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Long-term Outcomes of Boston Type 1 Keratoprosthesis Implantation

A Retrospective Multicenter Cohort

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Purpose: To study the long-term outcomes of Boston type 1 keratoprosthesis (KPro) surgery.

Design: Retrospective, multicenter case series.

Participants: A total of 158 eyes of 150 patients underwent KPro implantation at 5 participating tertiary centers in the United States between January 2003 and December 2006. Of those, 139 eyes of 133 patients were included in the analyses.

Methods: The medical records of consecutive adult patients who received KPro surgery were reviewed. All patients with at least 1 postoperative visit were retained in the outcomes analyses. In eyes in which a repeat KPro procedure was performed, only the outcomes of the initial surgery were analyzed.

Main Outcome Measures: Visual acuity (VA) outcomes, postoperative complications, and device retention.

Results: The mean follow-up was 46.7±26 months with all but 4 eyes having at least 6 months of follow-up. Preoperatively, only 10.8% of the eyes had VA of ≥20/200. Postoperatively, the VA in 70% of eyes improved to ≥20/200. The probability of maintaining VA of ≥20/200 at 7 years was 50%. The device retention rate was estimated at 67% at 7 years. The 7-year cumulative incidence of complications was 49.7% for retroprosthetic membrane formation, 21.6% for glaucoma surgery, 18.6% for retinal detachment, and 15.5% for endophthalmitis.

Conclusions: Although the risk for complications with longer follow-up seemed to increase, this large multicenter cohort demonstrates favorable outcomes with KPro, with a large number of patients achieving and retaining useful vision over a 7-year period. *Ophthalmology 2014;■:1–6 © 2014 by the American Academy of Ophthalmology.*

Over the past decade, the Boston type 1 keratoprosthesis (KPro) has emerged as a viable treatment option for eyes at high risk of failure with traditional donor penetrating keratoplasty. Since the US Food and Drug Administration granted marketing clearance in 1992, the KPro has undergone multiple design revisions to maximize the outcomes.[1] Although once considered a procedure of last resort, there has been a renewed interest in KPro implantation after the publication of multiple studies that have reported favorable outcomes.[2–7] As of August 2013, 8140 KPros have been implanted in patients worldwide: 5406 in the United States and 2734 abroad (Gelfand L, personal communication, 2013).

Thus far, the majority of the KPro studies reporting results have had a limited number of eyes or limited follow-up. Although short-term results suggest excellent visual outcomes with acceptable complication rates,[2–10] studies reporting long-term outcomes after this procedure are few,[5,7,10] and the follow-up periods are highly variable in these studies. It is currently unknown whether the complication rates will stabilize with time or significantly worsen after a certain length of time after surgery. To that end, we report the visual acuity (VA) outcomes, complications, and retention rates in the longest longitudinal cohort of patients after KPro surgery.

Methods

This is a retrospective, multicenter review of patients who underwent KPro implantation surgery between January 2003 and December 2006 by experienced surgeons at 5 tertiary referral centers in the United States (A.J.A., J.V.A., S.B.H., M.B., E.K.A.). The study was reviewed and approved by the institutional review board at each site in accordance with the Declaration of Helsinki and was Health Insurance Portability and Accountability Act compliant. Information from each eye/patient was collected retrospectively between May 2011 and April 2012 and entered in a uniform Microsoft Excel spreadsheet (Microsoft Corp, Redmond, WA) at each site. De-identified data were then reviewed by 2 of the authors (D.S. and B.M.) for completeness and consistency. Patients aged younger than 18 years of age at the time of surgery or without at least 1 postoperative follow-up visit were excluded from the analyses. Eyes that underwent KPro removal and subsequent repeat KPro implantation in the same eye (n = 19) during the specified time period were included only once

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in the study. For the retention analyses, these eyes were counted as failures. The VA was analyzed in 2 ways. In 1 analysis, all eyes regardless of KPro retention status were included, and the vision at the last visit was defined as the final vision. In a separate analysis, only the VA of the eyes that retained the initial KPro device were assessed. Demographic, clinical, and VA data were collected. One eye belonged to a patient with severe mental retardation such that VA could not be assessed and was excluded from the VA analysis but included in other outcomes assessments.

In regard to device retention analyses, eyes were divided into 5 categories based on the indication for KPro implantation and comorbid conditions: (1) ocular surface disease (OSD), which included eyes with severe keratoconjunctivitis sicca, cicatrizing conjunctivitis from chemical or thermal trauma, or autoimmune cause such as mucous membrane pemphigoid, Stevens–Johnson syndrome, or atopic disease; (2) congenital corneal abnormalities, including eyes with Peters' anomaly, aniridia, and congenital glaucoma; (3) infectious keratitis, including eyes with known or presumed viral, bacterial, fungal, or parasitic keratitis; (4) bullous keratopathy/corneal dystrophy, including isolated stromal or endothelial disorders such as Fuchs' endothelial corneal dystrophy, pseudophakic or aphakic bullous keratopathy, and keratoconus; and (5) unknown, including eyes with a diagnosis other than those listed or for which the original indication for keratoplasty was unknown. A subgroup analysis with respect to device retention was performed on the basis of these diagnostic categories.

The VA information was collected preoperatively, best ever, at 6 months after surgery and yearly thereafter. The VA was measured using the Snellen chart with manifest refraction. The VA was recorded as no light perception if the eye was enucleated during the follow-up. The final VA was the level of best-corrected vision measured at the last follow-up visit. The achievement and maintenance of a $\geq$20/200 VA and postoperative complication rates were estimated with Kaplan–Meier survival curves for the entire cohort. Eyes with a repeat KPro were censored from the Kaplan–Meier survival curves at the time of removal of the first KPro. Statistical analyses were performed using SAS software version 9.3 (SAS Inc, Cary, NC).

Table 1. Baseline Characteristics (n = 139 Eyes)*

Characteristic	
Mean age at the time of surgery (SD)	63.9 yrs (18.3)
Female (%)	54.7
Indication for surgery (%)	
Prior failed graft	72.6
Primary keratoprosthesis	27.3
Initial corneal diagnosis (%)	
OSD	23.0
Congenital corneal abnormalities	12.9
Known/presumed infectious keratitis	12.2
Bullous keratopathy/dystrophy†	35.3
Unknown	16.5
Lens status (%)	
Phakic	17.3
Aphakic	22.3
Pseudophakic	60.4
Glaucoma status (%)	
Known history of glaucoma	58.3
Previous glaucoma surgery (tube shunt, trabeculectomy, diode)	30.4
Retina status (%)	
History of retinal detachment	13.7
Other retinal disease (macular degeneration, epiretinal membrane, diabetic retinopathy)	19.4
Other associated conditions (%)	
Uveitis	5.8
Chronic hypotony	2.2
Length of postoperative follow-up (SD)	46.2 mos (26)
Median (IQR)	48.7 mos (23.8–66.1)
% Eyes with >4 yrs of postoperative follow-up	52.5

IQR = interquartile range; OSD = ocular surface disease; SD = standard deviation.
*The study group included 133 patients (139 eyes). Six patients had bilateral keratoprosthesis implantation surgery.
†Corneal dystrophy group included patients with Fuchs' endothelial dystrophy, keratoconus, and other stromal dystrophies.

Results

All included eyes in this study received a KPro device with a 7- or 8.5-mm fenestrated back plate. A total of 158 eyes of 150 patients underwent KPro implantation surgery for the first time between January 2003 and December 2006 at the mentioned sites. Of these, 13 patients (15 eyes) were aged younger than 18 years of age at the time of surgery, and 4 patients (4 eyes) had no postoperative follow-up data and thus were excluded from the analysis, leaving 139 eyes of 133 patients. The mean follow-up for all eyes included was 46.7±26 months (range, 6 weeks to 8.7 years) with more than half of the eyes (52.5%) having more than 4 years of follow-up. Fifteen eyes had 7 years of follow-up. All but 4 included eyes had a postoperative follow-up of at least 6 months. Two patients were lost to follow-up within 6 months after surgery, and 1 patient died of unrelated causes 2 months after surgery. One patient with severe OSD underwent explantation of the device because of sterile corneal necrosis 6 weeks after the implantation. These 4 eyes were still included in all of the analyses.

The baseline characteristics of the included eyes are summarized in Table 1. The mean age of the patients at the time of surgery was 63.9 years, with nearly equal men and women in the cohort. The indication for KPro surgery was prior donor graft failure in the majority of eyes (73%); 27% of the eyes underwent a primary KPro procedure without having received a previous donor keratoplasty. Approximately one-fourth (23.0%) of the eyes had OSD. More than half (58.3%) of the eyes had a known history of glaucoma. Approximately one-third of the eyes (30.4%) had received prior glaucoma surgery. One-third of the eyes had preexisting retinal disease, with 13.7% having a history of retinal detachment.

Seventy percent (97/139) of the eyes had at least 1 concomitant procedure at the time of the KPro procedure. Twenty-five percent of the eyes required an anterior vitrectomy, and more than one-fifth of the eyes (21%) underwent simultaneous glaucoma surgery.

Postoperative Outcomes

Visual Acuity. The distribution of vision preoperatively, best-ever postoperatively, and at last visit in all patients regardless of whether or not they were able to retain the initial KPro device is shown in Figure 1. The group included 138 eyes for the preoperative and best-ever postoperative VA. One mentally retarded patient who could not have vision measured accurately was excluded completely from vision analysis. Eight eyes with device removal with no post-removal acuity recorded were excluded from VA assessment at the last visit. Figure 2 shows the distribution of VA information in the 103 eyes in which the initial KPro device was retained. Preoperatively, 10.8% of the eyes had a best-corrected VA of $\geq$20/200. Postoperatively, 70% of the eyes

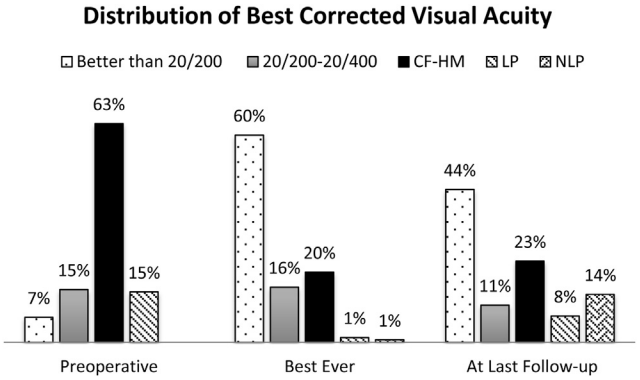

Figure 1. Preoperative visual acuity (VA) in comparison with best-ever vision measured at any time point during follow-up (n = 139) and the vision measured at the last visit (n = 130) in a retrospective cohort of patients who underwent Boston type 1 keratoprosthesis (KPro) surgery before 2007 at 5 tertiary care centers in the United States. The VA at the last follow-up is presented for all eyes in the cohort regardless of retention of the device. One patient with mental retardation could not have vision measured accurately and was excluded from this analysis. Eight eyes with device removal did not have a post-removal acuity recorded and were not included in the distribution for the last visit. The VA was recorded as no light perception if the eye was enucleated during the follow-up. The totals do not add up to exactly 100% because of rounding. CF = counting fingers; HM = hand motions; LP = light perception; NLP = no light perception.

(97/138) achieved ≥20/200 at a median time of 6.3 months (interquartile range, 3.8−11.5). One-third of the eyes (29.7%, 41/138) never achieved ≥20/200 after surgery because of preexisting posterior segment conditions. Figure 3 shows the Kaplan−Meier survival curve for maintenance of ≥20/200 VA at the last follow-up in 97 eyes that had a best-ever VA of ≥20/200 postoperatively. The probability of maintaining a vision of ≥20/200 was estimated to be 50% at 7 years.

Complications. Cumulative incidences of complications over 7 years are summarized in Table 2. The most common postoperative complication was formation of a retroprosthetic membrane with a cumulative incidence of 49.7%. The incidence seemed to plateau after the first 3 years. Not all patients with a retroprosthetic membrane required intervention; 33.0% underwent a YAG membranotomy, and 18.6% required a surgical membranectomy. Glaucoma development or exacerbation of preexisting glaucoma was a frequent complication, with 36.2% of the eyes that had previously stable intraocular pressures developing elevated intraocular pressure during follow-up. Furthermore, 21.6% of eyes required surgical intervention for the glaucoma management in the form of tube shunt surgery or diode ciliary body ablation. The need for glaucoma surgery did not differ when comparing eyes with and without preexisting glaucoma (20.6% vs. 17.2% respectively, $P = 0.99$). Eyes were further stratified as undergoing or not undergoing glaucoma surgery before or at the time of KPro

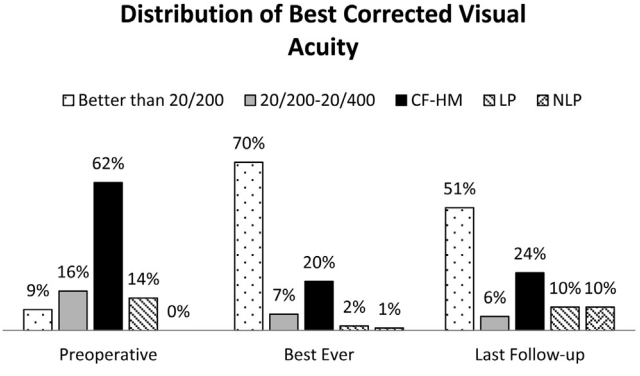

Figure 2. The visual acuity (VA) distribution preoperatively, best-ever vision measured at any time point during the follow-up, and vision measured at last follow-up in 103 eyes. Only the eyes that were able to retain the initial device at the last visit were included in the analysis. The totals do not add up to exactly 100% because of rounding. CF = counting fingers; HM = hand motions; LP = light perception; NLP = no light perception.

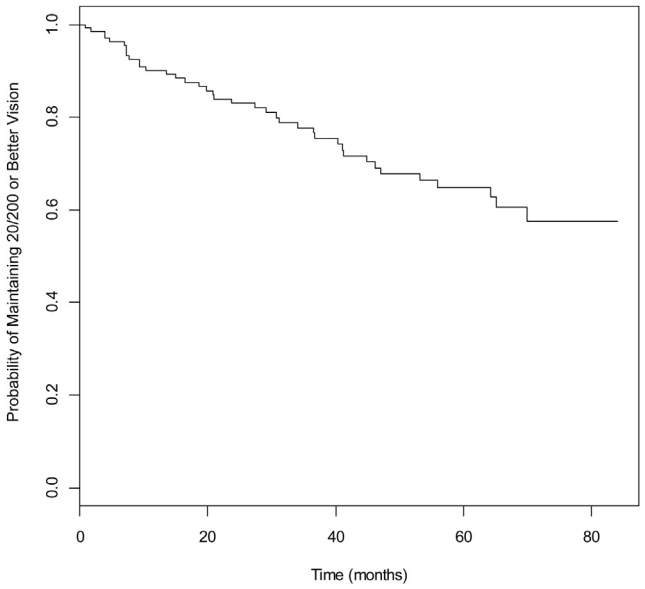

Figure 3. Kaplan−Meier survival curve for maintenance of ≥20/200 visual acuity (VA) at last follow-up in eyes that had a best-ever VA of ≥20/200 postoperatively. Ninety-seven of 138 eyes (70.2%) achieved ≥20/200 at a median time of 6.3 months (interquartile range, 3.8−11.5) after device implantation. Forty-one eyes (29.7%) never achieved 20/200 after surgery because of preexisting posterior segment conditions.

Table 2. Cumulative Incidence of Postoperative Complications in a Retrospective Cohort of Patients Who Underwent Boston Type 1 Keratoprosthesis Surgery before 2007 at 5 Tertiary Care Centers in the United States

% Complication	Years after Surgery				
	1	*2*	*3*	*5*	*7*
KPro device removal	5.9	16.2	20.9	33.2	33.2
Retroprosthetic membrane formation	29.5	35.5	44.9	49.7	49.7
Glaucoma requiring additional surgery	7.8	10.4	13.6	18.9	21.6
Sterile corneal necrosis	6.7	11.1	12.2	19.5	19.5
Retinal detachment	4.6	8.1	11.2	16.1	18.6
Infectious endophthalmitis	3.1	4.8	4.8	10.5	15.5
Persistent epithelial defect	4.4	6	7.1	8.2	8.2
Infectious corneal infiltrate	0.8	3.4	3.4	3.4	3.4

KPro = Boston type 1 keratoprosthesis.

implantation. There was a trend for increased need for glaucoma surgery postoperatively in eyes without compared with eyes with prior or concurrent glaucoma surgery (31.4% vs. 18.9%), although the difference did not reach statistical significance ($P = 0.10$).

Sterile corneal necrosis (19.5%), retinal detachment (18.6%), endophthalmitis (15.5%), cystoid macular edema (10.1%), persistent epithelial defects (8.2%), and infectious keratitis not progressing to endophthalmitis (3.4%) were noted less frequently.

Retention Rates. In one quarter (25%, 35/139) of the eyes, the KPro was removed (30/139) or the eye underwent enucleation (5/139) because of device-related complications during the entire follow-up. A Kaplan–Meier curve (product limit estimator) estimated an overall device retention rate of 67% at 84 months (Fig 4). A separate survival analysis for the 5 different corneal diagnostic subgroups also was performed (Fig 5). Eyes with a history of bullous keratopathy/corneal dystrophies had the highest device retention rate (85% at 84 months). Figure 6 further compares the device retention rates in eyes with versus without OSD. Eyes with OSD had significantly lower retention rates (only 35% at 84 months) compared with eyes without (78% at 84 months; log-rank test $P < 0.001$). No differences in KPro retention were noted between eyes that had a primary KPro versus those that had previously failed 1 or more donor grafts and eyes that had an aphakic versus pseudophakic KPro device implanted.

Discussion

This study provides information on long-term outcomes after KPro surgery in a multicenter, longitudinal cohort of eyes with a mean follow-up of 46 months, which is significantly longer than all previously reported series (the mean follow-up in previous reports ranged from 8.5 to 24 months).[2–9] More than one half of the eyes (52.5%) in this series completed more than 4 years of follow-up, and 15 eyes had at least 7 years. This study found an overall probability of retention of 84% at 2 years and 67% at 7 years. Of note, the survival curve for device retention in

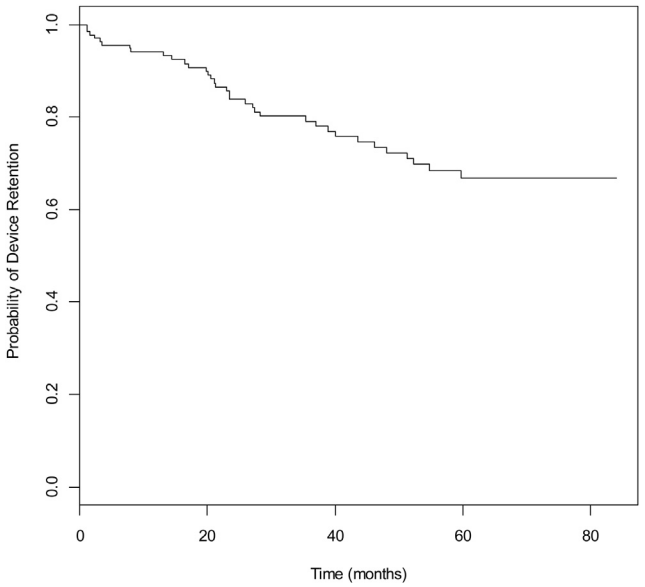

Figure 4. Kaplan–Meier survival curve demonstrating retention rate of the Boston type 1 keratoprosthesis (KPro) device over time.

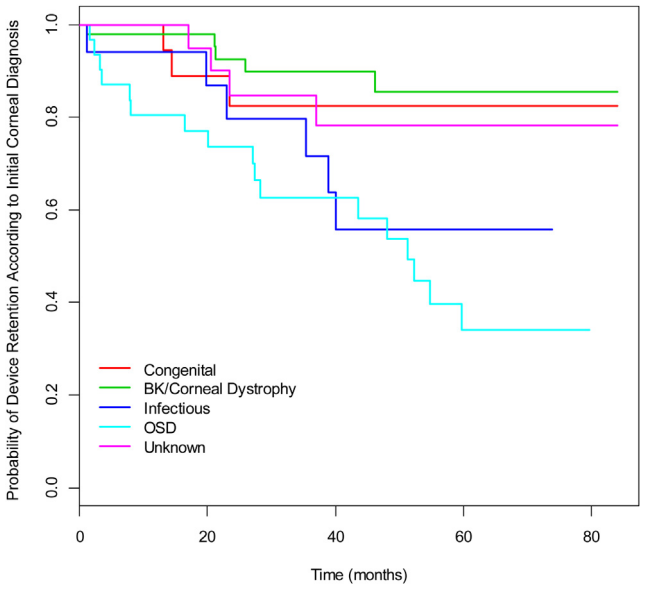

Figure 5. The Boston type 1 keratoprosthesis (KPro) device retention rates according to initial corneal diagnosis. The congenital group (n = 18) included eyes with Peters' anomaly, aniridia, and congenital glaucoma. The bullous keratopathy/corneal dystrophy group (n = 49) included eyes with pseudophakic or aphakic bullous keratopathy and isolated stromal or endothelial corneal dystrophies, such as Fuchs' endothelial dystrophy and keratoconus. The infectious group (n = 17) included eyes with known or presumed bacterial, viral, fungal, or parasitic keratitis. The ocular surface disease (OSD) group (n = 32) included eyes with severe keratoconjunctivitis sicca, limbal stem cell deficiency, and cicatrizing conjunctivitis. The unknown group (n = 23) included eyes with no other known corneal diagnosis. BK = bullous keratopathy.

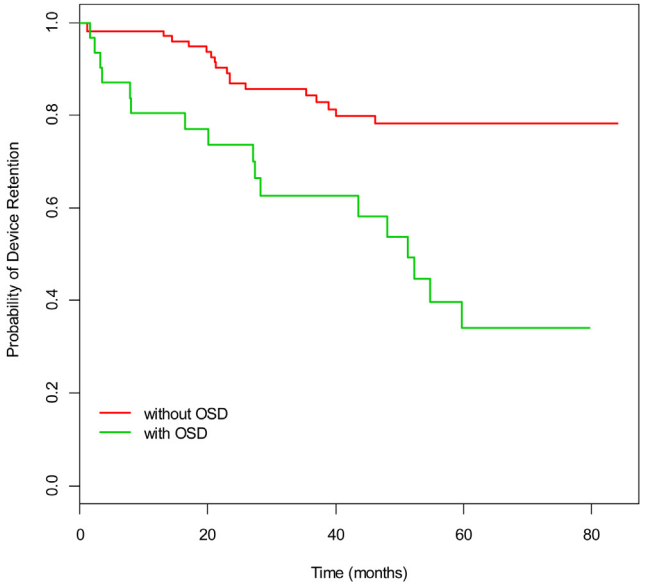

Figure 6. The Boston type 1 keratoprosthesis (KPro) device retention rate in eyes with ocular surface disease (OSD) (n = 32) in comparison with eyes without OSD (n = 107). Log-rank test was $P < 0.001$ for the difference between the curves.

eyes without OSD seemed to plateau at approximately 3 years. The most recent published report from a large, multicenter cohort involving 300 eyes receiving KPro implantation and average follow-up of 17.1±14.8 months found a probability of retention of 89% at 2 years.[10]

The patient characteristics in our cohort are similar to those previously reported in that the most frequent indication for KPro surgery was prior failed grafts.[2–10] There was a higher frequency of ocular comorbidity then in some of the previous series,[3,8] with a substantial number of the eyes having been diagnosed with glaucoma or retinal disease. Two-thirds of the eyes in this series had a concomitant surgery at the time of the KPro implantation. This is likely because of our patient referral patterns and the fact that the sites involved are tertiary care centers for corneal surgery.

Despite a high prevalence of ocular comorbidity in this cohort, the majority of the patients in this cohort achieved a significant increase in their vision after KPro implantation. Patients without improvement invariably had preexisting posterior segment comorbidity, the most common being advanced glaucoma. The most recent report from The Swedish Cornea Transplant Registry demonstrated poorer visual outcomes for patients who underwent re-grafts as opposed to primary donor corneal grafts.[11] Less than 70% of patients who underwent a re-graft for bullous keratopathy ever achieved a vision of 20/200, and >60% of the grafts failed within 2 years of follow-up. In our series, approximately 70% of patients achieved a vision of >20/200 during the follow-up period. Approximately one half of those maintained this level of vision at their last visit, which is considerably longer than 2 years. The patients in this series had significantly more complex eyes with worse preoperative vision and more frequent serious ocular comorbidities compared with patients included in the Swedish Cornea Transplant Registry. In addition, we did not find a difference in KPro retention in eyes with a primary KPro versus those with 1 or more prior failed grafts.

As consistent with previous reports,[10,12] the presence of OSD was shown to be associated with a significantly increased risk of KPro failure and complications. These eyes indeed are known to be at a higher risk of failure with donor keratoplasty as well.[13] However, because of the inadequate number of cases in this group, we were not able to perform subgroup analyses to assess whether there could be differences between, for example, patients with chemical burns and patients with severe inflammatory OSDs, such as mucous membrane pemphigoid or Stevens−Johnson syndrome.

With respect to postoperative complications, as in prior cohorts, the most common complication was the development of a retroprosthetic membrane, which occurred in approximately 50% of eyes and tended to develop in the first 2 years after surgery. This percentage is similar to those in the other cohorts, which range from 27% to 55% depending on the length of postoperative follow-up.[3,6,14]

Although glaucoma is a preventable cause of vision loss, it is the leading cause of poor visual outcome after KPro surgery. Management of glaucoma tends to be challenging in eyes with the KPro device because of difficulty in measuring intraocular pressure and obtaining standard testing reliably for follow-up. Elevation in intraocular pressure, with the subsequent need for glaucoma surgery, was the second most frequent complication in this cohort. The presence of preexisting glaucoma did not seem to affect the need for glaucoma surgery postoperatively. Because such a high percentage of patients develops glaucoma postoperatively, we advocate simultaneous or prior glaucoma surgery unless the patient has no history of glaucoma and with normal intraocular pressures while on no topical pressure-lowering eye drops.[4,5,9] Indeed, in this cohort, the subset of the eyes that had prior or concurrent glaucoma surgery tended to require glaucoma surgery after KPro implantation less frequently, perhaps suggesting better glaucoma control. However, even in eyes that underwent glaucoma surgery, elevations in intraocular pressure and progression of glaucoma might occur and require vigilant follow-up.

Although the rates of retinal detachment and endophthalmitis were slightly higher than previously reported,[2,4,8] this would be expected owing to the longer follow-up, because 2-year rates were not significantly different than in previously published reports.

In conclusion, our study shows favorable long-term outcomes with KPro with a device retention rate of approximately 70% at 7 years. Half of the eyes with a retained KPro maintained a VA of ≥20/200 at the last follow-up. Serious complications, including endophthalmitis, retinal detachment, and worsening glaucoma, continue to occur in these eyes long after surgery, albeit at a low chronic rate, suggesting the need for continued close follow-up of these eyes.

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Abbreviations and Acronyms:
KPro = Boston type 1 keratoprosthesis; **OSD** = ocular surface disease; **VA** = visual acuity.

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