OPEN

Techniques for Learning Descemet Membrane Endothelial Keratoplasty for Eyes of Asian Patients With Shallow Anterior Chamber

Takahiko Hayashi, MD, PhD,† Itaru Oyakawa, MD,‡§ and Naoko Kato, MD, PhD¶*

Purpose: To describe several essential surgical techniques that overcome difficulties in performing Descemet membrane endothelial keratoplasty (DMEK) for inexperienced surgeons, especially those who perform DMEK on eyes of Asian patients.

Methods: Nine eyes of 9 Asian patients with bullous keratopathy who underwent DMEK were analyzed retrospectively. All patients were given a diuretic such as D-mannitol or acetazolamide shortly before surgery, with retrobulbar anesthesia and a Nadbath facial nerve block. Core vitrectomy before DMEK was performed in several cases in which a high vitreous pressure during surgery was predicted. The donor graft was stained with trypan blue, and a 25-G anterior chamber maintenance cannula was used to maintain the anterior chamber depth during graft insertion in all eyes.

Results: The cornea became clear in all eyes. The best spectacle-corrected visual acuity had improved significantly 6 months after the surgery compared with preoperative values ($P = 0.026$). The corneal endothelial cell density was 1371 cells per square millimeter at postoperative 6 months.

Conclusions: Although DMEK is technically difficult, especially for inexperienced surgeons who operate on eyes of Asian patients, controlling anterior chamber pressure using various manipulations may help to prevent iatrogenic primary graft failure and lead to successful DMEK.

Received for publication September 6, 2016; revision received October 9, 2016; accepted October 11, 2016. Published online ahead of print December 20, 2016.

From the *Department of Ophthalmology, Yokohama Minami Kyosai Hospital, Kanagawa, Japan; †Department of Ophthalmology, Yokohama City University School of Medicine, Yokohama, Kanagawa, Japan; ‡Department of Ophthalmology, Heart Life Hospital, Okinawa, Japan; §Department of Ophthalmology, Ryukyu University, Okinawa, Japan; and ¶Department of Ophthalmology, Saitama Medical University, Saitama, Japan.

The authors have no funding or conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.corneajrnl.com).

Reprints: Naoko Kato, MD, PhD, Department of Ophthalmology, Saitama Medical University, Morohongo 38, Moroyamacho, Iruma, Saitama 350-0495, Japan (e-mail: naokato@bc.iij4u.or.jp).

Copyright © 2016 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Key Words: bullous keratopathy, Descemet membrane endothelial keratoplasty, shallow anterior chamber, vitreous pressure

(*Cornea* 2017;36:390–393)

Descemet membrane endothelial keratoplasty (DMEK)[1–3] transplants just one layer of the endothelium and the 20-μm-thick Descemet membrane and results in less irregularity on the corneal stromal back surface, achieving quick and consistent improvement in postoperative visual acuity and reduced postoperative graft rejection.[4–6] Many ophthalmologists in Europe and the United States have begun to perform DMEK for patients with corneal endothelial dystrophy.[7] However, many surgeons are reluctant to perform DMEK because of technical difficulties.[8]

DMEK is especially difficult to perform in eyes of Asian patients. The thin membrane graft with the fragile endothelial layer on the outside is easily injured when manipulated. Asians tend to have a narrow palpebral fissure and small deep-set eyes, with a relatively shallow anterior chamber and dark iris (Fig. 1; see Table, Supplement Digital Content 1, http://links.lww.com/ICO/A472). All of these characteristics of Asian eyes may become obstacles to performing DMEK.[9] Another reason is that the causes of corneal endothelial decompensation in Asians vary and differ from those in whites. Bullous keratopathy after laser iridotomy or complicated cataract surgery and endotheliopathy in pseudoexfoliation syndrome are frequently seen in Japan.[10,11] In contrast, Fuchs corneal endothelial dystrophy is the most common reason for endothelial keratopathy in Europe and the United States.[12–14] These various eye conditions may result in diverse problems during and after surgery.

This article outlines several approaches and precautions for DMEK in Asian eyes. The study may be useful when performing surgery for difficult eye conditions, such as a shallow anterior chamber eye or dark iris, in populations other than whites.

METHODS

Patients

Patients with bullous keratopathy who underwent DMEK at Yokohama Minami Kyosai Hospital from January 2015 to July 2015 and were followed for at least 6 months were analyzed retrospectively using medical records. The study protocol was approved by the Institutional Review Board of the Yokohama Minami Kyosai Hospital.

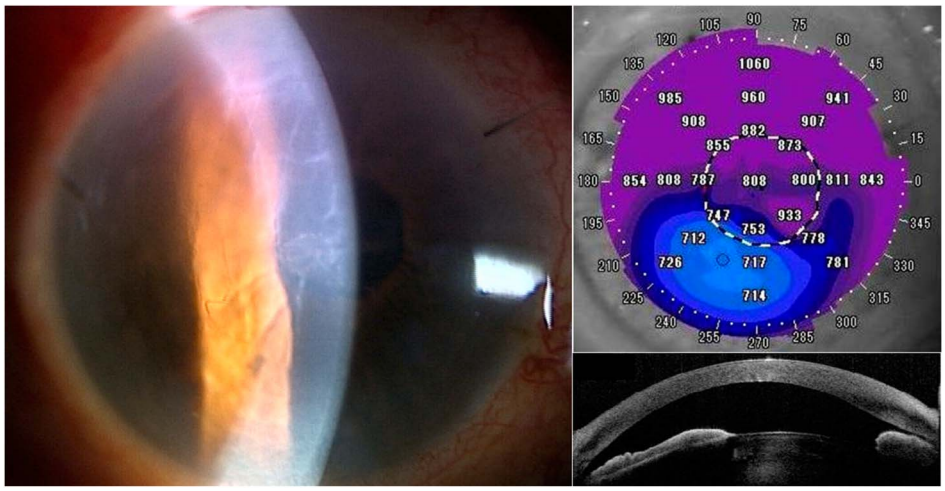

FIGURE 1. Photographs of bullous keratopathy in an eye from an Asian patient (case 8). Left, The bullous keratopathy is advanced, the anterior chamber is shallow, and the iris color is dark. These characteristics are all challenges for DMEK surgery. Right top, Pachymetry map shows that the cornea is more than 800 μm thick at the apex, indicating that the bullous keratopathy is advanced. Right bottom, The Scheimpflug image shows that the anterior chamber is shallow.

Nine eyes of 9 patients (8 females and 1 male; age, 71.3 ± 9.3 years) were included. All DMEK surgery was performed on pseudophakic eyes. Seven eyes underwent only DMEK, and 2 eyes (cases 6 and 7) underwent cataract surgery simultaneously with DMEK. Four eyes underwent cataract surgery with intraocular lens implantation at other hospitals, and the remaining 3 eyes underwent cataract surgery with intraocular lens implantation at our hospital. The etiology of bullous keratopathy varied: 3 eyes had Fuchs corneal endothelial dystrophy and 2 eyes had corneal endotheliopathy due to pseudoexfoliation syndrome (PEX). Four eyes had iatrogenic bullous keratopathy, 2 eyes had undergone argon laser iridotomy, and 2 eyes had previous cataract surgery. The anterior chamber depth of 5 eyes that underwent cataract surgery before the DMEK varied from 1.03 to 2.14 mm. The anterior chamber depth before DMEK was 3.07 ± 0.09 mm (range, 2.91–3.19 mm) after intraocular lens implantation (see Table, Supplement Digital Content 1, http://links.lww.com/ICO/A472).

Surgical Techniques and Postoperative Treatment

All patients were given a diuretic such as D-mannitol or acetazolamide shortly before surgery and had a urethral catheter inserted. We performed all surgery under local anesthesia. After retrobulbar anesthesia and a Nadbath facial nerve block, we performed ocular compression using a Honan balloon for 15 minutes.

A precut donor graft (SightLife, USA) was settled on a vacuum punch (Disposable donor punch, Moria, Japan). Then, Descemet membrane was stripped from the corneal stroma with a standard technique.[2,3,13] The Descemet membrane of the donor graft was carefully cut with a 7.25- or 7.5-mm-diameter donor punch. Three small marks indicating the direction of the donor graft were placed on the edge of the disc,[15] and the donor disc was again stained with 0.06% trypan blue. The donor disc was stripped from the underlying stroma and the graft was stored in balanced salt solution (BSS plus; Alcon, Fort Worth, TX) until insertion into the anterior chamber.

For the recipient cornea, 2 paracenteses and a 2.7-mm upper corneal or corneoscleral incision were made. The recipient's Descemet membrane with the endothelium was stripped using a reverse Sinskey hook (ASICO, Westmont, IL) and removed from the eye using Hayashi DMEK stripping–peeling forceps (ASICO). A 25-G anterior chamber maintenance cannula was inserted in one side port. An anterior vitreous cutter was inserted in the other side port and peripheral iridectomy was made at the 6 o'clock position using a 25-G anterior vitrectomy cutter. We performed core vitrectomy using a pars plana microincision system when we predicted that the vitreous pressure would be high and the iris would be elevated during surgery. We placed a trocar-mounted microcannula on an appropriate point on the sclera, 3.5 mm from the limbus, inserted a 25-G vitreous cutter into the vitreous cavity, and cut the vitreous for several seconds until the eye was softened. Then, the donor graft disc loaded on an intraocular lens inserter (WJ-60M; Santen, Osaka, Japan) was gently inserted into the anterior chamber. The anterior chamber was infused using an anterior chamber maintainer, and when the graft was completely inserted, infusion was immediately stopped before the inserter was removed. Then, the corneoscleral incision was sutured using 10-0 nylon. When the rolled inserted graft was unfolded using 0.05 mL of air or the double cannula technique,[16] 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. After 15 minutes, the air was partially replaced with BSS. At the end of the procedure, 0.4 mg of subconjunctival betamethasone (Rinderon; Shionogi, Osaka, Japan) and 1.5% levofloxacin eye drops (Cravit; Santen) were administered. Postoperative medications included 1.5% levofloxacin (Cravit; Santen), 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 tapered thereafter.

Examinations

In addition to a standard ophthalmic examination, the best spectacle-corrected visual acuity, corneal endothelial cell density (ECD), corneal pachymetry, and graft adaptation were evaluated preoperatively and up to 6 months postoperatively.

Copyright © 2016 The Author(s). Published by Wolters Kluwer Health, Inc.

Graft adaptation was assessed by observation using slit-lamp microscopy and anterior segment optical coherence tomography (CASIA SS-1000; Tomey, Nagoya, Japan). Pachymetry was measured by corneal topography (CASIA SS-1000). The preoperative ECD was determined by reviewing the records of donors from the eye bank. Intraoperative and postoperative complications were also recorded, and the postoperative ECD was measured using a specular microscope (SP-3000P; Tomey).

Statistical Analysis

The *t* test was used to compare mean values where appropriate. All analyses were performed using the statistical software StatView (Abacus Concepts, Berkeley, CA). $P < 0.05$ was considered significant.

RESULTS

All of 9 enrolled eyes showed graft adhesion throughout the observation period. In those 9 eyes, the best spectacle-corrected visual acuity (logMAR) improved significantly from 0.71 ± 0.26 preoperatively to 0.15 ± 0.12 at 6 months postoperatively ($P = 0.026$). The central corneal thickness decreased from 709.5 ± 114.6 μm preoperatively to 540.1 ± 32.5 μm 6 months postoperatively ($P = 0.001$). The postoperative corneal ECD was 1371 cells per square millimeter at 6 months, which was a 44.1% ± 16.9% decrease from the preoperative ECD of the donor graft.

One eye (case 3) had idiopathic bleeding from the iris during surgery that prolonged the operating time. Although the implanted graft was attached to the recipient's corneal stroma, it did not become clear. Three weeks postoperatively, we deemed this graft to have failed and performed DMEK again. The second DMEK surgery was uneventful and the cornea became clear. 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 3 eyes 4 to 14 days after surgery, and the graft showed complete attachment after the rebubbling in all 3 eyes.

DISCUSSION

The causes of corneal endothelial dysfunction vary in eyes of Asian patients, and frequently include PEX corneal endotheliopathy, bullous keratopathy due to laser iridotomy or complicated cataract surgery, or viral infection such as herpes simplex or cytomegalovirus infections.[17,18] In PEX eyes, the entire ocular tissue, including the pigment epithelium, vascular endothelial cells, stromal cells of the iris, zonular fibers, and lens epithelium are affected, rendering the anterior part of the eye vulnerable.[19] In eyes with bullous keratopathy after argon laser iridotomy, the eyeball is usually small because of hyperopia, and the anterior chamber is also very shallow because of the fragile and sometimes even partially ruptured zonule fibers.[20] In such eyes, the vitreous pressure is easily elevated during surgery, narrowing the anterior chamber and interfering with insertion of the graft into the anterior chamber. The graft can easily be bent over or expelled through the incision.

To solve these problems, the anterior chamber pressure should be controlled during the graft insertion. We administer not only retrobulbar anesthesia but also a Nadbath facial nerve block in all cases when we perform DMEK surgery under local anesthesia to reduce the external eye pressure by grimacing. A diuretic such as D-mannitol or acetazolamide should be given shortly before surgery to reduce the vitreous pressure and a urethral catheter inserted that helps to stop the patient from moving during surgery by providing uresiesthesia. When the vitreous pressure was still high, we performed core vitrectomy just before graft insertion.

We also used an anterior chamber maintainer during graft insertion. At this time, the pressure should be set at 15 to 20 mm Hg to keep the anterior chamber sufficiently deep and wide and not to interfere with graft insertion.

Furthermore, corneal edema of bullous keratopathy in Asian eyes is often advanced, which decreases the visibility of the anterior chamber during surgery. In addition, it is difficult to identify and manipulate the DMEK graft in the anterior chamber in Asian eyes with a dark iris. Therefore, it is necessary to use marks to identify the top and bottom surfaces[15] and stain the graft with a dye as previously recommended.[9] Abrasion of the host edematous epithelium can also improve the visibility of the anterior chamber in some advanced cases.

Using the previously described techniques, the postoperative corneal ECD decreased 44.1% ± 16.9% when compared with the preoperative ECD of the donor graft. Previous studies reported an endothelial loss of 28% to 65% at 6 months after surgery.[5,15,21–24] When considering that we used precut donor tissue transported from the United States, we consider our ECD loss in this investigation to be satisfactory.

Unfolding the graft is generally believed to be easier when the anterior chamber depth is narrower. However, endothelial cells are irreversibly damaged if the endothelial graft is barely inserted into the anterior chamber, and thus pushed back by the aqueous pressure and stuck between the corneoscleral incision or paracentesis. During DMEK in small eyes with a shorter axial length and shallow anterior chamber, uneventful graft insertion into the anterior chamber is the most important determinant of successful surgery. Once the graft is completely inserted, manipulation within the anterior chamber is similar to that of eyes with a deep anterior chamber, as long as we select a smaller donor punch based on the corneal diameter of the recipient.

Taken together, the techniques we introduced in this study should assist surgeons with limited experience in performing DMEK for bullous keratopathy in the eyes of Asian patients, to prevent iatrogenic primary graft failure and to optimize the chances of successful surgery.

REFERENCES

1. Price MO, Gorovoy M, Price FW, Jr, et al. Descemet's stripping automated endothelial keratoplasty: three-year graft and endothelial cell survival compared with penetrating keratoplasty. *Ophthalmology*. 2013; 120:246–251.
2. Melles GR. Posterior lamellar keratoplasty: DLEK to DSEK to DMEK. *Cornea*. 2006;25:879–881.

Copyright © 2016 The Author(s). Published by Wolters Kluwer Health, Inc.

3. Melles GR, Ong TS, Ververs B, et al. Descemet membrane endothelial keratoplasty (DMEK). *Cornea*. 2006;25:987–990.
4. 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;50:3151–3158.
5. Anshu A, Price MO, Price FW, Jr. Risk of corneal transplant rejection significantly reduced with Descemet's membrane endothelial keratoplasty. *Ophthalmology*. 2012;119:536–540.
6. Tourtas T, Laaser K, Bachmann BO, et al. Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty. *Am J Ophthalmol.* 2012;153:1082–1090.
7. Ang M, Wilkins MR, Mehta JS, et al. Descemet membrane endothelial keratoplasty. *Br J Ophthalmol.* 2016;100:15–21.
8. Dapena I, Ham L, Droutsas K, et al. Learning curve in Descemet's membrane endothelial keratoplasty: first series of 135 consecutive cases. *Ophthalmology*. 2011;118:2147–2154.
9. 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;8:91–93.
10. Shimazaki J, Amano S, Uno T, et al. National survey on bullous keratopathy in Japan. *Cornea.* 2007;26:274–278.
11. Ang LP, Higashihara H, Sotozono C, et al. Argon laser iridotomy-induced bullous keratopathy a growing problem in Japan. *Br J Ophthalmol.* 2007; 91:1613–1615.
12. 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;118:2368–2373.
13. Kruse FE, Schrehardt US, Tourtas T. Optimizing outcomes with Descemet's membrane endothelial keratoplasty. *Curr Opin Ophthalmol.* 2014;25:325–334.
14. Rodríguez-Calvo-de-Mora M, Quilendrino R, Ham L, et al. Clinical outcome of 500 consecutive cases undergoing Descemet' membrane endothelial keratoplasty. *Ophthalmology*. 2015;122:464–470.
15. 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;149:922–925.
16. Liarakos VS, Dapena I, Ham L, et al. Intraocular graft unfolding techniques in Descemet membrane endothelial keratoplasty. *JAMA Ophthalmol.* 2013; 131:29–35.
17. Anshu A, Chee SP, Mehta JS, et al. Cytomegalovirus endotheliitis in Descemet's stripping endothelial keratoplasty. *Ophthalmology*. 2009; 116:624–630.
18. Suzuki T, Hara Y, Uno T, et al. DNA of cytomegalovirus detected by PCR in aqueous of patient with corneal endotheliitis after penetrating keratoplasty. *Cornea*. 2007;26:370–372.
19. Naumann GO, Schlötzer-Schrehardt U, Küchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist. Intraocular and systemic manifestations. *Ophthalmology*. 1998;105:951–968.
20. 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;250:1043–1050.
21. Hamzaoglu EC, Straiko MD, Mayko ZM, et al. The first 100 Eyes of standardized Descemet stripping automated endothelial keratoplasty versus standardized Descemet membrane endothelial keratoplasty. *Ophthalmology*. 2015;122:2193–2199.
22. Ang M, Mehta JS, Newman SD, et al. Descemet membrane endothelial keratoplasty: preliminary results of a donor insertion pull-through technique using a donor mat device. *Am J Ophthalmol.* 2016;107:27–34.
23. Price MO, Giebel AW, Fairchild KM, et al. Descemet's membrane endothelial keratoplasty: prospective multicenter study of visual and refractive outcomes and endothelial survival. *Ophthalmology*. 2009;116: 2361–2368.
24. Monnereau C, Quilendrino R, Dapena I, et al. Multicenter study of Descemet membrane endothelial keratoplasty: first case series of 18 surgeons. *JAMA Ophthalmol.* 2014;132:1192–1198.

Copyright © 2016 The Author(s). Published by Wolters Kluwer Health, Inc.