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Outcomes of Descemet Membrane Endothelial Keratoplasty in Patients with Prior Glaucoma Surgery

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Abstract

Purpose—To evaluate outcomes of Descemet membrane endothelial keratoplasty (DMEK) in eyes with prior trabeculectomy or drainage device.

Methods—This is a retrospective study of 108 consecutive DMEK performed between October 2013 and December 2015. All eyes were divided into three groups: surgical treatment [ST] group, medical treatment [MT] group, and control group. Visual improvement, endothelial cell (EC) loss, and postoperative complications, including rejection, graft failure, and IOP elevation (25 mm Hg) were evaluated.

Results—The length of follow-up was 9.7 ± 7.3 months. Best-corrected visual acuity (BCVA) improved postoperatively in 85.3% of the ST group, 100% of the MT group, and 93% of the control (p=0.24). Significantly more lines of BCVA were gained in the ST and MT groups (8.1±8.1 and 9.2±6.3 lines, respectively) than in the control (4.8 ± 5.6 lines, p<0.05). The mean time to BCVA was 2.9 ± 2.8 months for the ST group, 4.7 ± 5.3 months for the MT group, and 3.0 ± 3.3 months for the control (P=0.75). EC loss was greater in the ST group ($44.6\pm17.8\%$) than in the MT group ($29.9\pm12.0\%$) and the control group ($32.7\pm11.3\%$, P=0.001). There was one primary failure and no secondary graft failures. The overall rejection rate was 0.9%. Postoperative IOP elevation was less common in the ST group (14.7%) and control (23.3%) than in the MT group (50.0%, P=0.04). There was no difference in the air injection rate among all groups (P=1.0).

Conclusion—DMEK in eyes with previous trabeculectomy and drainage device can result in very good short-term outcomes.

Keywords

Descemet Membrane Endothelial Keratoplasty (DMEK); endothelial keratoplasty; glaucoma; glaucoma surgery

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INTRODUCTION

Endothelial keratoplasty (EK) has become the standard of care for endothelial dysfunction. Descemet's stripping endothelial keratoplasty (DSEK) remained the most commonly performed type of EK in the United States in 2014, although the number of Descemet's membrane endothelial keratoplasty (DMEK) procedures has doubled every year since 2011; however, DMEK accounted for only 11% of total keratoplasties in 2014.¹

It has long been recognized that glaucoma has an adverse effect on the survival of penetrating keratoplasty (PK).^{2–4} DSEK has been reported as a feasible technique in eyes with previous trabeculectomy or tube shunt implantation and is effective in improving vision in the majority of these eyes; however, DSEK for patients with a history of glaucoma, treated either medically or surgically, carries a higher risk of secondary endothelial failure.^{5–7}

Mounting evidence indicates that DMEK provides better visual outcomes and faster visual rehabilitation than DSEK and PK.^{8–10} In addition, endothelial cell (EC) loss after DMEK is comparable to that seen with DSEK in the treatment of uncomplicated Fuchs endothelial corneal dystrophy (FECD) and pseudophakic bullous keratopathy (PBK).^{8, 9, 11–13} DMEK has been shown to have a significantly lower risk of immunological rejection than DSEK and PK,^{14, 15} and requires less topical corticosteroid therapy postoperatively without a significant increase in the rejection rate.^{16, 17} Thus, DMEK offers significant advantages over DSEK in patients whose vision is already limited by advanced glaucoma and whose intraocular pressure (IOP) control is challenging postoperatively.

There are few data about the outcomes of DMEK in patients with glaucoma who have been treated surgically. Only four case reports have indicated that DMEK has a higher rate of complications such as the need for air injection and secondary graft failure.^{18–21}

The current study which consists of the largest series of consecutive DMEK in patients with prior glaucoma surgery investigates the clinical outcomes of DMEK in this population using a standardized surgical technique.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board at the University of California, Los Angeles (UCLA Institutional Review Board #15-001250). A total of 108 consecutive DMEK procedures in 108 eyes performed between October 1, 2013, and December 31, 2015, by a single surgeon (SXD) was classified into three groups: eyes that had undergone trabeculectomy or tube shunt implantation prior to DMEK (the ST group), eyes that had been treated medically with or without prior laser treatment (the MT group), and eyes without a history of glaucoma (the control group). The diagnosis and severity of glaucoma was made by the referring glaucoma specialists prior to DMEK.

All patients underwent a comprehensive preoperative evaluation before DMEK. Bestcorrected visual acuity (BCVA) measured with a Snellen chart and intraoperative and postoperative complications at each postoperative follow-up visit were reviewed. EC density

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measured by specular microscopy (Konan Medical Inc., Irvine, CA), if available, was evaluated.

Surgical Procedure and Postoperative Management

Pre-stripped donor tissues prepared by eye banks were used in 107 of the 108 cases. Donor corneal preparation and the surgical technique of DMEK have been described in detail previously²² and did not differ among the three groups. The donor graft was unfolded with the use of a "touch, no touch" technique in which a 30-gauge cannula was used to manually unfold the Descemet membrane (DM) scroll on the DM side without touching the endothelium. All surgeries were performed under monitored anesthesia care and retrobulbar block. If the surgery was a combined DMEK and cataract surgery, the cataract was removed by phacoemulsification first. Trimming of the tube shunt and/or lysis of the anterior iris synechiae was performed prior to insertion of the DM tissue when necessary.

All patients were instructed to stay in a supine position in the recovery room for 1 to 2 hours, and examination was subsequently performed to confirm graft attachment using a portable slit lamp. IOP was estimated by digital palpation. If IOP exceeded low 20s', a small amount of air or aqueous was released. The patient was instructed to remain supine for 24 to 48 hours. Patients were examined at postoperative day 1, week 1, month 1, and every 2 months thereafter. Postoperative air injection was performed under aseptic conditions if the patient had visually significant graft edema or symptoms of corneal edema within the first 4 weeks after surgery. Topical fluoroquinolone therapy administered 4 times daily began 2 days prior to surgery and continued 7 days after surgery or until the epithelial defect healed. Topical 1% prednisolone acetate was administered 4 times daily, with the dosage tapered to once daily over a period of approximately 4 to 6 months. Topical glaucoma medications used before DMEK were generally resumed 1 day after the surgery.

Primary graft failure was defined as the failure of the DM to attach or persistent corneal edema after the first postoperative month despite an attached graft. Secondary graft failure was defined as irreversible edema of the host cornea that developed after previously successful DMEK. Endothelial rejection was defined as the presence of keratic precipitates or an endothelial rejection line on the DM, with or without edema of the host cornea or a decrease in vision. Elevated IOP was defined as a single measurement 25 mm Hg that lasted more than 1 week at any time during the postoperative period or that required any additional glaucoma treatment after the first postoperative week.

Statistical Analysis

Statistical analysis was performed by using SAS software version 9.4 (SAS, Inc., Cary, NC). The differences in the mean values of continuous variables with a skewed distribution (e.g., age, duration of follow-up, percentage of EC loss and visual acuity improvement) between patient subgroups were compared by the Kruskal-Wallis test, and the differences in the percentages of categorical variables (e.g., sex, visual acuity, and surgical indication) between patient subgroups were compared by the Fisher exact test. A P value 0.05 was considered statistically significant.

RESULTS

Patient Demographics

Of the 108 consecutive eyes that underwent DMEK, 34 eyes (31.5%) comprised the ST group. Twenty-three of the 34 eyes had previously undergone tube shunt implantation (5 eyes also had undergone trabeculectomy), and 11 eyes had undergone previous trabeculectomy only. Five eyes had 2 shunts, and 1 eye had 3 shunts. Fourteen eyes (13%) were treated with glaucoma medication and comprised the MT group, and 60 eyes (55.6%) had no history of glaucoma and comprised the control group. The mean (±SD) length of follow-up was 9.7 months (range, 0.3–27.6 months). There was no significant difference in the age, sex distribution, or mean follow-up length among the 3 groups (Table 1).

The mean age of donor tissues was 59.5 years (range, 52 to 68 years) in the control group, 58.7 years (range, 50 to 63 years) in the MT group, and 60.6 years (range, 55 to 68 years) in the ST group (P=0.48).

The indications for surgery differed among the 3 groups. FECD was more common in the control group (81.7%) and MT group (57.1%) than in the ST group (5.9%, P <0.0001), whereas PBK was more common in the ST group (64.7%) than in the MT group (21.4%) and control group (8.3%, P <0.0001; Table 1).

DMEK was performed concomitantly with one or more procedures in 50 of the 108 eyes (46%). Two or more concomitant procedures were performed significantly more frequently in the ST group (29.4%) than in the MT group (7.1%) and control group (3.3%; p = 0.0007). The most commonly performed concurrent procedures in the ST group were trimming of the glaucoma shunt (47.0%) and lysis of irido-cornea adhesions (35.3%). In contrast, cataract extraction was the most common procedure performed concomitantly in the MT group (21.4%) and control group (30%) (Table 1).

Overall, 24.1% of eyes were phakic prior to DMEK. Cataract extraction and posterior chamber intraocular lens implantation were performed as concurrent procedures in all phakic eyes except 3 (1 eye in the ST group and 2 eyes in the control group). Eight eyes had previous vitrectomy and 4 eyes underwent anterior vitrectomy as concurrent procedure prior to DMEK (Table 1).

Visual Outcomes

All eyes except one (primary graft failure) were included in the vision analysis. The mean preoperative BCVA was significantly worse in the ST and MT groups than in the control group (Table 2).

Postoperative BCVA improved in 91.6% of all eyes, 85.3% of eyes in the ST group, 100% eyes in the MT group, and 93.2% of eyes in the control group (P = 0.24, Table 2). No eye lost vision. BCVA was unchanged in 9 eyes (8.4%) after DMEK: 2 eyes retained a BCVA of 20/20 postoperatively, but the glare and halos that were the indication for DMEK improved significantly; 3 eyes had end-stage glaucoma; 1 eye had epiretinal membrane diagnosed prior to DMEK; one eye had corneal surface irregularity secondary to limbal stem cell

deficiency; one eye developed cystoid macular edema; and 1 eye did not have manifest refraction at the last follow-up.

The percentage of eyes that ever reached BCVA of 20/20 and 20/40 was 21.6% and 52.9%, respectively in the ST group, 71.4% and 92.7%, respectively in the MT group, and 59.3% and 88.1%, respectively in the control group. Significantly more lines of vision were achieved by the ST group (8.1 ± 8.1 lines) and the MT group (9.2 ± 6.3 lines) than by the control group (4.8 ± 5.6 lines, p=0.002) after DMEK. The mean time (\pm SD) to achieve visual improvement was defined as the number of months to reach the best achieved visual acuity from the day of surgery, and it was similar in all three groups: 2.9 ± 2.8 months for the ST group, (p=0.75). The preoperative median VA (LogMar) was 0.4 (range, 0 to 3.0) in the control, 0.8 (range 0.2 to 2.0) in the MT group, and 1.0 (range, 0 to 4.0) in the ST group. The postoperative median VA (LogMar) in the control, MT, and ST groups was 0.18 (range, -0.12 to 3.0), 0.18 (range, 0.0 to 1.0), and 0.51 (range, 0.0 to 3.0), respectively, at postoperative month 1. At postoperative month 3, the median VA (LogMAR) were 0.10 (range, 0.0 to 1.0) in the control group, 0.18 (range, 0.0 to 0.54) in the MT group, and 0.3 (range, 0.0 to 3.0) in the ST group.

Complications

There was no total detachment or upside down graft in any groups. Partial detachment of the DMEK graft that required air injection was the most common complication, occurring in 23.2% of the eyes. There was no difference in the air injection rate among the ST group (23.5%), the MT group (21.4%), and the control group (23.3%, P = 1.0). One eye in the control group and 1 eye in the MT group required a second air injection, and 1 eye with prior trabeculectomy in the ST group required a third injection in which sulfur hexafluoride 6 gas was used. Eight eyes developed cystoid macular edema and the incidence in each group was not significantly difference (P=0.9).

One case of primary graft failure (control group) and no cases of secondary graft failure occurred during the follow-up period. Immunogenic rejection developed in 4 eyes; 3 of them were in patients who self-discontinued topical steroid therapy within the first 3 months of the postoperative period, and rejection resolved after topical steroid therapy was resumed. Only 1 eye (0.9%), which was in the control group, developed true rejection (0.9%) 9 months after DMEK. In this case, increasing prednisolone acetate from once daily to 4 times daily resulted in resolution.

Postoperative IOP elevation was observed in 24.1% of all eyes. A significantly higher percentage of eyes in the MT group (50%) developed IOP elevation than did those in the ST group (14.7%) and the control group (23.3%) (P = 0.043). Overall, 4.6% of the eyes required surgical intervention for IOP control after DMEK, but it was significantly more common in the ST group (n=3, 8.8%) and the MT group (n=2, 14.3%) than in the control group (n=0, 0%) (Table 3).

Endothelial Cell Loss

The mean preoperative EC density (cells/mm²) was 3007 ± 187 in the control group, 3130 ± 143 in the MT group, and 2941 ± 165 in the ST group (P=0.006). The mean EC loss was greater in eyes with prior glaucoma surgery ($44.6\pm17.8\%$) than in those eyes without ($29.9\pm12.0\%$ in the MT group and $32.7\pm11.3\%$ in the control group, P=0.001) during the follow up period. The greatest EC reduction occurred during the first 3 months after surgery in all groups; however, there was no difference in the EC reduction among three groups at 3 month (p>0.05).

DISCUSSION

The current study is the largest series of consecutive DMEK in patients with prior glaucoma surgery. DMEK has been mostly performed in eyes with a normal anterior segment.^{23–26} The outcomes of DMEK in patients who had undergone prior glaucoma surgery have reported in only a few cases.^{18–21} DMEK can be more challenging in eyes with prior glaucoma surgery because of the abnormal anterior segment because of the shunt and anterior synechiae. Rebubbling was reported to be as high as 50% and secondary graft failure developed in 75% of eyes at 18 months of follow-up.²⁰

In order to make DMEK feasible in these complex eyes, concomitant procedures were often required. In the current series, 68% of eyes with prior glaucoma surgery required up to 3 procedures to re-create sufficient space in the anterior chamber prior to the insertion of the DM graft. Despite more complex surgery, visual acuity improved in more than 85% of these eyes, and none developed primary graft failure. Our results demonstrate that DMEK can be successfully performed in these complicated situations when a standardized technique is utilized without an increase in intraoperative and immediate postoperative complications.²²

The ST group had a dramatic improvement of BCVA by 3 months after DMEK that has not been reported after DSEK or PK. Medically and surgically treated eyes with glaucoma had worse preoperative visual acuity than did those without glaucoma. This difference is likely due to the presence of underlying advanced glaucoma and more severe corneal edema. The preoperative visual potential of these eyes with glaucoma was impossible to determine because the corneal edema was long-standing and it was unclear whether the IOP control was adequate to prevent further permanent visual loss after the onset of corneal edema. Previous studies reported improvement of BCVA in 71%-87% of patients who underwent DSEK after prior glaucoma surgery.^{6, 27, 28} A decrease in BCVA was observed in 13% of eyes in one study.²⁸ However, the degree of BCVA improvement that resulted after DMEK and DSEK could not be compared because the degree and the speed of BCVA recovery after DSEK have not been reported. In light of the earlier finding that DMEK yields greater visual recovery than DSEK in eyes without glaucoma,^{8–10, 13} DMEK likely provides greater vision improvement than DSEK in eyes with glaucoma as well. Importantly, the degree of visual acuity improvement was significantly greater in eyes with glaucoma than in those without glaucoma after DMEK, and the time to achieve BCVA was the same in eyes with glaucoma and the control eyes despite a longer duration of corneal edema prior to DMEK.

In the present study, only 1 eye (0.9%), which was in the control group, developed true rejection. This rejection rate is comparable to that reported previously for eyes without glaucoma after DMEK.^{14, 15} This finding suggests that prior glaucoma surgeries or medical glaucoma treatment do not increase the risk of immune rejection after DMEK. Three more eye developed rejection because these patients achieved very satisfactory visual outcome and self-stopped prednisolone acetate less than 3 months after surgery. These rejections would not have occurred if these patients were compliant with their medication.

As reported in other studies,^{9, 11, 24, 25, 29} the most common postoperative complication is graft detachment requiring air injection. The lack of difference among the 3 groups in the present study demonstrates that the presence of a trabeculectomy or a drainage shunt does not increase the risk of partial graft detachment. The overall air injection rate was reduced to 13% after the surgeon completed the first 50 procedures, although these later cases were more complex than the initial ones. In addition, the threshold for air injection in a majority of the cases was very low because of patients' strong desire of faster visual recovery. This factor contributed to the higher air injection rate in the current study.

The current study found that a higher incidence of IOP elevation in the MT group than the other 2 groups which is consistent with that observed after DSEK.^{5, 6}. Moreover, IOP elevation is a common occurrence not only in eyes with a history of glaucoma but also in eyes without a history of glaucoma. Therefore, close monitoring of IOP in all eyes after endothelial keratoplasty is necessary. In eyes that have undergone concurrent procedures with DMEK, a higher level of postoperative inflammation occurs, and these eyes would require a longer duration of topical corticosteroid therapy.

The reduction in EC density was higher in eyes with surgically treated glaucoma. This finding is consistent with that observed after DSEK in eyes with surgically managed glaucoma. A significantly better graft survival is seen in individuals without prior glaucoma surgeries than in those with after DSEK.^{5–7, 27, 28} The reduction in EC density in the absence of rejection episodes suggests that factors other than immunologic rejection are responsible for the difference in EC density and subsequent secondary graft failure in patients with prior glaucoma shunt implantation. Such potential factors include an increased level of plasma proteins involved in apoptosis in the aqueous humor, oxidative stress, and inflammation after tube shunt implantation, which is an indicator of a breakdown of the blood–aqueous barrier and potentially a cause of endothelial damage.^{30, 31} The greater loss of endothelial cells in surgically treated glaucoma eyes is not due to surgical manipulations because there was no difference in the EC reduction at 3 month among all groups.

In summary, the current study demonstrates that DMEK can be successfully performed in eyes that have undergone previous trabeculectomy and glaucoma drainage device implantation and provides excellent visual improvement without an increase in early postoperative complications. DMEK should be considered in this these group of patients to achieve the best possible visual rehabilitation. Additional study is needed to investigate the long-term outcomes.

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Table 1

Patient Demographics, Indications for Surgery and Concurrent Procedures

	Control	Surgically Treated Glaucoma	Medically Treated Glaucoma	Total	P*
No. DMEK/ eye	60	34	14	108	
Age (mean ± SD) (year)	72.2 ± 10.3	69.1 ± 16.4	74.1 ± 7.1	71.5 ± 12.3	0.78
Sex, N (%)					0.59
Female	34 (57%)	19 (56%)	10 (71%)	63 (58%)	
Male	26 (43%)	15 (44%)	4 (29%)	45 (42%)	
Mean Follow-up (range, month)	9.8±7.5 (0.3 to 27.6)	8.4±6.9 (1.1 to 26.7)	11.7±7.6 (0.3 to 26.7)	9.7±7.3 (0.3 to 26.7)	0.34
Surgical indication. N, (%)					<0.0001 [†]
FECD	49 (81.7)	2 (5.9)	8 (57.1)	59 (54.6)	
PBK	5 (8.3)	22 (64.7)	3 (21.4)	30 (27.8)	
PK failure	2 (3.3)	2 (5.9)	2 (14.3)	6 (5.5)	
DSEK failure	2 (3.3)	7 (20.6)	0(0)	9 (8.3)	
DMEK failure	0 (0)	0 (0)	1 (7.1)	1(0.9)	
Endothelitis	2 (3.3)	1 (2.9)	0(0)	3 (2.8)	
Previous vitrectomy	3 (5)	4 (11.8)	1 (7.1)	8 (7.4)	0.38
Lens status, N (%)					0.0316‡
PCIOL	39 (65)	30 (88.2)	10 (71.4)	79 (73.1)	
Iris fixated IOL	1 (1.7)	1 (2.9)	1(7.1)	3 (2.8)	
Phakic	20 (33.3)	3 (8.8)	3 (21.4)	26 (24.1)	
Concurrent procedures, N (%)					
Cataract extraction with PCIOL	18 (30)	2 (5.9)	3 (21.4)	23 (21.3)	
Trimming of glaucoma drainage tube	0 (0)	16 (47)	0 (0)	16 (14.8)	
Lysis of irido-corneal adhesions	3 (5)	12 (35.3)	2 (14.3)	17 (15.7)	
Anterior vitrectomy	0 (0)	4 (11.8)	0 (0)	4 (3.7)	
Retrocorneal membrane peel	3 (5)	6 (17.6)	1 (7.1)	10 (9.3)	
Number of concurrent procedures, n (%)					0.007§
-	20 (33.3)	13 (38.2)	4 (28.6)	37 (34.3)	
2	2 (3.3)	2 (5.9)	1 (7.1)	5 (4.6)	

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	Control	Surgically Treated Glaucoma	Medically Treated Glaucoma	Total	\mathbf{P}^{*}
ĸ	0 (0)	8 (23.5)	0 (0)	8 (7.4)	
2	2 (3.3)	10 (29.4)	1 (7.1)	13 (12)	

DMEK, Descemet membrane endothelial keratoplasty; PBK, bullous keratopathy; FECD, Fuchs endothelial comeal dystrophy; PCIOL, posterior chamber intraocular lens; PK, penetrating keratoplasty.

 $\overset{r}{\mathcal{T}} \text{Comparing FECD, PBK and Failed corneal transplant.}$

 t^{\dagger} Comparing PCIOL, Iris fixated and lens status.

 $\int_{0}^{\infty} Comparing 1$ to 2 previous corneal transplants.

* Fisher's exact test.

Table 2

Visual outcome

	Control N (%)	Surgically Treated Glaucoma, N (%)	Medically Treated Glaucoma, N (%)	Total N (%)	\mathbf{P}_{*}
Pre-op BCVA (n)	59	34	14	107	
20/25	6 (10.2)	1 (2.9)	1 (7.1)	8 (7.5)	0.52
20/40	27 (45.8)	3 (8.8)	2 (14.3)	32 (29.9)	0.0002
20/200	53 (89.8)	18 (52.9)	8 (57.1)	79 (73.8)	<0.0001
Post-op BCVA ⁷	59	34	14	107	
20/25, n (%)	46 (78.0)	11 (32.4)	10 (71.4)	67 (62.6)	<0.0001
20/40, n (%)	52 (88.1)	18 (52.9)	13 (92.9)	83 (77.6)	0.0002
20/200, n (%)	59 (100)	29 (85.3)	14 (100)	102 (95.3)	0.0054
Change in BCVA from pre-op to post-op (eyes)					
Improved, n (%)	55 (93.2)	29 (85.3)	14 (100)	98 (91.6)	0.24
Unchanged (eyes), n (%)	4 (6.8)	5 (11.8)	0 (0)	9 (8.4)	
Worsened (eyes), n (%)	0 (0)	0 (0)	0 (0)	0 (0)	
P-value					

 \dot{f}^{t} Post-operative BCVA ever achieved.

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* Fisher exact test Author Manuscript

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Complications

	Control N (%)	Surgically Treated Glaucoma, N (%)	Medically Treated Glaucoma, N (%)	Total N (%)	P^*
Total # of DMEK	60	34	14	108	
Primary graft failure	1 (1.7)	0 (0)	0 (0)	1 (0.9)	1.0
Secondary graft failure	0 (0)	0 (0)	0 (0)	0 (0)	NA
Rejection	1 (1.7)	0 (0)	0 (0)	1 (0.9)	1.0
Total dislocation or upside down graft	0 (0)	0 (0)	0 (0)	0 (0)	NA
Air injection	14 (23.3)	8 (23.5)	3 (21.4)	25 (23.1)	1.0
IOP elevation	14 (23.3)	5 (14.7)	7 (50)	26 (24.1)	0.043
Surgery to control IOP	0 (0)	3 (8.8)	2 (14.3)	5 (4.6)	0.010
CME	4 (6.7)	3 (8.8)	1 (7.1)	8 (7.4)	0.87