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Case Report

Development of a Donor Tissue Holding Technique for Descemet's Membrane Endothelial Keratoplasty Using a 25-Gauge Graft Manipulator

Akira Kobayashi Hideaki Yokogawa Natsuko Mori Toshinori Masaki Kazuhisa Sugiyama

Department of Ophthalmology, Kanazawa University Graduate School of Medical Science, Kanazawa, Japan

Keywords

Descemet's membrane endothelial keratoplasty · Argon laser iridotomy · 25-gauge graft manipulator

Abstract

Purpose: To report a modified surgical technique called the "donor tissue holding technique for Descemet's membrane endothelial keratoplasty (DMEK)" using a newly developed 25-gauge graft manipulator. ***Methods:*** Six consecutive patients exhibiting endothelial dysfunction were enrolled and treated by DMEK. In brief, after insertion of a DMEK donor into the anterior chamber, the edge of the roll was grasped using a graft manipulator and this grasp was maintained throughout the centering and opening of the roll (holding technique). The following parameters were evaluated in comparison to the previous 10 consecutive DMEK cases in which the no touch technique was used: time of graft unfolding, incidence of intra-/postoperative complications, and best spectacle-corrected visual acuity (BCVA) and endothelial cell density (ECD) 6 months after the procedure. ***Results:*** In both technique groups, neither intra- nor postoperative complications were noted in any case. No differences were observed between the two groups in postoperative BCVA (p = 0.88). Also, no differences were observed between the two groups in postoperative ECD (holding technique group: 2,108.3 cells/mm^2, no touch technique group: 1,491.7 cells/mm^2) (p = 0.08) Most notably, the time of graft unfolding prior

Akira Kobayashi, MD, PhD
Department of Ophthalmology
Kanazawa University Graduate School of Medical Science
13-1 Takara-machi, Kanazawa-shi, Ishikawa-ken 920-8641 (Japan)
E Mail eyekoba@gmail.com

to filling with air was significantly reduced in the holding technique group (305.5 s) compared to that of the no touch technique group (1,310.0 s; $p = 0.01$). ***Conclusions:*** This donor tissue holding technique enabled rapid and safe DMEK in a reproducible manner, even in Asian eyes with shallow anterior chambers with high vitreous pressure.

Introduction

Currently, Descemet's stripping automated endothelial keratoplasty (DSAEK) is widely used for the treatment of bullous keratopathy [1–6]. The advantages of DSAEK compared to penetrating keratoplasty include completely eliminating the need for full-thickness corneal incisions and many sutures, maintaining much of the anatomical integrity of the cornea, and inducing minimal refractive changes [6, 7]. However, the percentage of patients who achieve 20/20 best-corrected visual acuity (BCVA) is less than expected after DSAEK relative to the visual potential [4–10], and immunological graft rejection remains a possibility, although with low incidence [11]. To circumvent these problems, Melles et al. [12–15] established a procedure of selective transplantation of donor Descemet's membrane (DM) and endothelium, known as Descemet's membrane endothelial keratoplasty (DMEK). The visual outcomes after DMEK were impressive compared to DSAEK [16–21].

However, the surgical techniques required for the DMEK procedure are quite challenging, especially for Asian eyes, since these patients tend to have advanced bullous keratopathy with shallow anterior chambers, high vitreous pressure, and dark brown irises, all factors which complicate DMEK [10, 22, 23]. Moreover, in Japan, the incidence of Fuchs' dystrophy as a causative factor for bullous keratopathy is relatively low.

In the current study, we report a novel surgical technique called the "donor tissue holding technique for DMEK" using a newly developed 25-gauge graft manipulator. The utility and safety of this technique as well as preliminary clinical outcomes are presented.

Methods

This was a prospective interventional case series. The study was approved by the Ethics Committee of Kanazawa University Graduate School of Medical Science and followed the tenets of the Declaration of Helsinki. Six consecutive patients (1 male and 5 females; mean age, 73.2 years) exhibiting endothelial dysfunction were enrolled and treated by DMEK using the holding technique. The time required for graft unfolding during the procedure (using a surgical video), the incidence of intra-/postoperative complications, and the best spectacle-corrected visual acuity (BCVA) and endothelial cell density (ECD) 6 months after surgery were compared to the previous 10 consecutive DMEK cases (5 males and 5 females; mean age, 65.7 years) in which the no touch technique was used. The causative diseases in the patients of the holding technique group included argon laser iridotomy-induced bullous keratopathy ($n = 4$), posterior polymorphous corneal dystrophy ($n = 1$), and birth injury due to delivery forceps ($n = 1$). The causative diseases in the control patients of the no touch technique group included argon laser iridotomy-induced bullous keratopathy ($n = 3$), pseudophakic bullous keratopathy ($n = 3$), Fuchs' corneal dystrophy ($n = 2$), failed penetrating keratoplasty ($n = 1$), and cytomegalovirus corneal endotheliitis ($n = 1$). For statistical analysis, the unpaired t test (SPSS Statistics version 23; IBM) was used.

Surgery

No Touch Technique

DMEK surgery was performed under peribulbar anesthesia according to previously reported methods [18, 19]. In brief, after removal of the edematous host epithelial cells for better visualization of the anterior chamber, approximately 9.0 mm in diameter of the host DM was removed after filling the anterior chamber with viscoelastic materials. An inferior iridectomy at the 6 o'clock position was created using a 25-gauge vitreous cutter. All pre-stripped and s-stamped DMEK donor tissues were internationally shipped from a US eye bank (SightLife, Seattle, WA, USA). The DM roll (8.0 mm in diameter) stained with 0.06% trypan blue (Vision Blue®; DORC, Zuidland, The Netherlands) for 4 min was then inserted into the anterior chamber via a 2.4-mm temporal clear corneal incision using a DMEK shooter (G-38630; Geuder, Heidelberg, Germany). After securing the wound with one 10-0 nylon suture, the DMEK roll was correctly oriented with the endothelium side facing down. A small air bubble was then injected over the DM graft and used to unfold the graft. To obtain further visualization, oblique light via an endoillumination probe held by an assistant surgeon was used. The endoillumination probe was not inserted into the anterior chamber but was attached at the peripheral cornea. This technique improved the contrast between the blue-stained DM roll and the background of the dark brown iris. Additionally, the orientation of the DMEK donor was confirmed using intraoperative spectral-domain optical coherence tomography using the RESCAN 700 (Carl Zeiss Meditec, Germany). Finally, the anterior chamber was filled with air to completely attach the DM graft to the posterior stromal surface. No corneal fenestrations were made to drain interface fluid. To improve donor recipient adhesion, no scraping of the recipient's peripheral stroma was performed. The anterior chamber was kept full of air and the patient was instructed to lie on his or her back for 2–3 h.

DMEK Donor Holding Technique

The general surgical procedure of the holding technique is similar to that of the no touch technique; the difference is the use of a newly developed 25-gauge graft manipulator (Catalog No. AE-4933, AE-4934; ASICO, Westmont, IL, USA; Fig. 1). This 25-gauge DMEK manipulator has a ring-shaped tip (vertical and horizontal type), which is less traumatic to the DM when the surgeon grasps the membrane edge. Moreover, this forceps is able to grasp the edge of the donor DM without tearing during DMEK, enabling precise and rapid donor centering before and after air injection into the anterior chamber. After insertion of the trypan blue-stained DM roll into the anterior chamber via a 2.4-mm temporal clear corneal incision using a DMEK shooter (Fig. 2a, b), the edge of the roll was grasped using the 25-gauge graft manipulator and this grasp was maintained throughout the centering and opening of the roll (Fig. 2c–g); this was performed by adjusting the depth of the anterior chamber, sometimes using fluid through an infusion cannula and tapping of the corneal surface (referred to as the holding technique). Finally, a large amount of air was inserted under the graft (Fig. 2h, i).

Results

In both technique groups, neither intra-/postoperative complications, including graft detachment, upside-down graft placement, graft rejection, nor early graft failure were noted in any case. Mean BCVA improved from 0.18 to 0.63 decimal visual acuity in the no touch technique group, and from 0.43 to 0.85 in the holding technique group 6 months after surgery;

there was no statistical difference in postoperative BCVA between these two groups ($p = 0.88$). Also, no differences were observed between the two groups in postoperative ECD (holding technique group: 2,108.3 cells/mm^2, no touch technique group: 1,491.7 cells/mm^2) ($p = 0.08$). The rate of ECD loss after 6 months was 30.5 ± 14.6% in the holding technique group, whereas that of the no touch technique group was 49.9 ± 49.5% ($p = 0.09$). Most notably, the surgical time required between graft unfolding and filling with air was significantly reduced in the holding technique group (305.5 ± 104.7 s) compared to that of the no touch technique group (1,310.0 ± 1,036.3 s; $p = 0.01$).

Discussion

As reported previously by our group [10, 22] and others [23], it is more challenging to perform DMEK in Asian eyes with endothelial dysfunction, since they tend to have advanced bullous keratopathy with shallow anterior chambers, high vitreous pressure, and dark brown irises. To circumvent these difficulties, we [22] and others [24] have previously advocated the use of oblique light from an endoillumination probe to prevent the problem of upside-down donor placement during DMEK in Asian eyes. The oblique light helps visualize the stained DMEK graft against the background of the dark brown irises typical of Asian eyes. We have also adopted the use of an s-stamp on the DMEK graft to avoid upside-down donor placement [25]. Even with these techniques, it is still often cumbersome and takes quite a long time to unwrap and center the DMEK donor using the no touch technique.

Here we report a novel DMEK technique called the "donor tissue holding technique" using a newly developed 25-gauge graft manipulator. For comparison, the previous consecutive DMEK cases treated with the no touch technique were also evaluated. Although both techniques were successful and lacked any serious complications both during surgery and postoperatively, the holding technique enabled DMEK to be performed much faster (mean = 305.5 s) compared to the no touch technique (mean = 1,310.0 s) with high statistical significance ($p = 0.01$) even in the eyes of Asian patients. However, as a limitation of the holding technique, it may be possible to cause a graft tearing during DMEK.

The unscrolling time in the no touch technique reported herein seems to be relatively longer than that of experienced DMEK surgeons in western countries. One may think that surgeons who overcome the learning curve could unfold the DMEK graft within 10 min, especially in cases of shallow anterior chamber. However, we presume that Asian eyes with shallow anterior chamber tend to have high vitreous pressure, which makes DMEK graft unscrolling quite difficult. There have been two previous reports regarding tissue unscrolling time and endothelial cell loss [26, 27]. Although Heinzelmann et al. [26] suggested a relationship between longer unscrolling times and greater endothelial cell loss, Sáles et al. [27] reported no such correlation. However, in the current study, an analysis of unscrolling time, cell loss rate, and donor age was not performed.

A technical note for using this manipulator: a side port can be created at the limbus using a 25-gauge V-lance anywhere the surgeon prefers to grasp the donor tissue. Also, the rim of the rolled graft nearest to the iris plane should be identified using endoillumination and grasped; this allows correct orientation of the graft. Once the DMEK donor edge is grasped, the anterior chamber depth should be gradually reduced and the corneal surface should be tapped; this will slowly unwrap the graft. Finally, the manipulator should be pulled away through the corneal paracentesis with extreme care, as it could drag out the DMEK graft if not careful. The use of an anterior chamber maintainer is strongly recommended in the holding

technique. The anterior chamber tends to collapse when the edge of the DMEK roll is grasped using the graft manipulator, especially in cases with shallow anterior chamber. By using a small amount of fluid through the anterior chamber maintainer, unscrolling the graft is easily performed. However, meticulous care should be paid to the flow rate, since strong flow could flush the graft out of the eye.

In conclusion, the donor tissue holding technique using the newly developed 25-gauge graft manipulator enables rapid and safe DMEK in a reproducible manner, even in Asian eyes with shallow anterior chambers with high vitreous pressure. Further clinical study in a larger number of patients with different disease backgrounds will be required to fully confirm the effectiveness and safety of this technique.

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Statement of Ethics

The study was approved by the Ethics Committee of Kanazawa University Graduate School of Medical Science and followed the tenets of the Declaration of Helsinki.

Disclosure Statement

No authors have any financial/conflicting interests to disclose concerning any of the products mentioned in this article.

References

1 Melles GR, Eggink FA, Lander F, Pels E, Rietveld FJ, Beekhuis WH, et al. A surgical technique for posterior lamellar keratoplasty. Cornea. 1998 Nov;17(6):618–26.
2 Terry MA, Ousley PJ. Small-incision deep lamellar endothelial keratoplasty (DLEK): six-month results in the first prospective clinical study. Cornea. 2005 Jan;24(1):59–65.
3 Terry MA, Ousley PJ. Deep lamellar endothelial keratoplasty visual acuity, astigmatism, and endothelial survival in a large prospective series. Ophthalmology. 2005 Sep;112(9):1541–8.
4 Price MO, Price FW Jr. Descemet's stripping with endothelial keratoplasty: comparative outcomes with microkeratome-dissected and manually dissected donor tissue. Ophthalmology. 2006 Nov;113(11):1936–42.
5 Price FW Jr, Price MO. Descemet's stripping with endothelial keratoplasty in 200 eyes: early challenges and techniques to enhance donor adherence. J Cataract Refract Surg. 2006 Mar;32(3):411–8.
6 Gorovoy MS. Descemet-stripping automated endothelial keratoplasty. Cornea. 2006 Sep;25(8):886–9.
7 Bahar I, Kaiserman I, Levinger E, Sansanayudh W, Slomovic AR, Rootman DS. Retrospective contralateral study comparing descemet stripping automated endothelial keratoplasty with penetrating keratoplasty. Cornea. 2009 Jun;28(5):485–8.
8 Price MO, Baig KM, Brubaker JW, Price FW Jr. Randomized, prospective comparison of precut vs surgeon-dissected grafts for descemet stripping automated endothelial keratoplasty. Am J Ophthalmol. 2008 Jul;146(1):36–41.
9 Chen ES, Terry MA, Shamie N, Hoar KL, Friend DJ. Descemet-stripping automated endothelial keratoplasty: six-month results in a prospective study of 100 eyes. Cornea. 2008 Jun;27(5):514–20.

10 Kobayashi A, Yokogawa H, Sugiyama K. Descemet stripping with automated endothelial keratoplasty for bullous keratopathies secondary to argon laser iridotomy—preliminary results and usefulness of double-glide donor insertion technique. Cornea. 2008 Sep;27 Suppl 1:S62–9.
11 Wu EI, Ritterband DC, Yu G, Shields RA, Seedor JA. Graft rejection following descemet stripping automated endothelial keratoplasty: features, risk factors, and outcomes. Am J Ophthalmol. 2012 May;153(5):949–957.e1.
12 Melles GR, Lander F, Rietveld FJ. Transplantation of Descemet's membrane carrying viable endothelium through a small scleral incision. Cornea. 2002 May;21(4):415–8.
13 Melles GR, Ong TS, Ververs B, van der Wees J. Descemet membrane endothelial keratoplasty (DMEK). Cornea. 2006 Sep;25(8):987–90.
14 Melles GR. Posterior lamellar keratoplasty: DLEK to DSEK to DMEK. Cornea. 2006 Sep;25(8):879–81.
15 Melles GR, Ong TS, Ververs B, van der Wees J. Preliminary clinical results of Descemet membrane endothelial keratoplasty. Am J Ophthalmol. 2008 Feb;145(2):222–7.
16 Ham L, Dapena I, van Luijk C, van der Wees J, Melles GR. Descemet membrane endothelial keratoplasty (DMEK) for Fuchs endothelial dystrophy: review of the first 50 consecutive cases. Eye (Lond). 2009 Oct;23(10):1990–8.
17 Ham L, Balachandran C, Verschoor CA, van der Wees J, Melles GR. Visual rehabilitation rate after isolated descemet membrane transplantation: descemet membrane endothelial keratoplasty. Arch Ophthalmol. 2009 Mar;127(3):252–5.
18 Dapena I, Moutsouris K, Droutsas K, Ham L, van Dijk K, Melles GR. Standardized "no-touch" technique for descemet membrane endothelial keratoplasty. Arch Ophthalmol. 2011 Jan;129(1):88–94.
19 Kobayashi A, Yokogawa H, Yamazaki N, Masaki T, Sugiyama K. In vivo laser confocal microscopy after Descemet's membrane endothelial keratoplasty. Ophthalmology. 2013 May;120(5):923–30.
20 Saad HA, Terry MA, Shamie N, Chen ES, Friend DF, Holiman JD, et al. An easy and inexpensive method for quantitative analysis of endothelial damage by using vital dye staining and Adobe Photoshop software. Cornea. 2008 Aug;27(7):818–24.
21 Pavlovic I, Shajari M, Herrmann E, Schmack I, Lencova A, Kohnen T. Meta-Analysis of Postoperative Outcome Parameters Comparing Descemet Membrane Endothelial Keratoplasty Versus Descemet Stripping Automated Endothelial Keratoplasty. Cornea. 2017 Dec;36(12):1445–51.
22 Kobayashi A, Yokogawa H, Yamazaki N, Masaki T, Sugiyama K. The use of endoillumination probe-assisted Descemet membrane endothelial keratoplasty for bullous keratopathy secondary to argon laser iridotomy. Clin Ophthalmol. 2015 Jan;9:91–3.
23 Hayashi T, Oyakawa I, Kato N. Techniques for Learning Descemet Membrane Endothelial Keratoplasty for Eyes of Asian Patients With Shallow Anterior Chamber. Cornea. 2017 Mar;36(3):390–3.
24 Jacob S, Agarwal A, Agarwal A, Narasimhan S, Kumar DA, Sivagnanam S. Endoilluminator-assisted transcorneal illumination for Descemet membrane endothelial keratoplasty: enhanced intraoperative visualization of the graft in corneal decompensation secondary to pseudophakic bullous keratopathy. J Cataract Refract Surg. 2014 Aug;40(8):1332–6.
25 Veldman PB, Dye PK, Holiman JD, Mayko ZM, Sáles CS, Straiko MD, et al. The S-stamp in Descemet Membrane Endothelial Keratoplasty Safely Eliminates Upside-down Graft Implantation. Ophthalmology. 2016 Jan;123(1):161–4.
26 Heinzelmann S, Hüther S, Böhringer D, Eberwein P, Reinhard T, Maier P. Influence of donor characteristics on descemet membrane endothelial keratoplasty. Cornea. 2014 Jun;33(6):644–8.
27 Sáles CS, Terry MA, Veldman PB, Mayko ZM, Straiko MD. Relationship Between Tissue Unscrolling Time and Endothelial Cell Loss. Cornea. 2016 Apr;35(4):471–6.

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Fig. 1. Appearance of the 25-gauge graft manipulator for DMEK.

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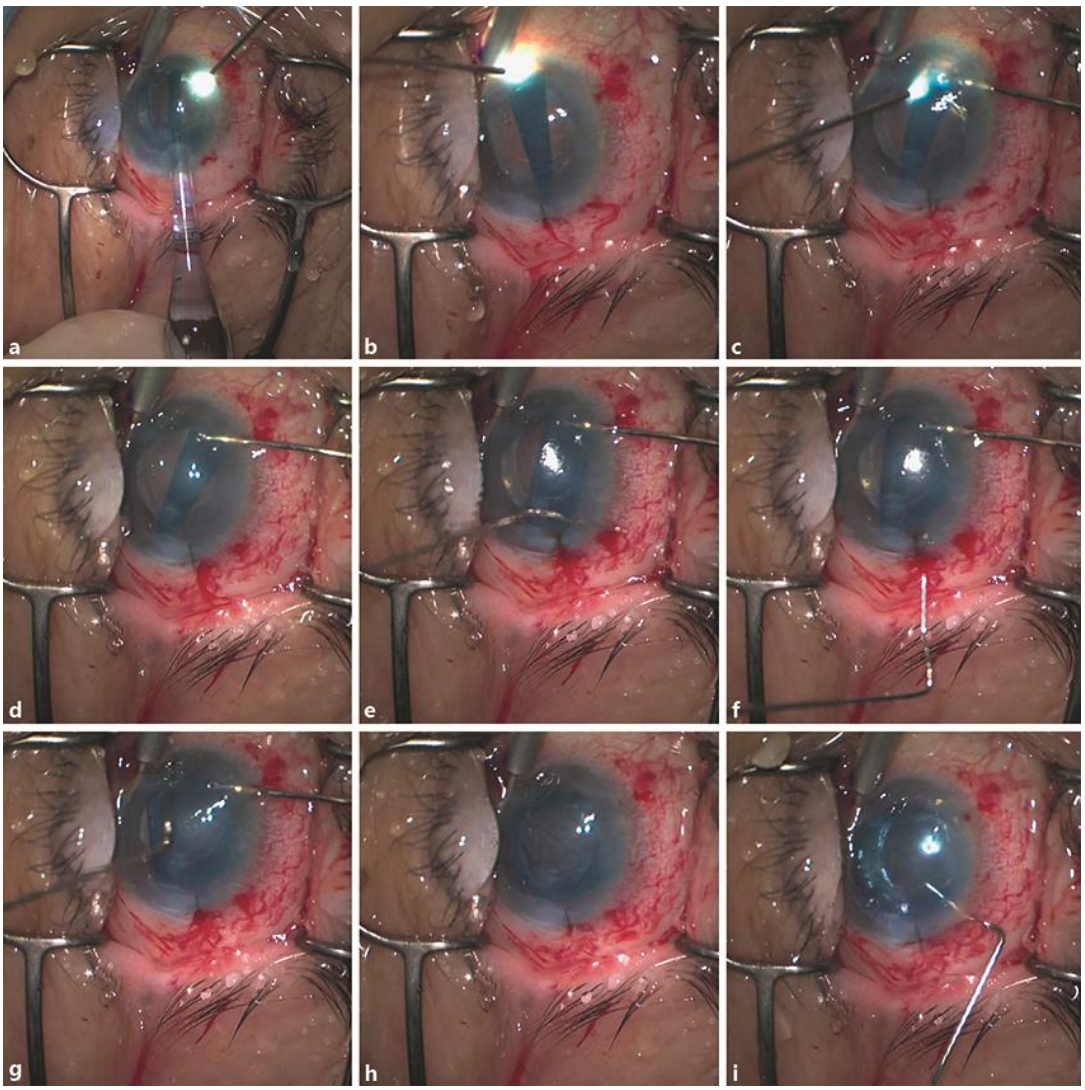

Fig. 2. DMEK donor holding technique. **a** A trypan blue-stained Descemet's membrane (DM) roll was inserted into the anterior chamber via a 2.4-mm temporal clear corneal incision using a DMEK shooter. In this case, due to preexisting paralytic mydriasis, inferior iridectomy was not performed. **b** The DM roll configuration was carefully observed using oblique light via an endoillumination probe. **c–g** The edge of the roll was grasped using a 25-gauge graft manipulator and the grasp was maintained throughout the centering and opening of the roll. This procedure was performed by adjusting the depth of the anterior chamber and tapping of the corneal surface. **h**, **i** Lastly, a large amount of air was inserted under the graft.