Original Investigation

Descemet Stripping Automated Endothelial Keratoplasty After Failed Penetrating Keratoplasty
Survival, Rejection Risk, and Visual Outcome

Danny Mitry, PhD; Maninder Bhogal, FRCOphth; Amit K. Patel, FRCOphth; Bryan S. Lee, MD; Shu Ming Chai, MD; Marianne O. Price, PhD; Francis W. Price Jr, MD; Albert S. Jun, MD; Anthony J. Aldave, MD; Jodhbir S. Mehta, FRCOphth; Massimo Busin, MD; Bruce D. Allan, FRCOphth

IMPORTANCE Descemet stripping automated endothelial keratoplasty (DSAEK) for isolated endothelial dysfunction has become the preferred surgical option for many corneal surgeons. However, there are limited large-scale reports on DSAEK survival and clinical variables affecting the risk of rejection and failure after failed penetrating keratoplasty (PK).

OBJECTIVE To report the survival, risk factors for graft rejection and failure, and visual outcome of DSAEK after failed PK.

DESIGN, SETTING, AND PARTICIPANTS A multicenter retrospective interventional case series included patients recruited from 6 tertiary referral surgical centers: 3 in the United States, 2 in Europe, and 1 in Asia. A total of 246 consecutive eyes (246 patients) that underwent DSAEK after failed PK, with a minimum follow-up period of 1 month, was included. Data comprising demographic details, preoperative and postoperative risk factors, time to rejection, time to failure, and corrected distance visual acuity were collected.

MAIN OUTCOMES AND MEASURES Cumulative probability of graft survival, hazard ratio estimates for survival, and corrected distance visual acuity were determined.

RESULTS The mean (SD) recipient age was 63.2 (16.6) years and the median follow-up period was 17 months (interquartile range, 6-30 months). One-third of the grafts (n = 82) had follow-up data for more than 2 years; 18.3% had more than 1 failed PK before DSAEK. In total, 19.1% (47 of 246) of DSAEK grafts failed. The cumulative probability of DSAEK survival after a failed PK was 0.89 (95% CI, 0.84-0.92), 0.74 (95% CI, 0.64-0.81), and 0.47 (95% CI, 0.29-0.61) at 1 year, 3 years, and 5 years, respectively. Based on multivariate analysis, significant preoperative risk factors for failure were young recipient age (hazard ratio [HR], 5.18 [95% CI, 1.57-17.18]), previous tube filtration surgery (HR, 5.23 [95% CI, 1.47-7.33]), and rejection episodes before PK failure (HR, 3.28 [95% CI, 1.47-7.33]); single-surgeon centers had a protective effect. Any rejection episode prior to PK failure was a significant predictor of post-DSAEK rejection, which in turn was a significant predictor of DSAEK failure. After a median follow-up of 17 months, 33.3% of the grafts achieved 0.3 or greater logMAR (20/40) corrected distance visual acuity.

CONCLUSIONS AND RELEVANCE Descemet stripping automated endothelial keratoplasty after failed PK combines greater wound stability and reduced suture-related complications, with visual outcomes and graft survival rates comparable to those of a second PK.

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Author Affiliations: Department of Corneal Surgery, Moorfields Eye Hospital, London, England, (Mitry, Bhogal, Allan); Department of Corneal Surgery, Birmingham Heartlands Hospital, Heart of England National Health Service Foundation Trust, Birmingham, England (Patel); Wilmer Eye Institute, The Johns Hopkins Hospital, Baltimore, Maryland (Lee, Jun); Department of Corneal Surgery, Singapore National Eye Centre, Singapore (Chai, Mehta); Cornea Research Foundation of America, Indianapolis, Indiana (M. O. Price); Price Vision Group, Indianapolis, Indiana (F. W. Price); Jules Stein Eye Institute, University of California, Los Angeles (Aldave); Department of Corneal Surgery, Villa Serena Hospital, Forli, Italy (Busin).

Corresponding Author: Danny Mitry, PhD, Department of Corneal Surgery, Moorfields Eye Hospital, City Road, London EC1V 2PD, England (mitryd@gmail.com).

Descemet stripping automated endothelial keratoplasty (DSAEK) has become the first-line treatment for corneal endothelial failure. In comparison with penetrating keratoplasty (PK), DSAEK results in less induced astigmatism and eliminates suture-related complications.[1] Because of these advantages, DSAEK has become, for many corneal surgeons, the preferred means of managing PK failure secondary to isolated endothelial dysfunction, particularly in cases in which the failed PK had healed with a satisfactory refractive shape profile. The DSAEK procedure also may be associated with a lower endothelial rejection rate than PK.[2-4] However, comparative studies[5,6] to date have focused on eyes in which DSAEK was the primary corneal procedure, and differing topical corticosteroid regimens in the PK and DSAEK groups may have influenced the results.

Several small single-center case series[7-10] have reported outcomes of DSAEK for the management of PK failure. In the present study, we aimed to examine the risk factors for and incidence of endothelial rejection and graft failure in DSAEK after failed PK in a larger multicenter data set to help guide surgical decisions and patient counseling in the management of PK failure.

Methods

This study was registered with and approved by the Clinical Audit Working Group at Moorfields Eye Hospital, London, England, and was performed in line with the principles of the Declaration of Helsinki. Additional individual institutional review board approval for participation in the study was obtained where required at each study site.

Data Collection

Data were collected retrospectively from 6 tertiary referral centers: Moorfields Eye Hospital, London (June 1, 2005-April 30, 2011); Price Vision Group, Indianapolis, Indiana (July 1, 2004-December 31, 2010); Wilmer Eye Institute, Baltimore, Maryland (September 1, 2010-August 31, 2011); Singapore National Eye Centre, Singapore (September 1, 2007-April 30, 2012); Villa Serena Hospital, Forli, Italy (September 1, 2006-April 30, 2011); and Jules Stein Eye Institute, Los Angeles, California (June 1, 2007- December 31, 2011). All eligible patients were identified through hospital records and a medical record review was conducted for data collection. Data derived from Price Vision Group consisted of individuals who had already been reported on, with shorter follow-up, in a previous study.[8] Inclusion criteria comprised all individuals with a failed PK who underwent DSAEK in the referral center. All included participants were required to have follow-up data for a minimum of 1 month. For individuals who had more than 1 DSAEK after PK, analysis was restricted to the first DSAEK. Data gathered included patient demographics, indications for initial PK, PK diameter, rejection episodes before PK failure, number of previous PKs, host risk factors before DSAEK, lens status, previous glaucoma surgery, DSAEK donor diameter, removal of the Descemet membrane before DSAEK, donor endothelial cell count, postoperative rejection episodes and time to first rejection episode, postoperative dislocation, follow-up duration, time to failure, and Snellen spectacle-corrected distance visual acuity (CDVA) at presentation and at final postoperative follow-up. Preoperative management, surgical technique, and postoperative care were provided according to each surgeon's customary routine. Endothelial rejection was defined as the presence of anterior chamber inflammation requiring an unscheduled increase in topical corticosteroid treatment. Graft failure was defined as irreversible loss of corneal clarity as a result of endothelial decompensation on consecutive clinic visits. The date of failure was the first clinic visit at which corneal edema was noted.

Statistical Analysis

We used a Kaplan-Meier product limit analysis to determine the cumulative probability of graft survival. Based on our power calculation, we estimated that a sample size of 250 would provide sufficient power (80%) to detect a difference in hazard ratio of 0.69 or greater at $P \leq .05$ (2-tailed). Using Cox proportional multivariate regression, we fit 3 separate models to describe the data. Model 1 was developed to examine for preoperative prognostic factors associated with DSAEK failure after PK. Model 2 was used to examine preoperative and postoperative risk factors for DSAEK failure after PK. Model 3 was used to examine preoperative and postoperative risk factors associated with rejection in DSAEK after PK. The survival period was defined as the time between the date of surgery and recorded date of failure. For individuals who had clear grafts at final examination and for cases lost to follow-up, survival time was calculated as the interval between the date of surgery and the date of the last clinic examination. Prognostic variables examined in model 1 (preoperative risk factors for DSAEK failure) comprised demographic characteristics (ie, recipient age, sex, and study center), graft characteristics (ie, indication for PK, PK graft diameter, DSAEK graft diameter, removal of the Descemet membrane prior to DSAEK, number of previous PKs, presence of deep neovascularization, and rejection episodes before PK failure), and clinical characteristics (ie, lens status, previous glaucoma surgery, the use of oral corticosteroids, and preoperative tissue matching). Variables examined in model 2 (preoperative and postoperative risk factors for DSAEK failure) comprised all model 1 variables as well as postoperative variables (ie, post-DSAEK rejection episodes and DSAEK dislocation). Variables examined in model 3 (preoperative and postoperative risk factors for DSAEK rejection) comprised all variables in models 1 and 2 and DSAEK dislocation.

To determine the best fit for each model, all categorical variables were analyzed individually by log-rank testing and all continuous variables were analyzed with univariate Cox proportional hazards regression modeling. Based on a purposeful method of covariate selection,[11] we adopted a threshold P value of ≤.2 to determine which factors were likely to have an important contribution to graft survival. All variables meeting this threshold on univariate analysis were analyzed using a multivariate Cox proportional hazards regression model. To ensure the best model selection, we fit a multivariate model with all significant univariate predictors and used stepwise backward selection to sequentially eliminate nonsignificant

variables (at $P \leq .05$). There were no significant interaction terms between any of the final model predictors. A 2-tailed P value of ≤.05 was considered statistically significant. Snellen CDVA measures were converted to logMAR units for analysis. All data analysis was conducted using Stata, version 12 (StataCorp).

Results

Demographics

In total, 246 cases of DSAEK after failed PK were available for analysis. The recipients' mean (SD) age was 63.2 (16.6) years (range, 10-95 years). The median follow-up period was 17 months (interquartile range [IQR], 6-30 months). One-third of the grafts (n = 82) had follow-up data for more than 2 years. In total, 52.8% (n = 130) of the participants were male. Most (74.8%) had a posterior chamber intraocular lens, 14.6% (36 eyes) were phakic, 6.5% (16) were aphakic, and 4% (10) had an anterior chamber intraocular lens. Approximately 81% (201) of the patients had undergone DSAEK after 1 failed PK, 13.0% (32) had 2 failed PKs before DSAEK, 3.7% (9) had 3 failed PKs before DSAEK, 1.2% (3) had 4 failed PKs before DSAEK, and 0.4% (1) had 5 PKs before DSAEK. Overall, 63.1% (155) of the PKs had a rejection episode before failure. **Table 1** highlights the main baseline characteristics of the study cohort together with data on dislocation and rejection episodes after DSAEK.

Graft Survival and Cox Proportional Hazards Analysis

In total, 19.1% grafts (47 of 246) failed. The cumulative probability of DSAEK survival after a failed PK graft in the entire cohort was 0.89 (95% CI, 0.84-0.92), 0.74 (0.64-0.81), and 0.47 (0.29-0.61) at 1 year, 3 years, and 5 years, respectively. The median survival time was 4.75 years (Table 1 and **Figure 1**). Excluding the cases previously reported,[8] the cumulative probability of DSAEK survival was 0.87 (95% CI, 0.80-0.91), 0.68 (0.55-0.79), and 0.30 (0.07-0.58) at 1 year, 3 years, and 5 years, respectively. Kaplan-Meier survival estimates for the univariate risk factors meeting inclusion threshold are presented in Table 1. In addition to young age, preoperative prognostic risk factors for failure (model 1) included tube filtration surgery and rejection before PK failure. Examining preoperative and postoperative risk factors for failure (model 2) identified young age, rejection before PK failure, shunt drainage, and post-DSAEK rejection as highly significant predictors of failure. Significant predictors of post-DSAEK rejection included rejection before PK failure (model 3). Excluding the cases previously reported by Anshu et al[8] did not alter the results of the multivariate analysis. **Table 2** summarizes the estimates for the individual models. Kaplan-Meier survival estimates stratified by age, center, previous glaucoma shunt surgery, and rejection episodes before PK failure are illustrated in the Supplement (eFigure).

Surgical Center

Accounting for other variables, a significant center effect was noted in all models of graft survival (Table 2). Using center 1 as a baseline comparison, centers 2, 4, and 5 (primarily single-surgeon centers) demonstrated a protective effect, suggesting a higher probability of graft survival from these sites.

Postoperative Risk Factors for Graft Failure

Early endothelial graft dislocation requiring refloating occurred in 19 individuals (7.7%). This was not a significant predictor of failure on multivariate testing. The dislocation rate was 7.4% in eyes without previous glaucoma surgery, 6.7% in eyes with a trabeculectomy, and 10.7% in eyes with a glaucoma filtration device. There was no significant difference in the dislocation rate by type of previous glaucoma surgery. A post-DSAEK rejection episode occurred in 41 individuals (16.7%), with 3 (7.3%) of these patients having a second rejection episode. The median (IQR) time to rejection was 13 (6-22) months. No significant age and rejection interaction term was present in the model, and 58.5% of rejection episodes were seen in patients younger than 59 years. At 1 year, the cumulative probability of survival was 0.70 (95% CI, 0.52-0.82) if a post-DSAEK rejection episode occurred compared with 0.94 (0.90-0.97) without a rejection episode. Of the 155 individuals who had a rejection episode prior to PK failure, 33 (21.2%) had a post-DSAEK rejection episode. This was more than 2-fold higher than the proportion of individuals who had a post-DSAEK rejection episode if they did not have a rejection episode before PK failure (8.8%; $P = .01$) The post-DSAEK corticosteroid regimen used by each surgical center is presented in the Supplement (eTable 1).

Post-DSAEK Surgical Procedures

In total, 22 of 36 individuals with phakic eyes had cataract extraction and intraocular lens implantation at the time of or after the DSAEK graft. Of 188 eyes without previous glaucoma surgery at the time of DSAEK, at final follow-up 4 had trabeculectomies and an additional 4 had glaucoma shunt filtration surgery. Of the 47 patients with failed grafts, 8 underwent an additional PK and 11 had an additional DSAEK. A second PK was performed in 1 patient with proliferative diabetic retinopathy in a previously vitrectomized eye, 2 patients with congenital glaucoma, 1 patient with persistent posterior segment uveitis, 1 patient with a large iris cyst needing excision, 1 patient with Peter anomaly, 1 patient with vitreous in the anterior chamber postoperatively, and 1 individual with an aphakic eye and a dislocated graft in the posterior segment. The Supplement (eTable 2) summarizes the characteristics and additional interventions of the 47 failed grafts.

Visual Outcome

Data on CDVA at the final postoperative visit were available for all 199 surviving grafts. The median final visit for all surviving grafts was 17 months postoperatively (IQR, 6-30 months). Four eyes (2.0%) had 0.3 logMAR or greater (20/40) CDVA preoperatively compared with 64 eyes (33.3%) after DSAEK. When the original indication for PK was keratoconus, 13 of 36 patients (36.1%) achieved 0.3 logMAR or greater CDVA at final follow-up. For pseudophakic bullous keratopathy and Fuchs endothelial dystrophy, 8 of 42 (19.0%) and 18 of 51 (35.3%) patients achieved 0.3 logMAR or greater CDVA after DSAEK,

Table 1. Patient Characteristics and Corresponding 1- and 3-Year Kaplan-Meier Estimates of the Probability of Graft Survival

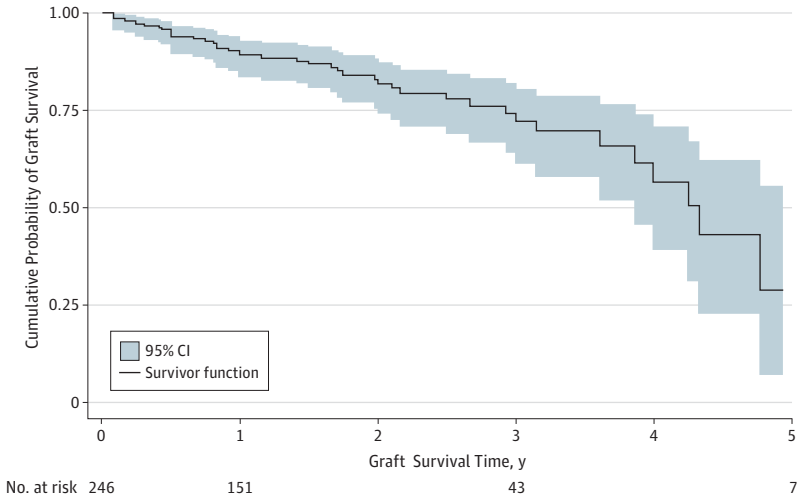
Characteristic	No. (%)	Probability of Graft Survival (95% CI)	
		1 y (n = 151)	3 y (n = 43)
Total	246	0.89 (0.84-0.92)	0.74 (0.64-0.81)
Age group, y[a]			
≥80	47 (19.1)	0.94 (0.78-0.98)	0.83 (0.63-0.93)
60-79	113 (45.9)	0.91 (0.83-0.95)	0.80 (0.66-0.88)
40-59	67 (27.2)	0.88 (0.76-0.94)	0.66 (0.42-0.82)
≤39	19 (7.7)	0.74 (0.43-0.89)	0.55 (0.25-0.77)
Center (No. of surgeons)[a]			
1 (4)	25 (10.2)	0.61 (0.39-0.78)	0.40 (0.17-0.62)
2 (1)	60 (24.4)	0.96 (0.86-0.99)	0.85 (0.68-0.93)
3 (2)	13 (5.3)	0.92 (0.57-0.98)	NA
4 (1)	30 (12.2)	0.86 (0.66-0.94)	0.81 (0.61-0.92)
5 (1)	105 (42.7)	0.94 (0.86-0.97)	0.75 (0.40-0.92)
6 (2)	13 (5.3)	0.83 (0.27-0.97)	0.44 (0.07-0.78)
Indication for first PK			
KC	43 (17.5)	0.91 (0.74-0.97)	0.71 (0.42-0.88)
PBK	51 (20.7)	0.91 (0.78-0.97)	0.74 (0.53-0.87)
FED	61 (24.8)	0.98 (0.88-0.99)	0.91 (0.63-0.98)
Other	91 (37.0)	0.81 (0.70-0.88)	0.64 (0.47-0.77)
Rejection episodes prior to PK failure[a]			
No rejection episode	91 (37.0)	0.96 (0.89-0.98)	0.86 (0.69-0.94)
Rejection episode	155 (63.0)	0.86 (0.78-0.91)	0.67 (0.55-0.77)
No. of previous PKs			
1	201 (81.7)	0.90 (0.84-0.94)	0.76 (0.65-0.84)
2	32 (13.0)	0.86 (0.66-0.94)	0.64 (0.36-0.83)
3	9 (3.7)	1 (NA)	0.80 (0.20-0.97)
4	3 (1.2)	0.67 (0.05-0.95)	NA
5	1 (0.4)	1 (NA)	NA
DSAEK donor diameter, mm			
≤7.5	8 (3.3)	0.63 (0.23-0.86)	NA
>7.5 to <8.5	67 (27.2)	0.88 (0.75-0.94)	0.62 (0.44-0.75)
≥8.5	156 (63.4)	0.92 (0.86-0.96)	0.86 (0.74-0.93)
NA	15 (6.1)		
Previous glaucoma surgery[a]			
None	188 (76.4)	0.92 (0.86-0.95)	0.79 (0.68-0.87)
Trabeculectomy	30 (12.2)	0.85 (0.64-0.94)	0.79 (0.56-0.91)
Shunt filtration surgery[b]	28 (11.4)	0.78 (0.58-0.90)	0.42 (0.17-0.66)
Trabeculectomy or shunt filtration surgery	58 (23.6)	0.81 (0.67-0.90)	0.57 (0.36-0.74)
PK Descemet membrane removal during DSAEK			
Yes	91 (37.0)	0.87 (0.80-0.92)	0.69 (0.50-0.82)
No	136 (55.3)	0.92 (0.82-0.96)	0.77 (0.64-0.87)
NA	19 (7.7)		
Lens status			
Phakic	36 (14.6)	0.88 (0.67-0.96)	0.75 (0.40-0.92)
PCIOL	184 (74.8)	0.91 (0.86-0.95)	0.73 (0.61-0.82)
ACIOL	10 (4.1)	0.69 (0.21-0.91)	0.69 (0.21-0.91)
Aphakic	16 (6.5)	0.78 (0.47-0.93)	0.78 (0.47-0.93)
Systemic immunosuppression			
Yes	119 (48.4)	0.89 (0.81-0.94)	0.74 (0.51-0.88)
No	127 (51.6)	0.89 (0.82-0.94)	0.72 (0.60-0.81)
Rejection episodes after DSAEK[a]			
Yes	41 (16.7)	0.70 (0.52-0.82)	0.34 (0.10-0.53)
No	206 (83.7)	0.94 (0.90-0.97)	0.86 (0.76-0.82)
DSAEK postoperative dislocation			
Yes	19 (7.7)	0.81 (0.51-0.94)	0.68 (0.31-0.88)
No	227 (92.3)	0.90 (0.85-0.94)	0.75 (0.64-0.82)

Abbreviations: ACIOL, anterior chamber intraocular lens; DSAEK, Descemet stripping automated endothelial keratoplasty; FED, Fuch endothelial dystrophy; KC, keratoconus; NA, not available; PBK, pseudophakic bullous keratopathy; PCIOL, posterior chamber intraocular lens; PK, penetrating keratoplasty.

[a] Indicates significant variables included in final model.

[b] All shunt filtration procedures were in the anterior chamber.

Figure 1. Kaplan-Meier Survival of All Grafts



Median survival time was 57 months (interquartile range, 36.0-70.8 months). The shaded region represents the 95% CI for the probability estimate with vertical inflections indicating censored data.

respectively. **Figure 2** highlights the changes in CDVA before and after DSAEK for failed PK.

Discussion

Endothelial keratoplasty after failed PK is a useful procedure that can provide a low rate of ocular surface disease and a favorable survival outcome.[7-10] The present study reports multicenter data on the survival of DSAEK after failed PK. After a median of 17 months, 19.1% of the grafts (47 of 246) had failed. The cumulative probability of DSAEK survival after a failed PK graft was 0.89, 0.74, and 0.47 at 1 year, 3 years, and 5 years, respectively. By using 3 individual models, we sought to analyze preoperative prognostic risk factors that can be used for patient counseling as well as postoperative risk factors that may influence time to failure or rejection. Significant independent preoperative risk factors for graft failure in multivariate analysis were young recipient age, previous glaucoma drainage device implantation, and rejection before PK failure. Relative protection was observed for patients having surgery in a single-surgeon setting. In addition, endothelial rejection episodes in failed PK was a significant predictor of post-DSAEK rejection, which is a strong predictor of subsequent graft failure.

These findings should be interpreted with reference to the following limitations. The retrospective design of the study meant that some variables of potential interest could not be assessed. For example, the preferential decision to perform DSAEK instead of a second PK after a failed PK was made by the operating surgeon. Individuals with isolated endothelial failure in an otherwise healthy penetrating graft with low astigmatism may have been more likely to undergo DSAEK, whereas a second PK may have been preferred in individuals with high corneal astigmatism. We were unable to collect detailed information on variations between centers in surgical technique or study population, which may have influenced results. Nonetheless, combined data from a cohort of 246 grafts originating from 6 surgical centers in Europe, Asia, and the United States should help to provide valid benchmarks for DSAEK survival after failed PK, which will be useful for audit and patient counseling in a range of surgical settings. Sixty cases in this cohort have been analyzed previously[8] but were included in the present multicenter analysis with longer follow-up. Excluding these cases did not alter the results of the survival and multivariate analysis, but care should be taken not to include both data sets in any future systematic reviews.

The 1-, 3-, and 5-year graft survival estimates of 89%, 74%, and 47%, respectively, for DSAEK after failed PK reported here are similar to survival estimates for a second PK. A second PK for keratoconus has estimated 1- and 5-year survival rates of 88% and 69%, which decrease to 65% and 49%, respectively, after a third graft.[12] The Collaborative Corneal Transplantation Studies Research Group[13] have reported that the risk of failure 3 years after PK increased from 17% without a previous graft to 53% with 2 or more previous grafts. Other reports[2-4] have suggested a 1-year survival estimate of between 98% and 63% for a first PK reoperation, decreasing to 45% to 28% at 5 years. Survival estimates from a recent multicenter study[14] of Boston keratoprostheses implanted for a variety of indications, the most common of which was PK failure, included an estimated 1-year retention rate of 92%, decreasing to 62% at 5 years.

Rejection is a risk factor for additional rejection episodes.[15] In the present study, rejection before PK failure was a significant risk factor for subsequent DSAEK failure. If postoperative risk factors are considered, the association between postoperative DSAEK rejection and DSAEK failure is highly significant. This effect is independent of age, surgical center, and the presence of a glaucoma shunt device. A long-term study[16] reported that endothelial rejection is more common and more likely to be irreversible if the recipient has had a history of irreversible corneal endothelial rejection; thus, individuals who have had a rejection

Table 2. Hazard Ratios for Statistically Significant Risk Factors in Each Model

Characteristic	Hazard Ratio (95% CI)	*P* Value
Model 1 (preoperative risk factors for DSAEK failure)		
Age, y		
≥80	1 [Reference]	
60-79	1.91 (0.75-4.86)	.17
40-59	2.46 (0.97-6.24)	.06
≤39	5.18 (1.57-17.18)	.007
Center		
1	1 [Reference]	
2	0.13 (0.05-0.32)	<.001
3	0.86 (0.23-3.20)	.82
4	0.09 (0.03-0.31)	<.001
5	0.12 (0.05-0.29)	<.001
6	0.52 (0.15-1.73)	.28
Previous glaucoma surgery		
None	1 [Reference]	
Trabeculectomy	2.10 (0.77-5.65)	.15
Shunt drainage	5.23 (1.47-7.33)	<.001
Rejection episodes prior to PK failure		
No episode	1 [Reference]	
Rejection episode	3.28 (1.47-7.33)	.004
Model 2 (preoperative and postoperative risk factors for DSAEK failure)		
Age, y		
≥80	1 [Reference]	
60-79	2.38 (0.89-6.30)	.08
40-59	3.98 (1.40-11.37)	.01
≤39	8.42 (2.23-31.69)	.002
Center		
1	1 [Reference]	
2	0.15 (0.06-0.39)	<.001
3	0.57 (0.14-2.26)	.43
4	0.11 (0.03-0.37)	<.001
5	0.16 (0.06-0.40)	<.001
6	0.54 (0.16-1.85)	.32
Previous glaucoma surgery		
None	1 [Reference]	
Trabeculectomy	2.12 (0.78-5.75)	.14
Shunt drainage	4.12 (1.63-10.41)	.003
Rejection episodes prior to PK failure		
No episodes	1 [Reference]	
Rejection episodes	2.41 (1.02-5.70)	.04
Post-DSAEK rejection		
No	1 [Reference]	
Yes	2.49 (1.18-5.26)	.01
Model 3 (preoperative and postoperative risk factors for DSAEK rejection)		
Rejection episodes prior to PK failure		
No episode	1 [Reference]	
Rejection episode	3.29 (1.46-7.14)	.004
Center		
1	1 [Reference]	
2	0.23 (0.09-0.61)	.003
3	1.67 (0.51-5.49)	.40
4	0.15 (0.04-0.49)	.002
5	0.16 (0.07-0.40)	<.001
6	1.16 (0.36-3.76)	.80

Abbreviations: DSAEK, Descemet stripping automated endothelial keratoplasty; PK, penetrating keratoplasty.

episode may carry a considerable rejection risk in a second graft. From the present study, apart from surgical center, the only significant predictor of DSAEK rejection was rejection before PK failure. One in 5 individuals who had any rejection episode before PK failure also had a post-DSAEK rejection episode. The cause of immune graft rejection is complex.[17] However, a recent clinical study[18] has suggested that trophic factors of the donor cornea may be influential in tissue intolerance and subsequent graft rejection.

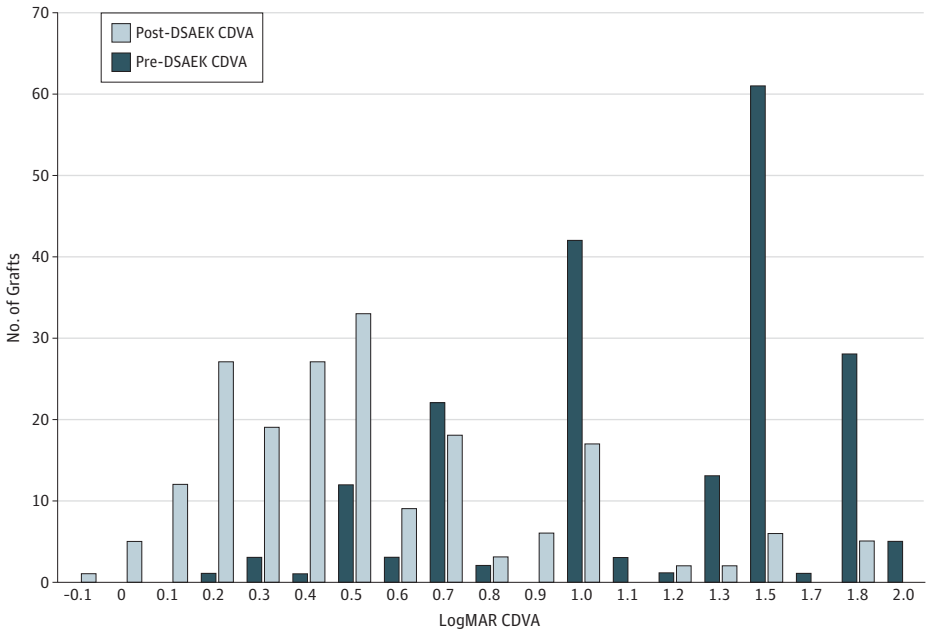
Contrary to a trend previously noted in primary PK survival,[19,20] in the present series younger recipient age was associated with a greater risk of failure. Better survival figures for younger patients in primary PK data may simply reflect a bias toward indications with a better prognosis in younger patients that was not present in our multicenter cohort. Only 32% of participants younger than 39 years evaluated in the present study had a first graft for keratoconus, pseudophakic bullous keratopathy, or Fuchs endothelial dystrophy.

After adjusting for other variables, we observed a significant center effect, with single-surgeon referral centers having a better graft survival outcome. This effect has been noted in previous studies[15,21] of corneal transplant. As discussed above, we were unable to collect detailed data on study population ethnicity, case selection, and surgical technique, which may help explain the differences in results between centers.

Previous trabeculectomy did not confer an increased risk of graft failure, but as noted in reports[8,22,23] from PK and DSAEK series, previous glaucoma drainage device (tube implant) surgery was associated with at least a 4-fold increase in the risk of failure when accounting for other factors. The physical presence of a filtration device in the anterior chamber and the known change in aqueous cytokines associated with the presence of a glaucoma shunt may account for the significant increased risk of failure observed.[24]

Although the study was sufficiently powered to detect moderate risk effects, several variables that we examined had no effect on graft survival or rejection. Males have been reported[19] to have a higher risk of PK failure, but we could not identify any sex effect. Lens status and treatment with oral corticosteroids before DSAEK similarly had no effect on

Figure 2. Corrected Distance Visual Acuity (CDVA) Before and at Final Follow-up After Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) in a Failed Full-Thickness Corneal Graft



Pre-DSAEK CDVA was known for 199 of 246 eyes; post-DSAEK CDVA at final follow-up was known for 192 of 199 eyes.

graft survival or rejection. Some surgeons advocate removal of the Descemet membrane before DSAEK, but this was not associated with an effect on survival or rejection. In addition, PK diameter, endothelial keratoplasty donor diameter, and the number of previous PKs were not predictors of graft failure or rejection.

Although we did not have information on the degree of preoperative astigmatism in our series, visual results for another transplant in the same eye appear to be better for DSAEK. One-third of our cases (64 of 192) achieved a final CDVA of 20/40 or better compared with between 5% and 31% in patients who underwent a second PK.[2,15,25] However, the visual outcome in our series was worse than after a primary DSAEK, for which up to 70% of patients achieve 20/25 acuity at 3 years.[26]

Conclusions

Studying a large international multicenter cohort of patients undergoing DSAEK after a failed PK, we found the overall 5-year graft survival to be approximately 50%. Glaucoma shunt surgery, younger recipient age, and endothelial rejection before PK failure are important preoperative predictors of failure. Any rejection episode before PK failure is an important predictor of rejection in the DSAEK graft, and post-DSAEK rejection is a strong predictor of subsequent graft failure. In summary, DSAEK after failed PK combines visual outcomes and rates of graft survival that are comparable to those of a second PK.

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Drafting of the manuscript: Mitry, Bhogal, Patel, Jun, Mehta, Allan.
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