Original Article

Outcomes of therapeutic penetrating keratoplasty in *Pythium insidiosum* keratitis managed with a combination of antibiotics

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Purpose: To describe the clinical outcomes of therapeutic penetrating keratoplasty (TPK) in patients with *Pythium insidiosum* keratitis following treatment with anti-pythium therapy (APT) consisting of linezolid and azithromycin. **Methods:** A retrospective review of medical records from May 2016 to December 2019 of patients with *P. insidiosum* keratitis was carried out. Patients who were treated with APT for a minimum of 2 weeks and then subsequently underwent TPK were included in the study. Data on demographic characteristics, clinical features, microbiology characteristics, and intraoperative details, postoperative outcomes were documented. **Results:** A total of 238 cases of *Pythium* keratitis were seen during the study period and 50 cases that satisfied the inclusion criteria were included. The median of the geometric mean of the infiltrate was 5.6 mm (IQR 4.0–7.2 mm). The patients received topical APT for a median of 35 days (IQR 25–56) prior to surgery. The most common indication of TPK was worsening keratitis (41/50, 82%). No recurrence of infection was observed. An anatomically stable globe was noted in 49/50 eyes (98%). The median graft survival rate was 2.4 months. A clear graft was present in 10 eyes (20%) with a final median visual acuity of 20/125 after a median follow-up period of 18.4 months (IQR 11–26 months). Graft size of less than 10 mm [OR: 5.824 (CI:1.292-41.6), $P = 0.02$] was found to be significantly associated with a clear graft. **Conclusion:** Performing TPK following the administration of APT has good anatomical outcomes. A smaller graft of <10 mm was associated with a higher chance of graft survival.

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Pythium insidiosum has been reported in the recent years as an important and challenging causative organism of microbial keratitis.[1] Although corneal infections due to *P. insidiosum* have been reported since 1987, the pathogen remained largely underdiagnosed because of its clinical and microbiological similarity with fungal filaments on the smear.[2,3] However, with the establishment of better diagnostic modalities in recent years, there has been a rise in the number of reported cases of *P. insidiosum* keratitis.[4] Due to similar microbiological features, initial treatment protocols were primarily based on antifungal agents with poor resolution rates and a higher need for surgical treatment.[5,6] This was attributed to the difference in the cell wall composition of fungal filaments and *P. insidiosum* as ergosterol is present only in the former.[6,7] As a result, antifungal medications are rendered ineffective in *Pythium* keratitis which led to the use of various antibiotics, such as linezolid, azithromycin, and minocycline, for the treatment of the same.[8,9] Of these, the combined use of linezolid 0.2% and azithromycin 1% is gradually being adopted as the preferred choice of medical anti-pythium therapy (APT) by several clinicians across the globe.[6,7,10–12]

The outcomes of therapeutic penetrating keratoplasty (TPK) following the use of antifungals have been described with good anatomical outcomes.[4,5,13–18] However, the functional outcomes in these studies were suboptimal with several studies reporting functional vision in less than 20% of the patients.[4,5,13–18] In the series by Nonpassopon *et al.* 2/6 (33%) had visual acuity better than 20/160.[19] Additionally, despite the low threshold for TPK in these studies, the rate of recurrent infection ranged from 20–100%.[4,5,13–19] The treatment regimen of *P. insidiosum* keratitis with APT is associated with a higher rate of medical resolution when compared to antifungals.[6,7,9] Nevertheless, nearly 25%–30% of patients still need TPK for eradication of infection.[7] We hypothesized that the patients undergoing TPK after having received APT would have better anatomical and functional outcomes when compared to those receiving antifungal therapy. And so, this present study was carried out to analyze the outcomes of TPK in cases who were initially treated with a combination therapy of linezolid and azithromycin.

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Methods

A retrospective chart review of all cases of culture and/or smear-proven *P. insidiosum* keratitis who were treated with topical linezolid 0.2% and azithromycin 1% for at least two weeks and then had undergone TPK from May 2016 to December 2019 was carried out. The study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Committee (LEC-BHR-R-09-22-940). Data regarding the baseline demographic details, clinical features, duration of preoperative anti-pythium therapy, surgical details, the postoperative course, and the outcomes of the grafts were collected.

All patients after microbiological confirmation of *Pythium* were subjected to a standard protocol for the management of *P. insidiosum* keratitis.[7] During the initial presentation, a detailed slit lamp examination was carried out and details of the ulcer were documented. This included the infiltrate size, location, and depth, presence of a hypopyon, corneal perforation, and associated limbal or scleral involvement. All patients underwent examination of the posterior segment if the media clarity permitted the same. The remaining patients were subjected to a b-scan ultrasonography. The microbiological diagnosis of *P. insidiosum* was initially made based on the presence of aseptate or sparsely septate, broad filaments with ribbon-like folds in the corneal scraping stained with 10% potassium hydroxide with 0.1% calcofluor white and viewed under a fluorescence microscope.[20] This was then confirmed by the growth of culture media followed by a demonstration of zoospores in an aquatic induction medium.[4] Once the organism was identified, anti-pythium treatment (APT) which consisted of hourly topical linezolid 0.2% with topical azithromycin (1% ointment twice a day) and oral azithromycin (500 mg, once a day for 2 weeks) was administered to the patient. The patients were then closely followed up and the progression of the ulcer was documented in terms of any increase in size, and development of impending or frank perforation. If any of these signs of worsening were noted, the patient was subjected to TPK for eradication of infection.

The surgery was performed under local or general anesthesia, based on the systemic and ocular suitability and cooperation of the patient. The intraoperative technique is similar to that described in the literature previously.[21] Of the 50 TPKs, 15 (30%) were performed by surgeons with surgical expertise of >5 years, while the rest (35 eyes, 70%) were performed by those who had <5 years of experience. The host trephination was oversized by 1.5 mm on either side of the maximum dimension of the infiltrate as per the protocol followed at our institute. The greater margin was taken in view of the higher rate of recurrence in *Pythium* keratitis.[5,14] Following the excision of the infected corneal button, one-half of the sample (across the middle of the involved cornea) was subjected to microbiological evaluation while the other half underwent histopathological examination as per the standard protocol.[21] Postoperatively the patients were continued on the same anti-pythium regimen. The initiation of topical steroids was started after 1–2 weeks of close observation for recurrence of infection. The outcome of the graft was categorized as a clear graft, primary or secondary graft failure. Graft failure was defined as irreversible corneal edema which was deemed secondary if the clarity was lost after 2 weeks of the surgery and the rest of the cases were considered primary failures. Additionally, the incidence of cataracts and secondary glaucoma was also documented along with the interventions performed for the same. Surgeries that were performed for visual rehabilitation as a second procedure were also recorded along with the final visual outcomes.

Statistical analysis was done with SPSS statistical software version 20 (SPSS, Inc., Chicago, IL, USA) and graphs were prepared using GraphPad Prism 9 (GraphPad Software, Inc., San Diego, CA). Data were described as percentages and continuous variables were reported as median with interquartile range (IQR). A P value of <0.05 was taken as statistically significant. Categorical data were described in proportions. The probability of graft survival following TPK was assessed with the Kaplan–Meier survival analysis. Regression analysis was carried out to assess factors associated with graft survival.

Results

A total of 238 cases of microbiologically confirmed *Pythium insidiosum* keratitis were seen during the study period. Of these, 50/238 cases (21%) satisfied the inclusion criteria and were included in the study. The demographic details and baseline clinical characteristics are presented in Table 1. The median of the geometric mean of the infiltrate was 5.6 mm (IQR 4.0–7.2 mm). Guttering around the area of the ulcer was present in 30/50 eyes (60%) and a hypopyon was noted in 26 eyes (52%). On microbiological examination, corneal scraping from all patients revealed filaments suggestive of *Pythium* on smears. *Pythium insidiosum* was found on culture in 40/50 scraping samples, of which 36/50 had a pure infection while the rest had a mixed infection [Fig. 1]. Details of the same are presented in Table 1. The patients had received topical APT for a median of 35 days (IQR 25–56) prior to undergoing keratoplasty. Of the 50 patients, 32 (64%) underwent additional procedures prior to TPK to either provide tectonic support or to reduce the load of infection. The most common surgery performed was the application of a tissue adhesive and bandage contact lens (19/50 eyes, 38%). The median time from presentation to keratoplasty was 35.5 days (IQR 23.8–58.5 days).

The most common indication for performing TPK was worsening of the keratitis (41/50, 82%) [Table 2]. The median donor graft size was 11 mm (IQR 9.5–12.5 mm), with a median endothelial count of 2460 cells/mm^2 (IQR 2200–2745 cells/mm^2). An intraoperative complication was noted in 10/50 eyes (20%) with the expulsion of the lens being the most common one (9/50 eyes, 18%). On histopathological evaluation of the corneal button, *Pythium* filaments could be detected in 25/50 buttons (50%) while the culture of pythium was obtained from 12/50 (24%) buttons. The postoperative regimen of APT has been presented in Table 3. A combination of topical linezolid and azithromycin was given in 37 eyes (74%). The patients received APT for a median of 21 days (IQR 15–30 days) and topical corticosteroids were started after a median of 13 days (IQR 8.5–16.8 days). A clinical suspicion of recurrent infection was present in 6/50 eyes (12%). Of these 6 eyes, three eyes had the presence of cellularity along the graft host junction, two eyes had anterior chamber exudates, and one eye had a combination of both. Two eyes underwent a repeat TPK; however, the culture of the half corneal button did not reveal *Pythium*. One eye underwent evisceration in view of a painful

Table 1: Baseline demographic and clinical features of eyes which underwent therapeutic penetrating keratoplasty

Demographic details and clinical features	*n*=50 eyes
Age (years), median (IQR)	42.5 (32-56.3)
Gender (n, %)	
Male	23 (46)
Female	27 (54)
Visual acuity at presentation (logMAR), median (IQR)	2 (1.2-2.0)
Poor visual acuity, (*n*,%)	
Hand movements	21 (42)
Perception of light	13 (26)
Infiltrate [median (IQR), mm]	
Vertical	5.5 (4.5-7.7)
Horizontal	5.7 (4.4-7.1)
Geometric mean	5.6 (4.0-7.2)
Ulcer features	
Endo-exudates	13 (26)
Tentacular infiltrates	38 (76)
Guttering	30 (60)
Pin-head lesions	36 (72)
Plaque formation	15 (30)
Hypopyon (*n*, %)	26 (52)
Scleral involvement (*n*, %)	2 (4)
Perforation (*n*, %)	
Impending	11 (22)
Frank	21 (42)
Culture, *n* (%)	
Pythium insidiosum	40 (80)
Staphylococcal sp.	3 (6)
Candida albicans	1 (2)
No growth	10 (20)
Duration of anti-pythium therapy, days; median (IQR)	
Topical	35 (25-56)
Oral	17 (10-25)
Time from presentation to TPK, days; median (IQR)	35.5 (23.8-58.5)
Adjunctive procedure (*n*, %)	32 (64)
TA	19 (38)
TA + AC reformation	7 (14)
TA + Intracameral linezolid	3 (6)
TA + Intrastromal linezolid	2 (4)
Intracameral linezolid	1 (2)
Duration of follow-up (months), median (IQR)	18.4 (11-26)

logMAR - logarithm of the minimum angle of resolution, IQR - interquartile range, TA - tissue adhesive, AC - anterior chamber

Table 2: Preoperative and intraoperative details of patients who underwent therapeutic penetrating keratoplasty

Indication (*n*, %)	
Worsening	41 (82)
Perforation/impending perforation	8 (16)
Large infiltrate at presentation	1 (2)
Median size of trephination, mm [median (IQR)]	
Host	10 (9-11)
Donor	11 (9.5-12.5)
Intraoperative complications (*n*,%)	
Lens expulsion	9 (18)
Lens expulsion + vitrectomy	1 (2)
Duration of surgery, minutes [median (IQR)]	114 (70-154)
Culture of HCB*, (*n*,%)	
Pythium insidiosum	12 (24)
Candida famata	2 (4)
Candida parapsilosis	1 (2)
Staphylococcus haemolyticus	1 (2)
No organism	22 (44)
No available information	12 (24)
Histopathology of HCB* (*n*,%)	
Pythium insidiosum	25 (50)
Candida famata	1 (2)
No organism	12 (24)
No records	12 (24)

IQR=Interquartile range, HCB=Half corneal button. *One patient had mixed bacterial and fungal infections

blind eye. No growth of *Pythium insidiosum* was noted from the eviscerated contents. The remaining eyes were managed medically with APT.

An anatomically stable globe was observed in 49/50 eyes (98%) following the TPK until the final median follow-up of 18.4 months (IQR 11–26 months). Primary graft failure was noted in 24/50 (48%) eyes, while the graft maintained clarity until the last visit in 10 eyes (20%) [Table 3, Fig. 2]. The final median visual acuity in the eyes with clear grafts was 20/125 (IQR logMAR 0.3–1.0). Secondary glaucoma and cataract were observed in 10/50 (20%) and 30/50 (60%) eyes, respectively. The underlying causes of glaucoma are presented in Table 3. A repeat surgical intervention was carried out in 29/50 eyes (58%) with cataract surgery being the most common one (15/50 eyes, 30%). The details of the other surgeries are presented in Table 3. Of the 39/50 eyes with primary or secondary graft failure, a repeat penetrating or endothelial keratoplasty was performed in 13 eyes (26%) and a visual recovery of ≥20/250 was observed in 8 eyes (16%). A Kaplan–Meier survival analysis predicted a graft survival rate of 33% at the end of 6 months which dropped to 13% at the end of 1 year [Fig. 3]. The median graft survival was 2.4 months. A logistic regression with "graft clarity" as outcome revealed a graft size of less than 10 mm [OR: 5.824 (CI: 1.292 to 41.6), $P = 0.02$] to favor a clear graft.

Discussion

Pythium keratitis accounts for a significant proportion of all fungal keratitis and is an important differential of atypical microbial keratitis, especially in eyes that clinically mimic fungal keratitis.[6,14,20] Several attempts have been made at establishing a standardized regimen of medical therapy for this organism, especially with the use of topical antibiotics.[5–7,14] The results of these studies have been promising; however, a significantly large subset of these eyes require surgical intervention either in the form of a TPK or an evisceration.[6,7,12] The current study describes the results of TPK performed after receiving treatment with a combination of topical linezolid and azithromycin. In nearly 98% of the eyes, a good anatomical outcome was observed with the preservation of globe integrity. Also, no microbiologically proven recurrent infection was noted. A good functional outcome was obtained in around one-third of the eyes and a complicated cataract and secondary glaucoma were the common postoperative complications.

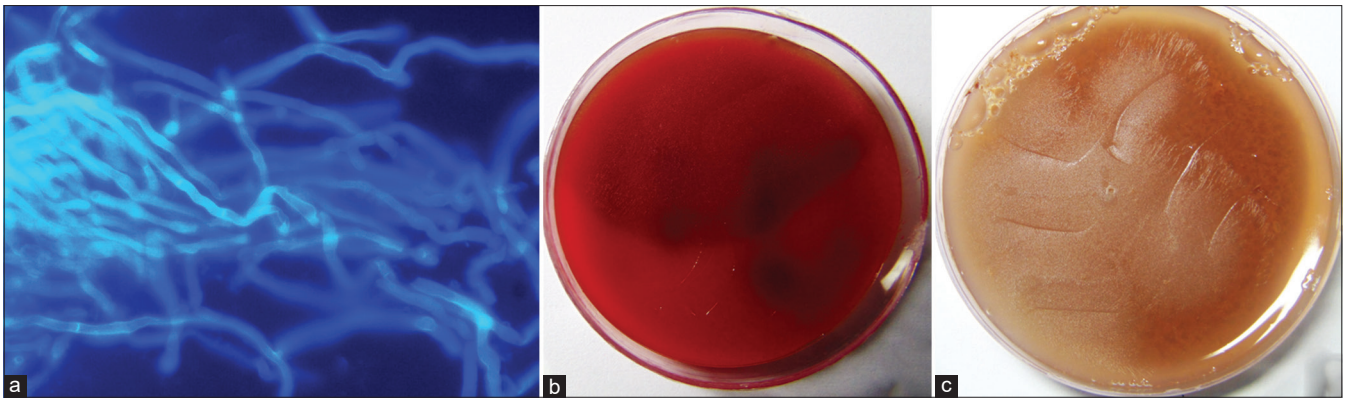

Figure 1: Collage of images depicting the smear and cultures of *Pythium insidiosum.* (a) Broad, aseptate, *Pythium* filaments stained with 10% potassium hydroxide and 0.1% calcofluor white stain, as seen under a fluorescence microscope (x400). (b) Flat, colorless, feathery colonies of *Pythium* on 5% sheep blood agar (c) *Pythium* colonies on chocolate agar

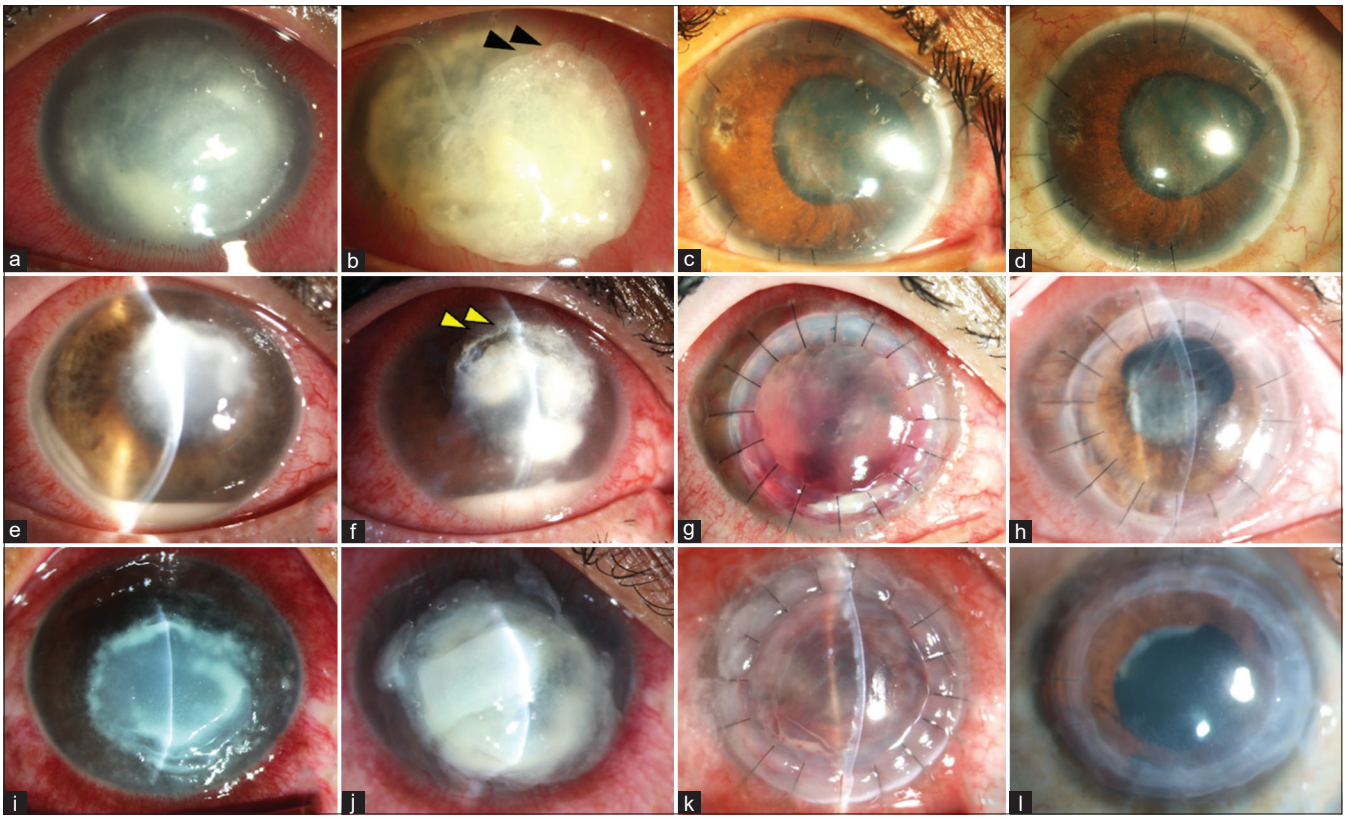

Figure 2: (a) Patient with *Pythium insidiosum* keratitis in the right eye showing a large infiltrate (b) which progressively worsened over the next month, requiring application of tissue adhesive and a bandage contact lens (TA + BCL) (black arrowheads). (c) The patient underwent a therapeutic penetrating keratoplasty (TPK). There was no evidence of any recurrent infection in the immediate postoperative period and a clear graft was observed at the 1-month and (d) 1-year follow-up visits. (e) Patient with *Pythium* keratitis in the right eye involving the central and paracentral cornea (f) which worsened over the next 1.5 months and required a TA + BCL (yellow arrowheads). (g) A TPK was performed nearly 2 months after presentation (h) The patient did not have any residual infection or recurrence in the subsequent visits and developed primary graft failure. (i) A similar presentation was observed in the third case of a central ulcer of *Pythium* keratitis in the right eye (j) A progressive increase in the ulcer size and density was observed over 1 month of follow-up (k) and the patient required TPK after 1.5 months of topical therapy (l) A primary graft failure was noted for which the patient underwent an endothelial keratoplasty after 6 months

Table 4 depicts the comparison of the current study with a series reporting TPK outcomes following the use of either antifungal (TPK-AF) or APT (TPK-APT). The anatomical success rate reported in TPK-APT studies was similar to that seen in our patients and ranged from 80–100%.[6,7,11,12] This was higher than the globe preservation rate observed in the TPK-AF series which varied from 44–100%.[4,5,14–19] Early TPK was found to have higher anatomical success by Gurnani *et al.*; however, 94% of the patients in the current study maintained globe integrity despite undergoing TPK after an average of nearly

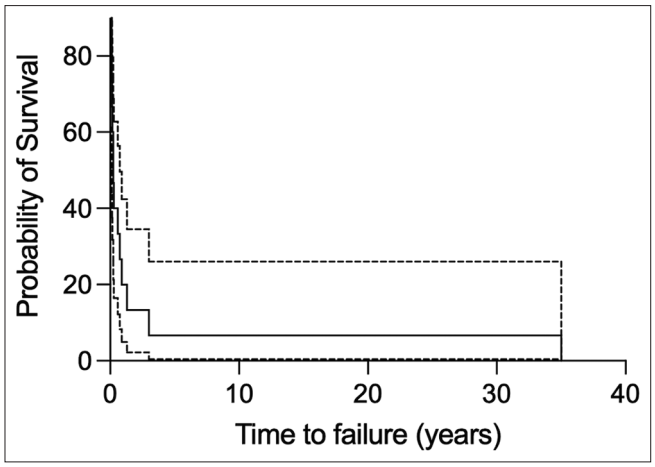

Figure 3: Kaplan–Meir survival analysis of grafts after therapeutic penetrating keratoplasty (solid line). The dotted lines represent the 95% confidence intervals

five weeks.[12] A wide variability was found in the proportion of eyes that had a good functional outcome in both TPK-AF and TPK-APT groups, with better outcomes in studies with smaller samples. The higher number of cases with a good visual recovery in the present study can perhaps be secondary to the initiation of topical corticosteroids within 2 weeks of the surgery. The use of donor tissues with a median ECD of 2460 cells/mm^2 could be another factor responsible for this.

The low recurrence rate seen in our study was similar to that reported by both Bagga *et al.* and Sane *et al.*[7,10] Although Gurnani *et al.* had a higher rate of recurrent infection following TPK-APT, this could be attributed to the fact that APT was started only after the organism was confirmed on culture reports.[12] Furthermore, the average time between presentation and TPK in this study was around 11 days.[12] Thus, the patients would have received APT for less than 2 weeks. This contrasts with the current study wherein the cases received APT for a median of 24 days which might have contributed to a decreased load of the infectious organism. The two-week time period for better outcomes has also been established by Bagga *et al.*[7] Vishwakarma *et al.* also reported a recurrent infection rate of nearly 27%; however, this was a combined rate of both TPK-AF and TPK-APT cases.[11] Studies with TPK-AF eyes had a very high recurrence rate ranging from 20–100%, with most studies having recurrent infections in more than half the eyes.[4,5,13–19] Thus, although a significant proportion of cases still require TPK despite the use of antibiotics, these eyes fare better following the surgery both in terms of anatomical and functional outcomes as well as the recurrence rates.

The cases with suspected recurrent infection in our series were managed medically or with repeat TPK and globe integrity was maintained in all cases. A similar management approach has been previously adopted with a surgical intervention being necessary for a majority of cases with recurrent infection.[12,14,15] Agarwal *et al.* reported poor outcomes in attempting medical management of recurrent *Pythium* infection and all these cases eventually required a repeat keratoplasty.[15] They also advocated the use of cryotherapy as a primary procedure to reduce the risk of recurrence, especially in eyes with the extension of the infiltrate beyond the limbus. However, most of their cases were managed with primary

Table 3: Postoperative outcomes of patients who underwent therapeutic penetrating keratoplasty

Graft outcomes, *n* (%)	
Clear graft	10 (20)
Primary graft failure	24 (48)
Secondary graft failure	15 (30)
Phthisis bulbi	1 (2)
Posterior segment complications, *n* (%)	
Endophthalmitis	1 (2)
Choroidal detachment	1 (2)
Retinal detachment	1 (2)
Postoperative medication - Topical, *n* (%)	
Natamycin + Azithromycin	1 (2)
Linezolid	8 (16)
Linezolid + Azithromycin	37 (74)
Antiglaucoma medications	4 (8)
Postoperative medication - Oral, *n* (%)	
Linezolid	3 (6)
Azithromycin	12 (24)
Acetazolamide	13 (26)
Secondary glaucoma, *n* (%)	10 (20)
Peripheral anterior synechiae	6 (12)
Pupillary block glaucoma	1 (2)
Idiopathic	3 (6)
Final visual acuity (logMAR), median (IQR)	0.9 (0.4-2)
Poor visual acuity, *n* (%)	
Hand movements	8 (16)
Perception of light	7 (14)
No perception of light	2 (4)
Additional procedures, *n* (%)	
DSAEK	12 (24)
Penetrating keratoplasty	6 (12)
Cataract surgery	15 (30)
VR surgery	3 (6)
Iridectomy	1 (2)
TSCPC	3 (6)

logMAR=logarithm of the minimum angle of resolution, IQR=interquartile range, DSAEK=Descemet stripping automated endothelial keratoplasty, VR=vitreoretinal, AGV=Ahmed glaucoma valve, TSCPC=transscleral cyclophotocoagulation

surgical intervention which contrasts with the present study. Thus, our low recurrence rate, in the context of the fact that this is the largest series of TPK-APT reported so far, signifies the efficacy of preoperative administration of APT. The oversizing of the host trephination greater than that of conventional TPK could have also contributed to the lower recurrence rate.[21]

A corneal perforation occurred in a significant proportion of our cases which could be because of the irregular corneal surface secondary to plaque formation. This plaque forms during the healing phase of the ulcer, and thus, these patients need to be followed up closely despite being in the resolution phase of the keratitis.[7] Carrying out TPKs in these eyes can be challenging and may result in lens expulsion or vitreous loss. Measures such as the use of scleral rings, non-compressive lid speculums, and preoperative osmotic diuretics can help reduce the risk of these complications. Nearly half the eyes in our study had primary graft failure which may have occurred because of intraocular inflammation. Furthermore, the delayed institution of topical corticosteroids in the immediate postoperative period could have also contributed to the failure of the graft. Several studies have attempted to study the risk factors associated with

Table 4: Outcomes of *Pythium* keratitis with antifungals and antibacterial medications from various published studies

Author	Number of eyes that underwent surgery (total sample size)	Medication prior to surgery	Primary surgery		Recurrence *n*, %	Anatomical success *n*, %	Functional success *n*, %
			TPK	Evisceration			
Thanathanee *et al* (2013)[13]	5 (5)	AF	5	0	3 (60)	4 (80)	0
Sharma *et al.* (2015)[4]	11 (13)	AF	10	1	2 (20)	9 (90)	3 (20)
Agarwal *et al.* (2017)[14]	10 (10)	AF	10	0	7 (70)	8 (80)	2 (20)
Agarwal *et al.* (2018)[15]	46 (46)	AF$^{\Psi}$	46	0	27 (59)	39 (85)	NA
Hasika *et al.* (2019)[5]	48 (71)	AF	48	0	26 (54)	21 (44)	5 (10)
Puangsricharern *et al.* (2021)[16]	21 (26)	AF	21	3	15 (71)	11 (52)	1 (5)
Zhang *et al.* (2021)[17]	6 (6)	AF	6	0	3 (50)	3 (50)	NA
Nonpassopon *et al* (2021)[19]	6 (6)	AF	6	0	1 (17)	6 (100)	2 (33)
Hou *et al.* (2021)[18]	3 (3)	AF	3	0	3 (100)	0	0
Vishwakarma *et al* (2021)[11]	15 (18)	APT/AF$^{\#\#}$	AF-10, APT-5	AF-1, APT-1	4 (27)	AF 9 (90) APT 4 (80)	AF-6 (60) APT-1 (20)
Bagga *et al.* (2018)[6]	88 (96) & 11 (18)	AF &APT	87&11	1&0	NA	9 (82) $^{\#\#\#}$	0$^{\#\#\#}$
Bagga *et al.* (2021)[7]	31 (69)	APT	31	0	0	31 (100)	9 (29)
Gurnani *et al.* (2021)[12]	19 (30)	APT$^{\#}$	19	0	7 (37)	90	NA
Sane *et al.* (2021)[10]	5 (21)	APT	4	1	0	4 (100)	0
Current Study (2022)	54 (54)	APT	54	0	0	53 (98)	21 (39)

TPK - Therapeutic penetrating keratoplasty, $^{\Psi}$Only one patient received LZ + AZ, $^{\Psi\Psi}$Nine patients did not receive any intervention, $^{\#}$Five patients received linezolid with azithromycin after therapeutic penetrating keratoplasty, $^{\#\#}$7/18 patients received linezolid and/or azithromycin while 11/18 received natamycin, $^{\#\#\#}$Data available for the group that received APT, AF - Antifungals, APT - Anti-pythium therapy

surgical intervention or a poor outcome. Vishwakarma *et al.* found a larger infiltrate and poorer final visual outcomes in patients presenting after 2 weeks of the onset of the disease.[11] A similar association was established by Puangsricharern *et al.* between advanced disease at presentation and increased globe removal rates.[16] They also found increased age and higher density of *Pythium* filaments on histopathology to have poor globe salvage rates. In the present series, smaller grafts had better chances of maintaining graft clarity during the follow-up period. Although graft survival following TPK-APT has not been studied, the survival rate in the present series is similar to that of TPK performed for bacterial and fungal keratitis.[21,22]

This is the largest reported series on the outcomes of TPK in *P. insidiosum* keratitis. Additionally, the combination of linezolid and azithromycin has had the best outcomes in terms of success with medical therapy and this is the largest series describing the outcomes of eyes that have undergone TPK following this regimen. Also, this is the first study to attempt to understand the preoperative and intraoperative factors that predict the outcome of the graft and graft survival rates following TPK for *P. insidiosum* keratitis. The retrospective nature of the study is a limitation. Additionally, confocal microscopy and polymerase chain rection (PCR) tests were not employed in the current study which could have provided an additional perspective. Future prospective studies can be designed which can help understand the demographic and clinical features that predict the risk of requiring surgical intervention and its subsequent outcomes.

Conclusion

In conclusion, although patients with *P. insidiosum* keratitis require TPK despite the use of APT, the anatomical and functional outcomes of these grafts are much better when compared to TPK following antifungal regimens. Also, the recurrence rates in TPK-APT are lesser than that of TPK-AF. The presence of larger grafts is associated with a higher risk of graft failure. Although early TPK has been practiced for P. insidiosum keratitis, the current study demonstrates the benefits of adequate preoperative administration of anti-pythium therapy which improves the global salvage rates. With judicious case selection and careful postoperative monitoring, a significant proportion of these eyes can be visually rehabilitated to provide good functional outcomes as well.

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Conflicts of interest

There are no conflicts of interest.

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