In summary, our study demonstrated that eyes with PEX syndrome have decreased cell densities in the cornea. The subbasal nerve density was also significantly decreased, and this was significantly correlated with clinically decreased corneal sensitivity. Our study sheds light on understanding the cause of impaired corneal sensitivity in patients with PEX syndrome. The PEX syndrome is probably a bilateral event in which the keratopathy of the fellow eye also must be observed.

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# Outcomes of cataract surgery in eyes with a low corneal endothelial cell density

Katsuya Yamazoe, MD, Takefumi Yamaguchi, MD, Kazuki Hotta, MD, Yoshiyuki Satake, MD, Kenji Konomi, MD, Seika Den, MD, Jun Shimazaki, MD

**PURPOSE:** To evaluate the surgical outcomes of cataract surgery in eyes with a low preoperative corneal endothelial cell density (ECD) and analyze factors affecting the prognosis.

**SETTING:** Tokyo Dental College, Ichikawa General Hospital, Chiba, Japan.

**DESIGN:** Noncomparative case series.

**METHODS:** Eyes with a preoperative ECD of less than 1000 cells/mm$^2$ that had cataract surgery between 2006 and 2010 were identified. Standard phacoemulsification with intraocular lenses was performed using the soft-shell technique. The rate of endothelial cell loss, incidence of bullous keratopathy, and risk factors were retrospectively assessed.

**RESULTS:** Sixty-one eyes (53 patients) with a low preoperative ECD were identified. Preoperative diagnoses or factors regarded as causing endothelial cell loss included Fuchs dystrophy (20 eyes), laser iridotomy (16 eyes), keratoplasty (10 eyes), traumatic injury (3 eyes), trabeculectomy (3 eyes), corneal endotheliitis (2 eyes), and other (7 eyes). The corrected distance visual acuity improved from 0.59 $\pm$ 0.49 logMAR preoperatively to 0.32 $\pm$ 0.48 logMAR postoperatively ($P$<.001). The mean ECD was 693 $\pm$ 172 cells/mm$^2$ and 611 $\pm$ 203 cells/mm$^2$, respectively ($P$=.001). The mean rate of endothelial cell loss was 11.5% $\pm$ 23.4%. Greater ECD loss was associated with a shorter axial length (AL) (<23.0 mm) and diabetes mellitus. Bullous keratopathy developed in 9 eyes (14.8%) and was associated with posterior capsule rupture.

**CONCLUSIONS:** The results suggest that modern techniques for cataract surgery provide excellent visual rehabilitation in many patients with a low preoperative ECD. Shorter AL, diabetes mellitus, and posterior capsule rupture were risk factors for greater ECD loss and bullous keratopathy.

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Corneal endothelial cell loss, a major complication that sometimes occurs after cataract surgery, can lead to corneal edema and decompensation if cell density falls to 500 cells/mm$^2$ or below. Causes of this complication are thought to include corneal distortion, ricocheting of nuclear fragments, intraocular lens (IOL) contact, and release of free radicals.[1–3] Bullous keratopathy is a vision-threatening complication, and pseudophakic bullous keratopathy is a leading indication for corneal graft surgery.[4] Although many procedures can reduce corneal endothelial damage, including the phaco-chop and soft-shell techniques,[5–8] there is often a reluctance to risk cataract surgery in cases in which the preoperative corneal endothelial cell density (ECD) is low, especially if it is below 1000 cells/mm$^2$.

To our knowledge, no large-scale studies have evaluated the outcomes of cataract surgery in eyes with a low preoperative corneal ECD. The aim of this study was to determine the outcomes of cataract surgery and which factors affect the prognosis in cases with a low preoperative corneal ECD.

## PATIENTS AND METHODS

Patients with a clear cornea and an ECD less than 1000 cells/mm$^2$ preoperatively were identified from those who had cataract surgery at Tokyo Dental College between January 2006 and May 2010 and were included in this retrospective study. All patients provided written informed consent. This study was performed in accordance with the tenets of the Declaration of Helsinki. Approval was obtained from the ethics committee at the institution.

 

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Patients had slitlamp microscopy and Landolt corrected distance visual acuity (CDVA), fundus, intraocular pressure (IOP), and ECD testing before and after cataract surgery. Exclusion criteria included preoperative bullous keratopathy with obvious corneal edema, cataract surgery by a technique other than phacoemulsification, combined surgical procedures including penetrating keratoplasty and Descemet-stripping automated endothelial keratoplasty (DSAEK), and a follow-up of less than 6 months. Bullous keratopathy was defined as persistent corneal edema resulting from a decreased ECD.

The central corneal ECD was measured using the EM-3000 device (Tomey Corp.) before surgery and at each follow-up visit. The ECD at the final visit was taken as representing the patient's postoperative ECD. Cataracts were evaluated according to the Emery-Little classification.[9]

## Surgical Technique

Phacoemulsification and aspiration were performed by 1 of 4 experienced surgeons (J.S., S.D., Y.S., T.Y.) using topical or sub-Tenon anesthesia of lidocaine 2%. A 2.75 mm clear corneal incision was placed superiorly or temporally. After instillation of sodium hyaluronate 1.0% (Opegan-Hi) and sodium hyaluronate 3.0%–chondroitin sulfate 4.0% (Viscoat) into the anterior chamber to stabilize the anterior chamber and protect endothelial cells (soft-shell technique), a continuous curvilinear capsulorhexis was created with a bent 27-gauge needle. After hydrodissection and standard endocapsular phacoemulsification of the nucleus was performed using the phaco-chop technique, the residual cortex was aspirated with a balanced salt solution using an Infiniti or Legacy phaco device (Alcon Laboratories, Inc.). The phaco device settings for the Infiniti device were bottle height, 60 to 65 cm; vacuum pressure, 250 mm Hg; flow rate, 25 mL/min; and longitudinal ultrasound power, 60%. The phaco device settings for the Legacy device were bottle height, 75 to 85 cm; vacuum pressure, 230 mm Hg; flow rate, 23 mL/min; and longitudinal ultrasound power, 60%. Viscoat was again placed in the anterior chamber to protect endothelial cells if remaining ophthalmic viscosurgical devices (OVD) were removed during the phacoemulsification. The lens capsule was inflated with a cohesive OVD, after which a foldable acrylic IOL was placed in the capsular bag. After IOL insertion, the OVD was thoroughly evacuated. The surgical protocols for each technique were standardized to reflect best practice by each surgeon.

Postoperative medications included levofloxacin (Cravit), diclofenac sodium 0.1% (Diclod), and betamethasone sodium phosphate 0.01% (Sanbetazon) 3 times a day for 1 to 2 months.

## Main Outcome Measures

Two outcome measures were used to determine and analyze the change in the endothelial cell count after surgery. First was the proportional loss of cells, defined as the percentage reduction in cell count at the patient's final visit. The mean percentage cell loss was calculated in various subgroups. The second outcome measure was the incidence of bullous keratopathy, which was diagnosed by slitlamp examination. Based on the preoperative evaluation, the patients were divided into several groups according to ECD, the cause of the low ECD, and other factors, including age, sex, cataract grade, visual acuity, axial length (AL), systemic hypertension, and diabetes mellitus. The 2 outcome measures were compared between the groups.

## Statistical Analysis

Differences in the percentage of endothelial cell loss were compared between the groups at every evaluation using the Mann-Whitney test, single-factor analysis of variance, or the Kruskal-Wallis test. The incidence of bullous keratopathy between the groups was evaluated using the Fisher exact test, chi-square for independence test, or Cochran-Armitage test. A $P$ value less than 0.05 was considered statistically significant. All statistical analyses were performed using SSRI software (SSRI Co. Ltd.).

# RESULTS

## Demographics and Clinical Features

During the study period, 3558 patients had cataract surgery; in this group, 61 eyes of 52 patients had a preoperative ECD less than 1000 cells/mm$^2$. Table 1 shows the patients' demographics. The proportion of women was greater than that of men. The mean follow-up was 14.6 months ± 11.0 (SD) (range 6 to 43 months). The most frequent preoperative diagnosis or factor regarded as causing endothelial cell loss was Fuchs dystrophy followed by laser iridotomy and keratoplasty (Table 1).

Table 2 shows surgical outcomes in the 61 eyes. The improvement in CDVA and the decrease in IOP from before surgery to after surgery were statistically significant (both $P<.001$). The postoperative ECD was unobtainable in 15 eyes, mainly because of the presence of corneal edema, including bullous keratopathy. There was a statistically significant decrease in ECD postoperatively ($P=.001$). The mean rate of endothelial cell loss was 11.5% ± 23.4%, and 9 eyes (14.8%) developed bullous keratopathy. Figure 1 shows the survival curve for all patients.

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From the Departments of Ophthalmology, Tokyo Dental College (Yamazoe, Yamaguchi, Satake, Konomi, Den, Shimazaki) Ichikawa General Hospital, and Kameda Medical Center (Yamazoe, Hotta), Chiba, and Keio University School of Medicine (Yamaguchi, Shimazaki), Tokyo, Japan.

Drs. Yamazoe and Yamaguchi contributed equally to this work.

Corresponding author: Katsuya Yamazoe, MD, Department of Ophthalmology, Ishikawa General Hospital, Tokyo Dental College, 5-11-13 Sugano, Ichikawa, Chiba, 272-8513, Japan. E-mail: kyamazoe1528@yahoo.co.jp.

**Table 1.** Patient demographics.

| Parameter | Value |
|---|---|
| Age (y) | |
| Mean ± SD | |
| Range | 72.3 ± 9.8 |
| Sex, n (%) | 32 to 95 |
| Male | 12 (22.6) |
| Female | 41 (77.4) |
| Mean preop AL (mm) ± SD | 23.2 ± 2.0 |
| Mean preop ACD (mm) | 3.7 ± 1.5 |
| Mean cataract grade* ± SD | 2.8 ± 0.9 |
| Cause of low ECD, n (%) | |
| Fuchs dystrophy | 20 (32.8) |
| Laser iridotomy | 16 (26.2) |
| Keratoplasty | 10 (16.4) |
| Trabeculectomy | 3 (4.9) |
| Trauma | 3 (4.9) |
| Corneal endotheliitis | 2 (3.3) |
| Other | 10 (16.4) |
| Diabetes mellitus, n (%) | |
| Present | 9 (14.8) |
| Absent | 52 (85.2) |
| Hypertension, n (%) | |
| Present | 23 (37.7) |
| Absent | 38 (62.3) |
| Complication, n (%) | |
| Capsule rupture/vitreous loss | 2 (3.3) |
| None | 59 (96.7) |

ACD = anterior chamber depth; AL = axial length; ECD = endothelial cell density
*Emery-Little classification

**Table 2.** Surgical results in all cases.

| Parameter | Preop | Postop | *P* value |
|---|---|---|---|
| CDVA | | | |
| Mean LogMAR ± SD | 0.59 ± 0.49 | 0.32 ± 0.48 | <.001 |
| Better than 20/20, n (%) | 3 (4.9) | 19 (31.1) | — |
| 20/40–20/20, n (%) | 17 (27.9) | 27 (44.2) | — |
| Worse than 20/40, n (%) | 41 (67.2) | 15 (24.6) | <.001 |
| Mean IOP (mm Hg) ± SD | 13.1 ± 3.9 | 11.3 ± 3.8 | <.001 |
| Mean ECD (cells/mm$^2$) ± SD | 693 ± 173 | 611 ± 203 | .001 |

CDVA = corrected distance visual acuity; ECD = endothelial cell density; IOP = intraocular pressure

## Clinical Characteristics and Surgical Outcomes

**In Relation to Preoperative Epithelial Cell Density** There were no statistically significant differences in clinical or surgical parameters between patients with a preoperative ECD less than 600 cells/mm$^2$, patients with a preoperative ECD between 600 cells/mm$^2$ and 800 cells/mm$^2$, and patients with a preoperative ECD between 800 cells/mm$^2$ and 1000 cells/mm$^2$ (Table 3). Although the rate of ECD loss was not significantly different between the 3 groups, the incidence of bullous keratopathy tended to be higher in the lower ECD groups ($P = .066$).

**In Relation to Cause of Low Endothelial Cell Density** There were no statistically significant differences in age, preoperative CDVA, IOP, prevalence of diabetes mellitus, or intraoperative complications between patients with Fuchs dystrophy, patients with laser iridotomy, and patients with keratoplasty (Table 4). The AL was significantly shorter in the laser iridotomy group ($P = .008$). The cataract grade was significantly lower in the keratoplasty group ($P = .002$). Hypertension was more common in the Fuchs dystrophy group ($P = .007$). The postoperative visual acuity was significantly better in the Fuchs dystrophy group than in the other groups ($P = .043$). Although the rate of ECD loss was not significantly different between the groups, the incidence of bullous keratopathy tended to be lower in the Fuchs dystrophy group. There were no cases of capsule rupture or vitreous loss in any of the 3 groups.

## Other Risk Factors

Table 5 shows the rate of ECD loss and the incidence of bullous keratopathy in the various groups. The rate of ECD loss was significantly higher in the shorter AL group ($P = .019$) and in patients with diabetes mellitus ($P = .049$). All cases with posterior capsule rupture developed bullous keratopathy, and a statistically significant difference was observed between eyes with posterior capsule rupture and eyes without posterior capsule rupture ($P = .020$). No differences were observed with regard to other factors.

## Keratoplasty for Bullous Keratopathy

Keratoplasty was performed in 4 eyes with bullous keratopathy (Table 6). Penetrating keratoplasty was

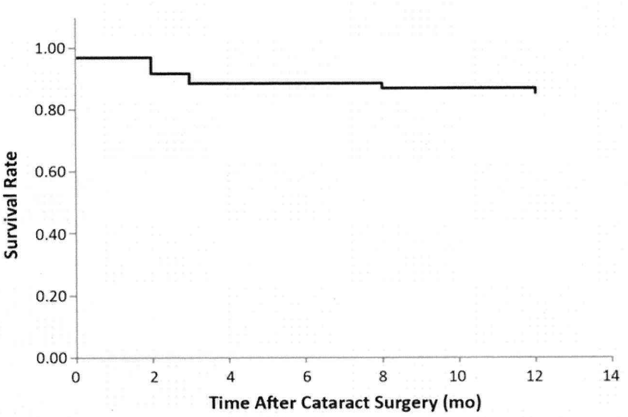


**Figure 1.** Survival curve of all patients having cataract surgery with low preoperative ECD.

Table 3. Characteristics and surgical results according to preoperative ECD.

| Parameter | Preoperative ECD (Cells/mm²) | | | P Value |
|---|---|---|---|---|
| | <600 | 600 to <800 | 800 to ≤1000 | |
| Eyes (n) | 18 | 26 | 17 | |
| Mean age (y) ± SD | 70.3 ± 5.4 | 71.9 ± 12.6 | 75.0 ± 8.5 | .289 |
| M/F sex (n) | 3/15 | 3/22 | 6/11 | .180 |
| Mean preop CDVA (logMAR) ± SD | 0.52 ± 0.36 | 0.64 ± 0.51 | 0.59 ± 0.58 | .725 |
| Mean preop IOP (mm Hg) ± SD | 11.8 ± 3.8 | 13.5 ± 4.4 | 14.2 ± 2.8 | .170 |
| Mean preop ECD (cells/mm²) ± SD | 486 ± 91 | 700 ± 55 | 901 ± 66 | <.001* |
| Mean AL (mm) ± SD | 22.7 ± 1.3 | 23.8 ± 2.3 | 22.8 ± 2.1 | .168 |
| Mean cataract grade ± SD | 2.94 ± 0.87 | 2.85 ± 0.92 | 2.53 ± 0.87 | .361 |
| Diabetes mellitus present (n) | 4 | 3 | 2 | .375 |
| Hypertension present (n) | 4 | 11 | 8 | .120 |
| Capsule rupture/vitreous loss (n) | 1 | 1 | 0 | .359 |
| Mean postop CDVA (logMAR) ± SD | 0.34 ± 0.59 | 0.32 ± 0.41 | 0.28 ± 0.48 | .935 |
| Mean postop IOP (mm Hg) ± SD | 10.2 ± 2.9 | 11.8 ± 4.0 | 11.9 ± 4.1 | .333 |
| Mean endothelial cell loss (%) ± SD | 4.4 ± 31.0 | 13.0 ± 17.8 | 16.2 ± 24.9 | .449 |
| Patients with bullous keratopathy (n) | 5 | 3 | 1 | .066 |

AL = axial length; CDVA = corrected distance visual acuity; ECD = endothelial cell density; IOP = intraocular pressure
*Statistically significant

performed in 2 eyes and DSAEK in 2 eyes. The CDVA improved in all cases after keratoplasty, and the grafts survived at the patients' last visits. The mean observation period after keratoplasty in the 4 eyes was 28.8 ± 6.3 months.

## DISCUSSION

We evaluated the outcomes of cataract surgery in cases with a low preoperative ECD. Although outcomes and factors affecting endothelial cell loss after cataract surgery have been reported, little information is available on cases with a low preoperative ECD. This makes an accurate postoperative prognosis for cataract surgery difficult. Therefore, we believe that the results in this study will provide surgeons and patients with much needed information about endothelial cell loss, the incidence of bullous keratopathy, and prognostic factors—all of which may be useful in deciding the indications for and timing of surgery.

Endothelial cell density decreases after ophthalmic procedures such as cataract surgery,[10,11] vitreoretinal surgery in aphakic eyes[12,13] and glaucoma,[14,15]

Table 4. Characteristics and surgical results according to cause of low ECD.

| Parameter | Fuchs Dystrophy | Laser Iridotomy | Keratoplasty | P Value |
|---|---|---|---|---|
| Eyes (n) | 20 | 16 | 10 | |
| Mean age (y) ± SD | 72.3 ± 8.1 | 73.3 ± 6.3 | 66.8 ± 13.2 | .416 |
| M/F sex (n) | 1/19 | 1/15 | 6/4 | <.001* |
| Mean preop CDVA (logMAR) ± SD | 0.37 ± 0.33 | 0.47 ± 0.26 | 0.66 ± 0.46 | .105 |
| Mean preop IOP (mm Hg) ± SD | 12.1 ± 3.0 | 13.6 ± 4.1 | 13.0 ± 4.8 | .492 |
| Mean AL (mm) ± SD | 23.1 ± 2.0 | 21.9 ± 0.7 | 24.1 ± 2.0 | .008* |
| Mean preop ECD (cells/mm²) ± SD | 725 ± 143 | 608 ± 146 | 746 ± 243 | .072 |
| Mean cataract grade ± SD | 2.9 ± 0.8 | 3.0 ± 0.8 | 1.9 ± 0.6 | .002* |
| Diabetes mellitus present (n) | 0 | 3 | 2 | .115 |
| Hypertension present (n) | 12 | 2 | 2 | .007* |
| Mean postop CDVA (logMAR) ± SD | 0.10 ± 0.16 | 0.22 ± 0.32 | 0.51 ± 0.69 | .043* |
| Mean postop IOP (mm Hg) ± SD | 10.4 ± 2.3 | 11.3 ± 2.9 | 11.5 ± 5.9 | .581 |
| Mean endothelial cell loss (%) ± SD | 13.5 ± 14.3 | 13.4 ± 33.2 | 3.1 ± 25.0 | .310 |
| Patients with bullous keratopathy (n) | 0 | 3 | 2 | .115 |

AL = axial length; CDVA = corrected distance visual acuity; ECD = endothelial cell density; IOP = intraocular pressure
*Statistically significant

**Table 5.** Risk factors for corneal endothelial cell loss and bullous keratopathy.

| Subgroup | Eyes (n) | Mean Cell Loss (%) | *P* Value | Patients with BK | *P* Value |
|---|---|---|---|---|---|
| Age (y) | | | .748 | | 1.000 |
| ≤69 | 19 | 11.0 | | 3 | |
| 70–79 | 30 | 9.6 | | 4 | |
| 80–90 | 12 | 16.8 | | 2 | |
| Sex | | | .414 | | .361 |
| Male | 12 | 19.6 | | 3 | |
| Female | 49 | 9.6 | | 6 | |
| Preop CDVA (decimal) | | | .379 | | .475 |
| ≥20/50 | 30 | 14.2 | | 3 | |
| <20/50 | 32 | 8.6 | | 6 | |
| Axial length | | | .019* | | .488 |
| ≤23.0 mm | 33 | 19.4 | | 6 | |
| >23.0 mm | 28 | 3.6 | | 3 | |
| Cataract grade | | | .228 | | .076 |
| NS1–NS2 | 26 | 2.5 | | 2 | |
| NS3 | 22 | 15.7 | | 3 | |
| NS4–NS5 | 13 | 10.7 | | 4 | |
| Diabetes mellitus | | | .049* | | .120 |
| Absent | 52 | 9.8 | | 6 | |
| Present | 9 | 19.6 | | 3 | |
| Hypertension | | | .406 | | .462 |
| Absent | 38 | 10.2 | | 7 | |
| Present | 23 | 14.0 | | 2 | |
| Capsule rupture/ vitreous loss | | | | | .020* |
| Present | 2 | — | | 2 | |
| Absent | 59 | 11.5 | | 7 | |

BK = bullous keratopathy; CDVA = corrected distance visual acuity; NS = nuclear sclerosis
*Statistically significant

pterygium surgery,[16] and keratorefractive surgery with the use of mitomycin-C.[17] In cataract surgery, several preoperative and intraoperative parameters can influence the risk for ECD loss. A high nucleus grade, long phaco time, high ultrasound energy, exfoliation syndrome, diabetes mellitus, and a short AL are all associated with an increased risk for endothelial cell damage.[10,18–23] In this study, cases with a low preoperative ECD showed an association between greater ECD loss and shorter AL (<23.0 mm) or diabetes mellitus. In eyes with diabetes mellitus, morphologic abnormalities and a delay in the resolution of postoperative corneal edema have been reported.[24–26] In a study by Lee et al.,[27] patients with diabetes had an increased central corneal thickness and coefficient of variation and a decreased ECD and percentage of hexagonal cells than healthy controls after cataract surgery. The results in the present study suggest that in diabetic patients, corneal endothelial cells are susceptible to damage and careful attention must be paid in deciding the timing of the surgery and during cataract surgery, especially in cases with a low ECD. Our study also found posterior capsule rupture to be a risk factor for bullous keratopathy. Challenging conditions, such as a hard nucleus, a shallow anterior chamber, and intraoperative corneal edema due to a low preoperative ECD, can cause intraoperative complications. Attention must be given to posterior capsule rupture during surgery to avoid a further decrease in ECD and the development of postoperative bullous keratopathy.

In this study, the mean ECD loss was approximately 80 cells/mm$^2$ (11.5%). Recent studies evaluating eyes with a normal preoperative ECD[7,20,28,29] report an endothelial cell loss of 1.8% to 15.0% after phacoemulsification. Previous studies[20,29] also found that the preoperative cell count was not predictive of corneal endothelial cell loss in eyes with a normal ECD. The rate of ECD loss in our study was almost the same as that in earlier studies, although the endothelial cells in the eyes in our study may have been under greater stress due to preoperative conditions. This suggests that the relatively low ECD loss in our study was because the soft-shell and phaco-chop techniques were used to reduce intraoperative endothelial cell damage.

**Table 6.** Prognosis in patients with subsequent bullous keratopathy who had keratoplasty.

| Before Cataract Surgery | | | | | | Before Keratoplasty | | After Keratoplasty | |
|---|---|---|---|---|---|---|---|---|---|
| Age | Sex | Primary Disease or Procedure | VA | ECD | Type of Cataract Surgery | CDVA | Type of Keratoplasty | CDVA | FU (Mo) |
| 71 | M | Trabec; uveitis | 0.40 | 352 | Phaco + IOL | 1.00 | DSAEK | 0.40 | 31 |
| 73 | M | LI | 0.82 | 574 | Phaco + IOL | 1.00 | DSAEK | 0.15 | 27 |
| 63 | M | PKP | 0.52 | 342 | Phaco + IOL | 2.30 | PKP | 0.52 | 36 |
| 72 | F | Unknown | 0.82 | 590 | Phaco + anterior vitrectomy | 0.40 | PKP | 0.10 | 21 |

CDVA = corrected distance visual acuity (logMAR); DSAEK = Descemet stripping automated endothelial keratoplasty; ECD = endothelial cell density; FU = follow-up; IOL = intraocular lens implantation; LI = laser iridotomy; PKP = penetrating keratoplasty; Phaco = phacoemulsification; Trabec = trabeculectomy

In this study, no eye in the Fuchs dystrophy group developed bullous keratopathy and the postoperative visual acuity in this group was significantly better than in eyes with laser iridotomy and eyes with keratoplasty. However, cataract surgery in eyes with Fuchs dystrophy and a low preoperative ECD remains a challenge. Seitzman[30] and Seitzman et al.[31] evaluated the clinical outcomes of cataract surgery in 136 Fuchs dystrophy cases; 5 cases had progression to keratoplasty within the first year postoperatively. Because Fuchs dystrophy is a progressive disorder, more comprehensive long-term evaluation is required in future studies.

With the recent advent of a new endothelial keratoplasty procedure, DSAEK,[32-34] the guidelines for the treatment of bullous keratopathy or cataract with a low preoperative ECD may have changed. However, it is still not known whether cataract surgery alone or a DSAEK triple procedure yields a better visual prognosis in patients with a low ECD. In our study, 75% of patients achieved a CDVA of better than 20/40. In earlier studies,[33-36] 55% to 80% of cases achieved that level of CDVA after DSAEK. Postoperative endothelial cell loss, which was 38% at 1 year in 1 study,[37] is a problem with DSAEK. Assuming no significant difference in visual outcome between cataract surgery and DSAEK, the results in our study suggest that cataract surgery with careful attention to preventing complications (eg, posterior capsule rupture) provides good visual rehabilitation in cases with a low preoperative ECD.

A limitation of this study was that we calculated the rate of ECD loss without taking into consideration the cases in which ECD was unobtainable due to bullous keratopathy. Therefore, we may have underestimated the loss of ECD. However, if the postoperative ECD in cases that developed bullous keratopathy was 400 cells/mm$^2$, the mean rate of ECD loss was 13.5% $\pm$ 23.6%, which is comparable to that in cases with a normal ECD. Other limitations were the follow-up period and that we did not evaluate intraoperative phaco time and the length of the corneal tunnel. Bullous keratopathy can occur several years after cataract surgery. Although we believe that the mean follow-up period in our study was sufficient to evaluate postoperative ECD loss and incidence of bullous keratopathy, we included patients with a follow-up of less than 12 months. In eyes with a shorter AL, IOLs with higher power might damage the corneal endothelial cells around the incision by direct contact with the cartridge or IOL. A longer observational prospective evaluation, including intraoperative ultrasound time or complications and postoperative ECD loss, would provide clinicians and patients with valuable information on ECD loss and the incidence of bullous keratopathy.

In conclusion, cataract surgery alone provided a safe and favorable surgical outcome in more than 85% of patients with a low preoperative ECD, although some of the patients required subsequent keratoplasty. A shorter AL, diabetes mellitus, and posterior capsule rupture were risk factors for greater ECD loss or incidence of bullous keratopathy. Although cataract surgery in eyes with a low preoperative ECD is a challenge, the rate of ECD loss in this study was almost the same as that in previous studies in eyes with a normal ECD.

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First author:
Katsuya Yamazoe, MD

*Department of Ophthalmology, Ishikawa General Hospital, Tokyo Dental College, Ichikawa, Chiba, Japan*

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CORNEA

# Surgical outcome of Descemet's stripping automated endothelial keratoplasty for bullous keratopathy secondary to argon laser iridotomy

**Masatoshi Hirayama · Takefumi Yamaguchi · Yoshiyuki Satake · Jun Shimazaki**

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**Abstract**
*Background* To report the 6-month clinical outcome of Descemet's stripping automated endothelial keratoplasty (DSAEK) for bullous keratopathy (BK) secondary to argon laser iridotomy (ALI), and compare the results with those of DSAEK for pseudophakic bullous keratopathy (PBK) or Fuchs' endothelial dystrophy (FED).
*Methods* A total of 103 patients (54 with ALI, 28 with PBK, 21 with FED) undergoing DSAEK were retrospectively analyzed. Simultaneous cataract surgery was performed in 37 patients with ALI and 13 with FED. Preoperative ocular conditions, best spectacle-corrected visual acuity (BSCVA), spherical equivalent refraction (SE), induced astigmatism, keratometric value, endothelial cell density (ECD), and complications were determined over 6 months postoperatively.
*Results* Mean axial length in the ALI group (21.8±0.8 mm) was significantly shorter than that in the FED ($P$=0.02) or PBK groups ($P$=0.003). Severe corneal stromal edema ($n$=6), advanced cataract ($n$=10), posterior synechia ($n$=3), poor mydriasis ($n$=5), and Zinn zonule weakness ($n$=1) were found only in the ALI group. A significant improvement was observed in postoperative BSCVA in all groups. No significant difference was observed in BSCVA, SE, induced astigmatism, keratometric value, ECD, or complications among the three groups.
*Conclusions* Descemet's stripping automated endothelial keratoplasty for BK secondary to ALI showed rapid postoperative visual improvement, with similar efficacy and safety to that observed in DSAEK for PBK or FED.

**Keywords** Descemet's stripping automated endothelial keratoplasty · Argon laser iridotomy · Fuchs' dystrophy · Pseudophakic bullous keratopathy · Posterior lamellar keratoplasty

## Introduction

The cause of bullous keratopathy (BK), one of the main reasons for corneal transplantation worldwide, differs by region. For example, in addition to cataract surgery, Fuchs' dystrophy is a major cause of BK in western countries [1]. In Japan, on the other hand, argon laser iridotomy (ALI) is the second most common cause for BK according to a recent national survey [2, 3]. Bullous keratopathy secondary to ALI (ALI-BK) can occur long after ALI, and both eyes with angle-closure glaucoma and those that have undergone prophylactic ALI may be affected. Descemet's stripping automated endothelial keratoplasty (DSAEK), a lamellar corneal surgical procedure, allows selective replacement of the posterior layers of the cornea in the treatment of BK [4, 5]. The advantages of DSAEK over conventional penetrating keratoplasty include the need for only a small incision to be

M. Hirayama (✉) · T. Yamaguchi · Y. Satake · J. Shimazaki
Department of Ophthalmology, Ichikawa General Hospital, Tokyo Dental College,
5-11-13, Sugano,
Ichikawa, Chiba 272-8513, Japan
e-mail: mar.hirayama@gmail.com

M. Hirayama · T. Yamaguchi · J. Shimazaki
Department of Ophthalmology,
Keio University School of Medicine,
Tokyo, Japan

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made, maintenance of structural integrity of the cornea, rapid visual recovery, and minimal induction of astigmatism [6–8]. However, when DSAEK is performed for ALI-BK, several challenges arise. These eyes characteristically have shallow anterior chambers which may render anterior chamber surgical maneuvers more difficult and risky. Therefore, DSAEK for ALI-BK is often technically challenging, even for well-experienced surgeons [9]. However, hitherto, reports on the surgical outcome of DSAEK for ALI-BK have only involved small patient samples [9, 10]. The incidence and management of the intra- and postoperative complications and visual outcomes of DSAEK for ALI-BK remain largely unknown. The aim of this study was to investigate the 6-month clinical outcome of DSAEK for ALI-BK, and to compare with those undergone DSAEK for other causes of BK (Fig. 1).

## Patients and methods

### Patients

The medical records of all consecutive patients undergoing DSAEK for BK resulting from ALI, Fuchs' endothelial dystrophy (FED), or pseudophakic bullous keratopathy (PBK) between April 2007 and December 2010 at Tokyo Dental College Ichikawa General Hospital were retrospectively reviewed (Table 1). Patients were excluded from the analysis because of the following reasons; combined causes suspected such as ALI and FED (three cases), previous history of penetrating keratoplasty (eight cases), macular dysfunction due to previous retinal detachment (two cases) or Axenfeld-Rieger syndrome (one case), and end-stage glaucoma without central visual field (one case), or BK due to birth injury with corneal stromal opacity (two cases). The present study adhered to the tenets of the Declaration of Helsinki.

### Surgical procedures and postoperative treatment

After sub-Tenon or retrobulbar injection of 2% lidocaine, a 5.0-mm temporal or superior corneoscleral incision was made (details in Table 2). An anterior-chamber maintenance cannula was inserted for paracentesis. Descemet's membrane stripping was performed with a diameter corresponding to the graft size, using a reverse-bent Sinsky hook (ASICO, Westmont, IL, USA) and an epithelial trephine marker. In most cases, the graft size was 8.0 mm, as shown in Table 2. Apart from seven eyes (13%) in the ALI group and four eyes (14%) in the PBK group in which nDSAEK were performed [10], the recipient's endothelium and Descemet's membrane were carefully removed by forceps. Pre-cut donor grafts were trephinated and the endothelial surface of the lenticle coated with a small amount of viscoelastic material (Viscoat®, Alcon, Fort Worth, TX, USA). Donor tissue was gently inserted into the anterior chamber using a Busin glide (ASICO, Westmont, IL, USA)/ IOL glide and Shimazaki DSAEK forceps (Inami, Tokyo, Japan). Pull-through technique was used to insert the donor graft, except in six eyes (three eyes in the ALI group, two eyes in the PBK group and one eye in the FED group) in which the folding technique was used. Air was carefully injected into the anterior chamber to unfold the graft. Fluid from between the recipient's stroma and the graft was drained via small incisions in the midperipheral recipient cornea. Ten minutes after air injection, most of the air was replaced with balanced salt solution (BSS plus®, Alcon, Fort Worth, TX, USA). At the end of the procedure, subconjunctival tobramycin 4 mg (Tobracin®, J-Dolph, Shiga, Japan) and betamethasone 0.4 mg (Rinderon®, Shionogi, Osaka, Japan) were administered. In patients with significant lens opacity, standard phacoemulsification and aspiration, and implantation of an intraocular lens were performed prior to DSAEK using the phaco-chop technique. Postoperative medication included 0.1% levofloxacin (Cravit®, Santen, Osaka, Japan) and 0.1% betamethasone sodium phosphate (Sanbetazon®, Santen, Osaka), starting at 5 times a day for 3 months and then tapering off thereafter.

### Examinations

Best spectacle-corrected visual acuity (BSCVA), spherical equivalent (SE), induced astigmatism [11], keratometric value (K value), and endothelial cell density (ECD) were measured pre- and postoperatively at 1, 3 and 6 months. Preoperative corneal opacity was semi-quantitatively graded using slit-

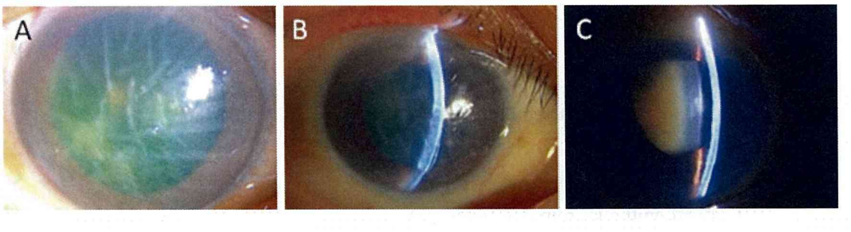


**Fig. 1** Slit-lamp photographs of three patients in ALI group taken preoperatively (a, b, c). Two cases (a, b) had severe corneal stromal edema with Descemet membrane fold with hard cataract. One case (c) had mild corneal stromal edema and rock-hard cataract with Zinn zonule weakness and poor mydriasis. DSAEK with cataract surgery had been performed safely on all patients

**Table 1** Patient demographics

| | ALI (N=54) | PBK (N=28) | *P* value | FED (N=21) | *P* value |
|---|---|---|---|---|---|
| Age (year) | 76±6.0 | 76±6.0 | NS* | 67±9.0 | NS* |
| Female/Male | 49/5 | 21/7 | 0.096† | 17/4 | 0.03† |
| Axial length (mm) | 21.8±0.8 | 23.1±2.4 | 0.018* | 22.8±1.5 | <0.001* |
| Presence of tube in anterior chamber (eyes, %) | 0 (0%) | 0 (0%) | - | 0 (0%) | - |
| Grade of corneal opacity (eyes, %) | | | | | |
| Grade 0 | 0 (0%) | 0 (0%) | - | 0 (0%) | - |
| Grade 1 | 14 (31.8%) | 8 (34.8%) | | 9 (45%) | |
| Grade 2 | 12(34.1%) | 8 (34.8%) | 0.68** | 8 (35%) | 0.22** |
| Grade 3 | 18 (34.1%) | 7 (30.4%) | | 4 (20%) | |
| Emery-Little Grading of cataract | | | | | |
| Mean of grade of cataract | 3.57±0.96 | - | - | 2.95±0.74 | 0.013* |
| Grade 1 cataract (eyes, %) | 0 (0%) | - | - | 0 (0%) | - |
| Grade 2 cataract (eyes, %) | 8 (14.8%) | - | - | 6 (28.6%) | 0.53† |
| Grade 3 cataract (eyes, %) | 17 (31.5%) | - | - | 10 (47.6%) | 0.81† |
| Grade 4 cataract (eyes, %) | 19(35.2%) | - | - | 5 (23.8%) | 0.12† |
| Grade 5 cataract (eyes, %) | 10 (18.5%) | - | - | 0 (0%) | 0.013† |
| Simultaneous cataract surgery (eyes, %) | 37 (68.5%) | 0 (0%) | - | 13 (61.9%) | 0.60† |
| Cataract surgery on beforehand (eyes, %) | 9 (7.4%) | 0 (0%) | | 0 (0%) | - |

* Mann–Whitney U test

** $\chi^2$ test † Fisher exact test

lamp biomicroscopy as follows: grade 0: clear and normal; grade 1: slightly hazy, but iris cleft visible; grade 2: iris cleft difficult to identify; grade 3: iris cleft impossible to identify. Cataracts were graded according to the Emery–Little

**Table 2** Details of surgical procedure of DSAEK in each groups

| | ALI ($n$=54) | PBK ($n$=28) | FED ($n$=21) |
|---|---|---|---|
| Descemet's stripping endothelial keratoplasty (eyes, %) | 47 (87%) | 24 (86%) | 21 (100%) |
| Non-Descemet's stripping endothelial keratoplasty (eyes, %) | 7 (13%) | 4 (14%) | 0 (0%) |
| Graft size (eyes) | | | |
| 7.0 mm | 1 | 0 | 0 |
| 7.5 mm | 1 | 0 | 0 |
| 7.75 mm | 1 | 1 | 1 |
| 8.0 mm | 51 | 26 | 19 |
| 8.25 mm | 0 | 0 | 1 |
| 8.5 mm | 0 | 1 | 0 |
| Location of corneoscleral incision (eyes, %) | | | |
| Temporal | 51 (94%) | 23 (82%) | 20 (95%) |
| Superior | 3 (6%) | 5 (18%) | 1 (5%) |
| Corneal epithelial removal (eyes, %) | 13/54 (24%) | 1/28 (3.6%) | 4 (19%) |
| Trypan blue staining (eyes, %) | 3/37 (8.1%) | 0 (0%) | 0 (0%) |
| Multiple sphincterotomy (eyes, %) | 3/37 (8.1%) | 0 (0%) | 0 (0%) |

classification. Poor preoperative mydriasis was defined as a pupil diameter of less than 5 mm after instillation of tropicamide and phenylephrine 3 times per 10 minutes. Decimal values of BCSVA were converted to logarithm for statistical analysis. Endothelial cell density was measured using a specular microscope (SP-3000P®, Tomey, Nagoya, Japan). Intra- and postoperative complications were also recorded.

### Statistical analysis

The Mann–Whitney U, Wilcoxon, Kruskal–Wallis, $\chi^2$ tests and Fisher's exact test were used for the statistical analysis. A *P* value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed with the SSRI software (SSRI Co. Ltd., Tokyo, Japan).

## Results

### Preoperative ocular conditions

Table 1 summarizes the demographic data on the 103 eyes with BK analyzed in this study, which included 54 with ALI-BK (ALI group), 28 with PBK (PBK group), and 21 with FED (FED group). The proportion of eyes that had simultaneous cataract surgery is shown in Table 1. Mean axial length was significantly smaller in ALI group than in FED ($P$=0.02) or PBK groups ($P$=0.0003, Mann–Whitney U test). As shown in Table 1, the grade of corneal opacity was similar in each group. However, severe corneal stromal edema with descemet's membrane fold occurred in six eyes (11%) in ALI group. Moreover, posterior synechia ($n$=3) and poor mydriasis ($n$=5) occurred more frequently in ALI group. Mean grade of cataract was significantly higher in ALI group than in FED group, with grade 5 cataract found only in ALI group (Table 1). Higher than grade 4 cataract occurred significantly more often in the ALI group than in the FED group ($P$=0.023; Fisher exact test). As shown in Table 2, various types of intraoperative manipulation, including corneal epithelium removal, trypan blue-assisted phacoemulsification and multiple sphincterotomy, were required only in ALI group.

### BSCVA, induced astigmatism, SE and K value

All eyes were followed up for a minimum of 6 months postoperatively. Clarity was maintained in the donor graft at postoperative month 6 in 50 eyes (92.6%) in ALI group, 26 eyes (92.9%) in PBK group, and 20 eyes (95.2%) in FED group. Table 3 summarizes BSCVA at preoperative and postoperative months 1, 3 and 6. With regard to postoperative BSCVA, 53 eyes (98.1%) in ALI group, 26 eyes (92.9%) in PBK group and 19 eyes (90.4%) in FED group showed improved BSCVA. Forty-four eyes (81.5%) in ALI group, 19 eyes (67.9%) in PBK group and 14 eyes (66.7%) in FED group achieved a BSCVA of 20/40 or better at 6 months. A significant improvement was observed in BSCVA from 1 month after DSAEK in each group ($P$< 0.0001 in ALI group, $P$=0.0006 in PBK group, and $P$= 0.0004 in FED group; Wilcoxon test). In ALI and PBK groups, BSCVA improved significantly from 1 month to 3 months postoperatively ($P$<0.0001 in ALI group and $P$= 0.0065 in PBK group; Wilcoxon test). Table 4 shows the results of refractive data. No significant difference was observed in induced astigmatism throughout the postoperative observation period in each group. No significant difference was observed in SE between the preoperative and postoperative 1-month values in any group. A significant difference was observed in SE between postoperative month 1 and 6 in FED group ($P$=0.046, Wilcoxon test). No significant differences were observed in preoperative and 1-, 3-, and 6-month postoperative K values in any group.

### Endothelial cell loss

Table 5 summarizes ECD of donor preoperatively and ECD at postoperative month 1, 3 and 6. Preoperative ECD

**Table 3** The average of best spectacle-corrected visual acuity (BSCVA)

| BSCVA (LogMAR±SD) | ALI (range) | PBK (range) | FED (range) | *P* value |
|---|---|---|---|---|
| Preoperative | 1.27±0.64 (0.16 to 3) | 1.41±0.59 (0.52 to 2.7) | 0.88±0.49 (0.3 to 2) | |
| 1 m | 0.60±0.63 (0.16 to 3) | 0.78±0.64 (0.3 to 2.7) | 0.44±0.46 (0.16 to 2) | NS* |
| 3 m | 0.43±0.57 (0 to 2.7) | 0.65±0.67 (0.1 to 2.7) | 0.39±0.44 (0.05 to 2) | NS* |
| 6 m | 0.34±0.60 (−0.08 to 2.7) | 0.50±0.65 (0 to 2.7) | 0.21±0.30 (0 to 1) | NS* |
| Eyes showing improved BSCVA (eyes) | 53 (98.1%) | 26 (92.9%) P=0.27† | 19 (90.4%) P=0.19† | |
| Postoperative BSCVA>20/40 (eyes) | 44 (81.5%) | 14 (66.7%) P=0.18†† | 19 (67.9 %) P=0.22†† | |

*Kruskal–Wallis test comparing the difference among three groups

† Fisher's test comparing the number of eyes showing improved BSCVA between in ALI group and PBK group or FED group

†† Fisher's test comparing the number of eyes showing postoperative BSCVA>20/40 between in ALI group and PBK group or FED group

**Table 4** Graft survival rate and refractive data

| | ALI | PBK | FED | *P* value |
|---|---|---|---|---|
| Graft survival rate at postoperative 6 m (eyes, %) | 50 (92.6%) | 26 (92.9%) | 20 (95.2%) | |
| Induced astigmatism (D) | | | | |
| 1 m | 1.4±1.2 | 2.5±2.1 | 2.3±1.4 | 0.007* |
| 3 m | 1.5±1.1 | 2.3±1.1 | 2.0±1.6 | 0.036* |
| 6 m | 1.5±1.0 | 1.8±0.7 | 1.7±1.3 | NS* |
| Spherical equivalence (D) | | | | |
| Preoperative | 0.69±2.6 | −0.74±1.86 | −0.25±1.5 | NS* |
| 1 m | 0.31±1.6 | −0.48±2.2 | −0.39±2.2 | NS* |
| 3 m | 0.17±1.2 | −0.94±2.0 | 1.6±5.26 | NS* |
| 6 m | −0.15±0.78 | −0.94±2.0 | −2.7±4.3 | NS* |
| Keratometric value | | | | |
| Preoperative | 44.5±2.4 | 43.8±2.0 | 44.5±2.3 | NS* |
| 1 m | 43.3±2.4 | 43.3±2.2 | 44.0±2.2 | NS* |
| 3 m | 44.0±2.2 | 43.6±1.9 | 43.5±2.6 | NS* |
| 6 m | 44.0±2.1 | 43.7±2.1 | 43.8±1.4 | NS* |

Data were presented as mean± SD. *Kruskal–Wallis test compared the difference among three groups

significantly decreased 1 month after DSAEK ($P<0.0001$ in ALI group, $P=0.043$ in PBK group, and $P=0.012$ in FED group; Wilcoxon test). In addition, postoperative ECD significantly decreased from month 3 (1174±361 cells/mm$^2$) to month 6 (944±386 cells/mm$^2$) in PBK group ($P=0.017$; Wilcoxon test), although no rejection episode occurred between 3 and 6 months in this group.

## Complications

Complications are summarized in Table 6. No significant differences were observed in incidence of intra- or postoperative complications among the three groups. Three eyes out of 37 eyes (8.1%) in ALI group showed posterior capsule rupture intraoperatively. In two of these three eyes, an intraocular lens was inserted into the capsular bag, while in the remaining eye the lens was fixed to the sulcus. Twelve out of 103 eyes (11.5%) (six eyes in ALI group, three eyes in PBK group and three eyes in FED group) showed dislocation of the donor corneal lenticle at day 1 postoperatively, with each undergoing successful reattachment with one or a pair of air bubble tamponades. Pupillary block glaucoma secondary to anterior chamber air bubble occurred in three out of 103 eyes (2.9%) (one eye in ALI group and two eyes in PBK group) on the day of surgery, and was successfully treated by air removal. One out of 103 eyes (0.97%) (PBK group) developed acute graft rejection characterized by mild inflammation in the anterior chamber and keratic precipitates on the donor endothelium. In this case, graft rejection was treated with intensive topical and intravenous corticosteroid therapy. No case underwent re-keratoplasty within 6 months. Postoperative ocular hypertension developed in six eyes (three eyes in ALI group, one eye in PBK group and two eyes in FED group) and was treated with antiglaucoma eye drops. Cystoid macular edema was found in one eye in ALI group, and was treated with intensive instillation of 0.1% diclofenac sodium (Diclod®, Wakamoto Pharmaceuticals, Tokyo, Japan).

**Table 5** Endothelial cell density (ECD)

| ECD(/mm$^2$±SD) | ALI | PBK | FED | *P* value |
|---|---|---|---|---|
| Donor preoperatively | 2339±284 | 2600±341 | 2701±332 | NS* |
| 1 m | 1360±467 | 1023±260 | 1158±487 | NS* |
| 3 m | 1217±485 | 1174±361 | 1388±612 | NS* |
| 6 m | 1124±427 | 944±386 | 1230±560 | NS* |

*Kruskal–Wallis test comparing endothelial cell density among three groups

## Discussion

We evaluated the 6-month clinical outcome of Descemet's stripping automated endothelial keratoplasty (DSAEK) for BK secondary to ALI and compare the results with those of DSAEK for pseudophakic bullous keratopathy (PBK) or Fuchs' endothelial dystrophy (FED). We demonstrated that DSAEK for BK secondary to ALI showed rapid postoperative visual improvement, with similar efficacy and safety to that observed in DSAEK for PBK or FED.

Bullous keratopathy secondary to ALI is becoming increasingly common in Asian countries, especially in Japan [2, 3, 12–15], where a national survey revealed that ALI-BK accounted for approximately one-fourth of BK cases

**Table 6** Complications

| | | ALI | PBK | *P* value* | FED | *P* value* | Total |
|---|---|---|---|---|---|---|---|
| Intraoperative | Posterior capsule rupture (eyes, %) | 3 (8.1%) | 0 (0%) | 0.54 | 0 (0%) | 0.56 | 3 (2.9%) |
| Postoperative; early | Dislocation (eyes, %) | 6 (11%) | 3 (11%) | 1 | 3 (14%) | 0.70 | 12 (12%) |
| | Pupillary block (eyes, %) | 1 (1.9%) | 2 (7.1%) | 0.27 | 0 (0%) | 1 | 3 (2.9%) |
| Postoperative; chronic | Rejection (eyes, %) | 0 (0%) | 1 (3.6%) | 1 | 0 (0%) | 1 | 1 (0.97%) |
| | Ocular hypertension (eyes, %) | 3 (5.5%) | 1 (3.6%) | 1 | 2 (9.5%) | 0.61 | 6 (5.8%) |
| | Cystoid macular edema (eyes, %) | 1 (1.9%) | 0 (0%) | 1 | 0 (0%) | 1 | 1 (0.97%) |

*Fisher exact test compared with ALI group

undergoing keratoplasty. Most cases of ALI-BK develop long after laser iridotomy, in which an argon laser is used [2]. However, the underlying mechanism of ALI-BK remains unclear. Several hypotheses have been postulated, including increased temperature in the local aqueous humor [16], high energy delivered during ALI breakdown of the blood–aqueous barrier, and change in aqueous humor fluid dynamics [17, 18].

This study demonstrated that surgery for ALI-BK is technically challenging, mainly due to the small size of the eyeball shallow anterior chamber and challenging simultaneous cataract surgery in ALI group. In the present study, the mean axial length of eyes receiving DSAEK for ALI-BK was less than 22 mm. In addition, advanced cataract is often associated with this disorder, and physicians are reluctant to perform surgery due to decreased endothelial density. Moreover, a shortage of donor grafts in Japan often gives rise to delayed keratoplasty, which makes the procedure even more challenging. There were also associated problems such as poor mydriasis and weak Zinn zonule in some cases. To overcome difficulties in surgery, various supporting surgical procedures are used, and simultaneous cataract surgery. Epithelial removal technique was performed in case of invisible anterior chamber by strong corneal epithelial edema. In addition, trypan blue staining was performed to stain anterior capsule for continuous curvilinear capsulorhexis (CCC) in the case of severe cataract. In this study, all trypan blue staining was combined with epithelial removal procedure. The postoperative outcome in eyes with ALI-BK was comparable to other groups, suggesting that combined DSAEK and cataract surgery can be performed without severe complications with the above-mentioned surgical technique in most cases.

In this study, the average BSCVA 6 month after DSAEK for ALI-BK was 20/29 with low induced astigmatism. Seven eyes (12.9%) achieved postoperative BSCVA of 20/20 or better. Clarity was maintained in the donor graft at postoperative month 6 in 50 eyes (92.6%). No case underwent re-keratoplasty within 6 months. These results are comparable with those of Gorovoy [5], Koenig [6], and Kobayashi [9] (Table 7). Endothelial cell loss was 52% at postoperative 6 months, similar to 6-month data reported previously [6]. Postoperative endothelial loss after DSAEK for ALI-BK was not significantly different from that in the other two groups. We were concerned about the possibility that the ALI group may experience a faster decrease in ECD than the other groups after DSAEK, because of the pathogenesis mechanism of ALI. However, the results of this study showed that the 6-month clinical outcomes of ECD in DSAEK for ALI-BK were comparable with those of DSAEK for BK caused by FED or PBK [20, 21]. One of the explanations may be that simultaneous cataract surgery eliminates the cause of endothelial cell damage by deepening the anterior chamber.

Our previous report on PK for ALI-BK showed a similar result in BSCVA to that of the present study (78.6% of patients achieved 20/40 or better); however, incidence of rejection (8.2%) and postoperative glaucoma (18.4%) was relatively high [22]. The refractive outcome at postoperative 6 months of our previous study indicated that PK for ALI-BK resulted in similar SE (the average was 0.19±4.6 D) to the present study, and higher induced astigmatism (the average; 3.3±2.4 D) (unpublished data). Although there was no report that showed postoperative refraction data of PK for ALI-BK in detail, PK usually results in unstable refraction as long as sutures are present, and even after their removal [23–26]. Bahar et al. reported the comparison of 12-month surgical outcomes of DSAEK and PK [8]. Stability of the refraction is a major advantage of all endothelial keratoplasty techniques as compared with PK. In current study, the postoperative refraction after DSAEK for ALI-BK was stable during follow-up terms.

In summary, this study of 6-month outcomes of DSAEK for BK secondary to ALI showed rapid postoperative visual improvement, with similar efficacy and safety to that observed in DSAEK for PBK or FED. Although many of the eyes in ALI group presented technical challenges during surgery, those challenges could be successfully managed by modification of the procedures and implements used.

**Table 7** Comparison of clinical outcome with previous reports

| Author Journal | Gorovoy et al. Cornea, 2006 [5] | Koenig et al. Cornea, 2007 [6] | Koenig et al. Ophthalmology, 2007 [7] | Bahar et al. Ophthalmology, 2008 [8] | Kobayashi et al. Cornea, 2008 [9] | Kobayashi et al. Am J O, 2008 [10] | Price et al. Ophthalmology, 2010 [19] | Hirayama et al. |
|---|---|---|---|---|---|---|---|---|
| Operation | DSAEK | DSAEK | DSAEK | DSAEK | DSAEK | nDSAEK | DSAEK | DSAEK/ nDSAEK |
| Study design | Retrospective | Prospective | Prospective | Prospective | Prospective | Prospective | Prospective | Retrospective |
| Number of eyes (eyes) | 16 | 34 | 26 | 45 | 14 | 6 | 173 | 54 |
| Disease (eyes) | FED 9 | FED 11 | FED 12 | FED 28 | ALI-BK 14 | ALI-BK 6 | FED 147 | ALI-BK |
| | PBK 7 | P/ABK 23 | P/ABK 14 | PBK 12 | | | P/ABK 23 | |
| | | | | ICE syndrome 2 | | | Other endothelial failure 3 | |
| | | | | Failed graft 3 | | | | |
| M:F | 7:9 | 6:28 | 6:20 | 20:25 | 1:13 | 2:4 | 69:104 | 5:49 |
| Mean age (years) | 66 | 73.8 | 75.9 | 70.2 | 74.2 | 74.5 | 72 | 76 |
| Follow-up time | 1 year | 6 months | 3 months | 9.8 months | 228 ±132 days | 6 months | 1 year | 6 month |
| Postoperative BSCVA | 20/40 or better (except three eyes with macular scar, optic dystrophy, primary graft failure) | Mean 20/42 (62% achieved 20/40 or better) | Mean 20/45 | Mean 20/44 | 20/40 or better (23% achieved 20/20) | More than 20/32 (33% achieved 20/20) | – | Mean 20/29 (13% achieved 20/20) |
| Postoperative SE (D) | – | 0.97 | 0.82 | 0.96 | – | – | – | −0.15 |
| Postoperative astigmatism (D) | – | 1.80 | 2.12 | 1.36 | 0.53 | 0.85 | – | 1.5 |
| Postoperative ECD (/mm$^2$) | 1,714 (except one eye of primary graft failure) | 1,396 | – | 1,735 | 1,654 | 2,391 | 1,743 | 1,124 |
| Cell loss | 41% | 50% | – | 36% | 45% | 26% | 38% | 52% |
| Complications during operation (eyes) | – | – | – | – | Vitreous prolapse 2 (14%) | None | – | Posterior capsule rupture 3 (5.5%) |
| Postoperative complications (eyes) | | | – | | | | | |
| Graft failure | 1 (6%) | 3 (9%) | – | 1 (2%) | – | 0 (0%) | – | – |
| Dislocaton | 4 (25%) | 9 (27%) | 9 (35%) | 7 (16%) | 2 (14%) | 1 (17%) | 10 (6%) | 6 (11%) |
| Acute rejection | – | 6 (18%) | 3 (12%) | 1 (2%) | – | – | 9 (5%) | 0 (0%) |
| Elevated IOP | – | – | – | 3 (7%) | – | – | 27 (16%) | 3 (6%) |
| Papillary block | – | 1 (3%) | 1 (4%) | – | – | 0 (0%) | 0 (0%) | 1 (2%) |
| Others | | | | Interface opacity 2 (4%) CME 1 (2%) | | Subclinical endothelial rejection 1 (17%) | Retinal detachment 1(<1%) Anterior synechiae 2 (1%) | CME 1 (2%) |

DSAEK; Descemet's stripping automated enthothelial keratoplasty, nDSAEK; non-Descemet's stripping automated enthothelial keratoplasty, FED; Fuchs' endothelial dystrophy, PBK; pseudophakic bullous keratopathy, ABK; aphakic bullous keratopathy, ALI-BK; bullous keratopathy secondary to argon laser iridotomy, ICE syndrome; iridocorneal endothelial syndrome, SE; spherical equivalent, ECD; endothelial cell density, IOP; intraocular pressure, CME; cystoid macular edema

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