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Early deep anterior lamellar keratoplasty for fungal keratitis poorly responsive to medical treatment

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Learning objectives

Upon completion of this activity, participants will be able to:

1. Describe the efficacy of therapeutic deep anterior lamellar keratoplasty in patients with fungal keratitis that is affecting the optical zone and is poorly responsive to medical treatment, based on a pilot study
2. Describe risk factors and causative organisms for fungal keratitis and inclusion criteria for therapeutic deep anterior lamellar keratoplasty, based on a pilot study
3. Describe clinical implications regarding therapeutic use of deep anterior lamellar keratoplasty in patients with fungal keratitis, based on a pilot study

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CLINICAL STUDY

Early deep anterior lamellar keratoplasty for fungal keratitis poorly responsive to medical treatment

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Abstract

Purpose **To investigate the efficacy of early therapeutic deep anterior lamellar keratoplasty (DALK) in eradicating fungal keratitis that is poorly responsive to medical treatment.**

Patients and methods **Twenty-three eyes (23 patients) underwent early therapeutic DALK within 15 to 50 days from the onset of symptoms. The adopted eligibility criteria for early DALK included the following: active fungal keratitis affecting the optical zone with ulcer confined in the 6.00 mm central cornea; deeper than 150 μm but not exceeding 300 μm; and poorly responsive to medical treatment.**

Results **The big bubble technique was accomplished in 74% (17) of eyes, whereas manual dissection was performed in the remaining 26% (6) of eyes. Histopathological examination did not show any sign of fungal colonization in the peripheral and deep stromal lamellae in any case. All grafts were transparent postoperatively, and no recurrence of infection occurred. Median best spectacle corrected visual acuity significantly improved from 2.0 (1.0 interquartile range) logMAR to 0.1 (0.1 interquartile range) logMAR ($P<0.01$). The mean follow-up was 32 ± 10 months. Neither episode of rejection nor graft failure was noted during the follow-up period.**

Conclusion **Early DALK could represent a safe therapeutic approach to eradicate fungal keratitis that affects the optical zone and is poorly responsive to medical treatment.**

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Introduction

Fungal involvement of the cornea represents a dramatic clinical event that is an important cause of blindness and visual impairment worldwide.[1–3] Managing fungal keratitis is challenging because of several issues. Delay in proper diagnosis and inappropriate treatment foster fungal growth.[4]

Once fungi reach the deep stroma, annihilating the infection becomes a challenge. Antifungal medications often fail to achieve adequate control of the keratitis, and long-standing tissue necrosis and host inflammation advance.[4] Fungi can colonize the deep stroma and penetrate through an intact Descemet membrane (DM), posing the globe at risk of endophthalmitis. Patients ultimately undergo penetrating keratoplasty (PK) for frank/impeding perforation or to avoid scleral extension of the infection; however, therapeutic control is not always achieved and graft failure and postoperative complications are common.[5]

Multiple treatment strategies have been proposed to manage the fungal keratitis recalcitrant to medical treatment; however, none has been shown to achieve the therapeutic and optical goals required to promote safe control of infection and restoration of corneal transparency.[6–12] We previously described the effectiveness of early deep anterior lamellar keratoplasty (DALK) for treating *Acanthamoeba* keratitis that is poorly responsive to medical treatment; the purpose of this study was to describe the outcomes of early DALK for fungal keratitis that is poorly responsive to medical treatment.[13]

Materials and methods

This retrospective, noncomparative, interventional, and consecutive case series adhered to the tenets of the Declaration of Helsinki. Informed consent for surgery was obtained from all participants, and attention was given to protect the identity of the study subjects. Patients with active fungal keratitis

poorly responsive to medical treatment who underwent early therapeutic DALK between January 2005 and December 2013 were considered eligible for this study.

The clinical suspicion of fungal keratitis was raised on the basis of suggestive clinical history and slit-lamp findings. The diagnosis was then confirmed following the direct microscopic examination (10% potassium hydroxide wet mounts and Gram-stained smear), inoculation, culture on Sabouraud dextrose agar, and PCR.

Once the diagnosis had been established, patients were required to follow our antifungal regimen protocol consisting of 1% voriconazole eye drops and 200 mg/day voriconazole tablets. Patients were required to use the eye drops every hour, day and night, during the first 2 days, and then hourly during the day from day 3. Amphotericin B 0.15% eye drops were then added if *Candida* or *Curvularia* were identified.

Patients were closely followed-up, at least once per day, to assess the therapeutic response to antifungal medications. All the fungal lesions were carefully studied in terms of location, depth, and progression during the treatment period. Objectifying the response to the medical treatment was difficult. Team briefing was conducted at the end of each day of treatment to discuss whether performing DALK was appropriate. The responsiveness to medical treatment was considered poor if neither improvement nor stabilization of lesion size was clearly observed.

Surgical indications

The parameters that we had followed for evaluating the response to the medical treatment included: subjective symptoms; size of lesions, appearance of new lesions; size of the epithelial defect; and degree of inflammation.

All the patients in this series showed an ulcer: (1) affecting the optical zone and confined within the 6.00 mm central cornea; (2) deeper than 150 μm but not exceeding 300 μm (anterior segment optical coherence tomography (AS-OCT); Optovue, Fremont, CA, USA); (3) with no associated signs of inflammation affecting the anterior chamber; and (4) poorly responsive to targeted medical treatment, as previously described.

Because of the dangerousness of fungal keratitis and the poor visual prognosis associated with lesions affecting the optical zone, DALK was performed early even in 'borderline' patients (ie, patients for whom the evaluation of response to treatment was not clear). This approach was chosen because large and deep lesions that are poorly responsive to medical treatment are prone to complications of perforation and intraocular extension of the infection.[14] Moreover, lesions affecting the optical zone are known to heal, leaving a scar that penalizes visual acuity.[14] DALK performed at an early stage would have increased the chances of eradicating the fungal infection poorly responsive to medical therapy.[13]

Data collection

Data collection for retrospective analysis included standardized patient demographics, preoperative and postoperative best spectacle-corrected visual acuity (BSCVA), causative microorganism and predisposing factor for fungal keratitis, trephination diameter, type of DALK achieved (descemetic (dDALK) or predescemetic (pdDALK)), histopathological examination of the removed stroma, postoperative recipient bed thickness (AS-OCT), episodes of postoperative infection recurrence, graft rejection, graft failure, follow-up duration, and postoperative endothelial cell density (ECD) at 6 and 12 months (Confoscan 3; Nidek, Milan, Italy; CSO SP02, Florence, Italy). Recurrence of infection was defined as a new episode of infection due to the same organism within 1 month after surgery.

All surgical procedures were performed by a single surgeon (VS) at 'Ambulatorio di Chirurgia Oculare Santa Lucia' and 'Misericordia Hospital' (Grosseto, Italy) within 15 to 50 days after the onset of symptoms. DALK technique was accomplished with the same modified technique described in our previous work regarding the management of *Acanthamoeba* keratitis poorly responsive to medical treatment, with the only exception being that irrigation of the exposed recipient bed was performed with targeted antifungal solution for 2 min instead of topical propamidine.[13,15–17]

The stromal tissue removed during surgery was evaluated for fungal colonization. Peripheral surgical margins were considered free of infection when at least 1.5 mm had no presence of pathogens. The deepest layer of stroma manually removed was analyzed to assess the pdDALK cases, whereas the last pieces of stroma removed after the opening of the big bubble were assessed for dDALK cases.

Postoperative treatment

Patients were required to keep following the treatment prescribed preoperatively. In addition to the antifungal medications, patients were also required to follow our post-keratoplasty therapeutic protocol consisting of: levofloxacin tablets (Levoxacin 500 mg; GlaxoSmithKline S.p.A., Verona, Italy) 500 mg/day for 1 week; ofloxacin 3 mg/ml eye drops (Exocin; Allergan S.p.A., Rome, Italy) four times/day for the first 2 weeks; and lubricant eye drops many times per day for at least 1 year. Dexamethasone 0.1%/tobramycin 0.3% eye drops (TobraDex; ALCON Italia S.p.A., Milan, Italy) were

introduced once surgical margins were found free from infection at histological analysis.

A minimum follow-up of 12 months was ensured for all patients.

Statistical analysis

The assumption of normal distribution was assessed with the Shapiro–Wilk test ($P>0.05$). BSCVA was measured with Snellen projector charts, and data were converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis.[18] Continuous variables were reported with the mean, s.d.; median and interquartile range (IQR) were also provided for nonparametric data. Range of values and 95% confidence interval (CI; reported as lower bound–upper bound) were shown for each variable. The related samples Wilcoxon signed rank test was used to evaluate changes in BSCVA, whereas paired sample *t*-test was performed to compare ECD. $P<0.05$ was considered statistically significant.

Results

Baseline data

Twenty-three patients were included in this retrospective case series; 11 were female (48%), with a median age of 33 (17) years (95% CI, 32–42; range, 24–65 years).

The causative microorganisms identified preoperatively included *Fusarium* species (9 cases), *Candida* species (8 cases), *Aspergillus* species (5 cases), and *Curvularia* species (1 case). Predisposing factors for fungal keratitis were soft contact lens wearing (14 cases), leukemia (5 cases), Sjögren syndrome (1 case), diabetes (2 cases), and trauma (1 case). Considering the response to antifungal medical treatment, DALK was deemed necessary: after 3 days for 1 case of *Fusarium*; after 6 days for 2 cases of *Fusarium*; between 7 and 14 days for 6 cases of *Fusarium*, for 7 cases of *Candida*, and for 4 cases of *Aspergillus*; and within 20 days for 1 case of *Curvularia*, 1 case of *Aspergillus*, and 1 case of *Candida*.

Surgical data

Donor graft matched the recipient cornea in terms of sizes of 8.5, 9.0, and 9.5 mm in 52.17% (12), 34.78% (8), and 13.04% (3) of eyes, respectively.

The big bubble technique was accomplished in 17 (74%) eyes, whereas manual dissection was performed in the remaining 6 (26%) eyes. The postoperative recipient bed thickness was quantified as $53\pm28\,\mu$m (range, 25–98; 95% CI, 24–83) by AS-OCT.

Postoperative outcomes

Histopathological examination did not show any sign of fungal colonization in the peripheral and deep stromal lamellae. All grafts were transparent postoperatively, and there was no recurrence of infection (Figure 1).

Postoperative data are listed in Table 1. There was a statistically significant improvement of BSCVA ($P<0.001$). Neither episode of rejection nor graft failure was noted during the follow-up period. The ECD was not measurable preoperatively and endothelial cell loss between 6 and 12 months postoperatively was 1.59%. The mean follow-up was 32 ± 10 months (range, 18–50; 95% CI, 27–36).

Discussion

Timing profoundly affects the delicate balance of the risks and benefits related to treatment. Establishing a prompt diagnosis and targeted antifungal treatment are the key factors to achieve optimal control of infections. Nonetheless, misdiagnosis, inappropriate therapy, and treatment delay compromise the success of antifungal regimens.[4]

Antifungal medications often fail to eradicate the active infection after fungi have gained access to the corneal

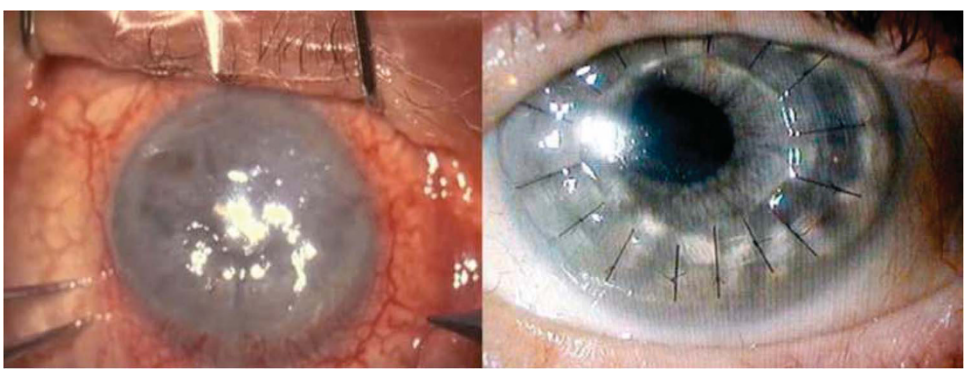

Figure 1 Fungal keratitis: preoperative (left) and postoperative (right).

Table 1 Postoperative outcomes

BSCVA	
Preoperative	
Median (IQR)	2.00 (1.00) logMAR
Range	1.30–3.00 logMAR
95% Confidence interval	1.92–2.45 logMAR
Postoperative	
Median (IQR)	0.10 (0.10) logMAR
Range	0.00–0.22 logMAR
95% Confidence interval	0.07–0.12 logMAR
ECD	
6 Months	
Mean ± SD	2517 ± 336 cells/mm^2
Range	1985–3102 cells/mm^2
95% Confidence interval	2372–2662 cells/mm^2
12 Months	
Mean ± SD	2477 ± 331 cells/mm^2
Range	1953–3052 cells/mm^2
95% Confidence interval	2334–2620 cells/mm^2

Abbreviations: BSCVA, best spectacle-corrected visual acuity; ECD, endothelial cell density; IQR, interquartile range; logMAR, logarithm of the minimum angle of resolution.
BSCVA results are displayed as median (IQR) given the nonparametric distribution of data. 95% Confidence intervals are expressed as lower bound–upper bound.

stroma.[19] The infection can progress through the DM into the anterior chamber and other intraocular structures, causing endophthalmitis that usually requires evisceration.[4,20]

Targeted drug delivery has been adopted in the form of intrastromal injections with the purpose of achieving optimal stromal antifungal concentrations, and it has been effective in controlling recalcitrant fungal keratitis, with different reported success rates.[10,11] However, therapeutic success is not invariably achieved with this approach; in a recent case series, 28% of the cohort required PK because of the progression of the infection and impending perforation.[11]

PK had been advocated as a therapeutic measure to control the progression of fungal keratitis recalcitrant to medications, to deal with impending or frank corneal perforations, and to prevent the scleral/intraocular extension of infection.[5–8] Even though PK has been reported to be effective in controlling fungal keratitis unresponsive to antifungal medications in several studies, graft clarity at 1 year postoperatively and the recurrence of infection have been found as high as 51.3% and 30%, respectively, in the case series of Chen and colleagues.[5–8,21,22] Major risk factors for recurrence of fungal keratitis after corneal transplantation include hypopyon, corneal perforation, and corneal infection expanding to limbus, and lens infection. The recurrence rates were, respectively, 5.09-, 2.06-, 4.31-, and 8.7-times higher in patients with these features than in patients without them.[23] Furthermore, unfortunately, fungal keratitis gets complicated more frequently with perforations and requires more therapeutic PK when compared with bacterial keratitis.[7,8]

When corneal perforations caused by fungal keratitis occur, the percentage of complications after PK include episodes of immune graft rejection (38.5%), recurrence of infection (15.4%), complicated cataract (19.2%), and secondary glaucoma (13.5%).[5] Repeating a full-thickness corneal graft leads to high failure rates: a retrospective analysis of 243 patients outlined that the overall survival rate of repeat PK was 49% at 5 years and that only 4.8% of patients had 20/40 or better visual acuity.[24]

The value of debulking the infected tissue in patients unresponsive to antifungal medical treatment was elucidated in 2002.[12] Specifically, Xie *et al*[12] reported the benefits of an early, large, and deep excision of the infected tissue and of washing the recipient stromal bed with 0.2% fluconazole. Following this approach, a high success rate (92.7%) for eradicating the fungal infection was obtained, and early surgery was therefore suggested to reduce surgical complications and ensure the return of good vision.[12] Nonetheless, histopathologic examination of the surgical specimens of the deep corneal stroma still displayed fungal hyphae in almost one-third of that case series (31%), suggesting that the posterior 150 μm corneal stroma had also been affected by the infection and that further surgeries were required for controlling the infection.[12,25]

Eventually, DALK, branching from the evolutionary tree of anterior lamellar keratoplasty, was also proposed for the management of fungal keratitis.[6,26] Although a proportion of patients affected by advanced fungal keratitis treated with PK developed endophthalmitis and underwent evisceration, none of the patients treated with DALK experienced these complications in a study comparing DALK and PK.[6] Nevertheless, even in that case series, the therapeutic success of DALK did not reach 100%; the retained corneal stroma was acknowledged as the culprit because all the unsuccessful cases had occurred when using the manual dissection technique and were eventually managed with further stromectomy.[6] The authors also reported that the patients of the PK group had more extensive and advanced lesions, suggesting that the more favorable outcomes seen in the DALK group would indicate that early intervention with lamellar surgery could be a reasonable option.[6] Conversely, early intervention with PK, carrying a high risk of endothelial rejection and perioperative risk of intraocular spread of the infection, would be highly discouraged at a stage when medical treatment may still be pursued.[6] Finally, Gao *et al*[26] reported very interesting outcomes following the use of DALK in patients who had unresponsive fungal infection or infiltrates affecting more than four-fifths of the corneal thickness, even when there was hypopion;

impressively, the infection was eradicated with the first attempt in 91.3% of patients.

Our previous case series regarding the management of *Acanthamoeba* keratitis unresponsive to medical treatment showed that therapeutic DALK led to complete therapeutic control if approached in a timely manner.[13] Similarly, the results of this case series confirm that an early surgical timing increase the chances of circumscribing the infected tissue with a trephination much deeper and larger than the actual focus of infection.

However, our surgical strategy was performed when infection was limited to the 6 mm central cornea and our results may not be extrapolated to eyes with more peripheral infections. Preserving the DM together with the healthy endothelium avoids the risks of any open-sky surgery and escapes the risk of endothelial corneal allograft rejection.[27]

One might argue that a period of 3 to 20 days is too short for assessing the responsiveness to medical treatment. However, we must highlight that the indication for surgery was made on the basis of several aspects and that the clinical response to the medical treatment was just one of the criteria. Location and depth of the lesion were fundamental to consider eligibility for surgery; all patients in our series were presumed candidates for undergoing keratoplasty at some point. Up to 38 and 15% of patients affected by fungal keratitis are reported to need PK or evisceration, respectively.[28,29] A recent case series of therapeutic PK using glycerol-preserved corneas performed for infectious keratitis, in which fungal etiology accounted for the majority of cases, showed that almost 41% of eyes required evisceration or enucleation.[30] The indication for such an early surgical approach comes from the authors' desire of not ' losing' any eye because of complications such as endophthalmitis, phthisis, or evisceration, and neither to perform a PK that has definitely lower graft survival and higher risk of more severe complications than DALK.[31]

Conclusion

This pilot study is, to the best of our knowledge, the largest case series published in the literature using early DALK to address fungal keratitis poorly responsive to medical treatment. Our results suggest that early DALK could represent a valid approach to effectively eradicate active corneal infections that are poorly responsive to medical treatment and are affecting the optical zone. Nonetheless, we would strongly suggest that only surgeons experienced in DALK, with low PK conversion rates, should perform this procedure.

Summary

What was known before

- Fungal keratitis represents a dramatic clinical event and an important cause of blindness and visual impairment worldwide. Multiple treatment strategies have been proposed to manage the fungal keratitis recalcitrant to medical treatment; however, therapeutic control is not always achieved.

What this study adds

- Early deep anterior lamellar keratoplasty could represent a safe therapeutic approach to effectively eradicate fungal keratitis that affects the optical zone and is poorly responsive to medical treatment.

Conflict of interest

The authors declare no conflict of interest.

References

1 Thomas PA, Kaliamurthy J. Mycotic keratitis: epidemiology, diagnosis and management. *Clin Microbiol Infect* 2013; **19**(3): 210–220.
2 Rose-Nussbaumer J, Prajna NV, Krishnan T, Mascarenhas J, Rajaraman R, Srinivasan M *et al.* Risk factors for low vision related functioning in the Mycotic Ulcer Treatment Trial: a randomised trial comparing natamycin with voriconazole. *Br J Ophthalmol* 2016; **100**(7): 929–932.
3 Gopinathan U, Sharma S, Garg P, Rao GN. Review of epidemiological features, microbiological diagnosis and treatment outcome of microbial keratitis: experience of over a decade. *Ind J Ophthalmol* 2009; **57**: 273–279.
4 Sharma S. Diagnosis of fungal keratitis: current options. *Exp Opin Med Diagn* 2012; **6**: 449–455.
5 Xie L, Zhai H, Shi W. Penetrating keratoplasty for corneal perforations in fungal keratitis. *Cornea* 2007; **26**: 158–162.
6 Anshu A, Parthasarathy A, Mehta JS, Htoon HM, Tan DT. Outcomes of therapeutic deep lamellar keratoplasty and penetrating keratoplasty for advanced infectious keratitis: a comparative study. *Ophthalmology* 2009; **116**: 615–623.
7 Lalitha P, Prajna NV, Kabra A, Mahadevan K, Srinivasan M. Risk factors for treatment outcome in fungal keratitis. *Ophthalmology* 2006; **113**: 526–530.
8 Wong TY, Ng TP, Fong KS, Tan DT. Risk factors and clinical outcomes between fungal and bacterial keratitis: a comparative study. *CLAO J* 1997; **23**: 275–281.
9 Xie L, Dong X, Shi W. Treatment of fungal keratitis by penetrating keratoplasty. *Br J Ophthalmol* 2001; **85**: 1070–1074.
10 Niki M, Eguchi H, Hayashi Y, Miyamoto T, Hotta F, Mitamura Y. Ineffectiveness of intrastromal voriconazole for filamentous fungal keratitis. *Clin Ophthalmol* 2014; **8**: 1075–1079.
11 Kalaiselvi G, Narayana S, Krishnan T, Sengupta S. Intrastromal voriconazole for deep recalcitrant fungal keratitis: a case series. *Br J Ophthalmol* 2015; **99**: 195–198.
12 Xie L, Shi W, Liu Z, Li S. Lamellar keratoplasty for the treatment of fungal keratitis. *Cornea* 2002; **21**: 33–37.

13 Sarnicola E, Sarnicola C, Sabatino F, Tosi GM, Perri P, Sarnicola V. Early deep anterior lamellar keratoplasty (DALK) for Acanthamoeba keratitis poorly responsive to medical treatment. *Cornea* 2016; **35**: 1–5.
14 Prajna NV, Krishnan T, Mascarenhas J, Srinivasan M, Oldenburg CE, Toutain-Kidd CM *et al.* Predictors of outcome in fungal keratitis. *Eye* 2012; **26**: 1226–1231.
15 Sarnicola E, Sarnicola C, Sabatino F, Tosi GM, Perri P, Sarnicola V. Cannula DALK versus needle DALK for keratoconus. *Cornea* 2016; **35**: 1508–1511.
16 Sarnicola V, Toro P, Gentile D, Hannush SB. Descemetic DALK and predescemetic DALK: outcomes in 236 cases of keratoconus. *Cornea* 2010; **29**: 53–59.
17 Sarnicola V, Toro P. Blunt cannula for descemetic deep anterior lamellar keratoplasty. *Cornea* 2011; **30**: 895–898.
18 Holladay JT. Proper method for calculating average visual acuity. *J Refract Surg* 1997; **13**: 388–391.
19 Maharana PK, Sharma N, Nagpal R, Jhanji V, Das S, Vajpayee RB. Recent advances in diagnosis and management of Mycotic Keratitis. *Indian J Ophthalmol* 2016; **64**: 346–357.
20 Hongyok T, Leelaprute W. Corneal ulcer leading to evisceration or enucleation in a tertiary eye care center in Thailand: clinical and microbiological characteristics. *J Med Assoc Thai* 2016; **99**: S116–S122.
21 Chen WL, Wu CY, Hu FR, Wang IJ. Therapeutic penetrating keratoplasty for microbial keratitis in Taiwan from 1987 to 2001. *Am J Ophthalmol* 2004; **137**: 736–743.
22 Ti SE, Scott JA, Janardhanan P, Tan DT. Therapeutic keratoplasty for advanced suppurative keratitis. *Am J Ophthalmol* 2007; **143**: 755–762.
23 Shi W, Wang T, Xie L, Li S, Gao H, Liu J *et al.* Risk factors, clinical features, and outcomes of recurrent fungal keratitis after corneal transplantation. *Ophthalmology* 2010; **117**: 890–896.
24 Al-Mezaine H, Wagoner MD. Repeat penetrating keratoplasty: indications, graft survival, and visual outcome. *Br J Ophthalmol* 2006; **90**: 324–327.
25 Garg P, Vemuganti GK. Lamellar keratoplasty for the treatment of fungal keratitis. *Cornea* 2002; **21**: 734–735 author reply 35.
26 Gao H, Song P, Echegaray JJ, Jia Y, Li S, Du M *et al.* Big bubble deep anterior lamellar keratoplasty for management of deep fungal keratitis. *J Ophthalmol* 2014; **2014**: 209759.
27 Sarnicola V, Toro P, Sarnicola C, Sarnicola E, Ruggiero A. Long-term graft survival in deep anterior lamellar keratoplasty. *Cornea* 2012; **31**: 621–626.
28 Ibrahim MM, Vanini R, Ibrahim FM, Fioriti LS, Furlan EM, Provinzano LM *et al.* Epidemiologic aspects and clinical outcome of fungal keratitis in southeastern Brazil. *Eur J Ophthalmol* 2009; **19**: 355–361.
29 Garg P, Gopinathan U, Choudhary K, Rao GN. Keratomycosis: clinical and microbiologic experience with dematiaceous fungi. *Ophthalmology* 2000; **107**: 574–580.
30 Thanathanee O, Sripawadkul W, Anutarapongpan O, Luanratanakorn P, Suwan-Apichon O. Outcome of therapeutic penetrating keratoplasty using glycerol-preserved donor corneas in infectious keratitis. *Cornea* 2016; **35**: 1175–1178.
31 Sarnicola V, Sarnicola E, Sarnicola C, Sabatino F, Tosi GM, Perri P. Reply. *Cornea* 2016; **35**: e14–e15.

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Early deep anterior lamellar keratoplasty for fungal keratitis poorly responsive to medical treatment

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1. Your patient is a 27-year-old man with fungal keratitis affecting the optical zone, in whom medical therapy has been ineffective. According to the pilot study by Sabatino and colleagues, which one of the following statements about efficacy of therapeutic deep anterior lamellar keratoplasty (DALK) is correct?

- A Manual dissection was required in more than half of eyes
- B About one-fifth of eyes had fungal colonization in the peripheral and deep stromal lamellae
- C Median best spectacle corrected visual acuity improved from 2.0 (1.0 interquartile range) logMAR to 0.1 (0.1 interquartile range) logMAR ($P<0.01$)
- D About one-fifth of eyes had recurrent fungal infection during follow-up

2. According to the pilot study by Sabatino and colleagues, which one of the following statements about risk factors and causative organisms for fungal keratitis and eligibility criteria for therapeutic DALK is correct?

- A Causative organisms were *Fusarium* species (9 cases), *Candida* species (8 cases), *Aspergillus* species (5 cases), and *Curvularia* species (1 case)
- B The most common predisposing factor was diabetes
- C Eyes with infections peripheral to the 6-mm central cornea were eligible for DALK
- D Eyes with infections deeper than 300 μm were eligible for DALK

3. On the basis of the pilot study by Sabatino and colleagues, which one of the following statements about clinical implications regarding therapeutic use of DALK in patients with fungal keratitis is correct?

- A DALK should be delayed to 30 days to allow time for response to medical therapy
- B Preserving the Descemet membrane together with the healthy endothelium has no additional benefit
- C Graft failure limited overall success of DALK
- D Only surgeons experienced in DALK, with low penetrating keratoplasty conversion rates, should perform this procedure