

Clinical results of non-Descemet stripping endothelial keratoplasty

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Abstract

• **AIM:** To investigate the impact of non-Descemet stripping endothelial keratoplasty (non-DSEK) on graft rejection rate, and its overall procedural effectiveness in patients.

• **METHODS:** Non-DSEK was performed on 65 eyes of 64 patients, and the procedural outcomes, including rejection episodes, failure and dislocation of the grafts, best corrected visual acuity (BCVA), endothelial cell density (ECD), and other complications, were analyzed retrospectively.

• **RESULTS:** Of the 65 eyes, 63 recovered from bullous keratopathy with a clear cornea. The mean follow-up time was 26.4mo (range, 6-84mo). The mean BCVA improved from 1.70 logMAR preoperatively to 0.54 logMAR at 3mo, 0.46 logMAR at 6mo, and 0.37 logMAR at 1y after surgery. The postoperative donor ECD of the 25 patients who successfully underwent specular microscopic examination was 1918 ± 534 cells/mm² (range, 637 to 3056 cells/mm²), and the mean endothelial cell loss was 41.9% at 24mo postoperatively. One eye developed secondary glaucoma and required regrafting *via* penetrating keratoplasty (PKP). Another eye had postoperative graft failure due to rejection at 26mo. Postoperative graft dislocation occurred in eight eyes. All of the eight dislocated grafts were reattached using air reinjection.

• **CONCLUSION:** Immunological graft rejection of the donor graft rarely occurs in non-DSEK. Therefore, non-DSEK is a safe, concise, and effective alternative to restore corneal decompensation when the Descemet membrane is disease-free.

• **KEYWORDS:** endothelial keratoplasty; non-Descemet stripping endothelial keratoplasty; endothelial dysfunction; Descemet membrane

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INTRODUCTION

Endothelial keratoplasty (EK) has become an effective alternative to penetrating keratoplasty (PKP) for treating bullous keratopathy caused by a dysfunctioning endothelium. Compared to PKP, the application of EK can lead to more rapid recovery of vision, minimize induced astigmatism, and, more importantly, better maintain the integrity of the globe^[1-4]. Moreover, clinical reports have shown that EK induces a lower graft rejection rate than does PKP. The rejection rates of Descemet stripping automated endothelial keratoplasty (DSAEK) have been reported to range from 0 to 45%, with an average rate of 10%^[5]. Meanwhile, Descemet membrane endothelial keratoplasty (DMEK) has a rejection rate of just 1%^[6-7]. Because of the inapplicability of DMEK in patients with serious edematous stroma or aphakic eyes, which have previously undergone vitrectomy, DSAEK is still used as the main procedure for EK. However, the rejection rate of DSAEK is still a serious concern. Since 2006, our team has applied non-Descemet stripping endothelial keratoplasty (non-DSEK) to treat various forms of bullous keratopathy. During the past 8y, none of the patients who have undergone non-DSEK have experienced any graft rejection, except those with failed PKP. Based on this finding, we hypothesized that non-DSEK might induce a very low graft rejection rate.

In this study, we have shown the low graft rejection rate induced by non-DSEK and its effectiveness based on the clinical results of 64 patients who underwent EK without the removal of the Descemet membrane (DM) for various indications.

SUBJECTS AND METHODS

This study was approved by the Institutional Review Board of the Aier School of Ophthalmology of Central South University, China. We retrospectively reviewed the medical records of 64 patients (65 eyes) who underwent non-DSEK between

Non-Descemet stripping endothelial keratoplasty

August 2007 and August 2014. The study was conducted in accordance with the tenets of the Declaration of Helsinki, and informed consent was obtained from each participant. Patients with less than 3mo of follow-up were excluded. The demographics, preoperative best corrected visual acuity (BCVA), postoperative BCVA, date and indications for non-DSEK, surgical technique, intraoperative/postoperative complications, subsequent surgical procedures, and date of last follow-up were reviewed. The condition of the donor graft adherence was investigated by optical coherence tomography of the anterior segment (Carl Zeiss Meditec, Inc. Dublin, CA, USA). The DM was examined by slit lamp and confocal microscope preoperatively. All the patients without fibrosis of DM were underwent non-DSEK surgery.

Surgical Techniques Donor graft dissection was performed using femtosecond laser apparatus (15 eyes, IntraLase 60, AMO, Irvine, CA, USA; 34 eyes, Wavelight FS200, WaveLight GmbH, Erlangen, Germany) or by manual dissection (16 eyes) by an experienced surgeon. Each donor corneal button with a 2-mm scleral margin was mounted on an artificial anterior chamber (Mediheica, Vostanya str, Kazan, Russia) filled with DisCoVisc (Alcon Laboratories, Fort Worth, TX, USA). The femtosecond laser was set to make full lamellar cuts from the epithelial side with a diameter of 8.0-8.5 mm, a cutting depth of cutting of 420-430 μm at the early surgical stage and 460-480 μm at the late surgical stage respectively, a raster energy of 1.5 mJ, and an anterior side cut at 90°. The thickness of the obtained donor graft ranged between 100 and 130 μm . The dissected donor graft was immersed in the medium-term corneal storage medium of Corneal chamber (AL.CHI.MI.A. S.RL, Viale Austria, Italy) for subsequent use.

All patients were under local anesthesia during the surgery. A main scleral tunnel incision (3-5 mm) was made in the superior or temporal sclera, and a peripheral transparent corneal incision was made using the 15° knife. The endothelial graft was then folded over with the endothelial side facing inward at a ratio of 4/6, and it was protected using viscoelastic matter (DisCoVisc, Alcon Laboratories, Texas, USA). For recipients with mild edema, the donor endothelial grafts were inserted using an implantable collamer lens injector (STAAR Surgical Company, Monrovia, CA, USA) through a 3-mm incision, while for the recipients with serious edema, they were inserted into the anterior chamber by using forceps (Moria, Antony, France) through a 5-mm incision. A suture was then used to seal the incision immediately. Sterile air was injected into the anterior chamber to assist to unfold the endothelial graft. Viscoelastic substance was applied for unfolding donor grafts that were too sticky to be unfolded using air injection, and the substance was later replaced with a balanced salt solution. Patients were maintained in a supine position for 2-4h postoperatively in the ward, and partial evacuation of air was then performed to prevent pupillary block.

Table 1 Total follow-up time of the individual patients *n* (%)

Follow-up time (mo)	Value (total eyes, <i>n</i> =65)
3-12	26 (40)
12-24	12 (18.5)
24-36	13 (20)
36-48	2 (3)
48-84	12 (18.5)

Table 2 Demographics and indications of the patients undergoing non-DSEK *n* (%)

Characteristics	Value (total eyes, <i>n</i> =65)
Mean age (a)	58.7±17.9
Male	36 (55.4)
Follow up time (mo), $\bar{x} \pm s$ (range)	26.4±21.4 (6-84)
Indication for procedure	
Pseudophakic bullous keratoplasty	52 (80.0)
Aphakic bullous keratoplasty	7 (10.8)
Failed PKP	6 (9.2)
The cases combined with history of previous surgery	
Prior ocular trauma	5 (7.7)
Prior vitreoretinal surgery	6 (9.2)
Previous glaucoma filtering surgery	14 (21.5)

Non-DSEK: Non-Descemet stripping endothelial keratoplasty; PKP: Penetrating keratoplasty.

Postoperative Medications Postoperatively, patients were treated with tobramycin/dexamethasone eye drops (TobraDex, Alcon, Fort Worth, Texas, USA) four times a day for two weeks; Thereafter, the administration frequency was reduced by one drop each week until the treatment ceased. The tobramycin/dexamethasone ointment was applied once at night for 1mo, and 40 mg prednisone was prescribed to be taken once per day, which was gradually tapered down to 5 mg every 5d until the treatment ceased. Either 0.1% FK506 (Senju Pharmaceutical, Hyogo-ken, Japan) twice a day or cyclosporin eye drops (North China Pharmaceutical Group Corporation, Shijiazhuang, China) four times a day was applied for one year, when the tobramycin/dexamethasone eye drops and the ointment were discontinued.

RESULTS

In our series, non-DSEK was performed in 65 eyes of 64 patients (36 men and 28 women). The mean age of the patients was 58.7y (range, 26 to 90 years old). The mean follow-up time was 26.4mo (range, 6-84mo) (Table 1). The indications for this study were pseudophakic corneal edema (52 eyes, 80.0%), aphakic corneal edema (7 eyes, 10.8%), and failed PK graft (6 eyes, 9.2%). The previously performed surgeries that were involved in some patients included previous glaucoma filtering surgery (14 eyes, 21.5%), prior ocular trauma (5 eyes, 7.7%), and prior vitreoretinal surgery (6 eyes, 9.2%) (Table 2).

Visual Acuity Of the 65 eyes, 63 recovered from bullous keratopathy with a clear cornea (Figure 1A, 1B). One eye

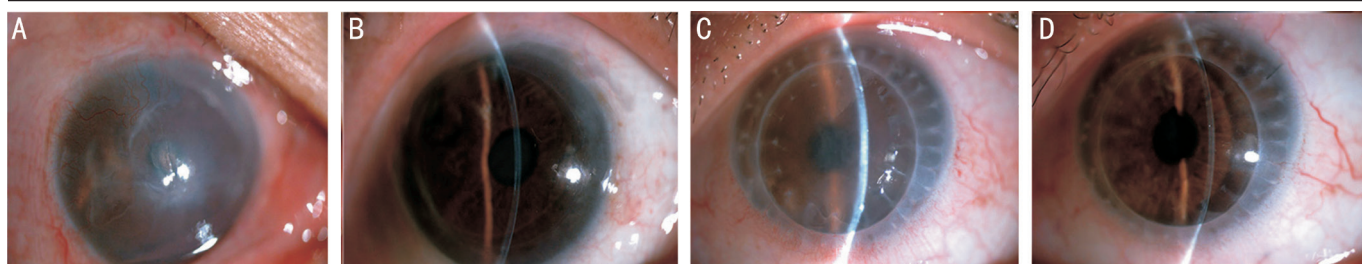


Figure 1 Representative slit-lamp photographs of two patients A: Representative slit-lamp photographs of patient with pseudophakic bullous keratopathy before the non-DSEK; B: Six years after non-DSEK, the cornea remains transparent. The BCVA improved from 2.00 logMAR preoperatively to 0.22 logMAR after surgery, without any graft rejection; C: PKP failure occurred two times in an eye with keratoconus that underwent non-DSEK and experienced rejection after 5mo postoperatively; D: The edematous cornea became transparent again 1mo after treatment with a topical steroid and cyclosporin eye drops.

developed secondary glaucoma because of the vitreous incarceration, which was regrafted using PKP. Another eye had postoperative graft rejection and progressed to graft failure at 26mo postoperatively. The mean BCVA improved from 1.70 logMAR (decimal visual acuity 0.02) preoperatively to 0.54 logMAR at 3mo (decimal visual acuity 0.29), 0.46 logMAR at 6mo (decimal visual acuity 0.35), and 0.37 logMAR at 1y after surgery (decimal visual acuity was 0.43) (Figure 2).

Endothelial Cell Counts The donor ECD was 3303 ± 430 cells/mm² (range, 2170 to 4100 cells/mm²). Twenty-five patients successfully underwent specular microscopic examination at the 2-year follow-up. The postoperative donor ECD of the 25 patients was 1918 ± 534 cells/mm² (range, 637 to 3056 cells/mm²), and the mean endothelial cell loss was 41.9% at 24mo postoperatively.

Operative Complications Two donor graft perforations occurred during the dissection using the femtosecond laser. New donor grafts were dissected for replacing the perforated ones. Two donor grafts were positioned upside down. One eye was found this disorder intraoperatively and was replaced with a new donor graft, while in the other eye, the cornea remained swollen until 1mo postoperatively and was then replaced with a new graft. The prolapse of the vitreous body occurred in one eye resulting in secondary glaucoma. This eye progressed to failure at 3mo postoperatively, and PKP was performed to recover visual acuity.

Postoperative Complications, Rejection and Failure Rate None had graft rejection for the innocent 59 eyes who had not undergone previous PKP with follow-up ranging from 6mo to 7y. However, two of the six eyes with failed PKP developed graft rejection. The rejection in one of these two eyes resolved after anti-rejection treatment (Figure 1C, 1D). However, the other eye progressed to graft failure and further treatment for the inferior preoperative visual function was withdrawn.

Graft dislocation Eight eyes had graft disc dislocation, which was resolved using air refilling to the anterior chamber. We noted that five of these eight eyes had a prior history of vitrectomy. Our experience of repositioning graft by injecting sterile air into the anterior chamber proved that this surgery was effective in managing dislocations.

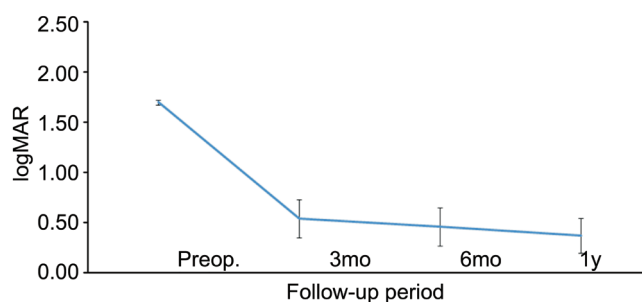


Figure 2 Visual results of patients undergoing non-DSEK The mean BCVA improved from 1.70 logMAR (decimal visual acuity, 0.02) preoperatively to 0.54 logMAR at 3mo (decimal visual acuity, 0.29), 0.46 logMAR at 6mo (decimal visual acuity, 0.35), and 0.37 logMAR (decimal visual acuity, 0.43) at 1y after surgery.

Primary graft failure Owing to the lack of experience of the surgeon at the early stage of this study, two endothelial grafts were inserted using an injector cartridge and unfolded automatically. The orientation of the endothelial lenticule in one unmarked eye could not be distinguished; it was later confirmed by the playback of the surgery video, and then the orientation of the endothelial graft lenticule was altered. The mark of another endothelial graft could not be identified because of a severely edematous cornea in the recipient; this resulted in the graft being placed in an inverted position and subsequent primary failure. One month later, the endothelial graft was replaced and the recipient's cornea became transparent.

DISCUSSION

Currently, EK is mostly performed with the removal of the DM^[4,8-11]. However, stripping the DM has several disadvantages. First, stripping the DM entirely is difficult, especially in recipients with serious edema. Second, the scope of the stripped DM is usually very hard to control, and this may result in incomplete donor graft coverage and topical edema in the recipients after EK. Furthermore, PKP wound dehiscence may occur during the injection of air into the anterior chamber^[12-13]. In contrast, the non-DSEK, which does not require the removal of the DM, has great merits. Non-DSEK has been shown to be potentially effective in simplifying the procedure, shortening the surgical period, and reducing inflammatory reactions. Moreover, non-DSEK may prevent fragments of the DM from falling into the vitreous cavity in patients with aniridic aphakic eyes.

Since 2006, our team has been performing non-DSEK to treat endothelial dysfunction after cataract surgery. According to the literature, EK without DM stripping was firstly performed by Price and his co-workers to resolve endothelial dysfunction in seven failed PKP cases, and they obtained excellent results^[8]. Thereafter, the effectiveness and safety of non-DSEK have been confirmed in several studies by Kobayashi *et al*^[14], Chaurasia *et al*^[13], Nottage *et al*^[15], Masaki *et al*^[12], Wu *et al*^[16], and Li *et al*^[17].

To the best of our knowledge, the number of patients in our case series of non-DSEK is the largest to date, with the longest follow-up time. Although some experts consider the possibility that stripping the DM may reduce the rate of endothelial graft dislocation, in our study, the total dislocation rate of non-DSEK was 12.3% (8/65). If the five cases of prior vitrectomy were excluded, the dislocation rate would be further reduced to 5% (3/60). For aniridic aphakic eyes with a prior history of vitrectomy, graft suturing of the lenticule could assist in the attachment of the donor graft^[18-19]. According to our own experience, refilling sterile air for correcting dislocated donor grafts can also effectively solve this disorder on the second postoperative day. Still, graft suturing of the lenticule is a dependable procedure in certain special cases during non-DSEK.

Moreover, the two eyes in which the endothelial grafts were positioned upside down were related to the condition of the patients and the experience of the surgeon, instead of the non-stripping of the DM. Asymmetrical marking of the donor may also be useful for determining graft orientation. In our study, one eye developed secondary glaucoma because of the prolapse of the vitreous body from the ruptured posterior capsule, which resulted from the trauma caused by the cataract surgery during the air injection for position of the donor lenticule.

Interface haze was not detected in any of our cases during regular examination by using slit lamp and confocal microscopy. Therefore, the retained DM of the recipients did not influence the postoperative clarity. Masaki *et al*^[12] reported that non-DSEK did not influence the attachment of donor grafts and the recovery of visual acuity when the DM is non-pathological. Except for the two eyes with endothelial decompensation resulting from rejection and secondary glaucoma, all patients had a clear graft. Most patients showed improvement in visual outcome with a postoperative BCVA better than the preoperative BCVA. The BCVA of 18 eyes at 1y postoperatively was better than 0.30 logMAR (decimal visual acuity, 0.5). The result of postoperative visual acuity indicated that the remnant DM did not interfere with the recovery of visual acuity. In our case series, 38 eyes had several co-morbid factors that affected the final visual acuity, such as a surgical history of glaucoma filtering surgery, prior vitreoretinal surgery, PKP, and ocular

trauma. The post-operative ECD of 25/27 patients who were followed up for more than 2y were available, with the values ranging from 637 to 3056 cells/mm². The mean ECD loss was 41.9% compared with that of the donor cornea at the 24mo postoperatively.

In our series, we also found an unexpected clinical result. Throughout the 7y of follow-up, no immunological graft rejection occurred in the eyes with regular endothelial dysfunction. This phenomenon was significantly different from that of other reported cases of DSAEK. The criteria of graft rejection in this study corresponded to the graft rejection criteria in previously published researches^[20-21]. Graft rejection occurred in two eyes (3.1%) of 65 eyes which underwent the non-DSEK. Both these eyes had a history of failed PKP with typical clinic features. While the complication in one eye resolved under treatment with a topical steroid and cyclosporin eye drops, the other eye progressed to graft failure and the further treatment for the inferior preoperative visual function was withdrawn. Price and his associates^[21] reported DSAEK rejection rates of 7.6% at 1y and 12.0% at 2y by using the Kaplan-Meier analysis. Anshu *et al*^[6] showed that the rejection rate is potentially time-dependent. However, in our study, 27 eyes with over 2y of follow-up did not experience any rejection episode. It is, nevertheless, possible that a temporary rejection was not identified by the doctors during an irregular follow-up in the clinical setting. Moreover, no difference in donor endothelial graft diameters was observed between our non-DSEK cases, which ranged from 8.0 to 8.5 mm, and those of another published reports on DSAEK cases. The use of drugs was sufficient for resisting immune rejection in our series, and this possibly resulted in the low rejection rate. Even so, a very low rejection rate is relatively uncommon. With the results presented in our study, it appears as though the surgical method of non-DSEK decreases the graft rejection rate. Considering the non-DSEK procedure described in our study, we hypothesized that the recipient's DM blocks antigen-presenting cells like the Langerhans cells from reaching the donor graft, reducing an immunologic reaction.

In summary, this modified EK technique (non-DSEK) for the treatment of endothelial dysfunction produced excellent clinical outcomes such as good visual acuity and low rejection rate. Non-DSEK is also a short surgical procedure that does not involve the removal of the DM. Therefore, non-DSEK may be a safe, concise, and effective alternative to restore corneal decompensation when the DM is disease-free.

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Authors' Contributions: study concept and design (Shao-Wei Li); data collection (Tao Zhang, Tie-Hong Chen, Jing-Liang He, Yan-Wei Kang, Fang-Qi Lyu, Jian-Hua Ning, Chang Liu); interpretation and analysis of data (Shao-Wei Li, Tao Zhang, Chang Liu) drafting of the manuscript (Tao Zhang); critical revision of the manuscript (Shao-Wei Li).

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