EXTENDED REPORT

Repeat penetrating keratoplasty: indications, graft survival, and visual outcome

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Aim: To determine graft survival and visual outcome after repeat penetrating keratoplasty (PKP).
Methods: Retrospective review of the medical records patients who underwent repeat PKP at the King Khaled Eye Specialist Hospital (KKESH) between 1 January 1991 and 31 December 2002.
Results: 243 repeat PKP performed in 210 eyes of 208 patients, who had also had initial PKP at KKESH, were included in the study. The mean follow up was 43 months (range 1–170). At the most recent examination, 114 (54.3%) grafts were clear. The overall survival rate was 98% at 1 year, 83% at 2 years, and 49% at 5 years. The best graft survival was in eyes with an original diagnosis of keratoconus (93.8%) and the worst was in eyes with Fuchs' dystrophy (23.1%). Overall, 29.6% of eyes achieved a final visual acuity greater than 20/200, while only 4.8% were 20/40 or better. The best visual prognosis was in eyes with an original diagnosis of stromal dystrophy and keratoconus.
Conclusion: Although the prognosis for repeat PKP is poorer than that of initial PKP, reasonable outcomes can be obtained with repeat PKP with careful case selection.

Repeat corneal transplantation continues to be an important and increasingly common indication for penetrating keratoplasty (PKP).[1–23] In most large eye care centres, repeat PKP is the second leading indication for corneal transplantation, accounting for a mean of approximately 18% (range, 6% to 41%) of cases performed.[1–23] In the United States, repeat PKP increased from 6.9% of cases performed in 1992 to 11.3% of cases performed in 1997. At the King Khaled Eye Specialist Hospital (KKESH) in Saudi Arabia, repeat PKP accounted for only 3.2% of cases of keratoplasty performed between 1988 and 1992, but accounted for 11.3% of cases performed between 1998 and 2002, despite a constant total number of corneal transplants.[23]

The present study provides insights into the contributions of indications for initial keratoplasty to repeat PKP, and provides valuable prognostic information that will assist ophthalmologists and patients in making the decision as to whether or not to proceed with another attempt after graft failure.

PATIENTS AND METHODS

After obtaining approval from the institutional review board, medical records of every patient who underwent repeat PKP at KKESH between 1 January 1991 and 31 December 2002 were retrospectively reviewed. Patients who had their initial PKP at KKESH were included in the study, while patients who had initial keratoplasty (lamellar or penetrating) elsewhere, but were subsequently referred to KKESH for repeat PKP were excluded from the analysis. Patients who had repeat PKP at KKESH after previous lamellar keratoplasty at KKESH were excluded from the analysis.

All cases were performed by members of the anterior segment division of the department of ophthalmology at KKESH utilising donor tissue that fulfilled all requirements of the Eye Bank Association of America. Topical corticosteroids and antibiotics were administered in tapering dosage after surgery. Topical antibiotics were discontinued after approximately 2 weeks, but topical steroid treatment continued for at least the first 6 months. Most patients were evaluated on the first postoperative day, after 2 weeks, after 3, 6, 9, 12, 18, 24 months, and yearly thereafter. The protocol for suture removal varied between ophthalmologists, with some removing all sutures after 12–36 months, and others only selectively removing loosened sutures or tight sutures that induced unacceptable astigmatism.

Data extracted included the original diagnosis responsible for the decision to perform the first corneal transplant, preoperative risk factors, concomitant operative procedures, postoperative complications, graft clarity, and visual acuity. Graft clarity was recorded at the most recent examination in all eyes, as well as just before additional repeat PKP. Graft failure was strictly defined as irreversible loss of central graft clarity, irrespective of the level of visual acuity. The time of graft failure was defined as the visit at which irreversible loss of graft clarity was first documented. Postoperative visual acuity was recorded at the most recent follow up examination. The best corrected visual acuity was used, if available. If the best corrected visual acuity was not available, uncorrected visual acuity was used for purposes of statistical analysis.

All data were entered onto a Microsoft Excel spreadsheet and analysed using two commercial statistical software packages, SPSS g (1998) and Epi-Info 6 (1994). The χ^2 test, the Fisher exact test, and the *t* test were used for analysis of variance. Nominal p values were used for all comparisons, and the term significance was accepted if the p value was <0.05. Graft survival curves were produced using the standard Kaplan-Meier methods and the life table. Data were entered and analysed separately for each eye for patients undergoing bilateral repeat PKP.

RESULTS

A total of 473 repeat PKP were performed at KKESH during the study period. Of these, 243 repeat PKP that were performed in 210 eyes of 208 patients after failure of initial PKP done at KKESH were included in the study. The

Abbreviations: ABK, aphakic bullous keratopathy; KKESH, King Khaled Eye Specialist Hospital; PBK, pseudophakic bullous keratopathy; PKP, penetrating keratoplasty

Table 1 Initial indication *v* repeat penetrating keratoplasty

Initial indication	Eyes	% (eyes)	Repeat PKP 1	Repeat PKP 2	Repeat PKP 3	Repeat PKP 4	Total cases	% (total cases)
PBK/ABK	62	29.5	62	5	2	0	69	28.4
Scar	53	25.2	53	5	3	1	62	25.5
Keratoconus	16	7.6	16	1	0	0	17	7.0
Fuchs' dystrophy	13	6.2	13	3	1	0	17	7.0
Therapeutic/tectonic	12	5.7	12	1	1	0	14	5.8
Stromal dystrophy	12	5.7	12	0	0	0	12	4.9
Others	42	20.0	42	10	0	0	52	21.4
Total	210	100.0	210	25	7	1	243	100.0

PBK/ABK, pseudophakic/aphakic bullous keratopathy; PKP, penetrating keratoplasty.

remaining 230 were done after failure of initial keratoplasty performed elsewhere or following failure of lamellar keratoplasty done at KKESH and were not included in the study. Among included cases, mean patient age at the time of surgery was 60.4 (SD 16.3) years (range 14–100). The mean follow up was 43 months (range 1–170).

The initial indications for corneal transplantation at KKESH in eyes that subsequently underwent single or multiple repeat PKP are summarised in table 1. Ten or more cases were performed for six different initial diagnostic categories. The leading indication for repeat PKP was pseudophakic/aphakic bullous keratopathy (PBK/ABK), followed, in order, by corneal scarring, keratoconus, Fuchs' dystrophy, therapeutic/tectonic PKP, and stromal dystrophy.

The number of eyes in which repeat PKP was done was 4.2% of the total number of primary PKP done in the same period (table 2). This ratio ranged from a high of 12.3% for eyes with PBK/ABK to a low of 1.2% for eyes with keratoconus. Eyes with PBK/ABK were significantly overrepresented as a relative contributing factor to repeat PKP compared to initial PKP (29.5% *v* 10.6%, $p = 0.001$), while those with keratoconus were significantly under-represented (7.6% *v* 27.9%, $p = 0.001$). There was no significant difference in the relative contributions of the indications of corneal scars, Fuchs' dystrophy, therapeutic/tectonic, or stromal dystrophy to initial or repeat keratoplasty.

There was a repeat PKP survival rate of 98% at 1 year, 83% at 2 years, and 49% at 5 years. At the most recent examination, 114 (54.3%) grafts were clear after one or more repeat PKP (table 3), ranging from a high of 93.8% in eyes in which the initial PKP was performed for keratoconus to a low of 23.1% in eyes with an initial diagnosis of Fuchs' dystrophy (table 4). The likelihood of survival of a repeat PKP was significantly correlated with the diagnosis leading to the initial PKP ($p<0.001$). The probability of graft survival was not significantly reduced with multiple repeat PKP compared to the first repeat PKP.

The relation between associated ocular conditions, concomitant operative procedures, and postoperative complications and graft survival is summarised in table 5. The presence of glaucoma or ocular surface disease was significantly associated with a higher rate of graft failure, while neovascularisation was not. Concomitant glaucoma surgery was a significant risk factor for graft failure, but simultaneous cataract surgery was not. Postoperative complications of endothelial graft rejection episodes, persistent epithelial defects, and microbial keratitis were all significantly associated with an increased risk of graft failure.

The final visual outcome after repeat PKP is summarised in table 6. Overall, 29.6% of eyes achieved a final visual acuity greater than 20/200, while 4.8% were 20/40 or better. The best visual prognosis was in eyes with an original diagnosis of stromal dystrophy and keratoconus, in which a final visual acuity greater than 20/200 was achieved in 75.0% and 68.8% of eyes, respectively, and 25% of eyes achieved a final visual acuity of 20/40 or better. Less than 25% of eyes with an

Table 2 Indications for initial and repeat penetrating keratoplasty (1991–2002)

Initial indication	Repeat PKP (eyes)	Relative contribution (%)	Initial keratoplasty (eyes)	Relative contribution (%)	p Value*	Repeat PKP/ initial keratoplasty (%)
PBK/ABK†	62	29.5	506	10.6	<0.001	12.3
Scar	53	25.2	1577	32.9	NS	3.4
Keratoconus	16	7.6	1339	27.9	<0.001	1.2
Fuchs' dystrophy	12	6.2	136	2.8	NS	9.6
Therapeutic/tectonic	12	5.7	397	8.3	NS	3.0
Stromal dystrophy	12	5.7	197	4.1	NS	6.1
Others	42	20.0	644	13.4	0.02	6.5
Total	210	100.0	4796	100.0		4.2

*Variation in relative contribution as a cause of initial PKP *v* relative contribution to repeat PKP.
†PBK/ABK, pseudophakic or aphakic bullous keratopathy; PKP, penetrating keratoplasty.

Table 3 Graft clarity *v* repeat keratoplasty

Repeat PKP No	Eyes	Clear	%	Failed	%	Clear grafts (cumulative)	%
1	210	98	46.7	112	53.3	98	46.7
2	25	13	52.0	12	48.0	111	52.9
3	5	2	40.0	3	60.0	113	53.8
4	3	1	33.3	2	66.7	114	54.3

PKP, penetrating keratoplasty.

Table 4 Survival of repeat penetrating keratoplasty *v* initial indication for surgery

		After initial repeat PKP				After all repeat PKP			
Initial indication	Eyes	Clear	%	Failed	%	Clear	%	Failed	%
PBK/ABK	62	27	43.5	35	56.5	30	48.4	32	51.6
Scar	53	23	43.4	30	56.6	26	49.1	27	50.9
Keratoconus	16	14	87.5	2	12.5	15	93.8	1	6.2
Fuchs' dystrophy	13	2	15.3	11	84.6	3	23.1	10	76.9
Therapeutic/tectonic	12	6	50.0	6	50.0	8	66.7	4	33.3
Stromal dystrophy	12	11	91.7	1	8.3	11	91.7	1	8.3
Others	42	15	35.7	27	64.3	21	50.0	21	50.0
Total	210	98	46.7	112	53.3	114	54.3	96	45.7

PBK/ABK, pseudophakic or aphakic bullous keratopathy; PKP, penetrating keratoplasty.

Table 5 Survival of repeat keratoplasty *v* risk factors

Risk factors	No	Clear	%	Failed	%	p Value*
Associated ocular conditions						
Glaucoma†	104	37	35.6	67	64.4	<0.001
Ocular surface disease	96	36	37.5	60	62.5	<0.001
Neovascularisation	36	16	44.4	20	55.6	0.20
Concomitant operative procedures						
Lens extraction	29	13	44.8	16	55.2	0.32
Glaucoma procedure	14	3	21.5	11	78.6	0.012
Postoperative complications						
Endothelial graft rejection	53	15	28.3	38	71.7	<0.001
Persistent epithelial defect	35	7	20.0	28	80.0	<0.001
Microbial keratitis	30	9	30.0	21	70.0	0.005

*Probability of graft survival *v* eyes without the same risk factor.
†Includes 68 eyes with pre-existing glaucoma and 36 eyes with new onset postoperative glaucoma.

original diagnosis of PBK/ABK, corneal scar, and Fuchs' dystrophy obtained visual acuity better than 20/200 after repeat PKP.

DISCUSSION

The ratio of repeat to initial keratoplasty is a function of not only the failure rate of initial grafts, but the willingness to repeat the procedure. Although graft failure rates range from a low of 8% for keratoconus to a high of 57% for therapeutic/tectonic grafts in our patient population,[24–27] the number of repeat PKP did not exceed 12.3% for any surgical indication, and only constituted 4.2% of total cases of initial PKP during the same time period. This low ratio of repeat to initial keratoplasty reflected caution for performing repeat PKP in a setting where the prognosis for successful surgery was often guarded and many patients were on the eye bank waiting list for initial surgery.[23]

Historically, repeat PKP have had a poorer prognosis for survival than initial keratoplasty. Repeat PKP share the same risk factors for graft failure as the initial keratoplasty with respect to the recipient diagnosis, but additional risk factors have been acquired since the original procedure such as increased age in all cases, and glaucoma escalation, development of neovascularisation, and worsening of ocular surface disease in many cases.[2 7 19 21] In a direct comparison of initial and repeat keratoplasty performed on 696 patients by a single surgeon, Weisbrod and associates[21] reported a significant difference in 5 year survival (64.6% *v* 45.6%, respectively; $p<0.001$). The 5 year Kaplan-Meier survival rate for all cases in the present series of 49% is comparable to other series in which there was a mean 5 year survival rate of 48%[5 7 20 21] (range 30%[20] to 66%[5]). There was considerable variation in overall graft survival between surgical indications in our series, with more than 90% of grafts remaining clear after repeat PKP in eyes with keratoconus and stromal dystrophies, approximately 50% remaining clear in eyes with PBK/ABK and corneal scars, and less than 25% remaining clear in eyes with Fuchs' dystrophy. As in previous studies,[2 7 19 21 28] the presence of preoperative ocular surface disease, the performance of simultaneous glaucoma surgery, the presence of postoperative glaucoma, the postoperative development of a persistent epithelial defect or microbial keratitis, or the occurrence of an endothelial rejection episode all contributed to an increased risk of graft failure after repeat PKP in our

Table 6 Visual outcome *v* original indication for keratoplasty

	All cases		PBK/ABK*		Scar		Fuchs' dystrophy		Keratoconus		Tectonic/ therapeutic		Stromal dystrophy		Others	
Visual acuity	No	Cum %	No	Cum %	No	Cum %	No	Cum %	No	Cum %	No	Cum %	No	Cum %	No	Cum %
≥20/40	10	4.8	2	3.2	0	0	0	0	4	25.0	1	8.3	3	25.0	0	0
20/50–20/160	52	29.6	13	24.2	10	18.9	2	15.4	7	68.8	5	50.0	5	75.0	10	23.9
CF-20/200	90	68.1	28	69.4	26	67.9	6	61.5	3	91.7	3	75.0	4	100.0	20	71.4
HM	36	85.2	13	90.3	11	88.7	5	100.0	0	91.7	2	91.7	0	100.0	5	83.3
LP	15	92.4	5	98.4	2	92.5	0	100.0	2	100.0	1	100.0	0	100.0	5	95.2
NLP	7	100.0	1	100.0	4	100.0	0	100.0	0	100.0	0	100.0	0	100.0	2	100.0
Total	210		62		53		13		16		12		12		42	

*Pseudophakic/aphakic bullous keratopathy.

patients. Conversely, the presence of neovascularisation or simultaneous cataract surgery did not significantly increase the risk of graft failure.

Unfortunately, the prognosis for visual outcome after repeat PKP was poor with less than 5% of eyes achieving a final visual acuity of 20/40 or better, and less than 30% of eyes obtaining vision that was better than 20/200. Our findings are consistent with three major Western studies in which the percentage of eyes with a visual acuity of 20/40 or better ranged from 3.6% to 9.0%, and less than 25% obtained vision that was better than 20/200.[2 4 7] As expected, eyes with stromal dystrophy and keratoconus, in which the prognosis for graft survival was excellent and other conditions compromising visual potential are usually absent, had a much better visual prognosis than eyes with diagnoses associated with poor graft survival and other associated conditions, such as macular oedema or optic atrophy, which further compromised the visual prognosis, even if graft clarity could be maintained.

KING KHALED EYE SPECIALIST HOSPITAL CORNEA TRANSPLANT STUDY GROUP

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