Recent innovations in minimally invasive anterior and posterior lamellar keratoplasty

Parker, J.

Chapter 8

Outcome of Descemet membrane endothelial keratoplasty in phakic eyes

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ABSTRACT

Purpose: To determine the clinical outcome of isolated Descemet membrane transplantation, i.e. Descemet membrane endothelial keratoplasty (DMEK), in phakic eyes.

Setting: Non-randomized, prospective clinical study, at a tertiary referral center.

Methods: From a larger group of consecutive 260 DMEK eyes that underwent DMEK for Fuchs endothelial dystrophy, 52 eyes were phakic. For the latter group, the best corrected visual acuity (BCVA), subjective and objective refractive data, endothelial cell density, and intra- and postoperative complications were documented at 1, 3 and 6 months.

Results: A total of 69% of phakic eyes reached a BCVA of ≥20/40 (≥0.5) within one week, and 85% reached ≥20/25 (≥0.8) at six months. Compared to an age-matched control group of pseudophakic eyes, phakic DMEK eyes showed a similar visual rehabilitation rate, final visual outcome, and endothelial cell densities of 1660 (±470) cells/mm^2 at 6 months follow-up, as well as a minor hyperopic shift (+0.74D) and a similar graft detachment rate (4%). Visual outcomes of ≥20/13 (≥1.5) were limited to phakic eyes, suggesting better optical quality with the crystalline lens in-situ. Temporary mechanical angle-closure glaucoma due to air bubble dislocation behind the iris was found to be the main complication (11.5%). Two eyes (4%) required phaco-emulsification after DMEK.

Conclusion: DMEK in phakic eyes may give excellent visual outcomes without an increased risk of complications. Visual acuities of ≥20/13 (≥1.5) may indicate that near normal anatomical repair in DMEK is associated with near perfect optical quality of the transplanted cornea.

KEYWORDS: Crystalline lens, Descemet membrane endothelial keratoplasty, posterior lamellar keratoplasty, corneal transplantation, Descemet membrane, endothelium, surgical technique

INTRODUCTION

Since 1998, we have introduced various techniques for endothelial keratoplasty, later popularized as 'deep lamellar endothelial keratoplasty' (DLEK), and Descemet stripping (automated) endothelial keratoplasty (DSEK/DSAEK).[1,2] More recently we described a technique for the selective transplantation of a donor Descemet membrane, now referred to as Descemet membrane endothelial keratoplasty (DMEK).[3,4]

To perform these various types of endothelial keratoplasty, a sufficiently deep recipient anterior chamber is required to maneuver the graft in position against the recipient posterior stroma.[5] Since removal of the crystalline lens also deepens the anterior chamber, there is a trend to routinely perform a cataract extraction prior or during the transplantation surgery. This is especially true given that the main indication for endothelial keratoplasty is a Fuchs endothelial dystrophy, many of which are accompanied by some degree of cataract that may be aggravated by the corneal surgery or the prolonged postoperative (steroid) medication.[6-8]

Clinical observation, however, suggests that 'phakic eyes do better' after endothelial keratoplasty, i.e. sparing the crystalline lens appears to be associated with higher visual outcomes.[9,10] This finding might be explained by bias due to selection of younger patients who on average have higher visual potential or a lower incidence of co-morbidity. On the other hand, cataract extraction could also induce some degradation of the optical quality of the eye, for example by posterior capsule opacification, loss of accommodation, and/or a change in the optical properties of the lens system.

In the current prospective study, we therefore prospectively evaluated the clinical outcome of 52 phakic DMEK eyes up to 6 months after surgery to determine what (dis) advantages may be associated with sparing the (clear) crystalline lens in DMEK.

MATERIALS AND METHODS

From a larger group of 260 eyes that underwent DMEK to manage Fuchs endothelial dystrophy, 52 eyes were phakic of which 48 consecutive phakic eyes of 43 patients, 24 male and 19 female, were enrolled in our prospective study. The average age was 52 (± 7) years (range 33 to 67) (**Table 1**). Two eyes were excluded from the visual acuity analysis because of graft detachment after DMEK, and two eyes were lost to follow-up.[11-12] From the larger group of 260 eyes that underwent DMEK to manage Fuchs endothelial dystrophy, we selected a group of 47 pseudophakic patients, which constituted the control-group in this study and age-matched the group of 48 phakic patients. The average age in the control group was 60 (± 5) years (range 48 to 66 years). All patients signed an IRB-approved informed consent.

Table 1. Demographics of phakic DMEK patients

Demographics of phakic DMEK patients		
Number of phakic patients	43	-
Number of phakic eyes	48	-
Mean age (yrs)	52.4 (±6.7)	-
Number of men/women	24/19	56/44%

Donor tissue

From donor globes obtained less than 24 hours post mortem, corneo-scleral buttons were excised and stored by organ culture in modified minimum essential medium (EMEM) 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 with a suction cup. Descemet's membrane (DM) was stripped from the posterior stroma, so that a 9.5 mm diameter flap of posterior DM with its endothelial monolayer was obtained.[13] Due to the elastic properties of the membrane, a 'Descemet-roll' formed spontaneously, with the endothelium at the outer side. Each Descemet–roll was then stored in organ culture medium until the time of transplantation.

Surgery

Surgeries were performed under retrobulbar anaesthesia, as previously described.[2-4] A 3.0 mm tunnel incision was made at the limbus, entering the anterior chamber approximated 3.0 mm within the clear cornea. With an inverted Sinskey hook (D.O.R.C. International, Zuidland, The Netherlands), a circular portion of DM was scored and stripped from the posterior stroma, so that a 9.0 mm diameter 'descemetorhexis' was created, and the central portion of DM was removed from the eye.[14]

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 (D.O.R.C International), to transfer the tissue from the culture medium vial to the anterior chamber.[4] Using the injector, the donor Descemet-roll was inserted into the anterior chamber and the graft was oriented endothelial side down (donor DM facing recipient posterior stroma) by careful, indirect manipulation of the tissue with air and fluid. While maintaining the anterior chamber with fluid and air, the graft was gently spread out over the iris. Then, an air bubble was injected underneath the donor DM to position the tissue onto the recipient posterior stroma.[4] The anterior chamber was completely filled with air for 45-60 minutes followed by an air-liquid exchange to pressurize the eye.

Data collection and Statistical analysis

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). In patient eyes, ECD was evaluated in-vivo 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.

Recipient eyes were examined before and after DMEK at 1, 3 and 6 months with biomicroscopy, Pentacam imaging (Oculus, Wetzlar, Germany), non-contact specular microscopy, and slit-lamp photography (Topcon Medical Europe BV). BCVA, ECD, as well as intraoperative and postoperative complications were recorded in a database.

Both the 'relative' and 'absolute' refractive changes were considered relevant to our study. To detect the presence or absence of a hyperopic shift, the myopic and hyperopic shift in spherical equivalent were averaged to show the relative, overall tendency in refractive change. The absolute change, whether in myopic or hyperopic direction, may illustrate the clinical impact of the refractive change.

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).[15] After correction, all P-values <0.05 represented statistical significance. Repeated measures AN(C)OVA (PASW Statistics 18) were used to test whether the pre- to postoperative decline in ECD and the pre- to postoperative change in logMAR visual acuity differs between the phakic group and the age matched pseudophakic control group.

RESULTS

Best corrected visual acuity (BCVA)

At six months, all eyes (100%) reached a BCVA of ≥20/40 (≥0.5), 85% ≥20/25 (≥0.8), 67% ≥20/20 (≥1.0), and 21% ≥20/17 (≥1.2) (n=48) (**Figure 1**). At one week these percentages were respectively 69%, 35%, 19%, and 0%; at 1 month 98%, 73%, 44%, and 4% and at 3 months 98%, 77%, 58% and 10% (**Figure 1**). The BCVA of the phakic eyes did not differ from that in age-matched pseudophakic eyes (*P*>0.1) (**Figure 1**).

Spherical equivalent of subjective refraction

The manifest spherical equivalent averaged -0.76D (±2.2 D) before surgery, 0.01D (±2.1D) at three months, and -0.02D (±2.1D) at six months after surgery (n=43) (**Table 2a**). Hence, the pre- to postoperative change in spherical equivalent (hyperopic and myopic shifts in corneal power averaged) was +0.77D (±0.8D) at three months (*P*=0.0000) and +0.74D (±0.8D) at six months (*P*=0.0000) (n=43) (**Table 2a**). The pre- to postoperative absolute change in spherical equivalent (absolute change in corneal power) averaged 0.96D (±0.6D) at three months and 0.84D (±0.7D) at six months (n=43) (**Table 2a**).

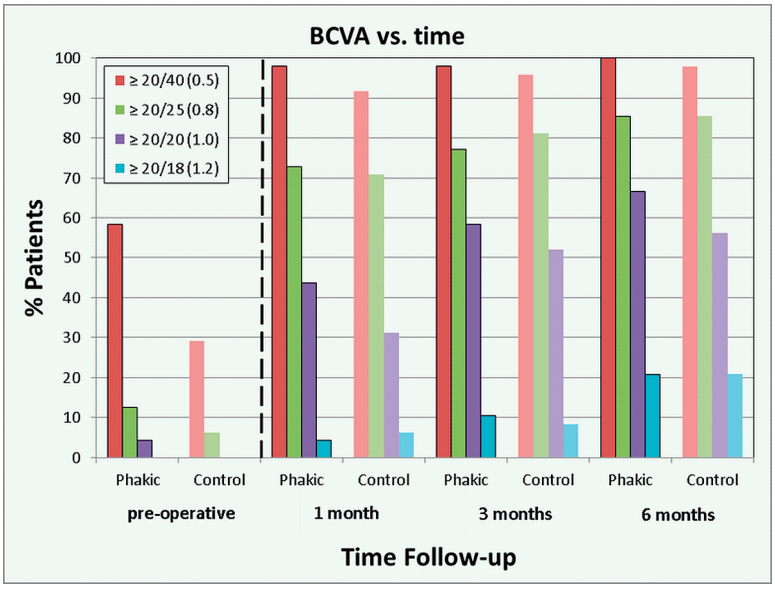

Figure 1. Graph displaying the best corrected visual acuity (BCVA) of all phakic eyes and the age-matched pseudophakic controls before and at 1, 3, and 6 months after DMEK surgery.

Table 2a

Subjective refractive outcome DMEK in phakic eyes (D) *n=43*[a]																		
	Pre-operative			3m postoperative			6m postoperative			ΔSE 3m vs preop	ΔSE 3m vs preop absolute	ΔSE 6m vs preop	ΔSE 6m vs preop absolute	ΔSE 6m vs 3m	Δ Cyl 3m vs preop	Δ Cyl 3m vs preop absolute	Δ Cyl 6m vs preop	Δ Cyl 6m vs preop absolute	ΔCyl 6m vs 3m
	SE	Sp	Cyl	SE	Sp	Cyl	SE	Sp	Cyl										
Average	-0.76	-0.26	-1.02	0.01	0.54	-1.07	-0.02	0.51	-1.05	0.77	0.96	0.74	0.84	-0.03	-0.05	0.87	-0.03	0.81	0.02
SD	2.2	2.2	1.0	2.1	2.3	0.9	2.1	2.1	1.0	0.8	0.6	0.8	0.7	0.7	1.1	0.7	1.0	0.6	0.8

Cylindric error of subjective refraction

The refractive cylinder averaged -1.02D (±1.0D) before surgery, -1.07D (±0.9D) at three months, and -1.05D (±1.0D) at six months after surgery (n=43) (**Table 2a**). Hence, the pre- to postoperative change in refractive cylinder (hyperopic and myopic shifts in cylindric power averaged) was -0.05D (±1.1D) at three months (*P*= 0.7581) and -0.03D (±1.0D) at six months (*P*=0.8214) (n=43) (**Table 2a**). The pre- to postoperative absolute change

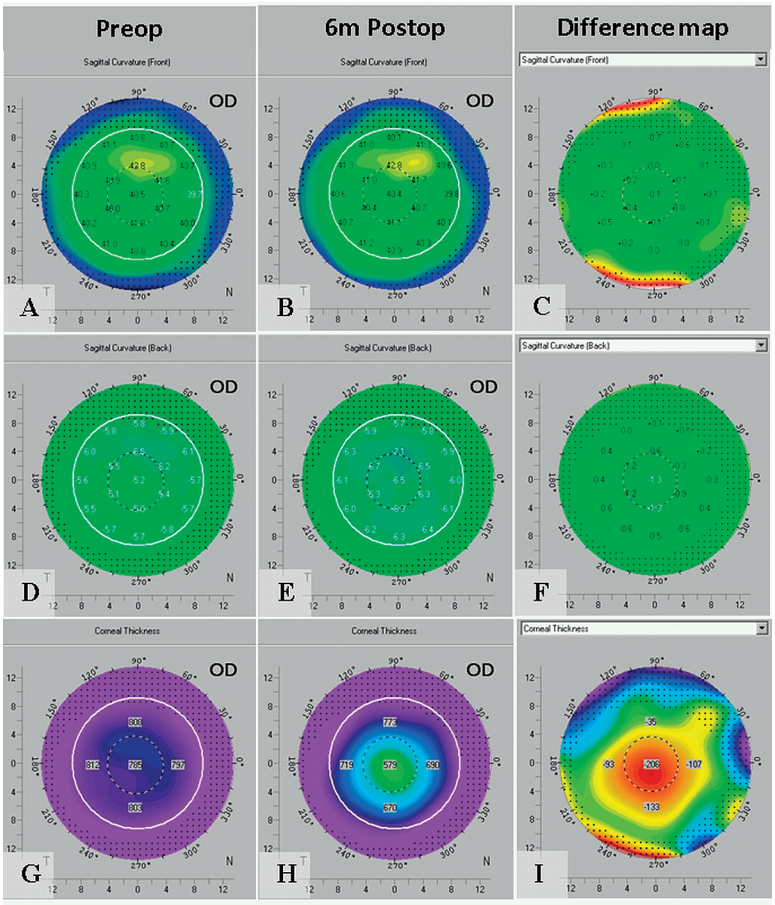

Figure 2. Topographic corneal power maps of the anterior corneal curvature (A-C), the posterior corneal curvature (D-F), and the corneal pachymetry (G-I) before DMEK (A, D and G), 6 months after DMEK (B, E, and H), and the difference maps (C, F and I). Note that the anterior corneal curvature is stable but the posterior curvature change of approximately 1.0D. Compare to Table 3a.

in refractive cylinder (absolute change in cylindric power) averaged 0.87D (±0.7D) at three months and 0.81D (±0.6D) at six months (n=43) (**Table 2a**).

Stability of refraction

The change in spherical equivalent before and at six months after surgery was ≤0.5D in 37% (16/43) of eyes and ≤1.0D in 61% (26/43) (**Table 2b**). The change in cylindric error before and at six months after surgery was ≤1.0D in 67% (29/43) of eyes (**Table 2b**).

From the three to six months postoperative time interval, 74% (32/43) of eyes did not show more than a 0.5D change in spherical equivalent, and 88% (38/43) was ≤1.0D (**Table 2b**).

Table 2b

Stability of refraction after DMEK in phakic eyes (D) *n= 43*[a]				
ΔSE 6m vs pre-op		ΔCyl 6m vs preop	ΔSE 6m vs 3m	
≤0.5D	≤1.0D	≤1.0D	≤0.5D	≤1.0D
37% 16/43	61% 26/43	67% 29/43	74% 32/43	88% 38/43

[a]n=43, because for 5 out of 48 patients no complete refractive dataset was available

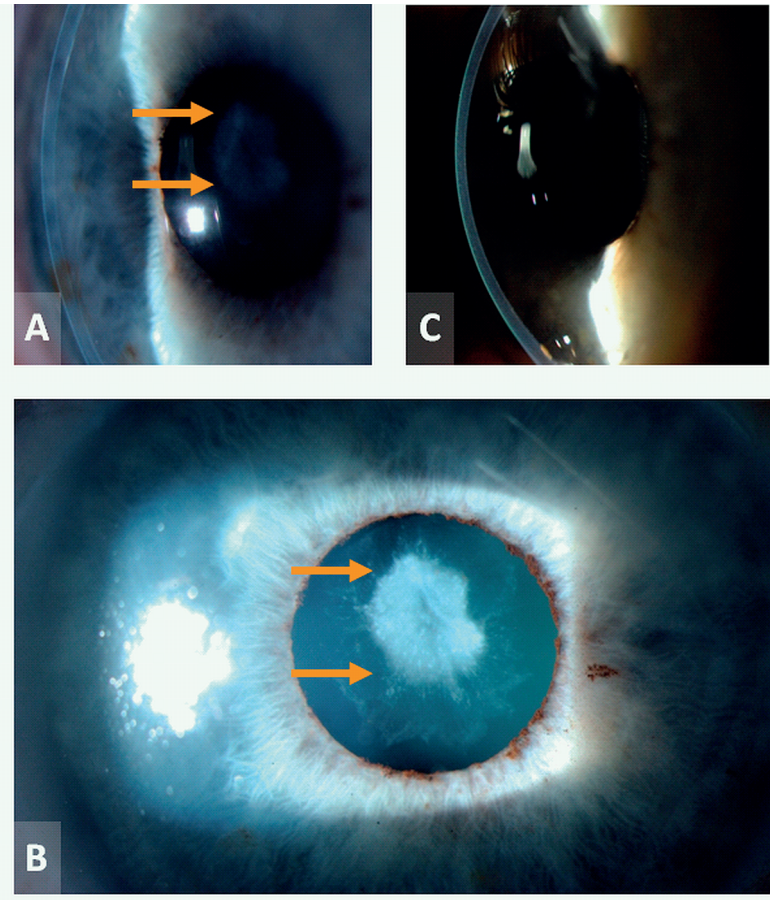

Figure 3. (A and B) Slit-lamp photographs of a cornea 6 months after DMEK complicated by air bubble dislocation behind the iris and air-bubble induced mechanical angle-closure glaucoma in the immediate postoperative phase. Note the anterior subcapsular cataract (orange arrows) for which a secondary phaco-emulsification was performed. (C) Three months after phacoemulsification (9 months after the initial DMEK), the Descemet graft is attached and functional.

Objective corneal power measurements

Using Pentacam topographic corneal power maps, the 'True Net Power' keratometric values were 42.8D (±2.3D) before surgery (n=45), 41.0D (±1.5D) at three months (n=41) (*P*=0.0000), and 41.0D (±1.5D) at six months after surgery (n=45) (*P*=0.0000). Anterior keratometric values changed from 43.2D (±1.7D) before (n=45), to 42.5D (±1.4D) at three months (n=41) (*P*=0.0000) to 42.5D (±1.5D) at six months after surgery (n=45) (*P*=0.0009), but posterior keratometric values increased from 5.4D (±0.7D) before surgery (n=45) to 6.4D (±0.3D) at three months (n=41) to 6.3D (±0.3D) at six months after surgery (n=45) (*P*=0.0000) (**Figure 2; Table 3a**).

Table 3a

Objective refractive outcome DMEK in phakic eyes (D) Pentacam measurements					
	Pre-operative (n=45)[a]	3m postoperative (n=41)[b]	6m postoperative (n=45)[a]	ΔK mean 3m vs preop	ΔK mean 6m vs preop
Average True Net Power	42.8	41.0	41.0	1.75	1.78
SD	2.3	1.5	1.5	0.83	0.76
P=				**0.0000**	**0.0000**
Average Cornea Front	43.2	42.5	42.5	0.75	0.74
SD	1.7	1.4	1.5	0.33	0.25
P=				**0.0000**	**0.0009**
Average Cornea Back	5.4	6.4	6.3	0.93	0.91
SD	0.7	0.3	0.3	0.42	0.37
P=				**0.0000**	**0.0000**

Pachymetry

Pentacam pachymetry measurements decreased from 665µm (±103µm) before surgery (n=45), to 510µm (±39µm) at three months (n=41) (*P*=0.0000), and 520µm (±44µm) at six months (n=45, *P*= 0.0000, **Table 3b**).

Table 3b

Central pachymetry after DMEK (µm) Pentacam measurements					
	Pre-operative (n=45)[a]	3m postoperative (n=41)[b]	6m postoperative (n=45)[a]	Δ pachymetry 3m vs preop	Δ pachymetry 6m vs preop
Pachymetry	665	510	520	155	145
SD	103	39	44	64	59
P=	-	-	-	**0.0000**	**0.0000**

Endothelial cell density

In phakic eyes, endothelial cell density averaged 2560 (±170) cells/mm^2 before surgery (n=46), and 1660 (±470) cells/mm^2 (n=46) at six months postoperative. The decline in ECD at six months was similar to that in the age corrected control group of pseudophakic DMEK eyes (n=47), which showed an average endothelial cell density of 2580 (±190) cells/mm^2 before surgery and 1660 (±500) cells/mm^2 (n=47) at six months postoperative. The ECD and cell loss of the phakic group was similar to the age-matched pseudophakic control group (*P*>0.1) (**Table 3c**).

Table 3c

Endothelial cell density (cells/ mm^2)		
	Phakic	Pseudophakic
Pre-op	2560 (±170)	2580 (±190)
6 m post-op	1660 (±470)	1660 (±500)
Cell loss (%)	35.4	35.5
N=	46[c]	47

[a]n=45, because for 3 out of 48 patients no preoperative and/or 6m postoperative Pentacam data were available

[b]n=41, because for 7 out of 48 patients no 3m postoperative Pentacam data were available

[c]n=46, because for 2 out of 48 patients no 6m postoperative ECD data were available

Side effects and complications

From a total of 52 phakic DMEK eyes, two eyes (4%) required phaco-emulsification at six months and 2.5 years after the initial DMEK surgery. Both of these eyes had developed anterior subcapsular opacifications within the first month after surgery, attributed to air bubble misdirection behind the iris in the immediate postoperative phase, causing mechanical angle-closure glaucoma in one case (**Figure 3**). Both phaco-emulsification procedures were uneventful and no graft displacements or other graft related problems were encountered.

Five other eyes (10%) showed a faint haze over the anterior lens capsule (similar to Glaukom-flecken) after surgery that may have been induced by air bubble trauma during or at the end of the DMEK procedure. Of these five eyes, all had at least 6 months of follow up, and the BCVA appeared similar to that of the overall group of phakic eyes: 100% reached ≥20/40 (≥0.5), 80% (4/5) ≥20/25 (≥0.8), 60% (3/5) ≥20/20 (≥1.0), and 20% (1/5) ≥20/18 (≥1.2).

Mechanical angle-closure glaucoma due to air bubble misdirection behind the iris in the immediate postoperative phase, was observed in a total of six eyes (11.5%) In all of these eyes, the air had shown a tendency to move underneath the iris during surgery. Another eye with pre-existing open-angle glaucoma presented with intermittent glau-

comatous crises within the first half year after surgery, for which secondary glaucoma surgery was performed.

Graft detachment occurring in two eyes (4%), was managed by a secondary DMEK in one eye, while the other eye showed corneal clearance despite graft attachment.[11-12] Other potential complications, such as primary or secondary graft failure, or allograft rejection did not occur in this series.

DISCUSSION

Clinical impression suggest that "phakic eyes do better" after DMEK surgery, as has also been reported after DSEK/DSAEK.[10] In the current study, however, we were not able to substantiate this observation: for the two main outcome criteria, the six months BCVA and the endothelial cell density, no overall difference could be found between the phakic DMEK eyes and an age-matched pseudophakic control group. In this age group, 85% of eyes reached a BCVA of ≥20/25 (≥0.8) within 6 months post-operative.

If all of the above is taken in consideration, should it be advocated to leave the crystalline lens in situ in the absence of a cataract? In DSEK/DSAEK, many corneal surgeons prefer to routinely perform a phaco-emulsification prior or during transplantation, because a deeper anterior chamber may facilitates tissue handling and in particular unfolding of the graft. After DSEK/DSAEK, cataract formation has been described to occur in about 37% of cases, however, when corrected for age (<50 yrs) the actual incidence reported was 7%.[10] In our series, only two DMEK eyes (4%) developed a clinically significant cataract, and with the standardized surgical technique currently available,[4] there may be little to gain by making the eye pseudophakic prior to DMEK. In addition, while reviewing the patients files, two rather subjective findings could explain our clinical impression that phakic eyes show better outcomes.

First, although statistical analysis did not show a difference in average BCVA between both groups, phakic eyes were frequently found to obtain visual acuities above 20/18 (>1.2), while none of the age-matched pseudophakic eyes reached this level of sight. This finding may suggest that, compared to a phakic eye, the optical system of the pseudophakic DMEK eye is somehow compromised. Furthermore, this finding may indicate that the anatomical restoration of the transplanted cornea after DMEK may allow for a near perfect optical quality of that cornea, because even minor aberrations would quickly limit the final visual acuity, even in virgin eyes. Second, the age-group eligible for sparing the (clear) crystalline lens (30-60 years of age) may still benefit from the accommodative power of the eye. For that reason the overall satisfaction with the DMEK procedure may be higher, i.e. when performed to manage an isolated Fuchs endothelial dystrophy, complete visual rehabilitation is commonly achieved, and also perceived as

such by the patient. It may be important to note that higher visual outcomes are associated with higher visual demands, so that relatively minor optical aberrations will be perceived as more disturbing to a patient.

Clinically, most DMEK patients continue to wear their 'own' glasses in the first months after surgery. This may be explained by the minor change in refractive power associated by the DMEK procedure: in about ⅔ of eyes of both the spherical equivalent and the cylindrical error were within 1.0D from the preoperative refractive error, partially due to a +0.74D refractive shift in hyperopic direction induced by stromal dehydration.[16] Pachymetry and refractive data demonstrated that the transplanted cornea stabilizes approximately three months after DMEK, so new glasses could usually be prescribed at this time point.

Detachment of the Descemet graft from the recipient posterior stroma may be the most common complication after endothelial keratoplasty.[17,18] During the 'learning curve period' in DMEK, graft detachment occurred in 10-20% of cases but declined to 2-5% or less with experience.[19,20] In the current series of phakic DMEK eyes, a similar graft detachment rate was found, i.e. 4% (two eyes). The most striking complication in our study was mechanical angle-closure glaucoma due to air bubble misdirection behind the iris in the immediate postoperative phase, occurring in six eyes (11.5%). In one of these eyes, the air-bubble dislocation seemed to have caused an anterior subcapsular cataract reducing BCVA to 20/40 (0.5) requiring secondary phaco-emulsification. In all of these six eyes, the air had already shown a tendency to move underneath the iris *during* surgery. Hence, to avoid this type of secondary angle-closure glaucoma, it may be advocated to reduce the final air-bubble size to approximately 25% or to remove all intracameral air at the termination of the surgery if the air tends to dislocate underneath the iris during surgery.

A YAG-laser iridotomy routinely made 1-2 weeks before the DMEK surgery may have prevented the occurrence of true pupillary block glaucoma in our series (since mechanical angle closure glaucoma induced by air-bubble misdirection does not result from a blockage of the pupillary outflow). One eye, however, developed clinically significant cystoid macular edema after the YAG-laser iridotomy that subsided over a period of 2 months. In another eye, pre-existing open-angle glaucoma may have been aggravated into intermittent glaucomatous crises by the DMEK surgery,[17] possibly by peripheral anterior synecchiae, perioperative inflammation, or the steroid medication.[21] No other glaucomatous or posterior segment complications were seen in this series, nor any other graft related problems such as primary or secondary graft failure, or allograft rejection. Therefore, because the latter cases may be considered incidental and mechanical angle-closure glaucoma can be avoided, DMEK in phakic eyes may be associated with a relatively low risk of complications.

SUMMARY

What was known before:

- In phakic eyes prior to endothelial transplantation, it is common practice to first remove the patient's crystalline lens, even in the absence of a cataract. This measure, while believed to facilitate DSEK/DSAEK surgery, and/or to reduce subsequent cataract formation, has not been studied in DMEK patients.

What this paper adds:

- In our study, we found that DMEK can be easily performed in phakic eyes, and that leaving the crystalline lens in-situ, rarely results in secondary cataract formation.
- Since better overall optical quality may be achieved in phakic DMEK eyes, while the accommodative functions are spared, it may be considered to leave the (clear) crystalline lens in situ prior to DMEK.

ACKNOWLEDGMENTS / DISCLOSURE

IRB/IC - Study conducted in compliance with the Institutional Review Board and Informed Consent requirements, in adherence to the tenets of the Declaration of Helsinki, at the Netherlands Institute for Innovative Ocular Surgery (Study registration no N.05.14). The study was submitted to http://www.clinicaltrals.gov (Study registration no NCT00521898).

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