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Dry Eye Disease after Refractive Surgery

Comparative Outcomes of Small Incision Lenticule Extraction versus LASIK

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Purpose: To compare small incision lenticule extraction (SMILE) versus LASIK for post-refractive dry eye disease.

Design: Prospective, comparative, nonrandomized clinical study.

Participants: Thirty patients scheduled for bilateral myopic SMILE and 30 age-, sex-, and refraction-matched patients scheduled for bilateral myopic LASIK were enrolled and followed for 6 months after the surgery.

Methods: Complete evaluation of dry eye disease was performed at 1 and 6 months postoperatively, which included vision-related quality of life (Ocular Surface Disease Index [OSDI]), clinical examinations (tear film breakup time [TBUT], Schirmer I test, corneal staining), and tear osmolarity measurements, together with an overall severity score. Function and morphology of the corneal innervation were evaluated by corneal esthesiometry and subbasal nerve imaging using in vivo confocal microscopy (IVCM).

Main Outcome Measures: Overall analysis of dry eye disease and corneal innervation.

Results: High incidence of mild to moderate dry eye disease was observed in both groups 1 month postoperatively, which remained significantly higher in the LASIK group than in the SMILE group 6 months after surgery (overall severity score [0−4]: 1.2±1.1 vs. 0.2±0.4, respectively, $P < 0.01$), leading to more frequent use of tear substitutes over the long term. Corneal sensitivity was better in SMILE than in LASIK eyes 1 month postoperatively (3.5±1.79 vs. 2.45±2.48, respectively, $P < 0.01$) and then recovered to statistically similar values at 6 months. Corneal nerve density, number of long fibers, and branchings as assessed by IVCM were significantly higher in the SMILE group compared with the LASIK group 1 and 6 months after surgery. Corneal sensitivity was negatively correlated with dry eye-related corneal damage ($R^2 = 0.48$, $P < 0.01$), and the long fiber nerve density was independently correlated with the OSDI score ($R^2 = 0.50$, $P < 0.01$) and the Schirmer test ($R^2 = 0.21$, $P < 0.01$) 6 months postoperatively.

Conclusions: The SMILE procedure has a less pronounced impact on the ocular surface and corneal innervation compared with LASIK, further reducing the incidence of dry eye disease and subsequent degradation in quality of life after refractive surgery. *Ophthalmology 2014;■:1−8 © 2014 by the American Academy of Ophthalmology.*

For the past 2 decades, LASIK has become the most popular corneal refractive surgery with approximately 1 million procedures per year in the United States.[1] Although a high satisfaction rate is reported, dry eye is still the most common adverse effect of LASIK. Many patients experienced mild-severity dry eye symptoms for a few months after LASIK, which are sufficiently eased using conventional tear substitutes, but patients still reported dry eye over the long term, with an occurrence of chronic dry eye disease ranging from 20% to 40% at least 6 months after surgery.[2] Dry eye causes damage to the ocular surface and symptoms of ocular discomfort associated with visual disturbance, which degrades not only the visual outcomes but also the quality of everyday life.[3–5] Thus, it could be assumed that hundreds of thousands of patients are likely to develop chronic dry eye disease after LASIK every year, further affecting the health status of this young and active population.

Total disruption of corneal nerves due to flap making combined with excimer photoablation is a likely cause of post-LASIK dry eye. A 90% decrease in central nerve fiber density has been reported in the first few months after LASIK, lasting for years until it recovers preoperative values or does not.[6] As a result, LASIK induces a decrease in tear film quality, tear secretion, blinking rates, and epithelial wound healing, all factors known to be involved in the pathogenesis of dry eye disease. Femtosecond laser was developed for LASIK to improve flap making and allows customization. However, the control and optimization of flap features brought few improvements in post-LASIK dry eye,[7] thus the need to develop new procedures to better protect the ocular surface after refractive surgery.

Small incision lenticule extraction (SMILE) is a recent procedure using femtosecond laser to create an intrastromal lenticule that is then removed through a small corneal

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incision.[8,9] Contrary to LASIK, this all-in-one femtosecond refractive surgery no longer needs excimer laser photoablation or a full flap cut. As a result, SMILE could constitute a minimally invasive approach to corneal refractive surgery because it only requires a small tunnel, which may have less impact on corneal innervation, thus further protecting patients against iatrogenic dry eye disease. Although clinical studies have reported refractive outcomes, corneal sensitivity, and clinical dryness after SMILE, nothing has been done to evaluate the overall severity of the disease, which requires a combination of objective tests and subjective symptom assessment as recommended by Delphi,[10] and its precise relationship with morphologic and functional changes in corneal innervation. Thus, uncertainty remains about long-term ocular surface recovery and subsequent patient health status after SMILE, which could become the new gold standard for corneal refractive surgery, provided its theoretic benefits are demonstrated.

This nonrandomized study was designed to prospectively compare SMILE with LASIK for surgically induced corneal changes and dry eye disease in accurately matched populations in terms of age, gender, and refraction. Clinical evaluation, a vision-related quality of life questionnaire, tear osmolarity assessment, corneal esthesiometry, anterior segment optical coherence tomography (OCT), and in vivo confocal microscope (IVCM) imaging were performed 1 and 6 months postoperatively to determine whether the SMILE procedure preserves the ocular surface and put an end to the common but sometimes deleterious post-refractive dry eye disease.

Methods

This prospective, comparative, nonrandomized clinical study was conducted in the Clinical Center for Investigation of Ocular Surface Pathology (Quinze-Vingts National Ophthalmology Hospital, National Institute for Health and Medical Research 503, Paris, France) in accordance with the Declaration of Helsinki, Scotland amendment, 2000. Previous approval was obtained from the National Ethical Research Committee (Comité de Protection des Personnes Ile de France V, National Agreement Number 10793). All patients gave informed consent to participate in the study.

Patients

Thirty European subjects scheduled for bilateral SMILE (J.F.F.) and 30 European age-, sex-, and spherical equivalent–matched subjects scheduled for bilateral LASIK (F.A.) were prospectively included. Inclusion criteria were planned myopic SMILE or LASIK (spherical correction range, −1 to −8 diopters; cylinder range, 0 to −1.5 diopters), willingness to participate in the study, and the ability to give informed consent. Exclusion criteria were any ocular pathology but myopia, any clinical sign or symptom of dry eye disease (Schirmer I test >10 mm/5 minutes, tear film breakup time [TBUT] >10 seconds, no corneal/conjunctival staining, no Meibomian gland dysfunction, and Oxford score = 0), previous ocular/eye lid medical or surgical treatment, systemic disorder, and pregnancy. All the examinations were performed 1 month and 6 months after the surgery, except OCT, which was performed at 6 months only. Detailed patient data are shown in Table 1.

Surgical Technique

All procedures were performed with topical anesthesia (0.8% oxybuprocaine tetrachloride) after standard sterile draping and insertion of an eyelid speculum. SMILE was performed bilaterally using femtosecond laser (Visumax, Carl Zeiss Meditec, Jena, Germany) with a 110-μm depth and a 6.5-mm diameter lenticule, and a 10-o'clock small tunnel incision. The lenticule was gently detached and extracted through the corneal tunnel using a spatula. The maximum lenticule thickness ranged from 51 to 152 μm. For the LASIK group, the corneal flap was made by femtosecond laser (IFS500, Abbot Medical Optics, Abbot Laboratories, Chicago, IL) with a 110-μm depth, 9-mm diameter flap, and 50° superior hinge. Excimer photoablation was performed (Allegretto, Alcon Laboratories, Fort Worth, TX) for a 6.5-mm optical zone, and then the flap was repositioned. In both groups, 0.3% tobramycin/0.1% with dexamethasone suspension (Tobradex, Alcon Laboratories) associated with preservative-free tear substitutes were used 3 times per day for 1 month, and then preservative-free fluid tear substitutes or gels were administered when needed.

Clinical Examinations and Questionnaire

Slit-lamp evaluations were conducted in a defined sequence[11] and included TBUT measurements (mean of 3 consecutive tests), ocular surface fluorescein staining (grade 0–5, according to the Oxford score), and the Schirmer I test (mm/5 minutes, without anesthesia). Before clinical examination, a trained interviewer

Table 1. Patient Features, Visual Outcomes, and Corneal Morphology as Assessed by Anterior Segment Optical Coherence Tomography

	SMILE Group (n=30)	LASIK Group (n=30)	*t* Test (*P*)
Preoperative data			
Age (yrs)	31.1±4.7	32.2±7.5	NS
Gender (M/F)	0.47	0.47	NS
Mean keratometry (D)	42.9±1.6	43.7±1.5	NS
Spherical equivalent (D)	−4.65±2.38	−4.42±1.78	NS
6-mo outcomes			
Mean keratometry (D)	40.9±1.4	39.9±2.5	NS
Spherical equivalent (D)	−0.03±0.41	0.13±0.4	NS
Distant best-uncorrected visual acuity (logMAR)	0.07±0.10	0.08±0.10	NS
Epithelial thickness (μm)	39.9±14.1	39.6±13.6	NS
Total corneal thickness (μm)	496.3±39.3	506.7±39.5	NS
Depth of the interface (μm)	117.2±4.6	117±4.5	NS

Data are reported as mean ± standard deviation. D = diopters; logMAR = logarithm of the minimum angle of resolution; NS = not significant; SMILE = small incision lenticule extraction.