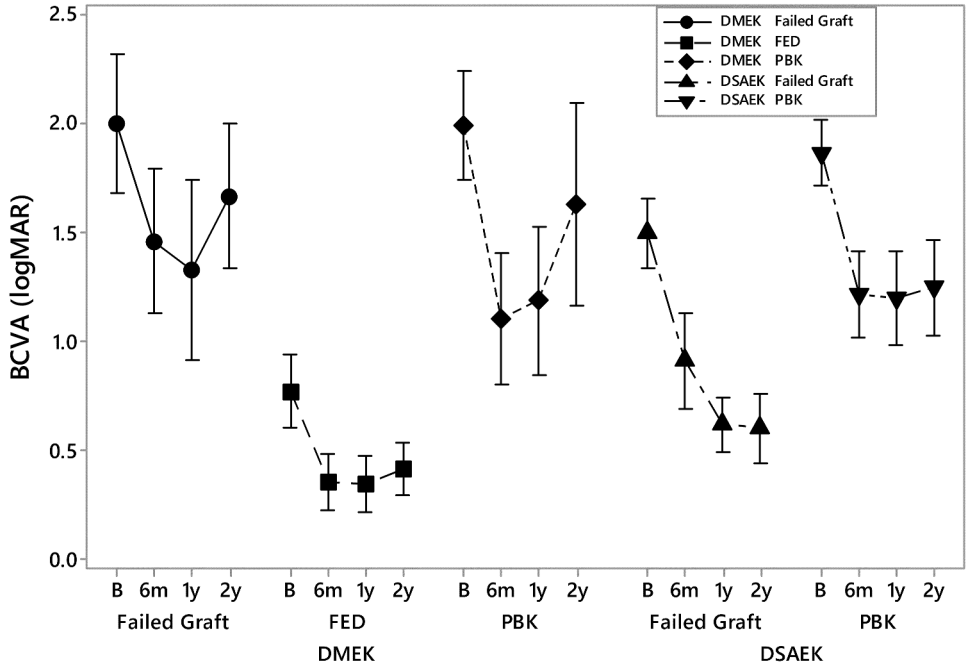

Figure 1. Entire cohort. Mean logMAR best spectacle-corrected visual acuity (BSCVA) at each visit stratified by indication for surgery (failed graft, Fuchs endothelial dystrophy (FED) or pseudophakic bullous keratopathy (PBK)) as well as type of surgery (DMEK or DSAEK). There were no cases of Fuchs in the DSAEK group. B: baseline, 6 m: 6 months, 1y: 1 year, 2y: 2 years, FED: Fuchs endothelial dystrophy, PBK: pseudophakic bullous keratopathy, BCVA: best-corrected visual acuity.

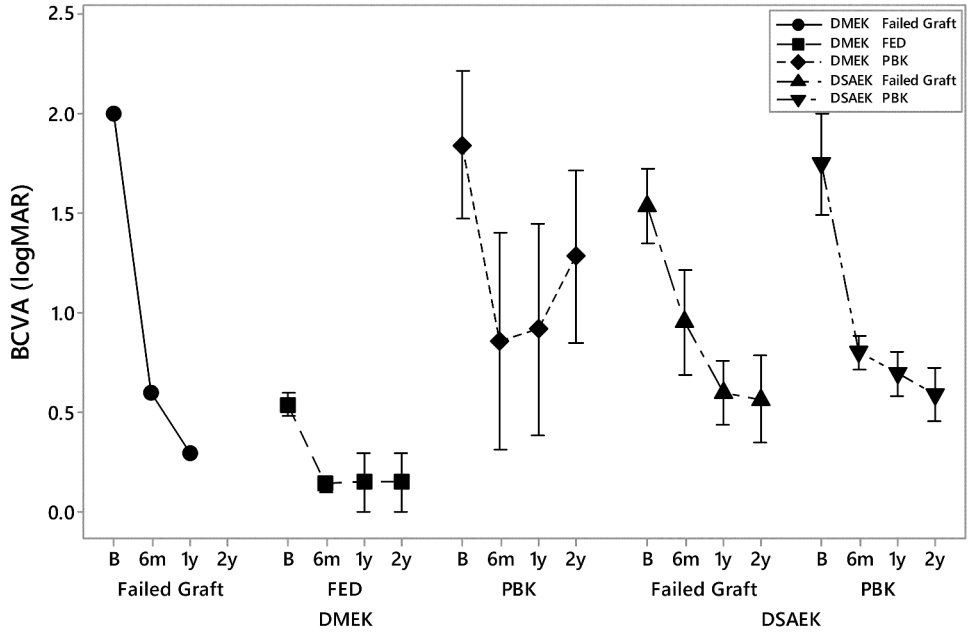

Figure 2. No visual comorbidities cohort. Mean logMAR best spectacle-corrected visual acuity (BSCVA) at each visit according to indication for surgery (failed endothelial keratoplasty (EK), failed penetrating keratoplasty (PKP), Fuchs or pseudophakic bullous keratopathy (PBK)) as well as type of surgery (DMEK or DSAEK). There were no cases of Fuchs in the DSAEK group. There was a significant improvement in visual acuity compared to baseline in both groups for all indications ($p < .05$ for all). B: baseline, 6 m: 6 months, 1y: 1 year, 2y: 2 years, FED: Fuchs endothelial dystrophy, PBK: pseudophakic bullous keratopathy, BCVA: best-corrected visual acuity.

Table 3. Comparison of complication rates between DMEK and DSAEK groups.

Serious Complication	DMEK	DSAEK	*P-value
Overall	50% (n = 13)	15% (n = 4)	0.02
Retinal detachment	19% (n = 5)	0% (n = 0)	0.05
CME	23% (n = 6)	0% (n = 0)	0.02
Graft failure	19% (n = 5)	12% (n = 3)	0.70
Glaucoma drainage device	15% (n = 4)	4% (n = 1)	0.35

CME: cystoid macular edema.
*Fisher's exact test.
Overall, there was a significantly higher proportion of serious adverse events in the DMEK group (50.0% versus 15.4%, $p = 0.02$).

decompensation in a previous PKP achieve better visual outcome with a DMEK than with a DSAEK.[5] In the current study, where both groups had a similar baseline visual acuity, there was no significant difference in BCVA at each follow-up visit although both groups did experience a significant improvement. The lack of an advantage of DMEK over DSAEK in vitrectomized eyes has several possible explanations with the most likely one being a lower visual potential in this group of patients.[13] Second, over half of the patients in both groups had complicated anterior segments rendering the centering and unfolding of a DMEK graft more complicated with more graft manipulation.[22–24] Indeed, significantly higher rates of diagnosed CME were observed in the DMEK group and a trend towards a higher rate of graft failures was identified in the DMEK group as well.

In the current study, there was a significantly higher proportion of serious adverse events in the DMEK group (50.0% versus 15.4%, $p = .008$). Specifically, there was a significantly higher proportion of RRD (19.2% versus 0.0%, $p = .02$) and diagnosed CME (23.1% versus 0.0%, $p = .009$). There were similar rates of RRD between eyes with prior PPV (9.4%) and those that had combined PPV (10.0%) and endothelial keratoplasty ($p = .94$). The higher proportion of RRD following DMEK may be explained in two possible ways. The first of which is the use of a pars plana infusion as was routinely performed in the current study as previously reported by our group.[8] We speculate that in some cases the pars plana infusion may have led to iatrogenic tears that ultimately lead to an RRD. An alternative explanation is that the centering and unfolding of a DMEK, especially in eyes with deep anterior chambers, may require more manipulation, shallowing and deepening of the AC and tapping when compared to straightforward cases.[9] It can also be speculated that in these complicated eyes with limited view, achieving a complete and thorough vitrectomy (whether prior to or during DMEK surgery) it is difficult to ensure. All of these may lead to more traction of the vitreous base which could lead to iatrogenic tears and RRD. Following the identification of higher retinal complications, some refinements have been made. Prior to surgery, we are more selective with choosing pars plana infusion DMEK over pull-through DSAEK. For instance, we no longer perform pars plana infusion DMEK in patients with aphakia or near-total\total aniridia.[25] Furthermore, we now put an emphasis on avoiding eyewall collapse as perhaps this led to the cannula of the infusion touching the peripheral retina and causing a tear. Last, any patient that undergoes pars plana infusion DMEK is dilated and monitored postoperatively to search for peripheral retinal tears.

A recent study by Inoda et al. reported CME in 15.6% of eyes undergoing DMEK and identified iris damage during the procedure as the single most important risk factor.[26] Others have reported similar or slightly lower rates of CME following DMEK.[27–30] We speculate that vitrectomized eyes with deep anterior chambers undergoing DMEK require additional manipulation and are therefore more likely to provoke pro-inflammatory markers and lead to subsequent CME. It may be

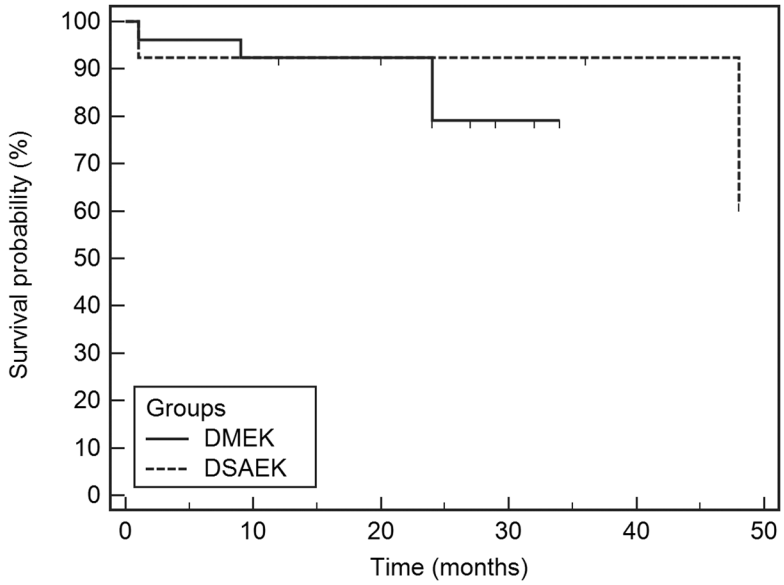

Figure 3. Kaplan-Meier survival curve demonstrating the cumulative survival rate of Descemet membrane endothelial keratoplasty and Descemet stripping automated endothelial keratoplasty grafts in vitrectomized eyes. Bars represent censored observations.

prudent to initiate a stricter prophylactic regimen in vitrectomized eyes undergoing DMEK as was reported by Hoerster et al.[29]

In the current study, graft detachment occurred more often in the DMEK group (53.9% versus 11.5%, p = .001). Despite 53.9% of the DMEK grafts experiencing some form of detachment, only 23.1% of them required rebubbling. This is supported by previous studies that have demonstrated that a majority of partial detachments undergo spontaneous adherence and corneal clearance.[31,32] A recent meta-analysis found that in eyes with Fuchs, rebubbling was 2.48 times more likely to occur following DMEK when compared to DSAEK[4] and although the current study assessed vitrectomized eyes, these eyes were also two times more likely to require rebubbling following DMEK when compared to DSAEK. Although a single rebubbling procedure does not increase the corneal densitometry, it has been shown that this results in significantly higher endothelial cell loss.[32]

There was no significant difference in failure rates between the DMEK and DSAEK groups (19.2% versus 11.5%, p = .44). When examining the two survival curves (Figure 2), they appear to be quite similar throughout the study period implying similar outcomes in this group of patients. This is supported by the findings of Price et al. who recently reported a 93% 5-year survival rate with DMEK and DSAEK in patients with Fuchs' endothelial dystrophy with no significant differences between the two procedures.[33] They reported that although DMEK had a significantly lower risk of immunologic rejection, rejection episodes rarely resulted in graft failure. It seems as though in vitrectomized eyes, graft failure rates are not significantly different, a fact that is encouraging consider the greater amount of graft manipulation required during DMEK in these eyes.

In the current study, the majority of eyes had visual comorbidities with 61.5% and 57.7% in the DMEK and DSAEK group, respectively. Furthermore, 50.0% of the DMEK group and 71.3% of the DSAEK group were classified as having a complicated anterior segment. As such, the findings of the study reflect the outcomes of complex vitrectomized eyes and could explain the relatively low improvement in vision in the entire cohort and the high complication rates in the DMEK group. Our group has reported high failure rates when performing DMEK in aphakic and\or aniridic eyes[25] and has since then abandoned this technique in this group of eyes. Similarly, we have reported higher failure and rejection rates in eyes with prior glaucoma surgery[34] and have since then been more aggressive with our perioperative topical immunosuppressive therapy. Refinements of DMEK are warranted in this group of complex vitrectomized eyes in order to improve outcomes. Furthermore, surgeons should weigh the advantages and disadvantages of DMEK and DSAEK in each case individually.

This study has several limitations. First of which is its retrospective nature that can lead to several biases one of which is a potential selection bias stemming from a tendency to turn to DSAEK for more complicated eyes and reserve DMEK for simpler cases. Unique to this retrospective study is that both groups were treated at the same facility with each group having all operations performed by the same surgeon and each surgeon performing their procedure of choice for vitrectomized eyes, thereby limiting the effect of a selection bias. In addition, the actual duration of surgery was not available to us, another metric that could have been of interest to compare. Furthermore, endothelial cell counts are not routinely performed in all patients and as such, limited data regarding cell counts were available. As all patients in the DMEK group underwent a pars plana infusion technique for unfolding the graft, the findings of this study may not apply to other unfolding techniques in vitrectomized eyes, where perhaps an infusion is unnecessary such as a pull-through tri-folded technique.[35] In addition, the heterogeneity in diagnosis of the groups and the relatively small number of patients in each subgroup entails a call for caution when

analysing the results. Furthermore, a multivariate analysis accounting for type of DMEK injector (lens cartridge versus glass), DSAEK glide (Busin versus Macaluso) and tamponade (SF6 versus air) could not be performed due to the cohort's characteristics. In addition, the DSAEK arm was not composed of ultra-thin grafts and therefore this study's findings do not apply to ultra or nano-thin DSAEK grafts. Furthermore, several outcomes were assessed in order to compare several outcomes between both groups which could have led to a type 1 error. Large multicentric prospective studies may be warranted, although when considering that vitrectomized eyes that are eligible for endothelial keratoplasty are heterogeneous and rare. Such a study might meet some patient recruitment challenges which could potentially be overcome in a multicentric study.

Nevertheless, this study, the first of its kind, reports a significant and similar improvement in BCVA following DMEK and DSAEK in vitrectomized eyes. The findings of this study reinforce those of a smaller study produced by our group where we reported high rates of complications following DMEK in vitrectomized eyes.[8] When performing endothelial keratoplasty in vitrectomized eyes, if a complete vitrectomy cannot be ensured, pars plana infusion should be avoided and a DMEK should be reconsidered. Furthermore, the added optical benefit of a DMEK may not be realized in eyes with limited visual potential, and added surgical manipulation is likely to increase the risk of serious complications rather than lead to better optical results.

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