Outcomes of Descemet Membrane Endothelial Keratoplasty in Aphakic and Aniridic Patients

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Purpose: To evaluate the outcomes of Descemet membrane endothelial keratoplasty (DMEK) in aphakic and aniridic eyes.

Methods: A retrospective chart review of either aphakic or aniridic patients who underwent DMEK at Toronto Western Hospital, Canada, between 2015 and 2019 was performed. Demographic characteristics, intraoperative and postoperative complications, and best corrected visual acuity (BCVA) were analyzed.

Results: Nine eyes of 9 patients, aged 51.0 ± 8.6 years, were included (3 aniridic, 5 aphakic, and 1 combined). The average follow-up was 15.7 ± 12.7 months. The best corrected visual acuities before surgery and 3 and 6 months after surgery were 1.28 ± 0.47, 1.33 ± 0.98, and 1.03 ± 0.56 LogMAR, respectively. Six eyes (67%) had graft detachment, with 3 of them larger than 30% of the graft area. One eye (11%) developed hyphema. The overall failure rate was 88% (8 of 9 eyes), meaning only one was viable at the last follow-up. Primary graft failure was seen in 4 eyes (44%) after detachment (n = 3) and intraoperative hyphema (n = 1). Secondary failure occurred in 4 eyes (44%) at 7, 12, 15, and 36 months. The secondary failure at 36 months was after rejection. Failures were managed with penetrating keratoplasty (n = 2), repeat DMEK (n = 3), Descemet stripping automated endothelial keratoplasty (n = 1), and observation because of poor vision potential (n = 2). Cumulative graft survival probabilities at 12 and 24 months were 44% and 17%, respectively.

Conclusions: Aniridic and aphakic patients experienced unacceptably high detachment and failure rates after DMEK. Before performing DMEK, the risks and benefits should be carefully weighed and perhaps other keratoplasty techniques should be used.

Key Words: DMEK, aphakia, aniridia

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Over the past few decades, corneal transplantation has evolved from full thickness grafts to lamellar grafts of decreasing thickness and increased safety. Descemet membrane endothelial keratoplasty (DMEK) has emerged as a preferred technique for endothelial pathologies of the cornea including Fuchs endothelial dystrophy and pseudophakic bullous keratopathy.[1] This technique offers a shorter recovery period, better visual acuity, and lower rejection rates, and thus, whenever appropriate, DMEK has become a standard of care in treatment of endothelial failure.[2–4]

However, the surgical technique of DMEK surgery makes it challenging both for novice and experienced surgeons, more so in certain scenarios where DMEK unfolding and handling is complex.[5] In aniridic and aphakic eyes, the posterior plane of the anterior chamber is partially or completely missing, rendering those eyes unicameral and thus a more challenging scenario for unfolding and attaching the graft.[6] The use of intracameral air tamponade (descematopexy) to apply pressure to the thin graft to the posterior stroma of the cornea may be less effective because the bubble behaves differently in unicameral eyes.[7] In addition, the thin endothelial graft used in DMEK could easily dislocate into the vitreous cavity because there is no physical barrier between the anterior and posterior segments.[7]

Owing to the complexity of DMEK in such cases, many surgeons favor Descemet stripping automated endothelial keratoplasty (DSAEK) or even penetrating keratoplasty in those eyes.[8,9] Some authors have also described combining transplants with intraocular lens (IOL) fixation to sclera with pupilloplasty or fixation of an artificial iris to the sulcus or to the sclera.[10] To the best of our knowledge, there are no published series on the outcomes of DMEK performed in this subset of patients. This study presents the outcomes of DMEK performed in eyes with aphakia or aniridia.

METHODS

A retrospective medical and surgical chart review (performed by 2 independent investigators) of aphakic or aniridic patients who underwent DMEK between 2015 and 2019 at Toronto Western Hospital was performed. This retrospective interventional case series received Research Ethics Board approval by the University Health Network (Toronto Western Hospital, Toronto, ON, Canada) and adhered to the principles of the tenets of the Declaration of Helsinki.

Demographics, best corrected visual acuity (BCVA), clinical characteristics, surgical complications, previous eye conditions, and postoperative follow-up data, including

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additional surgeries, were collected during the chart review. Data were recorded in Microsoft Excel (16.31, 2019 Microsoft). Graft survival was analyzed using the Kaplan–Meier survival analysis.

Surgical Technique

The Eye Bank of Canada, Ontario division, provided all of the donor tissues. These were stored in Optisol storage solution (Bausch and Lomb, Rochester, NY). Characterization of donor tissue is found in Table 1, The procedures were all performed by a single experienced corneal surgeon (D.S.R.), who had already performed more than 250 DMEK surgeries before attempting these complicated cases.

The DMEK graft preparation was performed as previously described.[1] The modified Melles technique was used for tissue preparation using a "F" marking through a scleral window.[11] For total or near total aniridia an anterior chamber maintainer was inserted through a corneal paracentesis. For cases with sufficient iris tissue, a pars plana infusion was inserted by using an inferotemporal 23-gauge trocar at a distance of 3.0 mm from the limbus and was then connected to a 23-gauge posterior infusion cannula. Infusion was adjusted and turned on and off according to anterior chamber depth. A temporal clear corneal incision was performed (2.4 mm). The diameter of the descemetorhexis was marked on the cornea. In addition, 2 paracenteses were performed at the 2 and 10 o'clock limbus positions. Ophthalmic viscosurgical device (OVD) was used in some cases to maintain anterior chamber space to allow for descemetorhexis using a reverse Sinskey hook. Otherwise, when possible, BSS infusion was used to maintain the chamber. Vision Blue (D.O.R.C., Zuidland, The Netherlands) was injected into the anterior chamber to ensure the complete removal of Descemet membrane anterior to the descemetorhexis. The size of the donor Descemet membrane was chosen according to recipient white-to-white measurements and was approximately 3 mm less than the horizontal white-to-white measurement. In an effort to improve success of DMEK in these unicameral eyes, the graft was loaded into an IOL cartridge intentionally rolled endothelial side in using a modified Busin technique[12] and pulled into the anterior chamber through the clear corneal incision using intraocular forceps (MST, Redmond, WA).[12] Infusion was turned on and off as needed to keep the vitreous cavity full. The graft was kept in place using the intraocular forceps until it unfolded over the flow from the anterior chamber maintainer or pars plana infusion. Unfolding of the graft was variable depending on the anterior segment condition of the patient, additional maneuvers to unfold the graft were needed: in some cases using a small air bubble under the graft to unfold the scroll while holding the edge of the graft with intraocular forceps and in other cases tapping and infusion helped the graft unfold while holding it with the intraocular forceps in the right orientation. Once the graft was opened, the posterior infusion was stopped, and the unicameral eye was then filled with SF6 20% as much as possible. Illustrations of the technique are found in Figure 1. Corneal wounds were sutured using 10-0 nylon if needed, and the sclerotomy site was sutured using 7-0 Vicryl (Ethicon Inc, Somerville, NJ), if it did not seal. Video illustration provided Supplemental Video 1 (see Supplemental Digital Content 1, http://links.lww.com/ICO/B35).

After each case, patients remained supine for 2 hours and then "as much as possible" at home until the next morning. Two hours after the procedure, patients were examined to ensure the correct positioning of the graft and the presence of the SF6 bubble. Eyes were kept patched over the first postoperative night. Day 1 postoperatively, patients were instructed to instill 0.1% dexamethasone sodium phosphate and 0.3% tobramycin antibiotic (Tobradex; Alcon, Mississauga, ON, Canada) eye drops 4 times daily for 1 week. After 1 week, the medication was changed to 0.1% dexamethasone sodium phosphate (Maxidex; Alcon) and was tapered down to once daily during a 3-month period. Patients were asked to remain supine as much as possible as long as the bubble was present.

TABLE 1. Donor Characteristics

	Mean ± SD
Donor age (yr)	67.4 ± 4.3
Time from death to preservation (h)	15.7 ± 8.0
Time from death to transplant (h)	168 ± 44
Endothelial cell density (cells/mm^2)	2744 ± 225

RESULTS

Nine eyes of 9 patients (5 men and 4 women), aged 53.1 ± 8.6 years, were included. Five of them were aphakic, 3 were aniridic (pseudophakic), and 1 was both aphakic and aniridic. Aphakia was secondary to cataract surgery for Marfan's Syndrome associated subluxated crystalline lens (n = 2), congenital cataract (n = 2), and juvenile rheumatoid arthritis associated to complicated cataract surgery (n = 1). All aniridic eyes (n = 3) had congenital aniridia secondary to Axenfeld Rieger Syndrome. The remaining eye was aphakic and aniridic secondary to aphakic bullous keratopathy after complicated cataract surgery.

Two eyes had intraoperative trimming of a preexisting glaucoma tube, and 1 eye had pupilloplasty and anterior vitrectomy performed at the time of surgery. One case had intraoperative anterior chamber bleeding. No grafts were lost during the procedure.

The average follow-up was 15.7 ± 12.7 months. The BCVAs before surgery, and 3 and 6 months after surgery were 1.28 ± 0.47, 1.33 ± 0.98, and 1.03 ± 0.56 LogMAR, respectively. Six eyes (67%) had graft detachment, with 3 of them being larger than 30% of the graft area. One eye (11%) developed hyphema. Primary graft failure was seen in 4 eyes (44%)—3 of those because of detachment and 1 because of intraoperative hyphema. Secondary failure occurred in 4 eyes (44%) at 7, 12, 15, and 36 months. The secondary failure at 36 months was after rejection. Two failures were managed with penetrating keratoplasty, 1 with DSAEK and 3 with repeat DMEK. Only 1 graft was viable at the last follow-up, and his endothelial cell counts 6 months postoperative was 1362 cell per square millimeter. The remaining 2 were observed because of poor vision potential. A Kaplan–Meier survival analysis showed

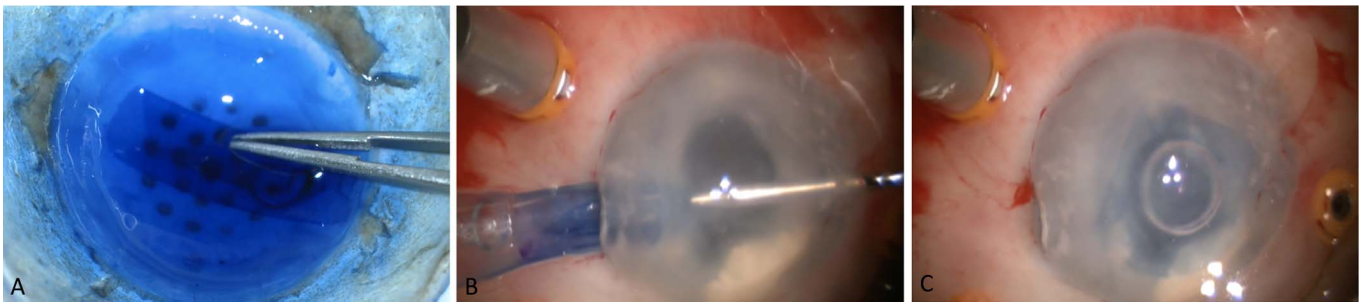

FIGURE 1. Intentional folding of the graft endothelium side in modified Busin technique (A). Graft loaded on intraocular lens cartridge being inserted with intraocular forceps (B). Unfolding of the graft using an air bubble below the graft holding it against the posterior stroma (C).

cumulative graft survival probability at 12 and 24 months to be 33% and 17%, respectively (Fig. 2).

Postoperative complications included corneal ulcer in 1 eye and retinal detachment in 2 eyes. Two eyes had rejection episodes of rejection at 6 and 12 months postoperatively. The intraocular pressures of the patients after surgery are stated in Table 2. Briefly, there were no cases of uncontrolled ocular hypertension; however, there were 3 cases of immediate postoperative hypotony (intraocular pressure ≤ 5 mm Hg). Patient #3 had transient hypotony which resolved at the 1-week visit and their graft survived for 36 months. Patients #4 and #9 had persistent hypotony and their grafts did not survive beyond 1 month.

DISCUSSION

This study evaluated the outcomes of DMEK performed in aphakic and aniridic patients. We speculate that because of the bigger challenges, these cases pose for the DMEK surgeon, a series of this size, to the best of our knowledge, have not been published before. The main challenge encountered in these eyes is the absence or reduced stability of the iridolenticular diaphragm that supports both the DMEK graft during unfolding and the gas bubble that keeps the graft in place and ensures its attachment to the recipient corneal stroma.[6]

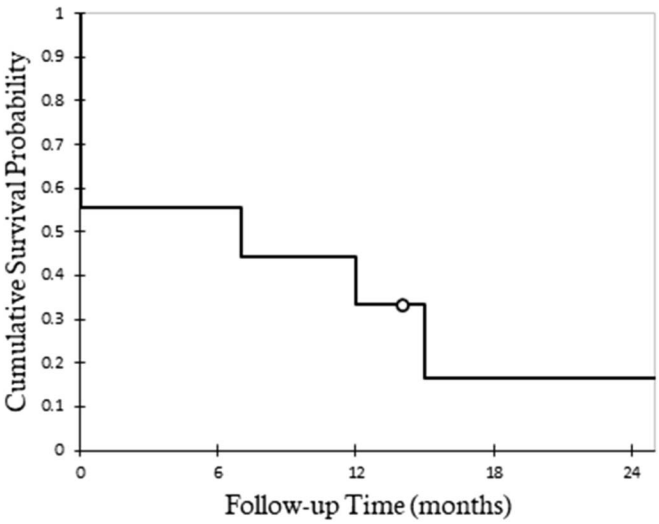

FIGURE 2. Kaplan–Meier survival curve showing the cumulative survival rate of Descemet membrane endothelial keratoplasty grafts in aphakic and aniridic eyes. Circles represent censored observations. Cumulative graft survival probability at 12 and 24 months was 33% and 17%, respectively.

Weller et al[10] described outcomes of DMEK in 24 eyes with complex anterior segments, included 2 eyes with aphakia. However, both aphakic eyes in that study underwent IOL exchange several months before DMEK. Therefore, the iridolenticular diaphragm in those eyes had been restored before the DMEK procedure. Interestingly, the only DMEK graft in our series that was viable on the last follow-up (14 months postoperatively) was in an eye that had IOL implantation and fixation performed simultaneously with DMEK. Therefore, this eye may have behaved as a bicameral eye, helping to keep the gas bubble to more efficiently tamponade the graft. All the other cases that remained unicameral postoperatively, developed either primary or secondary graft failure. This could suggest that simultaneous or previous IOL insertion in those cases may improve outcomes, although larger numbers would be necessary to substantiate this concept. Indeed, a recent study has shown that DMEK can be successfully performed in eyes with scleral- and iris-fixated lenses.[13]

Previous literature describes the use of DSAEK in complex eyes, including aphakic and aniridic eyes, with good outcomes.[8,9] However, even with DSAEK, preventing the graft from migrating into the vitreous cavity is challenging.[14] This difficulty can be managed using safety sutures,[8,9] and even wheel-spoke sutures.[15] Multiple approaches to suture-assisted DSAEK have been reported, highlighting the difficulty aphakic and aniridic eyes present for the corneal surgeon.[8,16] Unfortunately, a technique for suture-assisted insertion of DMEK grafts has yet to be developed.

All of the surgeries in our cohort were performed by an experienced DMEK surgeon (D.S.R.). Although there were no cases of intraoperative graft loss and only 1 significant intraoperative complication (1 case of intraoperative bleeding), the survival rate of our grafts was suboptimal. For instance, one of the main risks that predisposes DMEK grafts to primary failure is the upside-down placement of the graft. However, we did not have any grafts upside down because the correct orientation in all of the grafts was confirmed using a previously validated marking technique.[11] This is likely because of using a modified-trifolded Busin technique[12] that allows the graft to

TABLE 2. Table Showing IOP of Patients in Postoperative Visits

Patient	IOP day 1	IOP 1 wk	IOP 1 mo
1	19	9	11
2	15	14	16
3	5	18	20
4	5	0	0
5	16	10	15
6	12	12	16
7	14	19	23
8	18	6	8
9	0	2	5

unfold over the flow of BSS from an anterior chamber maintainer or pars plana infusion. An additional benefit of this pull-through technique is that it reduces the risk of tissue dislocation into the posterior segment of these unicameral eyes.[12] Although manipulating the graft into endothelium side in configuration could have partially damaged the endothelium and therefore contribute to graft failure, previous studies have indicated that this is unlikely[17,18] and injecting the graft would have been a relatively risky maneuver and this is why it was avoided. Postoperative hospitalization was not considered at the time of surgery and this should be considered if future attempts were to be performed. A similar technique has been previously described in DSAEK[8,9] because DSAEK grafts can also be lost in the posterior cavity. Owing to similar challenges faced in vitrectomized eyes, the procedures were performed in conjunction with a posterior pars plana infusion that has been described to facilitate DMEK under these circumstances.[19]

Our cohort of aphakic and aniridic eyes had very high detachment and failure rates, compared with DMEK performed in other scenarios.[20,21] Despite its multiple advantages, DMEK performed in this subset of patients presents great challenges and is not the most suitable technique, at least not with the current techniques used. Three of the cases had postoperative hypotony at day 1, 2 of which had persistent hypotony, and in those cases, the graft did not survive beyond 1 month. It has been previously reported that hypotony may be associated with higher detachment and failure rates after endothelial keratoplasty.[22,23] One alternative could be to treat in a stepwise approach, restoring the iridolenticular diaphragm using a fixated IOL with or without an iris implant.[24] This approach would decrease the risks of the unicameral status of the eye at the time of transplantation, facilitating the manipulation of the graft in the anterior chamber. Perhaps new innovations in technique will assist in accomplishing greater DMEK success in such challenging cases.

Donor corneas are a precious resource worldwide. In fact, a recent survey globally quantified the shortage of corneal graft tissue and concluded that there was only 1 cornea available for every 70 needed worldwide.[25] Hence, considering that when performing an aniridic/aphakic DMEK, the chances of success beyond 1 year are suboptimal/poor, we believe that the use of this limited resource may be unfair toward the patient, the donor and their family, and the health care system. As such, our group has reverted back to DSAEK in these extremely complex eyes and advise others to consider the same.

This study is limited by its retrospective nature and cohort size. In addition, because of the high rate of early failures, there were insufficient data available on endothelial cell counts. Nevertheless, it is, to the best of our knowledge, the first series describing the outcomes of DMEK in eyes with aphakia and aniridia. The high failure rate described may pose a barrier to performing prospective studies of this nature. Larger group samples could be studied retrospectively, if available, to add further information on this topic.

In conclusion, aniridic and aphakic patients experience high detachment and failure rates after DMEK. Other keratoplasty techniques, such as DSAEK, are advisable in these circumstances.

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