

Effects of Cataract Surgery on Endothelium in Transplanted Corneal Grafts: Comparison of Extracapsular Cataract Extraction and Phacoemulsification for Complicated Cataract after Penetrating Keratoplasty

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Abstract

Background: The endothelium should be carefully evaluated when choosing a surgical technique for cataract removal. Therefore, we aimed to study the effects of different cataract surgery techniques on endothelial cell loss in transplanted corneal grafts.

Methods: A total of 54 patients who received complicated cataract surgery in post-penetrating keratoplasty (PKP) eyes at the Shandong Eye Institute between February 2001 and June 2014 were included, and clinical records were reviewed. Baseline demographic details, clinical characteristics, endothelial cell density (ECD), and best-corrected visual acuity (BCVA) were recorded. Wilcoxon rank-sum test and Wilcoxon signed-rank test were used to test the equality of medians. A regression model was constructed to compare the reduced rate of ECD.

Results: Of the 54 eyes included in this study, extracapsular cataract extraction (ECCE) was performed in 34 eyes of 33 patients (ECCE group) whereas phacoemulsification was performed in 20 eyes of 20 patients (phacoemulsification group). There was no significant difference in the median age ($P = 0.081$) or preoperative ECD ($P = 0.585$) between the two groups. At 6 months after cataract surgery, ECD in ECCE group was significantly higher than that in phacoemulsification group ($P = 0.043$). In addition, the endothelial cell loss rate in ECCE group was significantly lower than that in phacoemulsification group at 2 months ($P = 0.018$), 4 months ($P < 0.001$), and 6 months ($P < 0.001$) after cataract surgery. Endothelial cell loss rate after cataract surgery increased over the 6-month study duration in both ECCE group ($P < 0.001$) and phacoemulsification group ($P < 0.001$), but phacoemulsification resulted in a greater reduction in ECD than that of ECCE in transplanted corneal grafts ($P < 0.001$). There was no significant difference in postoperative BCVA between the two groups ($P = 0.065$).

Conclusion: ECCE is more suitable than phacoemulsification in cataract surgery in complicated cataract after PKP.

Key words: Complicated Cataract; Corneal Endothelial Cell; Extracapsular Cataract Extraction; Penetrating Keratoplasty; Phacoemulsification

INTRODUCTION

Cataracts, a leading cause of blindness worldwide, are not only largely senile or age-related in origin but also a well-recognized complication of corneal transplantation. Underlying corneal disease pathology, inadvertent injury to the lens during corneal transplantation, and the use of therapeutic procedures such as corticosteroidal agents after keratoplasty can induce cataracts.

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In normal corneal physiology, loss of endothelial cells occurs gradually during the aging process. However, with a corneal transplant, the rate of endothelial cell loss accelerates significantly. After penetrating keratoplasty (PKP), the annual rate of endothelial cell loss averages 7.8% between the 3rd and 4th postoperative years and 4.2% between the 6th and 10th postoperative years.^[1,2] The reason underlying this phenomenon remains unclear. So far, this effect may be explained, in part, by immunological mechanisms.

The degree of endothelial cell loss is unchanged between patients after combined keratoplasty and cataract surgery versus staged surgery.^[3] Ohguro *et al.*^[4] reported a similar rate of endothelial cell loss in transplanted corneal grafts versus normal corneas after extracapsular cataract extraction (ECCE) and posterior chamber intraocular lens (PC-IOL) implantation. However, Kim *et al.*^[5] found a higher rate of endothelial cell loss after cataract extraction in transplanted corneal grafts than in normal corneas. In a prospective randomized study, Acar *et al.*^[6] revealed that transplanted corneal grafts after ECCE had a lower endothelial cell loss rate than that of transplanted corneal grafts after phacoemulsification. The endothelium should be carefully evaluated when choosing a surgical technique for cataract removal in both normal and transplanted corneal grafts. Therefore, it is necessary to study the effects of different cataract surgery techniques on endothelial cell loss in transplanted corneal grafts. This retrospective study compared the endothelial cell density (ECD) and cell loss rate after ECCE versus phacoemulsification in treating complicated cataract in post-PKP eyes.

METHODS

Patients

This study was approved by the Institutional Review Board of the Shandong Eye Institute. We retrospectively reviewed medical records. Patients who received phacoemulsification or ECCE in eyes with complicated cataract and previous PKP were included. Cases with the following conditions were excluded: Uveitis, proliferative diabetic retinopathy, preoperative ocular hypertension or newly detected glaucoma, low baseline endothelial cell count (<1000 cells/mm²), prior intraocular surgery except PKP, preoperative factors known to prolong surgical time (i.e., peripheral anterior synechiae, shallow anterior chamber, and pseudoexfoliation), combined cases of cataract extraction and other ocular surgery, episodes of immunologic graft reaction after PKP, or complications up to 6 months after cataract surgery. A total of 54 cases were included in this study. These cases of cataract surgeries were carried out between February 2001 and June 2014 at Shandong Eye Institute, China.

Surgical procedure

This retrospective study compared eyes that received ECCE (ECCE group) and phacoemulsification (phacoemulsification group) after PKP. Assessment before cataract surgery included medical history, visual acuity, slit lamp biomicroscopy,

dilated fundus evaluation, and applanation tonometry. Nuclear hardness was classified using the Emery-Little lens opacities classification system.^[7] Postoperatively, topical corticosteroids were administered in low doses for 3–6 weeks in most patients. Central corneal ECD together with percentage of hexagonal endothelium measured by specular microscope and best-corrected visual acuity (BCVA) was collected at 2, 4, and 6 months after cataract surgery.

The surgical techniques are described here in brief. Periocular anesthesia and preoperative digital ocular massage were administered to most eyes. In most eyes, ECCE was performed using the W-shaped incision [Figure 1],^[8] followed by a continuous curvilinear capsulorhexis (CCC). A PC-IOL was placed. The wound was sutured using a 10-0 nylon suture. In most eyes, phacoemulsification was performed via a 3.0 mm clear corneal incision and a CCC whose diameter is approximately 5.5 mm. A PC-IOL was placed. No sutures were used for closure. All the surgeries were performed by two very sophisticated surgeons. Central corneal ECD, percentage of hexagonal endothelium, and BCVA at 2, 4, and 6 months after cataract surgery were recorded.

Statistical analysis

Measurement data were processed using SAS 6.12 (SAS Institute Inc., Cary, NC, USA). Nonparameter statistical methods such as Wilcoxon rank-sum test and Wilcoxon signed-rank test were used to test the equality of medians. Endothelial cell loss rate was expressed as a percentage of the preoperative cell density. A regression model was constructed to compare the cell loss rate of ECD with time between the two groups. A $P < 0.05$ was considered significantly different.

RESULTS

A total of 54 eyes (53 patients) were included in this study, including 34 eyes of 33 patients (19 males and 14 females) receiving ECCE and 20 eyes of 20 patients (10 males and 10 females) receiving phacoemulsification. In ECCE

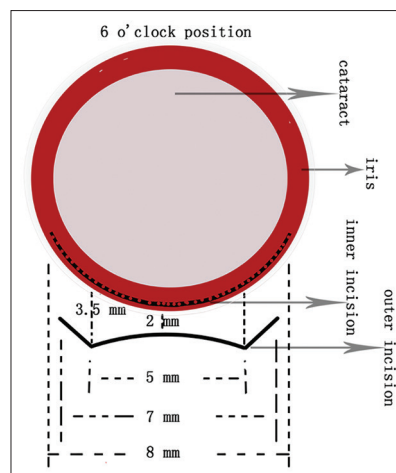


Figure 1: Improved frown incision in extracapsular cataract extraction.

group ($n = 34$), the mean postoperative examination time at 2, 4, and 6 months was 60.8 (range 51.0–74.0), 118.3 (range 105.0–133.0), and 188.9 (range 167.0–208.0) days, respectively. In phacoemulsification group ($n = 20$), the mean postoperative examination time at 2, 4, and 6 months was 60.6 (range 53.0–70.0), 118.8 (range 106.0–131.0), and 180.9 (range 167.0–197.0) days, respectively.

Preoperative data for the cases are shown in Tables 1 and 2. Figure 2 presents preoperative BCVA in the treatment groups. Postoperative ECD and cell loss rate are shown in Table 3. Figure 3 presents all the endothelial density versus examination time in both groups.

Since the age in ECCE group was not normally distributed (Shapiro-Wilk test, $P = 0.008$), Wilcoxon rank-sum test was used to test the equality of the median age between the two groups. The median age of ECCE and phacoemulsification groups was 60.0 years and 51.5 years, respectively, and there was no statistically significant difference ($W = 452.5$, $P = 0.081$, two-tailed). Since the preoperative ECD in phacoemulsification group was not normally distributed (Shapiro-Wilk test, $P = 0.004$), Wilcoxon rank-sum test was used to test the equality of the median ECD between the two groups. The median ECD of ECCE and phacoemulsification groups was 1968 cells/mm² and 1882 cells/mm², respectively, and there was no statistically significant difference ($W = 519$, $P = 0.585$, two-tailed) [Table 1].

Since the ECD in phacoemulsification group at 2, 4, and 6 months after cataract surgery was not normally distributed (Shapiro-Wilk test, $P = 0.004$, 0.003, and 0.003,

respectively), Wilcoxon rank-sum test was used to test the equality of median between the two groups. The median ECD had no statistically significant difference between the two groups at 2 ($W = 514$, $P = 0.525$) and 4 months postoperatively ($W = 466$, $P = 0.136$); however, at 6 months after cataract surgery, ECCE group had a significantly higher median ECD than phacoemulsification group ($W = 437$, $P = 0.043$, two-tailed) [Table 3]. Wilcoxon rank-sum test was also used to compare the median cell loss rate between the two groups. Statistically significant difference in the median cell loss rate was noted at 2 ($W = 418$, $P = 0.018$), 4 ($W = 251$, $P < 0.001$), and 6 months ($W = 211$, $P < 0.001$) between the two groups after PKP [Table 3].

Wilcoxon signed-rank test indicated that endothelial cell loss rate displayed a gradually rising tendency in ECCE ($Z = -3.92$, $P < 0.001$) and phacoemulsification groups ($Z = -5.069$, $P < 0.001$) during the 6-month follow-up after cataract surgery [Figure 4]. The regression line slope of phacoemulsification group is steeper than that of ECCE group. To test whether this phenomenon was statistically significant, the following regression model was introduced:

$$\text{Cell loss rate} = \mu + (\beta + \beta_i) \times \text{day} + \alpha_i + \epsilon \quad (i = 1, 2)$$

where μ and β denote the common intercept and slope, α_i and β_i denote the intercept and slope corresponds to ECCE group when $i = 1$ and phacoemulsification group when $i = 2$, respectively, ϵ denotes the error term. The estimated result is $\hat{\beta}_1 - \hat{\beta}_2 = -0.001$ ($P < 0.001$), meaning that slope of phacoemulsification group was significantly steeper than that of ECCE group. In other words, ECD reduced faster when phacoemulsification was used rather than ECCE in transplanted corneal grafts.

Since BCVA after cataract surgery in both groups was not normally distributed (Shapiro-Wilk test, $P < 0.001$ in ECCE group and $P = 0.016$ in phacoemulsification group), Wilcoxon rank-sum test was used to test the equality of the median BCVA between the two groups. The median BCVA

Table 1: Precataract surgery clinical characteristics of patients with complicated cataract in postpenetrating keratoplasty eyes

Characteristics	ECCE ($n = 34$)	Phacoemulsification ($n = 20$)
Age (years)	60.0 (14.0–75.0)	51.5 (11.0–72.0)
Endothelial cell density (cells/mm ²)	1968 (1072–3287)	1882 (1021–4039)
Percentage of hexagonal endothelium (%)	54 (31–75)	58 (25–78)

Data are shown as median (range). ECCE: Extracapsular cataract extraction.

Table 2: Original cornea diseases of patients who received complicated cataract surgery in postpenetrating keratoplasty eyes, n

Diseases	ECCE ($n = 34$)	Phacoemulsification ($n = 20$)
Keratoconus	1	0
Keratitis	27	14
Dystrophy	3	1
Corneal scar	1	0
Trauma and burn	2	4
Unknown etiology	0	1

ECCE: Extracapsular cataract extraction.

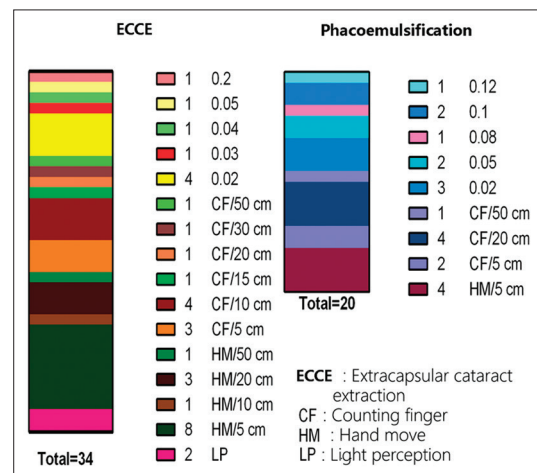


Figure 2: Preoperative best-corrected visual acuity in ECCE and phacoemulsification groups. ECCE: Extracapsular cataract extraction.

Table 3: Postcataract surgery clinical characteristics of patients who received complicated cataract surgery in postpenetrating keratoplasty eyes

Postoperative time (months)	ECCE (<i>n</i> = 34)			Phacoemulsification (<i>n</i> = 20)		
	Cell density (cells/mm ²)	Cell loss rate (%)	Percentage of hexagonal endothelium (%)	Cell density (cells/mm ²)	Cell loss rate (%)	Percentage of hexagonal endothelium (%)
2	1816 (957–3012)	6.6 (1.5–12.9)*	54 (41–68)	1712 (961–3631)	10.1 (1.9–16.5)	54 (35–68)
4	1770 (949–2944)	9.8 (5.3–17.1)*	50 (41–58)	1538 (842–3421)	17.6 (6.4–22.9)	51 (41–63)
6	1740 (940–2896)*	11.9 (7.8–19.3)*	51 (42–59)	1448 (746–3242)	22.9 (19.0–26.9)	52 (40–62)

Data are shown as median (range). **P*<0.05 compared with the phacoemulsification group. ECCE: Extracapsular cataract extraction.

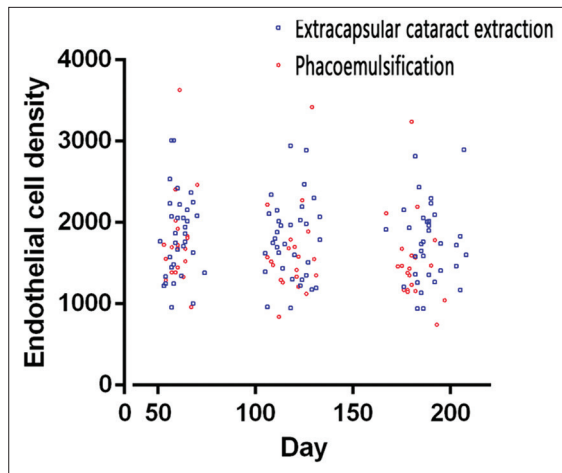


Figure 3: Scatter plot of endothelial density versus examination time.

in ECCE and Phacoemulsification groups was 0.200 and 0.300, respectively, and Wilcoxon rank-sum test indicated no statistically significant difference ($W = 832.5$, $P = 0.065$, two-tailed).

DISCUSSION

In transplanted corneal grafts, endothelial cell loss after cataract surgery can result from multiple factors: Mechanical damage to the grafted endothelium during cataract surgery or IOL implantation, ocular hypertension, and postoperative immunological reactions. We retrospectively reviewed 54 cases of patients who received complicated cataract surgery after PKP and added new discoveries to complicated cataract surgery in post-PKP eyes. Based on our study, phacoemulsification damaged more endothelial cells than ECCE at 6 months after cataract surgery in transplanted corneal grafts, and phacoemulsification resulted in a significantly higher endothelial cell loss rate than ECCE in transplanted corneal grafts at 2, 4, and 6 months after surgery.

In normal corneas, there is no significant difference between the effects of ECCE and phacoemulsification on the endothelial cell loss rate.^[9] Bourne *et al.*^[10] found a similar 10% decrease in endothelial cell count after phacoemulsification and conventional ECCE; the authors suggested that ECCE was preferred over phacoemulsification for hard nuclear cataracts removal,

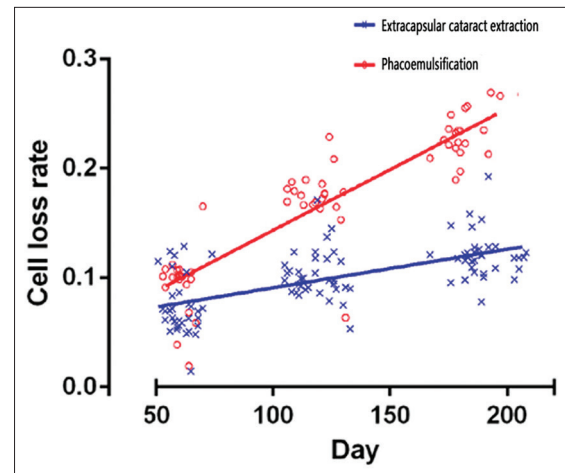


Figure 4: Endothelial cell loss rate changes with time in ECCE and phacoemulsification groups. ECCE: Extracapsular cataract extraction.

given that phacoemulsification caused greater endothelial cell loss rate than ECCE in such cases. Similarly, Acar *et al.*^[6] showed that ECCE caused less endothelial cell damage than phacoemulsification in post-PKP eyes with hard nuclear cataracts in a clinical trial of 26 patients during the 6-month follow-up, and they also observed that phacoemulsification resulted in a significantly greater endothelial cell loss rate in post-PKP eyes (16 eyes) than eyes with no previous surgery (20 eyes).^[11] We found that the ECD was significantly reduced in the phacoemulsification group versus the ECCE group at 6 months after cataract surgery in transplanted corneal grafts. In addition, phacoemulsification resulted in a significantly higher endothelial cell loss rate than ECCE in transplanted corneal grafts at 2, 4, and 6 months after surgery. Thus, our study provides a clear comparison of the effects of ECCE and phacoemulsification on the endothelial cell loss rate in post-PKP eyes with complicated cataract for the first time.

It was found that ECD was not significantly different before and after IOL implantation in transplanted corneal grafts during the 6-month follow-up in 26 eyes.^[12] Ohguro *et al.*^[4] reported no significant difference in the endothelial cell loss rate 3 months after ECCE with PC-IOL implantation in transplanted corneal grafts (6.2%, $n = 18$) and normal corneas (4.7%, $n = 18$) in a case series. The endothelial cell loss rate increased gradually over 6 months after cataract

surgery and IOL implantation in transplanted corneal grafts in our series ($n = 54$).

In cases of uneventful ECCE, the mean endothelial cell loss rate varies from 6% to 17% whereas the mean endothelial cell loss rate in complicated cases exceeds 40%.^[13] We found that the median endothelial cell loss rate was 7.3% at 2 months after ECCE and 7.3% at 2 months after phacoemulsification in post-PKP eyes; the median endothelial cell loss rate was 10.2% at 4 months after ECCE and 17.0% at 4 months after phacoemulsification in post-PKP eyes; finally, the median endothelial cell loss rate was 12.1% and 23.0% at 6 months after ECCE and phacoemulsification, respectively, in post-PKP eyes. Moreover, the median endothelial cell loss rate was significantly higher in the phacoemulsification group than in the ECCE group at 2, 4, and 6 months after cataract surgery in transplanted corneal grafts.

In our study, the ECD of transplanted corneal grafts in the phacoemulsification group was noticed to reduce faster than that in the ECCE group. The major reasons for this natural phenomenon are as follows. First, the maneuverability of ECCE is high, and thus in ECCE group, the incision can be created in a large size (W-shape) and the nucleus can be removed conveniently. It was reported that W-shaped incision benefited the extraction of hard nucleus, the implantation of IOL with large optic zone, and reduced the time to reach refractive stability.^[8] Second, the nucleus of complicated cataract after PKP is usually hard (the percentage of nuclear hardness \geq IV was 83% in our cases), and thus in these cases, more energy is required in phacoemulsification, which deteriorates the endothelial cells. Concerning ECCE, ample training, and a large size incision can make the extraction of hard nucleus be more convenient, and meanwhile, the number and quality of corneal endothelial cells can be maintained well. In contrast, the stability of anterior chamber is hard to be maintained in phacoemulsification surgery. Despite the premise of ample training, it is seldom accomplished to decrease the energy used in phacoemulsification when dealing with hard nucleus. Therefore, corneal endothelial cells may be damaged more severely in phacoemulsification than ECCE.

Accumulating evidence supports that some putative progenitors for the corneal endothelium reside in the transition area between the peripheral corneal endothelium and the anterior nonfiltering portion of the trabecular meshwork,^[14] and microenvironment plays an important role in determining the proliferative capacity of human corneal endothelial cells.^[15] The discovery that phacoemulsification resulted in a significantly higher postoperative endothelial cell loss rate than ECCE in transplanted corneal grafts may be partly explained by a conjecture that phacoemulsification damages more putative progenitors for corneal endothelium and affects microenvironment of human corneal endothelial cells more than ECCE does; however, the lack of evidence does not permit anyone to unravel it at present. The possible discrepancy of postoperative viscoelastics residue levels

between the two groups may be another factor responsible for the discovery.

There was significant progress in phacoemulsification in the past years, and corneal endothelial cells can be effectively preserved. Microincision cataract surgery technique effectively preserves corneal endothelial cells and reduces risk of corneal edema.^[16] Micropulse technique increases anterior chamber stability^[17] and decreases thermal effect.^[18] Torsional ultrasound mode reduces phacoemulsification time and energy.^[19] New ophthalmic viscosurgical devices, such as Viscoat, Provisc, and soft-shell technique, decrease thermal effect.^[20] Thus, in certain cases of complicated cataract after PKP such as cases in which nuclear hardness is \leq III, better postoperative visual acuity is demanded, and an advanced technology IOL is preferred, phacoemulsification should be suggested. Our study has potential limitations as a retrospective cohort study which spanned 13 years. The 6-month study duration was relatively short. Further randomized controlled trials are needed with a larger sample size and longer study duration to further elucidate this topic.

In conclusion, ECCE causes less damage than phacoemulsification on the vulnerable endothelium in transplanted corneal grafts up to 6 months after cataract surgery. Based on our results, ECCE causes less damage than phacoemulsification on the vulnerable endothelium.

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Conflicts of interest

There are no conflicts of interest.

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