Learning curve of Descemet membrane endothelial keratoplasty (DMEK) worldwide – Multicenter trial on DMEK

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Abstract

Purpose: The learning curve of Descemet Membrane Endothelial Keratoplasty (DMEK), like any surgical technique, may be discouraging for novel surgeons. Our purpose was to evaluate the clinical outcome of standardized 'no-touch' DMEK and its complications during the learning curve of surgeons starting with DMEK in different centers worldwide.

Material and methods: Retrospective multicenter interventional study. DMEK was performed in 431 eyes of 401 patients diagnosed with either Fuchs endothelial Dystrophy (FED; 68%) or Bullous Keratopathy (BK; 32%). The surgeries represented the learning curve of novel surgeons in 18 different centers in 11 different countries. Best corrected visual acuity (BCVA), endothelial cell density and intra- and postoperative complications were recorded.

Results: Overall, BCVA improved in 94% of the cases, remained unchanged in 4% and deteriorated in 2%. Visual acuity data up to 6 months were pooled and showed that 79% reached a BCVA of ≥20/40 (≥0.5), 43% ≥20/25 (≥0.8), and 22% ≥20/20 (≥1.0). Average decrease in endothelial cell density at 6 months was 47% with a wide variation between different centers. Intraoperative complications were rare (1%), including difficulties in inserting, unfolding or positioning of the graft. The main postoperative complication was graft detachment (35%); 20% underwent a single re-bubbling procedure, occasionally requiring a second (3%) or a third re-bubbling (1%) and 18% underwent a secondary keratoplasty. Regression analysis indicated that the type of inserter, the graft storage medium and the airbubble time may affect graft detachment incidence.

Conclusions: This first multicenter DMEK trial worldwide showed that the standardized DMEK technique was feasible in most hands. Surgeons starting with DMEK achieved results comparable to more experienced groups and were encouraged to continue. Differentiations in the technique may (or may not) affect the outcome. When successful, the visual outcome after DMEK may be relatively independent of the technique's learning curve.

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Since 1998, the Netherlands Institute for Innovative Ocular Surgery (NIIOS) introduced various techniques for endothelial keratoplasty, currently referred to as deep lamellar endothelial keratoplasty (DLEK), Descemet stripping (automated) endothelial keratoplasty (DSEK/DSAEK), and Descemet membrane endothelial keratoplasty (DMEK).[1-6] The latter technique, in which only the donor Descemet membrane (DM) and its endothelium are transplanted, allows for better outcomes than all other keratoplasty techniques currently available, with 94% of eyes reaching a best (spectacle) corrected visual acuity (BCVA) of ≥20/40 (0.5), while 77% reach ≥20/25 (0.8), and 47% ≥20/20 (1.0) within 6 months.[7,8]

With DLEK and DSEK/DSAEK, we noticed that surgeons were sometimes unable to successfully start with these techniques, owing to difficulties with donor tissue preparation and/or a lack of technique standardization. With DMEK, we therefore designed both the technique for preparing the

donor DM and the surgery itself, as standardized 'no-touch' procedures.[9,10] The first DMEK outcomes of former NIIOS course participants were collected in order to document their experiences in starting out with DMEK as well as to evaluate its clinical outcome.

Because recognition of the problems and complications associated with commencing with a new procedure may enable further technique improvements, recommendations and/or logistic support, the aim of our study was to evaluate the clinical outcome of 431 DMEK eyes, i.e. the first clinical series of 18 different surgeons, located in 11 different countries.

Keywords: Descemet membrane endothelial keratoplasty, Fuchs endothelial dystrophy, bullous keratopathy, surgical technique.

Materials and Methods

A total of 431 eyes of 401 patients that underwent DMEK for endothelial disorders from July 2008 to April 2012 were analyzed retrospectively (Table 1). Surgeries were performed in 18 different centers in 11 different countries (Figure 1). The average number of DMEK surgeries performed per surgeon was 24. Patients signed an institutional review board approved informed consent. The study was conducted in accordance with the Declaration of Helsinki.

Table 1: Demographics of patients included in the multicenter trial

	No. (%) (n=431 eyes)
Patients	401
Mean age (SD), [range in years]	70 (11%) [21-97]
Men	162 (40%)
Women	239 (60%)
Lens condition	
Pseudophakic	*358 (83%)*
Phakic	*69 (16%)*
Aphakic	*3 (1%)*
Unknown	*1 (0.2%)*
Indication	
Fuchs Endothelial Dystrophy	*294 (68%)*
BK	*137 (32%)*
-Pseudophakic BK	*122 (28%)*
*-Secondary BK**	*15 (4%)*

SD; Standard Deviation
BK; Pseudophakic Bullous Keratopathy
**penetrating keratoplasty failure, surgical trauma, herpes, argon laser iridotomy, DMEK failure*

Figure 1. Participating Centers

1. Instituto Oftalmológico Fernández-Vega, Universidad de Oviedo, Spain
2. Augentagesklinik und Laserzentrum Hamburg, Germany
3. Centro Oftalmologico Sertãozinho, Brazil
4. Gemini Eye Clinic Zlin, Czech Republic
5. Callahan Eye Hospital, Birmingham, Alabama, USA
6. Heinrich-Heine-Universität Dusseldorf, Germany
7. Augenklinik am Neumarkt Köln, Germany
8. Cornea Bank Mainz, Germany
9. Noor Ophthalmology Research Center, Tehran, Iran
10. Kanazawa University, Japan
11. Hospital Ramon y Cajal Madrid, Spain
12. Moscow Helmholtz Eye Research Institute, Russia
14. AKh Linz, Austria
13. Clinica Palmaplanas, Palma de Mallorca, Spain
15. Banco de Olhos de Sorocaba, Brazil
16 University Eye Clinic Genova, Italy
17. Philipps University Marburg, Germany
18. Tuen Mun Eye Center Hong Kong, China
Coordination: Netherlands Institute for Innovative Ocular Surgery, Rotterdam, The Netherlands

Donor preparation

Preparing an isolated DM-graft was performed by stripping the DM from a corneo-scleral rim (NIIOS technique) by 15 surgeons in 385/431 (89%) surgeries.[10] One surgeon employed the 'submerged cornea using backgrounds away' (SCUBA) technique 5/431 (1%), one surgeon a combination of both techniques 25/431 (6%), and one surgeon used an air-bubble to separate the DM from a corneo-scleral rim 16/431 (4%).[11, 12] Twelve surgeons prepared 282/431 (65%) of the grafts themselves immediately prior or up to six days before surgery, two surgeons (42/431 grafts; 10%) used grafts prepared by an eye bank up to one week before surgery; in four surgeons (107/431 grafts; 25%) preparation differed per surgery (Table 2). Preparation of the DMEK

Table 2. Variations of the applied surgical technique

Type of technique	No. of surgeons (n=18)	No. of eyes (% of total eyes) (n=431)	
Donor preparation			
Pre-dissected by eye bank	2	42	(10%)
Pre-dissected by surgeon			
Up to 6 days before surgery	*3*	*60*	*(14%)*
Shortly before surgery	*9*	*222*	*(52%)*
Pre-dissection by both eye bank and surgeon	4	107	(25%)
Peripheral iridotomy			
Yes, prior to surgery	7	163	(38%)
Yes, during surgery	4	87	(20%)
No	7	181	(42%)
Graft diameter			
9.5 mm	15	365	(85%)
8.0 – 8.5 mm	3	66	(15%)
Graft injection			
Glass pipet (glass material)	10	179	(42%)
IOL injector (plastic material)	5	72	(17%)
Glass cannula (glass material)	1	37	(9%)
18 Gauge intravenous cannula (plastic material)	1	74	(17%)
Unspecified	1	69	(16%)
Duration of air fill			
< 1 hour	2	69	(16%)
1-2 hour	12	304	(71%)
>2 hours	4	58	(13%)
Extent of air fill remaining in AC after surgery			
100 %	6	232	(54%)
80-90 %	4	36	(8%)
60-70 %	4	87	(20%)
50 %	2	55	(13%)
0 %	1	16	(4%)
Unspecified	1	5	(1%)

IOL; Intraocular Lens
AC; Anterior Chamber

graft performed by the surgeon himself proved successful in 93% of cases. Seven surgeons routinely had a back-up cornea in case preparation failed.

Grafts were either stored in cold storage medium (Optisol-GS, Bausch & Lomb Surgical, USA; Eusol-C, Alchimia, Italy) or organ culture medium (Modified minimum essential medium, CorneaMax, Eurobio AbCys France, and Tissue-C, Alchimia, Italy) (Table 3). Six surgeons used organ culture (113/431; 26% of grafts), 7 used cold storage (104/431; 24%), 4 used either method (140/431; 32%), whereas one surgeon used freshly prepared grafts from a whole globe (74/431; 17%).

Table 3: Different types of storage of the donor graft used

Influence of storage type	Cold storage No.	(%)	Organ culture No.	(%)	Both No.	(%)	Fresh globes No.	(%)
Surgeons	7		6		4		1	
No. of grafts	104		113		140		74	
Detachments								
Partial ≤1/3	*16*	*(15%)*	*16*	*(14%)*	*23*	*(16%)*	*25*	*(34%)*
Partial >1/3	*19*	*(18%)*	*12*	*(11%)*	*0*	*(0%)*	*0*	*(0%)*
Full	*1*	*(1%)*	*1*	*(1%)*	*13*	*(9%)*	*3*	*(4%)*
Unknown percentage	*0*	*(0%)*	*1*	*(1%)*	*12*	*(9%)*	*0*	*(0%)*
In total	36	(35%)	30	(27%)	48	(34%)	28	(38%)
Rebubbling	25	(24%)	33	(29%)	*31*	*(22%)*	13	*(18%)*

Surgical technique

All surgeons used basically the standardized DMEK techniques as described in the literature (Figures 2 and 3). [9, 13] Small variations were reported, which are summarized in Table 2. These variation relate to the diameter of the graft

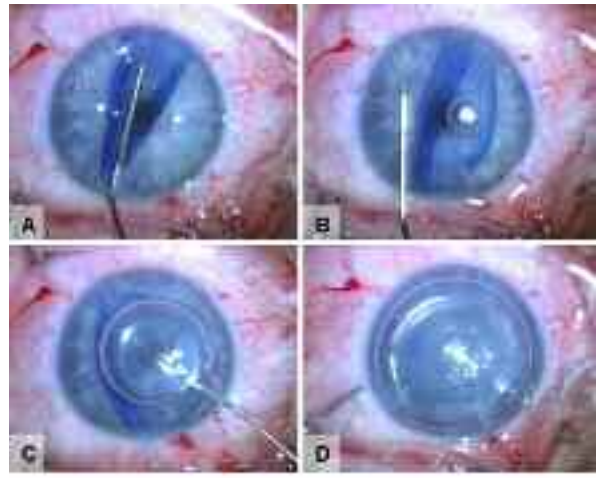

Figure 2. Standardized DMEK technique. A-D: Successive steps for unfolding the DM graft in a 'no-touch' manner (adapted from Liarakos et al. JAMA Ophthalmol. 2013)

(8.0-9.5mm), the material of the injector used (glass or plastic), the duration of the air fill (from less than 1 hour up to longer than 2 hours) as well as the size of the air bubble left (0-100%).

Outcome measurements

Of the 431 eyes that enrolled the study, several eyes (45/431) were excluded from the analysis because of low visual potential due to concomitant eye diseases unrelated to the corneal transplant. BCVA data, were available for 275

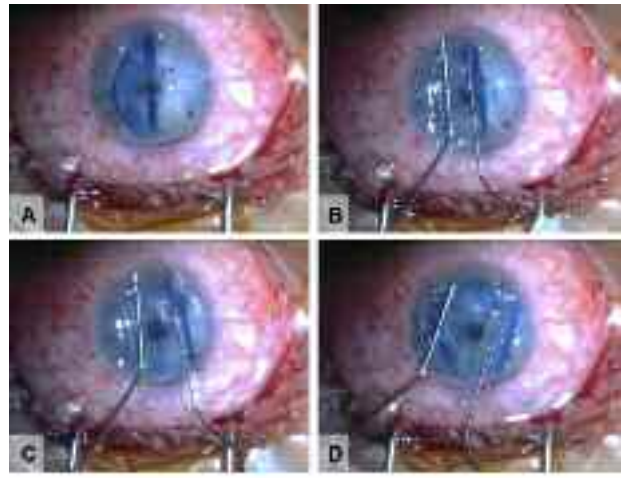

Figure 3. Unfolding techniques in DMEK. Various alternative techniques may be used for unfolding the DM graft in DMEK, based on the case. A-D: Successive steps for unfolding the DM graft in a 'no-touch' manner with a 'double-cannula' maneuver (adapted from Liarakos et al. JAMA Ophthalmol. 2013)

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No. of grafts	104		113		140		74	
Detachments								
Partial ≤1/3	*16*	*(15%)*	*16*	*(14%)*	*23*	*(16%)*	*25*	*(34%)*
Partial >1/3	*19*	*(18%)*	*12*	*(11%)*	*0*	*(0%)*	*0*	*(0%)*
Full	*1*	*(1%)*	*1*	*(1%)*	*13*	*(9%)*	*3*	*(4%)*
Unknown percentage	*0*	*(0%)*	*1*	*(1%)*	*12*	*(9%)*	*0*	*(0%)*
In total	36	(35%)	30	(27%)	48	(34%)	28	(38%)
Rebubbling	25	(24%)	33	(29%)	*31*	(22%)	13	(18%)

eyes, of which 176 had six months of follow-up, 43 three months, and 56 one month.

Preoperative donor endothelial cell density (ECD) was measured by providing eye banks, using specular microscopy or inverted light or phase contrast microscopy (Noncon Robo, Konan Medical Inc., Hyogo, Japan; Kerato Analyzer, Konan Medical Inc.; Nikon inverted microscope, Tokyo, Japan; Topcon SP1000, Topcon Medical Europe BV, Capelle a/d IJssel, The Netherlands; Axiovert inverted light microscope, Zeiss, Göttingen, Germany). Postoperative ECD was measured up to six months postoperative using specular microscopy (Noncon Robo, Konan Medical Inc.; Topcon SP2000/SP3000, Topcon Medical Europe BV; Bon Optic EM-2 specular microscope, Carleton Ltd., Buckinghamshire, England; CSO specular microscope, CSO S.r.I., Firenze, Italia; EM 3000, Tomey GmbH, Erlangen-Tennenlohe, Germany).

Statistical analysis

Statistical analysis was performed with the SPSS v.15.0 for Windows (SPSS Inc., Chicago, IL). Analysis of variance (ANOVA) and the student's paired t-test were used to compare ECD between different subgroups and different time points. Regression analysis was performed in order to evaluate the potential effect of different factors on the outcome of the surgeries. Statistical significance was determined as $P< 0.05$.

Results

A total of 431 consecutive eyes underwent standardized 'no-touch' DMEK with various modifications (Table 2).[9, 13]

Best corrected visual acuity

BCVA improved two or more Snellen lines in 258/275 eyes (94%), 12/275 eyes (4%) remained unchanged, and 5/275 eyes (2%) deteriorated. For all eyes with a follow-up of 1-6 months, 217/275 eyes (79%) reached a BCVA ≥20/40 (≥0.5), 117/275 eyes (43%) ≥20/25 (≥0.8), 61/275 (22%) ≥20/20 (≥1.0), and 8/275 eyes (3%) ≥24/20 (≥1.2).

Endothelial cell density

Complete pre- and six months postoperative ECD measurements were available for 133 eyes. Mean donor ECD was 2625 (±333) cells/mm^2 before, and 1399 (±533) cells/mm^2 at six months after surgery, i.e. overall decrease in ECD was 47 (±20) % (P=0.017) between the preoperative and six months postoperative measurements. EC loss presented a wide variation among different surgeons probably due to the different (not standardized) ways and different devices that were used in order to calculate it. Therefore, statistical analysis did not have enough power to correlate EC loss with possible parameters responsible such as lens status, type of inserter (plastic or glass), air bubble time and size, donor storage medium, surgeon or eye bank prepared grafts or the individual surgeon (P=0.441).

Complications

Intraoperative complications included difficulties during insertion, unfolding, and/or positioning of the Descemet graft and were observed in five eyes (1%) (Table 4). In two cases (0.5%) a small intraoperative hemorrhage occurred (Table 4). No other intraoperative complications were reported.

The most frequent postoperative complication was partial graft detachment, which occurred in 124/431 eyes (35%) (Table 4), of which 80 (19%) had a detachment ≤1/3 of the graft surface area, and 31 (7%) >1/3 of the surface area. For 13 cases (3%), the size of the detachment was not specified. Complete detachment, i.e. a roll in the AC, occurred in

Table 4: Complications regarding DMEK surgery

Complications	No. of complications (% of total eyes) (n=431)	
Intraoperative complications		
Failure to unfold / insert / position DMEK graft	5	(1%)
Intraoperative hemorrhage	2	(0.5%)
Postoperative complications and associated pathology		
Total grafts detached	149	(35%)
Partial detachment ≤1/3	*80*	*(19%)*
Partial detachment >1/3	*31*	*(7%)*
Partial detachment unknown extent	*13*	*(3%)*
Graft upside down	*7*	*(2%)*
Complete detachment	*18*	*(4%)*
Detachments resulting in secondary keratoplasty	43	(10%)
Primary graft failure	10	(2%)
Secondary graft failure	27	(6%)
Rejection (acute/chronic)	16	(4%)
Epithelial defect / erosion	13	(3%)
Secondary glaucoma ("de novo")	10	(2%)
DM folds/wrinkling affecting visual axis	8	(2%)
Cystoid macular edema	5	(1%)
Anterior synechiae	4	(1%)
Hypotonia	3	(1%)
Pupillary block	2	(0.5%)
Dendritic keratitis / endothelitis	2	(0.5%)
IOL vitreous luxation	1	(0.2%)
Cataract	1	(0.2%)
Melting ulcus corneae	1	(0.2%)
Subepithelial haze	1	(0.2%)
Macula pucker	1	(0.2%)
Interface pigment deposits	1	(0.2%)
Secondary interventions		
Total rebubbling procedures (102 eyes)	119	
1 x	*88*	*(20%)*
2 x	*11*	*(3%)*
3 x	*3*	*(1%)*
Total reoperations (79 eyes)	87	
Secondary DMEK	*46*	*(11%)*
Secondary DSEK / DSAEK	*15*	*(3%)*
Secondary PKP	*15*	*(3%)*
Tertiary DMEK	*2*	*(0.5%)*
Quintary DMEK	*1*	*(0.2%)*

DM; Descemet Membrane
IOL; Intra Ocular Lens
DMEK; Descemet Membrane Endothelial Keratoplasty
DS(A)EK; Descemet Stripping (Automated) Endothelial Keratoplasty
PKP; Penetrating Keratoplasty

18/431 eyes (4%), and in 7/431 cases (2%) the graft was positioned upside down. Of these (partially) detached grafts, 43/124 required a secondary transplantation (Table 4). Regression analysis showed that the use of plastic inserters (P=0.005), cold storage medium (P=0.005) and a short air bubble time (<1h) during surgery (P=0.019) correlated positively with the incidence and the extent of postoperative graft detachment. In addition, cold storage correlated with more extensive detachments than grafts stored using organ culture (P=0.01).

Other postoperative complications included primary graft failure owing to endothelial insufficiency (10/431 cases; 2%), secondary graft failure (27/431 cases; 6%), allograft rejection (16/431; 4%), epithelial defects and/or erosion (13/431; 3%), secondary glaucoma (12/431; 3%) of which 5 cases were steroid responders and significant folds or wrinkles of the Descemet graft (8/431; 2%) (Table 4).

Secondary corneal procedures

A total of 102/431 eyes (24%) required a re-bubbling procedure. A single re-bubbling procedure was performed for 88/431 eyes, while 11/431 eyes needed a secondary and 3/431 eyes a third procedure (Table 4). Re-bubbling proved successful in 83/102 eyes (81%), while the remaining 19 eyes required a secondary transplantation.

Overall, 79/431 eyes (18%) needed a secondary corneal procedure, of which 46 cases obtained a secondary DMEK. Fifteen eyes underwent a secondary DSEK/DSAEK and 15 eyes a secondary PKP (Table 4).

After a secondary DMEK, pre- and postoperative BCVA was available for 20 eyes, showing an increase in BCVA in 15/20 eyes (75%) from <20/40 (<0.5) to ≥20/40 (≥0.5). Seven eyes (35%) obtained a BCVA of ≥20/25 (≥0.8) and 3 (15%) of ≥20/20 (≥1.0).

Discussion

In the current multicenter trial, we evaluated the first series of DMEK surgeries performed by 18 corneal surgeons in various clinical settings and different countries, in order to document the logistic and technical problems, the clinical outcome, as well as the complications encountered when starting with DMEK. As such, our findings may assist other surgeons in making the switch from DSEK/DSAEK to DMEK, in choosing the best approach for their specific setting, and in shortening their learning curve. All surgeons had long term experience with penetrating keratoplasty and/or DSEK/DSAEK, so that in this study group the clinical results after DMEK justified making the switch from DSEK/DSAEK to DMEK.

Clinical outcome

Within the first six months after DMEK, 79% of eyes reached a BCVA of ≥20/40 (≥0.5), 43% of ≥20/25 (≥0.8), and 22% of ≥20/20 (≥1.0) (Figure 2). Hence, although during the learning curve, the majority of patients may already obtain a visual acuity level that allows them to perform their daily activities and to obtain or keep their driving license. In a previous study,[14] the learning curve did not seem to influence BCVA and ECD, but the number of functional (attached) grafts increased with surgical experience. In the current study, visual outcome did seem to vary with surgical experience. Considering that 13 out of the 18 surgeons performed fewer than 25 DMEK surgeries at the time of data collection, this may explain the visual outcome to be lower than in large series of DMEK, but still favorable as compared to that reported for DSEK/DSAEK.[7,8,15-17]

Our study showed an average ECD decrease of 47% at 6 months. Other investigators have reported an average ECD

decrease of 34-41% at the same postoperative time interval.[7,17-19] These numbers may be interpreted with some caution, because 50% of surgeons prepared the donor tissue themselves immediately before surgery. As a result, the decrease in ECD may have been overestimated, since ECD before DM stripping was used for comparison with postoperative ECD values. We had anticipated that DM stripping by the surgeon would have been more traumatic compared to preparation in an eye bank, especially during the surgeon's learning curve. However, the decrease in ECD did not prove to differ significantly between surgeon and eye bank prepared grafts, at least in this group of surgeries.

Complications

Intraoperative complications during the DMEK learning curve were relatively rare (1.5%), which agrees with previous findings.[13,20-22] The relative low number of intraoperative complications may in part be explained by the fact that all surgeons participated in a wetlab instruction course (at the NIIOS in Rotterdam), suggesting that such training sessions are effective in avoiding the most common pitfalls.

As in earlier studies, by far the most frequent postoperative complication after DMEK was (partial) graft detachment.[7,14,23] Of the 149 graft detachments reported in our study, 80 (54%) consisted of relatively small, peripheral detachments (less than one third of the graft surface area). Such detachments are usually clinically insignificant, since they spare the visual axis. If no graft adherence is obtained, the recipient cornea overlying the detachment tends to clear with time, owing to endothelial re-population of the denuded recipient posterior stroma.[24] Larger detachments (21% of the detached grafts) were often managed by re-bubbling, while a secondary DSEK/DSAEK or re-DMEK was employed in the event of complete detachment (12% of the detached grafts) or when the graft was positioned upside-down (5% of the detached grafts) (Table 4). Hence, about 10% of cases (29% of the detached grafts) may require a secondary surgical intervention in some form resulting from a detached graft.

Our study showed that there may be three main factors contributing to inadvertent graft detachment, all of which may be relatively easy to manage or avoid: the use of 'cold storage' media, the type of inserter used, and the air bubble time during surgery. In 2011 Laaser et al. reported a difference in detachments between DSAEK grafts stored in Optisol-GS (cold storage) and CorneaMax medium (organ culture): Grafts stored in Optisol-GS required more often re-bubbling than those stored in organ culture medium.[25] Our study seemed to confirm this trend with 35% detachments with cold storage versus 27% with organ culture (Table 3). Also, plastic (instead of glass) graft inserters correlated with higher postoperative graft detachment rates. This agrees with our initial in-vitro experiments, that showed more variable endothelial cell damage with plastic than with glass inserters and a somewhat different 'behavior' of the graft during insertion and unfolding, possibly due to electrostatic forces induced by plastics. In this study, all surgeries performed with an injector made of plastic material, the air fill time was ≥1h; subsequently, no correlation between plastic injectors and short air fill time could be identified. Air fill time <1h (short) was reported in 69 DMEK surgeries. In all of them, an inserter made of glass material had been used. Subsequently, the factor "short air fill time" was independent of a possible positive correlation with a "plastic injector". Finally, it may be advocated to leave the patient in a supine position with a complete air fill of the anterior chamber for ≥1 hour, to minimize the risk of (partial) graft detachment. In other words, an 'air-bubble time' of less than one hour may on average be insufficient to obtain complete graft attachment. Interestingly, after reducing the air-bubble size at termination of the surgery, the actual size of the air bubble left behind in the anterior chamber may have little effect on final graft detachment (rate).

Secondary graft failure within the first six months occurred in 6% of eyes, and may be attributed to endothelial damage during donor tissue preparation and/or manipulation of the tissue during or after insertion of the graft into the anterior chamber, or postoperative events. Compared to an incidence of 5-12% after DSEK/DSAEK, a lower allograft rejection rate has been reported for DMEK, varying from 1-5% within the first postoperative year.[18, 26-31] In the present study, 4% of eyes showed an allograft rejection: 8 surgeons reported rejections in one or more cases, while others observed none. It may be important to note that the risk of rejection may vary considerably among study populations, for example, Asian people may show a stronger immune response to corneal grafts, and require higher steroid regimes than Caucasian. All other reported complications seemed incidental and not specifically related to DMEK or its learning curve (Table 4).

Secondary procedures

The majority of the secondary procedures were performed to manage (partial) graft detachment after DMEK, in particular re-bubbling in 24% (Table 4). This procedure proved successful in 81%, while the remaining eyes required re-transplantation. Hence, re-bubbling was quite effective in the current study.[16] However, previous experience suggested that, especially with small, peripheral detachments over a limited graft surface area, spontaneous corneal clearance or re-attachment may be awaited.[7] Re-DMEK procedures were also effective since 75% of these eyes had a final BCVA of ≥20/40 (≥0.5).

Conclusion

This first multicenter DMEK trial worldwide showed that the standardized DMEK technique was feasible in most hands. Surgeons starting with DMEK achieved results comparable to more experienced groups and were encouraged to continue. Differentiations in the technique may (or may not) affect the outcome. More complex cases like bullous keratopathy in the presence of an anterior chamber intraocular lens (AC-IOL) or failed penetrating keratoplasty (PK) grafts may be successfully treated with DMEK; [32,33] however, such cases should be preferably excluded from the learning curve. Complications rate is comparable to more experienced centers. When successful, the visual outcome after DMEK may be relatively independent of the surgeons' learning curve.

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