LASIK Outcomes in Patients with Underlying Systemic Contraindications

A Preliminary Study

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Objectives: To determine the anatomic and functional outcomes of photorefractive surgery in patients with underlying systemic diseases that are traditionally listed as relative or absolute contraindications.

Design: Observational retrospective case–control study.

Participants: The case groups were composed of 275 eyes of 141 consecutive patients who underwent a LASIK procedure with any of the following underlying conditions: autoimmune connective-tissue disorders (n = 62), psoriasis (n = 91), intestinal inflammatory diseases (n = 67), diabetes mellitus (n = 44), and history of keloid formation (n = 18). Twenty-nine patients (56 eyes) were receiving systemic immunosuppressive therapy. The control group comprised 358 eyes of 181 patients without the above-mentioned conditions who underwent LASIK.

Methods: The study had 2 parts, relating to the anatomic and functional (visual and refractive) outcomes. For anatomic outcome, we compared the entire sample of both groups. For functional outcome, only myopic eyes of each group were compared. Independent comparisons were performed between each disease group and the control group.

Main Outcome Measures: Anatomic outcomes included perioperative and postoperative epithelial, flap, and interface complications. Functional outcomes were evaluated using visual and refractive indicators, percentage of eyes undergoing enhancement, and number of postoperative visits.

Results: Mild anatomic complications were observed in the case and control groups with similar percentages, and there were no statistical differences between groups. Regarding functional outcome, the only significant finding was a worse refractive outcome in the collagen vascular diseases group compared with controls. There were no other statistical differences detected in the other systemic disease groups.

Conclusions: In our experience, LASIK can be performed effectively and safely in selected patients with stable and controlled systemic diseases with favorable postoperative anatomic and visual outcomes. The absolute exclusion of certain systemic contraindications should be reconsidered. *Ophthalmology 2006;113: 1118–1124 © 2006 by the American Academy of Ophthalmology.*

Since the beginning of laser refractive surgery, the United States Food and Drug Administration, guided by the recommendations of the first excimer laser companies, established a group of absolute and relative contraindications for the procedure, which included ocular and systemic diseases. Among the systemic diseases are autoimmune and connective-tissue disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis, psoriatic arthritis, Sjögren's syndrome, and other types of systemic vasculitis. Diabetes mellitus, antecedent keloid formation, immunosuppression, treatment with some drugs, and, recently, atopia and allergic conjunctivitis were also included as relative contraindications or risk conditions. The reasons for these exclusions were the risk of a higher postoperative inflammatory response, a potentially damaging effect on the postoperative healing properties of the cornea, and that surgery theoretically could trigger a latent predisposition for corneal melting and significant scarring.

These concepts were introduced with the first photorefractive procedures (photorefractive keratectomy [PRK]) because of the mechanism of healing of this technique, in which the corneal stroma is exposed during a significant postoperative period until re-epithelialization is complete.[1] The subsequent evolution of LASIK as the main photore-

Originally received: April 15, 2005.
Accepted: February 20, 2006. Manuscript no. 2005-332.

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No author has a proprietary interest in any method or product mentioned.

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ISSN 0161-6420/06/$–see front matter
doi:10.1016/j.ophtha.2006.02.023

fractive procedure, however, did not significantly change these guidelines despite the marked improvement in the healing process that the LASIK technique involves. In addition, the Food and Drug Administration–established contraindications have remained unchanged because LASIK is associated with an iatrogenic dry-eye syndrome known as LASIK-induced neurotrophic epitheliopathy,[2] which might worsen a preexisting dry eye, often associated with the above-mentioned diseases.

A recent guideline from the American Academy of Ophthalmology cataloged the antecedent of connective tissue or autoimmune diseases and systemic immunosuppression as relative contraindications and only uncontrolled diseases and uncontrolled ocular allergy as absolute systemic contraindications.[3] Nevertheless, these concepts have remained confusing despite this guideline, and in practice, patients with autoimmune systemic disorders are routinely excluded by most surgeons, even in asymptomatic and stabilized patients, as reflected in the "Materials and Methods" section of most publications.

Moreover, the contraindication of these systemic diseases for refractive surgery has not been supported by the literature, and the few published reports are based on isolated cases and small series with contradictory opinions from different expert physicians. Some examples are RA (1 case of corneal infiltrates after LASIK),[4] SLE (2 eyes with corneal opacities and perforation after PRK),[5,6] and keloid formers (3 patients, 6 eyes with uneventful PRK).[7] Fraunfelder and Rich[8] reported a clinical case–control study of 30 diabetic eyes with poor anatomic and refractive outcomes. In recent years, atopic disease has been associated with a higher risk of diffuse lamellar keratitis,[9] haze, and myopic regression after PRK,[10] but other authors have not found allergic conjunctivitis to be a risk factor for LASIK.[11] Finally, we found no reports addressing modern surface ablation procedures such as laser epithelial keratomileusis (LASEK) in patients with underlying systemic diseases.

In addition, there is also confusion about the potential damage of chronic treatment with immunosuppressive drugs or as to whether those with other immunologic-based disorders, such as psoriasis, ulcerative colitis, Crohn's disease, oculodermatologic diseases, and other retinal vasculitis, should be excluded from refractive surgery. Recently, some authors (Alió et al[12]) reported good outcomes in selected patients with controlled rheumatic diseases who underwent a LASIK procedure to correct myopic refractive defects. In a series of 42 eyes of 22 patients, they found no operative or postoperative vision-threatening complications.

Definitively, these concepts have not been actualized, despite current ophthalmic technology advances and actual systemic medical therapy, which can control, diminish, and inactivate the disease for longer periods.

The objective of the present study was to determine the anatomic and functional outcomes of a group of patients with at least one of the above-mentioned diseases who underwent a photorefractive procedure, and compare these patients with a healthy control group.

Table 1. Underlying Diseases Associated with Case Group

Underlying Disease	No. of Eyes	Follow-up Time (mos) (SD)	Observations
Rheumatoid arthritis	29	6.26 (3.8)	
Systemic lupus erythematosus/discoid lupus	31		6 cases of discoid lupus
Spondylitis	2		
Psoriasis	91	5.75 (4)	10 cases of psoriatic arthropathy
Crohn's disease/ ulcerative colitis	67	4.58 (3.7)	
Keloids	18	3.7 (2.2)	
Diabetes mellitus	44	6.26 (5)	19 ID/21 NID/4 not specified
Immunosuppressive therapy	56	5 (3)	32 corticosteroids, 21 immunosuppressive drugs, 3 combined therapy

ID = insulin dependent; NID = not ID; SD = standard deviation.

Patients and Methods

In a retrospective observational case–control study, during the period from January 2002 to August 2004 the medical records of consecutive patients who underwent a LASIK procedure and had any of the systemic diseases listed in Table 1 were reviewed. Clínica Baviera is a private ophthalmologic institution with 22 centers located throughout Spain that performs a high volume of refractive surgical procedures (>16 000 per year). Since 2002, the records of all the clinical data and procedures (surgeries and office examinations) have been entered into a computer database. We conducted a search of the medical history section of the database using multiple keywords, such as *rheumatoid arthritis, systemic lupus erythematosus, collagen-connective/tissue-autoimmune diseases, vasculitis, diabetes mellitus, psoriasis, Crohn's, ulcerative collitis, immunosuppression, keloids,* etc. and their abbreviations. One hundred forty-one patients (275 eyes) were identified.

We also selected a healthy control group to compare anatomic and functional results. Control patients were obtained from consecutive patients examined in January 2003 (first visit), who underwent a refractive surgery during 2003 or 2004 and were exempt from diseases known to alter the immune system, diabetes, or keloid formation antecedents (181 patients, 358 eyes). Both groups, case and control eyes, were operated on by different experienced surgeons. The clinical charts of every patient were reviewed, and the protocol study form fields were completed.

Description of Study Groups

The case group comprised 275 eyes of 141 patients (age range, 21–65 years; mean [± standard deviation (SD)], 37.1±8.8 years; 59.3% female and 40.7% male). The underlying diseases are summarized in Table 1: collagen vascular autoimmune diseases (RA, SLE, and idiopathic spondylitis), intestinal inflammatory diseases, and psoriasis were the most common disorders. Seven patients presented with ≥2 coexisting systemic diseases. Follow-up time by disease group is shown in Table 1. Twenty-nine patients (56 eyes) were receiving immunosuppressive therapy with chronic corticosteroids and/or immunosuppressive drugs. With regard to the autoimmune disorders group, there was a variable time for the underlying disease as the diagnosis (>3 years in most patients), and by the time of refractive surgery, patients appeared

stable, under good medical control, and asymptomatic, with mild extraocular manifestations of the diseases (arthritis and skin disorders). In most cases, systemic disease stability was confirmed by speaking with the corresponding physician.

The control group comprised 358 eyes of 181 patients (mean age, 33.7 years [7.8 SD]; range, 20–56 years; 54.8% female). The refractive data and mild biomicroscopic and funduscopic preoperative findings of both groups are listed in Table 2 (available at http://aaojournal.org).

We also report the results of a small group of LASEK patients associated with these underlying diseases (14 cases) that were not included in the study, but are presented here only for description purposes.

All patients had a stable refraction for at least 1 year before the procedure, had no significant ocular pathology, and signed an informed consent form for their refractive surgery. The surgical procedure was similar for every patient and involved presurgical anesthesia with topical eyedrops of tetracaine hydrochloride (0.01%) supplemented with oral sedation (alprazolam, 0.25 mg). The keratectomies were performed in all cases with the same microkeratome, the Moria LSK-One (Microtech, Inc., Moria, France). The Technolas Keracor 217C (Bausch & Lomb, Claremont, CA) and MEL 80 (Zeiss-Meditec, Jena, Germany) excimer lasers were used.

We studied the following variables: preoperative data included type of underlying systemic disease and treatment (presence of immunosuppressive therapy) in the case group, refractive error data, best-corrected visual acuity (BCVA) (Snellen chart), slit-lamp biomicroscopy, indirect ophthalmoscopy, topography (Orbscan corneal topographer, Bausch & Lomb, Claremont, CA), and intraocular pressure (pneumotonometer) in both groups. Intraoperative data included type of laser; pachymetric values of total, flap, and bed corneal thicknesses (DGH pachymeter, DGH Technology, Inc., Exton, PA); optical zone; and the presence of any intraoperative complications. Postoperative data included visual and refractive results, enhancement percentage, and the presence of anatomic complications, including biomicroscopic and fundus examination. We also included the number of postoperative office visits as an indicator of postoperative evolution. There was an average of 4 postoperative visits from surgery to discharge; we considered a high number of visits to be a marker of a poorer or slower recovery.

The study was divided into two sections for the anatomic results and one for the functional results: for anatomic outcome, we compared the entire sample of both groups, which included eyes with myopic, hyperopic, and mixed astigmatic defects. For functional and refractive outcome, only myopic eyes (spherical, simple, or compound myopic astigmatic defects) from each group were included to compare homogeneous groups.

Anatomic Results

We searched for intraoperative (epithelial defect or flap repositioning alterations) and postoperative complications such as recurrent epithelial erosions, interface alterations (diffuse lamellar keratitis, epithelial ingrowth), microstriae, and/or other ocular surface problems.

Functional and Refractive Results

We defined predictability indicators as the percentage of eyes that achieved a postoperative spherical equivalent (SE) of ±1.00 diopters (D) and ±0.50 D. For visual outcome indicators, efficacy was represented as the percentage of eyes with a difference between postoperative uncorrected visual acuity (UCVA) and preoperative BCVA ≥ 0 Snellen lines, and safety was defined as the percentage of eyes with a loss of ≥1 lines between preoperative and postoperative BCVAs.

Statistical Analysis

Independent group differences for continuous quantitative variables were tested using the unpaired Student's *t* test. For comparison of percentages, the Pearson chi-square and Fisher exact test were used when n was <20 or when 25% of the theoretical values were <5. Statistical differences were considered significant when the *P* value was <0.05.

Results

Anatomic Results: Comparative Analysis

Anatomic complications (perioperative and postoperative) are described in Tables 3 and 4 (the latter available at http://aaojournal.org). Table 3 shows the biomicroscopic complications of the case and control groups; there were no statistical differences: the groups had similar frequencies of corneal complications. Table 4 shows the distribution of corneal lesions by the underlying disease, and the pathology was homogeneously distributed. Psoriasis was the most frequent disease with associated corneal complications. Nevertheless, the index of anatomic complications was not higher with RA and SLE. Most of the complications were transient and resolved with medical treatment without persistent sequelae, and in only one case of epithelial ingrowth (psoriatic group) was surgical debridement necessary. The microfolds and interface reactions described were mild and peripheral, without clinical repercussion.

One patient (42 years old; SE of −9.0 D) with underlying discoid lupus erythematosus and treatment with chronic corticosteroids had a new outbreak of the skin disease 6 months after LASIK surgery. There were no anatomic or functional ocular repercussions.

Functional Outcomes

For this purpose, we compared only myopic eyes (spherical, myopic simple, or compound astigmatism) between the 2 groups. We identified all the myopic eyes of the case group to assess the following absolute frequencies: collagen autoimmune diseases

Table 3. Anatomic Perioperative and Postoperative Complications: Comparative Analysis [n (%)]

	Cases	Controls	Statistical Significance*
Perioperative complications			
De-epithelialization	7 (2.5)	5 (1.4)	NS
Bed irregularities	0 (0)	1 (0.2)	NS
Flap complications (free/incomplete/broken flap)	3 (1)	2 (0.5)	NS
Postoperative complications			
Epithelial defects	3 (1)	6 (1.6)	NS
Punctate keratitis	10 (3.6)	16 (4.4)	NS
Interface reaction/debris	2 (0.7)	5 (1.4)	NS
Epithelial ingrowth	2 (0.7)	2 (0.5)	NS
Microfolding	4 (1.4)	6 (1.6)	NS
Conjunctivitis	1 (0.3)	4 (1.1)	NS

NS = nonsignificant.
*Fisher exact test.

Table 5. Functional Results: Preoperative and Perioperative Data, Homogeneity among Groups, and Comparison with Controls (Only Myopia) [Mean (Standard Deviation), *Statistical Significance*]

	Collagen Diseases (n = 46)	Psoriasis (n = 75)	Intestinal Inflammatory Diseases (CD, UC) (n = 57)	Diabetes (n = 38)	Keloids (n = 16)	Controls (n = 165)
Gender (% female)	76	46.6	50.8	50	68.7	56.7
	*<0.01**	*NS**	*NS**	*NS**	*NS**	
Age (yrs)	39.4 (7.1)	34.14 (7)	36.3 (8)	39.13 (11)	31.3 (3)	37.36 (6.7)
	NS†	*<0.01*†	*NS*†	*NS*†	*<0.01*†	
Sphere (D)	−3.99 (2.1)	−3.8 (2)	−3.36 (1.8)	−3 (1.8)	−3.23 (1.2)	−3.84 (2)
	NS†	*NS*†	*NS*†	*<0.05*†	*NS*†	
Cylinder (D)	−1 (1)	−0.88 (0.9)	−0.77 (0.7)	−1.1 (0.8)	−0.8 (0.8)	−1 (1)
	NS†	*NS*†	*NS*†	*NS*†	*NS*†	
SE (D)	−4.5 (2)	−4.3 (2)	−3.75 (1.7)	−3.6 (1.78)	−3.6 (1.34)	−4.3 (1.86)
	NS†	*NS*†	*NS*†	*<0.05*†	*NS*†	
BCVA	0.9 (0.18)	0.94 (0.1)	0.95 (0.1)	0.92 (0.1)	0.98 (0.04)	0.96 (0.08)
	<0.01†	*NS*†	*NS*†	*<0.05*†	*NS*†	
Flap thickness (μm)	98.9 (23)	96.5 (23)	92.4 (18)	99.25 (25)	110.6 (32)	101.3 (18)
	NS†	*NS*†	*<0.01*†	*NS*†	*NS*†	
Optical zone (mm)	5.9 (0.2)	5.88 (0.2)	5.9 (0.1)	5.89 (0.3)	6 (0.4)	5.8 (0.2)
	NS†	*NS*†	*NS*†	*NS*†	*NS*†	

BCVA = best-corrected visual acuity; CD = Crohn's disease; D = diopters; NS = nonsignificant; SE = spherical equivalent; UC = ulcerative colitis.
*Comparison with control group, Pearson chi-square test.
†Comparison with control group, Student's *t* test.

(n = 46 eyes), intestinal inflammatory diseases (n = 57 eyes), psoriasis (n =75 eyes), keloids (n =16 eyes), and diabetes (n = 38 eyes). For the control group, a homogeneous (by age and degree of myopia) subgroup of 165 myopic eyes was selected randomly. We studied the following variables described in "Patients and Methods": efficacy, predictability in ±0.5 D and ±1.0 D, safety, percentage of enhancement, and number of postoperative office visits until discharge.

Each disease was compared independently preoperatively and postoperatively with the control group. Table 5 shows preoperative and perioperative data to confirm homogeneity between groups. Table 6 shows the postoperative visual and refractive results and individual comparisons with the control group. Bivariate comparisons indicated only a statistically significant poorer predictability outcome of the collagen autoimmune diseases group. This worse refractive finding was mainly due to undercorrection of the sphere defect (regression), without induced astigmatism (mean final postoperative cylinder was −0.18±0.3 D) and without topographic abnormalities.

Results of LASIK in Pharmacologically Immunosuppressed Patients

We studied a specific group of patients (n = 29 patients, 56 eyes) who were under chronic immunosuppressive therapy (high doses

Table 6. Functional Results: Postoperative Data and Comparison with Controls (Only Myopia)

	Collagen Diseases (n = 46)	Psoriasis (n = 75)	Intestinal Inflammatory Diseases (CD, UC) (n = 57)	Diabetes (n = 38)	Keloids (n = 16)	Controls (n = 165)
Efficacy* (%)	67	82.6	73	73.6	87.5	73.9
	NS†	*NS*†	*NS*†	*NS*†	*NS*†	
Safety‡ (%)	0	2.6	1.7	7.8	0	2.4
	NS†	*NS*†	*NS*†	*NS*†	*NS*†	
Predictability,§ ±0.5 D (%)	78.2	82.6	87.7	92	100	88.2
	NS†	*NS*†	*NS*†	*NS*†	*NS*†	
Predictability,§ ±1.0 D (%)	89	93.3	94.7	94.7	100	99
	<0.01†	*NS*†	*NS*†	*NS*†	*NS*†	
Enhancement (%)	4.3	6.6	0	5.2	6.2	3.9
	NS†	*NS*†	*NS*†	*NS*†	*NS*†	
Postoperative visits [mean (SD)]	4.7 (1.9)	5 (2.6)	3.9 (1)	4.76 (4)	4.13 (0.8)	4.8 (1.7)
	NS‖	*NS*‖	*<0.001*‖	*NS*‖	*NS*‖	

CD = Crohn's disease; D = diopters; NS = nonsignificant; SD = standard deviation; UC = ulcerative colitis.
*Percentage of eyes with difference between postoperative uncorrected visual acuity and preoperative best-corrected visual acuity (BVCA) ≥ 0 Snellen lines.
†Statistical significance, comparison with control group, Pearson chi-square test.
‡Percentage of eyes with loss of ≥1 lines between preoperative and postoperative BCVAs.
§Percentage of eyes with postoperative spherical equivalent of ±0.5 D or ±1.0 D.
‖Statistical significance, comparison with control group, Student's *t* test.

of systemic corticoids (n = 32 eyes), immunosuppressive drugs (principally methotrexate and azathioprine; n = 21), or a combination of more than 2 drugs (n = 3). The associated underlying diseases were RA, SLE, psoriasis, and inflammatory intestinal diseases. The anatomic outcomes were as follows: no perioperative complications and 2 cases of postoperative superficial punctate keratitis. There were no flap or interface alterations and no signs of infection.

Results of Laser Epithelial Keratomileusis in Patients with Systemic Disease

The outcomes of 14 eyes of patients with a systemic disease, which were not included in the study, are shown for descriptive purposes because of the specific healing mechanism of LASEK, which is similar to that of the PRK technique. The underlying systemic diseases were RA (n = 7), SLE (n = 2), psoriasis (n = 3), ulcerative colitis (n = 1), and keloids (n = 1). Refractive data included 12 myopic, 1 hyperopic, and 1 mixed astigmatism cases. There were no perioperative complications and trivial postoperative anatomic complications (6 eyes with mild haze and 2 eyes with late mild punctate keratitis). The refractive and visual results were excellent, enhancement rate was 0%, and number of postoperative office visits was 6.7±3.7 (comparable to standard LASEK parameters).

Discussion

Although it is well established that some systemic diseases are contraindications for refractive surgery, surprisingly an analysis of the literature reveals a shortage of clinical studies that demonstrate a potentially damaging effect of these diseases on corneal healing, and most publications are based on anecdotal single reports or small series. The purpose of the present study was to clarify, with objective data, the repercussions of the above-mentioned diseases, such as autoimmune disorders, on LASIK surgery.

Connective Tissue Diseases

The association between autoimmune diseases and ocular pathology, including keratoconjunctivitis sicca, scleritis, episcleritis, keratitis, peripheral corneal ulceration, and other less common entities, such as choroiditis, retinal vasculitis, episcleral nodules, retinal detachment, and macular edema, is well known. Rheumatoid arthritis is probably the most emblematic autoimmune disease because of its strong association with ocular surface pathology and keratoconjunctivitis sicca (Sjögren's syndrome). Some anecdotal reports[13–17] describe severe corneal complications after intraocular surgery—principally lens surgery procedures, such as corneal melting, corneal infiltrate, peripheral ulceration, sclerokeratitis, and corneal perforation. In most of the reports, there was a preoperative history of sicca syndrome. There are no similar reports, however, of external photorefractive procedures. There is only one reported case of peripheral infiltrates after myopic LASIK, located on previous corneal scarring in a patient with stable RA.[4]

Regarding SLE, there are 2 case reports in which the authors associated the systemic disease with corneal complications after PRK: Seiler and Wollensak,[5] investigating the complications of PRK, described a patient with active SLE who developed a severe noninfectious corneal ulcer with perforation after PRK; the second case was a 41-year-old female that developed severe reticular corneal scarring that required surgical debridement for its resolution several years after uneventful PRK, concurrent with the appearance of the systemic disease.[6]

However, Alió et al[12] found good functional outcomes and no severe anatomic complications in a series of 42 eyes of 22 patients suffering from different rheumatic diseases, including 9 eyes with RA and 5 eyes with SLE. Our study is consistent with Alió et al's findings. We studied the postoperative evolution of 62 eyes associated with RA and SLE/discoid lupus, finding good anatomic and functional results, with the only exception being poorer predictability in the ±1.0-D range, and the remaining analyzed parameters were consistent with the control group. In Alió et al's study, there is a relatively high index of enhancement (14.3%) that reflects results consistent with the present study.

There were no cases of severe complications such as melting, corneal ulceration, or interface alterations. One limitation of the present study is the lack of measurements of tear function and corneal dryness. Only mild and moderate superficial punctate keratitis was observed, and there was no clinically significant dry eye (no eye required punctal plug occlusion). Wilson[2] suggested the term *LASIK-induced neurotrophic epitheliopathy* for a condition of transient ocular surface abnormality, such as punctate keratitis after LASIK, attributable to interruption of sensory nerve input to the corneal epithelium, which might last for ≥6 months postoperatively. He also suggested that preexisting dry eye is a risk factor for LASIK-induced neurotrophic epitheliopathy. Toda et al,[18] however, demonstrated that previous dry-eye status did not affect the efficacy of LASIK, measured as UCVA and BCVA, manifest refraction, and patient satisfaction, and there was no higher index of anatomic complications. Alió et al[12] also found that tear function indexes returned to normal preoperative levels after LASIK.

Keloids

A history of dermatologic keloid formation was classified initially by the Food and Drug Administration as a contraindication to PRK because of the perceived risk of developing a corneal scar with visual compromise. Tanzer et al[7] reported the outcomes of PRK in a group of African American patients in which there were 3 patients (6 eyes) with a history of cutaneous keloid formation. They found excellent visual results, comparable to those of the group of nonkeloid formers. Our results are consistent with Tanzer et al's, and although the patient sample is small (16 eyes), it is the largest published experience. There was no difference (anatomic and/or functional results) with the control group, and a successful LASIK outcome can be expected in this group of patients.

Diabetes Mellitus

Diabetes mellitus is prevalent (4%–8%), and an increasing number of diabetic patients will request refractive surgery. Diabetes, however, is cataloged as a relative contraindication, principally for patients with poor control and insulin-dependent disease.[8,19] Ocular manifestations of diabetes mellitus include vitreoretinal complications, increased risk of cataracts, refractive instability, and ultrastructural abnormalities in every layer of the cornea. Multiple morphologic alterations have been demonstrated at every corneal layer: epithelium (decrease in number of cells, polymorphism, superficial debris, etc.), thickening and rupture of basement membranes, epithelial barrier dysfunction, biochemical corneal nerve alterations, ultrastructural changes in the stroma, Descemet's membrane, and endothelium. These abnormalities predispose to corneal complications termed diabetic keratopathy.[20] Diabetic keratopathy includes superficial punctate keratopathy, persistent and recurrent corneal erosions, neurotrophic keratopathy, tear dysfunction, and endothelial dysfunction that result in increased epithelial fragility, poorer epithelial healing, and a consequent higher risk of infection.

There is only one clinical report regarding the anatomic and functional results of patients with diabetes mellitus after LASIK. In this study, Fraunfelder and Rich[8] described a statistically significant rate of epithelial complications in 30 diabetic eyes that underwent a LASIK procedure compared with the control group (47% vs. 6.9%, $P<0.01$), as well as poorer refractive outcomes. Jabbur et al[19] analyzed risk factors for interface epithelialization after LASIK, recommending against LASIK in patients with long-standing diabetes mellitus, especially insulin-dependent diabetes; they described 2 cases of interface epithelialization associated with underlying diabetes that required several surgical debridements.

The present study describes 44 eyes of diabetic patients with a low incidence of anatomic complications: 1 case of intraoperative de-epithelialization, 2 cases of postoperative superficial punctate keratopathy, 1 case of mild epithelial ingrowth, and a peripheral interface reaction, all of them resolved without significant sequelae. In addition, visual and refractive results and the number of postoperative visits did not differ significantly from the control group. These differences with Fraunfelder and Rich's study can be attributed to differences in the myopia range and in the refractive measurement parameters used in both studies.

Psoriasis

In the present study, there were more subjects in this group, comprising 91 eyes (10 were associated with a psoriatic arthropathy). Two percent had intraoperative epithelial defects and 4.4% had postoperative epithelial defects, which resolved without sequelae. Refractive and visual results were comparable to those of the control group. There are no other reports analyzing LASIK-specific outcomes in patients affected by psoriasis. In Alió et al's study,[12] there were described 4 patients affected with psoriatic arthritis who had generally good outcomes.

Inflammatory Intestinal Diseases

This group comprised 67 eyes of patients/subjects suffering from Crohn's disease and ulcerative colitis. Rates of intraoperative and postoperative epithelial defects were 4.4% and 6%, respectively, which also were resolved without sequelae. The patients achieved excellent refractive and visual results and 0% enhancement, and required a significantly lower number of postoperative visits than the healthy control group. We are aware of no similar studies with which to compare our results, with the exception of Alió et al's,[12] in which there were 2 patients with Crohn's disease and 1 patient with ulcerative colitis and arthritis. Although they do not report specific data for these cases, the general results show no significant complications in this subgroup.

LASIK and Pharmacologic Immunosuppression

There were 56 eyes that underwent LASIK surgery under systemic pharmacologic immunosuppression associated with one of the above-mentioned diseases. This group had good biomicroscopic outcomes (only 2 cases of mild superficial punctate keratitis), did not require a higher number of visits, and had no signs of corneal infection. In Alió et al's study,[12] there is no reference to the type of therapy, but they did not find any case of postoperative infective complication.

Laser Epithelial Keratomileusis and Systemic Diseases

The LASEK sample is small (14 eyes), but as this technique is essentially a variation of the PRK technique, we showed the results of this group to determine if this specific procedure is associated with poorer postoperative healing when there was an underlying autoimmune disease. We did not find any difference regarding time of re-epithelialization, number of postoperative visits, significant haze, or functional outcome relative to what we observed in healthy patients who underwent LASEK procedures.

Final Considerations

Although the present study is the first controlled study to analyze the results of photorefractive surgery in patients with underlying systemic diseases in a significant sample, some shortcomings were unavoidable, such as the retrospective nature of the study, small sample sizes when considering the independent subgroups, and short follow-up time to rule out the most important postoperative complications. Regarding sample size, although no patients had corneal melting, we can only assume that the risk of corneal melting in patients with collagen autoimmune diseases is less than 3/62 or 4.8% based on the rule of 3/n described by Schachat et al.[21]

In relation to follow-up time, although we cannot guarantee that there will be no further complications, the study supports that the major postoperative concerns, such as corneal melting, progressive ulcers, and perforation, do not occur during a substantial postoperative time. Most of the

published postoperative severe corneal complications associated with autoimmune diseases develop in a relatively short postoperative time (days to weeks[4,5,15,17]). In fact, we have not had any case of late complications after discharge, and one patient with discoid lupus had a flare-up 6 months after the LASIK surgery, without any repercussions for the previous surgery. In addition, causes other than underlying diseases, such as mild ocular trauma or mild infections, can produce severe scarring of the cornea several months after PRK.[22]

The results of the present study must be interpreted with caution because all the cases seemed to have stable and controlled underlying diseases without any other ocular pathology. We recommend maintaining the contraindications in cases of systemic and/or ocular activity, especially in patients with diabetes mellitus.

In conclusion, our data indicate that LASIK can be performed effectively and safely in appropriate and selected patients with stable and controlled systemic diseases with favorable postoperative anatomic and visual outcomes, and without severe adverse events. The absolute exclusion of certain systemic contraindications should be reconsidered, and larger studies should be performed to confirm and clarify these concepts to provide rational guidelines.

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Table 2. Ophthalmological Data of Case and Control Groups

	Cases (n)	Controls (n)
Refractive data		
Myopia	232	322
Hyperopia	33	22
Mixed astigmatism	10	14
Biomicroscopic findings		
Normal	231	311
Blepharitis	10	17
Pinguecula/pterygium	2	5
Minimal lens opacities (without visual significance)	17	8
Corneal alterations		
Subendothelial pigment	2	—
Leukoma	7	11
Punctate keratitis	3	4
Posterior embryotoxon	—	2
Iris atrophy	1	—
Subconjunctival hemorrhage	2	—
Intraocular pressure (mmHg)	15.2 (3.3)	15 (3.1)
Funduscopic findings		
Normal	247	335
Peripheral retinal degenerations	17	13
Myopic maculopathy	4	4
Fundus flavimaculatus	—	2
Equatorial drusen	2	—
Chorioretinal scars	5	4

Table 4. Anatomic Complications in Case Group: Distribution by Underlying Diseases

Underlying Disease	Perioperative Complications	Postoperative Complications
Rheumatoid arthritis (n = 29)	1 free cap	4 SPKs 1 microfold
Systemic lupus/discoid lupus (n = 31)	1 partial de-epithelialization	1 SPK 2 flap microfolds
Intestinal inflammatory disease: Crohn's disease/ulcerative colitis (n = 67)	3 partial de-epithelializations	2 SPKs 2 epithelial defects
Psoriasis (n = 91)	1 partial de-epithelialization 1 complete de-epithelialization 1 free cup	1 severe epithelial ingrowth 1 peripheral interface reaction 1 epithelial defect/SPK 1 conjunctivitis
Diabetes mellitus (n = 44)	1 partial de-epithelialization	1 peripheral mild epithelial ingrowth 1 microfold 1 interface reaction 2 SPKs
Keloids (n = 16)	1 incomplete flap	—

SPK = superficial punctate keratopathy.