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Keratoprosthesis: Preoperative Prognostic Categories

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Purpose. Recent advances aimed at preventing and treating complications after keratoprosthesis surgery have improved prognosis, but it has been suspected that various preoperative diagnoses may carry substantially different postoperative outcomes. This article attempts to clarify the ranking of prognostic categories for patients undergoing keratoprosthesis surgery. **Methods.** A retrospective review of the outcome in a recent series of 63 patient eyes operated at the Massachusetts Eye and Ear Infirmary between 1990 and 1997 and followed up for a minimum of 21 months. Anatomic retention of the device and the loss of vision caused by complications were recorded. The patients were divided into four categories according to preoperative cause. **Results.** Anatomically, one keratoprosthesis extruded spontaneously. Another 10 were permanently removed because of complications. Of the 63 eyes, 10 never achieved a visual acuity of at least 20/200 vision because of preexisting retinal or optic nerve damage. The remaining 53 had a visual acuity of 20/200 to 20/20 as follows: Stevens–Johnson syndrome ($n = 7$), after 2 years: 33%, after 5 years: 0%; chemical burn ($n = 17$), after 2 years: 64%, after 5 years: 25%; ocular cicatricial pemphigoid ($n = 20$), after 2 years: 72%, after 5 years: 43%; graft failure in noncicatrizing conditions (dystrophies, degenerations, or bacterial or viral infections) when a repeat graft was expected to have a poor prognosis ($n = 19$), after 2 years: 83%, after 5 years: 68%. The difference in outcome between the Stevens–Johnson syndrome outcome group and the graft failure group or the ocular cicatricial pemphigoid group was statistically significant. In the group of 53 eyes, visual acuity was restored to 20/200 to 20/20 for a cumulative total of 138 years. **Conclusion.** Outcome of the keratoprosthesis surgery varied markedly with preoperative diagnosis. Most favorable was graft failures in noncicatrizing conditions, whereas Stevens–Johnson syndrome was the worst. Ocular cicatricial pemphigoid and chemical burns occupied a middle ground. The difference between the groups seemed to correlate with the degree of past preoperative inflammation.
Key Words: Keratoprosthesis—Preoperative prognostics.

The concept of using a keratoprosthesis in eyes with corneal blindness has been known for more than 200 years.[1] Even in recent times, postoperative complications have been so frequent and severe that this approach is rarely resorted to outside a few centers with special interest. One of the gaps of knowledge that has retarded progress in this field has been uncertainty of prognosis in the various categories of disease that can lead to corneal blindness. Some authors have commented on the severity of glaucoma after chemical burns,[2] the relatively benign course in corneal edema,[3,4] and the difficulties with patients with Stevens-Johnson syndrome.[5] However, strict numerical comparisons have been absent. We have suggested that the various pathologic causes differ markedly and can be ranked.[6] We have tried to quantify and modify this ranking scheme based on analysis of keratoprosthesis surgery performed during the period from 1990 to 1997. The history of keratoprosthesis designs, materials, and methods have been reviewed extensively elsewhere.[7]

METHODS

In our practice, an all-polymethylmethacrylate device was used in all cases. The mechanical specifications and the manufacturing of the two types of keratoprosthesis used, namely the Dohlman-Doane type I and type II keratoprostheses (Fig. 1), have been described previously.[8,9] All procedures were performed by one surgeon (C.H.D.). In general, to be considered for this operation, the eye to be operated on did not have a visual acuity better than 20/400 (Table 1), and the opposite eye also had to have poor visual acuity. A B-mode ultrasound was used to help rule out preexisting intraocular abnormalities, such as end-stage glaucoma and retinal detachment, although it was not always reliable in this respect. The stepwise surgical technique used in implanting both types of keratoprostheses has been described previously.[10] In the postoperative period, the patients were routinely treated with topical antibiotic drops and topical anticollagenase medication, 1% medroxyprogesterone (diluted from Provera, Pharmacia-Upjohn, Kalamazoo, MI, U.S.A.), for a prolonged period. The antibiotics were rotated every 3 or 4 months to prevent development of resistant organisms. The details of postoperative follow-up regimen in these patients have been described in the past.[6]

Outcome after keratoprosthesis surgery has often been expressed as comparison between preoperative vision and postoperative vision at one point in time ("final" vision). This method is particularly treacherous in the field of keratoprosthesis, because disastrous complications can occur many years after surgery. The following definitions are used in this article: anatomic success, defined as the number of keratoprosthesis devices remaining in the

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FIG. 1. Keratoprosthesis designs used in the study. Type I (left) is used in eyes with good tearing and blink function. Type II (right) has an added anterior nub for through-the-lid placement in eyes with end-stage dry eye.

eyes without extrusion or without a need for replacement, regardless of visual acuity; the number of postoperative repair procedures performed; the number of eyes with preexisting retinal or severe glaucomatous optic nerve damage before the keratoprosthesis surgery precluding them from achieving a visual acuity of 20/200 or better at any time in the postoperative period; incidence of postoperative disastrous complications, such as endophthalmitis, retinal detachment, or end-stage glaucoma, which not only reduced visual acuity markedly but also eliminated hope of restoration of vision in the future; cumulative vision-year functional success, defined as the ratio of the cumulative years with visual acuity of 20/200 or better to total duration of time since surgery.

RESULTS

Keratoprostheses were inserted in 63 eyes of 60 patients between March 1990 and July 1997. The patients' mean age was 64 years (range, 24–93 years; standard deviation, 19.5 years). Follow-up at the time of analysis ranged from 21 months to 101 months (mean, 47 months; standard deviation, 23 months). The preoperative and postoperative visual acuity as of April 1999 are noted in Table 1 . Ten patients finishing with visual acuity of hand motions or finger counting had the keratoprosthesis well in place but had unrecognized severity of glaucoma or retinal problems that must have existed before surgery. Most patients with postoperative visual acuity of light perception (LP) or no light perception (NLP) had severe complications, such as infection or retinal detachment.

TABLE 1. *Pre- and postoperative visual acuity as of April 1999*

	Number of eyes	
Last VA	Preoperative	Postoperative (last exam)
20/20		4
20/25		6
20/30		5
20/40		2
20/50		1
20/60		3
20/70		2
20/80		1
20/100		1
20/200		6
20/400	2	1
CF @1′	2	
CF @2′	7	4
CF @3′	1	
CF @4′	1	
HM	26	5
LP	24	11
NLP		11

VA, indicates visual acuity; CF, count finger; HM, hand motion; LP, light perception; NLP, no light perception.

Approximately half the eyes were phakic and underwent extracapsular cataract extraction (52%) and partial or total iridectomy (53%). Vitrectomy was performed in 26 (45%) of those eyes, and a glaucoma shunt was placed in 45 (72%). Type I keratoprosthesis was implanted in a total of 42 (67%) eyes, and type II was implanted in 21 (33%) eyes (Fig. 2). The most common complications encountered in the course of follow-up were glaucoma in 29 (46%) patients, retroprosthetic membrane in 23 (37%), tissue necrosis and melting in 18 (29%), retinal detachment in 12 (19%), and endophthalmitis in 5 (8%). These complications were largely overlapping.

The patients' preoperative conditions were grouped into four categories. These included repeat graft failure in noncicatrizing conditions, such as dystrophies, degenerations, bacterial or viral keratitis, and uveitis; ocular cicatricial pemphigoid; chemical burn; and Stevens–Johnson syndrome. The numbers of patients in each category are listed in Table 2.

In terms of anatomic outcome, 7 of 42 type I (17%) and 3 of 21 type II (14%) keratoprosthesis were permanently removed because

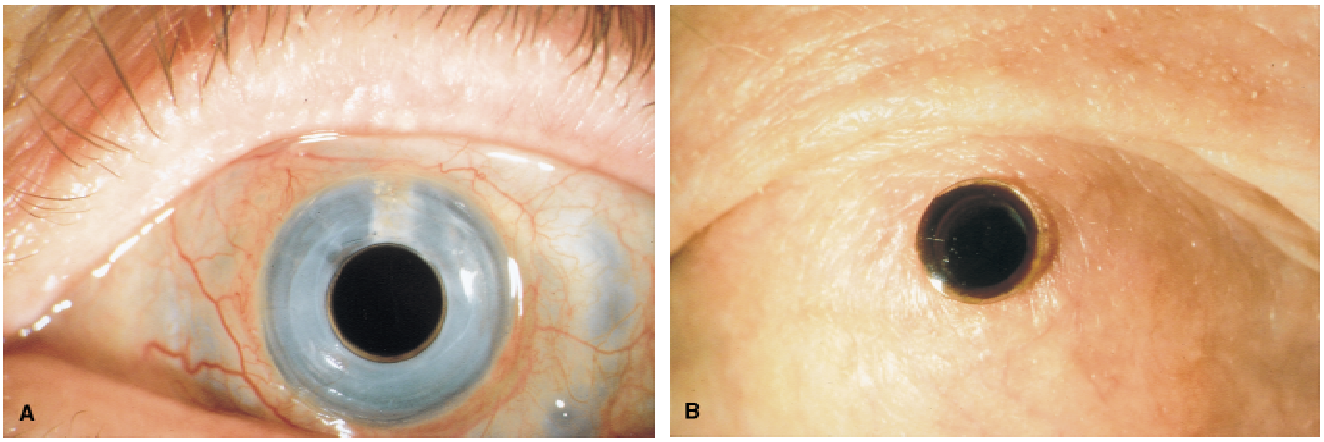

FIG. 2. Example of successful implantation of a type I **(A)** and type II **(B)** keratoprosthesis. The patient on the left had edema and multiple graft failures after bacterial keratitis. Two and a half years after surgery, visual acuity is 20/25. The patient on the right had pemphigoid. Three years later, visual acuity is 20/30.

TABLE 2. *Postoperative repair procedures*

Preop diagnosis	Number of eyes			
	Total	Major† repairs	Minor‡ repairs	Yag laser membranectomies
Graft failure*	19	6 (32%)	8 (42%)	7 (37%)
Pemphigoid	20	8 (40%)	10 (50%)	7 (35%)
Chemical burn	17	4 (24%)	7 (41%)	4 (24%)
Stevens-Johnson syndrome	7	5 (71%)	6 (86%)	5 (71%)
Total	63	23 (37%)	31 (49%)	23 (37%)

* Includes corneal edema,[11] lattice dystrophy,[1] salzmann's degeneration,[1], herpes simplex,[2] Zoster,[2] atopy.[1]

† Includes procedures performed in the main operating room, such as keratoprosthesis removal and replacements, glaucoma shunt revisions, and vitrectomi.

‡ Includes procedures performed in the office or in the minor surgery suite, such as tissue melt repair in type I and skin revisions in type II (the three categories of major repairs, minor repairs, and Yag membranectomies heavily overlap).

of complications. In addition, five (12%) type I and one (5%) type II keratoprosthesis were replaced. The number of major repairs performed in the main operating room, the number of minor repairs performed in the minor surgical suite or the office, and the number of yttrium–aluminum–garnet (YAG) laser membranectomies performed in each of the four diagnostic category are summarized in Table 2. The minor repairs in type I prosthesis mainly consisted of tissue melt repairs by insertion of a sliver of cornea or collagen material under the front plate. Type II occasionally required tightening of the skin around the anterior nub of the keratoprosthesis. When major repairs were needed, the number of operations ranged from one to two in those patients (mean, 1.5; standard deviation, 0.5) and included procedures such as keratoprosthesis revision or replacement and glaucoma shunt revision. Similarly, in those patients who needed minor repairs, they ranged from one to eight procedures (mean, 2; standard deviation, 2.1), and the number of YAG laser membranectomies ranged from one to five procedures per patient (mean, 2; standard deviation, 1.6). The numbers in the three categories of major repairs, minor repairs, and YAG membranectomies performed overlapped heavily. The numbers of any repairs (major, minor, or YAG capsulotomies) performed in the four diagnostic categories were 7 (100%) in Stevens–Johnson syndrome, 12 (57%) in pemphigoid, 8 (47%) in chemical burns, and 7 (39%) in the repeat graft failure group. The overall number of any repairs performed in all groups was 36 (57%).

Ten eyes never achieved a visual acuity of 20/200 or better after keratoprosthesis surgery, despite an uneventful operative and postoperative course. These patients had preexisting conditions that were unrecognized until after the keratoprosthesis surgery. The severity of the preexisting disease in those eyes (Table 3) could explain the poor postoperative visual acuity reported in those patients.

TABLE 3. *Diagnostic findings in eyes that never achieved 20/200 or better visual acuity after surgery*

Diagnostic finding*	Number of eyes
Age-related macular degeneration with subretinal neovascularization	1
End-stage glaucoma	5
Macular and retinal scarring	3
Chronic posterior uveitis with retinitis	1
Total	10

* Preexisting conditions noted after keratoprosthesis surgery.

In the remaining 53 eyes, at some point after achieving a visual acuity of 20/200 or better, 23 (42%) lost the gained vision (Tables 4 and 5, Fig. 3). The primary complications leading to visual loss in those 23 eyes in decreasing frequency were end-stage glaucoma, total retinal detachment, endophthalmitis, and severe recurrent retroprosthetic membrane that was not responsive to YAG laser capsulotomy (Table 4). Of the 10 eyes that lost vision because of end-stage glaucoma, seven had glaucoma shunt operation at the time of the surgery. Furthermore, of the seven eyes that lost vision because of a total retinal detachment, three had undergone a vitrectomy at the time of the keratoprosthesis surgery.

Determining the functional outcome in terms of cumulative vision-years in the 53 eyes is a convenient way to measure success after keratoprosthesis surgery. In the group of eyes with graft failure, for example, 47 years of cumulative visual acuity of 20/200 or better was achieved in 54 years of cumulative follow-up. Therefore in this study, eyes with graft failure without inflammation had a postoperative visual acuity of 20/200 or better for 86% of their cumulative time since the surgery. This is what was defined as the vision-year functional outcome. The vision-year functional outcome for each of the four diagnostic groups is listed in Table 5. The overall vision-year functional outcome in all diagnostic categories was 138 years with 208 years of cumulative follow-up. This should be related to the fact that slightly more than half of the operated eyes (57 %) had a visual acuity of 20/200 or better as of April 1999. Examples of successful clinical outcome are shown in Figure 2.

A Cox proportional hazard analysis was used to model vision failure against disease type. The primary endpoint was vision failure to worse than 20/200. Death with no vision failure, loss to follow-up with no vision failure, and absence of vision failure at the completion of the study period were all treated as censored event times. A significantly greater rate of vision loss in the

TABLE 4. *Severe complications leading to a loss of the achieved visual acuity of 20/200 or better after surgery*

Preoperative diagnosis	Primary complications		
	Endophthalmitis, no. eyes	End-stage glaucoma, no. eyes	Retinal detachment, no. eyes
Graft failure	1	1	1
Pemphigoid	2	2	1
Chemical burn	0	3	3
Stevens-Johnson syndrome	2	2	2
Total	5	8	7

TABLE 5. *Visual outcome of 55 patient eyes that achieved at least 20/200 visual acuity at some time postoperatively*

Preoperative diagnosis	No. eyes		Cumulative years	
	Total	Eventually lost VA of 20/200 or better	Postoperative	With VA of 20/200 or better
Graft failure	15	3 (20%)	54	47
Pemphigoid	18	6 (33%)	62	44
Chemical burn	14	6 (43%)	62	37
Stevens-Johnson syndrome	6	6 (100%)	30	10
Total	53*	23 (43%)	208	138

* Patients with preexisting conditions incompatible with 20/200 or better visual acuity were excluded from this table (follow-up time and results refer to the data of April 1, 1999).

VA indicates visual acuity.

Stevens–Johnson syndrome group relative to the graft failure group ($p = 0.01$) and ocular cicatricial pemphigoid group ($p = 0.03$) was seen (Fig. 3). There was a trend toward greater vision loss relative to the chemical burn group, but this did not reach statistical significance ($p = 0.1$). There was no statistically significant difference between the graft failure, ocular cicatricial pemphigoid, and chemical burn groups noted.

A Kaplan-Meier graph loses clarity when some groups have low numbers, especially at the end of the follow-up period. Such a graph also does not represent the learning curve of the surgeon. Therefore, the outcome of the individual patients are also illustrated as lines, starting with the year of surgery (Fig. 4).

DISCUSSION

In eyes with severely diseased corneas such that standard corneal transplantation has poor prognosis, a keratoprosthesis can provide good visual acuity when successful. However, it can also result in disastrous complications. In contrast to failure after corneal transplantation, these severe complications are not infrequent and seem to be able to strike even a long time after the surgery. In eyes with a preoperative visual acuity of light perception or hand motions, such disasters may not have caused much reduction of vision in the end as compared with the starting point, but they usually make any future restoration hopeless. Clearly, the goal of further developments in this field must be to improve long-term safety. Some success in this direction has recently been achieved by adopting temporary postoperative tissue coverage, antiulcerative topical treatment, heavy dosage of antiinflammatory drugs, design changes of the device, glaucoma shunts, and simpler and more effective repair procedures.[6]

Because of the frequency of severe complications, analysis of outcome after keratoprosthesis surgery is important in enabling surgeons to approach future patients with the knowledge of indications and prognosis. Our analyses include duration of attained vision, anatomic success, the number of postoperative repair procedures, frequency of previously unidentified but preexisting posterior segment disease precluding good vision, and the incidence of disastrous complications.

Our results should be translated cautiously into general recommendations for indications. As long as a standard penetrating keratoplasty has a reasonable chance of success, a keratoprosthesis is clearly not indicated. Also, in general, if the opposite eye has substantial vision, there is no need to subject the patient to this type of elaborate surgery and follow-up examinations. A keratoprosthesis currently might be indicated in end-stage pemphigoid and after severe chemical burns. In addition, there may be cases of noncicatrizing conditions in which repeated grafts have failed but might benefit from keratoprosthesis. Patients with Stevens–Johnson syndrome, however, have so far proven to have too great a risk for keratoprosthesis. This overall difference seems to be strongly related to the degree and chronicity of past inflammation

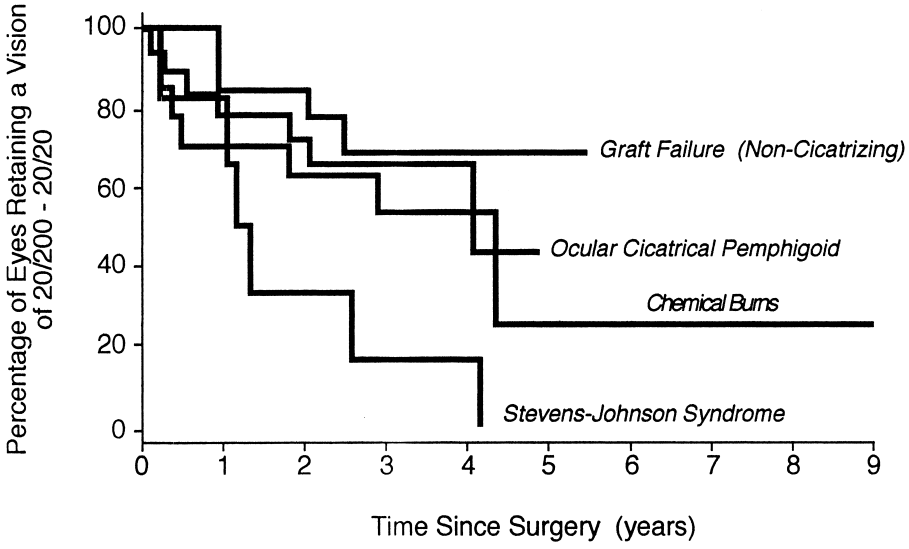

FIG. 3. Kaplan-Meier analysis of 53 eyes with keratoprosthesis that at one time reached a postoperative vision of 20/20 to 20/200. The attrition of eyes with this level of vision with time is indicated for each of the four patient categories.

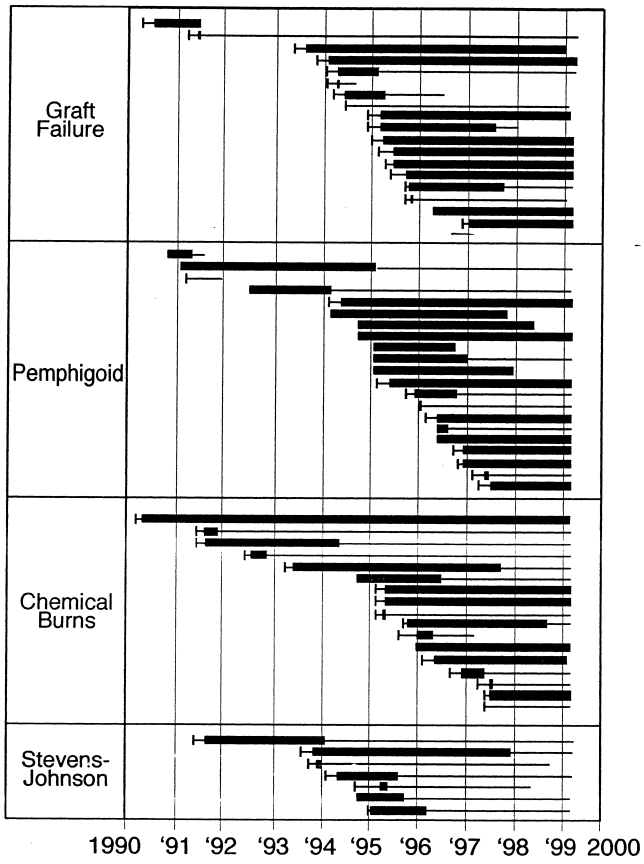

FIG. 4. A supplementary way to show visual attrition in the same group of 53 patient eyes. The lines represent the individual patients and their follow-up time. Sections with thick bars indicate periods with a vision of 20/200 to 20/20. The thin line represents time with visual acuity less than 20/200.

in the eyes to undergo surgery. In Stevens–Johnson syndrome, for instance, the chronic inflammation around the keratoprosthesis makes the tissue vulnerable to necrosis, melting, leakage, and infection. As the field progresses, indications may change, but a conservative approach currently is recommended because this procedure is complicated, has a narrow safety margin, and requires intensive follow-up. There are other special aspects in terms of prognosis. Patients with severe chemical burns, for example, may have occult damage to the retina or the optic nerve that may become observable only after providing media clarity. In addition, patients with chemical burns seem to be extremely sensitive to any increase in intraocular pressure. There is often a progression of glaucoma in this group of patients despite the presence of a functioning glaucoma valve shunt and normal intraocular pressure.[11] It is possible in these patients that the ganglion cells have been damaged by the initial chemical injury, making them particularly vulnerable to further insult.

Finally, it must be emphasized that the outcome results reflect only our keratoprosthesis design, our surgical techniques, and our postoperative follow-up regimens. It is possible that with other types of prostheses, and in the hands of other surgeons, different results may emerge. This is less likely, however, and we have good reason to believe in the generally adverse role of past ocular inflammation in the eyes undergoing keratoprosthesis surgery in relation to visual outcome.

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