DONOR CORNEAL TRANSPLANTATION VS BOSTON TYPE 1 KERATOPROSTHESIS IN PATIENTS WITH PREVIOUS GRAFT FAILURES: A RETROSPECTIVE SINGLE CENTER STUDY (AN AMERICAN OPHTHALMOLOGICAL SOCIETY THESIS)

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ABSTRACT

Purpose: To compare short-term outcomes of repeat penetrating keratoplasty (PK) to those of Boston type 1 keratoprosthesis (KPro). Our hypothesis was that visual outcomes were superior for KPro compared to PK.

Methods: This is a retrospective, nonrandomized, intermediate-term case series. Consecutive adults with one or more failed PKs who underwent either PK or KPro between January 2008 and December 2010 were included. Demographics, indication for the initial PK, comorbidities, concomitant procedures, and complications were considered. Only one procedure in each eye was included. All KPro procedures were retained in the analyses.

Results: Fifty-three patients underwent PK and 27 received KPro. Mean follow-up was 19.5 months in the PK group and 16.5 months in the KPro group. KPro eyes had worse mean preoperative vision (hand motions vs counting fingers, *P*=.01) and more comorbidities. In the postoperative period, 35% of PK eyes and 45% of KPro eyes attained best-ever visual acuity of 20/70. Forty-seven percent of PK eyes vs 40% of KPro eyes were able to retain this visual acuity. Two-year rate of failure to retain visual acuity better than the baseline was higher for PK eyes, though not at a statistically significant level (hazard ratio [HR]=1.67; 95% CI, 0.78-3.60; *P*=.19). Two-year cumulative rate of graft failure (loss of clarity for PK and removal/replacement for KPro) was higher for PK eyes (HR=3.23; 95% CI, 1.12-9.28; *P*=.03). Retinal detachment, endophthalmitis, and glaucoma rates were similar (*P*=.6 for all).

Conclusions: These results demonstrate less frequent graft failure, greater visual improvement, and greater likelihood of maintaining the visual improvement in KPro eyes vs PK.

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INTRODUCTION

Clarity of the cornea is important in visual function. Loss of corneal transparency is a major cause of blindness, affecting 8 million people worldwide.[1] Allogeneic donor corneal transplantation has played an integral role since the 1950s for the management of corneal opacity. During the past century, advances in surgical technique and instruments, newer and more effective postoperative medications, and developments in eye banking have contributed to the emergence of corneal transplantation as a safe and successful ocular surgical procedure. Currently, keratoplasty is the most frequently performed organ transplant in the developed countries.

Although most patients who undergo a donor keratoplasty enjoy a great success, not all patients are equally likely to benefit from it. Conditions associated with a relatively low risk for graft failure include keratoconus or Fuchs' endothelial dystrophy, with overall success rates ranging between 70% and 95% over a period of 5 to 15 years.[2-7] Endothelial allograft rejection is regarded as the leading cause of graft failure in these cases.[3,5,7] The risk for rejection following a corneal transplant is highest during the first year after the transplant.[8] Failure of donor endothelium not directly as a result of allograft rejection also plays a significant role in the failure of the donor graft.

Multiple recent publications have demonstrated that the single most important factor affecting the success of donor keratoplasty, defined as graft clarity, is the preoperative diagnosis, or *indication for the surgery.*[9] The overall success rate decreases to less than 50% over 5 to 15 years of follow-up when, for example, the indication is bullous keratopathy, and is even lower if the eye is aphakic.[4,6,7,9] Presence of significant neovascularization of the host bed, anterior chamber synechiae, history of glaucoma or previous glaucoma surgery, and history of previous herpetic infections are some of the host factors that further decrease the likelihood of graft survival.[4,6,7] In particular, whether from an immunologic rejection or primary endothelial failure from other reasons, re-grafts have been consistently associated with lower survival rates. High-risk patients often require multiple corneal transplants, with each subsequent graft having a significantly lesser chance of remaining clear.[9] In addition, the visual outcome in successive corneal transplants has been reported to be significantly worse in comparison to primary grafts.[10] For example, according to the most recent report from the Swedish Cornea Transplantation Register, only fewer than 20% of patients with bullous keratopathy undergoing a successive corneal transplant attained a visual acuity ≥20/50.[10] Of note, the visual acuities in these studies are frequently "best corrected vision" and do not reflect the daily experience of those with aphakia or significant refractive error who would normally require hard contact lenses for vision correction and cannot wear or be fitted with them due to corneal curvature issues. Because patients repeatedly seek restoration of vision, previous graft failure has now become the second most common indication for full-thickness donor corneal transplantation in the United States.[11]

An alternative is available for patients who are likely to have donor graft failure. The Boston type 1 keratoprosthesis (KPro) is a three-piece prosthetic device made of polymethyl methacrylate (PMMA).[12] KPro is a Category B, Class II device intended to provide a transparent optical pathway through an opaque cornea. KPro received 510(k) marketing clearance by the US Food and Drug Administration in 1992 to be used "in an eye that is not a reasonable candidate for a donor corneal transplant." KPro is a double-plated

From the Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland.

collar button prosthetic cornea composed of a front plate (diameter sizes of 5.5 mm or 7 mm) that houses the optical stem, a back plate, and a titanium locking c-ring (Figure 1). The device is available in either a standard plano power for pseudophakic eyes, or customized powers based on axial length for aphakic eyes. The anterior plate optical stem bears the refractive power. The back plate is generic regardless of the lens status of the eye. The back plate comes in diameter sizes of 7 mm and 8.5 mm. The 7-mm-diameter back plate has one row of larger holes, whereas the 8.5-mm plate has double rows of 8 holes (16 total). The smaller devices are generally used for pediatric eyes but can be considered for adult eyes as well. The anteroposterior length of the stem is 3.7 mm, with a diameter of 3.35 mm, allowing a visual field of 60 degrees. The device is currently machined from medical grade PMMA in a family-operated machine shop (J.G. Machine Co, Inc) in Woburn, Massachusetts. During implantation, the device is assembled with a donut-shaped piece of donor corneal tissue positioned between the front and back plates, which is then sutured into the recipient bed in a similar fashion to PK using 16 interrupted 10-0 nylon sutures (Figure 2).

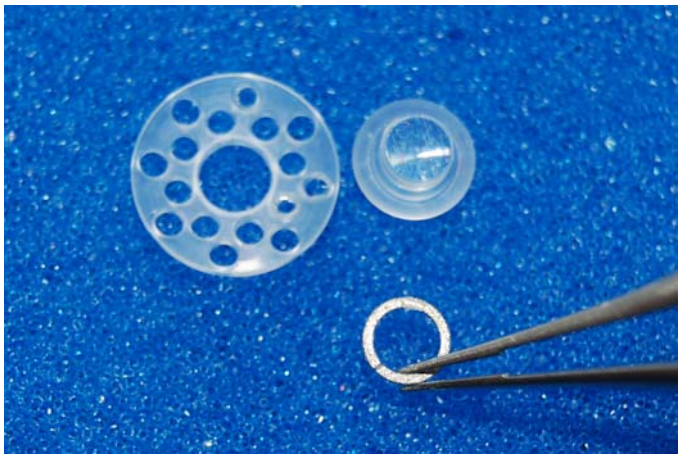

FIGURE 1

Boston type 1 keratoprosthesis is a 3-piece collar button device with an anterior and a posterior plate as well as a titanium locking c-ring.

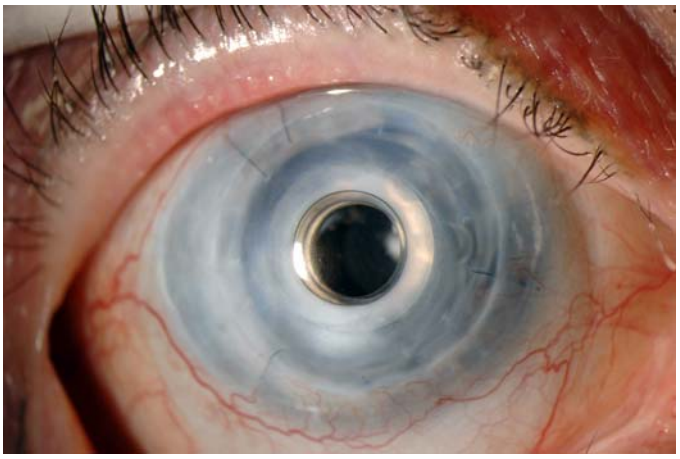

FIGURE 2

Slit-lamp appearance of a Boston type 1 keratoprosthesis in situ.

Prospective studies examining the long-term outcomes of KPro implantation following corneal transplant failure are lacking. Multiple retrospective reports showed that KPro has a favorable prognosis in patients with a wide variety of corneal conditions, such as previous allograft rejections or endothelial failure, and congenital corneal abnormalities.[12-16] Revisions in design, surgical technique, and postoperative clinical management have greatly reduced the perioperative complications associated with KPro.[11,12,16,17] Although KPro implantation was once considered as a procedure of last resort, interest in the procedure has been renewed after publication of several recent studies reporting favorable outcomes.[14-20] As of August 2013, 8,140 KPros have been implanted worldwide—5,406 domestically and 2,734 abroad (L. Gelfand, Boston Keratoprosthesis, Massachusetts Eye and Ear Infirmary, written communication, September 28, 2013).

In the last decade, multiple studies have examined the outcomes of successive donor corneal transplants[21-27] as well as KPro implantation *separately* in patients with graft failure.[28-34] A recent review of the *Cochrane Database of Systematic Reviews* demonstrated no reports directly comparing the outcomes of these two surgical procedures in similar patient populations (prospectively or retrospectively).[35] As such, there is insufficient evidence to guide corneal surgeons and their patients in the relative merits of these two procedures. The purpose of this retrospective study is to provide preliminary data on that topic by comparing the short-term clinical outcomes of patients with prior failed donor corneal transplants who underwent either a KPro or another full-thickness, penetrating corneal transplant (PK) for visual rehabilitation. Our hypothesis was that visual outcomes of KPro were superior to successive PK over an intermediate follow-up period, due to superior optical qualities of KPro.[36]

METHODS

Approval was obtained retrospectively from the Johns Hopkins University Institutional Review Board to proceed with review of medical records in accordance with the Declaration of Helsinki. The study was compliant with the Health Insurance Portability and Accountability Act. A list of patients who underwent any corneal transplant procedure at the Wilmer Eye Institute over a period of 3 years, from January 2008 through December 2010, was generated electronically using current procedural terminology (CPT) codes of 65730, 65750, 65755, and 65770 used for corneal transplantation. Medical records of these patients were reviewed retrospectively, and clinical data were abstracted in a standardized fashion. For the purpose of this study, only the procedures performed on patients who had previously undergone at least one full-thickness donor corneal transplant with failure of the graft were included. Primary donor corneal transplants, as well as primary KPro implants, were excluded. Patients with underlying severe autoimmune ocular surface diseases, grafts performed for tectonic purposes, and pediatric patients (younger than 18 years) were excluded. Only the KPro

procedures using Boston type 1 device were included. Lamellar grafts (eg, Descemet stripping endothelial keratoplasty) performed for graft failure in patients who previously failed a full-thickness transplant were also excluded from this review. The surgical procedures were performed in a reasonably uniform manner. Generally, the donor in successive PK was oversized by 0.25 to 0.5 mm and sutured in recipient bed using 16 interrupted 10-0 nylon sutures. The donor in KPro procedures was oversized by 0.5 mm and sutured in recipient bed using 16 interrupted 10-0 nylon sutures. A 7-mm fenestrated posterior plate was used in all cases. All patients received subconjunctival as well as intravenous injections of corticosteroids (dexamethasone) and antibiotics (cefazolin) at the end of the procedure and were patched overnight. In patients who received KPro, a large-diameter bandage contact lens was used to cover the eye prior to patching.

All patients who underwent KPro had been deemed ineligible to receive another donor corneal transplant. Patients with reasonable chance of success with another PK, based on clinical grounds, were grafted with a donor tissue. Postoperative management was tailored to the individual patient's needs in regard to corticosteroid eye drops used and other topical treatments, such as for glaucoma. Most frequently, topical corticosteroids (prednisolone 1% drops) were used every 2 hours immediately in the postoperative period for several weeks before tapering down to once a day over several months. In patients with a prior history of endothelial graft rejection, systemic corticosteroids, starting from 1 mg/kg/day with quick taper and discontinuation over 4 to 6 weeks, were used at the surgeon's discretion. Systemic immunosuppressants (such as mycophenolate, methotrexate, or azathioprine) were used in some patients with a history of endothelial rejection undergoing a successive PK or in patients with comorbid uveitis regardless of the corneal surgery they received. Topical antibiotics were continued until complete epithelization of the donor graft.

In KPro patients, topical antibiotics (vancomycin and moxifloxacin), as well as corticosteroids (prednisolone 1%), were continued two to four times per day indefinitely. A bandage contact lens was maintained indefinitely with frequent exchanges. Topical artificial tear drops or ointments were used for dry eye or epithelial defects as necessary. Patients with a known history of glaucoma were comanaged with specialists from the Glaucoma Division at Wilmer Eye Institute prior to the corneal procedure as well as afterwards. Topical glaucoma medications were used based on patients' intraocular pressure measured with applanation tonometry in patients who underwent PK and estimated by digital palpation in patients who received KPro. Whenever possible, optic nerve pictures and visual fields were also obtained for evaluation. Intraocular pressure values measuring or estimated to be greater than 25 were generally considered "elevated," necessitating either initiation/escalation of topical treatment or surgery when there was no room for additional medical treatment. Glaucoma tube shunt insertion was the preferred surgical method for KPro patients. In PK patients, trabeculectomy or diode laser was also used as deemed necessary due to elevated pressures.

All patients were seen on postoperative day 1. Further visits were based on the postoperative outcome and typically performed at about 7 to 10 days after surgery and at 6 to 10 weeks. All KPro patients were seen frequently, about every 2 to 4 months, either at the Wilmer Eye Institute or by their referring physicians. The outside medical records, mostly including anterior segment and optic nerve pictures, were evaluated by the operating surgeon at Wilmer on a regular basis when a patient was comanaged by referrers. Uncorrected visual acuity, spectacle-corrected visual acuity using manifest refraction, intraocular pressure assessment, slit-lamp examination, and dilated fundus examination were performed at every visit. Patients with clear grafts but inadequate spectacle-corrected visual acuity due to aphakia or high refractive errors were referred for contact lens fitting. In patients who wore contact lenses for vision correction, the visual acuity was assessed with the lens. Snellen visual acuity data were converted to decimal values and then logMAR values for analysis. For vision in the range of counting fingers to no light perception, decimal values were assigned according to previously published reports.[37] Visual acuities of counting fingers at 3 feet, 2 feet, 1 foot, and "at face" were assigned values of 3/200, 2/200, 1/200, and 1/400, respectively, whereas visual acuities of hand motions, light perception, and no light perception were assigned values of 20/10,000, 20/12,500, and 20/15,400, respectively.

In regard to data collection, attention was paid to demographics, preoperative corneal diagnosis, comorbid conditions, concomitant surgical procedures, major postoperative complications, and visual outcomes. Only one eye of each patient was included. If a patient had surgery in both eyes during the specified time period, the first eye was included. Whenever a patient had multiple successive PKs in the same eye, only the first one was retained. Thus each patient was entered into the database only once. To retain all KPro cases in the analyses, if a patient had a KPro following a successive PK during the study period, only the KPro procedure was included. All KPro procedures were the initial ones; no successive KPro procedures were included. Chart review (performed by S.H. and K.D.) was completed as of November 2012 to allow maximum postoperative follow-up. Whenever there were questions in regard to the clarity of a graft or complication, one examiner (E.K.A.) was the final arbiter. Graft failure for PK procedures was defined as irreversible loss of clarity of the graft that prevented recovery of useful vision. This was determined on the basis of the clinical examination following previously established guidelines.[38] The KPro failure was determined when the device had to be explanted and the patient was re-grafted with either donor PK or a successive KPro or if the eye was enucleated for complications. Any patient with fewer than 3 months of follow-up at the time of data collection was excluded from visual acuity analyses but included in assessment of complications. Data analyses were performed using SAS version 9.3 (SAS Institute, Inc).

STATISTICAL METHODS

Comparisons between repeat PK and KPro groups were made using *t* tests and continuity-adjusted chi-square tests. Kaplan-Meier survival analysis was used to compare the success of PK and KPro surgery over time, with failure defined as (1) either donor graft opacity/haze/edema obscuring vision in the PK group or need for corneal successive surgery (another PK or KPro or enucleation) in both groups, and (2) vision returning to the preoperative visual acuity or worse during a 2-year follow-up period.

RESULTS

DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

A total of 80 eyes of 80 patients who had at least one previously failed full-thickness donor corneal transplant and who underwent either PK or a Boston type 1 KPro during the specified time period that satisfied the previously described inclusion criteria were included. The demographic features of the patients are summarized in Table 1. Fifty-three eyes underwent successive PK, and 27 eyes received a KPro device. There were no statistically significant differences between the two groups in regard to gender or mean age at the time of surgery. KPro eyes had a mean of 1.9 prior failed grafts compared to 1.5 for the PK eyes (*P*=.02). Mean postoperative follow-up time after successive surgery was 19.5 months in the PK group and 16.5 months in the KPro group (*P*=.09).

TABLE 1. DEMOGRAPHICS OF PATIENTS WHO UNDERWENT A SUCCESSIVE FULL-THICKNESS CORNEAL TRANSPLANT (PK) VS BOSTON TYPE 1 KERATOPROSTHESIS (KPRO) AFTER HAVING FAILED ONE OR MORE PK PROCEDURES IN A RETROSPECTIVE SAMPLE AT A SINGLE, TERTIARY CARE INSTITUTION

CATEGORY	PK	KPRO
No. of patients	53	27
% Male	45.3	63.0
Mean age at surgery (yr)	72	67
Mean No. of previous grafts	1.5	1.9
Mean postoperative follow-up (mo)	19.5	16.5

Primary corneal diagnoses leading to the initial donor corneal transplant are listed in Table 2. The most common primary diagnosis was aphakic or pseudophakic bullous keratopathy for both groups, consisting of almost half the patients. Nineteen percent of patients in the KPro group had a primary diagnosis of congenital corneal condition such as aniridia or Axenfeld-Rieger syndrome, which are known to have poor prognosis with PK.

TABLE 2. PRIMARY DIAGNOSIS OF PATIENTS WHO UNDERWENT A SUCCESSIVE FULL-THICKNESS CORNEAL TRANSPLANT (PK) VS BOSTON TYPE 1 KERATOPROSTHESIS (KPRO) AFTER HAVING FAILED ONE OR MORE PK PROCEDURES IN A RETROSPECTIVE SAMPLE AT A SINGLE, TERTIARY CARE INSTITUTION

DIAGNOSIS	PK (n=53)	KPRO (n=27)
Pseudophakic/aphakic bullous keratopathy	25 (47%)	11 (41%)
Fuchs' dystrophy	8 (15%)	2 (7%)
Keratoconus	6 (11%)	1 (4%)
Iridocorneal endothelial syndrome	1 (2%)	0 (0%)
Infectious keratitis	4 (8%)	3 (11%)
Traumatic injury	4 (8%)	2 (7%)
Glaucoma-associated corneal decompensation	2 (4%)	1 (4%)
Chronic uveitis	3 (5%)	2 (7%)
Congenital corneal disorders (Axenfeld-Rieger syndrome, aniridia)	0 (0%)	5 (19%)

Table 3 demonstrates that eyes in the KPro group had a significantly higher rate of ocular comorbidities compared to PK eyes prior to surgery; however, only corneal neovascularization reached statistical significance (*P*=.003).

Table 4 lists the additional surgical procedures simultaneously performed at the time of successive PK or KPro procedures. Because of the relatively larger number of patients with comorbidities (previous history of glaucoma, subluxated intraocular lens implants, hypotony, and concurrent retinal detachments) in the KPro group, a disproportionate number of additional procedures were performed at the time of surgery (*P*=.0001).

TABLE 3. PREOPERATIVE COMORBIDITIES IN PATIENTS WHO UNDERWENT A SUCCESSIVE FULL-THICKNESS CORNEAL TRANSPLANT (PK) VS BOSTON TYPE 1 KERATOPROSTHESIS (KPRO) AFTER HAVING FAILED ONE OR MORE PK PROCEDURES IN A RETROSPECTIVE SAMPLE AT A SINGLE, TERTIARY CARE INSTITUTION[*]

CATEGORY	PK (n=53)	KPRO (n=27)
All preoperative risk factorsn	53 (100%)	27 (100%)
Known history of glaucoma	36 (68%)	23 (85%)
Prior glaucoma surgery	22 (42%)	18 (67%)
Hypotony	2 (4%)	3 (11%)
Pseudophakia	42 (79%)	18 (67%)
Aphakia	10 (19%)	8 (30%)
Uveitis	6 (11%)	5 (19%)
Recurrent HSV keratitis	5 (9%)	0 (0%)
History of retinal detachment	7 (13%)	7 (26%)
Optic nerve atrophy	8 (15%)	7 (26%)
Corneal neovascularization	9 (17%)	13 (48%)
Lagophthalmos	0%	2 (7%)
Degenerative myopia	0%	1 (4%)

HSV, herpes simplex virus.

[*]Some of the patients had more than one comorbidity.

TABLE 4. CONCOMITANT PROCEDURES PERFORMED IN PATIENTS WHO UNDERWENT A SUCCESSIVE FULL-THICKNESS CORNEAL TRANSPLANT (PK) VS BOSTON TYPE 1 KERATOPROSTHESIS (KPRO) AFTER HAVING FAILED ONE OR MORE PK PROCEDURES IN A RETROSPECTIVE SAMPLE AT A SINGLE, TERTIARY CARE INSTITUTION[*]

PROCEDURE	PK (n=53)	KPRO (n=27)
All concomitant procedures	18 (34%)	24 (89%)
Intraocular lens implantation	5 (9%)	0 (0%)
Intraocular lens explantation	3 (6%)	18 (67%)
Tube shunt placement	0 (0%)	3 (11%)
Tube shunt removal	0 (0%)	2 (7%)
Anterior vitrectomy	6 (11%)	17 (63%)
Retinal detachment repair	2 (4%)	1 (4%)
Synechiolysis	4 (8%)	5 (19%)
Pupilloplasty	1(2%)	0 (0%)
Iridectomy	2 (4%)	0 (0%)
Epiretinal membrane peel	3 (6%)	0 (0%)
Retrocorneal/pupillary membrane removal	1 (2%)	1 (4%)

[*]Some of the patients had more than one concomitant procedure.

VISUAL OUTCOMES

The mean preoperative and postoperative visual acuity (logMAR) by surgery group at various follow-up time points is displayed in Figure 3. Eyes undergoing KPro had significantly worse mean preoperative visual acuity compared to eyes undergoing successive PK (hand motions vision vs counting fingers visual acuity on average, *P*=.01). Additionally, at each postoperative time point there was a greater mean improvement in visual acuity as compared to baseline for eyes undergoing KPro as compared to eyes undergoing successive PK (Figure 4).

Figure 3.

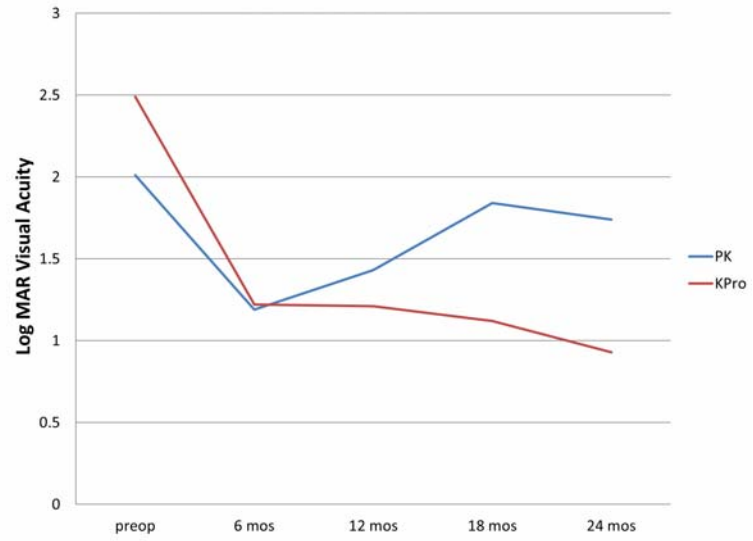

FIGURE 3

Mean preoperative and postoperative logMAR visual acuity at various postoperative time points (in months) in patients who underwent successive donor corneal transplant (PK) or Boston type1 keratoprosthesis (KPro) for previously failed PK in a retrospective sample at a single, tertiary care institution.

Figure 4.

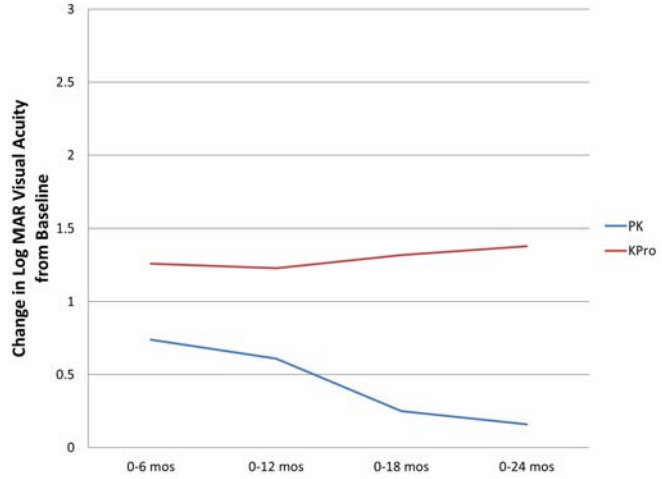

FIGURE 4

Mean change in vision (in logMAR) from preoperative values at various postoperative time periods (in months) in patients who underwent successive donor corneal transplant (PK) or Boston type1 keratoprosthesis (KPro) for previously failed PK in a retrospective sample at a single, tertiary care institution.

The distribution of actual visual acuity levels in the KPro and repeat PK groups is shown for the preoperative visit in Figure 5 upper, whereas the best-ever visual acuity and the visual acuity measured at the last postoperative visit by group are shown in Figure 5 middle and Figure 5 lower, respectively. As seen in the graphs, the improvement in vision was greater in the KPro group as compared to the PK group. Twenty-one of 27 patients (78%) in the KPro group and 5 of 49 patients (92%) in the PK group had better postoperative vision than prior to surgery. Among the patients who had any degree of improvement in their vision following the corneal surgery, about a third of the patients in the PK group (17 of 49, 35%) and about a half in the KPro group (10 of 21, 48%) attained a best-ever visual acuity of 20/70 or better. However, during the postoperative follow-up, only about half in each group (8 of 17 PK patients [47%] vs 4 of 10 KPro patients [40%]) were able to retain this level of vision at the end of the 2-year period.

Table 5 demonstrates the preoperative as well as mean, median, best-ever, and worst postoperative logMAR (Snellen) visual acuity levels in each group, at each postoperative time. The mean and median visual acuities at any time point were not statistically different between the two groups. However, in the KPro group, 70% (95% CI, 49%-85%) of eyes were able to retain vision better than baseline throughout the first year, and 66% (95% CI, 45%-81%) remained at vision better than baseline throughout the first 2 years. In the PK group, 66% (95% CI, 51%-77%) of eyes remained at vision better than baseline throughout the first year, whereas only 42% (95% CI, 25%-57%) of eyes retained vision better than baseline by the end of 2 years. Failure to retain vision better than baseline was more rapid in PK eyes as compared to KPro eyes (hazard ratio [HR]=1.67; 95% CI, 0.78-3.60; *P*=.19), though the observed differences were not statistically significant.

One patient with high axial myopia (axial length, 32.7 mm) in the KPro group had suprachoroidal hemorrhage intraoperatively, which resulted in no light perception vision on postoperative day 1. One additional patient also ended up with no light perception due to worsening of glaucoma. Only one patient in the PK group had no light perception vision at the last visit.

Figure 5 (upper)

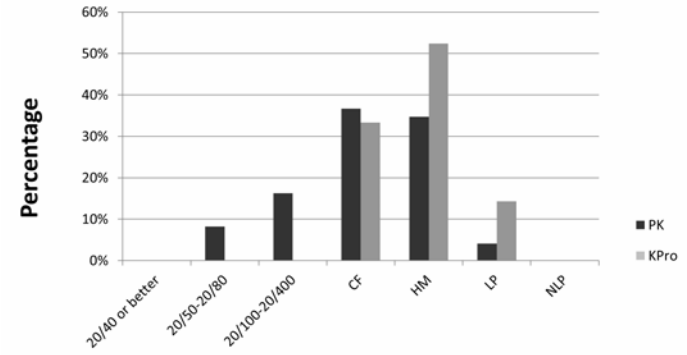

Figure 5 (middle)

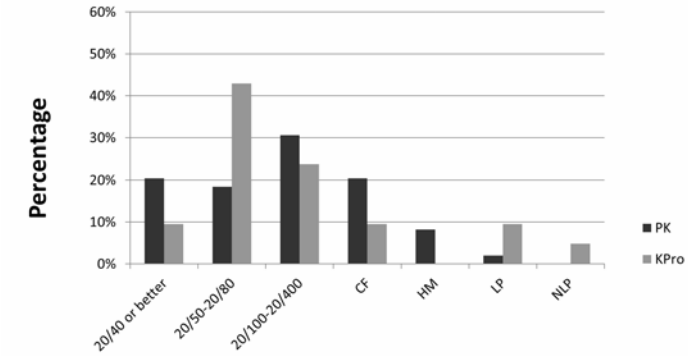

Figure 5 (lower)

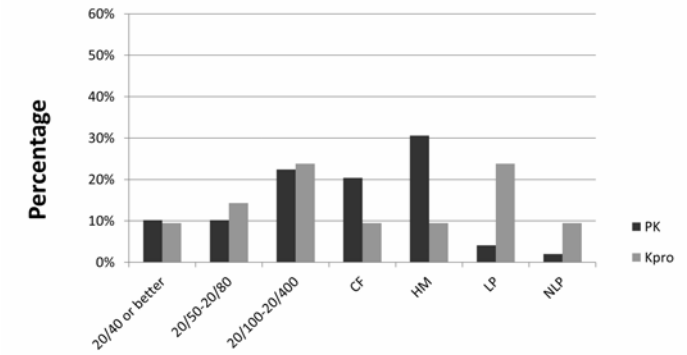

FIGURE 5

Preoperative visual acuity (upper), best-ever postoperative vision attained (middle), and visual acuity measured at the last examination (lower) in patients who underwent successive full-thickness corneal transplant (PK) vs Boston type 1 keratoprosthesis (KPro) for previously failed PK in a retrospective sample at a single, tertiary care institution. CF, counting fingers; HM, hand motions; LP, light perception; NLP, no light perception.

TABLE 5. SUMMARY OF LOGMAR (SNELLEN) VISUAL OUTCOMES IN PATIENTS WHO UNDERWENT A SUCCESSIVE FULL-THICKNESS CORNEAL TRANSPLANT (PK) VS BOSTON TYPE 1 KERATOPROSTHESIS (KPRO) FOR PREVIOUSLY FAILED PK IN A RETROSPECTIVE SAMPLE AT A SINGLE, TERTIARY CARE INSTITUTION

GROUP	VISUAL ACUITY	POSTOPERATIVE				
		PREOPERATIVE	6 mo	12 mo	18 mo	24 mo
PK*	n	53	48	38	31	16
	Mean	2.01 (20/2,000)	1.19 (20/310)	1.43 (20/540)	1.84 (20/1,400)	1.74 (20/1,100)
	Median	2.60 (20/8,000)	1.00 (20/200)	1.10 (20/250)	2.00 (20/2,000)	2.15 (20/2,800)
	Best	0.48 (20/60)	0.20 (20/32)	0.00 (20/20)	0.17 (20/30)	0.17 (20/30)
	Worst	2.80 (20/12,500)	2.70 (20/10,000)	2.80 (20/12,500)	2.80 (20/12,500)	2.80 (20/12,500)
	Mean change†		0.74	0.61	0.25	0.16
KPro	n	27	24	21	16	8
	Mean	2.49 (20/620)	1.22 (20/330)	1.21 (20/320)	1.12 (20/260)	0.93 (20/170)
	Median	2.70 (20/10,000)	0.89 (20/160)	1.10 (20/250)	0.85 (20/140)	0.44 (20/55)
	Best	1.00 (20/200)	0.17 (20/30)	0.00 (20/20)	0.17 (20/30)	0.10 (20/25)
	Worst	2.80 (20/12,500)	2.89 (20/15,400)	2.89 (20/15,400)	2.89 (20/15,400)	2.80 (20/12,500)
	Mean change†		1.26	1.23	1.32	1.38

*Three PK eyes (6%) were missing postoperative visual acuity data at one or more time points.
†Change is calculated as preoperative logMAR visual acuity – postoperative logMAR visual acuity; therefore a positive value is an improvement.

POSTOPERATIVE COMPLICATIONS

Postoperative complications are summarized in Table 6. Most of the patients in both the KPro and repeat PK group had at least one postoperative complication. The most common postoperative complication was glaucoma-related in both groups. Over a fifth of the patients in both groups (6 of 27 [22%] and 12 of 53 [23%] in the KPro and PK group, respectively, *P*=.97) subsequently underwent an additional glaucoma surgery during the postoperative follow-up for worsening of glaucoma. Of note, most of the patients in the KPro group had already had glaucoma surgery prior to the corneal surgery, most commonly a tube shunt (18 of 27 [67%] vs 22 of 53 [42%] in the KPro vs PK eyes). An additional 2 of 27 patients (11%) in the KPro group received concomitant glaucoma tube shunt at the time of corneal surgery.

Interestingly, the rate of presumed endophthalmitis (defined as intraocular infection diagnosed on clinical grounds requiring treatment by vitreous tap and intravitreal injection regardless of the growth in vitreous samples) was low and the same for both groups (2 of 53 in the PK group and 1 in 23 in the KPro group; 4%). Corneal epithelial defects treated with topical lubrication as well as antibiotic drops with or without positive corneal cultures were slightly more common in the KPro group (3 of 27 [11%] vs 3 of 53 [6%], *P*=.38). A similar proportion of those in the KPro group compared to the repeat PK group had postoperative retinal detachment (3 of 27 [11%] vs 5 of 53 [9%], respectively, *P*=.81) and/or macular edema and/or epiretinal membrane formation (5 of 27 [19%] and 8 of 53 [15%], respectively, *P*=.69). The most common postoperative complication in the KPro group was a retroprosthetic membrane formation (7 of 27, 26%). Although the patients in the PK group also developed retrocorneal membranes, the rate was much lower (2 of 53 [4%], *P*=.003). The majority of the retroprosthetic membranes in the KPro eyes were addressed with YAG laser membranotomy.

A Kaplan-Meier analysis was completed in which failure was defined as loss of graft clarity or need to remove/replace the original corneal transplant or enucleation of the eye (Figure 6). Using these criteria, 1- and 2-year survival in KPro eyes was 92% (95% CI, 71%-98%) and 86% (95% CI, 61%-95%), respectively. One- and 2-year survival in PK eyes was 78% (95% CI, 68%-87%) and 44% (95% CI, 28%-60%), respectively. Failure to retain graft clarity or avoid transplant replacement was significantly more rapid in PK eyes as compared to KPro eyes (HR=3.23; 95% CI, 1.12-9.28; *P*=.03).

TABLE 6. POSTOPERATIVE COMPLICATIONS NOTED IN PATIENTS WHO UNDERWENT A SUCCESSIVE FULL-THICKNESS CORNEAL TRANSPLANT (PK) VS BOSTON TYPE 1 KERATOPROSTHESIS (KPRO) AFTER HAVING FAILED ONE OR MORE PK PROCEDURES IN A RETROSPECTIVE SAMPLE AT A SINGLE, TERTIARY CARE INSTITUTION[*]

COMPLICATION	PK	KPRO
All postoperative complications	49 (92%)	22 (81%)
Glaucoma		
New-onset glaucoma	5 (9%)	0 (0%)
Worsening glaucoma requiring surgery	12 (23%)	6 (22%)
Hypotony	2 (4%)	5 (19%)
Presumed endophthalmitis	2 (4%)	1 (4%)
Corneal melt/nonhealing epithelial defects	3 (6%)	3 (11%)
Removal of device	NA	4 (15%)
Graft rejection/failure	24 (45%)	NA
Retroprosthetic/retrocorneal membrane formation	2 (4%)	7 (26%)
Retinal detachment	5 (9%)	3 (11%)
Macular edema/epiretinal membrane	8 (15%)	5 (19%)
Suprachoroidal hemorrhage[†]	0	1 (4%)

NA, Not applicable.
[*]Some of the patients had more than one postoperative complication.
[†]One patient in the KPro group had *intraoperative* suprachoroidal hemorrhage.

Figure 6.

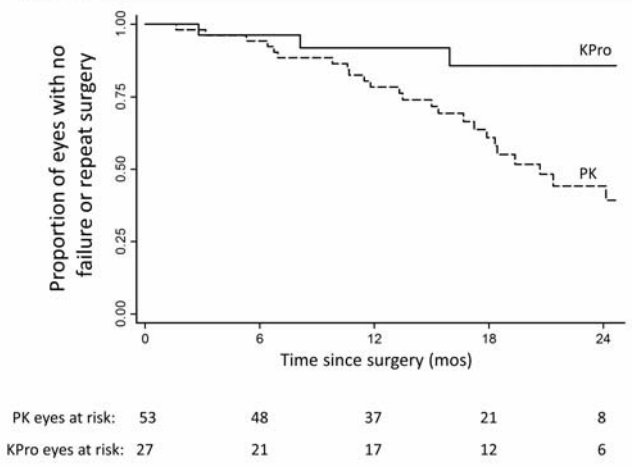

FIGURE 6

Kaplan-Meier survival curve demonstrating the proportion of eyes that were able to retain the original corneal transplant at various time points during a 2-year postoperative follow-up period, in patients who underwent a successive full-thickness corneal transplant (PK) vs Boston type 1 keratoprosthesis (KPro) after having failed one or more PK procedures in a retrospective sample at a single, tertiary care institution. Failure to retain graft clarity or avoid a successive transplant was significantly more rapid in PK eyes as compared to KPro eyes (HR=3.23; 95% CI, 1.12-9.28; *P*=.03).

DISCUSSION

Corneal transplant is becoming an increasingly common procedure to improve vision in eyes with opaque corneas. Currently, donor corneal transplantation is the most frequently performed organ transplant in developed countries.[38] In the United States alone, a total of 46,892 keratoplasty procedures were performed in 2013.[11] It is well known that donor corneal transplantation has excellent success rates, particularly in patients at low risk of graft failure, such as those with keratoconus, endothelial failure from dystrophy, or traumatic corneal scars. For those patients undergoing their initial corneal transplant, success rates are approximately 90% at 3 to 10 years follow-up.[2-7] However, there are certain patient profiles that are known to be associated with a significantly worse prognosis. Several recent publications have demonstrated that the single most important factor affecting the success of corneal transplantation is the preoperative diagnosis or indication for surgery.[9,10] The overall success rate decreases to less than 50% over the long term when the indication is corneal edema and is even lower if the eye is aphakic.[21,23,25,26] In addition, the rate of failure is likely underestimated in these studies, as successive transplants are generally performed only on patients in whom "there is a reasonable chance of success" with subsequent transplant. Presence of significant neovascularization of the host bed, history of glaucoma, and previous herpetic infections are known to decrease the likelihood of graft survival.[3,5,7] In particular, whether from an immunological rejection or primary endothelial failure from other reasons, re-grafts are consistently associated with lower survival rates.[9,10,21-27] Notably, 17% of those undergoing a PK in the United States in 2013 were successive corneal transplants, representing the second most common indication for full-thickness donor corneal transplantation after keratoconus.[11] This is in line with rates from other countries as well.[6,10,25]

In the United States, patients who have failed multiple corneal transplants may be offered an artificial corneal transplant, most commonly a Boston type 1 KPro. Prospective studies examining the long-term outcomes of KPro implantation in patients who have failed previous donor corneal transplants are lacking. However, multiple intermediate-term, retrospective studies demonstrate promising results with retention rates consistently above 80% and postoperative visual acuity 20/200 or better in most (over 70%) of the patients at an overall mean follow-up of 8.5 to 33.6 months.[29-33] The most recent multicenter, long-term outcomes analysis of KPro included 158 eyes of 150 patients from five centers in the United States.[34] Patients with autoimmune ocular surface diseases with severe dry eye were not excluded. All but three patients had at least 6 months of postoperative follow-up with a mean follow-up of 46.7± 26 months. Preoperatively 91% of the eyes had a visual acuity of 20/200 or worse. Postoperatively 70% of eyes improved to better than 20/200. Patients without improvement in their vision invariably had preexisting posterior segment comorbidity, most commonly advanced glaucoma. Of those, 50% retained this level of vision at 7 years. Device retention rate was 67% at 7 years. The cumulative incidence of complications was 49.7% for retroprosthetic membrane formation, 21.6% for requirement of glaucoma surgery, 18.6% for retinal detachment, and 15.5% for endophthalmitis. 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.[10] Fewer than 70% of patients who underwent a re-graft for bullous keratopathy ever attained a visual acuity of 20/200, and over 60% of the grafts failed within 2 years of follow-up. Importantly, the patients in the KPro series had significantly more complex eyes with worse preoperative vision and more frequent serious ocular comorbidities compared to the patients included in the Swedish Cornea Transplant Registry. Additionally, there was no difference in KPro retention in eyes with a primary KPro vs those with one or more prior failed grafts.

In particular, patients with a history of previous donor transplant failure from immunological rejection have high success rates with KPro implantation, as it essentially eliminates the risk of transplant rejection and failures and will not opacify. Patients who are well known to have poor prognosis with donor corneal transplantation, such as patients with aniridia,[14] severe ocular trauma (particularly chemical burns),[17] and herpetic keratitis,[18] also seem to have favorable prognosis with KPro. One advantage of KPro is rapid visual recovery with excellent *uncorrected* visual acuity in the early postoperative period even in aphakic patients. KPro eliminates the need for intraocular lens implantation and leaves virtually no refractive error (mean spherical refractive error of -0.57 D and mean astigmatism of 0.10 D).[36] KPro also has an advantage related to speed of visual recovery. Over 7% of patients attain their best-corrected visual acuity at 1 day, 24.6% at 1 week, and 70.6% at 3 months, cumulatively.[36] The patients who attained their best-corrected visual acuity after the first 3-month period most often are the ones who required multiple surgical procedures owing to either preexisting conditions or postoperative complications.

This retrospective study provides information on short-term outcomes of KPro in comparison to PK in a small group of patients who received a subsequent corneal procedure at a tertiary ophthalmological care center using relatively standard surgical technique and postoperative care. Only a third of the eyes receiving a subsequent PK ever attained a best-corrected visual acuity of 20/70 or better. About half of the successive PKs in this series failed within 2 years. This is in line with previously published series that demonstrated poorer visual outcomes for patients who underwent re-grafts as opposed to primary donor corneal grafts.[9,10]

This study does not address the question of under what circumstances and clinical grounds a corneal surgeon should go forward with another donor corneal transplant vs consider a KPro in a patient who already had failed a donor graft. However, our results show that over an intermediate-term postoperative follow-up period, the patients receiving KPro are more likely to attain improvement in their visual acuity and retain this improvement than patients receiving another PK. In distinct contrast to common perceptions, the postoperative complication profiles were similar in each group, except retroprosthetic membrane formation, which was significantly more common in KPro eyes.

As with all retrospective studies, our results must be interpreted cautiously. In this study, patients were not randomized. Eyes

receiving KPro tended to have a more complicated ocular history with significantly worse preoperative vision, a higher incidence of preoperative comorbidities, and more concomitant procedures performed along with the transplant. The study was performed at a single, tertiary referral care practice. As such, there might be potential bias toward having patients with more complex eyes with the possibility of lower visual potential and greater chances of failure with successive donor PK than previously reported series. The graft failure rate and best-corrected visual acuity in our PK patients were consistent with several previous reports[9,10] with the exception of a single study[24] that reported a 2-year survival rate of 78% for the third grafts and 73% for the fourth grafts. These results have yet to be duplicated. The mean improvement in the visual acuity in our KPro patients was less than in previous reports.[17-20] This might be due to the fact that most of the patients were new or referred to our practice with completely opaque corneas, influencing our ability to assess permanent damage to the optic nerve and retina and determine the level of expected improvement of vision in the postoperative period. This also had an influence on what type of surgery was offered to the patient. As such, the type of surgical procedure that the patient would receive was largely based on preoperative slit-lamp examination findings in regard to the feasibility of a PK and the number of previously failed donor PKs. The postoperative care in either group was not tightly standardized, but was tailored to the individual patient.

The follow-up period was short in both the PK and KPro patients. Follow-up time is likely to be very important in comparisons of the two procedures, since the varying complications have different rates of onset. Regrettably, we did not have enough numbers of cases in each group with longer follow-up. The main reason for this is that most of the patients who received surgery are referral cases and became lost to follow-up after several years. In addition, most of the patients who failed a successive PK subsequently underwent a KPro surgery. Those eyes could not be included, as we had aimed to include only the initial surgical procedure that was performed during the study period in order to eliminate the bias. Further, a portion of the cases with KPro also underwent successive KPro procedures due to complications. As stated in the "Methods" section, only the initial KPro procedures were included in this study, and once a KPro was removed, the eye was censored and not included in the analyses. The sample studied is too small to look at subgroups that may do much better with one or the other procedure. Nevertheless, this retrospective, intermediate-term case series is the only such study comparing the outcomes of successive PK to KPro in patients who have previously failed a full-thickness donor corneal transplant.

In conclusion, the logic to proceed with a subsequent PK or perform a KPro at a clinical setting remains unclear. Based on our limited data, in the selected patients who have failed one or more full-thickness donor corneal transplants, KPro might be a superior alternative to provide visual rehabilitation with similar postoperative risks to PK surgery in regard to serious complications. The preoperative patient profile predicting success with each of these procedures needs to be determined in prospective, randomized studies with longer postoperative follow-up.

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