

# Clinical features, antimicrobial susceptibilities, and treatment outcomes of patients with culture positive endophthalmitis after penetrating keratoplasty



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## ABSTRACT

**Purpose:** To report the clinical features organisms and treatment outcomes in patients with endophthalmitis after penetrating keratoplasty (PK)

**Methods:** Retrospective noncomparative case series.

**Results:** Eleven eyes of 11 patients with culture positive endophthalmitis after PK were included. The time to diagnosis of endophthalmitis from last PK was less than 1 week in 3/11 (27%), between 1 and 4 weeks in 3/11 (27%), and greater than one month in 5/11 (46%) (range 2–924 days). The distribution of isolates included gram positive (GP) 9/11 (82%), gram negative (GN) 1/11 (9%), and fungal 1/11 (9%) species, respectively. Of GP bacteria tested, 9/9 (100%) were sensitive to Vancomycin. Of fungal isolates tested, none (0/1) were sensitive to Amphotericin, Fluconazole, and/or Voriconazole. Among patients with rim culture data available, 1/7 (14%) donor rims were culture positive for *Candida glabrata* and 6/7 (86%) were culture negative. Patients were treated with primary tap and inject in 10/11 (91%) and primary vitrectomy in 1/11 (9%). VA of  $\geq 5/200$  was present in 2/11 (18%) at time of endophthalmitis diagnosis, and was recorded in 6/11 (55%) at last follow-up.

**Conclusions and Importance:** Patients with endophthalmitis after PK presented at variable time points after surgery. Gram positive organisms were the most common isolate. VA outcomes after treatment were generally poor.

## 1. Introduction

Endophthalmitis after penetrating keratoplasty (PK) is a rare but devastating post-operative complication with poor visual prognosis. The incidence of post PK endophthalmitis has been reported 0.1–2.47%,<sup>1–4</sup> and pooled estimate from 1972 to 2002 in 90549 PKs was reported as 0.382%.<sup>5</sup> Etiologies for post PK endophthalmitis include donor contamination, intraoperative seeding, post-operative suture related complication, wound dehiscence, and post-operative keratitis. The association between infectious keratitis and post PK endophthalmitis has been well described, with an incidence of 0.05% culture positive endophthalmitis after 9934 corneal cultures for suspected infectious keratitis from 1995 to 2009 at Bascom Palmer Eye Institute, Miami, FL (BPEI).<sup>6</sup> Reported risk factors for endophthalmitis include long term use of topical steroids, fungal keratitis, trauma, corneal thinning, and keratitis adjacent to a prior surgical wound. The purpose of this study was to identify the clinical features, organisms,

and treatment outcomes in patients with endophthalmitis after penetrating keratoplasty (PK).

## 2. Methods

The study was approved by the University of Miami, Miller School of Medicine Medical Sciences Subcommittee Institutional Review Board. Data for this retrospective, noncomparative, consecutive case series was obtained from medical records of all patients with endophthalmitis and history of PK in the same eye who were treated at Bascom Palmer Eye Institute (BPEI) between January 1, 2006 through December 31, 2016. Not all patients had their PK performed at BPEI and only patients with culture positive endophthalmitis were included. Positive cultures from this institution's microbiology lab were reverse screened for diagnoses of endophthalmitis and keratoplasty, yielding 35 cases. From 35 cases, 5 were excluded because they had undergone Descemet stripping automated endothelial keratoplasty (DSAEK) but

**Abbreviations:** BPEI, Bascom Palmer Eye Institute; CE, cataract extraction; DMEK, Descemet membrane endothelial keratoplasty; DSAEK, descemet stripping automated endothelial keratoplasty; GN, gram negative; GP, Gram positive; HM, Hand motion; IOL, intraocular lens implant; LP, Light perception; NLP, No light perception; PK, penetrating keratoplasty; PPV, vitrectomy; TAP, tap and inject

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**Table 1**  
Demographics, past medical and ocular history of patients with endophthalmitis after PK.

Case	Gender	Age (Years)	Ocular history	Indication for PK	PK surgery
1	Male	66	Keratoconus	Keratoconus	PK/Phaco/IOL
2	Female	74	PXF Glaucoma, GDI, DSAEK x2, Phaco/Ant vit/Sulcus IOL, IOL exchange for ACIOL, CME s/p IVA/IVT, PBK	PBK, Failed DSAEK x2	PK/ACIOL explant/Ant Vit/Scleral fixated IOL
3	Female	73	SB/PPV/MP/EL/FAX/C3F8, PPV/PPL/Sulcus IOL/GDI, Glaucoma	PBK	PK
4	Male	73	Fuchs, Phaco/IOL, PBK, prior PK aborted due to dull trephine	Fuchs, PBK	PK
5	Female	62	Hexagonal refractive syndrome, Yag capsulotomy	Hexagonal refractive syndrome	PK/Phaco/IOL
6	Female	62	Fuchs	Fuchs	PK/ECCE/Ant Vit/ACIOL
7	Female	80	Complicated Phaco/IOL	PBK	PK
8	Female	74	Phaco/IOL, PBK, PK/IOL exchange, Inferior trab, Failed PK x2, Glaucoma, CME	Failed PK	PK
9	Male	65	Pt died of sepsis from SBO/Splenitis, Phaco/IOL, PBK, IOL dislocation	PBK	PK/Ant Vit/IOL explant/Sutured IOL
10	Male	42	Congenital Glaucoma, PPV/PPL/IOL/MP/EL for RD, IOL removal, ABK, GDI x2	ABK	PK
11	Male	57	Pseudomonas keratitis	Keratitis	PK

No patients were immunocompromised.

ABK = aphakic bullous keratopathy; ACIOL = anterior chamber intraocular lens; Ant vit = anterior vitrectomy; C3F8 = perfluoropropane tamponade; CME = cystoid macular edema; DSAEK = descemet stripping automated endothelial keratoplasty; FAX = fluid air exchange; ECCE = extracapsular cataract extraction; EL = Endolaser; Fuchs = Fuchs dystrophy; GDI = glaucoma drainage implant; IOL = intraocular lens; IVA = intravitreal bevacizumab; IVT = intravitreal preservative-free triamcinolone acetate; MP = membrane peel; PBK = pseudophakic bullous keratopathy; Phaco = phacoemulsification; PK = penetrating keratoplasty; PPL = pars plana lensectomy; PPV = pars plana vitrectomy; PXF = pseudoexfoliation; RD = retinal detachment; SB = scleral buckle; SBO = small bowel obstruction; Trab = trabeculectomy.

not PK, 10 were excluded due to PK procedure following (not preceding) endophthalmitis, 8 were excluded due to keratitis-associated endophthalmitis, and one patient was excluded given positive anterior chamber culture but negative vitreous culture. Thus 11 cases remained to be analyzed. Patients with a history of non PK surgical procedure or keratitis within 1 month of the diagnosis of endophthalmitis were excluded, so as not to re-report patients with keratitis-related or corneal suture-related endophthalmitis previously described at this institution.<sup>6,7</sup> Clinical features before, at the time of, and after the diagnosis of endophthalmitis were noted. Culture results and treatments outcomes were reviewed.

### 3. Results

Endophthalmitis after PK (excluding those associated with acute keratitis) was diagnosed in 11 eyes of 11 patients. The clinical features of these patients are summarized in Table 1. The median age was 66 years (range 42–80). Mean follow-up after infection was 36 months (range 0.3–135). The indications for PK were corneal edema or bullous keratopathy in 7/11 (64%), corneal ectasia in 2/11 (18%), graft failure in 1/11 (9%), and keratitis in 1/11 (9%). At time of PK, concurrent procedures included 2/11 (18%) cataract surgery with intraocular lens implant (IOL), and 3/11 (27%) IOL exchange with anterior vitrectomy. The time to endophthalmitis from most recent PK was less than 1 week in 3/11 (27%), between 1 and 4 weeks in 3/11 (27%), and greater than one month in 5/11 (46%) (range 2–924 days). Among patients with history of prior anterior vitrectomy and open posterior capsule at time of PKP, 6/6 (100%) presented with endophthalmitis within 1 month after PKP. At time of endophthalmitis diagnosis, the lens status of patients included 9/11 (82%) pseudophakic, 1/11 (9%) phakic, and 1/11 (9%) aphakic.

The organisms isolated from vitreous specimens (Table 2) were Gram positive (GP) 9/11 (82%), gram negative (GN) 1/11 (9%), and fungal species 1/11 (9%), respectively. The isolates included coagulase negative *Staphylococcus* species 5/11 (45%), *Streptococcus* species 2/11 (18%), *Candida albicans* 1/11 (9%), and miscellaneous organisms (Fig. 1). Of GP bacteria tested, 9/9 (100%) were sensitive to Vancomycin. Of fungal isolates tested, 0/1 (0%) was sensitive to Amphotericin, Fluconazole, and/or Voriconazole. Among all patients with rim culture data available, 1/7 (14%) donor rims were culture positive for *Candida glabrata* and 6/7 (86%) were culture negative. The donor rim

matched the vitreous isolate in 0/7 (0%) cases. 10/11 (91%) patients received primary tap and inject (TAP) and 1/11 (9%) received primary vitrectomy (PPV). All 11 patients received and intravitreal vancomycin and ceftazidime. Of those who underwent primary TAP, 2/10 (10%) had secondary TAP while 3/10 (30%) had secondary PPV for worsening infection. One of one (100%) patient with primary PPV also underwent secondary PPV for worsening infection. Other subsequent procedures included repeat PK 3/11 (27%), retinal detachment repair 2/11 (18%), glaucoma drainage implant 1/11 (9%). At time of last follow-up, VA was better than 20/400 3/11 (27%), 5/200–20/400 3/11 (27%), Hand motion (HM) – Light perception (LP) 4/11 (36%) and No light perception (NLP) 1/11 (9%) (see Figs. 2, 3 and 4).

### 4. Discussion

Variations in post PK rates reported lie in varying study methodologies, inclusion criteria, and study definition of endophthalmitis (Table 3). Additionally, outside of the United States, septicemia is not always a contraindication to tissue donation, different sterilization technique at time of retrieval, and long death to preservation time may also contribute to a higher reported international estimate 0.38% endophthalmitis after PK.<sup>5</sup> In the UK annual incidence of post PK endophthalmitis was reported as high as 0.67% in 11 320 first PKs from 1999–2006.<sup>8</sup> Incidence was not calculated in this study given several cases were referred from outside institutions, thus the total number of PK procedures performed was not known.

In contrast to other categories of post-operative endophthalmitis, which tend to have acute onset,<sup>9,10</sup> there was a wide distribution of time between PK to endophthalmitis diagnosis among patients in the current study. This time distribution is comparable to a similar prior report.<sup>11</sup> The results of vitreous isolate data in this studies showed predominance of *Staphylococcus* and *Streptococcus* species, and is consistent with prior post PK and generalized post-operative endophthalmitis data.<sup>2,9,10,12–14</sup> While there has been suggestion of increased incidence of fungal endophthalmitis after PK in recent years (0.1%<sup>12,15,16</sup>–0.22%<sup>2,17–19</sup>), only 1/11 cultures were positive for fungal species in the current series. This lower incidence of post PK fungal endophthalmitis may result from of different microbial biomes, small study number, or differing study inclusion/exclusion criteria.

While concordance of donor rim or preservation medium with positive vitreous culture have been reported higher in fungal than

**Table 2**  
Endophthalmitis after PK: Causative organisms, Age of PK, Interval from Last Surgical Procedure to Diagnosis, Risk factors, and Follow-Up Data.

Case	Duration of PK (days)	Sutures present	Lens status	Organism	Follow-up Post-Infection (months)	Last Recorded VA	Primary treatment	Further Surgical Intervention
1	240	Yes	IOL	<i>Staphylococcus epidermidis</i>	0.3	20/400	TAP V/C/D	None
2	9	Yes	IOL/open posterior capsule	<i>Streptococcus oralis</i>	12.0	HM	TAP V/C	Secondary PPV for worsening (PK removal/Temp Kpro/IOL removal/PPV/IV V/C/Vori/PK), late RD repair, Kpro/SOI for graft rejection
3	2	Yes	IOL/open posterior capsule	<i>Streptococcus agalactiae</i>	1.1	LP	PPV V/C/D	Secondary PPV for worsening
4	262	Yes	IOL	<i>Staphylococcus epidermidis</i>	13.5	20/800	TAP V/C/D	Late PPV/SB/AFX for RD
5	216	Yes	IOL/open posterior capsule	<i>Staphylococcus epidermidis</i>	8.9	20/70	TAP V/C/D	None
6	5	Yes	ACIOL/open posterior capsule	<i>Staphylococcus epidermidis</i>	135.2	LP	TAP V/C	Repeat TAP with IV Vanco, Late repeat PK for wound dehiscence and external drainage of HCD
7	924	No	IOL	<i>Staphylococcus hominis</i>	64.0	20/200	TAP V/C	None
8	6	Yes	IOL/open posterior capsule	<i>Enterococcus faecalis</i>	38.7	20/800	TAP V/C/D	GDI
9	36	Yes	IOL/open posterior capsule	<i>Candida Albicans</i>	99.6	20/100	TAP V/C	Secondary PPV with IV Ampho for worsening, AC washout × 2 with Vori/Ampho, late repeat PK for graft rejection
10	17	Yes	Aphakic/open posterior capsule	<i>Methicillin resistant staphylococcus aureus</i>	13.7	HM	TAP V/C	Secondary PPV for worsening
11	212	Yes	Crystalline lens	<i>Pseudomonas aeruginosa</i>	6.2	NLP	TAP V/C/D	Repeat TAP with IV Cefaz

AC = anterior chamber; ACIOL = anterior chamber intraocular lens; AFX = air fluid exchange; Ampho = intravitreal Amphotericin B; C/Cefaz = intravitreal Cefazidime; D = intravitreal Dexamethasone HM = hand motions; GDI = glaucoma drainage implant; HCD = hemorrhagic choroidal detachment; IOL = intraocular lens; IV = intravitreal; Kpro = keratoprosthesis; LP = light perception; NLP = no light perception; PK = penetrating keratoplasty; PPV = pars plana vitrectomy; RD = retinal detachment; SB = scleral buckle; SOI = silicone oil injection; TAP = vitreous paracentesis and intravitreal injection; Temp Kpro = temporary keratoprosthesis; V/Vanco = intravitreal Vancomycin; Vori = intravitreal Voriconazole.

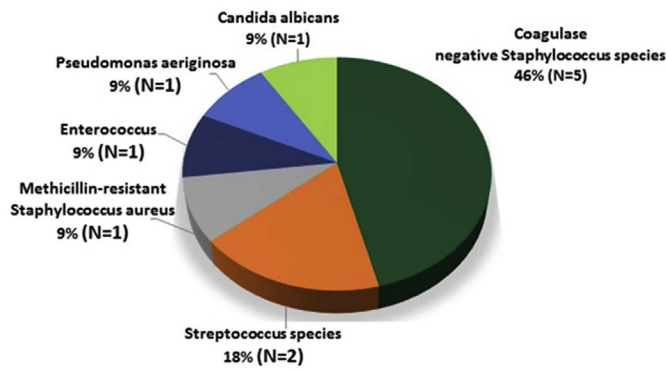


Fig. 1. Vitreous culture results in 11 patients.

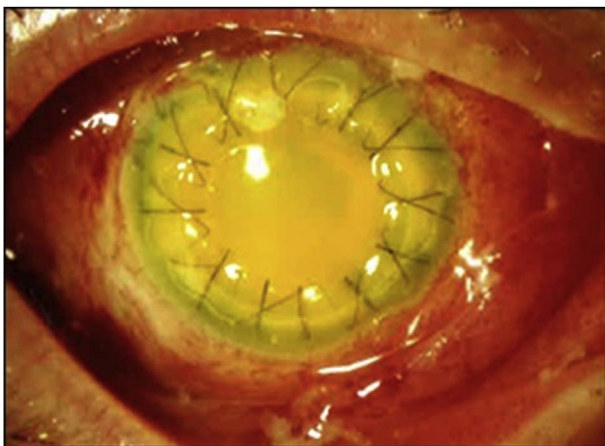


Fig. 2. Case 3: Clinical photograph at time of endophthalmitis diagnosis, 9 days after PK. Marked conjunctival injection, intact corneal sutures, and dense fibrinous anterior chamber reaction are noted. The vitreous isolate was *Streptococcus agalactiae*. At last recorded visit, VA was LP due to corneal and anterior chamber opacity.

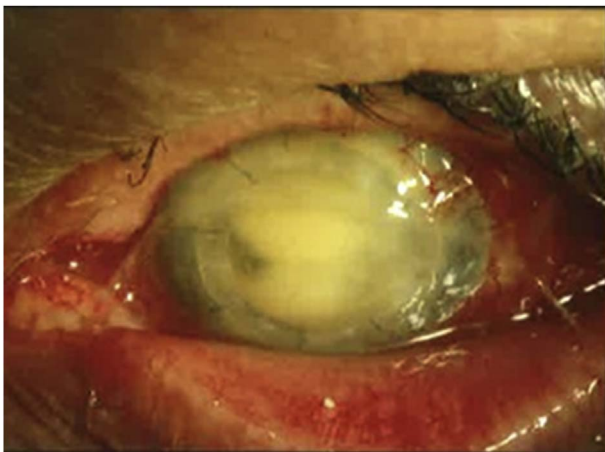


Fig. 3. Case 7: Clinical photograph at time of endophthalmitis diagnosis, 924 days after PK. Marked conjunctival injection, intact corneal sutures, and dense fibrinous anterior chamber reaction are noted. The vitreous isolate was *Staphylococcus hominis*. At last recorded visit, VA was 20/200 due to vitreous opacities and corneal edema.

bacterial endophthalmitis,<sup>19</sup> this was not present in this series. One of 7 rim cultures were positive for *Candida glabrata*, 1/11 vitreous cultures was positive for *Candida albicans*, and neither positive culture matched its counterpart. There is no clear consensus of predictive and prognostic value of donor rim culture in the literature.<sup>20,21</sup> In one study, bacterial contamination of donor rim was common (12–39%), but transmission rate was low.<sup>22</sup> In another study, endophthalmitis was 12 times more

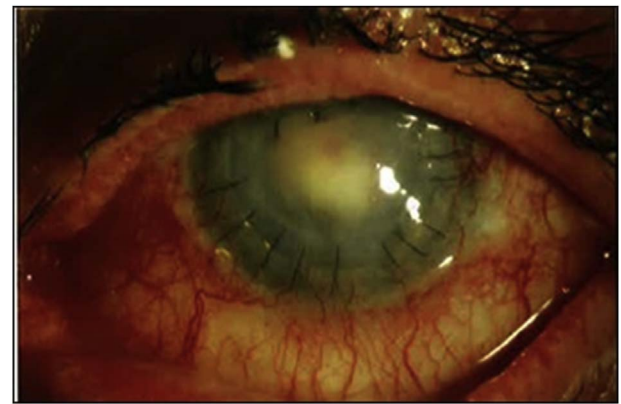


Fig. 4. Clinical photograph at time of endophthalmitis diagnosis, 214 days after PK. Marked conjunctival injection, intact corneal sutures, and dense fibrinous anterior chamber reaction are noted. The vitreous culture was negative, thus this patient was not included in the current series. The anterior chamber isolate was *Candida albicans*. At last recorded visit, VA was 20/200 due to corneal edema after multiple repeat PKs and removal of pupillary membrane.

likely with positive donor rim culture (95% CI 5–29%) more likely in positive rim. Based on these data, the routine use of antifungal agents in preservation media or the use of rim culture data in guiding management is not well defined.

Regarding risk factors, prior studies suggest risk factors for post PK endophthalmitis include prolonged used of steroids, keratitis, suture related complication, and wound dehiscence.<sup>6</sup> The following trends were recorded in the current study: combined CE/IOL at time of PK 5/11 (45%), anterior vitrectomy at time of PK 3/11 (27%), sutures present at time of endophthalmitis 10/11 (91%), recent suture removal 0/11 (0%), and wound leak 0/11 (0%). Nine of 11 patients in this study were pseudophakic, 1 phakic, and 1 aphakic. Patients with open posterior capsule at time of PK had earlier presentation with endophthalmitis (within 1 month of PK) likely due to greater ease of passage of pathogens from anterior to posterior chamber. It should also be noted that a majority of patients in this series received primary PK for corneal edema or bullous keratopathy, many of whom were referred from outside institutions. At this institution since 2006, it is uncommon practice to pursue a primary PK for corneal edema unless the patient has already failed prior Descemet stripping automated endothelial keratoplasty (DSAEK) or Descemet membrane endothelial keratoplasty (DMEK) procedures.

The predominance of TAP compared to PPV as initial treatment in this study reflects the lack of a defined protocol and management selection by individual surgeons. It is likely that the opacity of the PK graft in the setting of acute onset endophthalmitis precluded a satisfactory view for safe PPV. Due to the small number of patients, correlation between treatment and final visual acuity could not be performed; however, the wide variation in procedures including repeat TAP, secondary PPV, repeat PK, among others reflects the individuality of each patient presentation and lack of defined treatment protocol on which patients benefit most from surgical versus medical intervention. Data from study isolates support the continued use of vancomycin and ceftazidime as first line empiric intravitreal antibiotics, and the use of intravitreal antifungal agents when identified by culture results from the patient or the donor rim.

Limitations of this study include retrospective design, small number of patients, and lack of standardized prospective protocol. In cases where the infection clears, vision is often limited by other complications including secondary glaucoma, cystoid macular edema, graft failure and/or rejection, hypotony, cataract, retinal detachment. Cases of refractory or recurrent post PK endophthalmitis are also reported and management in these cases can be especially challenging.<sup>17</sup> Routine culture of donor rims and preservative media must be continued for

**Table 3**  
Comparison of post PK endophthalmitis studies.

	Leveille <sup>1</sup>	Guss <sup>2</sup>	Pardos <sup>3</sup>	Kloess <sup>4</sup>	Taban <sup>5</sup>	Henry <sup>6</sup>	Chen <sup>7</sup>	Kunimoto <sup>10</sup>	Antonios <sup>11</sup>	Cameron <sup>12</sup>	Alharbi <sup>13</sup>	Cameron <sup>14</sup>	Keyhani <sup>15</sup>	Edelstein <sup>17</sup>	Hassan <sup>18</sup>		
Year of publication	1983	1983	1982	1993	2005	2013	2015	2004	1991	1991	2014	1998	2005	2016	2005		
Country	USA	USA	USA	USA	0	USA	UK	USA	Saudi Arabia	Saudi Arabia	Saudi Arabia	Saudi Arabia	USA	USA	USA		
Number of PKs	1876	445	1880	1010	90549 <sup>00</sup>	-	11320	-	2210	3000	6752	16	2466	195859	-		
Number of reported endophthalmitis cases	4	11	2	4	-	5	76	14	9	10	55 <sup>c</sup>	4	3	37	234		
Reported incidence of endophthalmitis	0.21%	2.47%	0.1%	0.40%	0.38% <sup>00</sup>	-	0.67% <sup>•</sup>	-	0.41%	0.33%	0.68%	-	0.12%	0.018%	-		
Number of culture positive endophthalmitis cases	4/4	10/11	1/2	4/4	-	5/5	13/24 <sup>••</sup>	13/14	9/9	6/10 <sup>•</sup>	49/55 <sup>c</sup>	4/4	3/3	77/99 <sup>•</sup>	176/234		
Etiology																	
Suture related complication	-	0/11	0/2	-	-	5/5	-	-	-	0/6	19/55 <sup>c</sup>	0/4	0/3	-	-	-	
Wound leak/dehiscence	-	0/11	0/2	4/4	-	0/5	-	-	-	0/6	4/55 <sup>c</sup>	0/4	0/3	-	-	-	
Keratitis	-	6/11	0/2	1/4	-	5/5	-	-	-	1/6	47/55 <sup>c</sup>	0/4	0/3	-	-	-	
Contaminated donor	3/4	0/11	1/2	3/4	-	0/5	-	-	5/9	6/6	-	4/4	3/3	-	-	-	
Other	1/4	5/11	0/2	-	-	0/5	-	-	-	0/6	-	0/4	1/3	-	-	-	
Isolate																	
Gram positive	3/4	8/10	0/1	2/4	-	5/5	9/13 <sup>•••</sup>	10/13	6/9	2/6	68/80 <sup>••</sup>	3/4	0/3	27/82 <sup>••</sup>	130/176 <sup>l</sup>	-	
Gram negative	1/4	1/10	1/1	0/4	-	-	9/13 <sup>•••</sup>	3/13	0/9	1/6	10/80 <sup>••</sup>	0/4	0/3	2/82 <sup>••</sup>	130/176 <sup>l</sup>	-	
Fungal	0/4	1/10	0/1	2/4	-	-	4/13	0/13	3/0	3/6	2/80 <sup>••</sup>	1/4	3/3	53/82 <sup>••</sup>	46/176	-	
Primary management																	
Intravitreal antimicrobials	1/4	4/11	0/2	1/4	-	4/5	-	-	?	6/6	38/53 <sup>•••</sup>	2/4 <sup>†</sup>	-	-	-	-	
PFV	2/4	7/11	2/2	3/4	-	2/5	-	-	?	0/6	13/53 <sup>•••</sup>	0/4	-	-	-	-	
Evisceration	1/4	0/11	0/2	0/4	-	-	-	-	-	0/6	15/53 <sup>•••</sup>	0/4	-	-	-	-	
Last VA																	
< 5/200	2/4	9/11	2/2	4/4	-	3/5	-	-	?	3/6	48/55 <sup>c</sup>	2/4	-	-	-	-	
≥ 5/200 (better)	2/4	2/11	0/2	0/4	-	2/5	-	-	?	3/6	7/55 <sup>c</sup>	2/4	-	-	-	-	

patient safety. The role and timing of vitrectomy for post PK endophthalmitis with persistent corneal opacity and vitreous haze requires further study.

**5. Conclusion**

Endophthalmitis after PK is uncommon. The current study suggests that patients at highest risk are those with a concurrent procedure at time of PK, intraoperative complication (anterior vitrectomy), and those with open posterior capsule. Patients may present at variable time points after PK. Gram positive organisms were the most common isolate. VA outcomes were generally poor.

**Patient consent**

This report does not contain any personal information that could lead to the identification of the patient. A Waiver of HIPAA Authorization was approved by the University of Miami, Miller School of Medicine Medical Sciences Subcommittee Institutional Review Board for this study in accordance with IRB requirements.

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**Conflicts of interest**

The following authors have no financial disclosures: KDT, NAY, NS, NAP, DM, GA, AMB, HWF.

**Authorship**

All authors attest that they meet the current ICMJE criteria for Authorship.

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