Outcomes and complications of excimer laser surgery in patients with collagen vascular and other immune-mediated inflammatory diseases

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PURPOSE: To assess refractive and visual outcomes and postoperative complications in a large number of patients with well-controlled collagen vascular and other immune-mediated inflammatory diseases.

SETTING: Optical Express, Glasgow, United Kingdom.

DESIGN: Retrospective case series.

METHODS: The files were reviewed of patients who had collagen vascular and other immune-mediated inflammatory diseases and who had excimer laser surgery between 2008 and 2015. In all cases, the disease was well controlled with no flare or symptoms for a minimum of 6 months preoperatively.

RESULTS: The study comprised 622 patients (1224 eyes) with 1 of the following underlying diseases: rheumatoid arthritis (50.6% of patients), systemic lupus erythematosus (19.5%), psoriatic arthritis (10.5%), sarcoidosis (10.0%), ankylosing spondylitis (6.4%), multiple sclerosis (1.9%), or scleroderma (1.1%). Laser in situ keratomileusis (LASIK) was performed in 1114 eyes (91.0%) and photorefractive keratectomy (PRK) in 110 eyes (9.0%). The mean follow-up was 10.9 months. The preoperative spherical equivalent ranged between −10.13 diopters (D) and +4.13 D (LASIK) and −9.50 D and +4.00 D (PRK). Postoperatively, 81.8% LASIK eyes and 82.3% PRK eyes were within ±0.50 D. The uncorrected distance visual acuity was 20/20 or better in 76.8% and 73.4%, respectively. Complications were mostly those that would be expected after excimer laser surgery in a population of patients without disease with the exception of 1 peripheral flap melt that responded to treatment with topical steroids.

CONCLUSION: Excimer laser surgery can be safely performed in patients with well-controlled collagen vascular or other immune-mediated inflammatory disease.

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Both the U.S. Food and Drug Administration (FDA) and the American Academy of Ophthalmology guidelines consider collagen vascular diseases as a relative contraindication to excimer laser surgery.[1,2] However, data supporting these recommendations were not based on clinical studies but rather on case reports[3–8] or on complications reported during other non-laser ocular surgical procedures.[9–15]

The main reasons for excluding patients with collagen vascular diseases from excimer laser surgery is the fear of increased postoperative inflammation or unpredictable healing response; a higher risk for corneal melting, scarring, or ulceration; and an increased risk for infection in patients on immunosuppressive medications.[1,2] Collagen vascular diseases also might have ocular involvement, including keratoconjunctivitis sicca,

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scleritis/episcleritis, uveitis, or conjunctivitis,[1] that can complicate the outcome of any ocular surgery.

Despite the FDA recommendations against treatment of patients with collagen vascular diseases, a few retrospective studies[16–18] have suggested that laser in situ keratomileusis (LASIK) might be safe in some patients with well-controlled disease and minimal ocular involvement. However, the combined sample size for each particular disease in these studies was small, and they did not address the issue of surface ablation in the setting of immune-mediated inflammatory disease. In addition, since the time these studies were published 10 or more years ago, there has been no new evidence guiding surgeons about how to manage patients with immune-mediated inflammatory diseases who inquire about refractive surgery.

The aim of this study was to present visual and refractive outcomes as well as postoperative complications in a large number of patients with well-controlled collagen vascular or other immune-mediated inflammatory disease who had excimer laser surgery.

PATIENTS AND METHODS

This retrospective noncomparative study was deemed exempt from review by the Committee of Human Research at the University of California, San Francisco, because it used only retrospective de-identified patient data. Informed consent to have LASIK or photorefractive keratectomy (PRK) was obtained from all patients before surgery.

A retrospective data review was performed to identify patients who had rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, sarcoidosis, ankylosing spondylitis, multiple sclerosis, or scleroderma documented on their preoperative health questionnaire and who had a primary LASIK or PRK procedure between January 2008 and February 2015. Preoperatively, all patients were required to obtain a letter from their treating physician or primary care practitioner confirming that their condition was well controlled, with no flare or symptoms within the past 6 months. Patients with ocular pathology or active inflammation, abnormal tear breakup time, or a history of primary or secondary Sjögren syndrome were deemed unsuitable for excimer laser ablation. Furthermore, patients had to meet general inclusion criteria for excimer laser surgery, such as normal topography, a calculated postoperative corneal stromal bed thickness greater than 250 μm (LASIK patients) or greater than 350 μm (PRK patients) in each eye, visual acuity correctable to at least 20/32 in each eye, and age over 18 years.

Patient Examinations

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, slitlamp biomicroscopy, dilated fundus evaluation, noncontact tonometry, corneal topography, ultrasound pachymetry, and wavefront aberration measurement.

Postoperative visits were scheduled for 1 day, 1 week, 1 month, 3 months, and thereafter, as required. The PRK patients had an extra postoperative visit at 4 days to remove the therapeutic contact lens, providing the process of reepithelialization was complete. On the first postoperative day, a detailed slitlamp examination was performed to evaluate flap position and the integrity of the cornea. At the remaining visits, manifest refraction, UDVA, CDVA, and slitlamp examinations were performed. The data of the last available clinical visit are presented in this study.

At all postoperative visits, patients were questioned about their symptoms of ocular comfort and dryness and the results were recorded; a standardized questionnaire was not used. Because patient reports of dry eye were not assessed in a standardized way, a binary outcome of either the presence or absence of dry-eye complaints was used. For all patients, an extensive review of each follow-up patient visit after surgery was performed and documented reports of a dry sensation as well as examination findings of dryness were recorded. Based on patients' symptoms and corneal examination, patients were divided into the following 4 categories at each follow-up visit: 1 = patient reports mild dry eyes without clinical signs of punctate epithelial erosions; 2 = mild punctate epithelial erosions (up to grade 1.5); 3 = moderate punctate epithelial erosions (grade 2 to 3); 4 = severe punctate epithelial erosions (grade 3+) or filamentary keratitis. Grading was based on what the clinician documented at time of examination. Because this was a retrospective study, this grading system was designed for classification and analysis of the recorded clinical data. A standardized grading system was not used at the time of the actual clinical examination. For each eye, the dry-eye category and duration of symptoms (last available visit at which dry-eye symptoms were present) were noted.

Surgical Technique

All procedures were performed by 21 experienced surgeons at 33 surgical centers using the Visx Star S4 IR excimer laser system (Abbott Medical Optics, Inc.). Eyes had a conventional ablation profile or a wavefront-guided ablation profile (Advanced Customvue, Abbott Medical Optics, Inc.).

In LASIK patients, corneal flaps were created using a femtosecond laser (iFS, Abbott Medical Optics, Inc.) or a mechanical microkeratome (Moria Evo3 One Use-Plus, Moria

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SA). The diameter of the femtosecond flaps ranged from 8.0 to 9.2 mm, and the programmed depth ranged from 100 to 120 μm. The 130 μm head was used for the mechanical microkeratome. All surgical procedures were performed under topical anesthesia. The standard postoperative treatment for all patients consisted of topical levofloxacin 0.5% and topical prednisolone acetate 1.0% 4 times a day for 1 week and preservative-free artificial tears.

In PRK patients, epithelial debridement was performed over a 9.0 mm central diameter using 20% ethanol. After a 30- to 40-second application, the alcohol was carefully drained with a surgical spear, the epithelium was removed with a blunt spatula, and the ablation was performed. For stromal ablations greater than 70 μm, a circular sponge soaked in mitomycin-C 0.02% was applied for 20 seconds; the eye was then thoroughly rinsed with 15 mL of a balanced salt solution. A therapeutic contact lens (Purevision, Bausch & Lomb, Inc.) was placed on the eye and left in place until the cornea reepithelialized. Postoperative medications consisted of topical levofloxacin 0.5% 4 times a day for 1 week and 4 weeks of a tapering dose of topical fluorometholone ophthalmic solution 0.1% in the following sequence: 4 times a day for 1 week, 3 times a day for 1 week, 2 times a day for 1 week, and once a day for 1 week. Patients also were prescribed preservative-free artificial tears.

For both LASIK and PRK patients, the postoperative drop regimen was the same used in patients without systemic diseases.

Statistical Analysis

All eyes (regardless of the length of follow-up) were included in the analysis of complications. Snellen visual acuity was converted into logMAR for statistical analysis, and all continuous variables were described with mean and interquartile range (IQR), which is the range between first quartile and third quartile. Normality of data samples was tested with Kolmogorov-Smirnov test. The paired Student *t* test or Wilcoxon rank-sum test (depending on normality assumption) was used for comparisons between preoperative visits and postoperative visits. The unpaired *t* test or Mann-Whitney *U* test was used to compare independent groups of patients (PRK and LASIK). The chi-square test was used to compare percentages. Statistical analysis of dry-eye symptoms was performed on a per-patient basis, with data from the worse eye used. All data were analyzed using Microsoft Office Excel software (2007 program, Microsoft Corp.) The level of significance was a *P* value equal to 0.05.

RESULTS

The review identified 622 patients (1224 eyes) with immune-mediated inflammatory diseases. The majority of patients were women (417, 67.0%), and the mean preoperative age of the study group was 45 years (IQR = 18; range 19 to 70 years). Rheumatoid arthritis (315 patients [50.6%]), systemic lupus erythematosus (121 patients [19.5%]), and psoriatic arthritis (65 patients [10.5%]) were the most common diseases represented, followed by sarcoidosis (62 patients [10.0%]), ankylosing spondylitis (40 patients [6.4%]), multiple sclerosis (12 patients [1.9%]), and scleroderma (7 patients [1.1%]). Of all 622 patients, 577 (92.8%) attended a minimum follow-up of 1 month, 479 (77.0%) of 3 months, and 330 (53.1%) of 6 months follow-up or longer.

The mean preoperative manifest spherical equivalent (SE) of the whole study group was −1.68 diopters (D) (IQR = 4.88; range −10.13 to +4.13 D). The type of preoperative refractive error was as follows: hyperopia/hyperopic astigmatism 377 eyes (30.8%), mixed astigmatism 22 eyes (1.8%), and myopia/myopic astigmatism 825 eyes (67.4%). Patients with preoperative myopic sphere had the mean sphere of −2.87 D (IQR = 2.50) and the mean preoperative sphere in hyperopic patients was +2.05 D (IQR = 1.50). Monovision was targeted in 33 eyes (2.7%) and 110 eyes (9.0%) required an enhancement.

Of all eyes, 300 (24.5%) had a conventional ablation profile and 900 (75.5%) had a wavefront-guided ablation profile. Laser in situ keratomileusis was performed in 1114 eyes (91.0%) and PRK in 110 eyes (9.0%). In LASIK patients, corneal flaps were created with a femtosecond laser in 892 eyes (80.1%) and by a mechanical microkeratome in 222 eyes (19.9%).

Only eyes with a minimum follow-up of 3 months with an emmetropic target (916 eyes: 837 LASIK eyes, 79 PRK eyes) were included in the analysis of refractive predictability and efficacy, while all eyes with a minimum follow-up of 3 months (regardless of postoperative target) were included in analysis of postoperative CDVA (945 eyes: 864 LASIK eyes, 81 PRK eyes). The mean follow-up of this subgroup of patients was 13.6 months (IQR = 12.0; range 3 to 79 months) for LASIK patients and 15.2 months (IQR = 11.5; range 3 to 81 months) for PRK patients. Of eyes targeted for emmetropia, 685 (81.8%) of LASIK eyes and 65 (82.3%) of PRK eyes (P = .92) were within ±0.50 D and 778 (93.0%) of LASIK eyes and 77 (97.5%) of PRK eyes (P = .12) were within ±1.00 D of emmetropia (Figure 1).

Table 1 shows the mean postoperative refractive outcomes for LASIK and Table 2 for PRK. Figure 2 and Figure 3 show the attempted SE versus the achieved SE for LASIK and PRK, respectively.

Of all eyes aimed for emmetropia, 643 (76.8%) of LASIK eyes, and 58 (73.4%) of PRK eyes (P = .50) had the postoperative UDVA 20/20 or better (Figure 4). The mean postoperative UDVA was −0.01 logMAR (IQR = 0.08) for LASIK eyes and 0.0 logMAR (IQR = 0.18) for PRK eyes (P = .56).

Of all LASIK eyes, 1.2% (10 eyes) lost 2 lines or more of CDVA (Figure 5), and 2.2% (19 eyes) gained 2 or more lines of CDVA. Of the 10 eyes that lost 2 or more lines of CDVA, the loss in 9 of them was associated with dry eyes/presence of punctate epithelial erosions; the remaining patient developed severe nystagmus associated with a multiple sclerosis relapse that limited CDVA. Further exploration of eyes that lost 2 or more

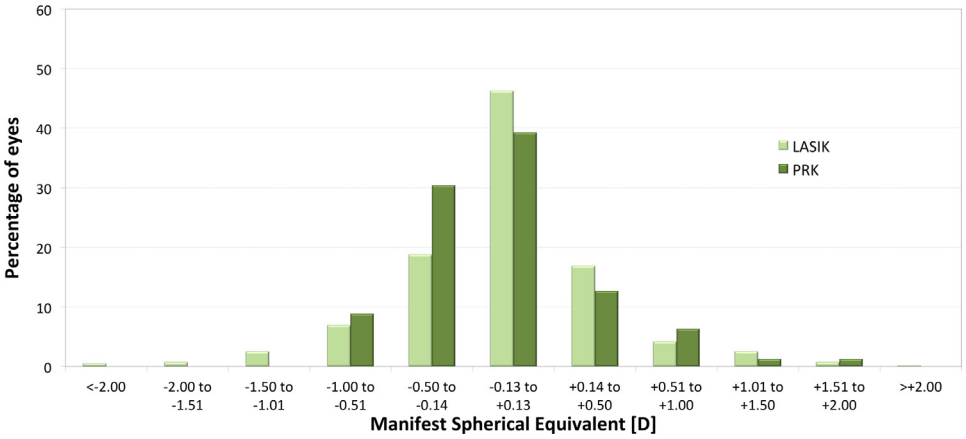

Figure 1. Refractive outcomes in eyes targeted for emmetropia and follow-up longer than 3 months (n = 837 LASIK eyes, n = 79 PRK eyes) (LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy).

lines of CDVA can be found in the complications section. No eye in the PRK group lost 2 or more lines of CDVA (Figure 5). The mean CDVA did not change from preoperatively to postoperatively for LASIK eyes (P = .71; Table 1) or PRK eyes (P = .16; Table 2).

Complications

Laser In Situ Keratomileusis In the LASIK group, 47 eyes (4.2%) developed mild (grade 0.5 to 1.0) diffuse lamellar keratitis (DLK), which was detected at early postoperative visits and treated with an increased

Table 1. Refractive and visual outcomes of all LASIK eyes that had a minimum of 3 months of follow-up (n = 864 eyes).

Parameter	Preoperative	Last Visit	*P* Value
Sphere (D)*			
Mean	−1.18	+0.11	<.01
IQR: Q1, Q3	−3.25, +1.75	0.00, +0.25	
Range	−9.75, +4.00	−2.50, 2.50	
Cylinder (D)			
Mean	−0.78	−0.30	<.01
IQR: Q1, Q3	−1.00, −0.25	−0.50, 0.00	
Range	−5.00, 0.00	−2.00, 0.00	
MSE (D)*			
Mean	−1.57	−0.04	<.01
IQR: Q1, Q3	−3.75, +1.38	−0.25, +0.13	
Range	−10.13, +3.88	−2.69, +2.25	
Monocular UDVA (logMAR)			
Mean	0.82	−0.01	<.01
IQR: Q1, Q3	0.52, 1.30	−0.08, 0.00	
Range	0.00, 1.30	−0.18, +1.00	
Binocular UDVA (logMAR)*			
Mean	—	−0.05	—
IQR: Q1, Q3	—	−0.08, 0.00	
Range	—	−0.18, 0.90	
CDVA (logMAR)			
Mean	−0.07	−0.06	.71
IQR: Q1, Q3	−0.08, −0.08	−0.08, 0.00	
Range	−0.18, 0.30	−0.18, 0.80	

CDVA = corrected distance visual acuity; IQR = interquartile range represented by 1st quartile (Q1) and 3rd quartile (Q3); MSE = manifest spherical equivalent; UDVA = uncorrected distance visual acuity
*Eyes targeted for monovision (n = 27) were excluded from the calculations of sphere, MSE, and UDVA

Table 2. Refractive and visual outcomes of all PRK eyes that had a minimum of 3 months of follow-up (n = 81).

Parameter	Preoperative	Last Visit	*P* Value
Sphere (D)*			
Mean	−1.91	+0.14	<.01
IQR: Q1, Q3	−3.25, −0.75	0.00, +0.50	
Range	−8.00 +4.25	−0.75 +2.00	
Cylinder (D)			
Mean	−0.99	−0.34	<.01
IQR: Q1, Q3	−1.50, −0.50	−0.50, 0.00	
Range	−3.00, 0.00	−1.25, 0.00	
MSE (D)*			
Mean	−2.41	−0.03	<.01
IQR: Q1, Q3	−3.63, −1.44	−0.25, +0.13	
Range	−9.50 +4.00	−1.00 +1.63	
Monocular UDVA (logMAR)			
Mean	0.80	0.00	<.01
IQR: Q1, Q3	0.52, 1.30	−0.08, 0.10	
Range	0.00, 1.30	−0.18, 0.60	
Binocular UDVA (logMAR)*			
Mean	—	−0.05	—
IQR: Q1, Q3	—	−0.08, 0.00	
Range	—	−0.18, 0.30	
CDVA (logMAR)			
Mean	−0.07	−0.06	.16
IQR: Q1, Q3	−0.08, −0.08	−0.08, −0.08	
Range	−0.18, 0.10	−0.18, 0.10	

CDVA = corrected distance visual acuity; IQR = interquartile range represented by 1st quartile (Q1) and 3rd quartile (Q3); MSE = manifest spherical equivalent; UDVA = uncorrected distance visual acuity
*Eyes targeted for monovision (n = 2) were excluded from the calculations of sphere, MSE and UDVA

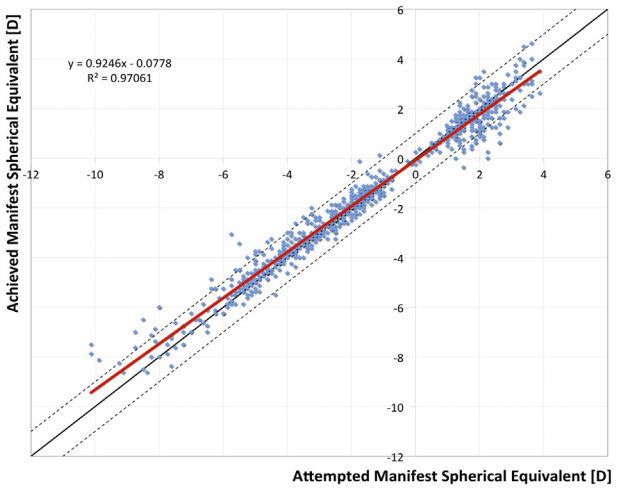

Figure 2. Predictability of manifest SE: attempted preoperative versus achieved postoperative correction in LASIK eyes. The area between 2 dashed lines represents manifest SE within 1.0 D. The solid red line represents linear regression (n = 837 eyes).

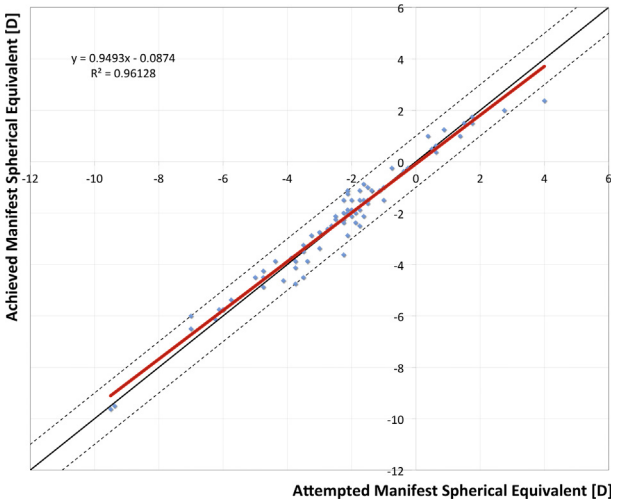

Figure 3. Predictability of manifest SE: attempted preoperative versus achieved postoperative correction in PRK eyes. The area between 2 dashed lines represents manifest SE within 1.0 D. The solid red line represents linear regression (n = 79 eyes).

dose of topical steroids. In all cases, the DLK resolved within 2 weeks of diagnosis.

Seven eyes (0.6%) developed grade 2 to 3 DLK (6 at early postoperative visits, 1 late onset). The DLK resolved in 4 eyes with aggressive topical steroid treatment. One eye with grade 3 DLK required flap lift and irrigation of interface on the third postoperative day, and the DLK resolved without consequence after the surgical intervention. This patient had a diagnosis of sarcoidosis that had been quiescent for 15 years and had not required therapy during that time. In 1 eye, a dislocated flap was found on the first postoperative day; the patient had flap repositioning with removal of epithelium and insertion of a therapeutic contact lens. In this eye, grade 2 DLK was found on the third postoperative day and treated with topical steroid drops. In this patient, the postoperative course was also complicated by corneal edema and delayed reepithelialization with unstable epithelium, and the DLK required approximately 1 month to resolve. This patient was followed for 3 years for severe dry eyes associated with episodes of punctate epithelial erosions; however, dryness was present in both eyes, not only the eye that developed postoperative complications. The patient had a diagnosis of sarcoidosis for 25 years; the disease was inactive at the time of surgery and the patient was not on any medications.

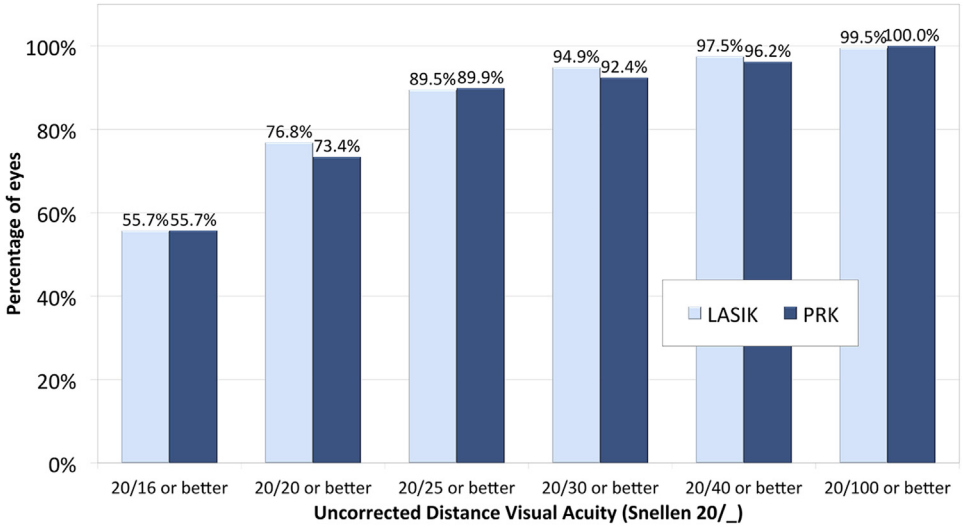

Figure 4. Cumulative monocular UDVA (n = 837 LASIK eyes, n = 79 PRK eyes) (LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy).

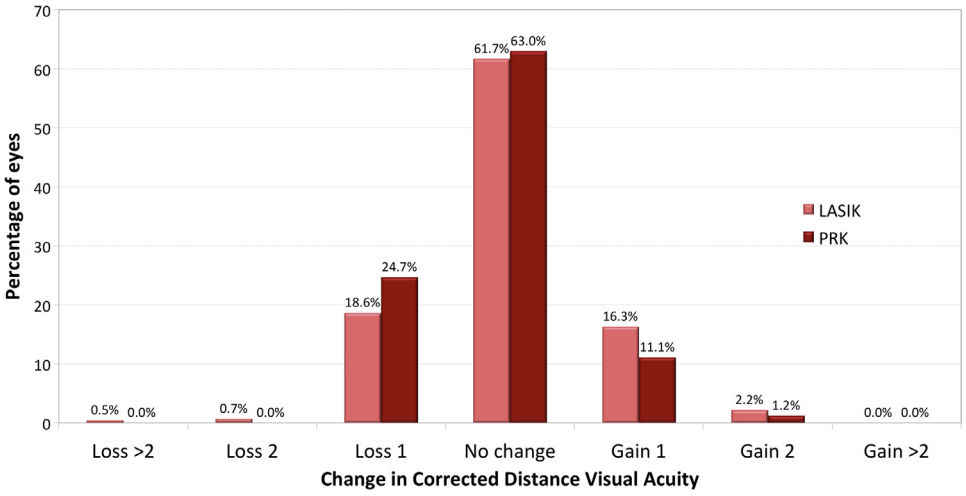

Figure 5. Safety: comparison of preoperative and postoperative CDV (n = 864 LASIK eyes, n = 81 PRK eyes) (LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy).

Late-onset DLK was noted 3 months after unilateral LASIK in a patient with sarcoidosis. The onset of DLK was observed approximately 10 days after the patient stopped treatment for sarcoidosis with a tetracycline derivative (lymecycline) 408 mg twice daily. The patient was managed with aggressive topical steroid treatment, and the lymecycline was restarted for the sarcoidosis. Because of ongoing dry-eye symptoms, the patient was monitored further for 3.5 years, during which time there was no recurrence of DLK.

Twenty-four eyes (2.2%) had microstriae that did not affect visual acuity and did not require surgical intervention (22 after primary LASIK, 2 following flap-lift enhancement). Three eyes (0.3%) required a flap lift for microstriae; 2 of these surgeries were uneventful. In the remaining 1 case, macrostriae were successfully smoothed with a flap lift; however, the patient developed recurring epithelial ingrowth at a later follow-up.

Epithelial ingrowth was noted in 6 eyes (0.5%). Five eyes had peripheral epithelial ingrowth outside of the pupillary area that stabilized and did not require intervention. One eye (case described above) developed epithelial ingrowth 3 months after a flap lift for macrostriae, and a flap lift with debridement was performed 6 months postoperatively. Unfortunately, epithelial ingrowth recurred 2 months later in the same location and another flap lift with an application of Tisseel glue (Baxter Healthcare) was performed. The patient was then monitored for a further 2 years, and there was no recurrence of epithelial ingrowth. There was no corneal melt in any patient with epithelial ingrowth in this study.

There were 3 cases of postoperative anterior uveitis; all of them were unilateral. In the first case, a patient with rheumatoid arthritis had an episode of anterior uveitis 3 months after LASIK. This patient had a history of recurrent anterior uveitis before laser vision correction (LVC) surgery with attacks 1 to 2 times per year. The second case of uveitis was also observed 3 months after LASIK in a patient with rheumatoid arthritis and no history of inflammatory eye disease. Another case of anterior uveitis was noted 2 weeks after uneventful LASIK in a human leukocyte antigen (HLA)-B27–positive patient with ankylosing spondylitis. This patient had 1 episode of uveitis 2 years before LASIK.

Seven cases (0.6%) of corneal abrasion were detected at early postoperative visits. Four abrasions were small and did not require treatment apart from intensive ocular surface lubrication. One abrasion was large and required insertion of a therapeutic contact lens. In 1 eye, a small corneal abrasion was noted on the second postoperative day; this was followed by symptoms of recurrent erosion syndrome for 6 months and managed with intense ocular surface lubrication. One patient had a large corneal abrasion followed by occasional episodes of recurrent erosions/abrasions for almost 3 years and required management with therapeutic contact lenses when symptomatic.

One case of unilateral marginal keratitis was diagnosed 23 days after uneventful LASIK in a patient with lupus; it resolved within 2 weeks with topical antibiotic–steroid treatment. One case of culture-negative microbial keratitis in a rheumatoid arthritis patient was noted 7 days postoperatively; it resolved with topical antibiotics within 2 weeks. One patient with rheumatoid arthritis in remission for 15 years developed bilateral corneal infiltrates 1 week after uneventful LASIK; this was followed by a minor peripheral flap melt. This was successfully treated with topical steroids, and no systemic intervention was required. The patient maintained 20/15 CDVA at the last follow-up.

Other complications include 1 patient who developed nystagmus in the postoperative period that severely affected corrected vision in the left eye. The

nystagmus was attributable to a relapse of a preexisting diagnosis of multiple sclerosis. In 10 eyes of 5 patients, low-grade stromal haze was noted at the follow-ups, but it had no effect on corrected visual acuity.

Photorefractive Keratectomy Four eyes (3.6%) developed mild haze (grade 1 or less) after primary PRK and 1 after PRK enhancement. All cases resolved within 6 months, and the final CDVA was 20/20 or better in all eyes.

One patient developed dense central haze 2 months after unilateral PRK enhancement over the LASIK flap. The haze was treated with topical steroids and eventually cleared; however, the patient had also extensive punctate epithelial erosions, reducing CDVA to 20/80. The CDVA gradually improved to the pre-enhancement level of 20/25 after approximately 12 months of intensive ocular surface treatment. The patient was taking methotrexate for psoriatic arthritis at the time of surgery.

Other complications included 2 patients with delayed epithelial healing, 1 after bilateral primary PRK and 1 after unilateral PRK enhancement. In both patients, the process of reepithelialization took 2 weeks. One case of a unilateral sterile infiltrate was observed in a patient after primary PRK; the infiltrate resolved within a few days with the use of topical antibiotics and steroids.

Dry-Eye Symptoms

Table 3 shows the results of dry-eye analysis for LASIK and PRK patients. Of all patients, 384 in the LASIK group (67.8%) and 33 in the PRK group (58.9%) experienced some dry-eye symptoms postoperatively ($P = .23$). Of all patients who experienced dry eyes, the duration of symptoms was 6 months or less in 256 LASIK patients (66.7%) and 18 PRK patients (54.5%) ($P = .22$).

The total percentage of patients with dry-eye symptoms for more than 12 months was 10.2% (58 patients) in the LASIK group and 8.9% (5 patients) in the PRK group ($P = .94$). Only a small percentage of LASIK patients (3.0%, 17 patients) had dry eyes associated with punctate epithelial erosions (dry-eye category 2 to 4) for longer than 12 months; there were no such erosions in the PRK group ($P = .38$).

Nine eyes lost 2 or more lines of CDVA due to corneal epitheliopathy. Of these, 5 patients (6 eyes) had a diagnosis of rheumatoid arthritis and 4 were taking methotrexate at the time of surgery. One patient (bilateral CDVA loss) had psoriatic arthritis and was also on methotrexate. The 1 remaining patient (unilateral CDVA loss) was on adalimumab for ankylosing spondylitis at the time of surgery. Of all eyes that had reduced CDVA from epitheliopathy at the last available appointment, none lost more than 3 lines of CDVA or had a CDVA worse than 20/32.

DISCUSSION

Patients with underlying collagen vascular or other immune-mediated diseases represent a challenging group for refractive surgery. After previous reports of sight-threatening complications, many clinicians are reluctant to perform laser surgery, even in patients with well-controlled or inactive disease.[3–15] In this study, we present, to our knowledge, the largest available group of patients with collagen vascular or immune-mediated inflammatory diseases, including conditions such as rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, sarcoidosis, ankylosing spondylitis, multiple sclerosis, and scleroderma.

Table 3. Dry-eye symptoms.

Dry-Eye Category*	Patients (n)	% of Whole LASIK/PRK Cohort	Duration (Mo)		Patients, n (% of Whole LASIK/PRK Cohort)			
			Mean	IQR	≤3 Mo	≤6 Mo	>6 Mo	>1 Y
LASIK								
1	213	37.6	8.6	2.7, 10.1	73 (12.9)	121 (21.4)	92 (16.3)	41 (7.2)
2	138	24.4	5.3	0.9, 6.0	85 (15.0)	106 (18.7)	32 (5.7)	15 (2.7)
3	31	5.5	2.0	0.3, 2.3	26 (4.6)	29 (5.1)	2 (0.4)	1 (0.2)
4	2	0.4	10.9	10.1, 11.6	0	0	2 (0.4)	1 (0.2)
PRK								
1	30	53.6	9.8	3.2, 10.8	8 (14.3)	15 (26.8)	15 (26.8)	5 (8.9)
2	2	3.6		2.5, —	2 (3.6)	2 (3.6)	0	0
3	0	0.0	—	—	—	—	—	—
4	1	1.8	—	—	1 (1.8)	1 (1.8)	0	0

IQR = interquartile range (range between 1st quartile and 3rd quartile); LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy
*1 = patient report of mild dry eyes without clinical signs of punctate epithelial erosions; 2 = mild punctate epithelial erosions (up to grade 1.5); 3 = moderate punctate epithelial erosions(grade 2–3); 4 = severe punctate epithelial erosions (grade 3+) or filamentary keratitis

In terms of visual acuity and predictability, good outcomes were achieved, with a mean postoperative UDVA close to 20/20 for both PRK and LASIK patients and a mean postoperative SE of −0.04 D for LASIK patients and −0.03 for PRK patients. Of all eyes for which the aim was emmetropia, 81.8% of LASIK eyes and 82.3% of PRK eyes had postoperative manifest SE within ±0.50 D of emmetropia and 76.8% of LASIK eyes and 73.4% of PRK eyes had a postoperative UDVA of 20/20 or better, which is an expected outcome in a group of patients slightly older (mean age 45 years) than a normal population of patients having laser surgery. To our knowledge, there are only 3 studies[16–18] presenting the outcomes in a group of patients with well-controlled collagen vascular diseases.

The first published study by Alió et al. in 2005[16] presented outcomes of LASIK in 42 eyes (22 patients) with well-controlled rheumatic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, scleroderma, ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease, and Behçet disease. No cases of corneal haze, melting, flap or interface complications were reported, and moderate dry-eye symptoms with duration longer than 6 months were recorded in 9.5% of eyes. This prompted the authors to conclude that LASIK can be safely performed in some patients with controlled rheumatic disease.

The findings of Alió et al. were later confirmed by Cobo-Soriano et al. in 2006[17] in a larger group of 141 patients (275 eyes) with underlying systemic diseases. That study presented outcomes of LASIK in patients with autoimmune collagen vascular disease, psoriasis, and inflammatory bowel disease as well as diseases that do not induce ocular inflammation, such as diabetes mellitus and a history of keloid formation. All reported complications were mild, and there was no statistically significant difference in complication rates between normal patients and the study group. However, patients with collagen vascular disease had worse predictability (89% within ±1.00 D of emmetropia, versus 99.0% of normal patients within ±1.00 D).

In 2006, Smith and Maloney[18] retrospectively reviewed complications in 26 LASIK patients (49 eyes) with well-controlled autoimmune diseases including systemic lupus erythematosus, rheumatoid arthritis, psoriatic arthritis, scleroderma, inflammatory bowel disease, Grave disease, Reiter syndrome, and Hashimoto thyroiditis. They found no instances of scleral or corneal complications, including corneal thinning or melting, persistent epithelial defect, central toxic keratopathy, scleral thinning, scleritis or scleromalacia.

There are, however, several individual reports of postsurgical complications, such as corneal ulcerations, corneal or scleral melting, and corneal perforation, after ocular surgery[9–15] (mainly intraocular surgery) in patients with collagen vascular disease. These complications often resulted in significant loss of CDVA, although in all reported cases, patients had a significant history of uncontrolled dry eyes, secondary Sjögren syndrome, or active systemic disease.

In 1992, Seiler and Wollensak[5] described a patient with active lupus who developed a perforating noninfectious corneal ulcer 1 month after PRK for 9.50 D of myopia. In 2002, Cua and Pepose[19] described a PRK patient with late-onset corneal haze requiring corneal debridement, concurrent with the development of systemic lupus erythematosus. The patient in that case report had bilateral PRK with a retreatment in the right eye 1 year later. The patient was diagnosed with lupus 2 months after retreatment and developed severe reticular corneal scarring 10 months later in the enhanced eye only. It is difficult to determine whether there was an association between the lupus and the development of haze because late-onset haze is a known complication of PRK, even in patients without autoimmune disease.[20] After these 2 case reports, the ophthalmology world became very cautious about performing surface ablation in eyes of patients with collagen vascular disease.

Previously reported complications after LASIK include a patient with rheumatoid arthritis who developed peripheral keratitis 5 days postoperatively.[3] A corneal infiltrate was present peripheral to the flap edge near a previously scarred area. A similar infiltrate appeared in the fellow unoperated eye. The patient was treated with aggressive antibiotic and corticosteroid therapy, and the peripheral keratitis resolved without vision loss. It is uncertain whether the rheumatoid arthritis played any role in this case; similar complications have been reported in patients without rheumatoid arthritis.[3,21]

Sterile corneal melting after LASIK has been reported in patients with collagen vascular disease. Li and Li[4] reported 12 cases of corneal melt after LASIK. Of these patients, 5 had collagen vascular diseases (2 with systemic lupus erythematosus, 2 with primary Sjögren syndrome, and 1 with rheumatoid arthritis). The severity and control of the disease in these patients was not disclosed.

Based on the cumulative experience in the literature, patients with Sjögren syndrome, secondary Sjögren syndrome, or keratoconjunctivitis sicca should probably not have elective refractive surgery because of the risk for severe corneal complications. During the initial consultation, patients who have evidence of abnormal corneal staining with fluorescein or bulbar conjunctival staining with lissamine green[22] should have further examinations to uncover the etiology of their epitheliopathy. A high level of clinical suspicion and surveillance is indicated when the patient has a known systemic inflammatory disorder. In this population, the presence of corneal epitheliopathy,

evidence of aqueous deficiency, and any dry-eye disease that is not easily treatable should serve as an indicator that the patient's underlying disease might be contributing to the dry-eye picture.

In our study, no catastrophic complications, such as corneal perforation, occurred. In our cohort of 622 patients (1224 eyes), 2 patients developed sterile corneal infiltrates (1 unilateral, 1 bilateral) and 1 developed unilateral marginal keratitis, all of which resolved with topical treatment. The patient with bilateral corneal infiltrates had a diagnosis of rheumatoid arthritis and developed a minor flap melt, which resolved without consequence. Interestingly, this patient's arthritis was inactive for 15 years before surgery. In the subgroup of LASIK patients (1114 eyes), 6 eyes had stable peripheral epithelial ingrowth and 1 eye required flap lifting for epithelial ingrowth. None of these cases progressed to corneal melting. There were a few cases of mild haze after PRK, as expected after surface ablation, and there was only 1 case of dense central haze after PRK enhancement on the LASIK flap, which also resolved without the need for corneal debridement.

Diffuse lamellar keratitis is a known complication of LASIK, with a reported incidence ranging between 0.75% and 32%.[23–26] In our case series, the incidence of mild DLK was 4.2% and the incidence of moderate (grade 2 to 3) DLK was 0.6%. There was 1 case of late-onset DLK (3 months after LASIK) in a patient with sarcoidosis, which occurred after the patient discontinued systemic treatment. There are sporadic reports of late-onset DLK in patients with autoimmune diseases. Díaz-Valle et al.[6] reported a case of DLK associated with acute anterior uveitis 3 years after LASIK in a patient with a history of ankylosing spondylitis and recurrent anterior uveitis. Javaloy et al.[27] described a case of recurrent late-onset DLK (4, 9, and 15 months after uneventful LASIK) in a patient who was later diagnosed with atypical Cogan syndrome. In our case of late-onset DLK, the patient was followed for 3.5 years with no recurrence of inflammation.

In this study, we found 3 cases of anterior uveitis, 2 in patients with rheumatoid arthritis and 1 in a patient with HLA-B27–associated anterior uveitis and ankylosing spondylitis. Two patients had a history of uveitis before LVC. In 2 patients, the inflammation occurred 3 months after surgery and was likely unrelated to the LVC. In the third patient, who had a diagnosis of HLA-B27–associated anterior uveitis and ankylosing spondylitis preoperatively, the inflammation occurred 2 weeks after LASIK, which might or might not indicate a link. Moshirfar et al.[28] assessed the incidence of acute anterior uveitis in HLA-B27–positive patients who had LASIK and compared them with a control group of HLA-B27–positive patients who did not have LASIK. With a follow-up of 5 years, the authors concluded that the occurrence of post-LASIK acute anterior uveitis was no higher than in a general population of HLA-B27–positive patients without refractive surgery. There are 2 other case reports of acute post-LASIK anterior uveitis in patients with autoimmune diseases. One is the previously discussed case of Díaz-Valle et al.,[6] in which acute uveitis was associated with late-onset DLK. Another case was published by Liu et al.,[8] who described a case of unilateral hypopyon anterior uveitis 15 days after uneventful LASIK in a patient with a history of ulcerative colitis.

Several complications in the literature have been reported in patients with inflammatory bowel disease (ulcerative colitis and Crohn disease).[6,29,30] Carp et al.[30] describe a case of necrotizing keratitis 3 days after LASIK in a patient with inflammatory bowel disease. The patient had a total colectomy for recurrent ulcerative colitis before LVC. Aman-Ullah et al.[29] reported 2 cases of necrotizing keratitis after LVC in patients with controlled Crohn disease. The first case occurred 1 day after LASIK and the other, 2 days after PRK. In both cases, the infiltrates resolved with aggressive systemic and topical corticosteroids without permanent sequelae. No patients in our study cohort had this diagnosis. It is our policy to offer LVC to patients with inflammatory bowel disease if they have had no ocular involvement and have stable disease that is well controlled on an immunosuppressive regimen per recommendation of their gastroenterologist or rheumatologist.

Although dry-eye symptoms after excimer laser surgery are commonly reported in the literature,[31–33] there is a potential risk that the normal transient post-LVC dryness might be exacerbated in patients with collagen vascular diseases.[1,2] It has been reported that nearly half of all LVC patients without collagen vascular diseases report symptoms of dryness for 6 months or more.[32] This is consistent with our findings, in which 67.8% of LASIK patients and 58.0% of PRK patients transiently reported dry-eye symptoms. In our study cohort, 10.2% in the LASIK group and 8.9% in the PRK group were attending clinic with dry-eye symptoms for longer than 12 months, although this percentage might be higher because some patients who did not return for long-term follow-ups might have also experienced dry-eye symptoms. It is difficult to compare our outcomes with those in the literature because patients had varying lengths of follow-up. It is also important to note that our study group was slightly older than normal groups of patients having LVC and that the majority of patients were women, which are both risk factors for increased dry-eye symptoms, irrespective of underlying disease.[34,35]

The main limitation of this study is its retrospective nature and short follow-up in some patients. Patients that attended early follow-ups only had mostly very good UDVA on their last available appointment;

therefore, we believe they would have returned to us if they had developed major complications. However, this argument is not strong enough to assume patients with a short follow-up did not develop any complications. Patients in this study had access to 131 clinics throughout the United Kingdom offering free aftercare service and a 24-hour emergency telephone line; therefore, they were likely to use us as a first point of contact in case of any postoperative complications. As this was a retrospective study, there was no standardized examiner or grading scale. Multiple examiners were involved in the care of these patients, so some bias is introduced by interexaminer differences and the lack of a standardized examination and a standardized patient-symptom questionnaire. Another limitation was that duration of dry eyes was calculated based on the last follow-up at which the patient presented with dry-eye symptoms. It is likely that in some patients, dryness persisted for a longer period (especially in those with mild dry-eye symptoms); however, we can assume that their symptoms were manageable and did not require a higher level of intervention because the patients no longer sought care.

In conclusion, we believe that LVC can be safely offered to patients with some inactive or well-controlled immune-mediated inflammatory diseases. Patients should be appropriately screened to ensure that there is no evidence of corneal involvement of their inflammatory disease or related dry eye before surgery and to ensure that their systemic disease is stable. Any evidence of dry eye postoperatively should be treated early and aggressively because this was overwhelmingly the cause of cases of lost CDVA in this study. Severe complications in our study group were extremely rare and were manageable with topical treatment. This is by far the largest study detailing postoperative outcomes and complications in this specific group of patients.

WHAT WAS KNOWN

- Collagen vascular diseases are considered a relative contraindication to excimer laser surgery.
- The literature on keratorefractive surgery in patients with collagen vascular diseases is scarce and mostly consists of case reports or studies with small samples of patients.

WHAT THIS PAPER ADDS

- Refractive and visual outcomes and complications rates in this large population of patients with collagen vascular diseases indicate that excimer laser surgery can be safely performed in some patients with well-controlled disease.

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