

Infectious Keratitis in 204 586 LASIK Procedures

Fernando Llovet, MD, PhD, Victoria de Rojas, MD, PhD, Emanuela Interlandi, MD, Clara Martín, MD, Rosario Cobo-Soriano, MD, PhD, Julio Ortega-Usobiaga, MD, PhD, Julio Baviera, MD

Purpose: To investigate the incidence, culture results, risk factors, and visual outcomes of infectious keratitis after LASIK, and examine treatment strategies.

Design: Retrospective study.

Participants: We included 107 613 patients who underwent LASIK at Clínica Baviera (Instituto Oftalmológico Europeo, Spain) from September 2002 to May 2008.

Methods: The medical records of post-LASIK patients (204 586 eyes) were reviewed to identify cases of infectious keratitis. Incidence, risk factors, clinical course, days to diagnosis, medical and surgical treatment, and final visual outcomes were recorded.

Main Outcome Measures: Incidence of post-LASIK infectious keratitis, culture results, response to treatment, and visual outcome.

Results: Post-LASIK infectious keratitis was diagnosed in 72 eyes from 63 patients. Onset of infection was early (within 7 days after surgery) in 62.5% of cases. Cultures were positive in 21 of 54 cases in which samples were taken. The most frequently isolated microorganism was *Staphylococcus epidermidis* (9 cases). Immediate flap lifting and irrigation with antibiotics was performed in 54 eyes; late flap lifting was subsequently required in 10 out of 18 cases initially treated with topical antibiotics alone. One case required flap amputation owing to flap necrosis. Final best spectacle-corrected visual acuity (BSCVA) was $\geq 20/20$ in 38 cases (52.7%) and $\geq 20/40$ in 67 cases (93.05%); final BSCVA was $< 20/40$ in 5 cases (6.94%).

Conclusions: The incidence of post-LASIK infectious keratitis was 0.035% per procedure. Infectious keratitis after LASIK is a potentially vision-threatening complication. The appearance of infections in asymptomatic patients highlights the need for a proper schedule of follow-up appointments. Prompt and aggressive management of this LASIK complication with early flap lifting, scraping, culture, and irrigation with antibiotics is strongly recommended. Proper management can result in preserving useful vision.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any of the materials discussed in this article. *Ophthalmology* 2010;117:232–238 © 2010 by the American Academy of Ophthalmology.



LASIK is currently the preferred method for the surgical correction of refractive errors, and thousands of procedures are performed worldwide every year. The procedure provides rapid recovery of visual acuity with a low incidence of complications.¹ However, microbial keratitis after LASIK has become an increasingly recognized, sight-threatening complication of refractive surgery.^{2–4} The incidence of infection is unknown, and in most cases, it is difficult to determine the origin. Predisposing factors include a history of corneal surgery, breaks in the epithelial barrier, excessive surgical manipulation, intraoperative contamination, delayed postoperative reepithelialization of the cornea, and use of topical corticosteroids.^{4,5}

The occurrence rate of post-LASIK keratitis remains difficult to estimate and can vary widely depending on the source of the data.

Two retrospective case series from 2 institutions have found an incidence of 2 infections in 1062 eyes⁶ and 1 infection in 1019 eyes⁷; however, the small number of cases prevents an integrated analysis of the data from being per-

formed and conclusions drawn on diagnosis and management. The largest series reported to date analyzed 15 eyes from 13 patients,⁵ although it included cases of infection referred to the Bascom Palmer Eye Institute from several parts of Florida, thus making it difficult to draw conclusions about incidence.

In a comprehensive review of the literature on post-LASIK infections, Chang et al⁴ state that incidence can vary widely (0%–1.5%). However, many cases of infection are probably not reported, and these numbers might underestimate the true incidence of infection. Conversely, atypical or worse cases could be reported more frequently, thus biasing results on incidence and outcome.

Further information about the incidence of infection and its more common etiologies has been obtained from surveys performed by the American Society of Cataract and Refractive Surgery (ASCRS), with a calculated incidence of 1 case in 2919 procedures² and 1 case in 2131 procedures.³ Nevertheless, this estimation is not conclusive, because it is subject to the nonresponse bias of surveys with a response rate of $< 66\%$.⁸

Because the frequency of post-LASIK infection is low, the analysis of a large series from a single center could reveal more data on several clinically relevant parameters and provide a better understanding of the presentation, etiology, and management of these infections. Series from a single center have the advantage of offering information about incidence in a setting in which most of the possible variables are controlled, because uniform protocols are followed by patients and surgeons before, during, and after surgery. However, given the low incidence of the condition, large numbers of patients would be needed to obtain meaningful conclusions, and such a high number is difficult to recruit from a single center. The largest series until the present study from a single center—10 cases of nonviral infection in 10 477 eyes—was recently published.⁹

We report the largest series to date of post-LASIK infectious keratitis, with all procedures carried out in the same institution. Cases were retrospectively reviewed to provide information on onset, etiology, clinical course, risk factors, and treatment, with the aim of improving our understanding of the prevention, diagnosis and management of this entity.

Patients and Methods

This retrospective case-series review comprised 204 586 eyes from 107 613 patients who underwent primary LASIK or enhancement surgery consecutively at Clínica Baviera between September 2002 and May 2008. More than 40 000 refractive procedures are performed each year at the clinic, a private ophthalmologic institution with 19 centers and 84 surgeons throughout Spain. Patients with a diagnosis of infectious keratitis within 6 months after LASIK were identified by an electronic search of medical histories using the key words LASIK and infectious or LASIK and keratitis. Diagnosis of infectious keratitis was based on symptoms, slit-lamp findings, and/or microbiological results. Clinical diagnostic criteria included the presence of corneal infiltrates compatible with infectious keratitis, excluding other causes of noninfectious keratitis (diffuse lamellar keratitis, peripheral sterile infiltrates, multifocal lamellar keratitis).^{9,10} The medical histories were reviewed to collect the following data: age, gender, involved eye, procedure type (primary versus enhancement), time from surgery to presentation, preoperative and postoperative best spectacle-corrected visual acuity (BSCVA), postoperative uncorrected visual acuity, risk factors, culture results, medical and surgical treatment, and complications. To obtain the average postoperative BSCVA, we converted Snellen visual acuities to their decimal equivalent to calculate mean final visual acuity. Data collection fulfilled Spanish legal requirements and institutional review board approval was obtained. Given the retrospective nature of the research design, no informed consent was needed.

Operative Technique

Patients underwent a complete ophthalmologic examination before surgery following a standard protocol to determine whether they were suitable candidates for corneal refractive surgery. Written informed consent was obtained before surgery in each case.

All procedures were performed according to standard protocols. The surgical suite met the criteria for ophthalmologic laser procedures and all instruments were autoclaved before LASIK surgery. Patients were instructed to perform lid hygiene during the 3 days before surgery. LASIK was performed using the Moria

LSK-One microkeratome (Microtech Inc., Moria, France). In bilateral cases, the same microkeratome blade was used in both eyes. The lamellar keratectomy was always performed first in the left eye and then in the right eye, and was followed by laser ablation first in the right eye and then in the left eye using the Technolas 217C, 217-Z-100 excimer laser (Bausch & Lomb, Claremont, CA) or the Mel 80 excimer laser (Carl Zeiss Meditec Inc., Jena, Germany). After surgery, a topical combination of tobramycin 3 mg/ml and dexamethasone 1 mg/ml (TobraDex, Alcon Laboratories, Barcelona, Spain) was prescribed 4 times a day for 1 week together with preservative-free artificial tears. All patients were examined 12 hours, 7 days, 1 month, and 3 months after surgery, unless complications required more frequent visits.

The outcome measures of the study were the incidence of infectious keratitis within 6 months after LASIK, culture results, response to treatment, and visual outcome.

Results

During the study period, 204 589 procedures (primary LASIK or enhancement) were performed on 107 613 patients. We identified 72 eyes from 63 patients (28 women, 44 men) with infectious keratitis (overall rate, 0.035% per procedure) within 6 months after LASIK. Mean age was 38.5 ± 10.08 years (range, 22–65). Thirty-four (47.22%) infections involved the right eye and 38 (52.77%) involved the left. Infection was bilateral in 9 patients. Sixty-eight (94.44%) infections presented after primary procedures and 3 infections appeared after an enhancement procedure (2 cases) or after lifting and ironing of flap folds (1 case; Table 1). Mean follow-up was 5.48 months (range, 1–42), and >6 months in 26 cases. Twelve cases did not complete the scheduled routine visit at 3 months (most of them were cases of early onset and rapid resolution). All patients attended visits until complete resolution of the infection so that no patient was lost to follow-up.

Time from surgery to the appearance of the initial symptoms was 16 ± 31 days (range, 1–180); onset was early (within 7 days after surgery) in 45 eyes (62.5%; mean, 3.5 ± 1.8 ; range, 1–7) and late (>7 days after surgery) in 27 eyes (37.5%; mean, 35.7 ± 43.7 ; range, 8–180). No clusters of cases were detected.

We detected the following risk factors: blepharitis (3 cases), intraoperative epithelial defect (6 cases; a bandage contact lens was applied in 3), dry eye (1 case), health professional (2 cases), and veterinarian (1 case).

Clinical symptoms were reported by 54 patients, whereas 9 were asymptomatic. In the asymptomatic patients, infection was diagnosed at one of the routine postoperative checkups. Thirty (41.6%) of the symptomatic eyes presented pain, 25 (34.72%) had

Table 1. Patient Demographics

Characteristic	Total
No. of eyes	72
No. of patients	63
Age (yrs)	
Mean \pm standard deviation	38.51 ± 10.08
Range	22–65
Gender	
Female	28 (38.38%)
Male	44 (61.11%)
Type of surgery	
Primary	69 (95.83%)
Reoperation	3 (4.16%)

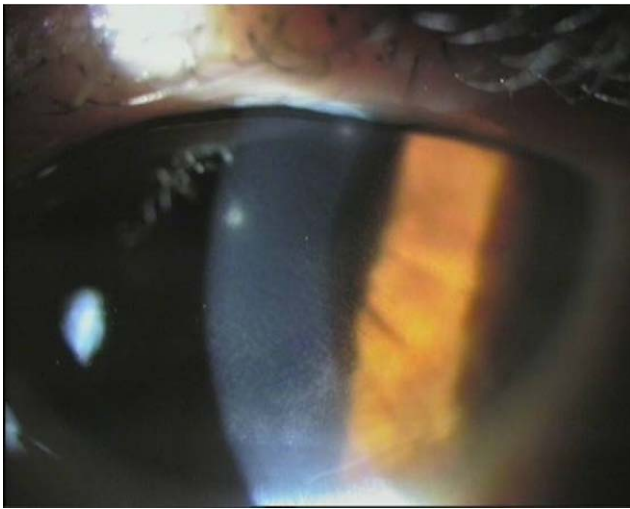


Figure 1. Slit-lamp photograph of case 18 showing 2 infiltrates with associated diffuse lamellar keratitis. The culture was negative.

decreased vision, and 40 (55.5%) had red eye. Photophobia was reported by 7 patients (9.7%) and 15 complained of tearing (20.83%).

Corneal infiltrates were detected in all cases (1 infiltrate in 39 eyes, 2 in 10 eyes, 3 in 5 eyes, and 4 infiltrates in 6 eyes, and >5 in the remaining cases; Figs 1–3). In 48 eyes, infiltrates were located at the interface and adjacent stroma without epithelial involvement, whereas in 18 cases, superficial involvement was noted with epithelial defects over the stromal abscesses (data missing for 6 eyes).

Samples were taken for microbiological analysis in 54 cases before treatment. Thirty-three of the samples were negative and 21 were positive. The microorganisms identified were *Staphylococcus epidermidis* (9 cases; 16.66%), *Streptococcus pneumoniae* (8 cases; 14.81%), *Streptococcus viridans* (2 cases; 3.7%), *Streptococcus pyogenes* (1 case; 1.85%) and *Staphylococcus aureus* (1 case; 1.85%) (Table 2; available online at <http://aaojournal.org>). Onset of symptoms was early in all cases with a positive culture except for 1 case (case 19), in which epithelial sloughing occurred during surgery. The patient had recurrent erosions and developed infec-



Figure 3. Slit-lamp photograph of the right eye of case 52 showing multiple interface infiltrates caused by *S. pneumoniae*.

tious keratitis in 1 of these episodes 25 days after LASIK, but 2 days after the onset of the recurrent erosion.

Immediate flap lifting and irrigation with antibiotics was performed in 54 eyes. Treatment was started empirically with topical fortified antibiotics in 18 cases, 10 of which required subsequent lifting and irrigation. The antibiotic treatment regimen is summarized in Table 2. A broad-spectrum combination consisting of fortified vancomycin with either an aminoglycoside (tobramycin or amikacin) or a fluoroquinolone was the most common regimen. A 4th-generation fluoroquinolone, moxifloxacin, was used in 5 cases. Oral doxycycline was added in 6 cases and minocycline in 2 cases. Oral ciprofloxacin and clarithromycin were used in 2 cases. One case required flap amputation owing to flap necrosis (Figs 3–6).

Fourteen of the 64 eyes that underwent a flap lifting procedure did not have a culture taken, and 4 eyes that did not undergo a flap lifting procedure did have samples taken for culture. Fourteen of the 18 eyes that did not have cultures taken underwent a flap lifting procedure.

Visual results are summarized in Table 2. The mean \pm standard deviation postoperative BSCVA was 1 ± 0 (range, 20/100–20/

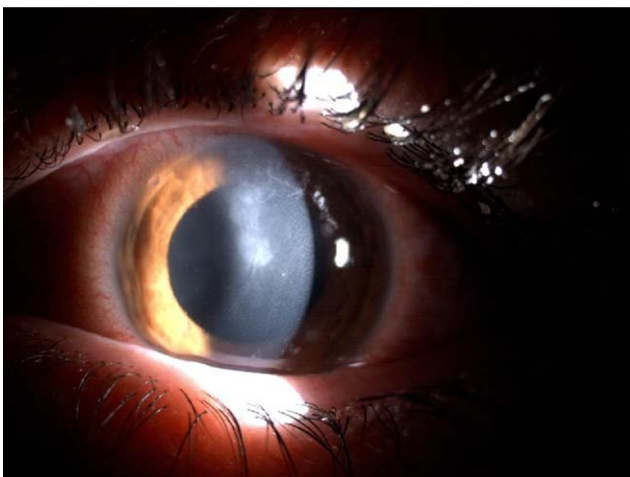


Figure 2. Slit-lamp view of the left eye in case 40 presenting with 2 dense infiltrates caused by *S. aureus*.

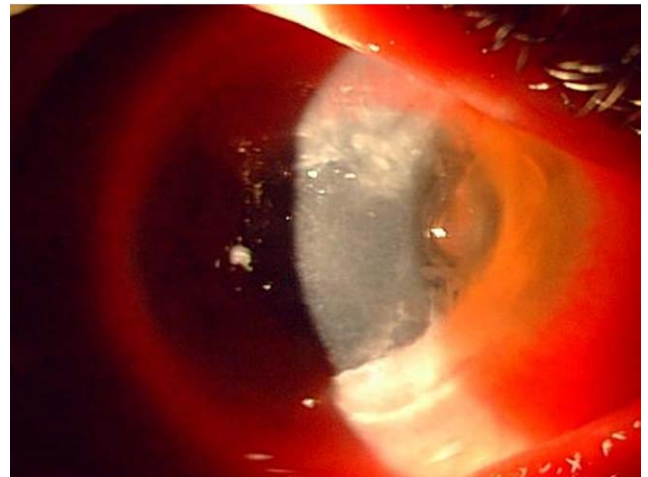


Figure 4. Case 52, right eye. The flap suffered severe necrosis despite intensive treatment.

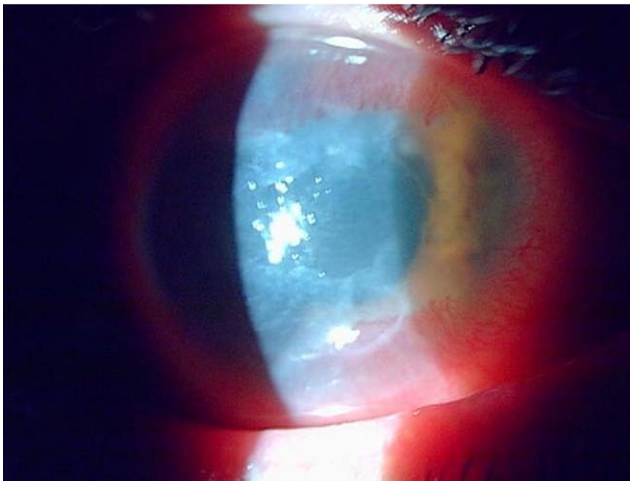


Figure 5. Case 52, right eye. Appearance of the cornea 5 days after flap amputation, presenting severe peripheral pannus.

12.5). Fifty-four cases maintained their BSCVA. Final BSCVA was $\geq 20/20$ in 38 cases (52.7%) and $\geq 20/40$ in 67 cases (93.05%); final BSCVA was $< 20/40$ in 5 cases (6.94%); 2 had low BSCVA of 20/200 and 20/50, cases 48 and 59, respectively). Residual corneal scars were recorded in 31 eyes. Visual rehabilitation procedures after resolution of infection included glasses (1 case), arcuate keratotomy (2 cases), phototherapeutic keratectomy (2 cases), LASEK (1 case), LASIK enhancement (1 case), and haze treatment with mitomycin C (1 case). The mean \pm standard deviation time between resolution and rehabilitation procedures was 4.75 ± 3.20 months (range, 2–7).

Discussion

LASIK is a relatively safe procedure; infection is a rare but sight-threatening complication.^{2–4} Corneal infection after an iatrogenic corneal wound is a traumatic experience for both the patient and the ophthalmic surgeon.

The actual incidence of post-LASIK infectious keratitis is unknown and varies widely depending on the source of the data. Moshirfar et al⁹ report data from a study on 10 477 post-LASIK eyes; 279 had a diagnosis of keratitis, which was infectious in 33 eyes (12%; 0.31% of the total) and noninfectious in 246 eyes (88%; 2.34% of the total). The infectious cases included 5 eyes (15%) with herpes simplex keratitis, 18 (55%) with adenoviral keratitis, and 10 (30%) with nonviral (including bacterial, fungal, and parasitic) keratitis.⁹

We found an occurrence rate of 72 cases in 204 586 LASIK procedures or an incidence of 0.035% per procedure (1 case in 2841 procedures). To our knowledge, this is the largest series of post-LASIK infectious keratitis reported to date. Our incidence is lower than that reported by Moshirfar et al⁹ and consistent with the estimated rate of 0.03% from an ASCRS survey in 2003.² The true incidence depends on our completeness of follow-up of the 204 586 eyes that underwent LASIK. If patients do not complete the follow-up, the possibility exists that cases of infectious keratitis would be missed. Nevertheless, it is our experience that

most patients attend all scheduled visits. Moreover, these visits are included in the cost of the procedure, so they are free of charge. Ours is a private ophthalmologic institution with 19 centers throughout Spain; therefore, any patient could reasonably be expected to attend the scheduled follow-up appointment if they experienced any change from their last visit. We believe, then, that the calculated incidence is reasonably accurate.

Infectious keratitis after LASIK has been classified as early onset (occurring within the 1–2 weeks after surgery) and late onset (occurring after 1 or 2 weeks to 3 months after the surgery).^{2,4} In the review of the literature performed by Chang et al,⁴ symptoms appeared within 7 days of the refractive procedure in 49.4% of cases and > 10 days after surgery in 50.6%. The results of the present study differ slightly, with a higher percentage of eyes (62.5% of eyes) classified as early onset infections (before 7 days) and the remaining cases as late-onset infections (between 7 and 180 days).

In the study by Chang et al,⁴ the mean time of presentation in the early onset group was 2.7 ± 4.2 days (range, 0–7) and in the late-onset group 27.4 ± 3.6 days (range, 10–90). Moshirfar et al⁹ retrospectively reviewed the records of all patients who developed keratitis within 4 weeks of the procedure. However, infections caused by atypical mycobacteria have been described to appear as late as 6 months after the procedure.¹¹ We chose 6 months, based on the time frame of presentation in these previous reports on this condition.^{4,9,11} Any infection related to the operative procedure would be present within this interval and, therefore, no case would be missed.

The microorganisms detected in the current series were gram-positive and presented before 7 days. According to Chang et al,⁴ gram-positive infections were more likely to present < 7 days after LASIK. No cases of polymicrobial or mycobacterial infection were detected. However, all cases with a negative result had a late presentation. Taking into account the fact that late infections are more likely to be

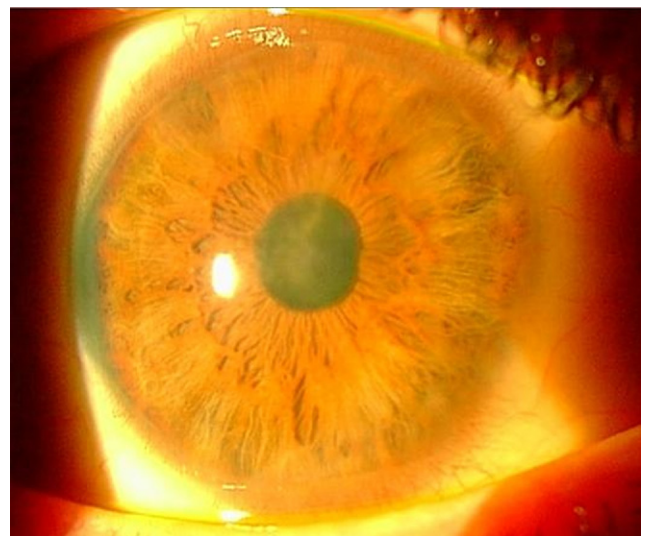


Figure 6. Case 52, right eye showing residual scarring after flap amputation and resolution of the keratitis. Uncorrected visual acuity was 20/32.

caused by atypical organisms (mycobacteria and fungi),^{4,5} and that these germs are associated with higher rates of negative culture results,¹¹ some of these late infections could have been caused by mycobacteria. These are difficult to grow in culture; specific plates might not have been used in some cases, they typically have a late onset, and some could have resolved under treatment with amikacin, which was used in some cases in our study. Indeed, atypical mycobacteria have been reported to be the first^{4,9} or second cause of infection after LASIK,² depending on the series. Fungal infection cannot be ruled out either in a context of negative culture results, although this seems unlikely; antifungal therapy was not used or required in any case.

Regarding culture results, a possible shortcoming of the current study is the high rate of negative cultures, which could be due to technical reasons (scant samples, sample alteration during transport to the reference microbiology laboratory, or previous antibiotic therapy which could inhibit growth of the microorganism) or infections caused by atypical organisms for which specific plates may not have been used in some cases. Awareness of the need to include specific plates to grow mycobacteria became evident and increased since the publication of the review of the literature by Chang et al⁴ in 2004 and the ASCRS White Paper by Donnenfeld et al³ in 2005; therefore, specific media for these organisms may not have been included in some cases before 2004. Even in cases in which proper media are used, atypical mycobacteria and fungi are difficult to grow and have been associated with higher rates of negative cultures.¹¹

Several sources of infection have been reported and include surgical instruments, surgeons' hands, environmental factors, and periocular flora. There are also reports of clusters of cases (all caused by atypical mycobacteria) in which the source of infection was detected,^{12–14} although in most cases, it is difficult to determine the origin of the infection.¹⁵ The rate of corneal interface contamination during LASIK was measured in a recent study and found to be 24.5%.¹⁵ As in other studies of contamination during intraocular surgery,^{16–18} the most commonly retrieved organism was *S. epidermidis*. This was expected because it is a normal inhabitant of the eyelids, eyelashes, and conjunctiva, and it is believed that the bacteria that cause postoperative complications originate from the eyelids and conjunctiva. However, in 38.8% of the contaminated cases, cultures of the eyelid margins, conjunctiva, and instruments were negative. Therefore, the sources of contamination in these cases could not be determined.¹⁵

The potential risk factors involved in post-LASIK keratitis reported in the literature include blepharitis, dry eyes, epithelial defects, bandage contact lenses, and the health care environment.^{3–5,19} Blepharitis, dry eye, and epithelial defects were detected in some patients in the current series. This highlights the importance of proper preoperative examination and treatment of the lids and dry eye disease.² The use of eyelid hygiene, included in our preoperative protocol, decreases the bacterial load on the surface; therefore, it is reasonable to believe that this measure could be associated with a decreased risk of infection, although this has not been demonstrated elsewhere or in this study. Treatment is started 3 days before surgery, because eyelid hy-

giene for longer periods may change the pattern of distribution of the saprophytic ocular flora.²⁰

Solomon et al¹⁹ recently published a review of cases of post-LASIK infectious keratitis caused by methicillin-resistant *S. aureus* (MRSA) in which 9 of 12 patients were exposed to a health care setting. Two of our patients were health care workers, although cultures were negative in both cases. Some studies^{2,4,9} found atypical mycobacteria to be the most common organisms involved in infectious keratitis after LASIK, although most recent studies detected an increase in infectious keratitis caused by *Staphylococcus* (Donnenfeld et al³) and MRSA after LASIK (Kim T. Results of an ASCRS-sponsored survey on infectious keratitis. Paper presented at Cornea Day, ASCRS meeting, April 2008, Chicago, Illinois). This change may reflect the increased awareness of the need to perform LASIK surgery under strict aseptic conditions (which would account for the decrease in mycobacteria) and the realization that the patient's ocular flora became the main source of germs causing infections. The increased rate of MRSA infections could reflect the carriage rate of MRSA in the community, as it has recently been documented.²¹ A similar trend toward a rise in the number of infections caused by MRSA has been detected by Deramo et al²² for postoperative endophthalmitis. However, we did not find any cases caused by MRSA and the only possible explanation for this discrepancy seems to be differences in the carriage rate in the community between the United States and Europe, in addition to the limitations posed by the high rate of negative cultures in our series.

Bilateral infections were found in 9 patients. The blade is not routinely changed between eyes. Some clinicians recommend performing monocular surgery or using separate instruments when performing bilateral surgery,²³ although this is not the practice of the members of the ASCRS Cornea Clinical Committee.²

The rate of symptom presentation was similar to that reported elsewhere.⁴ More important, 10 eyes from 9 patients were asymptomatic and the infections in these patients were detected at one of the postoperative scheduled appointments, thus highlighting the need for appropriate follow-up. Given that 62.5% of the cases appear within 1 week and 90.27% within 1 month, we strongly recommend the postoperative follow-up visit scheduled in our clinics as described.

The mean follow-up time for the cases in this study was 5.48 months (range, 1–42). Twelve cases did not complete the 3-month scheduled routine visit. Most of them correspond with cases with early onset and rapid resolution. Patients would have been expected to attend the scheduled follow-up appointment if they experienced any change from their last visit.

The hallmark of infectious post-LASIK keratitis is the presence of focal infiltrates at the interface. The most common signs on slit-lamp biomicroscopy were corneal infiltrates, which were present in all cases, a result that is consistent with those of Chang et al.⁴ These infiltrates must be differentiated from other causes of keratitis after LASIK, particularly from diffuse lamellar keratitis. Interface infections may initially be confused with diffuse lamellar kera-

titis, thus delaying appropriate treatment.²⁴ Conversely, given the high rate of negative cultures in the current series, the possibility of misdiagnosing diffuse lamellar keratitis should be taken into account. However, all cases included had clear focal infiltrates, which are the hallmark of infection; therefore, we do not believe that negative cultures correspond to cases of diffuse lamellar keratitis.

The management of post-LASIK infectious keratitis is challenging. Atypical organisms beneath the flap can pose diagnostic and therapeutic dilemmas. Location at the interface can make it more difficult to culture the organism and prevent adequate penetration of topical antibiotics. Empiric therapy is not recommended, because the organisms responsible for these infections do not often respond to conventional therapy. Several authors strongly recommend an aggressive approach, with immediate lifting of the flap for scraping and culture and irrigation with fortified antibiotics.^{2,4,5} Current recommendations on antibiotic regimens to treat post-LASIK infections have been summarized in an ASCRS White Paper.² The flap interface and stromal bed should be irrigated with fortified vancomycin when onset is early and with fortified amikacin when onset is late. Topical treatment should consist of a 4th-generation fluoroquinolone alternating with cefazolin or vancomycin for early onset infections and a 4th-generation fluoroquinolone alternating with amikacin when onset is late. The addition of oral doxycycline is also recommended to inhibit collagenase production. These guidelines were published in 2005,² and the antibiotic regimen used in our cases (Table 2) reflects the endorsement of this regimen in our clinics, with the exception of 4th-generation fluoroquinolones, which are not yet commercially available in Spain. Only 5 cases received moxifloxacin after a special request.

In the current series, 18 of the 72 eyes did not have a sample taken for culture. However, we must point out that 14 of those 18 eyes did undergo a flap lifting procedure. The reason behind this apparent discrepancy is that our clinics are outpatient clinics (not part of a hospital environment); therefore, culture plates are not always available when the emergency treatment of lifting the flap and irrigation with antibiotics is performed. On the other hand, samples were taken in 4 cases in which a flap lifting procedure was not performed, because keratitis affected the superficial stroma.

Chang et al⁴ found that flap lifting performed within 3 days of symptom onset may be associated with a better visual outcome. The results of our series further support this recommendation, as 10 of 18 cases initially managed with topical therapy subsequently required flap lifting and irrigation of the interface. Operative intervention was necessary in 64 of 72 eyes with infection in our series. This involved flap lifting and irrigation with antibiotics in 64 cases; one of the eyes subsequently required flap amputation. Even with early and aggressive treatment, flap amputation is necessary in some cases. The flap does not allow adequate penetration of antibiotics; once it becomes necrotic, it not only loses its optical qualities, but it could also harbor sequestered microorganisms, thus posing an additional difficulty for the success of medical therapy. Flap amputation is not unusual in post-LASIK infectious keratitis,^{3,4} especially when atypical or aggressive organisms are

involved. In a review of 103 infections, 37 flaps were eventually removed.⁴ Most procedures were performed as a result of infections caused by mycobacteria or very aggressive microorganisms. Series involving clustered atypical mycobacterial infections show that almost 50% of affected eyes required flap amputation.^{12–14} In the series by Karp et al,⁵ 5 out of 15 eyes with post-LASIK infections—all caused by atypical mycobacteria—required flap amputation. In the reports by Moshirfar et al,^{9,25} 1 case of keratitis caused by *P. aeruginosa* from a total of 10 eyes with infectious keratitis required flap amputation,⁹ as did 1 case of MRSA infection.²⁵ In the study by Solomon et al,¹⁹ 2 flaps had to be amputated in 12 cases of MRSA infection.¹⁹ In the current series, the case that required flap amputation was caused by *S. pneumoniae*.

Visual acuity results in the current series are much better than those reported in previous series^{4,5,9} for several reasons. First, the results from Chang et al⁴ and Karp et al⁵ derive from the analysis of published reports or referred cases respectively; therefore, worse cases can be selected and results biased as a consequence. Second, we did not detect fungal or mycobacterial infections, although this does not mean that they were not present. Thirty-three cultures were negative, and it must be remembered that cases caused by germs other than fungi or mycobacteria have a much better prognosis.^{4,5} Infections caused by gram-positive organisms resolved quickly with excellent visual acuity in previous series.^{4,5} Our results are also better than those of Moshirfar et al,⁹ who applied the same therapeutic measures as our group. This group showed that only 30% of eyes with nonviral infectious keratitis achieved 20/40 acuity and only 20% of eyes with nonviral keratitis achieved 20/20 visual acuity. Again in this series, 4 out of 10 cases were caused by mycobacteria and there were also 2 polymicrobial infections, 1 involving *Acanthamoeba* and the other, *Alternaria*.⁹

In summary, the occurrence of post-LASIK infectious keratitis was 0.035% per procedure. Infectious keratitis after LASIK is a potentially vision-threatening complication, and the appearance of infections in asymptomatic patients highlights the need for a proper follow-up schedule. Prompt and aggressive management of this LASIK complication with early flap lifting, scraping, culture, and irrigation with antibiotics is strongly recommended. Proper management can enable useful vision to be preserved.

References

1. Azar DT, Farah SG. Laser in situ keratomileusis versus photorefractive keratectomy: an update on indications and safety. *Ophthalmology* 1998;105:1357–8.
2. Solomon R, Donnenfeld ED, Azar DT, et al. Infectious keratitis after laser in situ keratomileusis: results of an ASCRS survey. *J Cataract Refract Surg* 2003;29:2001–6.
3. Donnenfeld ED, Kim TK, Holland EJ, et al. American Society of Cataract and Refractive Surgery Cornea Clinical Committee. ASCRS White Paper. Management of infectious keratitis following laser in situ keratomileusis. *J Cataract Refract Surg* 2005;31:2008–11.

4. Chang MA, Jain S, Azar DT. Infections following laser in situ keratomileusis: an integration of the published literature. *Surv Ophthalmol* 2004;49:269–80.
5. Karp CL, Tuli SS, Yoo SH, et al. Infectious keratitis after LASIK. *Ophthalmology* 2003;110:503–10.
6. Stulting RD, Carr JD, Thompson KP, et al. Complications of laser in situ keratomileusis for the correction of myopia. *Ophthalmology* 1999;106:13–20.
7. Lin RT, Maloney RK. Flap complications associated with lamellar refractive surgery. *Am J Ophthalmol* 1999;127:129–36.
8. Peyman GA, Lee PJ, Seal DV. Endophthalmitis: Diagnosis and Management. London: Taylor & Francis; 2004:67–79.
9. Moshirfar M, Welling JD, Feiz V, et al. Infectious and non-infectious keratitis after laser in situ keratomileusis: occurrence, management and visual outcomes. *J Cataract Refract Surg* 2007;33:474–83.
10. Hadden OB, Patel D, Gray TB, et al. Multifocal lamellar keratitis following laser in situ keratomileusis. *J Cataract Refract Surg* 2007;33:144–7.
11. John T, Velotta E. Nontuberculous (atypical) mycobacterial keratitis after LASIK: current status and clinical implications. *Cornea* 2005;24:245–55.
12. Chandra NS, Torres MF, Winthrop KL, et al. Cluster of *Mycobacterium chelonae* keratitis cases following laser in situ keratomileusis. *Am J Ophthalmol* 2001;132:819–30.
13. Fulcher SF, Fader RC, Rosa RH Jr, Holmes GP. Delayed-onset mycobacterial keratitis after LASIK. *Cornea* 2002;21:546–54.
14. Freitas D, Alvarenga L, Sampaio J, et al. An outbreak of *Mycobacterium chelonae* infection after LASIK. *Ophthalmology* 2003;110:276–85.
15. Feizi S, Jadidi K, Naderi M, Shahverdi S. Corneal interface contamination during laser in situ keratomileusis. *J Cataract Refract Surg* 2007;33:1734–7.
16. Seal D, Reischl U, Behr A, et al, ESCRS Endophthalmitis Study Group. Laboratory diagnosis of endophthalmitis: comparison of microbiology and molecular methods in the European Society of Cataract & Refractive Surgeons multicenter study and susceptibility testing. *J Cataract Refract Surg* 2008;34:1439–50.
17. Endophthalmitis Vitrectomy Study Group. Results of the Endophthalmitis Vitrectomy Study: a randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. *Arch Ophthalmol* 1995;113:1479–96.
18. Assia EI, Jubran RZ, Solberg Y, Keller N. The role of intraocular lenses in anterior chamber contamination during cataract surgery. *Graefes Arch Clin Exp Ophthalmol* 1998;236:721–4.
19. Solomon R, Donnenfeld ED, Perry HD, et al. Methicillin-resistant *Staphylococcus aureus* infectious keratitis following refractive surgery. *Am J Ophthalmol* 2007;143:629–34.
20. Hueso Abancens JR, Mengual Verdu E, Schargel Palacios K, et al. Modification of the conjunctival flora with cleaning palpebral solutions [in Spanish]. *Arch Soc Esp Oftalmol* 2004;79:617–22.
21. Grundmann H, Aires-de-Sousa M, Boyce J, Tiemersma E. Emergence and resurgence of methicillin-resistant *Staphylococcus aureus* as a public-health threat. *Lancet* 2006;368:874–85.
22. Deramo VA, Lai JC, Winokur J, et al. Visual outcome and bacterial sensitivity after methicillin-resistant *Staphylococcus aureus*-associated acute endophthalmitis. *Am J Ophthalmol* 2008;145:413–7.
23. Kohnen T. Infections after corneal refractive surgery: can we do better? *J Cataract Refract Surg* 2002;28:569–70.
24. Peng Q, Holzer MP, Kaufer PH, et al. Interface fungal infection after laser in situ keratomileusis presenting as diffuse lamellar keratitis: a clinicopathological report. *J Cataract Refract Surg* 2002;28:1400–8.
25. Moshirfar M, Mirzaian G, Feiz V, Kang PC. Fourth-generation fluoroquinolone-resistant bacterial keratitis after refractive surgery. *J Cataract Refract Surg* 2006;32:515–8.

Footnotes and Financial Disclosures

Originally received: November 2, 2008.

Final revision: June 30, 2009.

Accepted: July 6, 2009.

Available online: December 12, 2009.

Manuscript no. 2008-1299.

The Clinica Baviera, Instituto Oftalmológico Europeo, Spain.

Financial Disclosure(s):

The authors have no proprietary or commercial interest in any of the materials discussed in this article.

Correspondence:

Fernando Llovet, Clinica Baviera. Instituto Oftalmológico Europeo, Spain, C/Marqués del Turia 9, 46005 Valencia, Spain.

Table 2. Summary of Cases of Infectious Keratitis After LASIK Between 2002 and 2008: Risk Factors,

Case N°	Age/Gender	Eye	Risk Factors	Day of Presentation	Culture Samples Taken	Organism
1	28/F	LE	—	5	Y	negative
2	35/M	RE	—	3	Y	<i>S pneumoniae</i>
3	52/M	LE	—	180	Y	negative
4	34/M	RE	—	2	Y	negative
5	35/F	LE	—	4	Y	negative
6	37/F	RE	—	2	N	
7	35/M	RE	—	2	N	
8	40/F	RE	—	26	Y	negative
9	42/M	RE	—	3	Y	<i>S pneumoniae</i>
10	44/M	LE	—	30	N	
11	42/M	RE	—	12	N	
	42/M	LE	—	12	N	
12	23/M	LE	—	6	N	
13	54/M	LE	—	2	N	
14	43/M	LE	—	3	N	
15	29/M	LE	—	45	Y	negative
16	29/F	LE	—	2	N	
17	40/M	RE	—	2	Y	negative
18	53/F	LE	—	7	Y	negative
19	48/M	RE	IED + BCL	25	Y	<i>S epidermidis</i>
20	65/F	RE	IED	21	Y	negative
21	42/F	RE	—	4	Y	<i>S epidermidis</i>
	42/F	LE	—	4	Y	<i>S epidermidis</i>
22	27/M	RE	—	159	Y	negative
23	29/M	RE	—	1	Y	<i>S epidermidis</i>
	29/M	LE	—	3	Y	<i>S epidermidis</i>
24	47/M	RE	—	98	Y	negative
25	59/F	LE	IED	17	Y	negative
26	31/F	RE	—	2	Y	<i>S epidermidis</i>
27	38/F	RE	—	7	Y	<i>S epidermidis</i>
	38/F	LE	—	7	Y	<i>S epidermidis</i>
28	47/M	RE	—	12	Y	negative
29	41/F	LE	—	2	N	
30	25/M	RE	—	2	Y	negative
31	47/F	RE	—	13	Y	negative
32	29/F	RE	—	4	Y	negative
	29/F	LE	—	4	Y	negative
33	33/F	LE	—	8	Y	negative
34	45/M	RE	—	26	Y	negative
35	55/M	RE	—	5	Y	<i>S pyogenes</i>
36	32/F	RE	—	1	Y	<i>S pneumoniae</i>
37	28/F	LE	—	15	Y	negative
38	60/M	RE	Dry Eye	9	N	
39	28/M	RE	—	33	Y	negative
40	40/M	LE	—	8	Y	<i>S aureus</i>
41	50/F	LE	—	27	Y	negative
42	29/M	RE	Blepharitis	4	Y	negative
	29/M	LE	Blepharitis	4	Y	negative
43	27/M	LE	—	4	Y	<i>S pneumoniae</i>
44	37/F	LE	Nurse	1	N	
45	39/M	RE	—	6	N	
46	30/M	LE	—	6	Y	negative
47	49/M	RE	IED + BCL	75	N	
48	33/F	LE	—	15	N	
49	38/M	LE	—	25	N	
50	43/F	LE	blepharitis	5	Y	negative
51	36/F	RE	—	2	Y	<i>S pneumoniae</i>
52	22/M	RE	—	2	Y	<i>S pneumoniae</i>
	22/M	LE	—	2	Y	<i>S pneumoniae</i>
53	44/F	LE	Health care w	17	Y	negative
54	41/F	LE	—	10	Y	negative
55	32/M	LE	IED	4	Y	negative

(Continued)

Onset After LASIK, Microorganisms, Surgical/Medical Treatment and Clinical Outcome

Medical Treatment	Surgical Treatment	Follow-up (m)	Preop BSCVA	Postop UCVA	Postop BSCVA
Vanc + Amik + Moxi + oral Doxycycline	FLIw/Vanc	6	20/25	20/20	20/20
Vanc + Oflox + oral Doxycycline	FLIw/Vanc	5.5	20/25	20/20	20/20
Vanc + Oflox + oral Doxycycline	FLIw/Vanc	3	20/32	20/25	20/20
Vanc + Tobra + Oflox	FLIw/Vanc	4	20/20	20/20	20/20
Vanc + Oflox	FLIw/Vanc	1.5	20/25	20/25	20/25
Tobra + Oflox	FLIw/Vanc	3	20/25	20/25	20/25
Tobra + Oflox	FLIw/Vanc	7	20/20	20/25	20/25
Vanc + Oflox	FLIw/Vanc	5.5	20/25	20/20	20/20
Vanc + Ceftaz + Oflox	—	2	20/20	20/20	20/20
Oflox + Tobra	—	3.5	20/25	20/25	20/25
Vanc + Tobra	FLIw/Vanc	7	20/20	20/20	20/20
Vanc + Tobra	FLIw/Vanc	7	20/20	20/20	20/20
Vanc + Tobra	FLIw/Vanc	3	20/20	20/20	20/20
Vanc + Ceftaz + oral Ciprofl	—	5	20/25	20/25	20/25
Vanc + Amik + Oflox + oral Minocycline	FLIw/Vanc	6	20/25	20/20	20/20
Vanc + Oflox	FLIw/Vanc	4	20/25	20/20	20/20
Vanc + Tobra + Oflox	FLIw/Vanc	2	20/20	20/20	20/20
Vanc + Tobra + Ciprofl + oral Doxycycline	FLIw/Vanc	3	20/30	20/25	20/25
Vanc + Tobra + oral Doxycycline	FLIw/Vanc + Tobra	2	20/30	20/32	20/32
Vanc + Oflox	FLIw/Vanc	6	20/20	20/25	20/25
Vanc + Amik + Oflox + oral Clarithromycin	FLIw/Vanc	3	20/20	20/25	20/25
Vanc + Oflox	FLIw/Vanc	6	20/25	20/20	20/20
Vanc + Oflox	FLIw/Vanc	6	20/25	20/20	20/20
Vanc + Oflox	FLIw/Vanc	5	20/25	20/25	20/25
Vanc + Ciprofl	FLIw/Vanc	2.5	20/25	20/20	20/20
Vanc + Ciprofl	FLIw/Vanc	2.5	20/25	20/20	20/20
Vanc + Amik + Oflox	FLIw/Vanc + Amik	7	20/20	20/20	20/20
Vanc + Amik + Oflox	FLIw/Vanc + Amik	6	20/20	20/25	20/20
Vanc + Ciprofl + Tobra	FLIw/Vanc	2.5	20/20	20/20	20/20
Vanc + Amik + Oflox	FLIw/Vanc + Amik	4.5	20/20	20/25	20/20
Vanc + Amik + Oflox	FLIw/Vanc + Amik	4.5	20/20	20/25	20/20
Vanc + Amik	FLIw/Vanc	10	20/25	20/32	20/25
Vanc + Oflox	FLIw/Vanc	6	20/20	20/20	20/20
Vanc + Amik	FLIw/Vanc	4	20/25	20/25	20/25
Vanc + Amik	FLIw/Vanc	7	20/20	20/40	20/25
Vanc + Ciprofl	FLIw/Vanc	14	20/20	20/30	20/30
Vanc + Ciprofl	FLIw/Vanc	7.5	20/20	20/20	20/20
Vanc + Oflox	FLIw/Vanc	2	20/25	20/20	20/20
Amik + Moxi	FLIw/Vanc	6.5	20/20	20/20	20/20
Vanc + Ceftaz	FLIw/Vanc	3.5	20/20	20/32	20/30
Vanc + Oflox	FLIw/Vanc	1	20/32	20/20	20/20
Vanc + Tobra	FLIw/Vanc	2.5	20/25	20/20	20/20
Vanc + Genta + Ciprofl	FLIw/Vanc	6	20/25	20/20	20/20
Vanc + Oflox	FLIw/Vanc	3.5	20/20	20/25	20/20
Vanc + Oflox	FLIw/Vanc	4	20/30	20/40	20/40
Vanc + Oflox + oral Doxycycline	FLIw/Vanc	12	20/30	20/25	20/25
Tobra + Neo + Pol + Gram + oral Doxycycline	—	5	20/20	20/20	20/20
Tobra + Neo + Pol + Gram + oral Doxycycline	—	5	20/20	20/20	20/20
Lomeflox + Tobra + Ciclopl.	—	6	20/25	20/100	20/100
Vanc + Ciprofl + Tobra	FLIw/Vanc	42	20/25	20/30	20/30
Tobra + Vanc	FLIw/Vanc	14.5	20/20	20/16	20/16
Vanc + Tobra + Ciprofl + Tobra	FLIw/Vanc	3.1	20/32	20/32	20/25
Vanc + Amik + Oflox	—	1	20/20	20/25	20/12.5
Oflox + Tobra	—	12	20/200	20/50	20/50
Vanc + Tobra + Ciprofl	FLIw/Vanc + Tobra	4	20/20	20/20	20/20
Tobra + Vanc + Tobra + oral Minocycline	FLIw/Vanc + Tobra	3	20/20	20/32	20/25
Vanco	FLIw/Vanc + Tobra	1	20/20	20/20	20/20
Moxi	FLIw/Vanc + Tobra + Amik & FA	3	20/25	20/32	20/30
Moxi	FLIw/Vanc + Tobra + Amik	3	20/25	20/200	20/100
Vanc + Oflox	FLIw/Vanc	4	20/25	20/20	20/20
Tobra + Amik + Oflox	FLIw/Vanc	4	20/20	20/16	20/16
Vanc	FLIw/Vanc	8	20/25	20/20	20/20

(Continued)

Table 2.

Case N°	Age/Gender	Eye	Risk Factors	Day of Presentation	Culture Samples Taken	Organism
56	51/M	RE	—	1	N	
	51/M	LE	—	1	N	
57	32/M	RE	—	4	Y	<i>S viridans</i>
	32/M	LE	—	4	Y	<i>S viridans</i>
58	23/F	LE	IED + BCL	6	Y	<i>S epidermidis</i>
59	53/M	RE	—	38	Y	negative
60	30/M	RE	—	6	Y	negative
61	30/M	LE	—	3	Y	<i>S pneumoniae</i>
62	43/M	LE	Vet	2	Y	negative
63	56/M	LE	—	8	Y	negative

Vanc: vancomycin 50 mg/ml; Amik: amikacin 35 mg/ml; Oflox: ofloxacin 3 mg/ml (Exocin® Allergan, Madrid, Spain); Ciprofl: ciprofloxacin 3.5 mg/ml Inc. Fort Worth, Texas, USA); Genta: gentamicine 16 mg/ml; Lomeflox: lomefloxacin 3mg/ml (Ocacin® Novartis Farmaceutica, Barcelona, Spain); di Torile Italia); IED: intraoperative epithelial defect; BCL: bandage contact lens; Health care w: health care worker; FL + Iw/: Flap lifting and irrigation with; right eye; LE: left eye; M: male; F: female; Y: yes; N: no.

(Continued.)

Medical Treatment	Surgical Treatment	Follow-up (m)	Preop BSCVA	Postop UCVA	Postop BSCVA
Vanc + Oflox	FLIw/Vanc	3	20/30	20/25	20/25
Vanc + Oflox	FLIw/Vanc	3	20/25	20/25	20/25
Vanc + Tobr + Amik	FLIw/Vanc	8	20/30	20/40	20/32
Vanc + Tobra + Amik	FLIw/Vanc	8	20/30	20/40	20/32
Vanc + Amik	FLIw/Vanc	11	20/20	20/30	20/30
Vanc + Oflox	FLIw/Vanc	5.5	20/50	20/50	20/50
Vanc + Tobra + Oflox	FLIw/Vanc	3	20/30	20/50	20/50
Vanc + Moxi + Oflox + oral Doxycycline	FLIw/Vanc	5	20/25	20/32	20/32
Vanc + Amik	FLIw/Vanc	3	20/25	20/25	20/25
Vanc + Oflox	FLIw/Vanc	3.5	20/40	20/40	20/40

(Oftacilox[®] Alcon, Barcelona, Spain); Tobra: tobramycin 16 mg/ml; Ceftaz: ceftazidime 50 mg/ml; Moxi: moxifloxacin 5 mg/ml (Vigamox[®] Alcon Laboratories, Neo + Pol + Gram: combination containing neomicine 1700UI, polymyxin B 5000UI and gramicidine 25 UI per ml (Oftalmowell[®] GlaxoSmithKline SpA S Polo FA: flap amputation; Postop: postoperative; Preop: preoperative; m: months UCVA uncorrected visual acuity; BSCVA: best spectacle-corrected visual acuity; RE: