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A comparison of endothelial and penetrating keratoplasty outcomes following failed penetrating keratoplasty: A registry study

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ABSTRACT

Purpose To compare graft survival and visual outcomes for endothelial keratoplasty (EK) after a first penetrating keratoplasty (PK), with outcomes of repeat PK after a first PK.

Methods 400 eyes with a second graft (65 EK, 335 PK) performed after failure of a primary PK were identified through the Australian Corneal Graft Registry, a national prospectively-followed cohort. Grafts were performed after January 2008 (follow-up of the second graft extending to 6.75 years maximum). Kaplan-Meier graft survival plots were constructed and Cox proportional hazards regression was used to identify independent risk factors for graft failure. Best corrected Snellen visual acuity (BCVA) at last follow-up was compared with pre-graft acuity.

Results Poorer Kaplan-Meier graft survival was observed for PK-EK compared with PK-PK (log-rank=29.66, $p<0.001$). Variables retained in multivariate analysis as significantly influencing survival of the second graft included graft type (PK-EK or PK-PK, $p<0.001$), length of survival of the previous PK (global $p=0.011$), graft era (global $p=0.018$), occurrence of rejection in the second graft ($p=0.005$) and a history of raised intraocular pressure at any time ($p=0.048$), but not indication for the first graft. BCVA improved in the majority of surviving grafts and attainment of 6/12 vision was similar for both PK-EK and PK-PK groups.

Conclusions Our Registry findings suggest that repeat penetrating keratoplasty may deliver a better outcome in terms of graft survival than endokeratoplasty after a failed PK that was performed initially for keratoconus or pseudophakic bullous keratopathy. For surviving grafts, visual outcomes appear equivalent across groups.

INTRODUCTION

Endothelial keratoplasty (EK), including Descemet stripping endothelial keratoplasty (DSEK) or Descemet stripping automated endothelial keratoplasty (DSAEK),[1-3] is increasingly used to treat corneal opacification. Despite the potential benefits of EK,[4-6] such procedures fail in the early post-operative period at a higher rate than do penetrating grafts.[7, 8] Recent practice has seen subsequent EK used as an alternative to repeat full-thickness transplantation.[9, 10] This option may be chosen when the corneal stroma and epithelium of the previous PK are still relatively healthy, but when endothelial cell loss or failure has led to a loss of vision.[4] Because survival of penetrating grafts decreases as the number of previous grafts increases,[1, 11] EK following PK is also used in cases for which the original indication for PK was keratoconus,[4, 10, 12] in the expectation that graft survival might be improved. However, EK has its own risk factors, and repeat EKs still exhibit poorer survival than first EKs.[5]

The impact of a previous PK on an EK, and the influence of the original pathology on the second graft, is not yet fully understood. In addition, uncertainties remain over the influence that technical variations exert on graft survival.[4, 9, 13] We analysed the survival and visual outcomes of DSEK/DSAEK following previous PK, in comparison to repeat PK, performed over the same time period in a national cohort. We further examined the comparative survival of PK-EK and PK-PK for common indications for graft.

METHODS

The Australian Corneal Graft Registry (ACGR) is a national, prospectively-followed cohort of over 30,000 corneal transplantations, performed in Australia since May 1985. The Institutional Ethics Committee of Flinders University approves the operations of the Registry,

which are carried out in accordance with the Declaration of Helsinki. The census date for the present analyses was June 2015. Data for this study were contributed by 69 surgeons. Records of grafts that matched the following criteria were identified: PK or DSEK or DSAEK (both manual and automated dissection techniques acceptable) performed on or after 1st January 2008; first repeat (second) graft in the eye; previous PK also registered with the ACGR; and follow-up information available within the ACGR. Grafts were categorised into two groups: eyes with repeat penetrating keratoplasty (hereafter abbreviated PK-PK), and eyes with DSEK/DSAEK following penetrating keratoplasty (PK-EK).

Data collection

Data collection methods employed by the ACGR are described in detail elsewhere.[7] Contributing surgeons listed ocular co-morbidities that might affect graft survival and/or visual acuity at graft registration and each follow-up visit thereafter, and at registration also specified the desired/anticipated outcome of keratoplasty: improved vision; relief of pain; structural repair (tectonic graft); improved cosmesis; any combination of these outcomes.

Best-corrected Snellen acuity (BCVA) was recorded at the time of graft and at each follow-up. BCVA was measured with prescribed correction (spectacles, contact lens, or both) but not with pinhole. The visual outcome of surviving grafts was assessed as the percentage of grafts for which BCVA had improved following transplantation, and whether a BCVA of 6/12 had been achieved at most recent follow-up.

Statistical analyses of graft survival

Kaplan-Meier survival analysis was performed in SPSS version 22 (IBM Corp, Armonk, NY, USA) to compare survival time of the second graft across the two groups (PK-PK; PK-EK),

using the log-rank statistic to test statistical significance. Further univariate subgroup analyses were performed to compare PK-PK and PK-EK survival for each main indication for graft, the influence of length of survival of the previous graft and history of rejection episodes in the first graft on survival of the second graft, and the impact of oversizing or undersizing the EK in comparison with the previous PK.

Variables identified in the 2015 ACGR report[1] as significantly affecting survival of PK, DSEK/DSAEK, or both were included in a multivariate Cox-proportional hazards regression analysis, clustered by patient, conducted in STATA 11 (Stata-Corp, College Station, TX, USA). The length of survival of the previous graft was also included. Allocation of continuous variables into categorical groups was performed based on review of the published evidence, the distribution of data, and the findings of the 2015 ACGR report.

The final model included variables with a p-value of $p<0.05$, with variables eliminated in a stepwise manner, beginning with the least significant variable, until all variables contributed significantly to the model. For categorical variables, a global test was applied to calculate the overall p-value. Tests were conducted to ensure that the assumption of proportional hazards was not violated and to identify any time-varying covariates.

RESULTS

Corneal graft survival and reasons for failure

We identified 335 PK-PKs and 65 PK-EKs in 400 eyes, performed by 69 surgeons (range 1-44 grafts), that met the inclusion criteria for analysis. Follow-up ranged from 1 day (for primary non-functioning grafts) to 6 years and 9 months. The difference in corneal graft survival between these groups was significant (log-rank=29.66, $p<0.001$), with diminished survival found for the PK-EK group compared with the PK-PK group (Figure 1).

Failure was reported for 77 PK (23.0%) and 25 EK (38.5%). Primary graft failure was reported for three PK (original indication for graft: one keratoconus, one pseudophakic bullous keratopathy [PBK], one fungal keratitis) and six EK (original indication for graft: two keratoconus, two PBK, one Fuchs endothelial corneal dystrophy [FECD], one penetrating eye injury). Graft detachment was reported for seven EK, of which six resolved with treatment, and one, performed for previous graft rejection following a penetrating eye injury, progressed to primary graft failure. Failures of five EK and 22 PK were attributed to irreversible immunological rejection. Other reasons for failure included: endothelial failure (11 PK, 7 EK); infection (7PK, 2 EK); corneal ulcer (5 PK); glaucoma (4 PK); trauma (2 PK, 1 EK); corneal opacity or scar (2PK, 1 EK); and unknown cause (2 PK).

Subgroup univariate analyses

A comparison of variables previously shown to influence the survival of PK,[1] EK or both revealed significant differences between recipients of PK-PK compared with PK-EK (Table 1). Specifically, recipients of PK-PK were more likely ($p<0.05$) to have been transplanted for keratoconus and less likely to have been transplanted for PBK or FECD, more likely to have exhibited pre-graft neovascularization, more likely to have undergone surgery in an earlier era, and more likely to be phakic, than recipients of PK-EK. The length of survival of the initial PK also differed significantly across groups ($Chi^2=8.08$, $p=0.044$) with 21% of grafts that had a repeat PK having previously failed within two years, compared with 11% that went on to have a subsequent EK.

Table 1 Characteristics of the total cohort

	Total (n=400)	PK-PK (n=335)	PK-EK (n=65)	P value
Indication for graft				0.003*
Keratoconus	122 (30.5%)	112 (33.4%)	10 (15.4%)	
Pseudophakic bullous keratopathy	83 (20.8%)	63 (18.8%)	20 (30.8%)	
Fuchs endothelial corneal dystrophy	62 (15.5%)	46 (13.7%)	16 (24.6%)	
Other	133 (33.3%)	114 (34.0%)	19 (29.2%)	
Reason for failure of first graft				<0.001*
Endothelial failure	152	108	45	
Rejection	98	78	20	
Recurrent keratoconus/astigmatism	64	64	0	
Other	85	85	0	
Rejection episode(s) in first graft	129 (32.3%)	105 (31.3%)	24 (36.9%)	0.378
Rejection episode(s) in second graft	64 (16.0%)	57 (17.0%)	7 (10.8%)	0.209
History of raised intraocular pressure	112 (28.6%)	92 (28.1%)	20 (31.3%)	0.614
Pre-graft inflammation or steroid use	244 (61.8%)	200 (60.6%)	44 (67.7%)	0.283
Pre-graft neovascularisation	221 (55.3%)	198 (59.1%)	23 (35.4%)	<0.001*
Length of survival of first graft				0.044*
Less than 2 years	76 (19.0%)	69 (20.6%)	7 (10.8%)	
2/3 years	67 (16.8%)	50 (14.9%)	17 (26.2%)	
4/5 years	47 (11.8%)	37 (11.0%)	10 (15.4%)	
6 years or longer	210 (52.5%)	179 (53.4%)	31 (47.7%)	
Recipient age group				0.076
Under 40 years	31 (7.8%)	28 (8.4%)	3 (4.6%)	
40 to 49 years	44 (11.0%)	40 (11.9%)	4 (6.2%)	
50 to 59 years	68 (17.0%)	62 (18.5%)	6 (9.2%)	
60 to 69 years	73 (18.3%)	56 (16.7%)	17 (26.2%)	
70 to 79 years	86 (21.5%)	72 (21.5%)	14 (21.5%)	
80 years or older	98 (24.5%)	77 (23.0%)	21 (32.3%)	
Donor age group				0.495
Under 40 years	30 (8.4%)	28 (8.4%)	2 (3.1%)	
40 to 49 years	25 (6.3%)	23 (6.9%)	2 (3.1%)	
50 to 59 years	70 (17.5%)	56 (16.7%)	14 (21.4%)	
60 to 69 years	132 (33.0%)	110 (32.8%)	22 (33.8%)	
70 to 79 years	97 (24.3%)	81 (24.2%)	16 (24.6%)	
80 years or older	46 (11.5%)	37 (11.0%)	9 (13.8%)	
Interstate transportation of donor cornea	27 (6.8%)	21 (6.3%)	6 (9.2%)	0.384
Donor central endothelial cell count density**				0.125
<2500 cells/mm²	25 (9.8%)	19 (9.2%)	6 (12.5%)	
2500 to 2999 cells/mm²	93 (36.6%)	73 (35.4%)	20 (41.7%)	
3000 to 3499 cells/mm²	115 (45.3 %)	93 (45.1%)	22 (45.8%)	
3500+ cells/mm²	21 (8.3%)	21 (10.2%)	0 (0.0%)	
Graft size				0.482
8 mm or smaller	165 (43.3%)	142 (44.7%)	23 (36.5%)	
8.25 mm to 8.5 mm	143 (37.5%)	116 (36.5%)	27 (42.9%)	
8.75 mm or larger	73 (19.2%)	60 (18.9%)	13 (20.6%)	
Graft era**				0.009*
2008/2009	146 (37.0%)	131 (39.3%)	15 (24.2%)	
2010/2011	132 (33.4%)	113 (33.9%)	19 (30.6%)	
2012/2013	117 (29.6%)	89 (26.7%)	28 (45.2%)	
Surgeon had <25 followed grafts	46 (11.5%)	38 (11.3%)	8 (12.3%)	0.824

Eye phakic post-graft	100 (25.0%)	95 (28.4%)	5 (7.7%)	<0.001*
Desired outcome of graft				0.453
To improve visual acuity and reduce pain	71 (17.8%)	57 (17.0%)	14 (21.5%)	
To improve visual acuity, no pain present	277 (69.3%)	231 (69.0%)	46 (70.8%)	
To reduce pain, no improved vision expected	11 (2.8%)	10 (3.0%)	1 (1.5%)	
Other reason***	13 (3.3%)	13 (3.9%)	0 (0.0%)	
Not specified	28 (7.0%)	24 (7.2%)	4 (6.2%)	

* p<0.05 ** Grafts from 2014 excluded from analysis (2 PK:PK, 3 PK:EK); Grafts with unknown endothelial cell count density excluded from analysis (129 PK:PK, 17 PK:EK); ***Other reasons included structural repair (12) and improved cosmesis (1).

Graft survival for PK-PK and PK-EK data combined, differed significantly overall based on original indication for graft (log-rank=9.65, p=0.022). Further analysis showed that diminished graft survival was observed in the PK-EK group compared with the PK-PK group in cases for which the original indication was keratoconus (Figure 2a; PK-PK: n=112, PK-EK: n=10; log-rank=27.61, p<0.001) or PBK (Figure 2c; PK-PK: n=63, PK-EK: n=20; log-rank=19.67, p<0.001), but not FECD (Figure 2b; PK-PK: n=46, PK-EK: n=16; log-rank=1.46, p=0.228) or other indication (Figure 2d; PK-PK: n=114, PK-EK: n=19; log-rank=0.85, p=0.356). Exclusion of cases in which the repeat graft was performed for an indication other than rejection or endothelial failure reduced the log-rank values overall (PK-PK: n=186, PK-EK: n=65; log-rank=23.43, p<0.001), as well as for keratoconus (PK-PK: n=35, PK-EK: n=10; log-rank=9.72, p=0.002) and PBK (PK-PK: n=50, PK-EK: n=20; log-rank=16.34, p<0.001), but the comparisons remained significantly different.

Length of survival of the previous graft exerted a significant effect on survival of the second graft (log rank=23.27, p<0.001), with improved survival in cases in which the first graft had survived for at least two years, whereas occurrence of rejection episodes in the first graft did not influence survival of the second graft (log-rank=0.42, p=0.515). No significant difference was found in survival of PK-EK based on undersizing or oversizing the

second graft in comparison with the first (p=0.87).

Multivariate analysis of factors influencing PK-PK and PK-EK graft survival

A Cox proportional hazards regression model was developed to calculate adjusted risk factors for graft failure, controlled for potential confounders. Thirteen grafts were excluded because of missing data. The final model incorporated the type of second graft (PK or EK), the era over which the second graft was performed, history of raised intraocular pressure at any point, whether a rejection episode was reported in the second graft, and length of survival of the first PK, chi^2=75.23, p<0.001 (Table 2). Survival did not differ significantly between grafts that were performed in 2008/09 and 2010/11 (p=0.832). There were no significant effects on graft survival amongst the groups in which the original PK had survived for two or more years (all p>0.75).

Table 2 Cox proportional hazards regression model

	n	Hazard Ratio	Standard Error	p-Value	Global p-value	95% Confidence Interval
Type of second graft						
PK	325	1.00				
EK (DSEK/DSAEK)	62	3.67	0.96	<0.001		2.20 – 6.12
Length of survival of first graft						
Less than two years	74	1.00			0.011	
Two or three years	65	0.44	0.15	0.013		0.23 – 0.84
Four to five years	46	0.42	0.13	0.006		0.23 – 0.78
Six or more years	202	0.46	0.14	0.009		0.26 – 0.82
Graft Era						
2012/2013	116	1.00			0.018	
2010/2011	129	0.50	0.14	0.013		0.29 – 0.87
2008/2009	142	0.47	0.14	0.010		0.27 – 0.84
Rejection episode(s)						
None	323	1.00				
At least one	64	1.97	0.47	0.005		1.23 – 3.16
Raised intraocular pressure in past						
No	227	1.00				
Yes	110	1.59	0.37	0.048		1.00 – 2.51

Visual outcome

The desired outcomes from graft are shown in Table 1, with the majority performed to improve visual acuity. There were no significant differences in the desired outcome (Chi^2=3.669, p=0.453), or the pre-graft BCVA (Chi^2=2.304, p=0.512), of the two groups. Visual outcome (BCVA at last follow-up) for each of four main indications for graft (FECD, PBK, keratoconus, other) for grafts performed to improve vision are shown in Table 3. Comparative statistical analyses were not possible because of the low number of surviving PK-EK grafts with BCVA data provided. However, BCVA improved in the majority of surviving grafts. Attainment of 6/12 vision differed by indication for graft, but was similar for both PK-EK and PK-PK groups. Co-morbid conditions affecting visual acuity at last follow-up were not significantly different amongst groups (all p>0.1). The most common co-morbidity was glaucoma, which was reported in 14.9% of PK-PK and 7.7% of PK-EK. Grafts performed in eyes with glaucoma were less likely to attain 6/12 vision (11.3% vs. 33.6%).

Table 3 Post-operative visual outcome: BCVA at last follow-up in surviving grafts performed to improve vision

Indication, graft type	Surviving	Post-graft BCVA provided of surviving	Post-graft BCVA of 6/12 or better	Pre- and post-graft BCVA provided	BCVA improved pre- to post-graft
FECD					
PK-PK	33/43 (75.0%)	29/33 (87.9%)	18/29 (62.1%)	29/33 (87.9%)	23/29 (79.3%)
PK-EK	10/14 (71.4%)	7/10 (70.0%)	3/7 (42.9%)	7/10 (70.0%)	5/7 (71.4%)
PBK					
PK-PK	42/53 (79.2%)	37/42 (88.1%)	3/37 (8.1%)	32/42 (76.2%)	21/32 (65.6%)
PK-EK	8/18 (44.4%)	7/8 (87.5%)	2/7 (28.6%)	7/8 (87.5%)	6/7 (85.7%)
Keratoconus					
PK-PK	90/102 (88.2%)	88/90 (97.8%)	54/88 (61.4%)	86/90 (95.6%)	72/86 (83.7%)
PK-EK	5/10 (50.0%)	3/5 (60.0%)	2/3 (66.7%)	3/5 (60.0%)	3/3 (100.0%)

Other					
PK-PK	64/90 (71.1%)	55/64 (85.9%)	15/55 (27.3%)	55/64 (86.0%)	39/55 (70.9%)
PK-EK	14/18 (77.8%)	12/14 (85.7%)	1/12 (8.3%)	11/14 (78.6%)	8/11 (72.7%)
Total					
PK-PK	229/288 (79.5%)	209/229 (91.3%)	90/209 (43.1%)	202/229 (88.2%)	155/202 (76.7%)
PK-EK	37/60 (61.7%)	29/37 (78.4%)	8/29 (27.6%)	28/37 (75.7%)	22/28 (78.6%)

DISCUSSION

In our cohort of first repeat grafts following failed PK, graft survival was significantly better in eyes that had received a repeat PK, compared with those that had received a subsequent EK. The graft detachment rate for DSEK/DSAEK following PK was 10.8%, and the primary graft failure rate was 9.2%. These figures fall in the mid-range of those previously reported in cohort studies (detachment rate: 6-57%, and primary failure rate: 2-43%).[4-6, 9, 10, 12-18] The higher primary graft failure rate for PK-EK compared with PK-PK in our series likely reflects the greater early failure rate for EKs generally,[1, 7] possibly as a result of iatrogenic trauma. Tarantino-Scherrer et al found a higher graft detachment rate in EK performed under previous PK compared to first EK, and documented diminished endothelial cell survival following EK for a repeat PK compared with first EK.[19] This may have accounted for the high graft failure rate attributed to secondary endothelial failure in our series, but because endothelial cell counts at last follow-up were provided for fewer than 5% of grafts in our study, we were unable to explore this possibility further. Surgeon experience may also have influenced outcomes: data were contributed by 69 surgeons, with varying levels of experience. One-fifth of EK procedures were performed by surgeons with fewer than 10

prior registered EKs, and thus the primary graft failure rate observed may reflect a learning curve amongst surgeons taking up these new procedures.

A retrospective study by Kitzmann *et al*, analysing data from grafts in 24 eyes with a range of original indications, found no significant difference in graft survival (p=0.504) or visual acuity between PK-PK (17 eyes) and PK-EK (7 eyes).[15] However, in a previous large comparative cohort study, Ang *et al* reported results for repeat PK versus EK following failed PK in 113 eyes with an initial indication for graft of PBK.[9] Graft survival was better for the EKs compared with the repeat PKs (p=0.013), in contrast with our results in a comparable but smaller (n=83 eyes) cohort (p<0.001).

In our multivariate analysis, the length of survival of the first PK was retained as an independent variable influencing survival of the second graft (either PK or EK), with first PKs surviving for less than two years associated with poorer survival of second grafts. The reason is unclear, but is likely to be manifold and may relate to the reason for failure of the first graft, including primary graft failure, and eyes in which early rejection episodes were unable to be reversed. EK was less likely to be performed in these eyes, possibly indicating a surgeon preference for repeat PK in more complex cases. While a history of rejection in the original PK was found to influence graft survival significantly in univariate analysis, this variable was not retained in the multivariate model. However, consistent with previous findings for both first and repeat grafts,[1, 10] rejection episodes in the second graft led to diminished graft survival. A factor identified in previous studies as influencing graft survival in EK following PK is a history of glaucoma surgery.[4, 10] In our cohort, a history of raised intraocular pressure in the grafted eye was associated with an increased hazard ratio of 1.59 for subsequent failure.

Although we observed differences in survival between PK-PK and PK-EK in univariate

analysis, depending on indication for the original graft, these differences disappeared in multivariate analysis: indication for first graft was not an independent risk factor for failure of the second graft, irrespective of graft type. All PK-EKs were performed for endothelial failure or irreversible rejection of the original graft, whereas those in the PK-PK group exhibited a wider range of reasons for failure of the initial graft. However, indication for regraft was not retained in multivariate analysis, and when indication for regraft was limited to endothelial failure or rejection, the differences in survival remained significant.

The presence of co-morbid ocular conditions at the time of second graft did not differ significantly between PK-PK and PK-EK groups. Similarly, neither pre-graft BCVA nor the reported expectation that vision would improve following keratoplasty differed significantly. In consequence, it does not appear that our results have been unduly skewed by the inclusion of failed PKs that were unsuitable for subsequent EK, or by EK being performed in eyes with poor visual prognosis. However, only a randomised and controlled clinical trial in which patient groups are truly comparable will be able to provide a definitive answer.

Comparative outcomes for repeat PK versus EK following PK for keratoconus have not been previously reported, although some series include cases in which the original graft was performed for keratoconus, amongst other indications.[4, 10, 12] Our findings suggest that use of EK in these cases, as in others, results in a greater incidence of graft failure than repeat PK, which has previously been shown to exhibit diminished, albeit still acceptable, outcomes,[11, 20] although we acknowledge the low number of grafts in our PK-EK group. We recognise that many eyes in the PK-PK group exhibited no history of endothelial failure or rejection. Better outcomes might thus have been expected in PK-PK eyes. However, further analysis including only eyes in which the original PK for keratoconus had failed from rejection or endothelial failure still returned a significant result, supporting the need for

further investigation of the outcomes from secondary EK in eyes with keratoconus.

Previously published case series have reported follow-up ranging from three months to five years. Our follow-up is comparable: not all grafts in our cohort had been followed for six years (mean follow-up of two years). Kaplan-Meier analysis accounts for censoring of data with incomplete follow-up and our practice of analysing survival on a daily basis increases reliability. However, because requests for follow-up are made annually, graft failure is over-represented in the cohort of followed grafts performed in more recent years. Our multivariate model included the era in which the graft was performed, to control for this variable.

Previous studies have found significantly different survival of EK following failed PK, depending on whether the second graft was larger or smaller in diameter than the first; however results have been somewhat inconsistent.[4, 9, 13] We found no significant difference in survival of PK-EKs, based on undersizing or oversizing the second graft in comparison with the first (p=0.87).

Graft survival progressively diminishes as the number of previous grafts increases.[11] We specifically limited our cohort to first repeat grafts that have a better likelihood of survival, a criterion not previously employed in the majority of medium-sized case series reported in the literature.[4, 10, 15-17] We cannot extrapolate our findings to the likely outcome of grafts performed following multiple previous failures.

Endothelial keratoplasty continues to evolve and Descemet membrane endothelial keratoplasty (DMEK) is now preferred over DSEK/DSAEK by some surgeons in Australia, as elsewhere. However, we have insufficient follow-up of these grafts at present for meaningful analysis.

Visual outcomes in our cohort were comparable to those published previously, with

improvement in vision reported in 63-100% of surviving DSEK following PK, and attainment of 6/12 vision achieved in 33-66% of eyes.[5, 6, 10, 13, 14, 16, 17] Our findings suggest that visual outcome is related to the original pathology, as are the comparable results for repeat PK.

The limitations of a registry study include unequal graft follow-up times, the lag-time in receiving data on surviving grafts compared with failed grafts, variations (both known and unrecognised) between patient subgroups, and inevitable losses to follow-up over time. We chose statistical methods (Kaplan-Meier survival and multivariate analyses) to reduce the likelihood that these limitations would lead to misleading interpretation of data, but registry data are no substitute for prospective, randomised controlled clinical trials. However, while such a trial might be desirable to compare outcomes from different forms of keratoplasty, it seems unlikely that such a study will be undertaken in the foreseeable future, and a registry can provide at least some useful real-world information for surgeons.

The practice of performing an endothelial graft in eligible eyes with a failed PK continues to increase. Few studies have compared outcomes for these two groups. We found that survival for EK following PK was diminished compared to repeat PK, for grafts performed over the same time period, and irrespective of the original indication for first graft. Factors such as a history of raised intraocular pressure and length of survival of the original PK played an important role in survival of the second graft, and might be considered when surgery is contemplated. Endothelial grafts have some advantages over full-thickness grafts, in that they take less time to heal, involve the use of few (if any) sutures, permit fast visual recovery and more consistent refraction, and are less structurally invasive than is PK.[4-6] These factors may make a secondary endothelial graft a more attractive and appropriate option in some instances than a repeat PK, and surgeons should consider the

individual needs and circumstances of their patients when making treatment choices. However, repeat penetrating keratoplasty remains a viable treatment option, and may still achieve better outcomes in some cases.

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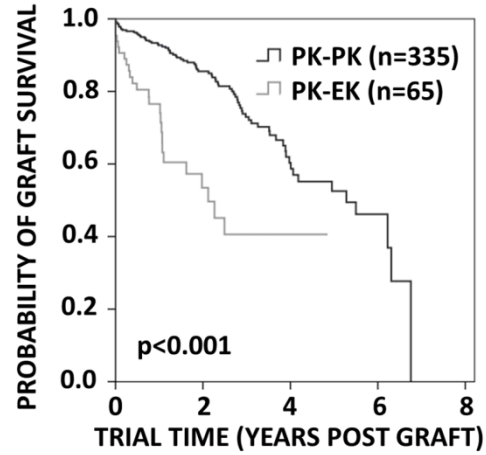
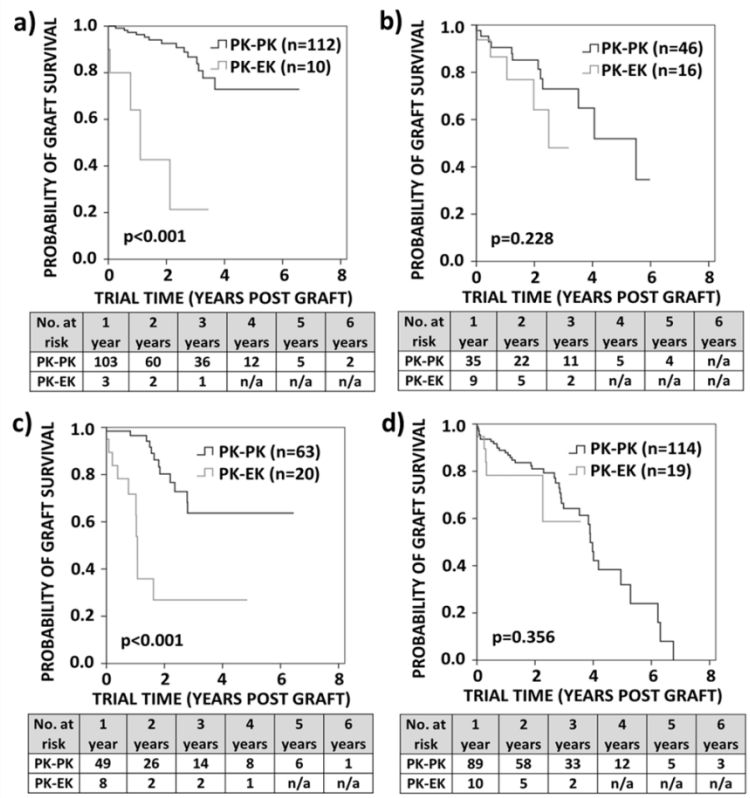
FIGURE LEGENDS



No. at risk	1 year	2 years	3 years	4 years	5 years	6 years
PK-PK	276	166	85	37	20	6
PK-EK	30	14	7	1	n/a	n/a

Figure 1 Kaplan-Meier survival plots of repeat penetrating corneal grafts (PK-PK) and subsequent endothelial grafts following failed penetrating procedures (PK-EK), performed from 2008 onwards. The numbers on the plot represent the number of grafts at risk in each stratum. The table shows the numbers at risk in each group at yearly intervals; n/a = not applicable. The difference between the curves is significant at P<0.001 (log-rank test). Repeat penetrating grafts fared significantly better than PK-EK procedures over the same era.



No. at risk	1 year	2 years	3 years	4 years	5 years	6 years
PK-PK	103	60	36	12	5	2
PK-EK	3	2	1	n/a	n/a	n/a

No. at risk	1 year	2 years	3 years	4 years	5 years	6 years
PK-PK	35	22	11	5	4	n/a
PK-EK	9	5	2	n/a	n/a	n/a

No. at risk	1 year	2 years	3 years	4 years	5 years	6 years
PK-PK	49	26	14	8	6	1
PK-EK	8	2	2	1	n/a	n/a

No. at risk	1 year	2 years	3 years	4 years	5 years	6 years
PK-PK	89	58	33	12	5	3
PK-EK	10	5	2	n/a	n/a	n/a

Figure 2 Kaplan-Meier survival plots of repeat penetrating corneal grafts (PK-PK) and subsequent endothelial grafts following failed penetrating procedures (PK-EK), performed from 2008 onwards, for grafts where the indication for graft was a) keratoconus, b) Fuchs endothelial dystrophy, c) pseudophakic bullous keratopathy or d) other. The numbers on the plots represent the number of grafts at risk in each stratum. The tables show the numbers at risk in each group at yearly intervals. The difference between the curves is significant at P<0.001 (log-rank test) for a) and c). Repeat penetrating grafts fared significantly better than PK-EK procedures over the same era in these cohorts.