Advances in endothelial keratoplasty

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Chapter 5

Clinical Outcomes of Descemet Membrane Endothelial Keratoplasty in Eyes with a Glaucoma Drainage Device

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ABSTRACT

Purpose: To evaluate the feasibility and clinical outcomes of Descemet membrane endothelial keratoplasty (DMEK) in eyes with a glaucoma drainage device (GDD).

Design: Retrospective, interventional case series.

Methods: Clinical outcomes of 23 DMEK procedures for bullous keratopathy (52%), failed previous transplant (39%) or Fuchs endothelial corneal dystrophy (9%) in 20 eyes (19 patients) with a GDD were retrospectively analyzed at two tertiary referral centers. Main outcome measures were best-corrected visual acuity (BCVA), endothelial cell density (ECD), postoperative complications, and graft survival.

Results: Mean length of postoperative follow-up after DMEK was 19 (±17) months. Kaplan-Meier survival analysis showed a 89% cumulative graft success rate at 1 year postoperatively. At 1 year postoperative (n=15), BCVA improved by ≥2 Snellen lines in 11 eyes (73%) and remained stable in 4 eyes (27%). Donor ECD decreased by 37% (n=14), 60% (n=11) and 71% (n=11) at 1, 6 and 12 months postoperatively, respectively. Postoperative complications up to two years postoperatively, comprised pupillary block in 1 eye successfully reversed by partial air removal, visually significant graft detachment requiring re-bubbling in 5 eyes (22%), allograft rejection successfully reversed with topical steroids in 2 eyes (9%), secondary graft failure in 2 eyes (9%) and cataract in one of 3 phakic eyes (33%). Re-keratoplasty was required in 2 eyes (9%).

Conclusions: With specific surgical modifications, DMEK provided acceptable clinical outcomes when taking the complexity of these eyes into account. However, presence of a GDD may reduce graft survival times and may pose a risk for more frequent re-grafting.

INTRODUCTION

Shifting paradigms in the field of corneal transplantation have led to an evolution in the management of corneal endothelial dysfunction in eyes with coexisting glaucoma and a glaucoma drainage device (GDD). With the introduction of Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK), penetrating keratoplasty (PK) has been replaced as the standard of care not only for endothelial disorders in general, but also for glaucomatous eyes with a GDD.[1-4]

Glaucomatous eyes may pose a challenge for corneal surgeons, as extensive corneal oedema often obscures visibility of the ocular structures, extensive peripheral anterior synechiae may require concurrent synechiolysis, and the presence of a GDD may necessitate adapted surgical protocols. Studies on the clinical outcomes of PK and DSAEK in eyes with endothelial dysfunction and a GDD are widely available and reveal increased allograft rejection rates and decreased graft survival rates compared to eyes without a GDD;[3-8] whereas reports on DMEK are sparse as it is a relatively new technique.[9-12]

With an increasing number of corneal surgeons adopting DMEK globally and employing it more and more in challenging cases, optimization of surgical technique and understanding of the clinical outcomes gain importance.[13] Thus, this study was intended to evaluate the feasibility and the clinical outcomes of DMEK in eyes with a GDD.

MATERIALS AND METHODS

Patient data

In this retrospective, interventional case series, 23 DMEK procedures were included that were performed in 20 eyes of 19 patients (mean age of 63.8 (±12.7); range 37-83 years) at two tertiary referral centers (Melles Cornea Clinic Rotterdam (Center 1) and Parker Cornea (Center 2)) (Table 1; Supplemental Table 1). All included eyes had a postoperative follow-up of at least 6 months. All patients signed an informed consent prior to surgery for research participation and the study adhered to the tenets of the Declaration of Helsinki.

Table 1. Patient and donor baseline characteristics

Characteristic	Result
Patient	
Number of procedures/ eyes/ patients	23/ 20/ 19
Recipient age, years (mean ±SD)	63.8 (±12.7)
Gender	
Female, n (%)	10 (53)
Male, n (%)	9 (47)
Race	
Caucasian, n (%)	15 (79)
African-American, n (%)	3 (16)
Other, n (%)	1 (5)
Lens status	
Phakic, n (%)	3 (13)
Pseudophakic, n (%)	20 (87)
Indication for surgery	
Bullous keratopathy, n (%)	12 (52)
Failed previous transplant, n (%)	9 (39)
Fuchs endothelial corneal dystrophy, n (%)	2 (9)
Type of Glaucoma	
Primary open angle glaucoma, n (%)	10
Secondary glaucoma, n (%)	5
Angle closure glaucoma, n (%)	3
Congenital glaucoma	2
Trabeculectomy, n (%)	13 (65)
Tube(s)	
1, n (%)	17 (85)
2, n (%)	3 (15)
Donor	
Donor age, years (mean ±SD)	68.6 (±7.4)
Donor gender	
Female, n (%)	11(48)
Male, n (%)	12 (52)
Donor death cause	
Cardiovascular/ stroke, n (%)	9 (39)
Respiratory, n (%)	4 (17)
Cancer, n (%)	8 (35)
Other, n (%)	2 (9)
Graft storage medium	
CorneaMax, n (%)	14 (61)
Optisol-GS, n (%)	9 (39)

SD= standard deviation; n= number

Donor tissue preparation

Corneosceral buttons were excised from donor globes less than 36 hours postmortem, and stored in organ culture medium (CorneaMax, Eurobio, Courtaboeuf, France) at 31 °C (Center 1) or in Optisol-GS corneal storage medium (Bausch & Lomb Inc, Rochester, United States; Center 2). For Center

1, donor tissue preparation was performed at Amnitrans EyeBank Rotterdam as previously described,[14,15] while for Center 2 donor tissue preparation was performed according to local protocol at the Alabama Eye Bank. Peripheral Descemet membrane was circumferentially stripped, preserving a small area still attached to the underlying posterior stroma in the center.

Surgical Technique

Surgeries were performed as previously described with some technique modifications.[16,17] A 3.0-mm clear corneal incision was created at the 12 o'clock position, avoiding the area of the GDD and the intracameral tube(s), and preserving the superior conjunctiva for future glaucoma surgery. Using a reversed Sinskey hook (DORC International, Zuidland, the Netherlands) and/ or custom-made scraper (Melles scraper; DORC International), scoring over 360 degrees and descemetorhexis were performed under air. In eyes with failed previous endothelial transplants (DSAEK or DMEK), grafts were stripped from the recipient posterior stroma in a similar fashion using identical instruments. After insertion, the graft was carefully unfolded and lifted against the recipient posterior stroma with an air bubble underneath, avoiding any contact between the graft and the tube(s). Subsequently, the anterior chamber was pressurized with air. Repetitive air injections were required for sufficient pressurization of the eye. The anterior chamber was then completely filled with air for on average >60 minutes and in most of the eyes the air-bubble was not reduced. If required, glaucoma tubes were trimmed during the DMEK procedure (n=6, 26%); none of the tubes was repositioned.

Postoperative management

For Center 1, the standard DMEK postoperative medication regimen included chloramphenicol 0.5% (6 times daily during the first week tapered to twice daily during the second week), ketorolac tromethamine 0.4% 4 times daily and dexamethasone 0.1% 4 times daily; switched to fluorometholone 0.1% 4 times daily at 1 month, and reduced to 3 times daily at 3 months, 2 times daily at 6 months, and once daily at 9 months postoperative.

For Center 2, postoperative medical therapy included Tobradex (tobramycin 0.3%/dexamethasone 0.1%; Novartis Pharmaceuticals Corporation, Hanover, New Jersey, USA) 4 times daily for 1 month; switched to prednisolone acetate 1% 4 times daily at 1 month postoperatively, tapered to 3 times daily at 3 months postoperatively, 2 times daily at 6 months postoperatively and once daily at 9 months postoperatively. In case of elevated intraocular pressure

(IOP), prednisolone acetate was replaced by fluorometholone. For pseudophakic eyes, bromfenac ophthalmic solution 0.07% was administered once daily during the first postoperative month.

Data collection and outcome analysis

In both centers, recipient eyes were examined at 1 day; 1 week; 1, 3, 6, 9 and 12 months; and every 6 months thereafter. Eyes were evaluated with anterior segment optical coherence tomography (AS-OCT) (Center 1: Heidelberg Slit Lamp-OCT; Heidelberg Engineering GmbH, Heidelberg, Germany; and Center 2: Zeiss Visante OCT; Carl Zeiss Meditec, Jena, Germany) and rotating Scheimpflug corneal tomography (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany). Endothelial cell density (ECD) was evaluated *in vivo* using non-contact specular microscopy (Center 1: Topcon SP3000p, Topcon Medical Europe BV, Capelle a/d Ijssel, the Netherlands; Center 2:Tomey EM-3000; CBD/Tomey, Phoenix, Arizona, USA).

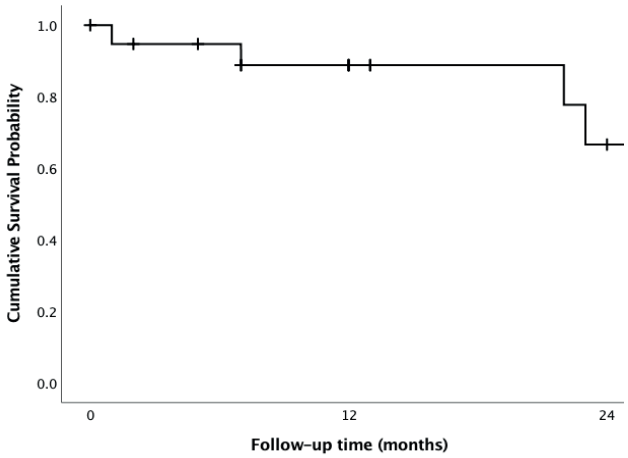
Secondary graft failure (SGF) was defined as corneal decompensation following an initially functional graft after DMEK. Best-corrected visual acuity (BCVA) was assessed using a Snellen letter chart.BCVA was defined as stable for changes ≤1 Snellen lines, and as improving or deteriorating for changes ≥2 Snellen lines. BCVA outcomes were converted to logarithm of the minimum angle of resolution units (LogMAR) for analysis. IOP was measured with applanation tonometry and increased IOP following DMEK was defined as an IOP ≥24 mmHg or an increase in IOP of ≥10 mmHg from baseline.

Kaplan-Meier survival analysis was performed using SPPS 25.0 (SPSS Inc, Chicago, Illinois, USA) to estimate the cumulative success probability of graft survival. Only primary eyes were included for the survival analysis (excluding 3 repeat-DMEK procedures). Descriptive data analysis was performed using SPSS 25.0 and Excel Software for Windows (Microsoft, Redmond, Washington, USA).

RESULTS

Clinical outcomes

All surgeries were uneventful. Mean follow-up after DMEK was 19 (±17) months. Kaplan-Meier survival analysis showed 89% and 67% cumulative graft success rates at 1 and 2 years, respectively (Fig. 1).



Time (months)		0	1	2	5	7	12	13	22	23	24
Cumulative success probability at FU	Estimate	.	.	0.95	0.95	0.95	0.89	0.89	0.89	0.78	0.67
	SE	.	.	0.05	0.05	0.05	0.08	0.08	0.08	0.12	0.15
Cumulative events		0	0	1	1	1	2	2	2	3	3
Remaining cases		20	19	18	17	16	13	10	8	7	7

Figure 1. Kaplan-Meier curve demonstrating the cumulative success rate of Descemet membrane endothelial keratoplasty in eyes with a glaucoma drainage device.
For eyes included twice in the study (n=3), only the first surgery was included for the survival analysis (n=20). The cumulative success probability was shown to be 0.89 and 0.67 at 1 and 2 years postoperatively, respectively. FU= follow-up, SE= standard error.

Median BCVA improved from 1.30 (IQR [2.00 – 0.82]) preoperatively, to 0.60 (IQR [1.30 – 0.40]) LogMar at 1 year after surgery, representing an improvement in Snellen equivalent from 20/400 (0.05) preoperatively to 20/80 (0.25) at 1 year after DMEK. At 1 year postoperatively (n=15), BCVA had improved by ≥2 Snellen lines in 11 eyes (73%) and remained stable in 4 eyes (27%) (Table 2).

Donor ECD decreased from 2810 (±330) cells/mm^2 before surgery (n=23) to 850 (±430) cells/mm^2 (-71%; n=11) at 1 year postoperatively (Table 2).

Mean pachymetry decreased from preoperatively 902 (±329) µm (n=18) to 633 (±165) µm (n=13) 1 year postoperatively. Mean IOP averaged 11.9 (±2.7) mmHg preoperatively and remained stable throughout the study period.

Table 2. Overview pre- and postoperative endothelial cell density, best-corrected visual acuity, central corneal thickness and Intraocular pressure.

	Cases (n)	Clinical outcome
LogMar BCVA, Median (IQR)		
Preoperative	23	1.30 (2.00 – 0.82)
1m FU	21	0.70 (1.65 – 0.52)
6m FU	17	0.60 (1.30 – 0.40)
12m FU	15	0.60 (1.30 – 0.40)
Change in BCVA from preoperative to 12m FU, n (%)	15	
Improved		11 (73)
Unchanged		4 (27)
Worsened		0
ECD in cells/mm^2, mean (SD) [ECD decrease in %, mean (SD)]		
Preoperative	23	2810 (±330)
1m FU	14	1820 (±510) [37 (±17)]
6m FU	11	1150 (±430) [60 (±15)]
12m FU	11	850 (±430) [71 (±13)]
CCT in µm, mean (SD)		
Preoperative	18	902 (±329)
1m FU	13	583 (±151)
6m FU	13	537 (±92)
12m FU	13	633 (±165)
IOP in mmHg, mean (SD)		
Preoperative	23	11.9 (±2.7)
1m FU	20	12.9 (±5.6)
6m FU	16	12.1 (±4.4)
12m FU	15	12.9 (±4.2)

BCVA: Best-corrected visual acuity
ECD: Endothelial cell density
FU: Follow-up
IOP: Intraocular pressure
IQR: Interquartile range
SD: Standard deviation

Postoperative complications

Pupillary block occurred in 1 of 23 (4%) cases (Case 12) and resulted in an IOP elevation, which could be reversed by partial air removal from the anterior chamber (Table 3). Interestingly, the same eye developed inflammation and spontaneous graft detachment (≥1/3 of the graft surface area) after the patient switched from dexamethasone to fluorometholone drops at 1 month post-operatively. After the eye was treated with an intensified regimen of topical steroids, it received secondary Descemet stripping endothelial keratoplasty

(DSEK). IOP elevation was observed in 2 of 23 (9%) cases (Cases 10 and 16) and occurred at 1 month and 6 months postoperatively, respectively. In both cases the patients were suspected to be steroid responders, and after the steroid load was reduced and topical beta-blockers were applied, the IOP normalized.

Visually significant graft detachment requiring re-bubbling was observed in 5 of 23 (22%) cases (Cases 3, 7, 13, 14a and 20). In case 3, all the air in the anterior chamber had escaped through the glaucoma shunt tube by the end of the operation. Because the postoperative AS-OCT showed a paracentral, ≥1/3 inferior detachment, the eye underwent immediate re-bubbling and the anterior chamber was left with a complete air fill. At 1 day postoperatively, AS-OCT examination showed a fully attached graft. Cases 7, 13 and 14a (<1/3 of the

Table 3. Postoperative complications

	n (%)
Follow-up time; mean (±SD)	19 (±17) months
Pupillary block	1 (4.3)
IOP decompensation	2 (8.7)
Graft detachment at 6m FU (n=17)	
Minor (<1/3)	10 (58.8)
Major (≥1/3)	2 (11.8)
Re-bubbling	5 (21.7)
Allograft rejection	2 (8.7)
Secondary graft failure	2 (8.7)
Re-keratoplasty	2 (8.7)
Cataract	1 (33.3) [a]

[a] 1 out of 3 phakic eyes developed cataract and underwent phacoemulsification at 15 months after DMEK.
SD= standard deviation; n= number

graft surface area) and Case 20 (≥1/3 of the graft surface area) underwent re-bubbling for graft detachment at 1 week postoperatively. In case 20, the graft detachment persisted and the eye underwent successful Descemet stripping automated endothelial keratoplasty (DSAEK) at 2 months postoperatively.

Allograft rejection was suspected in case 7 at 7 months postoperatively and was treated with an intensified regimen of topical steroids. Case 2 developed an allograft rejection at 9 months postoperatively and was successfully treated with topical steroids (Fig. 2). Secondary graft failure was observed in 2 of 23 (9%) cases (Cases 14a and 15a), which underwent successful re-DMEK at, respectively, 26 and 30 months postoperatively.

One of 3 phakic eyes developed cataract in the postoperative course and received phacoemulsification and posterior chamber lens implantation at 15 months postoperatively.

DISCUSSION

In the current study, the clinical outcomes of DMEK in eyes with a GDD were evaluated. While several research groups have reported outcomes of PK and DS(A)EK in eyes with a GDD, reports on DMEK are few, with small sample sizes and short-term follow-up (Table 4).[3-12,18-26] In addition, for the available keratoplasty studies heterogeneity in study design - for example 'mixed study groups' (shunt tube vs. trabeculectomy vs. trabeculectomy and shunt tube) - poses a challenge when interpreting results.

Our study showed lower graft survival rates for DMEK in eyes with a GDD compared to our standard DMEK cohort.[27] At 1 year postoperatively, survival probability was still at 89% for our study group, which decreased to 67% at 2 years postoperatively. This fast drop in survival probability was also reported after PK and DSAEK in eyes with a GDD (Table 4) and might be an inherent problem for this group of eyes taking their complexity into account. For these cases, counselling patients regarding the graft survival prognosis and the higher risk of needing to undergo re-endothelial keratoplasty may be even more important, so that patients can anticipate this.

The presence of a GDD also seems to negatively affect donor ECD, as ECD decrease was higher at 12 months postoperative (71%) than previously reported for our standard DMEK cohort.[27] The incidence of secondary graft failure was also higher than after standard DMEK, but occurred less frequently than compared to DSAEK (26-50%) and PK (30-70%) in eyes with a GDD.[3-5,8,18,19,21,22,24,25,26]

The underlying cause of the greater ECD decrease and higher graft failure rates in the presence of a GDD has been described to be 'multifactorial'. Firstly, changes in aqueous humour circulation patterns owing to a glaucoma shunt tube may adversely affect the endothelial cell viability.[23,24,28,29] Secondly, the GDD itself may induce a breach in the blood-aqueous barrier by intermittent tube-uveal touch and/ or chronic trauma by intermittent tube-corneal touch caused by heavily rubbing or forcefully blinking, resulting in an increase of influx of oxidative, apoptotic and inflammatory proteins, potentially causing

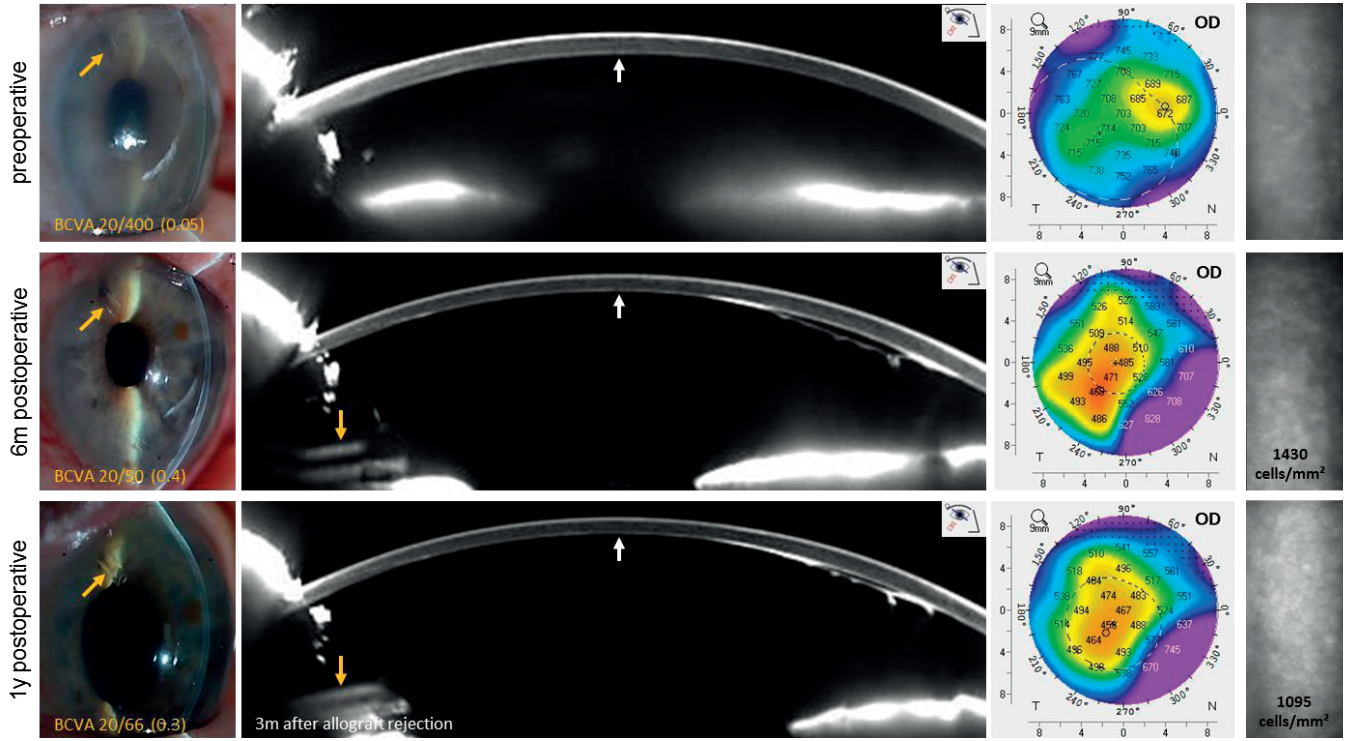


Figure 2. Slit-lamp images, Scheimpflug overviews and pachymetry and specular microscopy images before and after Descemet membrane endothelial keratoplasty (DMEK).

Images are shown for an eye (case 2) preoperatively (top row), at 6 months (second row) and at 1 year after DMEK (third row). Note the glaucoma drainage device superotemporally (orange arrows) and the deturgescence of the cornea (white arrows). The eye developed an allograft rejection at 9 months postoperatively, which was successfully reversed with an intensified regimen of topical steroids.

Table 4. Overview previously published studies on penetrating keratoplasty or endothelial keratoplasty in eyes with a glaucoma drainage device.

Type of surgery	Year	Author	No. of cases	Mean FU time (m)	Graft detachment % (n)	Allograft rejection n (%)	Graft survival (%)
PK	2001	Kwon et al.[18]	GDD n=55	34	n.a.	immunologic 7 (13%); non-immunologic 17 (31%)	70 (24m) 55 (37m) 40 (89m)
	2004	Alvarenga et al.[19]	GDD n=40	18	n.a.	n.a.	30
	2010	Witmer et al.[20]	GDD n=51	38	n.a.	1 (after cessation of topical steroids)	61
	2010	Hollander et al.[5]	GDD n=77	n.a.	n.a.	Overall 13 (17%)	89 (12m) 67 (24m) 64 (36m) 41 (48m)
	2012	Knape et al.[6]	GDD n=28	60	n.a.	13 (46%)	43
PK/ DSEK	2017	Iverson et al.[8]	PK GDD n=21 DSEK GDD n=12	23 14	n.a. 25 (3)	2 (10%) 0	62 58
DS(A)EK	2011	Wiaux et al.[2]	Surgically treated n=56 (52 eyes); GDD n=33 (29 eyes) Trab n=29	12	12.5 (7/56)	3/52 (6%)	87.5 (7/56)
	2012	DeCroos et al.[21]	Trab n=20; GDD n=27; multiple GDD n=12; GDD + Trab n=12	24	5 26 30 8.3	2 (3%)	95 74 80 66.7
	2012	Nguyen et al.[22]	Trab n= 18 Trab + GDD n=11 GDD n=35	44	16.7 18.2 17.1	n.a.	83.3 72.7 74.3
	2012	Kim et al.[23]	GDD n=11	20	36.4	36.4	18.2
	2012	Anshu et al.[3]	Trab n=26; Trab + GDD n=10; GDD n=10	Up to 60	n.a.	Overall 6 (13%)	Overall 59
	2013	Schoenberg et al.[24]	GDD n=18	24	50	n.a.	50

Table 4. Overview previously published studies on penetrating keratoplasty or endothelial keratoplasty in eyes with a glaucoma drainage device. (*continued*)

Type of surgery	Year	Author	No. of cases	Mean FU time (m)	Graft detachment % (n)	Allograft rejection n (%)	Graft survival (%)
	2014	Aldave et al.[4]	Total 76	21			
			Trab n=37;		13.5 (5/37)	5/35 (14.3%)	84
			GDD n=61;		18.0 (11/61)	6/52 (11.5%)	74
			Trab + GDD n=15		0	2/14 (14.3%)	93
	2015	Ni et al.[25]	GDD n=24		2	n.a.	
				12			87
				24			80
				36			70
	2016	Kang et al.[26]	129 cases/ 102 eyes	29		Overall 9 (8.8%)	
			Trab n=62		33.9 (21)		65
			GDD n=26;		42.3 (11)		54
			Trab + GDD n=14		35.7 (5)		57
	2017	Chiam et al.[7]	GDD n=14		Overall 0	Overall 1 (7.1%)	
				12			71
				24			36
				30			30
DMEK	2011	Bersudsky et al.[9]	GDD n=1	12	0	0	100
	2013	Heindl et al.[10]	GDD n=2	12	50	0	100
	2015	Liarakos et al.[11]	GDD n=1	6	0	0	100
	2017	Aravena et al.[12]	Total 60; GDD=23	10	Overall 23.2	Immunogenic 4 (3 after cessation of topical steroids and 1 in the control group)	100

EK = endothelial keratoplasty; no. = number; FU= follow-up; m=months; n= number; n.a.= not available; PK= penetrating keratoplasty; DS(A)EK= Descemet stripping (automated) endothelial keratoplasty; DMEK= Descemet membrane endothelial keratoplasty; GDD= glaucoma drainage device; Trab= trabeculectomy.

corneal endothelial damage.[28,30,31] Kim and associates similarly showed progressive decrease of the ECD in the first year after Ahmed valve implantation without keratoplasty in eyes with a GDD and even showed that cell loss was highest in the area of the tube.[32]

Graft detachment was the main postoperative complication, with 22% of eyes requiring a re-bubbling procedure. While this is comparable to rates reported in other series after DSAEK (17-50%) and DMEK (24%),[4,12,21-24] it is significantly higher than for our standard DMEK cohort.[27] This may reflect that eyes with a GDD are more prone to surgical complications, which is possibly related to the added difficulty of pressurizing these eyes with air at the conclusion of the operation.

The allograft rejection rate observed in this study is similar to the rates reported for DSAEK (7-14%)[3,4,7] but lower than the 10-40% reported for PK.[5,6,8,18] A possible explanation for the lower rejection rate may be the lower antigen load with reduction of the graft tissue. While our allograft rejection rate for DMEK in eyes with a GDD may seem higher than the 1-2% that we have reported for standard DMEK before,[33] the current study concerns a relatively small sample size and results should be interpreted with caution.

Most of the observed postoperative complications are thus inherent to the presence of a GDD but might partly be mitigated by special surgical considerations. These may include: 1) creating the main incision in such a way (more corneal rather than limbal) that a pre-existing filtering bleb of a trabeculectomy or a GDD is preserved and the superior conjunctiva is spared for possible future glaucoma surgery; 2) trimming or displacing the shunt tube laterally in order to avoid donor endothelial cell damage; 3) unfolding the Descemet graft over the tube rather than over the iris; 4) maintaining a complete air fill of the anterior chamber for 90-120 minutes (instead of 45-60 minutes) with repetitive air injections in between, if required; 5) leaving a 100% air bubble at termination of the surgery, since the risk of pupillary block glaucoma may be relatively small owing to the presence of a pre-existing peripheral iridotomy and the tube shunt.

The limitations posed by the retrospective study design and the relatively small sample size of this study may be surpassed by additional prospective studies of larger sample size and longer follow-up terms, possibly with control

groups (no glaucoma, medically treated glaucoma/ glaucoma without previous glaucoma surgery and trabeculectomy/ shunt tube only).

In conclusion, with specific surgical modifications, DMEK provided acceptable clinical outcomes when taking the complexity of eyes with a GDD into account. The presence of a GDD, however, may reduce graft survival times and may pose a risk for more frequent re-grafting.

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Supplemental Table. Overview Baseline Characteristics, Pre- and Postoperative Endothelial

Center	Patient							ECD (cells/mm²) [ECD decrease (%)]				BCVA (Snellen (decimal))	
	Case no.	Age (y) / Sex	Race	Eye	Indication for surgery	Lens status	Tube (n)	Pre-op	1m FU	6m FU	1y FU	Preop	1m FU
1	1a[a]	37 / F	C	OS	BK	Phakic	1	2500	N/A	n.p.	n.p.	1/60 (0.017)	1/300 (0.003)
1	1b[a]	40 / F	C	OS	Failed DMEK	Pseudo-phakic	1	2500	n.p.	n.p.	n.p.	1/300 (0.003)	1/60 (0.017)
1	2	63 /M	C	OD	PPBK	Pseudo-phakic	1	2500	1818 [27]	1428 [43]	1095 [56]	20/400 (0.05)	20/66 (0.3)
1	3	42 / F	C	OD	PPBK	Pseudo-phakic	1	2600		LTFU		20/200 (0.1)	LTFU
1	4	41 / M	C	OD	Failed PK	Phakic	1	2700	N/A	n.p.	590 [78]	3/300 (0.01)	N/A
1	5	60 / F	C	OD	PPBK	Pseudo-phakic	1	2400	897 [63]	525 [78]	n.p.	3/300 (0.01)	20/100 (0.2)
1	6	72 / F	C	OS	Failed thin DSEK	Pseudo-phakic	1	2600	N/A	689 [73]	504 [81]	3/300 (0.01)	20/100 (0.2)
1	7	80 /M	C	OS	PPBK	Pseudo-phakic	1	2600	1748 [33]	1495 [42]	1343 [48]	20/100 (0.2)	20/50 (0.4)
1	8	62 / F	C	OS	PPBK	Pseudo-phakic	2	2800	1513 [46]	1269 [55]	687 [75]	1/300 (0.003)	20/100 (0.2)
1	9	73 / F	C	OS	PPBK	Pseudo-phakic	1	2700	N/A	563 [79]	n.p.	3/300 (0.01)	1/300 (0.003)
1	10	62 / M	C	OD	Failed re-DMEK[c]	Pseudo-phakic	1	2700	2241 [17]	703 [74]	286 [89]	1/300 (0.003)	20/133 (0.15)
1	11	58 / M	SA	OS	PPBK	Pseudo-phakic	1	2800	2182 [22]	LTFU		20/133 (0.15)	20/40 (0.5)
1	12	73 / M	AA	OD	PPBK	Pseudo-phakic	1	2500	N/A	DSEK		1/300 (0.003)	3/300 (0.01)
1	13	65 / F	AA	OS	PPBK	Pseudo-phakic	2	2700	N/A	n.p.	n.y.a.	3/300 (0.01)	0.25/200 (LP+)
2	14a[a]	64 / M	C	OD	Failed re-DSEK	Pseudo-phakic	1	3155	2952 [6]	1293 [59]	620 [80]	*20/70*[e] *(0.28)*	*20/40*[b,e] *(0.5)*
2	14b[a]	66 / M	C	OD	Failed DMEK	Pseudo-phakic	1	3145	1585 [50]	1479[b] [53]	1334 [58]	*20/200*[e] *(0.1)*	*20/100*[e] *(0.2)*
2	15a[a]	64 / M	C	OS	Failed re-DSEK	Pseudo-phakic	2	2793	1937 [31]	1593 [43]	621 [78]	*20/80*[e] *(0.25)*	*20/40*[e] *(0.5)*
2	15b[a]	66 / M	C	OS	Failed DMEK	Pseudo-phakic	2	2882	1811 [37]	1455 [50]	n.y.a.	*20/50*[e] *(0.4)*	*20/50*[e] *(0.4)*
2	16	62 / M	C	OD	PPBK	Pseudo-phakic	1	3831	2279 [41]	1398 [64]	1639 [57]	*20/400*[e] *(0.05)*	*20/60*[e] *(0.3)*
2	17	72 / F	C	OS	3x Failed DSAEK[d]	Pseudo-phakic	1	3003	1627 [46]	N/A	664 [78]	*20/200*[e] *(0.1)*	*20/400*[e] *(0.05)*
2	18	83 / M	AA	OD	FECD	Phakic	1	2874	1805 [37]	N/A	n.y.a	*20/400*[e] *(0.05)*	*20/70*[e] *(0.28)*

Cell Density, Best-Corrected Visual Acuity and Central Corneal Thickness

BCVA (Snellen (decimal))		CCT (μm)				IOP (mmHg)				Graft detachment at 6m FU (surface area)	Remarks
6m FU	1y FU	Pre-op	1m FU	6m FU	1y FU	Pre-op	1m FU	6m FU	1y FU		
1/300 (0.003)	3/300 (0.01)	1213	525	569	556	12	10	10	12	<1/3	Phacoemuls. (15m)
1/60 (0.017)	20/400 (0.05)	1176	590	437	913	11	11	14	10	<1/3	
20/50 (0.4)	20/66 (0.3)	714	520	477	459	16	17	10	12	≥1/3	Allograft rejection (9m)
LTFU		788	LTFU			14	LTFU			N/A	Re-bubbling (1.5h postop); patient returned to own ophthalmologist for check-up
20/80 (0.25)	20/50 (0.4)	710	782[b]	675	750	11	N/A	12	12	<1/3	
20/66 (0.3)	20/200 (0.1)	727	533	552	605	10	12	11	12	<1/3	Extensive PAS
20/100 (0.2)	20/66 (0.3)	1129	725	509	588	14	11	11	17	<1/3	
20/40 (0.5)	20/200 (0.1)	588	539	557	510	17	15	17	17	Fully attached	Tube trimmed during surgery; Re-bubbling (1w); suspected allograft rejection (7m)
20/100 (0.2)	20/200 (0.1)	1147	575	589	616	10	11	16	16	<1/3	
20/400 (0.05)	1/60 (0.017)	817	1038	779	1012	15	19	14	14	<1/3	Extensive PAS
20/80 (0.25)	20/80 (0.25)	1084	457	469	564	8	28	14	10	<1/3	IOP decompensation (1m)
LTFU		933	499	LTFU		11	18	LTFU		N/A	Patient returned to own ophthalmologist for check-up
DSEK		1882	n.p.	DSEK		10	6	DSEK		n.p.	Pupillary block à Elevation IOP (1d); Switch Dexa to FML à inflammation à graft detached (1m)
0.25/200 (LP+)	n.y.a.	951	n.p.	n.p.	n.y.a.	15	10	N/A	n.y.a.	<1/3 (5m)	Re-bubbling (1w)
20/40[e] (0.5)	*20/25[e] (0.8)*	N/A	N/A	N/A	N/A	11	N/A	8	12	≥1/3	Re-bubbling (1w); SGF (23m)
20/50[e] (0.4)	*20/70[e] (0.28)*	N/A	427[b]	487	493	11	10	8	11	<1/3	
20/30[e] (0.67)	*20/25[e] (0.8)*	N/A	N/A	N/A	N/A	8	6	10	10	N/A	SGF (22m)
20/40[e] (0.5)	n.y.a.	586	485[b]	481	n.y.a.	7	16	10	n.y.a.	Fully attached	Tube trimmed during surgery
20/50[e] (0.4)	*20/40[e] (0.5)*	714	524	527	526	13	18	25	23	Fully attached	Tube trimmed during surgery; IOP decompensation (6m)
20/400[e] (0.05)	*20/400[e] (0.05)*	N/A	513	N/A	641	13	3	4	5	N/A	Tube trimmed during surgery; synechiolysis of ext. PAS
20/400[e] (0.05)	n.y.a.	524	400[b]	429	n.y.a.	16	16	12	n.y.a.	Fully attached	

Supplemental Table. Overview Baseline Characteristics, Pre- and Postoperative Endothelial

Center	Patient							ECD (cells/mm^2) [ECD decrease (%)]				BCVA (Snellen (decimal))	
	Case no.	Age (y) / Sex	Race	Eye	Indication for surgery	Lens status	Tube (n)	Pre-op	1m FU	6m FU	1y FU	Preop	1m FU
2	19	76 / F	C	OS	PPBK	Pseudo-phakic	1	3356	1098 [67]	N/A	n.y.a.	20/400 (0.05)	*20/80* [e] *(0.25)*
2	20	76 / F	C	OS	FECD	Pseudo-phakic	1	2941	N/A	DSAEK		PH: 20/60 (0.3)	20/400 (0.05)

ECD= endothelial cell density; CCT= central corneal thickness; µm= micrometer; IOP= intraocular pressure; Y= years; n= number; w= weeks; m= months; FU= follow-up; Preop= preoperative; F= female; M= male; C= Caucasian; AA=African American; SA=Saudi-Arabian; OS= oculus sinister; OD= oculus dexter; (PP)BK= (pseudophakic) bullous keratopathy; N/A = not available; n.p.= not possible; LTFU= lost to follow-up; SGF = Secondary graft failure; PGF = Primary graft failure; DMEK= Descemet membrane endothelial keratoplasty; PK= penetrating keratoplasty; dexa= dexamethasone; FML= fluorometholone; DSEK= Descemet stripping endothelial keratoplasty; FECD= Fuchs endothelial corneal dystrophy; PH= visual acuity measured with Pinhole; ext. PAS= extensive peripheral anterior synechiae; phacoemuls.= phacoemulsification.

Cell Density, Best-Corrected Visual Acuity and Central Corneal Thickness (*continued*)

BCVA (Snellen (decimal))		CCT (µm)				IOP (mmHg)				Graft detachment at 6m FU (surface area)	Remarks
6m FU	**1y FU**	**Pre-op**	**1m FU**	**6m FU**	**1y FU**	**Pre-op**	**1m FU**	**6m FU**	**1y FU**		
20/60 (0.3)	n.y.a.	797	534	512	n.y.a.	11	10	12	n.y.a.	Fully attached	Tube trimmed during surgery
DSAEK		N/A	N/A	DSAEK		10	10	DSAEK		N/A	Tube trimmed during surgery; Re-bubbling (1w); secondary DSAEK for persistent graft detachment (2m)

[a] 1a,1b / 14a,14b / 15a,15b = Subsequent operations in the same eye.
[b] 3 months follow-up
[c] First DMEK, patient did not have a glaucoma drainage device implant yet.
[d] Related to shunt tube
[e] *Italic* Uncorrected visual acuity, BSCVA not available.