The Boston Keratoprosthesis in Stevens-Johnson Syndrome

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PURPOSE: To evaluate the use of the Boston keratoprosthesis (KPro) in patients with Stevens-Johnson syndrome (SJS).

DESIGN: Retrospective, noncomparative, interventional case series.

METHODS: Sixteen eyes of 15 patients with SJS underwent KPro surgery at the Massachusetts Eye and Ear Infirmary from January 2000 through December 2005. The preoperative, operative, and postoperative findings were recorded. All patients underwent either the type I or type II Boston KPro surgery by one surgeon (C.H.D.). Retention of the prosthesis, best-corrected visual acuity, the need for surgical revision, and postoperative complications were recorded. The outcomes were compared with those of an earlier group of patients from the 1990s.

RESULTS: The mean age of patients was 50 ± 18 years (range, 23 to 74 years), and the mean duration of their disease was 10 ± 6.6 years. The mean follow-up period was 3.6 ± 1.5 years (range, 10.2 months to 5.6 years). Ten eyes underwent type II KPro surgery, whereas six eyes underwent type I KPro surgery. Twelve eyes (75%) achieved a visual acuity of 20/200 or better after surgery, with eight eyes (50%) achieving excellent vision of 20/40 or better. Visual acuity was maintained at 20/200 or better over a mean period of 2.5 ± 2.0 years. Preexisting glaucoma was found to be a significant risk factor for visual loss. There were no cases of KPro extrusion or endophthalmitis.

CONCLUSIONS: KPro in SJS has improved, largely because of the introduction of vancomycin prophylaxis and better glaucoma treatment. It seems to be superior to standard penetrating keratoplasty, with or without allografted stem cell transplantation, as judged from the literature. However, the outcome of the KPro in SJS is still substantially less favorable than in nonautoimmune diseases. (Am J Ophthalmol 2008;145:438–444. © 2008 by Elsevier Inc. All rights reserved.)

METHODS

WE REVIEWED ALL PATIENTS WHO UNDERWENT BOSTON KPro implantation from January 2000 through December 2005 at the Massachusetts Eye and Ear Infirmary. A total of 154 patients had undergone KPro surgery for complicated corneal disease or repeated failed corneal grafts. Among these patients, 16 eyes of 15 patients had
a basic cause of SJS, and the charts of these patients were reviewed retrospectively. All patients were operated on by the same surgeon (C.H.D.). The symptomatology, best spectacle-corrected visual acuity, physical findings, detailed ophthalmic examination results, surgical details, postoperative examination findings, and ocular complications were recorded on an itemized data collection form.
The preoperative evaluation included a detailed history, an assessment of the visual acuity and visual potential, tonometry, slit-lamp examination, fluorescein staining, and anterior segment photography. Light projection and color discrimination were used to evaluate the visual potential of the eyes. Particular attention was paid to the presence of glaucoma and ensuring that its treatment was optimal before KPro surgery. When the posterior pole could not be visualized, B-scan ultrasonography was performed to exclude preexisting retinal or optic nerve abnormalities.

To be considered for this operation, the eye to be operated on had to have a visual acuity at least light perception but worse than 20/400, and the opposite eye also had to have poor visual acuity. Eyes with some residual tear function underwent type I KPro surgery, whereas eyes that had clinically significantly reduced tear function or were completely dry were selected for type II KPro surgery. Glaucoma shunts, when indicated, were implanted either as a preliminary procedure, in conjunction with the KPro, or were implanted as a secondary procedure. The axial length of the eye was determined by A-scan biometry and the appropriate aphakic or pseudophakic KPro lens powers were selected. Donor corneal tissue was obtained from the Tissue Bank International (Baltimore, Maryland, USA).

- **SURGICAL PROCEDURE:** The surgery was performed under general anesthesia, unless contraindicated because of the medical status of the patient. The host corneal bed was prepared for trephination, which included releasing any symblepharon or fornical shortening that was present. Depending on the size of the cornea, an 8.0- or 8.5-mm corneal trephine was used. The KPro was assembled as previously described. Thus, briefly, the donor corneal carrier used was oversized by 0.5-mm compared with the recipient bed. The optic cylinder of the anterior plate was inserted through a 3-mm trephined central opening in the corneal button. The posterior plate of the prosthesis was screwed into firm apposition with the donor tissue, and, since 2003, a titanium locking ring has been applied to secure it in place.

Phakic eyes underwent extracapsular lens extraction and were left aphakic. Preexisting intraocular lenses were left in place if they were well positioned and fixated. Peripheral iridectomy was performed routinely. The donor corneal tissue with the assembled KPro was sutured in place with 10-0 or 9-0 nylon sutures. Finally, a Kontur soft contact lens (Kontur Contact Lens Co, Hercules, California, USA) 16.0 mm in diameter and with a 9.8-mm base curve was inserted over the type I KPro. In the type II counterpart, with the protruding anterior cylinder, an opening in the lid was created, usually during surgery, and the skin was tightened around the nub (Figure 1). Antibiotic drops and ointment were applied.

The postoperative medication consisted of topical vancomycin 14 mg/ml, fluoroquinolone 0.5%, and prednisolone acetate (1% suspension) eye drops, all administered four times daily initially. This dosage was tapered to twice daily over one month, to be continued as such for life. The postoperative examination included assessment of the visual acuity, intraocular pressure, optic disk, and fundus. Particular attention was paid to the intraocular pressure and whether signs of inflammation or infection were present. The soft contact lens was replaced if lost. The intraocular pressure could be estimated only by digital palpation of the globe. Other outcome measures that were assessed included retention of the prosthesis, best-corrected visual acuity over time, the need for surgical revision, and the presence of complications such as retroprosthesis membrane formation, infection, inflammation, or corneal melting. Cumulative vision-year functional success was defined as the number of years with visual acuity of 20/200 or better.

- **STATISTICAL ANALYSIS:** A Kaplan-Meier survival analysis was used to evaluate the visual outcome of the procedure. The influence of duration of disease, number of previous interventions, type of KPro implanted, age at surgery, and presence of glaucoma on the final visual outcome was evaluated using the log-rank test. Because of the small sample size, the P value of the two-sided log-rank test was obtained based on the permutation procedure. All analyses were conducted using Microsoft Excel for Windows software version 2003 (Microsoft Corp, Seattle, Washington, USA), with the level of significance taken as P < .05.

**RESULTS**

**SIXTEEN EYES OF 15 PATIENTS WITH SJS WHO UNDERWENT KPro surgery were studied. All but one patient had a severe form of SJS. One patient had the diagnosis of toxic epidermal necrolysis. Four patients were male and 11 were female. The mean age was 50 ± 18 years (range, 23 to 74 years), and the mean duration of their disease was 10 ± 6.6 years (range, two to 20 years). Nine eyes (56%) had previous failed penetrating keratoplasties, with four having three or more. Three had undergone limbal cell transplantation and one had undergone mucous membrane grafting. All eyes had a preoperative visual acuity of counting fingers at 1 foot or worse in the operated eye as well as in the fellow eye. The mean follow-up period was 3.6 ± 1.5 years (range, 10.2 months to 5.6 years).

Ten eyes (63%) underwent type II KPro surgery, whereas six eyes (38%) underwent type I KPro surgery. Seven eyes (44%) had lens extraction at the time of surgery and were left aphakic. Six eyes (38%) underwent anterior vitrectomy to remove vitreous in the anterior chamber that complicated previous cataract surgery. Ahmed shunts were placed in all 16 eyes (11 during KPro surgery, four before surgery, and one after surgery). In two cases, additional shunts had to be added later.
• VISUAL OUTCOME: Twelve eyes (75%) achieved a visual acuity of 20/200 or better (which was the equivalent of at least two lines of improvement in visual acuity) after surgery, with eight eyes (50%) achieving excellent vision of 20/40 or better (Table). Visual acuity in the 12 eyes was maintained at 20/200 or better over a mean period of 2.5 ± 2.0 years after surgery (range, six months to 5.4 years). Four eyes did not achieve a visual acuity of 20/200 or better after KPro surgery, despite an uneventful operative and postoperative course. These patients had preexisting ocular disease that was unrecognized until after the KPro surgery. The conditions included end-stage glaucoma in two eyes of the same patient, severe chronic uveitis in one eye, and severe, scarred age-related macular degeneration in one eye. The eye with macular degeneration retained good peripheral vision.

At the last follow-up visit, seven eyes (44%) retained good to excellent vision of 20/70 or better. Five eyes that had initial improvement in visual acuity subsequently deteriorated to less than 20/200 vision because of the following complications: corneal melting and leak in one eye, retinal detachment in two eyes, end-stage glaucoma in one eye, and vitreous hemorrhage in one eye. The latter four eyes (25%) subsequently lost all perception to light.

In terms of cumulative vision-years, 12 eyes (75%) that were able to reach a visual acuity of 20/200 or better were followed up for a total cumulative duration of 45.5 years. These eyes maintained a visual acuity of 20/200 or better over a period of 30 years cumulatively.

Kaplan-Meier survival analysis was used to evaluate the visual outcome of the procedure, with the primary end points being vision of 20/200 or worse, vision worse than the preoperative visual acuity, or loss of light perception. Patients who died, were lost to follow-up, or had no visual loss at the completion of the study period were treated as censored events (Figure 2).

However, the small sample size may reduce the quality of the Kaplan-Meier graph. Furthermore, it does not represent the individual changes in visual acuity until the full outcome is reached, and no inferences can be made on the learning curve of the surgeon. Therefore, the individual patient functional outcomes also are illustrated as color-coded bars, starting with the year surgery was performed (Figure 3).

• COMPLICATIONS: There were no cases of endophthalmitis, but in one patient, severe sterile inflammation developed immediately after the operation, causing inoperable retinal detachment. Complications that developed after KPro implantation included skin retraction, the formation of a retroprosthesis membrane, and worsening of glaucoma.

• TISSUE MELT AND LEAK: There were no cases of spontaneous extrusion of the implant. However, in four eyes (25%), aqueous leakage developed that was managed by replacement of the KPro in two type II KPro eyes and

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**Table:** Distribution of Eyes with the Various Visual Acuities before and after Implantation of a Keratoprosthesis and at the Last Postoperative Follow-up Visit

<table>
<thead>
<tr>
<th>Visual Acuity Preoperative</th>
<th>Best Visual Acuity Achieved</th>
<th>Visual Acuity at Last Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/15</td>
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<td></td>
</tr>
<tr>
<td>20/20</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
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<td>1</td>
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</tr>
<tr>
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<td>1</td>
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<tr>
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<td>20/100</td>
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<td>1</td>
</tr>
<tr>
<td>20/200</td>
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<tr>
<td>LP</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>NLP</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

CF = counting fingers; HM = hand movements; LP = light perception; NLP = no light perception.

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**Figure 2.** Kaplan-Meier analysis of eyes with SJS implanted with a KPro. Primary outcomes were loss of 20/200 vision or better (blue), loss of any vision better than preoperative (red), and loss of light perception (shaded area). The survival curve from Yaghouti and associates is reproduced for comparison (dotted gray line). Compared with eyes operated on between 1990 and 1997, a longer conservation of visual acuity was observed in this study. This can be attributed to advances in the KPro design, surgical technique, and management of postoperative complications, and particularly the long-term use of broad-spectrum antibiotics and a large diameter soft contact lens. NLP = no light perception.
replacement with a standard corneal graft in two other eyes. In the latter two cases, one patient had little vision because of underlying nerve damage secondary to glaucoma as well as chronic uveitis, and penetrating keratoplasty was performed to maintain light perception and for tectonic reasons. The other patient had severe leak and fistula formation along with choroidal hemorrhage that led to light perception visual acuity.

- **SKIN RETRACTION AROUND TYPE II KERATOPROSTHESIS:** In four of the 10 eyes (40%) that underwent type II KPro surgery, skin retraction developed around the stem of the KPro. Skin retraction was first noted an average of \(18.6 \pm 10.0\) months (range, 10 to 33 months) after surgery. These were managed by skin revision and wound closure at the site of retraction. Two eyes underwent two skin revisions and one eye required a third skin revision. Skin retraction continued to develop in the last eye despite two skin revisions, and subsequently the eye underwent replacement of the type II KPro, which prevented further recurrences.

- **RETROPROSTHESIS MEMBRANES:** Retroprosthesis membranes developed in nine eyes (56%), with subsequent recurrences in three eyes. The average time for the formation of the first retroprosthesis membrane was \(7.8 \pm 10.7\) months after KPro implantation. Of the 12 retroprosthesis membranes, eight were managed easily by neodymium: yttrium–aluminum–garnet (Nd:YAG) laser membranotomy (one session was enough except for one case that needed repeat YAG), three were removed by pars plana vitrectomy, and a last membrane was left untreated for the eye had lost vision because of a vascular event.

- **GLAUCOMA:** Twelve eyes (75%) had preexisting glaucoma before KPro surgery, reflecting the severity of anterior segment damage arising from SJS. Of these, six (50%) had previous failed corneal transplants, and three
had undergone limbal cell transplantation as well. Four eyes (25%) had glaucoma shunt procedures performed before surgery, 11 eyes (69%) had shunt implantation at the time of KPro surgery, and one eye (6%) had shunt implantation after surgery. Another two shunts were added after surgery because of failure of pressure control. In three eyes (19%), glaucoma developed after the operation. Of these cases of glaucoma, none were controlled by medication alone, and shunt surgery was required for medically uncontrolled glaucoma. End-stage glaucoma was a major cause for visual loss in operated eyes, resulting in one eye failing to achieve 20/200 vision and another two eyes losing best-corrected visual acuity after surgery.

**PROGNOSTIC FACTORS FOR VISUAL LOSS:** We looked at various possible risk factors for visual loss. The 12 patients with preoperative glaucoma had an average of 1.3 years of good vision (20/200 vision or better). This is in comparison with an average of 3.6 years in the four patients with no preoperative glaucoma. Comparing the survival curves of patients with and without preoperative glaucoma using the log-rank test results in a P value of .039, suggesting that the duration of vision is higher for patients without preoperative glaucoma.

Having had previous surgical interventions (e.g., penetrating keratoplasty, mucous membrane grafts, or limbal transplantation), implantation of a type I KPro (vs a type II KPro), long duration of the disease (more than 10 years), and advanced age of the patient (more than 50 years), were found not to be significantly correlated with a longer duration of good vision (P > .05). Caution should be exerted in interpreting this data, given the small size of the patient population.

**DISCUSSION**

STEVENS-JOHNSON SYNDROME IS A RARE AUTOIMMUNE disease which may lead to significant corneal changes and conjunctival scarring. It remains the worst prognostic category for KPro surgery. The prolonged severe inflammation associated with the disease makes the tissue around the KPro vulnerable to necrosis and melting, which can result in leakage, choroidals, and retinal detachment. Infection, in the form of endophthalmitis, also was a major concern in previous years. Yaghouti and associates previously reported the use of the Boston KPro in a series of patients that included seven eyes with SJS. None of these seven eyes retained 20/200 vision five years after implantation.

The results of the current study, however, are significantly better than the previous results, as demonstrated in the Kaplan-Meier survival analysis (Figure 2). Many eyes maintained an improvement over their preoperative vision at the last follow-up. This can be attributed largely to improvements to the KPro design, the surgical technique, and postoperative management, which have helped to improve significantly the visual outcome and to reduce the incidence of complications. These advances include a modification of the design to include perforation holes in the back plate to facilitate the nutrition and hydration of the corneal graft, which has reduced the incidence of corneal melting and aqueous leak. The recent addition of broad-spectrum topical antibiotics and the long-term use of a large-diameter therapeutic soft contact lens (in type I keratoprostheses) also have drastically reduced the risk of corneal melting, extrusion of the implant and endophthalmitis. The virtual elimination of postoperative endophthalmitis has been particularly important. The long-term prophylactic use of vancomycin eye drops combined with a third- or fourth-generation fluoroquinolone has had a dramatic effect. Nouri and associates previously reported that in 12% of patients undergoing KPro surgery in the 1990s (without vancomycin), endophthalmitis developed, with SJS patients having the highest incidence. In our more recent study in which all patients received vancomycin drops prophylactically, usually twice daily, in none of the 16 eyes did acute bacterial endophthalmitis develop, demonstrating the dramatic effect of this new antimicrobial medication regimen in preventing this devastating complication.

Another important problem related to KPro surgery is glaucoma. Preexisting glaucoma may worsen after surgery, especially in eyes that are inflamed, as is the case for SJS. Eyes that did not have a history of glaucoma also may develop glaucoma, probably because of the inflammation and progressive angle closure from peripheral anterior synechiae. In our study, we found that preexisting glaucoma was found to be a significant risk factor for eventual visual loss, which makes control of this condition particularly critical for good long-term visual outcome. Furthermore, the inability to obtain an accurate intraocular pressure measurement in the presence of a KPro makes assessment of the glaucoma treatment particularly difficult. Optic disk evaluation and sequential visual field assessment therefore are important in the assessment of glaucoma control. Whereas antiglaucoma eye drops are effective for type I implants, oral medications may be the only effective treatment for type II. In either case, optimization of the intraocular pressure control often is achieved with glaucoma shunt surgery, such as implantation of an Ahmed valve shunt. However, these chronically inflamed eyes are at a particularly high risk of failure of any glaucoma filtration surgery, and intraocular pressure control often requires both surgical and medical measures. Novel glaucoma shunt procedures to drain aqueous to extraorbital locations may be useful in the glaucoma management of these patients (Dohlman CH, Grosskreutz CL, Dudenhoefer EJ, Nouri M, Rubin PAD, unpublished data, “Connecting Ahmed valve shunt to the lacrimal sac..."
or nasal sinuses in severe glaucoma,” presented as a poster at the American Academy of Ophthalmology meeting, October 2002).

Retroprosthesis membrane formation is a common complication that is associated with all forms of KPro surgery.¹⁰,¹⁶ These membranes are postulated to form from inflammation induced by the release of allogeneic proteins in the anterior chamber and vary from condensations that coat the posterior surface of the optic to dense vascularized sheets of fibrotic tissue. In most of our cases, these were easily managed with Nd:YAG laser membranotomy. Only a few recurrent membranes that contained vessels or were too thick for laser treatment required surgical removal by pars plana vitrectomy.

In this study, we demonstrated that modifications to the design as well as the postoperative management of patients implanted with the Boston KPro have to significant improvements in the functional and anatomic outcome of this procedure over the situation existing just a decade ago. Operated eyes demonstrated a longer conservation of visual acuity compared with previous reports, and there was a dramatic decrease in serious sight-threatening complications, such as endophthalmitis. Still results are much inferior to those in patients with nonautoimmune diseases, and expectations must be adjusted accordingly. Patients with SJS who elect to have the procedure must be prepared for a life-long follow-up with an experienced KPro surgeon.

REFERENCES