Clinical outcomes of modern lamellar keratoplasty techniques

Dijk, K. van

Chapter 2

Near complete visual recovery and refractive stability in modern corneal transplantation: Descemet membrane endothelial keratoplasty (DMEK)

Korine van Dijk, Lisanne Ham, Win-Hou W. Tse, Vasilios S. Liarakos, Ruth Quilendrino, Ru-Yin Yeh, and Gerrit R.J. Melles

Cont Lens Anterior Eye 2013;36:13-21

ABSTRACT

Objective. To report the six months results of a large prospective study on Descemet membrane endothelial keratoplasty (DMEK) for management of corneal endothelial disorders.

Methods. DMEK was performed in 300 consecutive eyes with Fuchs endothelial dystrophy, bullous keratopathy or previous corneal transplant failure. Best spectacle-corrected visual acuity (BSCVA), refractive outcome and endothelial cell density (ECD) were evaluated before and at 1, 3, and 6 months after surgery. Intra- and postoperative complications were documented.

Results. At 6 months, 98% of eyes reached a BCVA of ≥20/40 (≥0.5), 79% ≥20/25 (≥0.8), 46% ≥20/20 (≥1.0), and 14% ≥20/18 (≥1.2) (n=221). The pre- to 6 months postoperative spherical equivalent (SE) showed a +0.33D (±1.08D) hyperopic shift (P=0.0000). Refractive stability was shown at 3 months after DMEK, i.e. no significant change in SE (P=0.0822) or refractive cylinder (P=0.6182) at 3 versus 6 months follow-up. Donor ECD showed a decrease from 2561 (±198) cells/mm^2 before, to 1674 (±518) cells/mm^2 at 6 months after surgery (n=251) (P=0.0000). The main complication was (partial) graft detachment occurring in 31 eyes (10%). Secondary ocular hypertension was seen in 13 eyes (6%): 6 induced by air-bubble dislocation posterior to the iris and 4 induced by steroids. Secondary cataract requiring phaco-emulsification developed in 3 out of 63 (5%) phakic eyes.

Conclusions. DMEK may provide a refractively neutral near complete, rapid visual rehabilitation with ECDs similar to earlier endothelial keratoplasty techniques. This combined with a relatively low complication rate, would indicate that DMEK is a safe and effective treatment for corneal endothelial disorders.

Keywords: Descemet membrane endothelial keratoplasty (DMEK), posterior lamellar keratoplasty, corneal transplantation, visual acuity, Fuchs endothelial dystrophy, bullous keratopathy

INTRODUCTION

From 1998, the authors have introduced various sutureless techniques for the replacement of diseased corneal endothelium. These techniques have been popularized as 'deep lamellar endothelial keratoplasty' (DLEK),[1] and 'Descemet stripping (automated) endothelial keratoplasty' (DSEK/DSAEK).[2-4] More recently, the authors further refined the concept of endothelial keratoplasty towards the selective transplantation of Descemet membrane (DM) and its donor endothelium, referred to as 'Descemet membrane endothelial keratoplasty' (DMEK).[2,5-7] Furthermore, Studeny et al. described a hybrid technique between DSEK/DSAEK and DMEK, in which transplantation of Descemet membrane with a peripheral stromal rim is performed, referred to as DMEK-S or DMAEK.[8]

The early forms of endothelial keratoplasty, DLEK and DSEK/DSAEK, may have shown that visual outcomes could compete with penetrating keratoplasty (PK), while the most frequent complications were minimized.[9] Endothelial keratoplasty shows minimally induced astigmatism because the recipient anterior corneal surface is not compromised; suture related problems are eliminated since endothelial keratoplasty requires no (corneal) sutures; and wound healing related complications are rare as the procedure can be performed through a self sealing limbal or scleral tunnel incision.

Initial results showed that DMEK enabled better visual outcomes than DLEK and DSEK/DSAEK with minimal refractive changes.[5-7,10-13] Given the growing interest worldwide, optometrists may soon become more involved in the referral and postoperative management of these patients. Hence, the aim of the current study was to evaluate a first series of 300 consecutive DMEK cases, with the main focus on visual and refractive outcomes.

METHODS

The first 300 consecutive eyes of 248 patients that underwent DMEK surgery enrolled in this prospective study. The mean age of the patients was 67 ±13 years (range 30 to 93 years) (Table 1). All patients signed an IRB-approved informed consent; the study was conducted according to the Declaration of Helsinki, and registered at www.clinicaltrials.gov (NCT00521898).

Donor tissue protocol

The procedure for harvesting a DMEK-graft has been previously described.[14] In short, corneo-scleral buttons were excised from donor globes ≤36 hours post mortem and stored by organ culture at 31°C. After one week of culture, endothelial cell morphology and viability were evaluated and the corneo-scleral buttons were mounted endothelial side up on a custom made holder. A 9.5-mm diameter Descemet-sheet with its endo-

Table 1. Demographic DMEK eyes (n=300)

Number of patients	248	-
Mean age (± SD)	67 (± 13) years	Range 30-93 years
Men/women	134/166	45/55%
Phakic eyes	63	21%
Fuchs endothelial dystrophy	272	90.7%
Bullous keratopathy	17	5.7%
Failed DSEK / PK	9 / 1	3.3%
Decompensation after perforation	1	0.3%

DMEK = Descemet membrane endothelial keratoplasty
DSEK = Descemet stripping endothelial keratoplasty
PK = Penetrating keratoplasty
SD = standard deviation

thelium was removed from the posterior stroma with the corneo-scleral rim immersed in balanced salt solution (BSS). Due to the elastic tissue-properties, a 'Descemet-roll' formed spontaneously, with the endothelium on the outer side. Each Descemet–roll was then stored for 5 to10 days in organ culture medium until the time of transplantation.[14]

Surgical protocol

All eyes were operated under local anesthesia (4 ml 1% ropivacain hydrochloride with 150IE Hyason), followed by ocular massage and a Honan's balloon for 10 minutes and the patient was positioned in the anti-Trendelenburg position. Surgeries were performed as previously described.[15] Three side ports were made, the anterior chamber was filled with air, a circular portion of Descemet membrane (DM) was scored and stripped from the posterior stroma with an inversed Sinskey hook (D.O.R.C. International, Zuidland, The Netherlands), thereby performing a 9.0-mm diameter 'descemetorhexis'.[16] A 3.0-mm tunnel incision was made at the limbus for insertion of the graft.

The donor Descemet-roll was stained with a 0.06% trypan blue solution (VisionBlue™, D.O.R.C. International) and sucked into a custom made injector (DMEK-inserter, D.O.R.C. International) to inject into the recipient anterior chamber. The graft was oriented endothelial side down (donor DM facing recipient posterior stroma) by indirect manipulation with air and BSS.[15] The graft was then gently spread out over the iris and an air bubble was injected underneath the graft to position it onto the recipient posterior stroma (Figure 1).[15] The anterior chamber was left completely filled with air for 60 minutes followed by an air-liquid exchange to pressurize the eye while leaving an approximately 30% to 50% air bubble in the anterior chamber. Each surgical procedure was recorded on DVD (Pioneer DVR-RT601H-S, Tokyo, Japan).

In all eyes, a YAG-laser peripheral iridotomy was made at 12 o'clock, 1 to 2 weeks before surgery to reduce the potential risk of postoperative pupil block glaucoma due to the air

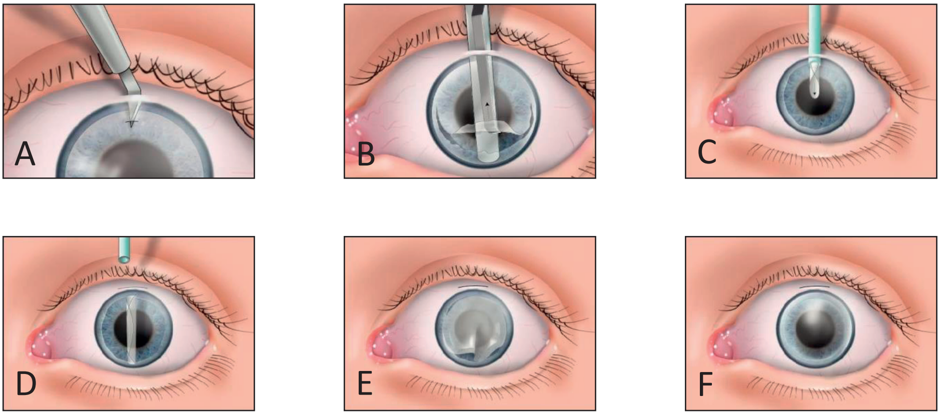

Figure 1. The DMEK procedure consists of the following steps: After the anterior chamber is filled with air through a side port at 3 or 9 o'clock, the main incision is made at 12 o'clock (A) and the recipient Descemet membrane is removed by creating a descemetorhexis through the main incision or through a side port (B). The donor DMEK-roll is inserted into the anterior chamber (C) and centered (D). Then, the DMEK-roll is unfolded by injecting BSS and/or air to the graft (E). Once completely unfolded and positioned against the recipient posterior stroma, the anterior chamber is filled with air for approximately 60 minutes (F). (*Figure has been used with permission of CORNEA*)

bubble left in the anterior chamber after surgery. The iridotomy was made at 12 o'clock as patients are requested to lay in a supine position after surgery. In this position, the air bubble is likely to be in the inferior angle of the eye due to Bell's phenomenon rotating the eye upward on closure.

Measurements and statistics

Patients were examined before and 1, 3 and 6 months after DMEK with Pentacam imaging (Oculus, Wetzlar, Germany), non-contact specular microscopy and slit-lamp photography (Topcon Medical Europe BV). Donor endothelial cell density (ECD) was evaluated *in-vitro* (Axiovert 40 inverted light microscope, Zeiss, Göttingen, Germany) and photographed (PixeLINK PL-A662, Zeiss, Göttingen, Germany).[13] *In-vivo* ECD was evaluated using a Topcon SP3000p non-contact autofocus specular microscope (Topcon Medical Europe BV, Capelle a/d IJssel, The Netherlands). Images of the central corneal window were manually corrected and three measurements were averaged.

Subjective refraction, best spectacle-corrected visual acuity (BSCVA) and ECD, as well as intraoperative and postoperative complications were recorded in a SQL-database. For all comparisons, two-sided paired-sample *t*-tests were performed (SPSS 18.0). *P*-values for the Pentacam and refractive data were corrected with the Benjamini&Hochberg correction (multiple tests increase false positives).[17] After correction, all *P*-values of less than 0.05 were considered to be statistically significant.

RESULTS

Demographics

Three hundred eyes of 248 patients underwent DMEK surgery (Table 1). In patients referred for combined cataract extraction and DMEK, phacoemulsification was performed one to two months prior to the cornea transplantation. Post-phacoemulsification measurements were used for preoperative DMEK refractive data.

Visual outcome

A total of 221 eyes were included for visual acuity analysis; 79 eyes were excluded because of low visual potential (n=38), a re-operation within 6 months (n=21), 'spontaneous corneal clearance' despite graft detachment (n=8),[18,19] or incomplete visual data (n=12) (Table 2). At six months, 79% of eyes reached a BSCVA of ≥20/25 (≥0.8), 46% ≥20/20 (≥1.0), and 14% ≥20/18 (≥1.2) (n=221) (Table 3 and Figure 2). At 1 month, these percentages were 57%, 24% and 3%, respectively and at 3 months 71%, 37% and 6% (Table 3 and Figure 2).

Table 2. Analysis clinical outcome DMEK (n=300)

Exclusion criteria	Analysis BCVA	Analysis subjective refractive data	Analysis Pentacam data	Analysis endothelial cell density
One or more follow-up measurement not available	12	54	63	19
Low visual potential	36	--	--	--
Secondary DSEK (*)	17(3)	17(3)	17(3)	17(3)
Secondary DMEK (*)	4(10)	4(10)	4(10)	4(10)
Spontaneous clearance despite graft detachment	8	8	8	8
Total number of eyes excluded	-79	-83	-92	-48
Total number of eyes evaluated	221	217	208	252

(*) All secondary DMEK/DSEK performed after the 6 months study evaluation interval
BCVA = Best corrected visual acuity
DMEK = Descemet membrane endothelial keratoplasty
DSEK = Descemet stripping endothelial keratoplasty

Table 3. Visual outcome after DMEK (n=221)

BCVA	Pre-operative	1 month	3 months	6 months
≥ 20/40 (≥ 0.5)	38% (84/n)	87% (193/n)	96% (212/n)	98% (216/n)
≥ 20/25 (≥ 0.8)	7% (16/n)	57% (126/n)	71% (157/n)	79% (175/n)
≥ 20/20 (≥ 1.0)	1% (2/n)	24% (53/n)	37% (82/n)	46% (103/n)
≥ 20/18 (≥ 1.2)	0% (0/n)	3% (5/n)	6% (13/n)	14% (32/n)

BCVA = Best corrected visual acuity
DMEK = Descemet membrane endothelial keratoplasty

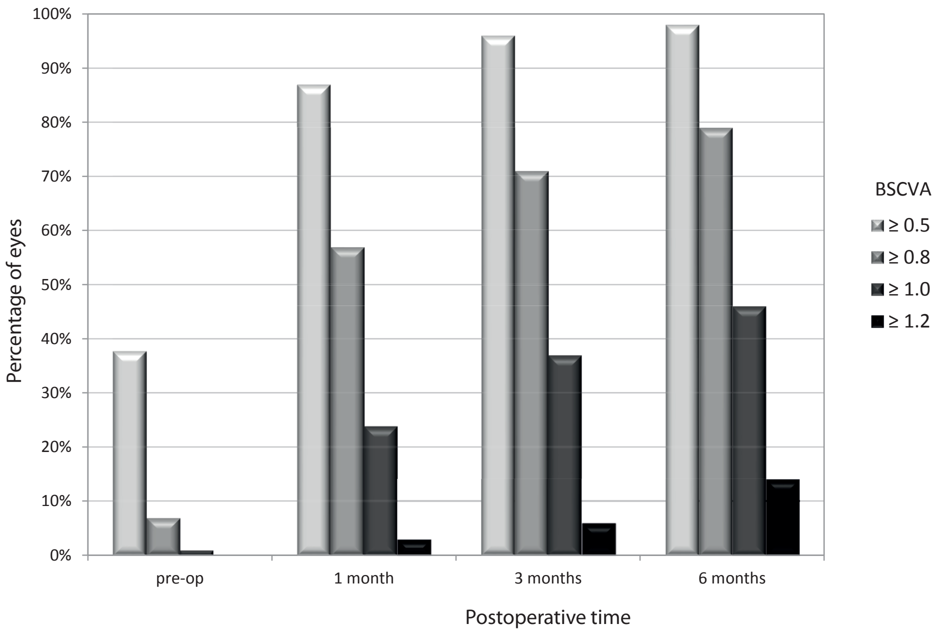

Figure 2. Bar graph displaying the best spectacle-corrected visual acuity (BSCVA) preoperatively and at one, three, and six months after DMEK surgery.

Subjective refraction

From 217 eyes subjective refractive data was available at all follow-up intervals (Tables 2, 4 and 5). Because the preoperative refraction may have been less reliable due to low visual acuity, we also performed the same analysis for 166 eyes with a preoperative BSCVA of ≥20/60 (≥0.3); however similar results were found (Table 6). The change in spherical equivalent (SE) from preoperative to 3 months after surgery was ≤0.50D in 41% and ≤1.00D in 65% of eyes and to 6 months postoperative ≤0.50D in 40% and ≤1.00D in 68%. The change in cylindrical error 3 months after surgery was ≤1.00D in 69%, and ≤2.00D in 95% of eyes, and at 6 months ≤1.00D in 66% and ≤2.00D in 95% (Table 6).

For the whole group (n=217), the pre- to postoperative change in SE (hyperopic and myopic shifts averaged) was +0.41 (±1.06) D (range -2.50D to 3.75D) (*P*=0.0000) at 3 months, and +0.33 (±1.08) D (range -2.50D to 3.75D) (*P*=0.0000) at 6 months (Table 4). The pre- to postoperative change in refractive cylinder (hyperopic and myopic shifts in cylindrical power averaged) was -0.36 (±1.07) D (range -4.00D to 3.75D) (*P*=0.0000) at 6 months (Table 4).

Of these 217 eyes, 50 were phakic and 167 pseudophakic. The mean change in SE at 6 months postoperatively was +0.60 (±0.86) D (range -2.13D to 2.75D) (*P*=0.0000) and +0.25 (±1.12) D (range -2.50D to 3.75D) (*P*=0.0074) in phakic and pseudophakic eyes, respectively. The change in SE was significantly higher in phakic than pseudophakic

Table 4. Subjective refractive outcome DMEK

	Pre-operative		3m postoperative		6m postoperative		ΔSE (D)					Δ Refractive cylinder (D)				
	SE (D)	Cyl (D)	SE (D)	Cyl (D)	SE (D)	Cyl (D)	Preop to 3m	Preop to 3m absolute	Preop to 6m	Preop to 6m absolute	3m to 6m	Preop to 3m	Preop to 3m absolute	Preop to 6m	Preop to 6m absolute	3m to 6m
Eyes with preoperative BCVA ≥ CF (≥ 1/60); n=217																
Average	-0.34	-0.99	0.07	-1.33	-0.01	-1.36	0.41	0.89	0.33	0.86	-0.08	-0.34	0.90	-0.36	0.88	-0.03
SD	1.82	0.91	1.78	0.95	1.82	0.96	1.06	0.72	1.08	0.73	0.73	1.15	0.79	1.07	0.71	0.82
P=	--	--	--	--	--	--	**0.0000**	--	**0.0000**	--	0.0822	**0.0000**	--	**0.0000**	--	0.6182
Eyes with preoperative BCVA ≥ 20/60 (≥0·3); n=166																
Average	-0.39	-1.00	0.07	-1.32	0.02	-1.37	0.46	0.86	0.40	0.82	-0.06	-0.31	0.86	-0.36	0.86	-0.05
SD	1.56	0.89	1.54	0.97	1.56	0.97	1.01	0.70	1.01	0.71	0.71	1.08	0.72	1.02	0.66	0.71
P=	--	--	--	--	--	--	**0.0000**	--	**0.0000**	--	0.3523	**0.0003**	--	0.4756	--	0.4089
Pseudophakic eyes with preoperative BCVA ≥ CF (≥1/60); n=167																
Average	-0.08	-0.99	0.27	-1.38	0.17	-1.43	0.36	0.88	0.25	0.87	-0.11	-0.39	0.92	-0.43	0.92	-0.04
SD	1.46	0.89	1.31	0.96	1.38	0.93	1.12	0.76	1.12	0.75	0.75	1.17	0.82	1.10	0.74	0.83
P=	--	--	--	--	--	--	**0.0001**	--	**0.0074**	--	0.0594	**0.0000**	--	**0.0000**	--	0.5265

BCVA = Best corrected visual acuity
CF = Counting fingers
DMEK = Descemet membrane endothelial keratoplasty
"Bold" = Significant ($P<0.05$)
SE = Spherical equivalent
Cyl = Cylinder
D = Diopter
m = months

Table 5. Stability of refraction after DMEK (n=217)

Δ SE				Δ Cylinder			
≤ 0.50 D Preop-3m	≤ 1.00 D Preop-3m	≤ 0.50 D Preop-6m	≤ 1.00 D Preop-6m	≤ 1.00 D Preop-3m	≤ 2.00 D Preop-3m	≤ 1.00 D Preop-6m	≤ 2.00 D Preop-6m
41% (89/217)	65% (141/217)	40% (86/217)	68% (148/217)	69% (150/217)	95% (205/217)	66% (143/217)	95% (206/217)

DMEK = Descemet Membrane Endotelial Keratoplasty
SE = Spherical equivalent
Δ = Change
m = months

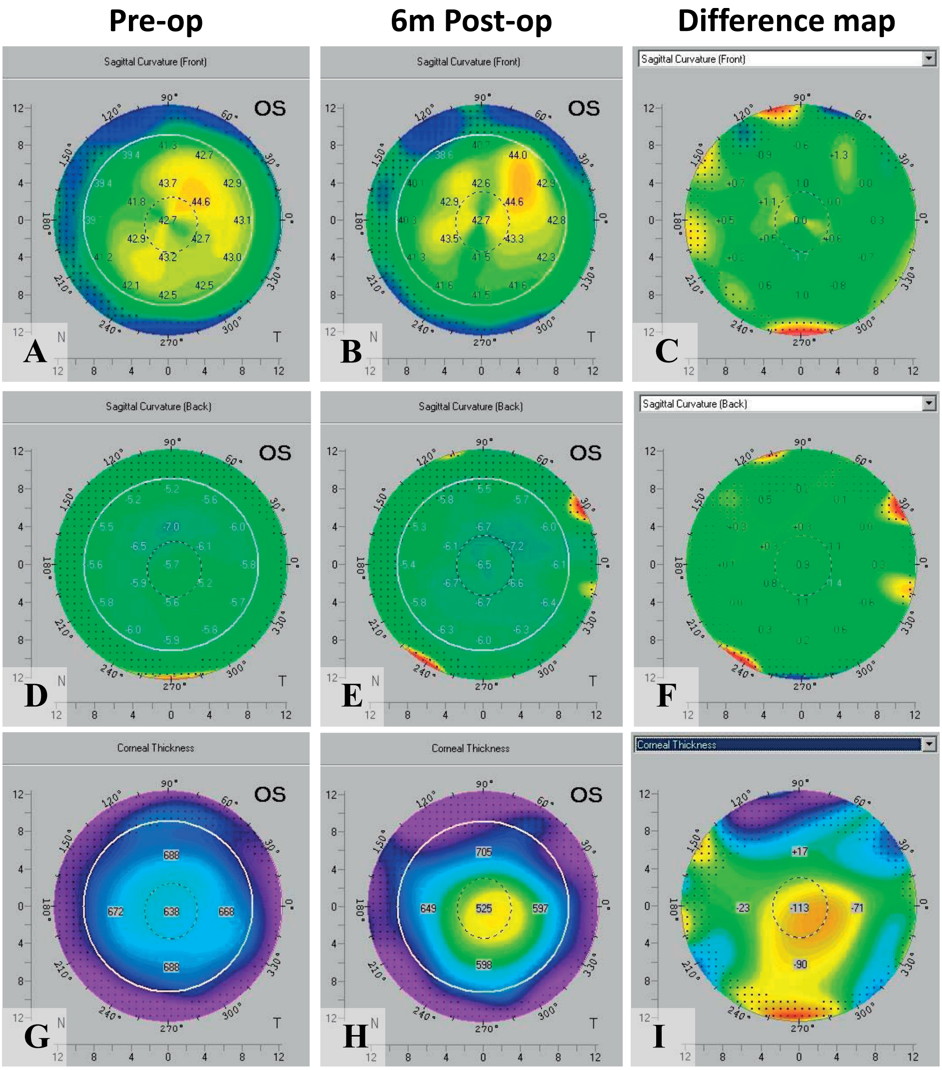

Figure 3. Topographic corneal power maps of the anterior corneal curvature (A-C), the posterior corneal curvature (D-F) and pachymetry (G-I), before DMEK (A, D and G), six months after DMEK (B, E and H), and the corresponding difference maps (C, F and I). Note that DMEK is associated with a virtual absence in curvature change at both the anterior and posterior corneal surfaces.

eyes (P=0.0227). The refractive outcome for the pseudophakic eyes (i.e. eyes in which any effect of the crystalline lens on the refraction could be excluded) was analyzed separately (Table 4).

Refractive stability after surgery was evaluated by comparing 3 to 6 months postoperative refractions (n=217), that showed no significant change in SE (P=0.0822) or cylindrical error (P=0.6182) (Table 4). All patients obtained full binocular vision, except for three cases: two with amblyopia, and one patient was a monoculus.

Pentacam analysis

Complete Pentacam data was available for 208 eyes. Eyes with incomplete data or where the image showed improper software auto-detection, were excluded (Table 2). At 3 and 6 months postoperatively, the change in the anterior corneal curvature was -0.5 (±1.2) D and -0.4 (±1.0) D, respectively (P=0.0000).The posterior corneal curvature changed -0.8 (±0.7) D and -0.7 (±0.7) D (P=0.0000) at 3 and 6 months (Figure 3; Table 6). Keratometric astigmatism did not increase from preoperative to 6 months postoperatively (P=0.1089) (Figure 3; Table 6).

Mean central corneal thickness decreased from 671 (±102) μm before surgery, to 525 (±56) μm at 3 months, and 524 (±51) μm at 6 months (n=208), a decrease of 146 (±109) μm and 147 (±101) μm (P=0.0000), respectively (Figure 3).

Endothelial cell density

Six months postoperative ECD measurements were available in 251 eyes and averaged 1674 (±518) cells/mm^2, compared to an average preoperative donor ECD of 2561 (±198) cells/mm^2, indicating a decrease in ECD of on average 34.6% (P=0.0000).

Postoperative complications

All transplanted corneas with an attached graft cleared in 1 to 12 weeks, except for 4 eyes. Of the latter eyes, 3 were among the first DMEK cases that underwent an early re-intervention when the cornea failed to clear within 3 weeks after the initial DMEK. With growing experience, we learned corneal clearance can be delayed for several weeks.[20] Therefore, it remained uncertain whether or not these 3 eyes had primary graft failure, since these corneas should have cleared if no secondary surgery had been undertaken. No secondary graft failures occurred within the 6 months follow-up interval (Table 7).

The major postoperative complication in this DMEK series was graft detachment, defined as a lack of adherence between the Descemet graft and the recipient posterior stroma requiring secondary surgical intervention (re-bubbling or re-graft). This could be a complete (frequently seen as a 'free-floating' Descemet-roll in the recipient anterior chamber) or partial detachment. Overall, 10.3% (31/300) of eyes showed a graft detachment; of these 5.7% (17/300) were partial and 4.7% (14/300) were complete detachments (Table 7).

Table 6. Objective refractive outcome (diopters) Pentacam measurements; n=208

	Pre-operative		3m postoperative		6m postoperative		Δ Sim K mean		Δ Cornea astigmatism	
	Sim K mean	Cornea astigmatism	Sim K mean	Cornea astigmatism	Sim K mean	Cornea astigmatism	Preop-3m	Preop-6m	Preop-3m	Preop-6m
Average True Net Power	42.4	1.8	41.0	2.2	41.2	1.9	-1.3	-1.1	0.4	0.1
SD	2.0	1.5	1.7	1.4	1.5	1.3	1.7	1.6	1.7	1.5
P=	--	--	--	--	--	--	**0·0000**	**0·0000**	**0·0026**	0·3767
Average Cornea Front	43.1	1.5	42.6	1.9	42.7	1.6	-0.5	-0.4	0.4	0.1
SD	1.7	1.2	1.8	1.7	1.5	1.1	1.2	1.0	1.8	1.1
P=	--	--	--	--	--	--	**0·0000**	**0·0000**	**0.0031**	0.1089
Average Cornea Back	-5.6	0.5	-6.4	0.5	-6.3	0.5	-0.8	-0.7	0.1	0.0
SD	0.7	0.4	0·4	0.4	0.4	0.5	0.7	0.7	0.6	0.7
P=	--	--	--	--	--	--	**0·0000**	**0·0000**	0.2452	0·9377

m = months
Δ = change
"Bold" = Significant (P<0.05)
Sim K = Simulated keratometry

An allograft rejection occurred in 3 eyes (1%). Only one patient presented with discomfort, reduced visual acuity due to corneal edema and a Khodadoust line. No subjective complaints were experienced by the other two patients, who discontinued their

Table 7. Complications after DMEK (n=300)

Intraoperative	
Failed to unfold/position DMEK graft	1 (0.3%)
'Vitreous pressure' during surgery	18 (6.0%)
Irisroot hemorrhage	4 (1.3%)
Postoperative	
Graft related	
Primary graft failure / Early re-intervention	4 (1.3%)*
Secondary graft failure	1 (0.3%)**
Graft detachment:	
Complete	14 (4.7%); first 150 cases: 10 (6.7%); second 150 cases: 4 (2.7%)
Partial	17 (5.7%); first 150 cases: 10 (6.7%); second 150 cases: 7 (4.7%)
Recipient raelated	
Remnant recipient Descemet at interface	17 (5.7%)
Allograft rejection	3 (1.0%)
Corneal infiltrate	3 (1.0%)
Intraocular pressure	
Hypotonic eye	1 (0.3%)
Pre-existing glaucoma	7 (2.3%)
Pupillary block glaucoma	0 (0.0%)
Air bubble induced angle closure glaucoma	6 (2.0%)
Steroid induced glaucoma	4 (1.3%)
Secondary glaucoma (other causes)	3 (1.0%)
Crystalline lens	
Iatrogenic induced cataract	3 (4.8%; 3 out of 63 phakic eyes)
Posterior segment	
Cystoid macular edema	3 (1.0%)
Macular hole	1 (0.3%)
Macular Pucker	3 (1.0%)
Retinal detachment	1 (0.3%)
Re-operations	
Re-bubbling	9 (3.0%)
Secondary DSEK	20 (6.7%)
Secondary DMEK	14 (4.7%)

* See text complications in results section

** No secondary graft failures occurred within the 6 months. One eye showed secondary failure 10 months postoperative

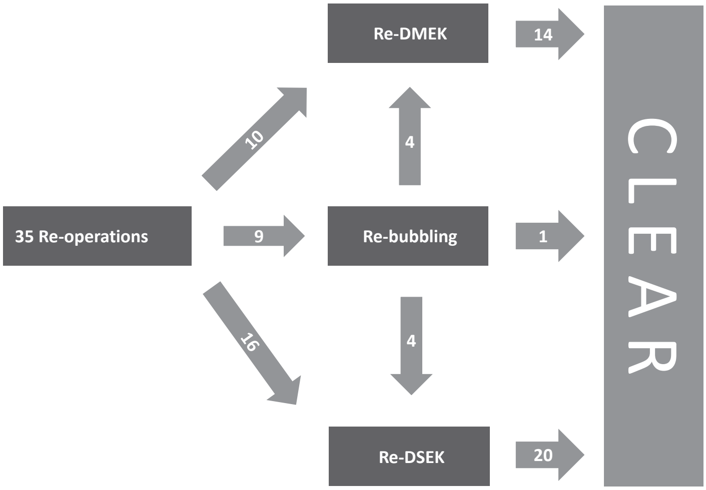

Figure 4. Diagram displaying the number and sequence of secondary interventions after the 300 DMEK surgeries performed in this study.

steroid medication prematurely. Three eyes (1%) presented with a peripheral corneal infiltrate in an area with remnant peripheral corneal edema that resolved with topical antibiotics (Table 7).

Intraocular pressure (IOP) elevation was found in 20 DMEK eyes (20/300, 6.7%), of which 7 eyes (2.3%) had an escalation of a pre-existing glaucoma and 13 eyes (4.3%) presented with a 'de-novo' IOP elevation (Table 7). Of these 13 eyes, secondary glaucoma due to air-bubble dislocation behind the iris and/or mechanical forward displacement of the iris-diaphragm occurred in 6 phakic eyes. Four eyes showed steroid induced intraocular pressure elevation within the first month after surgery (in one patient bilateral). The 3 remaining eyes developed secondary glaucoma due to peripheral anterior synechiae (necessitating glaucoma surgery in one eye). The aetiology of the IOP elevation was unidentified in 2 eyes (Table 7). Hypotony for several weeks was observed in one eye with a history of phacoemulsification, PK and vitrectomy (Table 7).

In phakic eyes, mild anterior crystalline lens opacities were sometimes observed after DMEK, these usually faded within months. However, in 3 out of 63 phakic eyes (5%), the induced lens opacities required phacoemulsification (Table 7).[21]

Cystoid macular edema developed in three eyes (1%; 3/300). One highly-myopic eye (0.3%; 1/300) presented with a retinal detachment two months after surgery requiring vitrectomy. A macular hole developed in one eye (0.3%; 1/300) and in three eyes a epiretinal membrane was observed after DMEK (1%; 3/300) (Table 7).

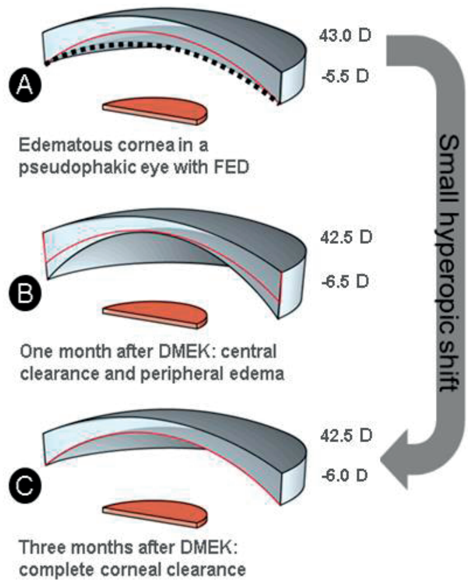

Figure 5. Diagrammatic representation of the corneal power shift in a pseudophakic eye before (A), and after DMEK (B and C). Before surgery, endothelial disease induces corneal edema, associated with flattening of the posterior corneal curvature and/or steepening of the anterior corneal surface may occur due to epithelial edema in more advanced cases. Hence, on both the anterior and posterior corneal surface a 'myopic shift' is induced by the endothelial dysfunction. In the early phase after DMEK surgery, the cornea shows central thinning while the periphery is still edematous, creating a steepening of the posterior cornea curvature and a flattening of the anterior cornea curvature, which results in a 'hyperopic shift'. As the transplanted cornea returns to a physiological hydration status, the induced hyperopic shift is again reduced, but still detectable in comparison to the preoperative power.

Secondary corneal procedures

In 35 eyes, reoperation was performed because of graft detachment (n=31) or alleged graft failure (n=4). A re-bubbling procedure was performed in 9 eyes (3%), of which only one was successful. Twenty eyes (6.7%) underwent a secondary DSEK, and 14 eyes (4.7%) had a re-DMEK (Figure 4; Table 7). All of the secondary DSEK and DMEK surgeries were successful, and visual outcomes were similar to primary DSEK or DMEK procedures.[22]

DISCUSSION

In the current study we evaluated visual performance, refractive outcome, ECD and postoperative complications of the first 300 DMEK cases. Compared to earlier EK techniques such as, DLEK and DSEK/DSAEK, our study showed that DMEK may provide significantly better visual outcomes and faster visual rehabilitation, while eliminating the most common complications associated with PK.[1,2,9,23-26]

Visual outcome and rehabilitation rate

In this study, the majority of DMEK eyes showed visual recovery in the first month after surgery with a continuing improvement up to 6 months (Figure 2). At one month after DMEK, about 90% of eyes had a BSCVA of ≥20/40 (≥0.5), a visual acuity level required for an independent lifestyle and driving. At 3 months 70% of eyes reached ≥20/25 (≥0.8). The rate of visual rehabilitation after DMEK appears to be faster as compared to DSEK/

DSAEK and PK, in which a visual acuity of ≥20/40 (≥0.5) may not be achieved before 6 or even 12 months after surgery.[2-4,23-27]

Visual rehabilitation after DMEK may also be more complete, as approximately 80% of eyes (with normal visual potential and an attached transplant) achieved a BSCVA of ≥20/25 (≥0.8) at six months and about 50% reached ≥20/20 (≥1.0), which compares favorably to visual outcomes after PK and DSEK/DSAEK. Historic studies on PK for endothelial disease reported visual results of ≥20/40 (≥0.5) at one year in 40-50% of patients.[26] Although DSEK/DSAEK may surpass PK, with mean visual outcomes up to 20/30 (0.6), only small percentages may reach ≥20/25 (≥0.8).[1-4,23-25] It has been suggested that (cultured) donor posterior stroma in DSEK/DSAEK grafts could degrade the optical quality of a transplanted cornea, possibly through a mismatch between donor and recipient cornea curvature.[2,28-30] In contrast, isolated Descemet grafts as used in DMEK may provide near normal anatomical restoration of the recipient cornea, which seems to be associated with a near normal optical performance of the transplanted cornea, with visual acuity levels up to 20/18 (1.2) or better.

Refractive change and stability

Refractive and pachymetric stability is largely obtained at approximately 3 months after DMEK, with pachymetry returning to normal and limited changes in refraction thereafter. Therefore, new glasses were usually prescribed at 3 months after surgery, while patients continued to wear their preoperative glasses in the immediate postoperative period.

Interestingly, our study showed a small pre- to postoperative hyperopic shift.[13] In DSEK/DSAEK, a hyperopic shift of +1.5D has been described, which may result from the 'negative lenticle' effect of the stroma carried by the endothelial transplant.[31] If so, no hyperopic shift would be expected after DMEK, in which only an isolated donor DM is transplanted. Surprisingly, however, a small shift of +0.33D was also found in our DMEK series, that persisted when phakic eyes were excluded from analysis (to eliminate any refractive bias induced by the crystalline lens) (Table 4). In the pseudophakic group, however, the hyperopic shift was only +0.25D, which should be of little clinical importance. Hence, DMEK may be the first technique in corneal transplantation that (on average) truly is refractive neutral. If so, intraocular lens power calculations for cataract extraction prior or during DMEK would become less critical, and even multifocal implants or accommodative intraocular lenses could be considered in suitable candidates. However, although the mean change in SE may not be of clinical significance, large differences in refractive shift were found among individuals (Tables 4 and 5), so that better refractive predictability, with more individual patients achieving emmetropia may still be pursued.

If not explained by a 'lenticle-shaped tissue effect', how is the hyperopic shift after DMEK to be explained? In our study, DMEK was associated with a -0.7D steepening of the posterior curvature and a -0.4D flattening of the anterior corneal curvature with a concurrent decrease in pachymetry. It may therefore be assumed that, pre- to postoperatively, the reversal toward a normal hydration status of the recipient cornea would largely explain the shift in SE after DMEK (Figure 5).[13,32] In eyes with mild Fuchs endothelial dystrophy, the change in anterior keratometric values may be negligible, so that routine nomograms may be used for intraocular lens power calculations. However, in more advanced cases and particularly in the presence of epithelial edema,[33] some flattening of the anterior corneal surface (ie lower keratometric values) may be anticipated for.

Endothelial cell density

At 6 months after DMEK, the ECD decreased by about 35% compared to preoperative donor cell counts, similar to values reported after DSEK/DSAEK and PK.[7,24,25,27,34-36] Since DMEK graft diameters (9.0-10.0-mm) exceed those in PK (7.0-8.0-mm) and DSEK/DSAEK (8.0-9.0-mm), more endothelium is transplanted, potentially providing longer graft survival in DMEK.

Complications

(Partial) graft detachment has been recognized as the most frequent complication in endothelial keratoplasty,[2-4,37,38] which also occurred in 31 eyes (10%) in our series. With growing experience, the incidence of detachments decreased from 20 in the first 150 cases (13%), to 11 in the second 150 cases (7%) (Table 7). This may be explained by technique adjustments and general precautions, such as a longer air-fill of the anterior chamber at the end of the surgery to support the graft and avoiding the use of plastic material.[20,39] In early cases, a 're-bubbling' procedure (repositioning of the graft by filling the recipient anterior chamber with air) was performed to manage these detachments. We have now learned that awaiting 'spontaneous corneal clearance' may be advocated because re-endothelialization of the recipient posterior stroma and subsequent restoration of the vision in the presence of a partially detached graft was observed within the first months after surgery in virtually all cases operated on for Fuchs endothelial dystrophy.[18,19,39]

An intriguing finding was the low incidence of allograft rejections in our series of only 1%, that has recently been confirmed by others.[7,40,41] Apparently, DMEK seems to be associated with a significantly lower risk of allograft rejection than with DSEK/DSAEK or PK, despite larger transplant diameters of ± 9.5mm.[40,41]

In phakic eyes, it has become common practice to first remove the crystalline lens, before commencing DSEK/DSAEK to gain a deeper anterior chamber and to facilitate tissue handling during surgery. We recently documented that there is a relatively low risk of inducing a secondary cataract and that visual outcomes may be better when an eye remains phakic.[42] Since overall patient satisfaction may also be better in these (relatively young) patients, when the accommodative functions are spared, it may be appropriate to leave the (clear) crystalline lens in-situ prior to DMEK.

Postoperative pressure elevation after DMEK may most often result from exacerbations of pre-existing glaucoma, steroid response, or secondary due to air-bubble misdirection behind the iris (after leaving a 30-50% air-fill of the anterior chamber at the end of the surgery).[43]

In conclusion, for corneal endothelial disorders, DMEK may be offered as an alternative to PK and/or DSEK/DSAEK, because it has the potential to provide faster and more complete visual rehabilitation, with only minimal changes in refraction and good refractive stability after surgery.

REFERENCES

1. Melles GRJ. Posterior lamellar keratoplasty. DLEK to DSEK to DMEK. Cornea 2006;25:879-881
2. Dapena I, Ham L, Melles GRJ. Endothelial keratoplasty: DSEK/DSAEK or DMEK - the thinner the better? Curr Opin Ophthalmol 2009;20:299-307
3. Price MO, Price FW. Descemet's stripping endothelial keratoplasty. Curr Opin Ophthalmol 2007;18:290-294
4. Gorovoy MS. Descemet-stripping automated endothelial keratoplasty. Cornea 2006;25:886-889
5. Ham L, Dapena I, van Luijk, et al. Descemet membrane endothelial keratoplasty (DMEK) for Fuchs endothelial dystrophy: review of the first 50 consecutive cases. Eye 2009;23:1990-1998
6. Ham L, Balachandran C, Verschoor CA, et al. Visual rehabilitation rate after isolated Descemet membrane transplantation: Descemet membrane endothelial keratoplasty (DMEK). Arch Ophthalmol 2009;127:252-5
7. Price MO, Giebel AW, Fairchild KM, Price FW Jr. Descemet's membrane endothelial keratoplasty: prospective multicenter study of visual and refractive outcomes and endothelial survival. Ophthalmology 2009;116:2361-2368
8. Studeny P, Farkas A, Vokrojova M, et al. Descemet membrane endothelial keratoplasty with a stromal rim (DMEK-S). Br J Ophthalmol 2010;94:909-914
9. Bahar I, Kaiserman I, McAllum P, et al. Comparison of posterior lamellar keratoplasty techniques to penetrating keratoplasty. Ophthalmology 2008;115:1525-1533
10. Dirisamer M, Ham L, Dapena I, et al. Efficacy of Descemet membrane endothelial keratoplasty: Clinical outcome of 200 consecutive cases after a learning curve of 25 cases. Arch Ophthalmol 2011;129:1435-1443
11. McCauley MB, Price MO, Fairchild KM, et al. Prospective study of visual outcomes and endothelial survival with Descemet membrane automated endothelial keratoplasty. Cornea 2011;30:315–319
12. Guerra FP, Arundhati A, Price MO, et al. Descemet's membrane endothelial keratoplasty: Prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology 2011;118:2368-2373.
13. Ham L, Dapena I, Moutsouris K, et al. Refractive change and stability after Descemet membrane endothelial keratoplasty (DMEK). J Cataract Refract Surg 2011;37:1455–1464
14. Lie JT, Birbal R, Ham L, et al. Donor tissue preparation for Descemet membrane endothelial keratoplasty. J Cataract Refract Surg 2008;34:1578-1583
15. Dapena I, Moutsouris K, Droutsas K, et al. Standardized 'no touch' technique for Descemet's membrane endothelial keratoplasty (DMEK). Arch Ophthalmol 2011;129:88-94
16. Melles GRJ, Wijdh RH, Nieuwendaal CP. A technique to excise the descemet membrane from a recipient cornea (descemetorhexis). Cornea 2004;23:286-288
17. Benjamini Y, Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. J R Statist Soc B 1995;57:289-300
18. Balachandran C, Ham L, Verschoor CA, et al. Spontaneous corneal clearance despite graft detachment in Descemet membrane endothelial keratoplasty (DMEK). Am J Ophthalmol 2009;148:227-234
19. Dirisamer M, Dapena I, Ham L, et al. Patterns of corneal endothelialization and corneal clearance after Descemet membrane endothelial keratoplasty for Fuchs endothelial dystrophy. Am J Ophthalmol 2011;152:543–555
20. Ham L, van der Wees J, Melles GR. Causes of primary donor failure in Descemet membrane endothelial keratoplasty. Am J Ophthalmol 2008;145:639-644
21. Dapena I, Ham L, Tabak S, et al. Phacoemulsification after Descemet membrane endothelial keratoplasty. J Cataract Refract Surg 2009;35:1314-1315

22. Dapena I, Ham L, van Luijk C, et al. Back-up procedure for graft failure in Descemet Membrane Endothelial Keratoplasty (DMEK). Br J Ophthalmol 2010;94:241-244
23. Chen ES, Terry MA, Shamie N,et al. Descemet-stripping automated endothelial keratoplasty: six month results in a prospective study of 100 eyes. Cornea 2008;27:514-520
24. Koenig SB, Covert DJ, Dupps WJ Jr, Meisler DM. Visual acuity, refractive error, and endothelial cell density six months after Descemet stripping and automated endothelial keratoplasty (DSAEK). Cornea 2007;26:670-674
25. Mearza AA, Qureshi MA, Rostron CK. Experience and 12-month results of Descemet-stripping endothelial keratoplasty (DSEK) with a small-incision technique. Cornea 2007;26:279-283
26. Williams KA, Muehlberg SM, Lewis RF, Coster DJ. How successful is corneal transplantation? A report from the Australian Corneal Graft Register. Eye 1995;9:219-227
27. Guerra FP, Arundhati A, Price MO, Price FW. Endothelial keratoplasty: Fellow eyes comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. Cornea 2011;30(12):1382-1386
28. Ham L, Dapena I, van der Wees J, Melles GR. Secondary DMEK for poor visual outcome after DSEK: donor posterior stroma may limit visual acuity in endothelial keratoplasty. Cornea 2010;29:1278-1283
29. Moutsouris K, Ham L, Dapena I, et al. Radial graft contraction may relate to subnormal visual acuity in Descemet stripping (automated) endothelial keratoplasty. Br J Ophthalmol 2010;94:951-953
30. Giebel AW, Price FW. Descemet's membrane endothelial keratoplasty: the bare minimum. In: Price FW Jr, Price MO, eds. DSEK: What you need to know about Endothelial keratoplasty. Thorofare, NJ: Slack Incorporated; 2009:119-146
31. Dupps WJ Jr, Qian Y, Meisler DM. Multivariate model of refractive shift in Descemet-stripping automated endothelial keratoplasty. J Cataract Refract Surg 2008;34:578–584
32. Brunette I, Sherknies D, Terry MA, et al. 3-D Characterization of the corneal shape in Fuchs dystrophy and pseudophakic keratopathy. Invest Ophthalmol Vis Sci 2011;52:206-214
33. Borboli S, Colby K. Mechanisms of disease: Fuchs' endothelial dystrophy. Ophthalmol Clin North Am 2002;15:17-25
34. Parker J, Dirisamer M, Naveiras M, et al. Endothelial cell density after Descemet membrane endothelial keratoplasty: 4-year follow-up. Am J Ophthalmol 2011;15:1107e2
35. Terry MA, Shamie N, Chen ES, et al. Precut tissue for Descemet's stripping automated endothelial keratoplasty: vision, astigmatism, and endothelial survival. Ophthalmology 2009;116:248-256
36. Price MO, Price FW Jr. Endothelial cell loss after Descemet stripping with endothelial keratoplasty influencing factors and 2-year trend. Ophthalmology 2008;115:857-865
37. Dapena I, Moutsouris K, Ham L, Melles GR. Graft detachment rate. Ophthalmology 2010;117:847e1
38. Suh LH, Yoo SH, Deobhakta A, et al. Complications of Descemet stripping with automated endothelial keratoplasty: survey of 118 eyes at one institute. Ophthalmology 2008;115:1517-1524
39. Dirisamer M, Van Dijk K, Dapena I, et al. Prevention and management of graft detachment in Descemet membrane endothelial keratoplasty. Arch Ophthalmol 2012;130:280-291
40. Dapena I, Ham L, Netukova M, et al. Incidence of early allograft rejection after Descemet membrane endothelial keratoplasty. Cornea 2011;30:1341-1345
41. Anshu A, Price MO, Price FW jr. Risk of corneal transplant rejection significantly reduced with Descemet's membrane endothelial keratoplasty. Ophthalmology 2012;119:536-540
42. Parker J, Dirisamer M, Naveiras M, et al. Outcome of Descemet membrane endothelial keratoplasty in phakic eyes. J Cataract Refr Surg 2012;38:871-877
43. Naveiras M, Dirisamer M, Parker J, et al. Causes of glaucoma after Descemet membrane endothelial keratoplasty. Am J Ophthalmol 2012; 153:958-966