Randomized, Prospective Comparison of Clinical Outcomes and Confocal Findings of Precut versus Manually Dissected Grafts for Descemet’s Stripping Endothelial Keratoplasty

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Abstract

**Purpose:** To compare the outcome of surgery and postoperative complications between using manually dissected cornea in Descemet’s stripping with endothelial keratoplasty (DSEK) and using eye bank automated precut cornea in Descemet’s stripping with automated endothelial keratoplasty (DSAEK).

**Methods:** Forty eyes with indication of endothelial keratoplasty (EK) were included in this randomized prospective clinical trial. The eyes were randomly divided into two groups. Donor cornea in one group was dissected with curved blade by the surgeon, while precut cornea from eye bank was used in other group. All surgeries were performed in one center by three surgeons, authors of the article. Patients were followed for 3 months.

**Results:** Baseline parameters and demographic features were not significantly different between the two groups. The most common indication of EK in both groups was pseudophakic bullous keratopathy (PBK) (60%). Endothelial cell loss in DSEK and DSAEK were 51.59% and 50.70%, respectively after 3 months follow-up (P=0.947). Best spectacle-corrected visual acuity (BSCVA) and intraocular pressure (IOP) after surgery and postoperative complications were not significantly different in both groups. Prevalence and intensity of interface opacity was significantly lower in DSAEK group after surgery. BSCVA equal or more than 20/100 was detected in 85% and 75% individuals in DSAEK and DSEK groups, respectively.

**Conclusion:** In conclusion, three months postoperative outcomes of EK were similar in the two groups of precut DSAEK and manually dissected DSEK. Smooth and uniform layer in precut DSAEK leads to lower interface opacity in patients.

**Keywords:** Endothelial Keratoplasty, Manually Dissected, Automated Dissected

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Introduction
Since the very first successful human lamellar corneal transplantation performed by Von Hippel¹ in 1886, endothelial keratoplasty (EK) and the technique of selectively replace the diseased layers of the cornea have been enormously evolved particularly, in the last decades. Many forms of EK have been surprisingly advanced recently.² Descemet’s stripping with endothelial keratoplasty (DSEK)³,⁴ is now considered the preferred surgical procedure replacing penetrating keratoplasty (PK) for corneal endothelial disorders. Structural integrity of the recipient eye is maintained in DSEK. Besides, rapid healing and early visual rehabilitation with satisfactory visual outcomes are the advantages of DSEK compared to PK. Moreover, the complication profile is much lower as DSEK requires fewer or no corneal sutures leading to an astigmatically neutral procedure in DSEK.²,⁵⁻⁷

Melles et al⁸ described posterior lamellar keratoplasty using curved blade in 1998 which was developed and became automated in 2006 using a microkeratome⁹ and presented as Descemet’s stripping with automated endothelial keratoplasty (DSAEK).

A microkeratome is a precision surgical device commonly used to create corneal flap in refractive laser eye surgery. Microkeratome and associated equipments are expensive and are not affordable for each hospital or eye surgery center. Accordingly, microkeratome facilities are purchased by some eye banks where trained technicians using developed standard operating procedures to provide the surgeons with standard dissected cornea. After dissection, endothelial health of donor tissue would be examined in eye bank by slit-lamp and specular microscopy before shipping to the surgeon. Such endothelial evaluation is not achievable when the dissection is performed by surgeon in operation room.¹⁰

There are many successful reports of using eye bank precut tissues, though to our knowledge, there was no report in literature comparing precut cornea with manually dissected ones. The only available prospective randomized clinical trial, compared eye bank predissected corneal grafts with surgeon-dissected grafts using a comparable microkeratome and same protocol in operation room.¹⁰ Consequently, we aimed to compare the clinical outcome and endothelial cell characteristics in manually surgeon dissected and eye bank predissected corneal grafts (precut).

Methods
Forty patients with endothelial decompensation and pseudophakic who were candidates for EK were entered into a randomized prospective clinical trial from May 2009 through March 2010. Patients were randomly divided into two groups. For 20 patients, donor tissue was manually dissected (DSEK group) and eye bank precut graft was used in the other twenty patients (DSAEK group). Study was conducted in Farabi Eye Hospital of Tehran University of Medical Sciences, a tertiary referral center in Iran. All patients read and signed an informed consent document. All surgeries were performed by three surgeons (MNH, FO, SHB).

Sample size was calculated using stata/SE8 software and db sanspsi order considering α=0.05 and β=0.10 (Power=90%). Demographic data was collected for all individuals. Best spectacle-corrected visual acuity (BSCVA), refraction (If was possible), intraocular pressure (IOP), and complete slit-lamp examination was performed for both groups before operation. Ultrasound B-scan of posterior segment was performed in patients who had severe corneal edema and fundoscopy was not conceivable. Table 1 shows the indications of EK in both groups.

All patients were examined using slit-lamp and followed one and three months after surgery by masked examiners regarding the tissue randomization. Endothelial cell density was measured using noncontact specular microscope (Kerato Analyzer EKA-98, Konan Medical Inc, Hyogo, Japan) after microkeratome tissue dissection (DSAEK group). The same was done for 16 corneoscleral tissues in DSEK group, while donor endothelial cell count in the 4 fresh globes was reported qualitatively as “very good”.

BSCVA, IOP, confocal scan results for pachymetry [Lenticule thickness, central corneal thickness (CCT)], endothelial cell
parameters (Hexagonality, mean cell area, polymegatism) and interface opacity as surgery outcomes were evaluated one and three months postoperatively, as well as complications. Zscan profile curves were used to measure lenticule thickness and CCT.

After the month three sutures were removed and refraction was performed for each patient. Endothelial evaluation was performed using a confoscan 3.4 confocal microscope (Nidek Technologies, Padova, Italy) and was analyzed using the manufacturer's semiautomated cell count software. The cell centers and exact borders of the area being counted were manually identified and average counts were done from three central photographs.

**Technique**

**Donor preparation**

**Manual dissection**

A donor corneoscleral shell was mounted on an artificial anterior chamber (AC), and the chamber was inflated with balanced salt solution (BSS). A 5 mm incision in limbus was made using a diamond blade set at 350 µm depth and dissection was done using a series of 3 curved blades as the Melles standard technique of dissection.

Fresh globe was used in four patients. After globe preparation, a 5 mm incision with 350 µm plate was selected and dissected as previously mentioned. Pachymetry was performed in none of the patients.

**Automated dissection**

Automated precut grafts were prepared in eye bank using the CB microkeratome (Moria, Antony, France). After epithelial removal 350 µm plate was selected and dissected without performing pachymetry before dissection. The precut donor corneas were shipped in optisol (Bausch & Lomb, Rochester, New York, USA) to the surgery center. In all patients, all precut grafts were transplanted within 48 hours after being dissected in the eye bank.

DSEK procedure was performed according to the standard method. 5 mm temporal clear cornea incision was performed on the recipient using monitored anesthesia with retrobulbar block or topical anesthesia. The recipient epithelium of center of cornea was marked and Descemete rhexis was performed with an 8 mm diameter (Except for the failed PK patients).

After dissection, the donor lenticule was folded into a taco configuration (With 8 mm diameter) and inserted into anterior chamber of the recipient eye using Kelman-McPherson forceps. After unfolding and centration, AC was filled with air for 10 minutes, and then 50% of the air was removed and replaced with BSS. All incisions were sutured and all patients were patched.

In 9 patients with the diagnosis of cataract and Fuchs endothelial dystrophy, phacoemulsification was performed initially using 3.2 mm temporal clear corneal incision before EK, and after finishing phacoemulsification, incision size was augmented to 5 mm for lenticule insertion. The next steps of EK were performed as standard method subsequent to complete washing of viscoelastic from AC and Miocohl-E (Acetylcholine) is used to constrict the pupil of the eye during surgery.

Standard EK without Descemet’s stripping was done in 3 patients with initial diagnosis of failed PK before operation. All three patients had PK more than one year prior to EK and all sutures were removed.

In 4 patients with failed DSEK, lenticule was separated and driven out using forceps and subsequently, the next steps of EK were performed using standard methods. Previous DSEK was performed less than one month before the second surgery for all four patients and 5 mm temporal clear incision was used in all.

Postoperatively, betamethasone 0.1% and chloramphenicol eye drops were prescribed 4 times a day for all patients. Topical antibiotics was discontinued after one week and steroid was continued for 2 months after surgery and tapered as one drop daily if there was not any signs of steroid induced ocular hypertension. IOP increased in 2 patients. Betamethasone was discontinued and fluorometholone and timolol was started twice daily for these two patients.

**Statistical analysis**

Man-Whitney test was used to compare BSCVA, IOP, endothelial cell count, CCT, lenticule thickness, hexagonality, polymegatism and postoperative complications between the two groups.
Comparing the parameters before and after surgery was performed by Wilcoxon signed-ranks and Fridman tests. Interface opacity grading was analyzed using cross-tabulation. P-values of less than 0.05 considered statistically significant. Study was approved by the ethics committee of Eye Research Center of Farabi Eye Hospital.

Results

In this study, mean age, male to female ratio, BSCVA, IOP, and donor endothelial cell density were not significantly different in both groups before the operation (Table 2). The most common indication of DSEK in both groups was pseudophakic bullous keratopathy (PBK) (60% totally).

Refraction assessment before operation was not possible due to advanced bullous keratopathy. Mean spherical equivalent (SE) three months after surgery and removal of sutures was 0.08±1.57 and 0.42±1.86 in DSEK and precut DSAEK groups, respectively, which was not significantly different (P=0.482).

Mean IOP before surgery, one and three months postoperatively is shown in table 3. No significant difference was observed between the two groups.

Table 4 shows mean BSCVA logMAR before surgery, one and three months postoperatively in the two groups. There was no significant difference between the two groups but in each group, before and after surgery a significant difference was observed (P<0.001). BSCVA equal or more than 20/100 was detected in 85% and 75% individuals in DSAEK and DSEK groups, respectively.

Endothelial characteristics, polymegatism and hexagonality were not different between the two groups, postoperatively. Although the mean cell area in DSAEK group was significantly more than DSEK group, 3 months after surgery. Endothelial characteristics, one and three months after surgery are shown in table 5.

Endothelial cell loss in DSEK and DSAEK were in respect 30.74% and 34.36% one month postoperation (P=0.169), and 51.59% and 50.70% after 3 months of follow-up (P=0.947).

Endothelial cell loss one month and three months after surgery for both groups is shown in table 6.

CCT and lenticule thickness calculations after one and three months in DSAEK group were significantly lower than DSEK group (Table 7).

Grading system was applied to assess interface opacity:

Grade 0
No interface opacity and keratocytes are completely visible with all their features (Figure 1).

Grade 1
Mild haziness: mild interface opacity, keratocytes are visible, although due to bright extracellular dense tissue, the details of keratocytes' borders are not completely definable (Figure 2).

Grade 2
Moderate haziness: keratocytes are visible, but due to intense light scattering subsequent to bright extracellular dense tissue, internal structures of keratocytes and the adjacent keratocytes' borders are not defined (Figure 3).

Grade 3
Severe haziness: keratocytes are not visible due to maximal diffuse reflectivity in stroma.

Interface opacity amounts are shown in table 8.

Intensity and prevalence of interface opacity in first and third month after surgery were more in DSEK group than DSAEK group, and opacity in both groups was significantly reduced by time.

Complications
Complication incidence was not significantly different between the two groups. Nine patients, 4 in DSEK group and 5 in DSAEK group presented postoperative complications (Shown in table 9).
Table 1. Surgery indication in patients who underwent Descemet's stripping with endothelial keratoplasty and Descemet's stripping with automated endothelial keratoplasty

<table>
<thead>
<tr>
<th>PBK</th>
<th>Failed penetrating keratoplasty</th>
<th>Fuchs endothelial dystrophy</th>
<th>Failed DSEK</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSEK</td>
<td>11 (55%)</td>
<td>2 (10%)</td>
<td>5 (25%)</td>
<td>20</td>
</tr>
<tr>
<td>DSAEK</td>
<td>13 (65%)</td>
<td>1 (5%)</td>
<td>4 (20%)</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>3</td>
<td>9</td>
<td>40</td>
</tr>
</tbody>
</table>

DSEK: Descemet's stripping with endothelial keratoplasty
DSAEK: Descemet's stripping with automated endothelial keratoplasty

Table 2. Comparison of demographic and baseline characteristic in Descemet's stripping with endothelial keratoplasty and Descemet's stripping with automated endothelial keratoplasty patients

<table>
<thead>
<tr>
<th></th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>11/9</td>
<td>12/8</td>
<td>0.749</td>
</tr>
<tr>
<td>Age mean (SD)</td>
<td>70.45 (12.05)</td>
<td>69.70 (9.19)</td>
<td>0.597</td>
</tr>
<tr>
<td>Preoperative IOP mean (SD)</td>
<td>14.75 (3.35)</td>
<td>14.90 (2.53)</td>
<td>0.663</td>
</tr>
<tr>
<td>Preoperative BSCVA (logMAR) mean (SD)</td>
<td>1.67 (0.37)</td>
<td>1.66 (0.36)</td>
<td>0.922</td>
</tr>
<tr>
<td>Preoperative endothelial donor cell count mean (SD)</td>
<td>3426.88 (270.97)</td>
<td>3273.90 (371.35)</td>
<td>0.171</td>
</tr>
</tbody>
</table>

DSEK: Descemet's stripping with endothelial keratoplasty
DSAEK: Descemet's stripping with automated endothelial keratoplasty
SD: Standard deviation
IOP: Intraocular pressure
BSCVA: Best spectacle-corrected visual acuity

Table 3. Preoperative and postoperative intraocular pressure in Descemet's stripping with endothelial keratoplasty and Descemet's stripping with automated endothelial keratoplasty patients

<table>
<thead>
<tr>
<th>IOP mean (SD)</th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>14.75 (3.35)</td>
<td>14.90 (2.53)</td>
<td>0.663</td>
</tr>
<tr>
<td>1 month postoperative</td>
<td>15.0 (4.08)</td>
<td>13.95 (3.58)</td>
<td>0.924</td>
</tr>
<tr>
<td>3 months postoperative</td>
<td>14.75 (3.82)</td>
<td>14.65 (2.45)</td>
<td>0.754</td>
</tr>
</tbody>
</table>

DSEK: Descemet's stripping with endothelial keratoplasty
DSAEK: Descemet's stripping with automated endothelial keratoplasty
SD: Standard deviation
IOP: Intraocular pressure

Table 4. Best spectacle-corrected visual acuity logMAR pre and postoperation

<table>
<thead>
<tr>
<th>BSCVA logMAR Mean (SD)</th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperation</td>
<td>1.67(0.37)</td>
<td>1.66(0.36)</td>
<td>0.922</td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>0.69(0.30)</td>
<td>0.66(0.39)</td>
<td>0.540</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>0.65(0.25)</td>
<td>0.63(0.37)</td>
<td>0.462</td>
</tr>
</tbody>
</table>

DSEK: Descemet's stripping with endothelial keratoplasty
DSAEK: Descemet's stripping with automated endothelial keratoplasty
SD: Standard deviation
BSCVA: Best spectacle-corrected visual acuity
Table 5. Endothelial cell characteristics pre and postoperation

<table>
<thead>
<tr>
<th></th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. cell count mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperation (Donor)</td>
<td>3426 (271)</td>
<td>3274 (371)</td>
<td>0.171</td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>2402 (433)</td>
<td>2120 (277)</td>
<td>0.005</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>1690 (341)</td>
<td>1597 (140)</td>
<td>0.182</td>
</tr>
<tr>
<td>B. Polymegatism (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>30.09</td>
<td>34.64</td>
<td>0.086</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>34.11</td>
<td>36.10</td>
<td>0.399</td>
</tr>
<tr>
<td>C. Hexagonality (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>49.32</td>
<td>57.20</td>
<td>0.574</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>43.32</td>
<td>47.59</td>
<td>0.148</td>
</tr>
<tr>
<td>D. Mean cell area mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>475 (118)</td>
<td>505 (76)</td>
<td>0.100</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>593 (209)</td>
<td>622 (95)</td>
<td>0.051</td>
</tr>
</tbody>
</table>

DSEK: Descemet’s stripping with endothelial keratoplasty
DSAEK: Descemet’s stripping with automated endothelial keratoplasty
SD: Standard deviation

Table 6. Endothelial cell loss one and three months postoperation

<table>
<thead>
<tr>
<th>Cell loss</th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month postoperation</td>
<td>30.74%</td>
<td>34.36%</td>
<td>0.164</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>51.59%</td>
<td>50.70%</td>
<td>0.947</td>
</tr>
</tbody>
</table>

DSEK: Descemet’s stripping with endothelial keratoplasty
DSAEK: Descemet’s stripping with automated endothelial keratoplasty

Table 7. Central corneal thickness and lenticule thickness in Descemet’s stripping with endothelial keratoplasty and Descemet’s stripping with automated endothelial keratoplasty patients

<table>
<thead>
<tr>
<th></th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal thickness Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>738.85 (46.61)</td>
<td>685.26 (61.06)</td>
<td>0.005</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>727.85 (48.93)</td>
<td>673.95 (56.79)</td>
<td>0.002</td>
</tr>
<tr>
<td>Lenticule thickness Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month postoperation</td>
<td>134.70 (13.53)</td>
<td>123.47 (13.40)</td>
<td>0.009</td>
</tr>
<tr>
<td>3 months postoperation</td>
<td>130.75 (12.30)</td>
<td>19.42 (12.33)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

DSEK: Descemet’s stripping with endothelial keratoplasty
DSAEK: Descemet’s stripping with automated endothelial keratoplasty
SD: Standard deviation
Table 8. Interface opacity grading number (%) in Descemet’s stripping with endothelial keratoplasty and Descemet’s stripping with automated endothelial keratoplasty patients one and three months postoperation

<table>
<thead>
<tr>
<th>Complications</th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month postoperation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>2 (10%)</td>
<td>9 (47.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Grade 1</td>
<td>9 (45%)</td>
<td>10 (52.6%)</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>9 (54%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>3 months postoperation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>6 (30%)</td>
<td>12 (63.2%)</td>
<td>0.038</td>
</tr>
<tr>
<td>Grade 1</td>
<td>14 (70%)</td>
<td>7 (36.8%)</td>
<td></td>
</tr>
</tbody>
</table>

DSEK: Descemet’s stripping with endothelial keratoplasty
DSAEK: Descemet’s stripping with automated endothelial keratoplasty

Table 9. Surgery complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>DSEK</th>
<th>DSAEK</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early donor detachment (Re bubbling)</td>
<td>2</td>
<td>3</td>
<td>0.633</td>
</tr>
<tr>
<td>Endothelial rejection</td>
<td>1</td>
<td>0</td>
<td>0.311</td>
</tr>
<tr>
<td>Primary graft failure (PGF)</td>
<td>0</td>
<td>1</td>
<td>0.311</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

DSEK: Descemet’s stripping with endothelial keratoplasty
DSAEK: Descemet’s stripping with automated endothelial keratoplasty

Figure 1. Grade 0 interface opacity (Confocal scan)
Discussion

EK is the method of choice for patients with endothelial dysfunction mostly evolved and widely used within the past decade. More rapid visual recovery, refractive outcomes, less postoperative complications, minimized induced astigmatism and better maintenance of globe integrity makes this method more preferred than standard PK.\textsuperscript{15-19}

The EK technique requires lamellar dissection of the donor graft performed either manually or automated. The automated lamellar dissection is usually performed using a microkeratome in eye banks to produce the precut tissue or in the operation room by the surgeon.

This prospective randomized trial suggests that using either eye bank precut cornea in DSAEK or manually dissected (DSEK) ones in the operation room are comparable regarding visual outcome, endothelial cell loss and postoperative complications.

We studied the endothelial characteristics one and three months postoperatively. Endothelial cell loss, refractive and visual outcomes were similar to Price et al\textsuperscript{10} results of 20 patients who were followed for 6 months. Terry et al and Koenig et al studies reported similar results as well.\textsuperscript{20,21}

BSCVA progressed one and three months after surgery both groups without significant difference. Seventy-five percent and 85%
patients in DSEK and precut DSAEK groups respectively, achieved VA$^2_{20}/100$ after three months while the mean visual acuity (VA) before operation was $20/800$ in both groups. In Price et al study$^{10}$ BSCVA $^{20}_{40}$ was achieved in 84% of precut DSEK and 75% of surgeon dissected grafts by microkeratome, and after omitting the patients with retinal and macular disorders. This result was obtained in 15% of our cases which was much lower than their results. In their study 90% of the patients were affected by Fuchs dystrophy and only 10% had PBK, while in our series 60% of the patients were affected with PBK. Sixty percent of them had a positive history of complicated cataract surgery, and Fuchs patients composed only 22.5% of our cases. In addition we did not exclude patients with retinal and macular disorders. In other investigations$^{22}$ endothelial cell loss is reported to be 25-54% of the eyes after 6 months and 24-61% of eyes one year after surgery. In our investigation postoperative endothelial cell lost was calculated to be 30.74% and 34.36% in DSEK and DSAEK after one month and 51.59% and 50.70% after 3 months, respectively. It seems that higher rate of cell loss in our study is related to our surgeons’ learning curve. Moreover, using Kelman-McPherson forceps that makes pressure on a larger area in donor taco compared to Goosey or Charlie forceps that make pressure on a smaller leading edge could be a cause of increase in cell loss in our cases.$^{23,24}$

Corneal and lenticule thickness, intensity and prevalence of interface opacity were significantly less in DSAEK group compared to DSEK group. Interface opacity was compared between the two groups, grade 2 opacity was significantly lower in DSAEK group, one month postoperatively (P=0.001). Significant lower grade 1 opacity was observed in DSAEK group 3 months after surgery (P=0.038). Grade 2 opacity was not observed in any of the patients after three months postoperatively. Price et al compared results of EK between two groups of manual dissected donor tissue and microkeratome dissected donor tissue. They suggested that visual recovery might be accelerated applying microkeratome which produces smoother layer and reduces interface irregularity.$^{23}$ Mean SE was 0.08±1.57 and 0.42±1.36 in DSEK and DSAEK groups and both groups had mild hyperopia after 3 months of surgery (P=0.482). Similarly, in Price et al study 0.66 Diopter (D) hyperopic shift is reported which is related to thinner dissection in center of lenticule than the periphery causing meniscus lenticules. Refractive shift determination in our study was not possible as patients’ refraction data prior to operation was not available.

Lenticule thickness and CCT in first and third month postoperatively was significantly different between the two groups. Thinner CCT in precut DSAEK group might be due to thinner lenticules in this group. Dissection in both groups was performed without pachymetry in 350 µm depth. In precut group dissection in 350 µm depth was done after epithelial removal while in manually dissected group, epithelial layer was intact. This can be a possible reason for thinner lenticule in precut DSAEK than DSEK group. In Price et al study, corneal epithelium was removed in all patient who underwent DSAEK using precut and surgeon dissected tissue by microkeratome in operation room. Consequently, CCT in two groups was not significantly different, 6 month and one year postoperatively.$^{10}$

Early postoperative donor dislocation happened in 2 patients of DSEK group and 3 patients in precut DSAEK group. Rebubbling in operation room was inevitable (P=0.633). In contrast, the donor dislocation rate was lower in Price et al$^{23}$ in microkeratome group compared with hand dissected ones. Lenticule was attached in all of our five patients but cornea was cleared in only 4 of them. Previous studies reported the rate of 4-50% for early donor dislocation. In our study dislocation rate was not significantly higher in manually dissected groups. However, smooth dissection layer in precut group might be the reason for higher rate of dislocation in this group (Physical mechanism). Another reason might be the more reduction in endothelial cell count in precut group and consequently reduction in endothelial pump function (Physiological mechanism). In addition, thinner lenticule in precut group may require more manipulations in insertion process and causes more detachment. However, two previous studies suggested that graft
dislocation subsequent to precut tissue transplantation is not a gratuitous concern.25,26

In one of precut DSAEK patients lenticule was inverted and due to major manipulations to flip and attach the lenticule,27 patient presented graft dislocation and severe corneal edema, the day after operation. After rebubbling and venting, lenticule was attached. However, corneal edema was not recovered subsequently and cell density determination and evaluation of postoperation endothelial characteristics was not possible in this case. The patient was suggested to have a second DSEK due to primary graft failure (PGF) but he did not accept to be reoperated. PGF rate in our study was 5% which is comparable to 5-18% in other studies.3,9,20,21,28,29 PGF rate in first 114 patients in Price et al3,9,20,21,28 study was 6% that was reduced to 0.5% in their next studies.24 Terry et al11 suggested skill and experience of the surgeon is correlated with reduction in the PGF rate in patients undergoing DSEK. Therefore, PGF occurrence after DSEK is mostly iatrogenic and is rarely due to eye bank processing. This is exactly in contrast with PGF after PK.11

In our case the mean IOP before and after surgery did not significantly changed in both groups. Only in one patient in DSEK group presented augmented IOP after two months that was controlled using timolol eye drop twice daily. Another patient in precut DSAEK group presented increased IOP, which was not responsive to medical therapy using timolol twice daily, dorzolamide three times a day, and brimonidine twice daily. Trabeculectomy was performed for the patient to control the ocular hypertension and glaucoma.

In month three after surgery, one of the DSEK patients presented signs of endothelial graft rejection following the discontinuation of topical steroid. Intensive topical steroid therapy was started immediately and inflammation symptoms were resolved and cornea becomes clear. In a multicenter retrospective study, graft rejection and epit’s incidence in deep lamellar endothelial keratoplasty (DLEK) and DSEK patients is reported to be 7.5% two years postoperatively. Topical high dosage of steroids might be the most important factors in preventing the graft rejection incidence.25-31 Price believes that standard regimen of prednisoln acetate 1% four times a day for four months and then tapering through 3 months to one drop daily and then continue indefinitely (Except in phakic patients or patients with increased IOP) would reduce the rejection rate to 3.6% up to six months after surgery. Moreover, graft rejection in a cohort study that discontinued topical steroid four months postoperatively is reported in 12% of cases.32

The limitation of our study was the short time follow-up (Three months). Longer follow-up periods with larger sample sizes are strongly suggested to determine the comparable outcomes between manually or precut automated EK. Another main limitation was the period between preparation and dissection of precut tissue in the eye bank and its use in the operation room which was 48 hours maximum. Longer periods should be considered in other studies.

Conclusion
In conclusion, the EK outcomes three months postoperatively were similar in two groups of precut DSAEK and manually dissected DSEK by the surgeon at the time of surgery. Surgery expenses for both operations considering artificial AC preparation process is equal. Moreover, smooth and uniform layer leading to lower interface opacity in precut DSAEK might cause more satisfaction in patient’s daily life.

It should be reminded that in centers and countries that eye bank or microkeratome instrumentation is not available an expert surgeon can gain excellent results performing DSEK manually.

References