Endophthalmitis Rates and Clinical Outcomes Following Penetrating and Endothelial Keratoplasty

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• PURPOSE: To evaluate endophthalmitis rates after penetrating keratoplasty (PK) and endothelial keratoplasty (EK) and to compare clinical outcomes.
• DESIGN: Retrospective cohort study.
• METHODS: The medical and billing records of several large academic private practices in Philadelphia, PA were electronically queried for all surgical visits during which a PK or EK was performed between April 1, 2012 and August 31, 2018. Demographic information and transplant characteristics were recorded for each patient and office visit. An additional query was performed to identify all cases of endophthalmitis based on diagnosis and procedure billing codes. Charts of patients with endophthalmitis were individually reviewed, and information was collected on triggering factors, clinical evaluation at presentation, management, culture data, visual outcomes, and graft survival rates. The main outcome measure was incidence of presumed infectious endophthalmitis following PK or EK.
• RESULTS: During the study period, 1676 PKs and 2292 EKs for 3069 patients were performed. The mean age of patients in this transplant cohort was 66.4 (± 17.5) years and 54.6% of patients were women. Sixteen cases of endophthalmitis occurred during the study period; 12 cases of endophthalmitis occurred after PK and 4 cases occurred after EK. The rate of endophthalmitis after EK (4 of 2292; 0.2%) was significantly lower than that after PK (12 of 1676; 0.7%) ($P = .01$). In addition, the odds of developing endophthalmitis after PK or EK performed in conjunction with anterior vitrectomy were significantly higher than after either PK or EK alone (odds ratio 8.66; 95% confidence interval 2.98-25.18; $P < .001$). Visual acuity outcomes were poorer after PK-related endophthalmitis than EK-associated cases ($P = .01$). The rate of graft failure at final follow-up was significantly higher in post-PK endophthalmitis ($P = .02$).
• CONCLUSIONS: In this large cohort of patients undergoing either PK or EK, rates of endophthalmitis were low for both procedures and significantly lower for EK compared with PK. Eyes with endophthalmitis after PK had poorer visual acuity outcomes and graft prognosis compared with those with endophthalmitis after EK. (Am J Ophthalmol 2019;205:82–90. © 2019 Elsevier Inc. All rights reserved.)

OVER THE PAST 15 TO 20 YEARS, SURGICAL TECHniques in corneal transplantation have advanced significantly. Penetrating keratoplasty (PK) remains the necessary surgical procedure in many cases, such as after trauma or severe infection in which full-thickness corneal scarring or pathology is present. However, selective endothelial replacement with either Descemet stripping endothelial keratoplasty (DSEK) or Descemet membrane endothelial keratoplasty (DMEK) has replaced PK as the preferred surgical method to manage endothelial disorders, such as Fuchs endothelial dystrophy or pseudophakic bullous keratopathy.[1–4] These advanced endothelial keratoplasty (EK) techniques offer the benefit of faster visual recovery, more predictable refractive outcomes, and lower rates of complications such as rejection or traumatic wound dehiscence compared with PK.[5–7]

Endophthalmitis is a feared and devastating complication of many ophthalmic procedures. Rates of infectious endophthalmitis after PK have been well-studied and are low, ranging from 0.11% to 1.05% in prior large series[8–14]; however, the rate of endophthalmitis after EK is largely unknown. Although adverse event reports are available from the Eye Bank Association of America (EBAA), these reports contain self-reported adverse events and may not be inclusive of all cases.[15,16] Aside from this, only case reports and smaller studies are available in the literature.[17–26]

The purpose of this study was to investigate the incidence and clinical outcomes of endophthalmitis following PK or EK in a large cohort of patients undergoing these procedures. Understanding the incidence and clinical outcomes

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TABLE 1. Baseline Characteristics of Patients (n = 3069) Undergoing Penetrating Keratoplasty or Endothelial Keratoplasty (n = 3968 Transplants)

	Penetrating Keratoplasty	Endothelial Keratoplasty	*P*
Number of patients,[a] n (%)	1334 (43.5)	1735 (56.5)	—
Age (y), mean (SD)	58.1 (21.1)	72.9 (11.1)	**< .001**
Sex, n (%)			**< .001**
Female	662 (49.6)	1014 (58.4)	
Male	672 (50.4)	721 (41.6)	

Statistically significant *P* values are indicated in bold.
[a]Patients who had both types of transplantation at different times are included in the group that represents their initial transplant type.

of this vision-threatening complication is important for comprehensive patient counseling.

METHODS

INSTITUTIONAL REVIEW BOARD APPROVAL WAS OBTAINED from the Wills Eye Hospital Review Board for this retrospective cohort study. All work was performed in accordance with the Health Insurance Portability and Accountability Act of 1996 and adhered to the tenets of the Declaration of Helsinki.

The electronic medical records of Corneal Associates and Ophthalmic Partners of Pennsylvania, comprising most of the Cornea Service at Wills Eye Hospital, were queried for all surgical encounters during which either a PK or an EK was performed between April 1, 2012 and August 31, 2018 using Current Procedural Terminology (CPT) codes. CPT codes also were used to determine if concurrent cataract extraction with intraocular lens insertion, lensectomy, intraocular lens insertion, removal, repositioning, or exchange, and/or anterior or pars plana vitrectomy were performed. *International Classification of Diseases, Ninth Revision* (ICD-9) and *10th Revision* (ICD-10) codes were used to determine the indication for each transplant. Basic demographic information also was extracted for each patient included in the study.

ICD-9 and ICD-10 codes for endophthalmitis were used to electronically identify cases of endophthalmitis following corneal transplantation. An electronic query was done to search both the electronic medical records of the cornea practices, as well as the medical records of the Mid-Atlantic Retina practice and the Wills Eye Hospital Retina Service. An additional search of the Mid-Atlantic Retina electronic health records was done using CPT codes for a vitreous tap and intravitreal antibiotic injection (vancomycin, ceftazidime, or voriconazole) to capture patients who may not have had a correct ICD diagnosis code. Cases were excluded from the study if subsequent additional procedures, such as cataract or glaucoma surgery or intravitreal anti–vascular endothelial growth factor injection, were performed within 30 days before the endophthalmitis diagnosis.

Charts from all possible cases of endophthalmitis from this electronic search were individually reviewed to confirm a diagnosis of presumed infectious endophthalmitis. For each case, information concerning the original transplant was extracted including laterality, indication for transplant, history of multiple prior transplants, concurrent intraocular procedures, and best Snellen visual acuity after the transplant. Data about the endophthalmitis event extracted included triggering factor for endophthalmitis, postoperative day after PK or EK, clinical evaluation and medications at presentation, management, culture data, and posttreatment visual acuity at 1, 3, and 6 months. We also reviewed ocular outcomes including graft failure, requirement for repeat transplantation, and need for enucleation or evisceration.

Presumed infectious endophthalmitis was defined based on a clinical decision to proceed with either a vitreous or anterior chamber tap and injection of intravitreal antibiotics/antifungals, or a pars plana vitrectomy with injection of intravitreal antibiotics/antifungals. Cases of posttransplant inflammation that were treated with intensive topical steroids and close monitoring alone without injection of intravitreal antibiotics were not included. Thorough chart review was done to obtain Gram stain and culture information for each case, if available.

All statistical analyses were conducted using SPSS, Version 25 (SPSS, Inc, Chicago, IL). Categorical variables were compared using a χ^2 test and continuous variables were compared using a 2-sample *t* test. Risk factors for endophthalmitis after corneal transplantation were assessed in univariate analyses. Concurrent procedures were determined based off of CPT codes, and surgeon experience was defined as the number of years from fellowship graduation to the date of transplant. Factors with $P < .25$

TABLE 2. Clinical History and Indications for Keratoplasty

	Total	Penetrating Keratoplasty	Endothelial Keratoplasty	*P*
Number of transplants, n (%)	3968	1676 (42.2)	2292 (57.8)	—
Procedure history, n (%)				**.030**
Initial transplant	2821 (71.1)	1161 (69.3)	1660 (72.4)	
≥ 1 prior transplants	1147 (28.9)	515 (30.7)	632 (27.6)	
Diagnosis, n (%)				
Endothelial corneal dystrophy	1258 (31.7)	43 (2.6)	1215 (53.0)	**< .001**
Secondary corneal edema	902 (22.7)	244 (14.6)	658 (28.7)	**< .001**
Graft failure	605 (15.2)	346 (20.6)	259 (11.3)	**< .001**
Corneal ectasia	273 (6.9)	273 (16.3)	0 (0.0)	**< .001**
Corneal scar/opacity[a]	227 (5.7)	227 (13.5)	0 (0.0)	**< .001**
Microbial ulcer	153 (3.9)	153 (9.1)	0 (0.0)	**< .001**
Graft dehiscence	123 (3.1)	123 (7.3)	0 (0.0)	**< .001**
Herpetic scar	43 (1.1)	43 (2.6)	0 (0.0)	**< .001**
Epithelial or stromal corneal dystrophy	22 (0.6)	17 (1.0)	5 (0.2)	**.001**
Aniridia	11 (0.3)	11 (0.7)	0 (0.0)	**< .001**
Concurrent procedures, n (%)				
CE/IOL	75 (19.1)	179 (10.7)	578 (25.2)	**< .001**
Lensectomy	18 (0.5)	14 (0.8)	4 (0.2)	**.002**
IOL insertion	91 (2.3)	67 (4.0)	24 (1.0)	**< .001**
IOL removal	32 (0.8)	31 (1.8)	1 (< 0.1)	**< .001**
IOL repositioning	11 (0.3)	5 (0.3)	6 (0.3)	> .99
IOL exchange	142 (3.6)	79 (4.7)	63 (2.7)	**.001**
Vitrectomy	202 (5.1)	117 (7.0)	85 (3.7)	**< .001**

CE = cataract extraction; IOL = intraocular lens.
Statistically significant *P* values are indicated in bold.
[a]Acquired or congenital.

were included in a multivariate logistic regression with a stepwise backward likelihood model selection procedure. A *P* value of less than .05 was considered statistically significant.

RESULTS

• **DEMOGRAPHICS:** Overall, 3968 corneal transplants performed on 3069 patients were included in this study. The mean age of patients in this cohort was 66.4 years and 54.6% of patients were women. Demographic characteristics of patients stratified by corneal transplantation type are described in Table 1.

• **TRANSPLANT CHARACTERISTICS:** Characteristics for the cornea transplant surgeries are provided in Table 2. Of the 3968 transplants, 1676 PKs and 2292 EKs were performed during the study period. Although cataract extraction with intraocular lens insertion was more commonly performed in combination with EK (578 of 2292; 25.2%) compared with PK (179 of 1676; 10.7%) ($P < .001$), anterior or pars plana vitrectomy was more commonly performed in patients undergoing PK (117 of 1676; 7.0%) compared with EK (85 of 2292; 3.7%) ($P < .001$). Lens manipulation, which was defined as lensectomy or intraocular lens insertion, removal, repositioning, or exchange, was more common in cases of EK (673 of 2292; 29.4%) than in cases of PK (366 of 1676; 21.8%) ($P < .001$). These characteristics are presented in Table 2.

The 10 most common indications for transplantation are listed in Table 2. PK was most commonly performed for graft failure (20.6%), whereas endothelial corneal dystrophy was the most common indication for EK (53.0%). Primary indication for transplantation based on ICD-9 or ICD-10 coding was unavailable for 335 cases (8.4%).

• **ENDOPHTHALMITIS CHARACTERISTICS:** Overall, 16 patients developed endophthalmitis. The clinical characteristics and outcomes of these patients are presented in Table 3. Mean time from transplantation to endophthalmitis was not significantly different between those who received PK (134.7 ± 136.8 days) and EK (214.5 ± 357.8 days) ($P = .69$). The median time from transplantation to endophthalmitis was 79.0 days for the PK group and 50.5 days for the EK group.

TABLE 3. Clinical Characteristics and Outcomes of Patients Who Developed Endophthalmitis After Keratoplasty

	Overall	Penetrating Keratoplasty	Endothelial Keratoplasty	*P*
Sex, n (%)				.60
Female	10 (62.5)	8 (66.7)	2 (50.0)	
Male	6 (37.5)	4 (33.3)	2 (50.0)	
Age, mean (SD)	68.8 (19.8)	65.3 (21.2)	79.2 (11.5)	.24
Right eyes, n (%)	8 (50)	6 (50.0)	2 (50.0)	> .99
Prior corneal transplants, n (%)				.77
0	10 (62.5)	7 (58.3)	3 (75.0)	
1	5 (31.3)	4 (33.3)	1 (25.0)	
2	1 (6.3)	1 (8.3)	0 (0.0)	
Concurrent procedures, n (%)				
Lensectomy	1 (6.3)	1 (8.3)	0 (0.0)	> .99
IOL exchange	3 (18.8)	2 (16.7)	1 (25.0)	> .99
Vitrectomy	5 (31.3)	4 (33.3)	1 (25.0)	> .99
Post-operative day of endophthalmitis diagnosis, mean (SD)	154.6 (202)	134.7 (137)	214.5 (358)	.69
1 month or less between surgery and endophthalmitis symptoms, n (%)	5 (31.3)	3 (25.0)	2 (50.0)	.55
Lens status at time of endophthalmitis, n (%)				.20
Aphakic	2 (12.5)	2 (16.7)	0 (0.0)	
Phakic	4 (25.0)	4 (33.0)	0 (0)	
PCIOL	10 (62.5)	6 (50.0)	4 (100.0)	
Initial endophthalmitis management, n (%)				> .99
Tap and inject	13 (81.3)	10 (83.3)	3 (75.0)	
Vitrectomy	3 (18.8)	2 (16.7)	1 (25.0)	
Average days of follow-up post-endophthalmitis, mean (SD)	644.9 (647.2)	540.2 (575.9)	959.3 (837.9)	.28
Graft failure, n (%)	9 (56.3)	9 (75.0)	0 (0.0)	**.02**
Repeat transplant, n (%)	3 (18.8)	3 (25.0)	0 (0.0)	.53
Enucleation/evisceration, n (%)	2 (12.5)	2 (16.7)	0 (0.0)	> .99

IOL = intraocular lens; PCIOL = posterior chamber intraocular lens.
Statistically significant *P* value is indicated in bold.

All patients except for one were on steroid drops at the time of the endophthalmitis diagnosis. Thirteen patients (81%) were on topical antibiotic drops at the time of the endophthalmitis diagnosis. Eleven patients developed endophthalmitis more than 1 month after undergoing corneal transplantation. Three of these patients had developed a corneal ulcer within the graft (independent of suture issues) and 4 patients developed endophthalmitis due to transplant suture-related infections. Two patients developed endophthalmitis after traumatic dehiscence of their PK graft. Other historical factors contributing to development of endophthalmitis after the immediate postoperative period were an exposed Gore-Tex suture and a case of glaucoma bleb–related infection.

Culture data were evaluated for each case of endophthalmitis, and 14 patients had information available for review. Four of the cultures (29%) had no growth. Seven patients had bacterial endophthalmitis with organisms including *Staphylococcus epidermidis*, methicillin-resistant *Staphylococcus aureus*, *Streptococcus dysgalactiae*, *Streptococcus mitis*, *Haemophilus influenzae*, *Enterococcus faecalis*, and *Serratia marcescens*. Three patients had fungal endophthalmitis; 2 cultures grew *Candida* species and 1 patient had endophthalmitis secondary to the mold *Colletotrichum truncatum*. The 3 patients with endophthalmitis secondary to a mold or fungus had undergone PK.

Visual acuity outcomes after endophthalmitis are presented in Figure. Compared with pre-endophthalmitis best available visual acuity, patients who developed endophthalmitis after PK had significantly poorer visual acuity at both 3 and 6 months after infection. Conversely, patients who developed endophthalmitis after EK did not have significantly poorer vision at 3 and 6 months compared with baseline visual acuity. A comparison of post-PK and post-EK endophthalmitis visual acuity demonstrated significantly better visual acuity for EK compared with PK patients at 6 months ($P = .01$) (Figure, A). A comparison of change in lines from baseline between post-PK and post-EK endophthalmitis approached statistical significance ($P = .06$)

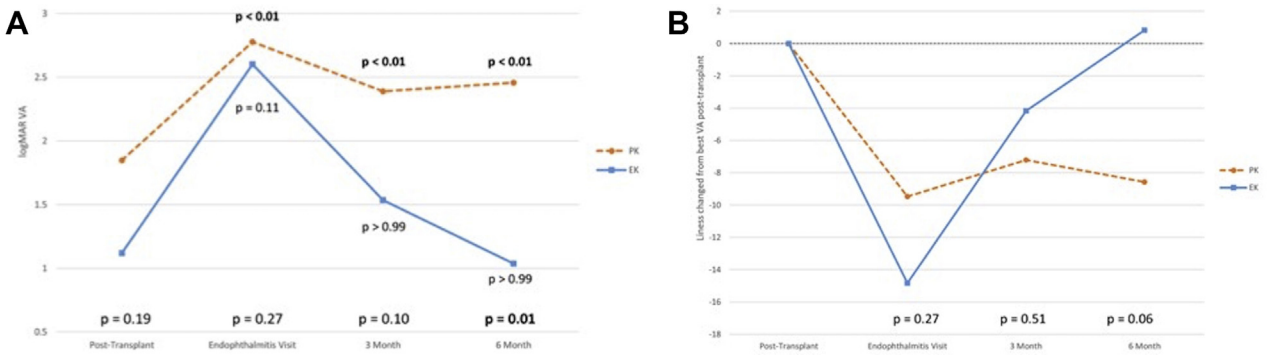

FIGURE. Visual acuity outcomes of eyes that developed endophthalmitis after penetrating (PK) and endothelial keratoplasty (EK). (A) *P* values on the individual transplant line graphs represent comparisons of visual acuities at each time point to the best visual acuity posttransplant. *P* values on the horizontal axis represent the difference between the visual acuities of the 2 transplant groups at each time point. Post hoc correction for multiple comparisons by the Holm-Bonferroni method was performed for all *P* values. (B) *P* values along the horizontal axis represent a comparison of mean lines changed from best posttransplant visual acuity between patients that received PK or EK before developing endophthalmitis.

TABLE 4. Multivariate Analysis of Risk Factors for Endophthalmitis After Keratoplasty

		Univariate Model		Multivariate Model	
	Endophthalmitis Rate, n (%)	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Procedure			**.01**		**.03**
Penetrating keratoplasty	12/1676 (0.7)	4.13 (1.33-12.81)		3.56 (1.14-11.18)	
Endothelial keratoplasty	4/2292 (0.2)	Reference		Reference	
Concurrent procedures			**< .001**		**< .001**
Vitrectomy	5/202 (2.5)	8.66 (2.98-25.18)		7.23 (2.46-21.21)	
No vitrectomy	11/3766 (0.3)	Reference		Reference	

Statistically significant *P* values are indicated in bold.

(Figure, B). There was a significant difference in the rates of graft failure after post-PK (75%) and post-EK (0%) endophthalmitis ($P = .02$) (Table 3).

There was no significant difference in post-endophthalmitis visual acuity at 6 months for patients who underwent tap and injection of antibiotics or antifungals versus those who underwent vitrectomy with injection of antibiotics or antifungals ($P = .79$).

• **RISK FACTORS FOR ENDOPHTHALMITIS:** Potential risk factors for developing endophthalmitis after corneal transplantation were assessed in univariate analyses and incorporated into a multivariate regression model if found to be significant. PK was found to be a risk factor for developing endophthalmitis. Patients undergoing PK had a 4 times higher odds of developing endophthalmitis compared with patients undergoing EK (odds ratio 4.13; 95% confidence interval 1.33-12.81; $P = .01$) (Table 4). In addition, concurrent vitrectomy was found to be a significant risk factor for endophthalmitis. Patients undergoing vitrectomy, either through the anterior or pars plana approach, had a more than 8 times higher odds of developing endophthalmitis compared with patients who did not undergo vitrectomy (odds ratio 8.66; 95% confidence interval 2.98-25.18; $P < .001$) (Table 4). Both of these factors remained significant with similar adjusted odds ratios in the multivariate model (Table 4).

A number of additional factors were evaluated and not found to be significant predictors of endophthalmitis including gender, age at transplantation, history of prior transplants, particular surgeon, and surgeon's years of experience ($P > .25$ for all). Each diagnosis was screened as a potential risk factor, and herpetic scar (1 in 43; 2.3%), microbial ulcer (2 in 153; 1.3%), and corneal scar/opacity (2 in 227; 0.9%) were the indications with the highest rate of postoperative endophthalmitis ($P = .08$, $P = .09$, and $P = .26$, respectively); however, the diagnosis necessitating corneal transplantation was not found to be an independent predictor of endophthalmitis in the multivariate model.

Endophthalmitis after corneal transplantation developed at similar rates between eyes that received concurrent cataract extraction or lens manipulation procedures (4 in 1039; 0.4%) as compared with those without these procedures (12 in 2929; 0.4%) ($P > .99$).

DISCUSSION

IN THIS STUDY, THE OVERALL RATE OF ENDOPHTHALMITIS following PK was 0.7%, whereas the rate of endophthalmitis after EK was 0.2%. The rate of endophthalmitis following PK in prior large series has been reported to range from 0.11% to 1.05%, which is consistent with our results.[8–14] On the other hand, there have not been large series describing the rate of endophthalmitis following EK. In many of the endophthalmitis cases, precipitating factors that altered the postoperative course such as corneal ulcer, graft dehiscence, exposed Gore-Tex suture, or bleb-related infection were identified.

The EBAA report of self-reported adverse events found an overall rate of endophthalmitis of 0.028% for all penetrating, anterior lamellar, and endothelial keratoplasties and keratoprostheses, which is much lower than previously reported rates for PK alone.[16] The EBAA report found a higher rate of endophthalmitis for EK compared with PK, although the difference was not statistically significant. It is possible that the self-reported nature of the adverse events studied in the EBAA report could affect the results, as not all adverse events were captured. Alternatively, it is also possible that the much larger sample size of this study (over 150,000 of both PK and EK) compared with our sample size allowed for a more accurate ascertainment of the rate of this rare complication.

There are multiple possible reasons why the endophthalmitis rate following PK was higher than the rate after EK in this study. First, as shown in Table 2, eyes underwent PK for a wider range of diagnoses compared with EK. Indications for PK but not EK included traumatic graft dehiscence and microbial ulcer (often associated with perforation), diagnoses previously associated with higher rates of endophthalmitis.[14,27] Furthermore, eyes with herpetic scars and aniridia were candidates for PK but not EK. These diagnoses are associated with other ocular comorbidities including neurotrophic keratopathy and limbal stem cell deficiency, both of which can increase the risk of infection.[28,29] Furthermore, patients with intraocular hardware, such as glaucoma tubes, may preferentially undergo PK instead of EK according to the surgeon's comfort level, and this additional foreign body may increase the development of biofilms and the subsequent risk of intraocular infection.[30] Finally, in our cohort, many cases of endophthalmitis developed after suture-related infections. EK grafts have fewer long-term sutures and fewer ocular surface issues than PK grafts, decreasing the risk of this complication.

Patients who underwent concurrent anterior or pars plana vitrectomy had an approximately 8 times higher odds of developing endophthalmitis compared with those who did not in both multivariate and univariate analyses. A case series of endophthalmitis following PK also noted a high number of patients who had undergone concurrent anterior vitrectomy.[31] Similarly, large studies of postcataract endophthalmitis have shown that vitreous loss significantly increases the odds of developing endophthalmitis.[32–34] Several factors could contribute to this finding. Cases undergoing PK and requiring anterior vitrectomy are often related to infectious perforation or trauma, which are also independently associated with an increased risk of endophthalmitis.[14,27]

In the EBAA report on self-reported adverse events after corneal transplantation, *Candida* species was the most commonly reported etiology for endophthalmitis after EK.[16] In this study, there were 4 cases of endophthalmitis following EK. However, there was no growth on the 3 available cultures; thus, a comparison is difficult. In the 12 cases of endophthalmitis following PK, 10 had culture data with growth available. Five were gram positive, 2 were gram negative, 2 cases were due to *Candida*, and 1 case was secondary to a mold species. This wide-ranging microbial spectrum is similar to a recent case series describing 11 cases of endophthalmitis following PK.[31] In contrast, this is a much more diverse microbial spectrum than for endophthalmitis after cataract surgery or pars plana vitrectomy, which has been shown to be most commonly caused by gram-positive bacteria in 90% to 95% of culture-positive cases.[35–38] This difference may be due to several factors, such as the frequent long-term use of topical steroids in patients with prior PK, predisposing the eye to fungal infection.

Unlike for endophthalmitis following cataract surgery, there is limited evidence to guide the initial management of endophthalmitis after corneal transplantation.[35] In addition, dense corneal edema or an associated ulcer may limit the view for a safe pars plana vitrectomy, which can restrict options for initial management. In this study, 3 patients underwent pars plana vitrectomy at the time of diagnosis, and an additional 3 patients underwent pars plana vitrectomy within 1 month of the endophthalmitis diagnosis. However, because of the small sample size, it is difficult to make sound conclusions regarding treatment choice and clinical outcomes.

In general, clinical outcomes were poor in patients who developed endophthalmitis after PK, with patients losing on average more than 7 lines of vision at final follow-up compared with baseline visual acuity before endophthalmitis diagnosis. Only 16.7% of eyes had 20/400 or better visual acuity at final follow-up. This is comparable to the

prior series from the Bascom Palmer Eye Institute, showing that only approximately one-quarter of patients had Snellen visual acuity of 20/400 or better 12 months after their post-PK endophthalmitis diagnosis.[31] Several additional factors such as graft failure or rejection, cystoid macular edema, or retinal detachment likely contributed to these poor visual outcomes. In cases in which visual potential was poor, such as from retinal detachment or glaucoma, repeat transplantation was not performed. In general, these poor visual outcomes are worse than what has been observed in endophthalmitis cases after cataract surgery, which tend to have more favorable outcomes.[35,39,40]

Clinical outcomes were worse after post-PK endophthalmitis compared with post-EK endophthalmitis, with poorer visual acuity and higher rates of graft failure. Eyes with prior PK had more comorbidities than those with prior EK, including glaucoma (and prior trabeculectomy or tube shunts), herpetic infection, or trauma. It may be that the cases of endophthalmitis were more severe in the PK group than the EK group. We had no objective way to quantify the severity of the endophthalmitis cases to explore this possibility, however, as the endophthalmitis cases were treated by different retina specialists at Wills. Alternatively, the microbial spectrum of endophthalmitis may differ between the 2 groups, with a higher load of steroids in the PK group resulting in a greater predisposition to fungal infection. Finally, patients in the PK group were more likely to have had prior transplants and prior graft failure, as shown in Table 2, which increases the risk of future graft failure.

This study has some limitations. Although there was a large sample size included in this study, endophthalmitis is relatively rare. Due to the low number of endophthalmitis cases, there were some limitations in the number of risk factors we were able to evaluate. Although we did find that concurrent vitrectomy was a significant risk factor for endophthalmitis, this result also should be evaluated in the context of the small number of endophthalmitis cases. In addition, because billing codes were used to identify the indication for corneal transplantation, some encounter information was sporadically missing from the practice database. However, the number of transplants with a missing clinical indication constitutes a small percentage of the overall large number of surgical cases included in this study and does not affect the primary outcome evaluated, namely the development of endophthalmitis. Furthermore, because billing codes and basic electronic medical record demographic data were used to identify patients for this study, we were not able to assess if historical factors, such as trauma or infection, were associated with the development of endophthalmitis. Finally, we used procedure codes to identify patients who had undergone EK. There was no systematic way to differentiate those who had undergone DSEK versus DMEK, as the two use the same procedural codes. It is possible that the rates of endophthalmitis after DMEK would be even lower than DSEK, given that DMEK is typically performed in eyes with fewer comorbidities, but we could not demonstrate this with our data.

Despite these limitations, this study has several strengths. To our knowledge, it is the largest study performed evaluating endophthalmitis rates after PK compared with EK and the only study comparing outcomes for endophthalmitis following these 2 procedures. Data were collected from 11 corneal surgeons at different practices and multiple locations, adding to the diversity of the study population and increasing generalizability. At the same time, surgeons had a relatively standardized operative protocol, which decreased the potential for unobserved confounders related to the development of endophthalmitis. In addition, although electronic diagnosis codes were used to identify cases of endophthalmitis, individual chart review was performed to verify the diagnosis and clinical course.

In summary, this study reports the rate of endophthalmitis following nearly 4000 corneal transplants. The rate of endophthalmitis after PK was comparable to prior reports, but there was a significantly lower rate of endophthalmitis after EK, which has not been reported previously. Concurrent anterior or pars plana vitrectomy was found to be a risk factor for development of endophthalmitis. Eyes with endophthalmitis after PK had an overall poorer visual prognosis than those with endophthalmitis after EK. In addition, patients with endophthalmitis after PK had a higher rate of graft failure. The findings of this study are valuable both for counseling patients on complication rates after keratoplasty and for advising clinicians of the typical clinical course of endophthalmitis following corneal transplantation.

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