

Post-operative outcomes associated with Boston type 1 keratoprosthesis implantation in Northeast China

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Abstract. The aim of the present study was to investigate the post-operative outcomes associated with Boston type 1 keratoprosthesis (Kpro-1) implantation in the treatment of patients with corneal blindness in Northeast China. Clinical data of patients who had undergone Kpro-1 implantation between July 2010 and November 2014 were retrospectively collected. The visual performance, implant retention and post-surgical complications were recorded for each patient. A total of 20 patients (20 eyes) with corneal blindness were included in the study. Prior to surgery, the patients exhibited poor vision and decreased levels of light perception. At 3 days, 1 month, 6 months, 1 year and 2 years post-surgery, logarithm of the minimum angle of resolution values were significantly decreased compared with the pre-operative values. The initial Kpro-1 implants were retained in 16 eyes. Regarding the post-operative complications, six patients exhibited retro-prosthetic membrane formation, two patients presented with endophthalmitis, two patients developed secondary glaucoma, two patients experienced optical cylinder detachment, two patients presented with corneal melting, three patients had retinal detachment, three patients developed corneal ulcers and one patient had secondary optic neuropathy. Overall, the results of the present study suggested that implantation with Kpro-1 may represent an alternative therapeutic strategy for patients following previously failed keratoplasty in Northeast China. Serious complications associated with Kpro-1 implantation are common, and thus, suitable patient selection, continuous follow-up and early treatment interventions are recommended.

Introduction

According to the statistics of the World Health Organization in 2012, 4.9 million individuals suffered from bilateral corneal blindness worldwide, which accounted for ~12% of all cases of blindness (1-3). It has been well established that penetrating keratoplasty (PK) may significantly improve post-surgical visual acuity of patients with corneal blindness; however, the long-term graft survival rates have been estimated to be 28-55% over 5 years and 11% at 10 years post-graft implantation in patients treated with repeated keratoplasty (4-7). Furthermore, PK has been reported to be associated with poor post-surgical visual outcomes, as well as surgical complications and/or failure in high-risk patients, including those suffering from aniridia, herpetic keratitis, severe chemical burns and cicatrizing diseases (8-11). Therefore, a novel strategy for the treatment of patients with PK and poor prognoses was required, which led to the development of the keratoprosthesis (Kpro) implantation strategy (12).

Boston type 1 Kpro (Kpro-1) is considered to represent an alternative therapeutic strategy for patients suffering from late-stage corneal blindness, which is not specified in standard keratoplasty. Several previous studies have investigated the symptoms, complications and post-surgical outcomes associated with Kpro-1 implantation (13-21); however, the majority of these studies were performed in the USA. Thus far, there has been limited research regarding the evaluation of Kpro implantation outside North America. To the best of our knowledge, only one study investigating the clinical outcomes associated with Kpro-1 implantation in Southern China has been published (22). Therefore, it is important that symptoms, clinical outcomes and complications associated with Kpro-1 implantation in patients in Northeast China are further investigated in future studies.

Materials and methods

Patients. Clinical data of patients with corneal blindness who had undergone implantation with Kpro-1 between July 2010 and November 2014 were collected in a retrospective manner. Patients were qualified for inclusion if they: i) had a history of PK surgical failure; ii) were not amenable to standard keratoplasty; iii) had no optic neuropathy or retinal neuropathy; and iv) had a good eyelid contour with normal eye blink. Cases with

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autoimmune diseases, including ocular cicatricial pemphigoid or Stevens-Johnson syndrome, were excluded from the present study. Written informed consent was obtained from each patient prior to surgery. The clinical and personal data of the patients were recorded, including age, sex, pre-operative diagnoses, symptoms, prior history of ocular surgeries, ocular and medical comorbidities and visual outcomes.

Surgical technique. A pre-operative assessment of the complete personal medical and family ocular history for each patient was performed. Each patient was subjected to ophthalmological examination to determine whether they were suitable for keratoplasty. The KPro-1 threadless design was purchased from the Massachusetts Eye and Ear Infirmary (Boston, MA, USA). Implantation with Kpro-1 was performed using a standard technique that has been previously described (23,24). Surgical procedures were performed by the same experienced surgeon. A contact lens was placed on the cornea of all patients following KPro implantation. During the post-operative follow-up period, contact lenses were adjusted, replaced and cleaned if required.

Patients' bandages were removed a total of 24 h post-surgery. Topical tropicamide eye drops (twice per day), levofloxacin eye drops (four times per day), prednisolone eye drops (four times per day) and tobramycin dexamethasone eye ointment (once per night) were administered over a 1-month time period. Following this, the frequency of topical eye drops administered to patients was reduced by half over a 6-month period. For patients that exhibited elevated intraocular pressure (IOP) post-surgery, loteprednol and anti-glaucoma eye drops, e.g. brimonidine tartrate, were administered twice per day. Following this, patients were subjected to systemic administration of numerous drugs for 6 months, including oral administration of minocycline (twice per day) and a liver-preserving drug as antifungal drugs may result in liver damage.

Outcome measures. Patients were subjected to follow-up examination at the following time intervals post-surgery: 3 days, 1 month, 6 months and every 1 to 3 months thereafter. At each follow-up examination, slit-lamp examination was performed, the logarithm of the minimum angle of resolution (LogMAR), IOP, optic disc and fundus were evaluated, and any possible complications were screened for. The post-operative characteristics were subsequently observed, including best spectacle-corrected visual acuity, device retention and post-operative medications. The incidence of post-operative complications, the timing of such complications and therapeutic regimens administered were also recorded.

Statistical analysis. Quantitative data are expressed as the mean \pm standard deviation and differences between groups were analyzed using one-way analysis of variance followed by Tukey's post-hoc test. Data analysis was performed using SPSS 19.0 software (IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Baseline characteristics. A total of 20 patients were included in the present study (14 males and 6 females; mean age, 47.15 ± 14.79 years; age range, 21-79 years). Of these patients,

17 cases had a history of failed PK, one had experienced three failed PK surgeries and only two patients had no history of failed PK. All patients were followed up at 3 days, 1 month, 6 months, 1 year and 2 years post-surgery. Details on the patients who received a KPro-1 implant are presented in Table I. Representative images of the patients' corneas prior to and post-implantation with Kpro-1 are presented in Fig. 1.

Visual acuity. Patients exhibited poor vision and decreased levels of light perception prior to surgery. Following Kpro-1 implantation, visual improvement was observed in all 20 eyes (100%). The LogMAR values obtained at 3 days, 1 month, 6 month, 1 year and 2 year post-surgery were significantly decreased compared with the pre-operative values ($P < 0.05$; Fig. 2).

Prosthesis retention. The mean follow-up period was 2.89 ± 1.56 years post-implantation (range, 3-5 years). During the follow-up period, the initial Kpro-1 was retained in 16 eyes (80%). In addition, corneal images (Fig. 1) and swept-source optical coherence tomography imaging (Fig. 3) revealed that the artificial and donor corneas in 14 patients were completely healed 1 year following Kpro-1 implantation.

Complications and management. Post-operative complications exhibited by patients are listed in Table II. A total of seven patients (35%) experienced one or more post-operative complications. A total of six patients developed retroprosthetic membrane formation (RPM) and mild-to-moderate visual loss. In these six patients, five eyes affected were treated using a neodymium-doped yttrium aluminum garnet (YAG) laser, and one eye was treated via surgical membrane removal; all eyes subsequently exhibited visual improvement. Optical cylinder detachment was observed in two patients at 1- and 2-year time intervals post-surgery, and their LogMAR values were slightly decreased to 0.25 and 1.85, respectively. Corneal ulcers occurred in three patients; however, inflammation was effectively managed and the visual acuity was improved following administration of active systemic and local anti-infective treatment. Retinal detachment occurred in two patients at 1 and 4 years post-operation. The retina was repositioned in one patient following vitrectomy, retinal reposition and silicone oil filling; the other patient also developed secondary endophthalmitis, however, this was subsequently managed via conservative and surgical treatment. Corneal melting occurred in two patients: One patient refused to undergo a second KPro implantation and the other patient received ophthalmectomy due to additional infective endophthalmitis. In total, endophthalmitis was observed in two patients. Secondary optic neuropathy occurred in one patient at a total of 4 years post-surgery; however, following 3 days of systemic hormone shock therapy combined with oral hormone sequential therapy, the patient's visual acuity remained at 0.2. Secondary glaucoma was detected in two patients. Following the administration of cyclocryotherapy and compound trabeculectomy to these patients, the IOP of the two eyes returned to normal.

Discussion

PK has provided patients with diseased, opacified or otherwise compromised corneas with a chance to regain sight. Although

Table I. Details of patients implanted with a KPro-1.

Age (years)/sex	Ocular diagnosis	Number of previous failed PK	Technique
49/F	Mycotic corneal ulcer	1	KPro-1 + iridectomy + AV
36/M	Leukoma	1	KPro-1 + ECCE
23/M	Mycotic corneal ulcer	1	KPro-1 + cataract removal + ILI
21/M	Alkali burn	1	KPro-1 + AV
49/M	Mycotic corneal ulcer	1	KPro-1 + AV
27/M	Bacterial corneal ulcer	1	KPro-1
40/M	Acid burn	3	KPro-1
79/F	Herpes simplex corneal ulcer	1	KPro-1 + AV
54/M	Leukoma + glaucoma	1	KPro-1 + CT + cyclocryotherapy
37/M	Mycotic corneal ulcer	1	KPro-1
42/M	Mycotic corneal ulcer	1	KPro-1 + ECCE + ILI
51/M	Leukoma		KPro-1 + ECCE
53/F	Mycotic corneal ulcer	1	KPro-1 + ECCE
45/M	Mycotic corneal ulcer + Mooren's ulcer	1	KPro-1 x2
56/F	Mycotic corneal ulcer	1	KPro-1
55/M	Leukoma	1	KPro-1 + AV
61/F	Glaucoma + CED		KPro-1 + AV
65/F	Leukoma + glaucoma	1	KPro-1 + iridectomy + AV
64/M	Alkali burn	1	KPro-1 + AV
36/M	Viral corneal ulcer	1	KPro-1 + cataract removal + ILI

PK, penetrating keratoplasty; CED, corneal endothelial decompensation; CT, compound trabeculectomy; ECCE, extracapsular cataract extraction; ILI, intraocular lens implantation; AV, anterior vitrectomy; M, male; F, female; Kpro-1, Boston type 1 keratoprosthesis.

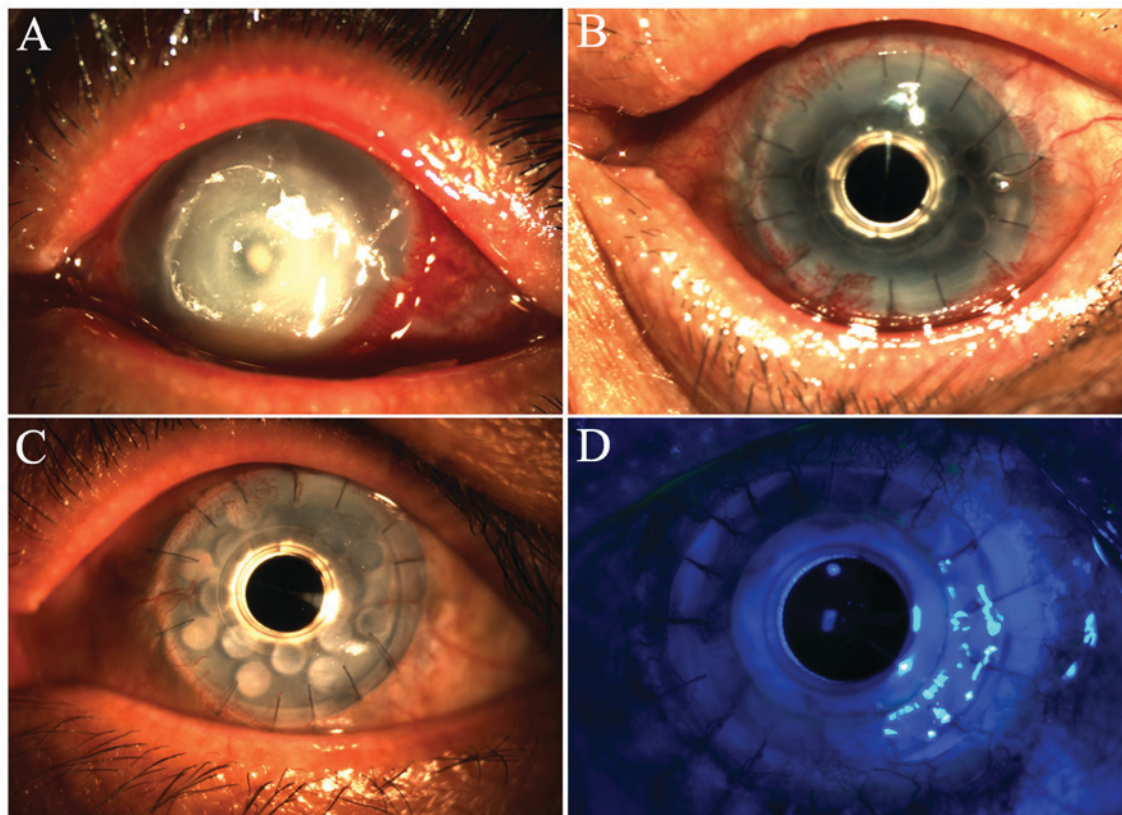


Figure 1. Corneal images from one patient with corneal blindness. (A) Prior to surgery, and at (B) 1 month and (C) 1 year post-implantation with a Boston type 1 keratoprosthesis. (D) Fluorescein staining at 2 years post-surgery revealed that there was no significant staining in the conjunctiva.

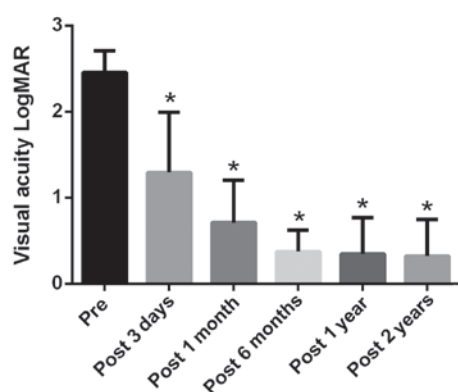


Figure 2. Visual acuity of the patients over a 2-year follow-up period. * $P < 0.05$ vs. Pre. LogMAR, logarithm of the minimum angle of resolution; Pre, pre-surgery; Post, post-surgery.

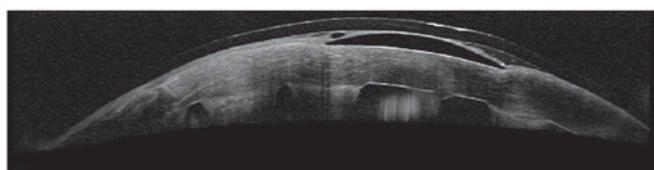


Figure 3. At 1 year post-implantation with Boston type 1 keratoprosthesis, the swept-source optical coherence tomography image of the anterior segment of one patient demonstrated that the corneal epithelium and the complex were fully healed.

this procedure represents the primary treatment option for such conditions, graft failure is a huge obstacle for surgical success. Despite the development of numerous novel drugs and increasingly advanced surgical techniques, ~40% of patients with PK have been reported to exhibit immunological rejection following corneal grafts over a 10-year follow-up period, and in half of these cases, this results in graft failure (7,8,25,26). The success rate of secondary corneal graft surgery is markedly lower (4).

Specific indications for Kpro implantation include PK surgical failure, chemical burns and severe corneal scarring vascularization (27,28). To identify patients that may be suitable for Kpro implantation, surgeons should consider causes of visual loss, lid position, ocular surface condition, and concomitant ocular and systemic diseases (29). In addition, Farias *et al* (30) demonstrated the successful use of intraocular videoendoscopic examination in the pre-operative evaluation of candidates for KPro implantation.

In the present study, the results revealed that the majority of patients exhibited a significant improvement in post-operative visual acuity following KPro implantation due to the removal of retro-KPro membranes and cataracts. Other factors resulting in poor eyesight following artificial cornea transplantation included secondary glaucoma with high intraocular pressure, vitreous opacity and optical cylinder detachment.

The incidence of RPM in the present study was 30%. A previous study by Stacy *et al* (31) reported an RPM incidence of 25-65% following Boston type 1 implantation and ~45% of those cases affected required further treatment, including YAG laser treatment or surgical membranectomy. In the present study, two patients presented with secondary glaucoma

Table II. Post-operative complications.

Complication	Cases
Retroprosthetic membrane formation	6
Endophthalmitis	2
Secondary glaucoma	2
Optical cylinder detachment	2
Corneal melting	2
Retinal detachment	2
Corneal ulcer	3
Secondary optic neuropathy	1

after the implantation. The development and progression of glaucoma in patients with KPro implants may be due to a compromised angle as a result of a crowded anterior chamber, routine topical steroid therapy or debris accumulation in the trabecular meshwork (22). In the present study, endophthalmitis occurred in two patients, which represents one of the most damaging and challenging complications associated with KPro surgery (32). Retinal detachment was observed in two patients of the present study. Patients with underlying autoimmune systemic disorders should be closely monitored for the development of retinal detachment following KPro surgery (33). In the present study, corneal melting occurred in two patients (10%), the rate of which was decreased compared with that reported by Cade *et al* (34). A recent study by Kammerdiener *et al* (35) suggested that the absence of lens implantation following KPro surgery may increase the risk of post-operative complications, including corneal melting. Therefore, extensive forniceal reconstruction performed to retain the lens may contribute to prolonged retention of the implanted KPros in patients with late-stage corneal blindness.

Of note, the present study had certain limitations. First, the study lacked a concurrent control group and follow-up data of 3 months post-surgery. Furthermore, all procedures in the present study were performed by a single surgeon. Therefore, no data were available for comparison between different surgical procedures or different surgeons. In addition, the size of the study population and the quantity of available OCT data were small. Therefore, future large-scale studies with long-term follow-up periods are required.

In conclusion, the results of the present study suggested that Kpro-1 represents an alternative therapeutic strategy for patients with previously failed keratoplasty in Northeast China. Serious complications are common, and thus, suitable patient selection, continuous follow-ups and early treatment interventions are recommended.

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Availability of data and materials

The data used to support the results of this study are available from the corresponding author upon request.

Authors' contributions

MG was a major contributor in the writing of the manuscript and performed the surgery. YC designed the present study and performed literature searches. JW analysed and interpreted the patient data. CW collected and assembled the data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the ethical committee of the General Hospital of Shenyang Military Area Command (approval no. 2010L05; Shenyang, China).

Patient consent for publication

Written informed consent was obtained from all patients prior to surgery, including for the use of personal information for research purposes.

Competing interests

The authors declare that they have no competing interests.

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