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ABSTRACT

Purpose. To report the clinical results, postoperative progress, and complications after therapeutic keratoplasty for corneal perforation. **Methods.** Twenty consecutive eyes (20 patients) that underwent therapeutic keratoplasty between December 2003 and May 2006 were included. The eyes were evaluated retrospectively for the cause of the corneal perforation, the type of surgical technique and intraoperative complications, anatomic cure rates, graft clarity, visual prognosis, and postoperative complications. **Results.** The causes of corneal perforation were herpetic keratitis (n=5), bacterial ulcer (n=1), fungal ulcer (n=1), neurotrophic ulcer (n=3), rheumatoid arthritis (n=2), Mooren's ulcer (n=2), Terrien's marginal corneal degeneration (n=1), keratoconus (n=1), and Wegener's granulomatosis (n=1). In three cases, the etiology was unknown. Six cases had a previous history of corneal transplantation. Anatomic cures were obtained in 16 (80%) of 20 eyes after the first transplantation procedure. Visual acuity (VA) equal to or better than the preoperative level was achieved in 17 (85%) of 20 eyes. The graft transparency rate was 67% in 15 eyes that underwent central penetrating keratoplasty with fresh donor tissue. Major postoperative complications included cataract (n=6), glaucoma (n=4), and recurrent disease (n=3).

Conclusions. Keratoplasty is valuable for maintaining the ocular integrity and VA. In cases

with severe preoperative inflammation of the anterior segment, it is difficult to achieve transparency after the first graft.

Key Words: Keratitis--Corneal perforation--Therapeutic keratoplasty

Corneal perforation is one of the most severe corneal pathologies. Perforated eyes need immediate treatment to protect the corneal anatomic integrity and avoid the development of complications such as endophthalmitis or secondary glaucoma. Conservative management of corneal perforation such as therapeutic soft contact lenses or surgical adhesive glue is used to block leakage of the aqueous humor, but the effect of adhesion is transient. A large perforation ultimately needs a therapeutic keratoplasty. Although keratoplasty is the best technique for treating corneal perforations, maintaining the condition of the corneal graft after transplantation is not easy, and the postoperative visual acuity (VA) is lower compared with cases in which the cornea is not perforated.¹⁻⁵ We report the clinical results of keratoplasty for corneal perforation.

METHODS

Twenty consecutive eyes of 20 patients (9 men and 11 women; mean age, 70.2±16.5 years) who underwent therapeutic keratoplasty for corneal perforation were included in this retrospective study. Written informed consent was obtained from all patients before corneal transplantation.

Three surgeons performed the procedures between December 2003 and

November 2006 at Asahikawa Medical College Hospital. All cases were followed for at least 6 months postoperatively (mean follow-up time, 19 months; range, 6-36 months).

The eyes were evaluated for the cause of the corneal perforation, the type of surgical technique and intraoperative complications, anatomic cure rates, graft clarity, visual prognosis, and postoperative complications. The patients in whom an anatomic cure was achieved were those with stable anatomic integrity of the eye, such as no leakage of aqueous humor, and the resolution of the original cause of the corneal perforation for at least 6 months.

RESULTS

Causes of corneal perforation

The causes of corneal perforation were categorized as infectious keratopathy (n=7), noninfectious keratopathy (n=10), and unknown (n=3). The causes of infectious keratopathy included herpetic keratitis (n=5), bacterial ulcer (n=1), and fungal ulcer (n=1). The causes of noninfectious keratopathy included neurotrophic ulcer (n=3), rheumatoid arthritis (RA) (n=2), Mooren's ulcer (n=2), Terrien's marginal corneal degeneration (n=1), keratoconus (n=1), and Wegener's granulomatosis (n=1). The etiology of the corneal ulcer

was unknown in three eyes, two of which had a paracentral inflammatory perforation and one a paracentral noninflammatory perforation (Table 1). The patients with RA and Wegener's granulomatosis were treated with systemic steroids for several years. All eyes had been treated with therapeutic soft contact lenses before keratoplasty. Two cases of neurotrophic ulcer had been treated with tarsorrhaphy and underwent amniotic membrane transplantation (AMT). The patients with bacterial and fungal keratitis, all with neurotrophic ulcers, and one with a perforation of unknown origin had undergone corneal transplantation. The organisms cultured in two cases of infectious keratopathy were *Corynebacterium*-like Gram-negative rod bacteria (Centers for Disease Control and Prevention coryneform groups G) and *Alternaria spp.* fungus.

Seven eyes were aphakic or pseudophakic with a history of cataract extraction.

Thirteen cases were phakic before therapeutic keratoplasty.

Surgical technique and intraoperative complications

Central penetrating keratoplasty (PK) was performed in 16 cases of central or paracentral perforation (herpetic keratitis, bacterial ulcer, fungal ulcer, neurotrophic ulcer, rheumatoid arthritis, keratoconus, and unknown paracentral ulcer). Fifteen of 16 eyes were

treated with fresh donor tissue in storage medium (OptisolTM-GS, Bausch & Lomb, Rochester, NY) within 7 days of the time of preservation. Frozen donor tissue stored at -80 °C was used in one case of bacterial keratitis.

Central PK was performed using 7.5-mm Barron's trephines to cut the recipient cornea, and an 8.0-mm graft was sutured into place using 10-0-monofilament nylon sutures. Fifteen cases were performed with interrupted sutures. One herpetic case was treated with continuous running sutures.

Five of the 16 eyes were pseudophakic or aphakic preoperatively, and 11 eyes had a crystalline lens. Four cases of infectious keratopathy and one of unknown perforation underwent open-sky extracapsular cataract extraction (ECCE) for advanced cataract combined with keratoplasty. Intraocular lenses (IOLs) were implanted after ECCE. IOLs were not implanted in the patient with unknown ulcer with severe inflammation of the iris and anterior chamber. Two cases underwent pupilloplasty with 10-0 nylon sutures as the result of severe iris damage. The crystalline lens was preserved in six of 11 cases. Three cases of neurotrophic ulcers underwent tarsorrhaphy after PK.

Peripheral lamellar keratoplasty (LK) was performed in four cases of limbal perforation (Mooren's ulcer, Terrien's degeneration, and Wegener's granulomatosis). These

cases had ulcer and perforation limited in limbal area. PK was not selected to retain clear optical zone and trabecular function. All eyes were treated with fresh donor tissue. After the melted cornea was removed, the graft that was cut free hand was sutured in place using 10-0 monofilament nylon sutures. Lensectomy was not combined with peripheral LK (Table 2).

A viscoelastic substance was used in all cases to remove peripheral anterior synechiae and protect the endothelia of the grafts.

All patients received postoperative topical antibiotics and sodium hyaluronate. Topical steroids were used in all cases of noninfectious disease. In infectious cases, a topical steroid was used after epithelialization was complete and resulted in a cure of the infection. Oral valacyclovir 1,500 mg/day was used for herpetic keratitis for at least 1 month postoperatively.

In two cases of herpetic keratitis, posterior capsular damage occurred during the ECCE procedure. The large capsular ruptures required anterior vitrectomy for vitreous loss and hernia. Each patient was implanted with a posterior chamber IOL.

Disease cures

An anatomic cure was obtained in 16 (80%) of 20 eyes after the first transplantation. Central PK or peripheral LK was unsuccessful in two cases of infectious disease and two cases of noninfectious disease. One case of herpetic keratitis recurred, which was complicated by fungal keratitis due to *Candida albicans* and caused graft failure and total conjunctivalization. One case of bacterial ulceration did not resolve after central PK, and the retina and the posterior ocular segment sustained severe damage. Vitrectomy and antibiotic injection for endophthalmitis were unsuccessful in this case. A neurotrophic ulcer after PK resulted in recurrent thinning of the graft and perforation. Tarsorrhaphy, AMT, and insertion of punctual plugs were not effective in this case. In the case of Wegener's granulomatosis, the graft melted and re-perforated. The case of neurotrophic ulceration resolved after a second PK with tarsorrhaphy and maintenance of the ocular surface moisture.

An anatomic cure was ultimately achieved in 17 (85%) of 20 eyes.

Graft clarity after PK using fresh donor tissue

Graft transparency was achieved in 10 (67%) of 15 eyes after central PK during which fresh donor tissue was transplanted. Among the infectious cases, the eyes with

herpetic keratitis were clear in four (80%) of five cases. Fungal ulceration had not achieved graft transparency. Among the noninfectious cases, graft transparency was achieved in two (67%) of three eyes with a neurotrophic ulcer and in two eyes with rheumatoid arthritis, keratoconus. Unknown ulcer was clear in one (33%) of three eyes.

The grafts failed in five (33%) of 15 eyes. Four of five eyes had severe anterior segment inflammation preoperatively. Herpetic keratitis recurred, complicated by fungal keratitis and total conjunctivalization. The grafts failed within 3 months postoperatively in three eyes with bacterial and fungal ulcerations. Two corneas were transparent after corneal re-grafting. In one case the unknown ulceration did not resolve. One case of neurotrophic ulceration resolved after a second PK.

Visual prognosis

The best-corrected visual acuity (BCVA) was equal to or better than the preoperative BCVA in nine (45%) of 20 eyes after the first corneal transplantation. In 11 (55%) of 20 eyes, the VA did not increase after the first treatment. The VA improved in five eyes after cataract surgery and in three eyes after corneal re-grafting. VA equal to or better than the preoperative level was achieved in 17 (85%) of 20 eyes finally (Figure 1). The

preoperative VA in 20 eyes could be categorized into two grades, i.e., 20/2000 to 20/20 (good VA group, n=10) and light perception (LP) to <20/2000 (poor VA group, n=10). The postoperative BCVA was better than the preoperative BCVA in eight (80%) eyes in the group with good VA but was limited in five (50%) eyes in the group with poor VA.

Postoperative complications

The major postoperative complication was cataract. Dense cataracts developed in six (30%) eyes, and five eyes that underwent cataract surgery had an improvement in VA. Cataract surgery was not performed in a patient with Wegener's granulomatosis because severe scleral and conjunctival inflammation remained.

Glaucoma developed in four eyes (20%). Three eyes had well-controlled intraocular pressure using β -blocker eye drops. One case of unknown ulcer with total peripheral anterior synechiae underwent trabeculectomy 30 months after PK. The original disease recurred in three (15%) with herpetic keratitis, neurotrophic ulcer, and Wegener's granulomatosis (Table 3).

Discussion

An anatomic cure was obtained in 16 (80%) of 20 eyes after the first transplantation procedure. Three eyes underwent corneal re-grafting. Seventeen (85%) of 20 eyes ultimately achieved a cure. Keratoplasty was valuable for maintaining the ocular integrity.

The BCVA was equal to or better than the preoperative in only nine (45%) of 20 eyes after the first central PK and peripheral LK, suggesting that treatment of corneal perforation should continue after the first therapeutic keratoplasty. Eleven (55%) of 20 eyes did not have an increase in VA after the first treatment. The first transplantation procedure should be performed to treat the perforated eye to ensure the anatomic integrity and avoid complications such as endophthalmitis or secondary glaucoma. After the emergent conditions have resolved, surgeons then can perform a procedure to increase the quality of vision. In this series of eyes, in some cases the inflammation was severe and did not decrease after the first surgery, resulting in graft failure. After the initial treatment, cataract surgery or corneal re-grafting can improve the visual prognosis. In our results, VA equal to or better than the preoperative level ultimately was achieved in 17 (85%) of 20 eyes. Keratoplasty was valuable for maintaining the VA. The preoperative VA in 20 eyes could be categorized into two different grades, i.e., 20/2000 to 20/20 (good VA group) and

LP to <20/2000 (poor VA group). There was a marked difference between the two groups.

The postoperative BCVA was better than the preoperative BCVA in 80% of the eyes in the group with good VA but limited in 50% of the eyes in the group with poor VA. The preoperative VA may suggest the postoperative VA outcome.

The graft transparency rate was 67% (10 in 15 eyes) after central PK in which fresh donor tissue was used. Graft clarity is limited after the first central PK. Infectious cases especially had a high rate of failed graft transparency (3/6, 50%). In this series, we did not use topical steroids immediately after PK for infectious cases. There are some instances when the use of topical steroids in combination with anti-infective agents is appropriate. We consider that cases of severe infection should not be treated with topical steroids until the infection begins to abate and re-epithelialization occurs. In cases of herpetic keratitis, oral valacyclovir is effective for reducing viral activity, four (80%) of five cases achieved transparency. All cases of bacterial and fungal ulceration may not achieve corneal transparency after the first graft because of strong infectious inflammation.

The VA after keratoplasty was sometimes reduced as a result of advanced cataract. In 13 cases of phakic eyes preoperatively, five eyes required lensectomy with keratoplasty and six eyes developed advanced cataract in the early phase after keratoplasty. Planning for

secondary cataract surgery in patients who undergo PK is a safe and reliable procedure to decrease the postoperative refractive error^{6, 7}; however, this option may not be easy for a patient undergoing therapeutic keratoplasty because the cataract can mature before the corneal wound is sufficiently healed to proceed to the next procedure.

Glaucoma was a common complication after keratoplasty. Secondary glaucoma developed in four eyes (20%). All cases were controlled with medical or surgical intervention.

Conservative management, such as continuous pressure patching with ointment, sometimes resolves cases in which there are small aqueous humor leaks after trauma or surgery. However, this treatment was inappropriate for perforations with large corneal ulcerations. Corneal melting with persistent epithelial defects requires more extensive procedures. The continuous use of a therapeutic soft contact lens promotes healing of epithelial defects.⁸ A surgical procedure is required in cases that do not respond to a medical approach.

Surgical adhesive glue is sometimes used to fill small corneal perforations,^{9,10} but it cannot replace the full thickness of the corneal stroma or sclera. The effect of adhesion is transient, and it sometimes delays normal wound healing and epithelialization.

Conjunctival cover was used frequently in the past in perforation cases that required emergent treatment, but we did not use this technique in this series, because conjunctival cover can cause neovascularization, fibrosis, and proliferation of abnormal epithelium. Inflammation and invading vessels caused by conjunctival tissue may be risk factors in further treatment, such as PK or other ocular surface reconstruction.

Amniotic membrane (AM) transplantation can reconstruct severe corneal or scleral ulcers. AM grafted into the ulceration can act as a supplement to the collagen layer and is effective for emergency cases.^{11,12} However, the wound rigidity with AM is limited and there is lack of transparency. In this series, two cases of neurotrophic ulceration had been treated with AM but a cure was not achieved. The effect of AM is limited in the absence of severe inflammation or infection.

A donor cornea may be the most suitable material for grafting to treat a damaged cornea. Corneal transplant is commonly used to treat corneal ulcer. There is also the risk of complications or graft failure after therapeutic keratoplasty, high-risk procedures,¹⁻⁵ because ulcerative perforation often induces severe persistent inflammation. Systemic corticosteroids may be beneficial for patients with noninfectious inflammatory diseases, such as RA and Wegener's granulomatosis. In this series, 2 cases of RA were well

controlled after keratoplasty with systemic corticosteroids, but the case of Wegener's granulomatosis did not achieve cure. Recently, anti-tumor necrosis factor α (anti-TNF- α) agents are increasingly used as therapies of ocular inflammation.^{13,14} Anti-TNF- α agents were not employed and available in this series. This new approach may be more beneficial and bring better control of inflammation than steroids alone. We think the interval of time from perforation to surgery is important and might influence cataract formation and glaucoma. In this series, we cannot discuss this factor because the time interval was unknown. It is uncertain when the ulceration started or perforation occurred in some cases. Although corneal perforation always requires meticulous treatment and resolution of the underlying conditions, the indispensable procedures and careful management after surgery make the results successful. We have documented the clinical results and postoperative risks of corneal perforation and believe that this study adds important information to the knowledge about emergency corneal procedures.

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Legend**TABLE 1.** *Causes of corneal perforation*

Group	Diagnosis	No.	%
Infectious keratopathy	Herpetic keratitis	5	25
	Bacterial ulcer	1	5
	Fungal ulcer	1	5
	Total	7	35
Noninfectious keratopathy	Post-PK neurotrophic ulcer	3	15
	Rheumatoid arthritis	2	10
	Mooren's ulcer	2	10
	Terrien's degeneration	1	5
	Keratoconus	1	5
	Wegener's granulomatosis	1	5
	Total	10	50
Unknown		3	15
Total		20	100

TABLE 2. *Surgical procedures*

Procedure	Additional procedure	Additional procedure			Total	%
		Infectious	Noninfectious	Unknown		
Central PK	(none)	3	5	2	10	50
	ECCE			1	1	5
	ECCE+IOL	3			3	15
	ECCE+IOL+PP	1			1	5
	PP		1		1	5
	Total		7	6	3	16
Peripheral transplant			4		4	20

ECCE: extracapsular cataract extraction

IOL: intraocular lens insertion

PP: pupilloplasty

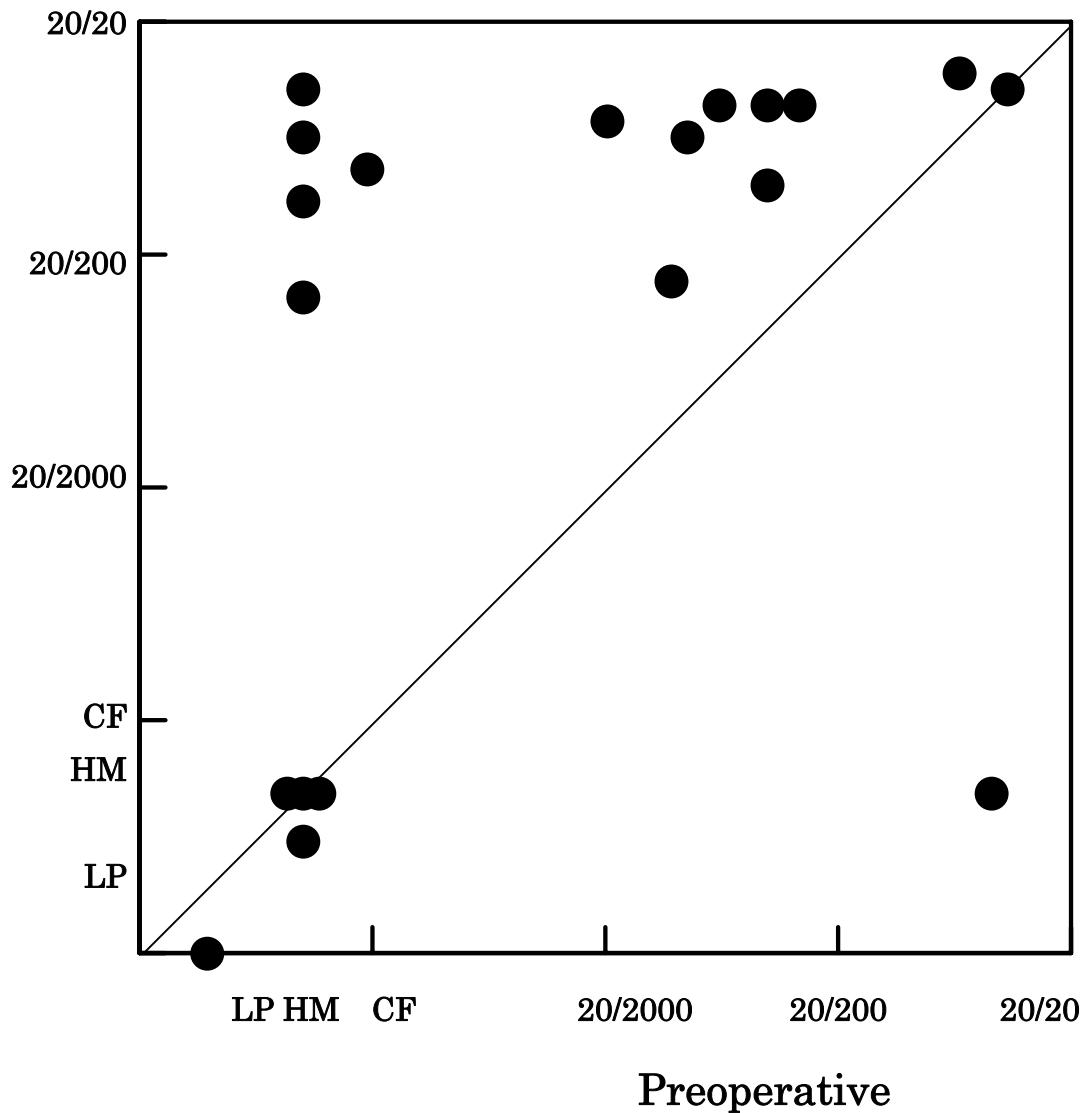
TABLE 3. *Postoperative complications*

Table 3. Postoperative complications

	Infectious (n=7)	Noninfectious (n=10)	Unknown (n=3)	Total	%
Glaucoma	3		1	4	20
Advanced cataract after keratoplasty		5	1	6	30
Persistent epithelial defect		1		1	5
Post-keratoplasty keratitis	1			1	5
Endophthalmitis	1			1	5
Recurrent disease	1	2		3	15
Graft failure after PK with fresh donor tissue (n=15)	3	1	1	5	33 (5/15 eyes)
Melting of peripheral graft (n=4)		1		1	25 (1/4 eyes)

FIG. 1. *Visual results.*

Postoperative



LP: light perception
 HM: hand motions
 CF: counting fingers