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Descemet membrane endothelial keratoplasty using ophthalmic viscoelastic devices for eyes with laser iridotomy-induced corneal endothelial decompensation

Analysis of 11 eyes

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Abstract

Graft insertion into the anterior chamber is one of the most important procedures for successful Descemet membrane endothelial keratoplasty (DMEK). Especially in eyes with fragile zonular fibers and a shallow anterior chamber, smooth graft insertion tends to become more difficult. Ophthalmic viscoelastic devices (OVDs) can usually help to retain the space in the anterior chamber and to improve the safety of manipulations during various ophthalmic surgeries. Therefore, we postulated that graft insertion into the anterior chamber could be improved by their use. The purpose of this study is to investigate the availability and efficacy of OVDs during graft insertion in DMEK surgery.

A total of 11 eyes of 9 patients with bullous keratopathy who underwent DMEK were retrospectively analyzed. The cause of bullous keratopathy was corneal endothelial decompensation following laser iridotomy in all eyes. We used low viscous dispersive OVD (Opegan) to maintain the anterior chamber depth during graft insertion in all of the eyes.

The graft insertion was uneventful in all of the eyes. The inserted graft was attached to the back surface of the cornea. However, 2 eyes needed rebubbling, and after rebubbling, all of the 2 grafts completely attached to the back surface of the cornea. The best spectacle-corrected visual acuity significantly improved 6 months after surgery (P < .001) and the central corneal thickness significantly decreased (P < .001).

The use of OVD facilitates safer graft insertion during DMEK, and subsequently prevents endothelial cell loss, which leads to a successful procedure.

Abbreviations: ACD = anterior chamber depth, BSCVA = best spectacle-collected visual acuity, CCT = central corneal thickness, DMEK = Descemet membrane endothelial keratoplasty, ECD = endothelial cell density, OVD = ophthalmic viscoelastic device.

Keywords: Descemet membrane endothelial keratoplasty, high vitreous pressure, laser iridotomy, ophthalmic viscoelastic devices, shallow anterior chamber

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TH and IO authors contributed equally to this work.

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1. Introduction

Descemet membrane endothelial keratoplasty (DMEK),^[1,2] involving transplantation of only 1 layer of the endothelium and the 20 µm thick Descemet membrane, results in quick and excellent improvement in postoperative visual acuity due to less irregularity on the anterior and posterior surfaces of the cornea, and to the very low incidence of postoperative graft rejection.^[3-5] Many ophthalmologists in Europe and the United States have started to perform DMEK in patients with Fuchs corneal endothelial dystrophy.^[6,7] However, it is thought to be a difficult procedure for Asian eyes, which tend to have a shorter axial length, narrower anterior chamber, darkly colored iris, and more advanced corneal edema resulting from various etiologies of bullous keratopathy, compared with Caucasian eyes.^[8,9] In Asian eyes, particularly those with a short axial length and narrow anterior chamber, successful insertion of the thin endothelial graft into the anterior chamber can sometimes be complicated by elevated vitreous pressure. Furthermore, the etiology for bullous keratopathy varies, in contrast to that of Fuchs corneal endothelial dystrophy, which is more commonly observed in Europe and the United States.^[10–12]

Laser iridotomy (LI) is a well-established procedure for the treatment and prevention of angle-closure glaucoma. Despite the relative safety of the procedure, the eventual development of focal or generalized corneal decompensation following LI have been described by several authors especially from East Asian countries.^[13–16] The characteristics of such eyes include a shorter axial length, a shallow anterior chamber, and fragile zonular fibers. Attempting DMEK on such eyes could sometimes be more difficult, while the iris is often susceptible to prolapse and the collapse of the anterior chamber during graft insertion, with occasional extrusion of the already inserted thin graft through sclerocorneal or corneal incision.

Ophthalmic viscoelastic devices (OVDs) are routinely used in cataract surgery to protect delicate ocular structures, compartmentalize within the eye, and pressurize the anterior chamber. However, they are believed to be contraindicated for use during DMEK surgery, because OVDs remaining in the anterior chamber possibly adhere to both the Descemet membrane and endothelial surfaces of the thin membrane graft. Thus, the OVDs cannot be properly rinsed, and as such, may interfere with the attachment of the graft to the corneal back surface. However, we recently developed the use of OVDs during graft insertion that may assist in surgical procedures.

In this report, we introduce a novel procedure using OVDs for DMEK in the eyes that underwent argon LI as a treatment or prevention of angle closure glaucoma. This procedure may assist surgeons, particularly those who must manipulate eyes under difficult conditions such as those with a shallow anterior chamber, weak iris-lens diaphragm, or high vitreous pressure.

2. Methods

2.1. Patients

Table 1

A total of 11 eyes of 9 patients with bullous keratopathy, who underwent DMEK at Yokohama Minami Kyosai Hospital from August 2015 to July 2016 and were followed up for > 6 months, were analyzed retrospectively. The patients included 1 male and 8 females with a mean age of 75.7 ± 4.1 years. All of the eyes only underwent DMEK. All eyes had a history to undergo LI due to acute angle-closure glaucoma previously. Cataract surgery using phacoemulcification and aspiration techniques with implantation of an intraocular lens were performed before the DMEK in all eyes. The detailed patients' profiles are indicated in Table 1. The study protocol was approved by the Institutional Review Board of the Yokohama Minami Kyosai Hospital.

2.2. Surgical techniques and postoperative treatment

All of the patients were given a diuretic such as D-mannitol and/or acetazolamide shortly before surgery and had a urethral catheter inserted. We performed all of the surgeries under local anesthesia. After retrobulbar anesthesia and a Nadbath facial nerve block, 2 small incisions and a 2.8 mm upper corneal or corneoscleral incision were made. A pre-cut donor graft (SightLife, Seattle, WA) was settled on a vacuum punch (One; Moria SK, Antony, France). Then, Descemet membrane was slowly stripped from the corneal stroma with 2 pairs of forceps, stained with trypan blue, and returned to its original position. Next, the Descemet membrane of the donor graft was carefully cut with a 7.5 or 7.75 mm diameter donor punch. Three asymmetric small marks indicating the direction of the donor graft were placed on the edge of the disc,^[17] and the donor disc was stained again with trypan blue. The donor disc was stripped from the underlying stroma and the graft was stored in a balanced salt solution (BSS Plus; Alcon, Fort Worth, TX) until insertion into the anterior chamber.

After the recipient's epithelium was removed for better visualization of the anterior chamber during surgery, the Descemet membrane with the endothelium was stripped using a reverse Sinskey hook (ASICO, Westmont, IL) and removed from the eye using a Hayashi DMEK stripping-peeling forceps (ASICO). A 25 G anterior-chamber maintenance cannula was inserted in 1 side port. An anterior vitreous cutter was inserted in the other side port and a peripheral iridectomy was made at the 6 o'clock position using a 25 G anterior vitrectomy cutter. We performed a core vitrectomy using a pars plana microincision system when we predicted that the vitreous pressure could be elevated during surgery. Then, we stopped the infusion into the anterior chamber, remove the aqueous fluid through the side port to make the anterior chamber pressure low, and injected a 0.05 to 0.1 mL of OVD (sodium hyaluronate 1%; Opegan, Santen, Osaka, Japan) into the anterior chamber in order to keep the space. After the donor graft disc was loaded on an intraocular lens inserter (WJ-60 M; Santen) with a 0.1 to 0.2 mL of OVD between the graft and the tip of the plunger (Fig. 1), we gently inserted the graft into the anterior chamber. Then, the wound was closed using 10-0 nylon sutures (Mani, Tochigi, Japan). We rinsed the OVD 3 or 4 times by injecting the BSS slowly via the

Preoperative profiles of the enrolled patients.								
Case	Sex	Age	OD/OS	Axial length, mm	ACD, mm	ACD post-phaco, mm	BCVA	ССТ, µ m
1	Μ	73	OD	22.1	1.78	2.82	20/4000	926
2	F	71	OD	21.8	1.453	3.097	20/1000	727
3			OS	21.7	1.330	2.988	20/60	744
4	F	75	OD	21.4	1.926	3.019	20/60	698
5	F	78	OS	22.4	1.959	3.491	20/100	703
6	F	81	OD	22.8	1.477	2.933	20/1000	763
7	F	77	OD	21.9	1.597	3.075	20/60	745
8	F	69	OS	21.3	1.660	2.822	20/60	716
9	F	75	OD	22.7	1.790	3.132	20/2000	934
10	F	82	OS	20.9	1.698	2.738	20/600	863
11			OD	21.0	1.701	2.778	20/400	876

ACD = anterior chamber depth, BSCVA = best spectacle-corrected visual acuity, CCT = central corneal thickness, OD = right eye, OS = left eye, post-phaco = post- phacoemulsification, aspiration, and intraocular lens implantation surgery.

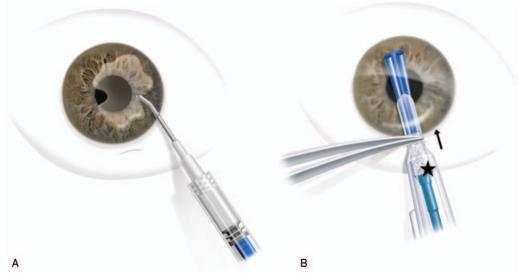


Figure 1. Schematic drawing showing how to use ophthalmic viscoelastic devices (OVDs) during Descemet membrane endothelial keratoplasty. (A) We placed a 0.05 to 0.1 mL of the OVD into the anterior chamber before insertion of the corneal graft. (B) The donor graft disc is loaded into an intraocular lens injector with the OVD (star) between the graft and plunger tip. As we pressed the plunger, the OVD pushed the graft smoothly into the anterior chamber in the direction indicated by the arrow.

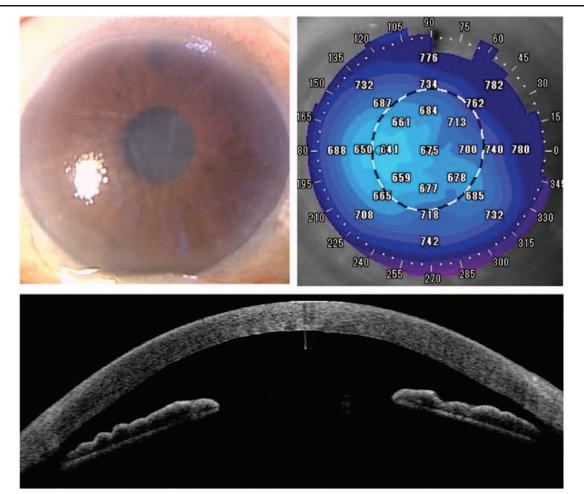


Figure 2. Preoperative photographs of a representative case with bullous keratopathy that has undergone previous laser iridotomy. Top left, slit-lamp microscope shows edematous corneal epithelium and stroma with folds of the Descemet membrane. Top right, the pachymetry map shows that the corneal thickness is more than $600 \,\mu\text{m}$ at the thinnest points. Bottom, the cross-sectional image using an anterior segment optical coherence tomography indicates corneal edema and shallow anterior chamber.

side port. After the rolled inserted graft was unfolded using 0.02 mL air or the double cannula technique,^[18] additional air was carefully injected into the anterior chamber underneath the graft so that the graft attached to the back surface of the recipient corneal stroma (supplemental video, http://links.lww.com/MD/C309). After 15 minutes, the air was partially replaced with a BSS. At the end of the procedure, 0.4 mg subconjunctival betamethasone (Rinderon; Shionogi, Osaka, Japan) and 1.5% levofloxacin eye drops (Cravit; Santen) were administered. Postoperative medications included 1.5% levofloxacin (Cravit), 0.1% betamethasone sodium phosphate (Sanbetasone; Santen), and 2% rebamipide ophthalmic solution (Mucosta; Otsuka, Tokyo, Japan), starting at 4 times per day for 3 months and then tapering thereafter.

2.3. Examinations

In addition to a standard ophthalmic examination, the best spectacle-corrected visual acuity (BSCVA), corneal endothelial cell density (ECD), corneal thickness, and graft adaptation were evaluated preoperatively and up to 6 months postoperatively. Graft adaptation was assessed by observation using slit-lamp microscopy and anterior segment optical coherence tomography (SS1000; Tomey, Aichi, Japan). Corneal thickness was measured by corneal tomography (SS1000). The preoperative ECD was determined by reviewing records of donors from the eye bank. Intra- and postoperative complications were also recorded, and the postoperative ECD was measured using a specular microscope (FA3509; Konan Medical, Hyogo, Japan).

2.4. Statistical analysis

The Wilcoxon test was used to compare mean values where appropriate. A *P* value less than .05 was considered statistically significant.

3. Results

The graft adhered to the corneal back surface in all of the cases throughout the observation period. The BSCVA (logMAR) improved significantly from 1.12 ± 0.55 preoperatively to $0.00 \pm$ 0.05 at 6 months postoperatively (P < .001). The central corneal thickness decreased from $790.5 \pm 86.5 \,\mu\text{m}$ preoperatively to $509.2 \pm 44.1 \,\mu\text{m}$ at 6 months postoperatively (P < .001). The

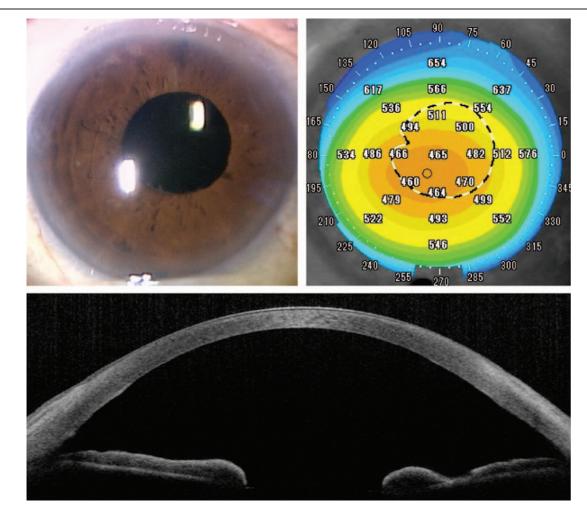


Figure 3. Postoperative photographs of a representative case. The same eye that is shown in Fig. 2. This eye underwent cataract surgery prior to the DMEK surgery. All of the photographs are taken on 6 months after DMEK. Top left, the corneal edema completely healed and whole cornea became clear. Top right, the pachymetry map shows that the corneal thickness dramatically improved. Bottom, the cross-sectional image using an anterior segment optical coherence tomography image shows the corneal edema improved with no increased scattering at the interface between the corneal stroma and the Descemet membrane.

postoperative corneal ECD was 1451.5 ± 424.3 cells/mm² at 6 months (a $43.8 \pm 14.8\%$ decrease from the preoperative ECD of the donor graft). No eyes showed signs of pupillary block, microbial infection, or endothelial rejection. Partial detachment of the graft that required rebubbling into the anterior chamber was observed in 2 eyes within 7 days after surgery, and the graft showed complete attachment immediately after the rebubbling in both eyes. There was no primary graft failure. The pre- and postoperative photographs of a representative case are shown in Figs. 2 and 3.

4. Discussion

Various injectors have been used for DMEK, but thus far an optimal injector has not been developed. If the anterior chamber is deep enough, a graft may successfully be inserted with the Melles glass tube or the Jones tube. However, in some eyes with shallow anterior chamber and high vitreous pressure, the tip of the tube sometimes cannot be inserted, even into the corneal/ corneoscleral tunnel, because of an elevated lens-iris diaphragm and iris prolapse. In such eyes, an OVD maintains the anterior chamber depth and protects the thin membrane graft from being pressed. In particular, placement of the OVD in the injector behind the DMEK graft helps to gently push the graft forward to enable smooth insertion of the graft into the anterior chamber.

The biggest concern is that the OVD used during DMEK may remain in the anterior chamber and interfere with the graft attachment during and after surgery. To prevent this complication, we used a small volume of low viscous dispersive OVD (Opegan), and gently rinsed it using aspiration with BSS within the anterior chamber after the graft insertion. As a result, only 2 of 11 eyes required postoperative rebubbling, which is infrequent for beginning DMEK surgeons. In addition, it helps prevent severe endothelial cell loss possibly due to mechanical damage occurring because of inadequate anterior chamber pressure control and/or spontaneous graft extrusion through the incision during surgery.

Our procedure using low viscous dispersive OVDs for DMEK surgery may be useful for surgeons with less experience and/or for eyes with narrower anterior chambers, shorter axial length, and high vitreous pressure frequently found in Asian patients. Especially, we believe that the use of OVDs prevents primary graft failure resulting from technical problems of surgeons with less experience, particularly in difficult cases, so its use could be helpful to these clinicians. In the future, additional surgical innovations should also improve the outcomes of DMEK.

Author contributions

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- Writing original draft: Takahiko Hayashi, Naoko Kato.
- Writing review & editing: Itaru Oyakawa, Nobuhisa Mizuki, Naoko Kato.

References

- Melles GR. Posterior lamellar keratoplasty: DLEK to DSEK to DMEK. Cornea 2006;25:879–81.
- [2] Melles GR, Ong TS, Ververs B, et al. Descemet membrane endothelial keratoplasty (DMEK). Cornea 2006;25:987–90.
- [3] Hayashi T, Yamagami S, Tanaka K, et al. Immunologic mechanisms of corneal allografts reconstituted from cultured allogeneic endothelial cells in an immune-privileged site. Invest Ophthalmol Vis Sci 2009; 50:3151–8.
- [4] Anshu A, Price MO, Price FWJr. Risk of corneal transplant rejection significantly reduced with Descemet's membrane endothelial keratoplasty. Ophthalmology 2012;119:536–40.
- [5] Tourtas T, Laaser K, Bachmann BO, et al. Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty. Am J Ophthalmol 2012;153:1082–90.
- [6] Ang M, Wilkins MR, Mehta JS, Tan D. Descemet membrane endothelial keratoplasty. Br J Ophthalmol 2016;100:15–21.
- [7] Dapena I, Ham L, Droutsas K, et al. Learning curve in Descemet's membrane endothelial keratoplasty: first series of 135 consecutive cases. Ophthalmology 2011;118:2147–54.
- [8] Kobayashi A, Yokogawa H, Yamazaki N, et al. The use of endoillumination probe-assisted Descemet membrane endothelial keratoplasty for bullous keratopathy secondary to argon laser iridotomy. Clin Ophthalmol 2015;8:91–3.
- [9] Ip JM, Huynh SC, Robaei D, et al. Ethnic differences in refraction and ocular biometry in a population-based sample of 11-15-year-old Australian children. Eye (Lond) 2008;22:649–56.
- [10] Guerra FP, Anshu 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;118:2368–73.
- [11] Kruse FE, Schlötzer-Schrehardt U, Tourtas T. Optimizing outcomes with Descemet's membrane endothelial keratoplasty. Curr Opin Ophthalmol 2014;25:325–34.
- [12] Rodríguez-Calvo-de-Mora M, Quilendrino R, Ham L, et al. Clinical outcome of 500 consecutive cases undergoing Descemet' membrane endothelial keratoplasty. Ophthalmology 2015;122:464–70.
- [13] Shimazaki J, Amano S, Uno T, et al. Japan Bullous Keratopathy Study GroupNational survey on bullous keratopathy in Japan. Cornea 2007;26:274–8.
- [14] Ang LP, Higashihara H, Sotozono C, et al. Argon laser iridotomyinduced bullous keratopathy a growing problem in Japan. Br J Ophthalmol 2007;91:1613–5.
- [15] Hirayama M, Yamaguchi T, Satake Y, et al. Surgical outcome of Descemet's stripping automated endothelial keratoplasty for bullous keratopathy secondary to argon laser iridotomy. Graefes Arch Clin Exp Ophthalmol 2012;250:1043–50.
- [16] Wang PX, Koh VT, Loon SC. Laser iridotomy and the corneal endothelium: a systemic review. Acta Ophthalmol 2014;92:604–16.
- [17] Bachmann BO, Laaser K, Cursiefen C, et al. A method to confirm correct orientation of Descemet membrane during Descemet membrane endothelial keratoplasty. Am J Ophthalmol 2010;149:922–5.
- [18] Liarakos VS, Dapena I, Ham L, et al. Intraocular graft unfolding techniques in Descemet membrane endothelial keratoplasty. JAMA Ophthalmol 2013;131:29–35.