Incidence of Intraoperative and Early Postoperative Adverse Events in a Large Cohort of Consecutive Laser Vision Correction Treatments

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• PURPOSE: To evaluate the incidence of adverse events (AE) following laser vision correction.
• DESIGN: Retrospective case series.
• METHODS: Optical Express, UK. PATIENTS/STUDY POPULATION: patients who underwent laser in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) between July 1, 2014, and June 30, 2016. INTERVENTION/OBSERVATION PROCEDURES: all AEs recorded in the electronic medical record were extracted and retrospectively reviewed. The total incidence of AE and serious adverse events (SAE) was calculated. Loss of 2 or more lines of corrected distance visual acuity (CDVA) was calculated for the entire cohort of patients that attended a minimum of 3 months follow-up. MAIN OUTCOME MEASURES: AEs; Preoperative and last available postoperative clinical data.
• RESULTS: A total of 31,921 (61,833 eyes) were included in the study for LASIK and 5,016 (9,467 eyes) for PRK. The total number of AE was 850 for LASIK (occurring in 783 eyes of 657 patients; incidence of 1.3% or 1:79 eyes) and 227 for PRK (occurring in 218 eyes of 170 patients; incidence of 2.3% or 1:43 eyes). In the LASIK group, there were 287 SAEs (271 eyes of 226 patients; incidence of 0.4% or 1:228 eyes), and the number of SAEs in PRK group was 65 (65 eyes of 39 patients; incidence 0.7% or 1:146 eyes). Combining LASIK and PRK data, the loss of 2 or more lines of CDVA was recorded in 0.37% of eyes.
• CONCLUSIONS: Contemporary LASIK and PRK are safe procedures with a low incidence of serious adverse events. (Am J Ophthalmol 2019;■:■–■. © 2019 Elsevier Inc. All rights reserved.)

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MODERN LASER VISION CORRECTION (LVC) OUTcomes demonstrate excellent precision and a high rate of patient satisfaction.[1–4] Given the large amount of published data, the expected visual outcomes for a wide range of refractive errors are well known.[2,5] Despite these reassuring numbers, the potential for complications that may ultimately lead to reduced best corrected visual acuity exist. A thorough understanding of the potential risks associated with LASIK and PRK is essential for treating physicians as well as prospective patients.

Although there are some recent large laser vision correction studies that discuss adverse event (AE) rates,[6,7] there is a need for better understanding of postoperative AEs as well as their impact on postoperative visual acuity. The aim of this study was to explore AEs and outcomes in a large multicenter clinical practice.

SUBJECTS AND METHODS

THIS STUDY WAS DEEMED EXEMPT FROM FULL REVIEW BY the Committee on Human Research (the institution-specific name for the Institutional Review Board) at the University of California San Francisco because the study used only retrospective deidentified patient data. All patients provided informed consent to undergo LASIK or PRK and agreed to the use of their deidentified data for statistical analysis.

All AEs following primary laser in situ keratomilousis (LASIK) and photorefractive keratectomy (PRK) of patients treated between July 1, 2014, and June 30, 2016, were extracted from Optical Express electronic database. An AE was defined as an event that had the potential to adversely affect patients' visual outcomes and could be related to the refractive surgery. A list of AEs was created, and each AE was clearly defined (Table 1). Subsequently, each AE was reviewed to ensure that all AEs were categorized correctly and in line with their definition. The list of AEs was derived from the US Food and Drug Administration clinical trials,[8] although the list of AEs was expanded, and stringent criteria were used for the definition of some of

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the AEs to ensure that any event that could have a potentially negative impact on the patient's outcome was captured.

All treatments were performed using the VISX STAR S4 IR excimer laser system (Johnson & Johnson Vision Care, Inc, Santa Ana, California) with either a conventional or a wavefront-guided ablation profile (iDesign or Advanced CustomVue; Johnson & Johnson Vision Care). Corneal flaps were created by using a femtosecond laser (IntraLase iFS or FS-60; Johnson & Johnson Vision Care). All surgeries were performed by 1 of 29 surgeons in 25 surgical centers located in the United Kingdom.

For all patients, the preoperative ophthalmic examination included manifest and cycloplegic refraction, monocular and binocular uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA) using a calibrated projected eye chart, low-light pupil diameter, slit lamp biomicroscopy, dilated fundus examination, noncontact tonometry, corneal topography, ultrasonography pachymetry, and wavefront aberration measurement. All patients were advised to return for 1- and 4-day (PRK patients only), 1-week, and 1-, 3-, and 6-month postoperative examinations, where manifest refraction (except for days 1 and 4), visual acuity, noncontact tonometry and slit-lamp examination were performed. Yearly eye care was also recommended. If patients experienced AEs or side effects that were not resolved by 3 months, they were provided with continuing care until their issues resolved.

All AEs were recorded in the Optical Express electronic medical record (EMR) system. The EMR system is a custom-built system specifically for Optical Express and consists of both clinical and operating room interfaces. It is designed to enable easy capture of pertinent examination data and operating room specifics and has specialized measurements built in to comprehensively capture AEs in order to enable rapid analysis of any potential AE issues. All providers who interface with the EMR, including physicians, optometrists, and operating room nurses and technicians, undergo formal training in its use, which includes instructions for capturing AEs. In order to maximize the reporting of AEs, each electronic visit record (operative and postoperative) has a drop-down list of common LVC AEs. The electronic visit cannot be closed without the user first selecting if an AE had occurred or not. Furthermore, the user can select more than 1 AE for either eye of a given patient, and there is a field for free text entries if the encountered AE does not exist in the prespecified list. Continuous quality monitoring of the EMR data is also undertaken to ensure data integrity. Postoperative variables are analyzed on a per-examiner basis and compared with expected norms. Any substantial outliers trigger a review process with retraining if necessary. Patients who were treated at an outside clinic for an AE were instructed to submit bills to Optical Express for reimbursement. Any outside AE treatment was incorporated into the EMR.

Specific to the operating room, the clinical personnel are trained to record all intraoperative AEs that were evident during a procedure, such as flap complications, suction loss, equipment failure, and so forth. The operating room nurse or technician was trained to enter any AE encountered, and separately the treating physician also was required to enter a free text explanation of the situation leading to the AE. Postoperatively; Patients were seen by qualified and experienced refractive optometrists. The only exception to this was that patients who experienced an intraoperative AE were generally seen by their treating physicians. Any postoperative AE was recorded in the EMR in the process specified above. The refractive optometrists are provided with and instructed in a protocol regarding the engagement of the treating ophthalmic surgeon for management of AEs. Depending on the nature and severity of the AE, the patient was either managed by the optometrist in close communication with the treating surgeon or the patient was immediately referred to the surgeon. All severe AEs were managed by the treating surgeon. Every refractive optometrist undergoes a program of annual education and training to identify and manage AEs.

• **STATISTICAL ANALYSIS:** The AEs were summarized, and the incidence rate was calculated based on the total number of eyes treated in the time period between July 1, 2014, and June 30, 2016. All percentages were calculated on a "per-eye" basis. Postoperative visual acuity outcomes and refractive outcomes for the last available appointment were separately presented for AEs marked as "serious" in Table 1. Loss of 2 or more lines of best-corrected spectacle acuity was calculated for patients who attended the 3-month or later follow-up visit. This time point was chosen because most of the patients had achieved stabile acuity and refraction at 3 months after LVC. All visual acuity and refractive outcomes calculations were done based on the last available follow-up. Data tabulation was performed using Office Excel software (Microsoft, Redmond, Washington) and STATA software (Stata Corp, College Station, Texas).

RESULTS

THE TOTAL NUMBER OF PATIENTS TREATED BETWEEN JULY 1, 2014, and June 30, 2016, was 31,921 (61,833 eyes) for LASIK and 5,016 (9,467 eyes) for PRK. Combining LASIK and PRK, the total numbers of patients who attended a minimum of 1-, 3-, 6-, and 12-month follow-up exams were: 89.4%, 60.3%, 40.9%, and 20.0%, respectively. The mean follow-up of the whole study group was 4.4 ± 4.9 months. Table 2 and 3 summarize the incidence of all postoperative AEs.

The clinical and demographic characteristics of patients with and without LASIK AEs was tabulated (Table 4).

TABLE 1. Definition of Adverse Events

AE	Serious AE	Definition
Abrasion		Corneal abrasion that occurred in immediate postoperative period and was likely to be related to the surgical procedure.
Crystalline lens changes within 12M of LVC	Yes	Crystalline lens changes recorded in the first 12 postoperative months
CTK	Yes	Noninfectious dense opacification of the central corneal stroma associated with loss of stromal tissue, hyperopic shift, loss of CDVA and long recovery.
Corneal edema	Yes	Corneal edema persisting for longer than 1 month postoperative
Decentered ablation	Yes	Decentered ablation appearance on postoperative topography, causing visual symptoms and/or irregular astigmatism and/or loss of corrected visual acuity.
Delayed healing		Epithelial defect persisting for longer than 2 weeks postoperatively
DLK grade 3		Diffuse lamellar keratitis graded based on clinical examination
DLK grade 4	Yes	
Ectasia[a]	Yes	Progressive keratometric and topographic steepening, with or without central or paracentral corneal thinning, and associated corneal irregularity, myopic shift and/or induced astigmatism
Epithelial Ingrowth (required intervention)	Yes	Progressive epithelial ingrowth requiring surgical intervention
Epithelial ingrowth (stable)		Epithelial ingrowth that required monitoring, but did not induce irregular astigmatism, topographic changes or cause visual symptoms.
Flap buttonhole	Yes	Intraoperative or postoperative complications evident during surgery or postoperative aftercare
Flap free		
Flap incomplete	Yes	
Flap torn	Yes	
Flap traumatic displacement	Yes	
Flap melt	Yes	
Irregular flap	Yes	
Gas break-through during femtosecond flap creation	Yes	
Equipment failure during excimer laser ablation	Yes	
Suction loss		Intraoperative suction loss that either resulted in change of the procedure to a surface ablation, or the procedure had to be aborted and rescheduled to a different day.
Flap lift (debris/fiber)		Debris/fiber under flap discovered during early postoperative period and required a flap lift to remove.
Flap striae	Yes	Flap striae resulting in secondary procedure to correct the striae and/or a loss of vision or significant visual symptoms attributed to the striae.
Haze or scar	Yes	Haze/scar that persisted for longer than 1 month after LASIK or longer than 3 months after PRK and resulted either in a loss of CDVA and/or required a course of steroids and/or required a secondary surgical intervention to reduce haze, such as mitomycin C application.
Incorrect treatment	Yes	Incorrect treatment endpoint (aim), or incorrect procedure performed (e.g. conventional ablation instead of wavefront guided).
Elevated IOP	Yes	Elevated intraocular pressure greater than 21 mm Hg or $>$10 mm Hg over baseline persisting for longer than 1 week postoperatively
Microbial keratitis	Yes	Culture positive or probable culture negative microbial keratitis based on clinical findings.
Herpes simplex keratitis	Yes	Herpes simplex keratitis based on clinical findings

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TABLE 1. Definition of Adverse Events (*Continued*)

AE	Serious AE	Definition
Recurrent erosions		Repeated breakdown of epithelium, causing discomfort and/or photophobia, requiring management with either ocular surface lubrication or therapeutic contact lenses.
Retinal tear	Yes	Retinal tear diagnosed on dilated fundus examination, requiring treatment
Retinal detachment	Yes	Retinal detachment diagnosed on dilated fundus examination, requiring urgent treatment
Other posterior segment event	Yes	Posterior segment events including central serous retinopathy, pigment epithelium detachment of posterior vitreous detachment with formation of significant floaters
Sterile infiltrates		Noninfectious corneal infiltrate(s)
Transient light sensitivity syndrome		Transient light sensitivity diagnosed based on patients symptoms of light sensitivity with no obvious slit-lamp findings, treated with a course of steroid drops.

AE = adverse event; CDVA = corrected distance visual acuity; CTK = central toxic keratopathy; LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy.

[a]Ectasia after laser vision correction can take many years to manifest and it is only included here to maintain a comprehensive list of all AEs that occurred in our study population.

Overall; Patients with AEs tended to have more cylinder and worse postoperative uncorrected and best-corrected acuity, but there was a wide variation with type of AE.

Table 5 compares clinical data and demographics between PRK AE patients and all remaining PRK patients. Postoperatively; Patients with AEs had, on average, a higher amount of residual cylinder and slightly worse visual outcomes, but again, there was a wide variation with type of AE.

LASIK AEs were recorded in 783 eyes of 657 patients (531 patients had unilateral events, and 126 patients had bilateral events) for an overall incidence of 1.27% of eyes (1:79 eyes) and 2.06% of patients (1:49 patients). Of all LASIK AE eyes (Table 2) that had preoperative CDVA 20/40 or better, 99.4% had a CDVA of 20/40 or better on the last recorded examination. Of all AE LASIK eyes that had preoperative CDVA of 20/20 or better, 91.7% had postoperative CDVA of 20/20 or better. The last recorded UDVA in all LASIK patients with an AE (regardless of preoperative CDVA) was 20/20 or better in 68.5% of eyes monocularly and 88.4% of patients binocularly. On the last recorded examination, 75.2% and 88.5% of eyes were within 0.50 diopter (D) and 1.00 D of emmetropia, respectively.

For PRK, AEs were observed in 218 eyes of 170 patients (122 patients unilaterally, 48 patients bilaterally) for an overall incidence of 2.30% of eyes (1:43 eyes) and 3.39% of patients (1:30 patients). Of all PRK AE eyes (Table 3) who had preoperative CDVA of 20/40 or better, 99.1% had a CDVA of 20/40 or better on the last recorded examination. Of all AE PRK eyes that had preoperative CDVA of 20/20 or better, 91.6% had postoperative CDVA of 20/20 or better. The last recorded UDVA in all PRK patients with an AE (regardless of preoperative CDVA) was 20/20 or better in 73.9% of eyes monocularly and 86.5% of patients binocularly. On the last recorded examination, 77.4% and 91.7% of PRK AE eyes were within 0.50 D and 1.00 D of emmetropia, respectively.

• **SERIOUS ADVERSE EVENTS:** Combining LASIK and PRK serious AEs, of all eyes that had preoperative CDVA of 20/40 or better, 98.5% achieved postoperative CDVA of 20/40 or better. Of all eyes that achieved a preoperative CDVA of 20/20 or better, 85.4% had postoperative CDVA of 20/20 or better. The percentage of eyes with serious AS (SAE) that achieved postoperative monocular UDVA of 20/20 or better was 54.8%, and 79.2% of patients achieved binocular UDVA of 20/20 or better. Of all eyes with SAEs, 68.3% were within 0.50 D of emmetropia, and 81.4% were within 1.00 D of emmetropia at the last recorded examination.

• **LOSS OF 2 OR MORE LINES OF CDVA:** Loss of 2 or more lines of CDVA was calculated for the entire LVC cohort (LASIK and PRK) who attended a minimum of 3-months follow-up examinations (43,131 eyes of 22,277 patients). The loss of 2 or more lines of CDVA was 0.37% (158 eyes of 138 patients) in the entire cohort. For LASIK, the loss of 2 or more lines was 0.37% (136 eyes of 118 patients) and 0.35% for PRK (22 eyes of 20 patients), a difference that was not statistically significant ($P = 0.058$).

For the combined LVC cohort, the most common reasons for CDVA loss were ocular surface issues which were

TABLE 2. LASIK AEs

Total Consecutive Treatments			61,833 Eyes of 31,921 Patients				
Total Adverse Events			850 (783 Eyes Of 657 Patients): 1.3% Or 1:79 Eyes				
Total Serious Adverse Events			287 (271 Eyes of 226 Patients): 0.4% or 1:228 Eyes				
AE	SAE	No of Eyes	Incidence	1:__ Eyes	Last CDVA ≥20/20[a]	Last CDVA ≥20/40[b]	Lost ≥ 2 lines CDVA[c]
Epithelial ingrowth (stable)		120	0.194%	1:515	94.8%	100.0%	1.0%
Flap striae[e]	Yes	107	0.173%	1:578	89.2%	99.1%	6.1%
Abrasion		100	0.162%	1:618	88.2%	100.0%	2.8%
Recurrent erosions		76	0.123%	1:814	93.0%	98.7%	4.5%
Sterile infiltrates		76	0.123%	1:814	98.6%	100.0%	0.0%
Haze or scar	Yes	74	0.120%	1:836	86.6%	100.0%	7.0%
Transient light sensitivity syndrome		70	0.113%	1:883	95.7%	100.0%	1.6%
DLK grade 3		69	0.112%	1:896	94.1%	100.0%	4.3%
Suction loss		31	0.050%	1:1,995	100.0%	100.0%	0.0%
Epithelial ingrowth (required intervention)	Yes	18	0.029%	1:3,435	77.8%	100.0%	7.1%
Flap lift (debris/fiber)		14	0.023%	1:4,417	100.0%	100.0%	0.0%
Crystalline lens changes within 12 months of LVC	Yes	10	0.016%	1:6,183	60.0%	90.0%	40.0%
Central toxic keratopathy	Yes	9	0.015%	1:6,870	75.0%	100.0%	14.3%
Corneal edema	Yes	8	0.013%	1:7,729	75.0%	100.0%	0.0%
Ectasia[d]	Yes	8	0.013%	1:7,729	42.9%	87.5%	50.0%
Flap traumatic displacement	Yes	7	0.011%	1:8,833	85.7%	100.0%	20.0%
Flap incomplete	Yes	6	0.010%	1:10,306	100.0%	100.0%	0.0%
Flap melt	Yes	5	0.008%	1:12,367	100.0%	100.0%	0.0%
Flap torn	Yes	5	0.008%	1:12,367	100.0%	100.0%	0.0%
Other posterior segment events	Yes	5	0.008%	1:12,367	0.0%	100.0%	100.0%
Delayed healing		4	0.006%	1:15,458	100.0%	100.0%	0.0%
Flap buttonhole	Yes	3	0.005%	1:20,611	100.0%	100.0%	0.0%
Flap free		3	0.005%	1:20,611	100.0%	100.0%	0.0%
Herpes simplex keratitis	Yes	3	0.005%	1:20,611	100.0%	100.0%	0.0%
Incorrect treatment	Yes	3	0.005%	1:20,611	100.0%	100.0%	0.0%
Decentred ablation	Yes	2	0.003%	1:30,917	0.0%	100.0%	50.0%
DLK grade 4	Yes	2	0.003%	1:30,917	50.0%	100.0%	–
Equipment failure during surgery	Yes	2	0.003%	1:30,917	100.0%	100.0%	0.0%
Gas break through during flap creation	Yes	2	0.003%	1:30,917	100.0%	100.0%	0.0%
IOP elevated	Yes	2	0.003%	1:30,917	100.0%	100.0%	0.0%
Microbial keratitis	Yes	2	0.003%	1:30,917	50.0%	100.0%	50.0%
Retinal detachment	Yes	2	0.003%	1:30,917	0.0%	0.0%	100.0%
Irregular flap	Yes	1	0.002%	1:61,833	100.0%	100.0%	0.0%
Retinal fear	Yes	1	0.002%	1:61,833	100.0%	100.0%	0.0%

AE = adverse event; CDVA = corrected distance visual acuity; CTK = central toxic keratopathy; DLK = diffuse lamellar keratitis; LASIK = laser in situ keratomileusis; LVC = laser vision correction.

Incidence is calculated as the percent of total eyes experiencing the particular adverse event. Acuity results are percentage of eyes with the particular AE achieving the listed acuity or better.

[a]last available CDVA 20/20 or better was calculated only for eyes that had preoperative CDVA 20/20 or better

[b]last recorded CDVA 20/40 or better was calculated only for eyes that had preoperative CDVA 20/40 or better

[c]Loss of ≥ 2 lines of CDVA calculated only for eyes that reached a minimum of 3 months follow-up

[d]Ectasia after laser vision correction can take many years to manifest and it is only included here to maintain a comprehensive list of all AEs that occurred in our study population.

[e]Visual acuity is calculated after repair

responsible for the loss of CDVA in 0.234% (101 eyes). The population with ocular surface issues was slightly older than the average age in the non-AE cohort (37.2 ± 11.6 vs 34.3 ± 10.5, respectively; $P < 0.001$), but there were no significant differences in refractive errors ($P = 0.75$ for myopia and 0.69 for hyperopia) nor sex ($P = 0.097$). Other reasons for loss of CDVA were: crystalline lens changes (0.030%; 13 eyes), haze or scarring (0.019%; 8 eyes), of

TABLE 3. PRK AEs

Total Consecutive Treatments			9,467 Eyes of 5,016 Patients				
Total Adverse Events (AE)			227 (218 Eyes of 170 Patients): 2.3% or 1:43 Eyes				
Total Serious Adverse Events (SAE)			65 (65 Eyes of 39 Patients): 0.7% or 1:146 Eyes				
AE	SAE	No of Eyes	Incidence	1:__ Eyes	Last CDVA ≥20/20[a]	Last CDVA ≤20/40[b]	Lost ≥ 2 Lines CDVA[c]
Recurrent erosions		104	1.099%	1:91	93.1%	99.0%	6.4%
Haze or scar	Yes	58	0.613%	1:163	93.0%	100.0%	3.4%
Sterile infiltrates		29	0.306%	1:326	93.1%	100.0%	4.2%
Abrasion		16	0.169%	1:592	93.8%	100.0%	0.0%
Delayed healing		13	0.137%	1:728	69.2%	100.0%	9.1%
IOP elevated	Yes	2	0.021%	1:4,734	100.0%	100.0%	0.0%
Microbial keratitis	Yes	2	0.021%	1:4,734	100.0%	100.0%	0.0%
Crystalline lens changes within 12 months of LVC	Yes	1	0.011%	1:9,467	100.0%	100.0%	0.0%
Ectasia[d]	Yes	1	0.011%	1:9,467	100.0%	100.0%	0.0%
Retinal detachment	Yes	1	0.011%	1:9,467	0.0%	0.0%	100.0%

AE = adverse event; CDVA = corrected distance visual acuity; IOP = intraocular pressure; LVC = laser vision correction; PRK = photorefractive keratectomy.

Incidence is calculated as the percent of total eyes experiencing the particular adverse event. Acuity results are percentage of eyes with the particular AE achieving the listed acuity or better.

[a]Last available CDVA 20/20 or better was calculated only for eyes that had preoperative CDVA 20/20 or better

[b]Last recorded CDVA 20/40 or better was calculated only for eyes that had preoperative CDVA 20/40 or better

[c]Loss of ≥ 2 lines of CDVA calculated only for eyes that reached a minimum of 3 months follow-up

[d]Ectasia after laser vision correction can take many years to manifest and it is only included here to maintain a comprehensive list of all AEs that occurred in our study population.

which scarring in one eye was caused by microbial keratitis, flap striae (0.012%; 5 eyes); posterior segment events (Table 1) (0.012%; 5 eyes), corneal ectasia (0.009%; 4 eyes), retinal detachment (0.007%; 3 eyes), central toxic keratopathy (0.002%; 1 eye), and decentered ablation (0.002%; 1 eye). In 17 eyes (0.038%), the loss of CDVA was unexplained. Note that the follow-up in this cohort was not sufficient to calculate an accurate rate of postoperative ectasia.

Of all 158 eyes that lost 2 or more lines of CDVA, 22 eyes (13.9%) had CDVA reduced to less than 20/40, but in all cases, the loss was unilateral. There were no patients in the study who had CDVA reduced to less than 20/40 in each eye.

DISCUSSION

DESPITE THE EMERGENCE OF ALTERNATIVE SURGICAL TECHniques, excimer laser surgery remains the most commonly performed refractive surgery in the world.[1] Excimer laser vision correction has a low incidence of AEs, with several large series published in the last decade reporting rates ranging between 0.6% and 2.8%.[2,6,7,9,10] However, the criteria of what constitutes a complication or AE varied among studies, making the comparison of outcomes to our study difficult. Additionally, the present authors explored the impact of each individual AE on patients' final visual acuities, which has not, to the present authors' knowledge, been reported in previous studies.

Using standardized definitions derived from Food and Drug Administration reporting criteria,[8] the total overall AE rate (intraoperative and postoperative) for LASIK was 1.3% and 2.3% for PRK. The incidence of significant, potentially sight-threatening AEs was low (0.4% for LASIK and 0.7% for PRK). None of the patients in the present cohort had the last recorded CDVA less than 20/40 in both eyes. Of all patients who experienced serious, sight-threatening AEs, 79.2% had the last recorded binocular UDVA of 20/20 or better.

The overall largest cause of vision loss in this study was postoperative ocular surface issues, responsible for 101 of the 158 eyes that lost CDVA. This population was, on average, slightly older than the population without ocular surface issues. Older patients have previously been reported to have more dry eye issues after undergoing LVC and overall more difficulties with epithelial adherence after LASIK.[11–14] However, the average age difference between the overall cohort and the cohort with CDVA loss secondary to surface issues was small (3 years) and, as such, is not clinically useful in screening patients. The fact that ocular surface issues were the largest factor in vision loss should serve as a reminder to clinicians to pay attention to the condition of the ocular surface both before and after refractive surgery and to treat ocular

TABLE 4. Clinical Data for Eyes with and without AEs after LASIK

Event	n Eyes	Age (y)	% Female (n Patients)	% Myopic (n Eyes)	Preop MSE Myopic	Preop MSE Hyperopic	Postop Sphere	Postop Cylinder	Postop UCVA	Postop CDVA
Cohort without AE	61.833	34.2 ± 4.8	49.7 (15,551)	90.7 (55,042)	−3.33 ± 1.93	+1.61 ± 0.92	+0.03 ± 0.44	−0.19 ± 0.27	−0.05 ± 0.15	−0.09 ± 0.06
Epithelial ingrowth (stable)	120	36.3 ± 10.6	45.8 (55)	71.7 (86)	−4.21 ± 2.18	+2.26 ± 1.03	+0.04 ± 0.48	−0.45 ± 0.45	0.002 ± 0.19	−0.08 ± 0.06
Flap striae	107	34.6 ± 10.7	39.2 (42)	94.4 (101)	−4.43 ± 2.51	+0.77 ± 0.24	+0.23 ± 0.77	−0.46 ± 0.41	0.05 ± 0.25	−0.05 ± 0.11
Abrasion	100	36.0 ± 11.6	47 (47)	77 (77)	−3.88 ± 2.14	+2.46 ± 1.11	−0.09 ± 0.66	−0.41 ± 0.32	0.04 ± 0.18	−0.04 ± 0.09
Recurrent erosions	76	34.2 ± 9.5	49.3 (37)	93.4 (71)	−3.80 ± 2.43	+2.18 ± 0.49	+0.11 ± 0.44	−0.50 ± 0.47	0.01 ± 0.15	−0.04 ± 0.10
Sterile infiltrates	76	36.0 ± 10.5	43.4 (33)	82.9 (63)	−3.54 ± 1.92	+1.66 ± 0.82	−0.14 ± 0.71	−0.36 ± 0.30	0.02 ± 0.25	−0.10 ± 0.07
Haze or scar	74	42.3 ± 12.9	43.2 (32)	52.7 (39)	−4.23 ± 3.05	+2.53 ± 0.79	−0.18 ± 1.17	−0.58 ± 0.71	0.15 ± 0.26	−0.02 ± 0.10
Transient light sensitivity syndrome	70	40.3 ± 11.3	72.9 (51)	85.7 (60)	−3.51 ± 2.01	+1.53 ± 0.76	−0.01 ± 0.53	−0.31 ± 0.25	−0.03 ± 0.18	−0.07 ± 0.06
DLK grade 3	69	32.5 ± 108	44.9 (31)	95.7 (66)	−3.30 ± 2.10	+2.13 ± 0.22	+0.15 ± 0.67	−0.44 ± 0.37	0.00 ± 0.19	−0.07 ± 0.08
Suction loss	31	30.3 ± 12.3	54.8 (17)	74.2 (23)	−2.98 ± 1.79	+1.66 ± 0.90	−0.05 ± 0.35	−0.18 ± 0.26	−0.01 ± 0.16	−0.06 ± 0.07
Epithelial ingrowth (required intervention)	18	37.8 ± 11.9	27.7 (5)	77.8 (14)	−3.08 ± 1.62	+2.34 ± 0.72	−0.36 ± 0.64	−0.56 ± 0.49	0.05 ± 0.24	−0.04 ± 0.10
Flap lift (debris/fiber)	14	32.1 ± 7.1	35.7 (5)	85.7 (12)	−4.09 ± 2.51	+2.31 ± 0.80	+0.14 ± 0.51	−0.50 ± 0.37	−0.03 ± 0.16	−0.10 ± 0.05
Crystalline lens changes	10	59.5 ± 7.1	60.0 (6)	60.0 (6)	−5.08 ± 2.02	+1.56 ± 0.26	−0.43 ± 1.61	−0.46 ± 0.39	0.43 ± 0.30	0.10 ± 0.23
Central toxic keratopathy	9	34.9 ± 10.5	33.3 (3)	100 (9)	−4.01 ± 2.43	–	+1.86 ± 0.84	−0.72 ± 0.52	0.17 ± 0.19	0.01 ± 0.11
Corneal edema	8	50.1 ± 5.6	62.5 (5)	87.5 (7)	−5.13 ± 2.28	+0.88	−0.34 ± 1.01	−0.56 ± 0.55	0.30 ± 0.30	0.01 ± 0.08
Ectasia	8	32.9 ± 5.6	37.5 (3)	87.5 (7)	−5.30 ± 3.27	+2.50	0.03 ± 2.11	−3.13 ± 1.60	0.43 ± 0.28	0.16 ± 0.27
Flap traumatic displacement	7	33.3 ± 11.8	12.3 (1)	100 (7)	−3.11 ± 2.30	–	−0.36 ± 0.53	−0.75 ± 0.46	0.01 ± 0.23	−0.08 ± 0.09
Flap incomplete	6	33.0 ± 7.8	66.7 (4)	100 (6)	−4.39 ± 1.97	–	+0.05 ± 0.27	−0.44 ± 0.38	−0.02 ± 0.04	−0.04 ± 0.05
Flap melt	5	42.4 ± 11.9	80.0 (4)	60.0 (3)	−3.63 ± 2.58	+2.25 ± 1.24	+0.35 ± 0.95	−0.56 ± 0.13	0.14 ± 0.16	−0.05 ± 0.04
Flap torn	5	30.6 ± 12.1	100 (5)	100 (5)	−3.18 ± 2.06	–	0.10 ± 0.42	−0.30 ± 0.27	−0.02 ± 0.13	−0.08 ± 0.00
Other posterior segment events	5	42.4 ± 5.1	20.0 (1)	80.0 (4)	−3.47 ± 2.19	+0.50	−0.35 ± 0.49	−0.15 ± 0.34	0.31 ± 0.12	0.023 ± 0.08
Delayed healing	4	41.3 ± 6.2	100 (4)	75.0 (3)	−3.29 ± 0.14	+0.63	−0.06 ± 0.31	−0.13 ± 0.18	−0.02 ± 0.09	−0.02 ± 0.09
Flap buttonhole	3	37.7 ± 14.0	33.3 (1)	66.7 (2)	−4.18 ± 3.80	+3.88	+0.08 ± 0.14	−0.50 ± 0.75	0.01 ± 0.18	−0.06 ± 0.05
Flap free	3	43.4 ± 9.0	66.7 (2)	66.7 (2)	−4.81 ± 3.09	–	+0.33 ± 0.52	−0.08 ± 0.14	−0.03 ± 0.05	−0.09 ± 0.01
Herpes simplex keratitis	3	40.0 ± 5.2	33.3 (1)	100 (3)	−3.00 ± 1.51	+1.88	+0.33 ± 0.29	−0.25 ± 0.00	−0.12 ± 0.10	−0.12 ± 0.10
Incorrect treatment	3	52 ± 3.6	33.3 (1)	66.7 (2)	−3.44 ± 0.97	+3.13 ± 1.60	−0.17 ± 0.76	−0.42 ± 0.14	0.01 ± 0.09	−0.11 ± 0.06
Decentred ablation	2	45.5 ± 0.7	100 (2)	0 (0)	0	–	−0.25 ± 0.0	−1.25 ± 1.77	0.30 ± 0.00	0.10 ± 0.00
DLK grade 4	2	23.5 ± 0.7	50.0(1)	100 (2)	−2.06 ± 1.68	–	+2.50 ± 0.71	−1.38 ± 0.18	0.26 ± 0.06	0.07 ± 0.21
Equipment failure during surgery	2	32.5 ± 2.1	100 (2)	100 (2)	−5.81 ± 0.62	–	0.00 ± 0.00	−0.13 ± 0.18	−0.13 ± 0.07	−0.13 ± 0.07
Gas break through during flap creation	2	48.5 ± 9.2	100 (2)	50.0 (1)	−1.00 ± 0.00	+0.63	+0.25 ± 0.00	−0.25 ± 0.35	−0.08 ± 0.00	−0.08 ± 0.00
IOP elevated[a]	2	19	0 (0)	100 (2)	−2.74 ± 0.00	–	0.00 ± 0.00	−0.38 ± 0.18	−0.08 ± 0.00	−0.08 ± 0.00
Microbial keratitis	2	46 ± 15.5	50.0 (1)	50.0 (1)	−4.38 ± 0.00	+1.88	−1.25 ± 0.53	−1.63 ± 0.88	0.70 ± 0.42	0.07 ± 0.21
Retinal detachment	2	51.5 ± 6.4	100 (2)	100 (2)	−8.25 ± 1.06	–	+1.875 ± 2.65	−0.25 ± 0.35	1.50 ± 0.70	0.70 ± 0.00
Irregular flap	1	37	0 (0)	100 (1)	−5.58	–	+0.50	−0.50	−0.08	−0.08
Retinal tear	1	37	100 (1)	100 (1)	−2.75	–	−0.25	−0.25	0.10	−0.08

AE = adverse event; CDVA = corrected monocular distance visual acuity; DLK = diffuse lamellar keratitis; LASIK = laser in situ keratomileusis; MSE = manifest spherical equivalent; UCVA = uncorrected monocular distance visual acuity.

[a]Both eyes of same patient.

TABLE 5. Clinical Data for Eyes with and without AE after PRK

Event	n Eyes	Age, y	% Female (n Patients)	% Myopic (n Eyes)	MSE Myopic (D)	MSE Hyperopic (D)	Postop Sphere (D)	Postop Cylinder (D)	Postop UCVA (LogMAR)	Postop CDVA (LogMAR)
Cohort without AE	9,467	33.2 ± 10.1	42.4 (3,984)	91.5 (8665)	−2.82 ± 1.99	+1.10 ± 0.74	+0.04 ± 0.49	−0.25 ± 0.33	−0.02 ± 0.17	−0.08 ± 0.08
Recurrent erosions	104	36.1 ± 11.9	48.0 (50)	79.8 (84)	−2.71 ± 2.13	+0.78 ± 0.40	+0.10 ± 0.54	−0.39 ± 0.44	0.00 ± 0.20	−0.07 ± 0.09
Haze or acar	58	30.8 ± 10.5	24.1 (14)	93.1 (57)	−4.94 ± 2.05	+1.75	+0.25 ± 0.97	−0.78 ± 0.93	0.04 ± 0.22	−0.07 ± 0.08
Sterile infiltrates	29	40.1 ± 8.6	55.2 (16)	82.8 (24)	−3.34 ± 2.00	+1.38 ± 1.10	−0.13 ± 0.71	−0.35 ± 0.24	0.00 ± 0.23	−0.09 ± 0.07
Abrasion	16	41.0 ± 14.2	43.6 (7)	68.6 (12)	−2.31 ± 1.45	+1.125 ± 0.43	+0.23 ± 0.45	−0.48 ± 0.53	0.05 ± 0.21	−0.05 ± 0.07
Delayed healing	13	42.2 ± 10.5	61.5 (8)	69.2 (9)	−5.47 ± 2.11	+0.71 ± 0.33	0.00 ± 0.77	−0.25 ± 0.35	0.09 ± 0.22	−0.03 ± 0.10
IOP elevated	2[a]	52.0 ± 0	0.0 (0)	100 (2)	−0.63 ± 0.35	–	−0.50 ± 1.77	0.00 ± 0.00	0.61 ± 0.55	−0.04 ± 0.06
Microbial keratitis	2	36.4 ± 21.0	0.0 (0)	100 (2)	−2.75 ± 1.06	–	−0.75 ± 0.53	−0.50 ± 0.38	−0.08 ± 0.00	−0.08 ± 0.00
Crystalline lens changes within 12 months of LVC	1	59.0	100 (1)	100 (1)	−1.50	–	0.00	0.00	0.22	−0.08
Ectasia	1	39.0	100 (1)	100 (1)	−2.00	–	−1.50	0.00	−0.18	−0.18
Retinal detachment	1	59.0	100 (1)	100 (1)	−0.25	–	–	–	1.3	0.7

AE = adverse event; CDVA = best spectacle corrected monocular distance visual acuity; D = diopter; IOP = intraocular pressure; LVC = laser vision correction; MSE = manifest spherical equivalent; PRK = photorefractive keratectomy; UCVA = uncorrected monocular distance visual acuity.

[a]Both eyes of same patient.

surface disease aggressively. Neuropathic pain has gained attention as a potential complication of LASIK.[15] Unfortunately, information for neuropathic pain symptoms was not gathered in this cohort, and the authors were unable to report its occurrence.

The intraoperative LASIK AEs encountered in the present study were mostly related to the creation of the flap. Flap-related AEs included torn flaps, incomplete flaps, free flaps, flap button holes, suction loss, and gas breakthrough during femtosecond flap creation, accounting for a total of 0.08% of all LASIK AEs in this study. A recent meta-analysis of femtosecond laser outcomes reported intraoperative AE rates ranging between 0.00% and 1.35%[16] for the same type of femtosecond laser that was used in the present study (IntraLase iFS, Johnson & Johnson Vision Care). Likewise, other large series using predominantly (although not exclusively) femtosecond lasers have reported incidence rates in the same spectrum for flap-related complications.[2,6]

Early flap-related postoperative AEs in this study included mainly flap striae, occurring in a total of 0.17% LASIK cases. Other early postoperative flap AEs (e.g., flap lift for debris or traumatic flap displacement) were relatively rare. In this review, only clinically significant striae that either necessitated intervention or resulted in the loss of CDVA were included. The present incidence of clinically significant flap striae is slightly lower than the range commonly cited in published reports (0.2%-1.5%)[17–19]; however, many of those studies were using a mechanical microkeratome. Femtosecond flaps have been shown to be more uniform and may have better adherence[20,21]; therefore, clinically significant striae may have a lower incidence in modern refractive surgery.

A group of AEs very specific to LASIK flap creation are those related to the flap interface.[22] Vision-threatening interface AEs such as clinically significant epithelial ingrowth (0.029%), DLK grade 4 (0.003%), or central toxic keratopathy (0.015%) had very low occurrence but did result in reduction of best-corrected acuity. Interface haze that persisted for longer than 1 month occurred in 0.120% cases. The potentially most devastating AE that often manifests in flap interface is microbial keratitis; microbial keratitis was relatively rare (incidence of 0.003%; 1:30,917 eyes). This is in agreement with a previous study of infectious keratitis from the present authors' group, who found it rarely occurred.[23]

There were no patients who experienced an intraoperative AE during the PRK procedure. Postoperative AEs were those commonly associated with PRK, such as corneal haze, although the incidence of haze persisting for longer than 3 months was relatively low (0.61%), and 93% of these eyes had CDVA of 20/20 or better at the last recorded examination. Mitomycin C was routinely used in all PRK cases, which has been shown to lower the rate of haze.[24] Patients who developed haze had a higher amount of preoperative myopia than those who did not (−4.94 ± 2.05 D

vs −2.82 ± 1.99 D, respectively), and were slightly younger (30.8 ± 10.5 vs 33.2 ± 10.1, respectively), both of which have also been shown to be a risk factors for the development of haze.[25,26]

Other PRK AEs were associated mainly with poor epithelial adherence, such as recurrent erosions (1.10%); corneal abrasion (0.17%) or delayed epithelial healing (0.14%), all of which tended to occur relatively more frequently in older patients. The incidence of epithelial complications in this series is less than that reported in some series (0.2%-0.5% for delayed healing, 2%-4% for recurrent erosions), which may be explained by differences in mitomycin C and epithelial removal protocols.[27–29] Older patients have been reported to have more difficulties with the epithelium during and after laser vision correction.[11–14] Recurrent erosions have also been reported to occur more often after PRK thank LASIK, which was observed in this series.[30] The most feared AE, microbial keratitis, had a slightly higher incidence in the PRK group than in the LASIK group (0.021%; 1:4,734 eyes), although the visual recovery was good with all eyes achieving CDVA of 20/20 or better at the last recorded exam.

In this case series, there were 3 cases of unilateral retinal detachment (2 after LASIK; incidence 0.003%; and 1 after PRK; incidence of 0.011%). The 2 cases of LASIK retinal detachment occurred 2 months after LASIK for −9.0 D of myopia and 12 months after LASIK for −7.5 D of myopia. The reported incidence of RD following LASIK was 0.033% to 0.25% and has been postulated to be associated with the suction ring application inducing vitreous traction.[31] However, it is not clear if there was any relationship between the suction applied during LASIK and RD.[32–34] In fact, the third case of retinal detachment in the present study occurred 9 months postoperatively in a plano presbyopic patient who underwent PRK to induce monovision, during which no suction was applied.

Another significant AE with a possible onset years after LVC is corneal ectasia. The reported post-LVC occurrence ranges between 0.04% and 0.6%.[35] The mean follow-up of the present study population was not adequate to accurately calculate the true incidence of corneal ectasia and should not be interpreted as such; this cohort may see additional ectasia cases develop in the future as these have been reported to occur years after the primary surgery.[35] The authors only included it to maintain a comprehensive list of all AEs that occurred in the present study population, and it is possible that more patients from this cohort will develop ectasia with time.

This study had several limitations. First, there is a possibility that some AEs might have been underreported. Several procedures were incorporated into the electronic medical record system to ensure the accurate capture of all AEs, such as mandatory entering of AE occurrence, and double-reporting of any operative AE. The second limitation is that the study was retrospective in nature and it is possible that some patients might not have returned for follow-up examinations to the authors' clinics. However, all patients received instruction on follow-up and were provided with a 24-hour phone number to call with any postoperative concerns. Care for patients who were treated for AEs at other sites was reimbursed by the refractive provider, which provided another avenue for AE capture. Given these precautions, the authors believe that this study offers the most inclusive picture of AEs possible given the large cohort; however, it is possible that some AEs may be underrepresented. Another limitation of this study was that long-term AEs, such as the development of ectasia, could not be accurately evaluated.

This study summarized the AEs of contemporary laser vision correction in a large population of patients. Outcomes show that excimer LVC is a safe procedure with low AE rates and most of the patients that encountered AEs recovered without significant vision loss. The most common cause for loss of best corrected vision in this cohort was ocular surface disease. This information should be useful to practitioners in counseling patients as to potential outcomes. It is reassuring that these rates are low, but it also provides a reminder that, as with any surgical intervention, there is a risk associated with the procedure. Further study of risk factors associated with individual AEs may assist improvements in patient counseling and selection.

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REFERENCES

1. Sandoval HP, Donnenfeld ED, Kohnen T, et al. Modern laser in situ keratomileusis outcomes. *J Cataract Refract Surg* 2016; 42:1224–1234.
2. Yuen LH, Chan WK, Koh J, Mehta JS, Tan DT. A 10-year prospective audit of LASIK outcomes for myopia in 37,932 eyes at a single institution in Asia. *Ophthalmology* 2010;117: 1236–1244.e1.
3. Sugar A, Hood CT, Mian SI. Patient-reported outcomes following LASIK: quality of life in the PROWL studies. JAMA 2017;317:204–205.
4. Moshirfar M, Shah TJ, Skanchy DF, Linn SH, Durrie DS. Meta-analysis of the FDA reports on patient-reported

outcomes using the three latest platforms for LASIK. *J Refract Surg* 2017;33:362–368.
5. Varley GA, Huang D, Rapuano CJ, Schallhorn S, Boxer Wachler BS, Sugar A. LASIK for hyperopia, hyperopic astigmatism, and mixed astigmatism: a report by the American Academy of Ophthalmology. *Ophthalmology* 2004;111:1604–1617.
6. Kamiya K, Igarashi A, Hayashi K, Negishi K, Sato M, Bissen-Miyajima H. A multicenter prospective cohort study on refractive surgery in 15 011 eyes. *Am J Ophthalmol* 2017;175:159–168.
7. Kamiya K, Igarashi A, Hayashi K, Negishi K, Sato M, Bissen-Miyajima H. A multicenter retrospective survey of refractive surgery in 78,248 Eyes. *J Refract Surg* 2017;33:598–602.
8. US Food and Drug Administration. FDA-approved lasers for PRK and other refractive surgeries. Available at: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/ucm192110.htm. Accessed November 12, 2017.
9. Haft P, Yoo SH, Kymionis GD, Ide T, O'Brien TP, Culbertson WW. Complications of LASIK flaps made by the IntraLase 15- and 30-kHz femtosecond lasers. *J Refract Surg* 2009;25:979–984.
10. Chang JS. Complications of sub-Bowman's keratomileusis with a femtosecond laser in 3009 eyes. *J Refract Surg* 2008;24:S97–S101.
11. Shoja MR, Besharati MR. Dry eye after LASIK for myopia: incidence and risk factors. *Eur J Ophthalmol* 2007;17:1–6.
12. Randleman JB, Lynn MJ, Banning CS, Stulting RD. Risk factors for epithelial defect formation during laser in situ keratomileusis. *J Cataract Refract Surg* 2007;33:1738–1743.
13. Chen YT, Tseng SH, Ma MC, Huang FC, Tsai YY. Corneal epithelial damage during LASIK: a review of 1873 eyes. *J Refract Surg* 2007;23:916–923.
14. Tekwani NH, Huang D. Risk factors for intraoperative epithelial defect in laser in-situ keratomileusis. *Am J Ophthalmol* 2002;134:311–316.
15. Theophanous C, Jacobs DS, Hamrah P. Corneal neuralgia after LASIK. *Optom Vis Sci* 2015;92:e233–e240.
16. Huhtala A, Pietila J, Makinen P, Uusitalo H. Femtosecond lasers for laser in situ keratomileusis: a systematic review and meta-analysis. *Clin Ophthalmol* 2016;10:393–404.
17. Vesaluoma M, Perez-Santonja J, Petroll WM, Linna T, Alio J, Tervo T. Corneal stromal changes induced by myopic LASIK. *Invest Ophthalmol Vis Sci* 2000;41:369–376.
18. Estopinal CB, Mian SI. LASIK flap: postoperative complications. *Int Ophthalmol Clin* 2016;56:67–81.
19. Wallerstein A, Gauvin M, Adiguzel E, et al. Clinically significant laser in situ keratomileusis flap striae. *J Cataract Refract Surg* 2017;43:1523–1533.
20. Kezirian GM, Stonecipher KG. Comparison of the IntraLase femtosecond laser and mechanical keratomes for laser in situ keratomileusis. *J Cataract Refract Surg* 2004;30:804–811.
21. Durrie DS, Kezirian GM. Femtosecond laser versus mechanical keratome flaps in wavefront-guided laser in situ keratomileusis: prospective contralateral eye study. *J Cataract Refract Surg* 2005;31:120–126.
22. Randleman JB, Shah RD. LASIK interface complications: etiology, management, and outcomes. *J Refract Surg* 2012;28:575–586.
23. Schallhorn JM, Schallhorn SC, Hettinger K, Hannan S. Infectious keratitis after laser vision correction: incidence and risk factors. *J Cataract Refract Surg* 2017;43:473–479.
24. Majmudar PA, Schallhorn SC, Cason JB, et al. Mitomycin-C in corneal surface excimer laser ablation techniques: a report by the American Academy of Ophthalmology. *Ophthalmology* 2015;122:1085–1095.
25. Lee DH, Chung HS, Jeon YC, Boo SD, Yoon YD, Kim JG. Photorefractive keratectomy with intraoperative mitomycin–C application. *J Cataract Refract Surg* 2005;31:2293–2298.
26. Netto MV, Mohan RR, Sinha S, Sharma A, Dupps W, Wilson SE. Stromal haze, myofibroblasts, and surface irregularity after PRK. *Exp Eye Res* 2006;82:788–797.
27. Alio JL, Artola A, Claramonte PJ, Ayala MJ, Sanchez SP. Complications of photorefractive keratectomy for myopia: two year follow-up of 3000 cases. *J Cataract Refract Surg* 1998;24:619–626.
28. Mohammadpour M, Shakoor D, Hashemi H, et al. Comparison of bandage contact lens removal on the fourth versus seventh postoperative day after photorefractive keratectomy: a randomized clinical trial. *J Curr Ophthalmol* 2017;29:103–107.
29. Kremer I, Ehrenberg M, Levinger S. Delayed epithelial healing following photorefractive keratectomy with mitomycin C treatment. *Acta Ophthalmol* 2012;90:271–276.
30. Hovanesian JA, Shah SS, Maloney RK. Symptoms of dry eye and recurrent erosion syndrome after refractive surgery. *J Cataract Refract Surg* 2001;27:577–584.
31. Faghihi H, Jalali KH, Amini A, Hashemi H, Fotouhi A, Esfahani MR. Rhegmatogenous retinal detachment after LASIK for myopia. *J Refract Surg* 2006;22:448–452.
32. Qin B, Huang L, Zeng J, Hu J. Retinal detachment after laser in situ keratomileusis in myopic eyes. *Am J Ophthalmol* 2007;144:921–923.
33. Salazar PF, Rodriguez FJ, Medina DM, Infante R, Rodriguez A. Outcomes of vitreoretinal surgery for retinal detachment after LASIK for myopia. *Eur J Ophthalmol* 2006;16:435–439.
34. Kang HM, Lee CS, Park HJ, et al. Characteristics of rhegmatogenous retinal detachment after refractive surgery: comparison with myopic eyes with retinal detachment. *Am J Ophthalmol* 2014;157:666–672.
35. Santhiago MR, Giacomin NT, Smadja D, Bechara SJ. Ectasia risk factors in refractive surgery. *Clin Ophthalmol* 2016;10:713–720.