A surgical alternative of fusiform penetrating keratoplasty for the management of severe infectious keratitis

Xiao–Lin Qi, Li–Chao Wang, Miao–Lin Wang, Hua Gao

Eye Hospital of Shandong First Medical University, State Key Laboratory Cultivation Base, Shandong Provincial Key Laboratory of Ophthalmology, Shandong Eye Institute, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan 250021, Shandong Province, China

Correspondence to: Hua Gao. Eye Hospital of Shandong First Medical University, 372 Jingsi Road, Jinan 250021, Shandong Province, China. hgao@sdfmu.edu.cn

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Abstract

● AIM: To describe the surgical procedure of fusiform penetrating keratoplasty (FPK) using multiple trephines of different sizes for treating patients with severe infectious keratitis.

● METHODS: Fourteen eyes underwent FPK, and 15 eyes received conventional penetrating keratoplasty (PK) were included in the study. The best-corrected visual acuity (BCVA), refractive outcomes, endothelial cell density, and postoperative complications were recorded.

● RESULTS: The FPK group was followed for an average of 15.3±2.1mo, whereas the PK group was followed for 16.1±1.9mo. The corneal ulcers were elliptical-shaped in all 14 eyes in the FPK group. The mean BCVA (logMAR, 0.26±0.13) showed no statistically significant differences from that in the PK group (logMAR, 0.21±0.12, P>0.05) at 1y after surgery. But the mean curvature, mean astigmatism, and mean spherical equivalent in the FPK group were lower than those in the PK group (P<0.05). Peripheral anterior synchia was observed in one patient in the FPK group, whereas 6 patients in the PK group. Suture loosening and neovascularization were observed in 4 and 5 eyes in the PK group, respectively. No graft immune rejection or elevation of intraocular pressure was observed in the two groups.

● CONCLUSION: For patients with elliptical-shaped corneas or corneal ulcers, FPK can avoid disrupting of corneal limbus, reduce the risk of postoperative complications, and can result in satisfactory visual quality.

● KEYWORDS: fusiform penetrating keratoplasty; multiple trephines; infectious keratitis; cornea

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INTRODUCTION

In current standard penetrating keratoplasty (PK), the graft is circular and is generally located centrally in the cornea, away from the vascular-rich corneal limbus[1-3]. In practice, however, the human cornea has a horizontally elliptical shape with a decreased vertical width of the clear area by a vascularized pannus. Given this configuration, conventional round corneal transplantation may inevitably disrupt the corneal limbus, and consequently, the corneal graft which is sutured to the corneal limbus may be at an increased risk of immune rejection. In the case where the corneal lesion is oval in shape, for example, the long diameter of the lesion is 9 mm and the short diameter is only 7 mm, in order to completely remove the diseased tissue, a circular trephine with a diameter of about 10 mm is usually used. However, this will result in a large area of corneal tissue being cut, which may involve or even destroy the limbus. Therefore, researchers have attempted to perform fusiform corneal transplantation that conforms to the morphology of corneal lesions. Initially, researchers used excimer laser to perform the surgery while avoiding the corneal limbus site[4-7]. However, the excimer laser cannot be applied to patients with infectious keratitis. In order to address this, we innovatively used multiple trephines of different sizes to create fusiform corneal grafts, and then created matching recipient beds with the assistance of an artificial anterior chamber for the treatment of patients with severe infectious keratitis, achieving good surgical results.

SUBJECTS AND METHODS

Ethical Approval This retrospective study was approved by the Ethics Committee of Eye Hospital of Shandong First Medical University (No.SDSYKYY201805-1). This study was conducted in compliance with the tenets of the Declaration of Helsinki. Each patient gave written informed consent to participate in this research after the risks and possible adverse consequences had been explained.
Subjects A consecutive series of 14 eyes (14 patients) underwent fusiform penetrating keratoplasty (FPK) for infectious keratitis at the Eye Hospital of Shandong First Medical University from June 2018 to June 2019. The inclusion criteria were as follows: 1) patients were suggested to undergo penetrating keratoplasty (PK), with over 4/5 of the corneal thickness infected or infiltrated as observed by slit-lamp microscopy and anterior segment optical coherence tomography (AS-OCT), and anti-infectious medication as reported in our previous studies was given for at least 2wk but was ineffective; 2) the long diameter of the corneal ulcers is 1 mm larger than the short one; 3) completing a follow-up of at least 12mo. To compare the postoperative outcomes, 15 patients (15 eyes) who received conventional PK for infectious keratitis by the same surgeon (Gao H) were included in the PK group. In the meanwhile, the age, sex, diagnosis, and preoperative best-corrected visual acuity (BCVA, logMAR) of the 15 patients were comparable with those who underwent FPK.

Surgical Procedure

Preparation of recipient eye All surgeries were performed under peribulbar anesthesia. First, a suitable trephine (Storz) was selected according to the size of the corneal ulcer, with the diameter of the trephine being 0.5–1 mm larger than the longest diameter of the ulcer. Then, two methylene blue marks were made with the ulcer included inside using the trephine, and the intersection of the two arcs was shown in a fusiform shape. Finally, remove the diseased cornea manually along the marks with a corneal scissor. The Castroviejo circle gauge was used to measure the longest and the shortest diameters of the fusiform recipient bed.

Preparation of donor tissue The donor tissue was mounted onto an artificial anterior chamber, and Optisol corneal storage medium was injected to stabilize the pressure in the artificial anterior chamber. The longest and the shortest diameter of the graft were set to be 0.5 mm larger than those of the recipient bed. First, a Castroviejo circle gauge was used to mark the longest and the shortest diameter on the graft. Then, the trephine was used to make indentations according to the marked longest and shortest diameter. The intersection of the two indentations was also fusiform. The puncture knife was then used perpendicularly-oriented to the anterior chamber with the viscoelastic agent being injected to support the anterior chamber, and the fusiform graft being cut along the indentation using corneal scissors.

Having prepared the recipient bed and the graft, the surgeon performed conventional PK, and the detailed surgical procedure was introduced in our previous report\cite{1,8}. The donor cornea was sutured to the recipient bed with 16–24 interrupted 10/0 nylon sutures. FPK: Fusiform penetrating keratoplasty.

Postoperative Treatment Anti-infective treatment was administered based on the preoperative or intraoperative pathology results according to our previous report\cite{8-13}. In patients with fungal and Acanthamoeba corneal ulcers, glucocorticoids were not used for 3wk after surgery\cite{14-15}. Afterwards, 0.1% fluorometholone was used 4 times daily for 6mo and tapered to 0.02% fluorometholone three times daily for at least 1y, tobramycin and dexamethasone ophthalmic
ointment was administered every night for 6mo and tapered to twice weekly. The 0.1% tacrolimus eye drops were given four times a day after surgery for 1mo and tapered to three times for 6mo and twice for at least 1y.

**Main Outcome Measures** All patients were observed daily during the first week after surgery, weekly during the next 2mo, and monthly thereafter. All sutures were removed at 1y after surgery. BCVA, intraocular pressure, healing time of the epithelium, corneal astigmatism, spherical equivalent, mean corneal curvature, endothelial cell density, and perioperative complications were evaluated 1y after surgery and 3mo after suture removal.

**Statistical Analysis** Statistical analysis was performed using SPSS 24.0, with the significance level set at $P<0.05$. The Kolmogorov-Smirnov test was used to check the normal distribution of data. The two-sample $t$ test was used to analyze independent continuous variables, and the Mann-Whitney $U$ test was instead for non-normally distributed continuous variables. Visual acuity was recorded in international standard eye chart and converted to logMAR for statistical analysis. The related-samples Wilcoxon signed-rank test was used to evaluate the postoperative improvement in BCVA. The Chi-square test and Fisher exact test were used to analyze categorical variables. The graft survival rates were analysed with the Kaplan-Meier survival curves, and the differences between groups were compared using the log-rank test.

**RESULTS**

**Patient Information** The FPK group was followed for an average of 15.3±2.1mo, whereas the PK group was followed for an average of 16.1±1.9mo. The intergroup comparisons of age, sex, diagnosis, and preoperative BCVA showed no significant differences (Table 1).

In the FPK group, the primary diagnoses included bacterial corneal ulcers in 6 eyes, fungal corneal ulcers in 5 eyes, herpes simplex keratitis in 2 eyes, and *Acanthamoeba* keratitis in 1 eye. The corneal ulcers were elliptical-shaped in all 14 eyes, the long and short diameters measured by Castroviejo circle gauge were 7 mm×5 mm in 5 eyes, and 9 mm×7 mm in 9 eyes. Hypopyon was present in 7 eyes. The diameter of corneal recipient bed/graft included 7.5/8.0 mm in 5 eyes, and 10/10.5 mm in 9 eyes (Table 1).

The primary diagnoses included bacterial corneal ulcers in 5 eyes, fungal corneal ulcers in 6 eyes, and herpes simplex keratitis in 4 eyes in the PK groups. The size of corneal ulcers included 8 mm×8 mm in 7 eyes, and 10 mm×10 mm in 8 eyes. The diameter of corneal recipient bed/graft included 8.5/9.0 in 7 eyes, and 10.5/11.0 in 8 eyes (Table 1).

**Visual Acuity and Refractive Outcomes** The mean healing time of the epithelium was 4.3±3.4d and 4.5±2.1d in the FPK and PK groups, respectively ($P>0.05$).

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### Table 1 Preoperative basic information of patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FPK group (n=14)</th>
<th>PK group (n=15)</th>
<th>t/$t$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>54.9±13.7</td>
<td>56.3±10.9</td>
<td>0.292</td>
<td>0.77</td>
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<tr>
<td>Sex (male/female)</td>
<td>4/10</td>
<td>3/12</td>
<td>0.281</td>
<td>0.61</td>
</tr>
<tr>
<td>Diagnoses</td>
<td></td>
<td></td>
<td>0.492</td>
<td></td>
</tr>
<tr>
<td>Bacterial keratitis</td>
<td>6 (42.9)</td>
<td>5 (33.3)</td>
<td>-</td>
<td>0.611</td>
</tr>
<tr>
<td>Fungal keratitis</td>
<td>5 (35.7)</td>
<td>6 (40.0)</td>
<td>-</td>
<td>0.53</td>
</tr>
<tr>
<td>Herpes simplex keratitis</td>
<td>2 (14.3)</td>
<td>4 (26.7)</td>
<td>-</td>
<td>0.81</td>
</tr>
<tr>
<td><em>Acanthamoeba</em> keratitis</td>
<td>1 (7.14)</td>
<td>0</td>
<td>-</td>
<td>0.30</td>
</tr>
<tr>
<td>Preop. BCVA (logMAR)</td>
<td>2.23±0.40</td>
<td>2.36±0.20</td>
<td>0.592</td>
<td>0.29</td>
</tr>
<tr>
<td>Hypopyon</td>
<td>7 (50.0)</td>
<td>11 (73.3)</td>
<td>0.421</td>
<td>0.09</td>
</tr>
<tr>
<td>Depth of hypopyon (mm)</td>
<td>1.92±1.19</td>
<td>2.40±1.40</td>
<td>0.329</td>
<td>0.345</td>
</tr>
</tbody>
</table>

**PK:** Penetrating keratoplasty; **FPK:** Fussiform penetrating keratoplasty; **BCVA:** Best corrected visual acuity. *Fisher’s exact test; Others: t test.

At 1y after surgery, all eyes maintained a clear graft in the two groups (Figure 2). The mean BCVA (logMAR) was 0.26±0.13 in the FPK group, which showed no statistically significant differences from that in the PK group, which was 0.21±0.12 ($P=0.110$; Figure 3). The mean curvature was 43.3±3.4 and 40.6±5.7 D in the FPK and PK groups, respectively ($P=0.032$). The mean astigmatism and mean spherical equivalent in the FPK group were lower than those in the PK group ($P<0.05$; Table 2).

At 3mo after suture removal, the mean BCVA (logMAR) was 0.28±0.10 in the FPK group, which showed no statistically significant differences from that in the PK group, which was 0.23±0.12 ($P=0.145$; Figure 3). The mean curvature was 43.6±2.1 and 40.8±2.3 D in the FPK and PK groups, respectively ($P=0.028$). The mean astigmatism and mean spherical equivalent in the FPK group were lower than those in the PK group ($P<0.05$; Table 2).

**Loss of Corneal Endothelial Cells** The mean endothelial cell density was 1783±165 cells per square millimeter at 1y after surgery in the FPK group, with no statistically significant differences compared with the density in the PK group, which was 1801±197 cells per square millimeter ($P=0.05$; Figure 4).

**Ultrasonic Biomicroscopy** Ultrasonic biomicroscopy was used to examine the structures of the anterior chamber angle after keratoplasty. Peripheral anterior synchia was observed in one patient in the FPK group, whereas 6 patients in the PK group (Figure 2).

**Intraoperative Complications** No cases of hyphema, iris damage, and lens dislocation were observed during the surgery in the two groups.

**Postoperative Complications** No cases of disease recurrence, or graft immune rejection were observed during the follow-up period in the two groups. In the PK group, suture loosening and neovascularization were observed in 4 and 5 eyes, respectively (Figure 2), while no eyes in the FPK group.

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Elliptical penetrating keratoplasty

Figure 2 Slit-lamp and ultrasonic biomicroscopy examination of the FPK group and PK group  
A: Preoperative slit-lamp photograph showed a patient with *Acanthamoeba* keratitis; B: A clear graft was observed at 1y after FPK; C: Ultrasonic biomicroscopy showed peripheral anterior angle is open; D: Preoperative slit-lamp photograph showed a patient with bacterial keratitis; E: Corneal neovascularization was observed at 1y after PK; F: Extensive peripheral anterior synechia was observed by ultrasonic biomicroscopy. PK: Penetrating keratoplasty; FPK: Fusiform penetrating keratoplasty.

DISCUSSION

Under normal circumstances, the horizontal diameter of the cornea is 1 mm larger than the vertical diameter. For patients with total corneal infection or corneal ulcers with large diameters and elliptical shapes, the corneal limbus is bound to be involved if it is trephined with a conventional circular trephine. Due to the rich vascular and lymphatic network in the corneal limbus, the closer the corneal graft is to the corneal limbus, the higher the chance of postoperative immune rejection\textsuperscript{[16-19]}. In addition, cutting and suturing at the corneal limbus site not only easily causes intraoperative bleeding, affecting the surgical field and increasing the difficulty of surgery, but it also destroys the structure of anterior chamber angle, increasing the risk of postoperative anterior synechia and secondary glaucoma. In order to address these issues, we proposed the method of manual fusiform corneal transplantation using multiple trephines of different sizes, thus decreasing the risks for corneal limbus destruction secondary to surgery, postoperative secondary glaucoma, and immune rejection.

Figure 3 Cumulative BCVA (logMAR) of the FPK group and PK group  
A: Patients’ cumulative BCVA preoperative, 1y after surgery and 3mo after suture removal in the FPK group; B: Patients’ cumulative BCVA preoperative, 1y after surgery and 3mo after suture removal in the PK group. PK: Penetrating keratoplasty; FPK: Fusiform penetrating keratoplasty; BCVA: Best corrected visual acuity.

Table 2 Postoperative refractive status of the FPK and PK groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1y after surgery</th>
<th>3mo after suture removal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FPK group</td>
<td>PK group</td>
</tr>
<tr>
<td></td>
<td>1y after surgery</td>
<td>3mo after suture removal</td>
</tr>
<tr>
<td>BCVA (logMAR)</td>
<td>0.26±0.13</td>
<td>0.21±0.12</td>
</tr>
<tr>
<td>Curvature (D)</td>
<td>43.3±3.4</td>
<td>40.6±5.7</td>
</tr>
<tr>
<td>Astigmatism (D)</td>
<td>2.01±1.3</td>
<td>4.08±1.3</td>
</tr>
<tr>
<td>Equivalent spherical radius</td>
<td>2.20±1.1</td>
<td>4.15±0.8</td>
</tr>
</tbody>
</table>

*FPK: Fusiform penetrating keratoplasty; PK: Penetrating keratoplasty; BCVA: Best corrected visual acuity.*

Figure 4 Attenuation of ECD in the FPK and PK group  
ECD: Endothelial cell density; PK: Penetrating keratoplasty; FPK: Fusiform penetrating keratoplasty.
The core method of FPK is to use an appropriately sized circular trephine to indent each side of the long axis of the corneal ulcer, with the intersection of the two indentations taking on a fusiform shape. The key point is to choose a trephine diameter that is 0.5–1 mm longer than the long diameter of the ulcer, thus ensuring complete coverage of the ulcer area. After the indentation, the Castroviejo gauge is used to measure the long and short diameters of the recipient bed, and then a fusiform-shaped graft is created, with both the long and short diameters of the graft requiring to be 0.5 mm longer than the recipient bed. After the graft is successfully created, the diseased cornea is removed, thus reducing the time of the open-skylight procedure and reducing the risk of prolapse of the ocular contents.[26-27] Other surgical procedures were the same as PK with no increase in surgical difficulty, and the mean endothelial cell density was 1783±165 cells per square millimeter at 1y after surgery, with no statistically significant differences compared with the density in the PK group which was 1801±197 cells per square millimeter (P>0.05). The consumables in this study included the routinely applied Storz trephines and an artificial anterior chamber, which did not impose additional financial burden on the patients, making this procedure suitable for clinical promotion and application.[23-24] In the PK group, because the corneal limbus was rich in blood vessels, the sutures closed at the corneal limbus were prone to loosening and tended to be tight, resulting in a mean astigmatism and mean spherical equivalent higher than that of the FPK group postoperatively. The visual quality was subsequently affected, despite the fact that the mean BCVA (logMAR) showed no statistically significant differences between the two groups. In addition, the sutures at the corneal limbus of five eyes had signs of inward neovascularization, which would increase the risk of immune rejection. In addition, trephining the cornea at the limbus could easily damage the structure of the chamber angle and lead to anterior synechia after surgery.[25] Ultrasonic biomicroscopy found that six patients in the PK group had anterior synechia,[26-27] while only one patient in the FPK group had anterior synechia. Although no elevation of intraocular pressures was detected during the follow-up, peripheral anterior synechia was found to be a high-risk factor for the development of glaucoma after PK,[28-30] which requires long-term follow-up and observation. Despite these findings, this study had shortcomings including a small number of enrolled patients and short follow-up times, which may affect the comparison of incidences of secondary glaucoma and immune rejection between the two groups. In addition, when preparing the implant bed during the operation, first of all, the surgeon selects a trephine with appropriate diameter according to the size of the lesion, then marks it, and finally cuts it. Follow the same steps to prepare grafts. Compared with conventional circular keratoplasty, the operation time may be longer, which may be a waste of time for new surgeons. In patients with elliptical-shaped corneas or corneal ulcers, FPK using multiple trephines of different sizes can effectively avoid disruption of the corneal limbus by trephination, with minimal postoperative astigmatism and satisfactory visual quality, while reducing the risk of postoperative complications such as secondary glaucoma, suture loosening, suture neovascularization, and immune rejection.

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