Long-Term Visual and Refractive Outcomes following Surface Ablation Techniques in a Large Population for Myopia Correction

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Purpose. To evaluate the visual and refractive outcome for four wavefront-guided surface ablation (WGSA) techniques (LASEK, LASEK flap-off [LASEK FO], Epi-LASIK, and Epi-LASIK flap-off [Epi-LASIK FO]) in a large myopic population.

Methods. This retrospective review included 1000 myopic eyes (spherical equivalent [SE] −1.0 to −8.0 diopters [D]) treated with WGSA (VISX STAR S4 with IR) using four different epithelial management techniques. Flaps were either retained (163 Epi-LASIK, 361 LASEK) or discarded (277 Epi-LASIK FO, 199 LASEK FO). Eyes in each group were stratified to either low, mild, moderate, or high myopia based on preoperative SE. Uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), manifest refraction spherical equivalent (MRSE), predictability, lines lost, and haze were compared at 3, 6, and 12 months.

Results. At 1 year, UDVA and CDVA of ≥20/20 and 20/15 were comparable across the four procedure groups and within each subgroup of myopia. Predictability was less than or equal to ±0.5 D of intended correction in 96% to 99% of eyes. LASEK FO and Epi-LASIK FO outperformed the EPI-LASIK in achieved MRSE, especially in the high myopia category (–0.012, 0.040, and –0.27 D, respectively, $P < 0.05$). No eyes lost more than one line of CDVA; and 50% to 60% of eyes in each group gained one or more lines. No significant haze was recorded in any group. There was no statistically significant difference between groups in the preoperative MRSE and efficacy indices except for LASEK FO.

Conclusions. At 1 year, there was no statistically significant difference in visual outcomes between techniques for any degree of myopia. However, the MRSE achieved with LASEK FO and Epi-LASIK FO were closer to emmetropia. (*Invest Ophthalmol Vis Sci.* 2013;54:609–619) DOI:10.1167/iovs.12-10387

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Photorefractive keratectomy (PRK) has stood the test of time as a safe and simple procedure to correct low to moderate levels of myopia and astigmatism.[1] Equally good results are achieved with use of an Amoils rotating brush, Paton spatula, 20% alcohol, or laser to remove the epithelium.[2,3] PRK is also considered a better option for patients with thin corneas, recurrent erosions, or work/sport-related predisposition to trauma or in patients for whom fitting a suction ring could have adverse consequences, such as those with glaucoma or retinal pathology.[4] However, visual recovery is relatively slow, and patients can experience postoperative discomfort/pain and haze.[5]

Laser-assisted subepithelial keratectomy (LASEK) was developed in 1998[6] with the intention of circumventing microkeratome-related complications of LASIK. With use of 20% alcohol, the epithelium can be separated within the basement membrane between the lamina lucida and lamina densa. The flap, when later replaced, covers the epithelial defect.[7] If the flap is completely removed, the procedure is termed LASEK flap-off (LASEK FO).[8] LASEK was initially felt to provide the advantages of LASIK, such as reduced incidence of postoperative pain, reduced corneal haze, and faster visual recovery than with PRK,[5,9] plus better visual quality through reduction of haze.[10] However, many authors have concluded that LASEK offers no additional clinical benefits over PRK.[11–15]

In 2001, Pallikaris introduced the epithelial laser in situ keratomileusis (Epi-LASIK) technique, in which the epikeratome is used to create the epithelial flap. In this procedure, separation occurs beneath the basement membrane, leaving an intact basal cell layer with more intact hemidesmosomes.[7] It was thought that these flaps, when replaced, might act as a barrier to protect the photoablated stroma from inflammatory responses, hence resulting in less postoperative pain and haze, with faster visual recovery.[16,17] However, no such advantages have been confirmed and, in fact, some have reported increased pain, delayed epithelial healing, and inferior early visual outcomes compared with flap-off techniques.[18–20]

The flap-off variant of this technique was termed Epi-LASIK flap-off (Epi-LASIK FO).[8,18] The advantage of Epi-LASIK and Epi-LASIK FO is absence of alcohol-related toxicity and possibly faster time to healing.[21]

With the wide variety of procedures available today to treat mild to moderate myopic astigmatism, the question remains as to which technique is superior. The aim of our study was to determine if there was any significant difference in long-term refractive or visual outcomes based on the type of surface ablation procedure (utilizing either alcohol or an epikeratome)

to create the epithelial defect with either flap replacement or removal, for varying degrees of myopia.

To the best of the authors' knowledge, this is the first report that compares all four surface ablation techniques using the same wavefront-guided ablation program in a large myopic population at one university eye institute.

Patients and Methods

This single-center, retrospective review was approved by the Research Ethics Board of the Ottawa Hospital Research Institute. All patients signed an informed consent in accordance with the tenets of the Declaration of Helsinki. The study included 1000 consecutive eyes of 585 patients with myopia or myopic astigmatism (manifest refraction spherical equivalent [MRSE] −1.0 to −8.0 diopters [D]) who underwent wavefront-guided surface ablation treatment at the University of Ottawa Eye Institute, Ottawa, Canada. Wavefront-guided surface ablations (Advanced CustomVue; Abbott Medical Optics, Santa Ana, CA) were performed on all eyes with VISX STAR S4 IR (Abbott Medical Optics) by two surgeons (WBJ and GM). The 1000 eyes included in this study are a subset of the total myopic population that met the following parameters: spherical equivalent (SE) −1.00 to −8.00 D with a cylinder of 0 to +2.00 D; had not had previous ocular surgery; had successful WaveScan capture; and elected to undergo surface ablation laser surgery. Eyes with a larger SE and/or astigmatism, previous ocular or refractive surgery, other ocular pathology, or unsuccessful wavefront capture, as well as those undergoing retreatment, were excluded from the analysis.

LASEK was the standard procedure used initially, followed by the introduction of Epi-LASIK. Patients chose to have either alcohol or an epikeratome epithelial removal. Over the course of several years, other techniques were explored. When it became clear that "flap-off" procedures were also successful, more of these procedures were performed. The flap-off was performed whenever the surgeon did not have a complete epithelial flap intraoperatively. Eyes were allocated into one of four procedure groups (163 Epi-LASIK, 277 Epi-LASIK FO, 361 LASEK, 199 LASEK FO) and further stratified based on the degree of preoperative SE (low, −1.0 to −1.9 D; mild, −2.0 to −3.9 D; moderate, −4.0 to −5.9 D; and high, −6.0 to −8.0 D). Patients had a minimum of 3 months' follow-up. Data from the 12-month visit was available for 70% to 85% of eyes in all four groups ($n = 138$ Epi-LASIK, 286 LASEK, 195 Epi-LASIK FO, 146 LASEK FO).

Eyes with a pachymetry less than 475 μm, a calculated residual bed depth less than 300 μm, and/or topographies suggestive of forme fruste keratoconus or other corneal abnormalities were not considered for surgery. Monocular distance visual acuity (i.e., uncorrected distance visual acuity [UDVA] and corrected distance visual acuity [CDVA]) by Snellen charts, external ocular examination, haze scoring by slit-lamp microscopy, and corneal topography by Pentacam (OCULUS Optikgeräte, Wetzlar, Germany) were recorded at baseline and at 1, 3, 6, and 12 months postprocedure. Haze levels by slit-lamp microscopy were reported as follows: 0 = no haze; 0.5 = visible only by tangential illumination; 1 = trace haze seen with difficulty under direct illumination; 2 = moderate haze (possible to observe iris in detail); 3 = marked haze (difficult to observe iris in detail); and 4 = severe haze (not possible to observe iris in detail).[22,23]

Surgical Techniques

Preoperatively, all patients received topical antibiotic prophylaxis with a fourth-generation fluoroquinolone four times a day and 500 mg vitamin C orally twice per day for 2 and 7 days before the procedure, respectively. Two drops of 0.5% proparacaine hydrochloride (Alcaine; Alcon Laboratories, Fort Worth, TX) and a single oral dose of 1 mg lorazepam were administered just before the surgery. Asepsis was achieved by cleaning the eyelid and eyelashes with 10% povidone. A Gebauer MicronEdge epithelial separator (Gebauer, Neuhausen, Germany) was used to create a flap in Epi-LASIK and Epi-LASIK FO. For LASEK and LASEK FO treatments, an 8 mm LASEK Epithelial Trephine (Camellin Style LASEK Trephine 8 mm; Katena Products, Inc., Denville, NJ) was used to score the epithelium, and then warm 20% alcohol was applied for 20 seconds using an 8.5 mm well (Camellin Style LASEK Alcohol Well 8.5 mm; Katena Products, Inc.). The loosened epithelium was separated with a micro hoe (Sloane LASEK Micro Hoe; Katena Products, Inc.) to attempt to create an intact epithelial flap. Surface ablations were done bilaterally at the same surgical sitting, targeting emmetropia, using the STAR S4 IR excimer laser system (AMO, Santa Ana, CA) and wavefront profiles obtained by Advanced CustomVue (AMO). As the WaveScan nomogram is set for LASIK treatments and more pulses are required to achieve the desired effect for surface ablation treatment, the surgeons increased the attempted correction by 6% to 8% in each treatment plan based on an analysis of our earlier data. Mitomycin C (MMC) 0.02% solution was applied with a Merocel surgical sponge (Merocel; Medtronic Xomed, Inc., Jacksonville, FL) for 30 seconds for all ablations exceeding 80 μm depth and/or cylinders ≥2.0 D, followed by cool balanced salt solution irrigation to reduce the chance of haze formation. Depending on the procedure, the epithelial flap was either replaced or removed (as previously reported).[24] The patients were fitted with a −0.50 D bandage contact lens with base curve of 8.6 (Shine Optical, Zevenaar, Netherlands) until the epithelium healed (3–7 days). Postoperatively, a nonsteroidal anti-inflammatory drop, ketorolac 0.5% (Acular LS; Allergan, Irvine, CA), was used at the time of surgery and continued four times a day for the first 24 hours. A solution of dilute tetracaine in artificial tears was given for use on an as-needed basis to mitigate ocular discomfort. In addition, fluorometholone ophthalmic suspension 0.1% (FML; Allergan) four times a day was prescribed in a tapering fashion over the ensuing three months. Oral vitamin C (500 mg twice per day), which was started a week before surgery, was continued twice a day for 1 week after surgery. Patients were encouraged to use ocular lubricants (Refresh Artificial Tears and/or Refresh Liquigel eye drops; Allergan) for the first two months and later if required.

Statistical Analysis

Data were analyzed using Microsoft Excel 2003 (Microsoft, Redmond, WA) and SigmaStat for Windows Version 3.5 (Systat Software, Inc., Chicago, IL) statistical software. One-way analysis of variance (ANOVA) on ranks was used to compare sphere and cylinder measurements between all the pre- and posttreatment groups and also between eyes stratified by the degree of preoperative myopia. χ^2 test was used to compare the percentage of the level of visual acuity achieved among different groups.

Root mean square (RMS) comparison was also performed using pairwise multiple comparison procedures (Dunn's method). A predictability distribution of each of these procedures and for each of the subgroups was calculated at 12 months. A P value < 0.05 was regarded as statistically significant.

Results

A total of 1000 eyes of 585 patients (38.5% males, 61.5% females) were analyzed. Mean age of patients in the four groups was similar (≈39 years, range 20–62 years, $P = 0.41$). There was a slight preponderance of females (59%–64%) compared with males (36%–41%) in all four groups. MRSE was higher in eyes undergoing LASEK FO compared to the other groups (−4.65 D vs. −3.98 to −4.23 D, $P < 0.001$), though the difference in MRSE and sphere between all other groups was not statistically significant. There were no significant differences in the preoperative variables between the groups, including cylinder values, age, and sex of the patients (Table).

Table. Patient Characteristics and Optical Performance Preoperatively

	WF Epi-LASIK	WF Epi-LASIK FO	WF LASEK	WF LASEK FO	*P* Value
Eyes, *n*	163	277	361	199	
Age, y, mean ± SD	39 ± 9.4	38 ± 9.1	38 ± 8.5	39 ± 9.3	0.4138*
Male/female, %	36/64	39/61	41/59	38/62	0.9080†
MRSE, D, mean ± SD	−4.15 ± 1.74	−3.98 ± 1.57	−4.23 ± 1.79	−4.65 ± 1.93	<0.001*
Sphere, D, mean ± SD	−4.42 ± 1.74	−4.28 ± 1.59	−4.53 ± 1.81	−4.98 ± 1.96	<0.001*
Cylinder, D, mean ± SD	+0.80 ± 0.52	+0.73 ± 0.50	+0.79 ± 0.54	+0.80 ± 0.55	0.3769*

n, Number of eyes in the group; MRSE, manifest refraction spherical equivalent; WF, wavefront; Epi-LASIK, epithelial laser in situ keratomileusis; LASEK, laser epithelial keratomileusis; FO, flap-off.

* One-way analysis of variance.

† χ^2 test for independence.

Uncorrected Distance Visual Acuity

Analysis of the total cohort at 1 year showed no statistically significant difference in the UDVA at the level of 20/20 or 20/15 between any of the procedures. Between 86% and 94% of patients in all four treatment groups achieved UDVA of 20/20 or better, while the rates of UDVA of 20/15 or better ranged from 58% to 70% (Figs. 1, 2). In addition, analysis of low, mild, moderate, and high myopia groups revealed no statistically significant difference between the groups ($P = 0.26$, 0.19, 0.66, and 0.154, respectively) (Figs. 3, 4).

Distance Corrected Visual Acuity

The proportion of eyes with preoperative CDVA of 20/20 (93%–100%) was similar between the four treatment groups. Postoperatively at 12 months, as expected, a greater proportion of eyes in the low myopia group (86%–100%) achieved a CDVA of 20/15 than in the high myopia group (40%–61%), with no significant difference ($P > 0.05$) between any of the treatment groups (Fig. 5).

Mean Manifest Refraction Spherical Equivalent

MRSE was quite stable from 3 months to 1 year in all groups. At 3 months postoperative, all eyes except the LASEK FO group showed an undercorrection of <0.25 D. At the 1-year follow-up, mean MRSE across the four groups ranged from –0.12 to –0.01 D, with a very tight standard deviation (SD) between the groups (SD = 0.13–0.32). However, eyes treated with LASEK FO and Epi-LASIK FO were closer to emmetropia than with other procedures at various follow-up periods postprocedure (Fig. 6). MRSE did not change more than ±0.25 D from 3 months to 1 year in 97% of eyes across the groups. This trend was consistent even when subanalysis was carried out for the different levels of myopia (Fig. 7).

Predictability

Predictability (achieved versus intended correction) of ±1.0 D was found in 100% of eyes in all treatment groups. At 12 months, achieved MRSE was within ±0.5 D of intended in 96% of eyes in the Epi-LASIK group and in 98% or 99% of eyes in all other treatment groups. Achieved MRSE of ±0.25 D of intended correction was attained in 86% to 97% of eyes (Fig. 8).

Safety

On average, approximately 50% (range 47%–58%) of eyes in each group gained one line of CDVA, and no eyes in any of the groups had lost had more than one line of CDVA at 12 months (Fig. 9). The distance safety index (ratio of the mean

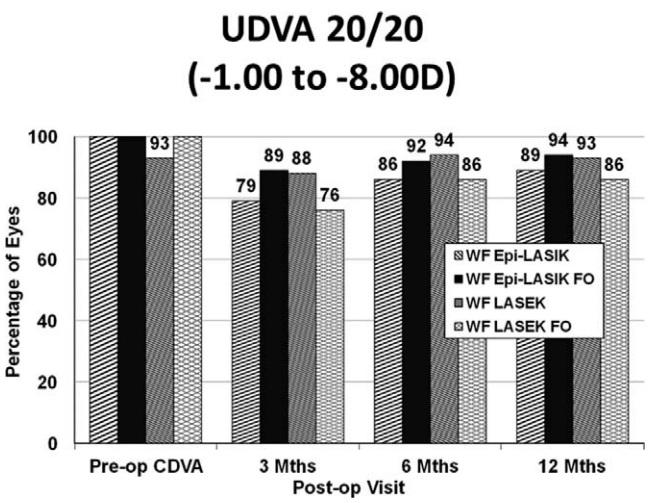

Figure 1. Uncorrected distance visual acuity (UDVA) of 20/20 or better for the entire range of treated refractive errors (–1.00 to –8.00 D) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO). There was no statistical significant difference in the UDVA at level of 20/20 between procedures at any point during the follow-up period.

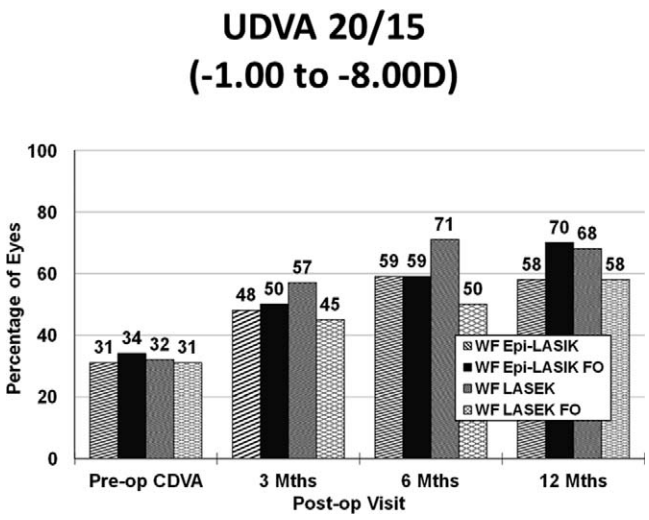

Figure 2. Uncorrected distance visual acuity (UDVA) of 20/15 or better for the entire range of treated refractive errors (–1.00 to –8.00 D) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO). There was no statistical significant difference in the UDVA at the level of 20/15 between procedures at any point during the follow-up period.

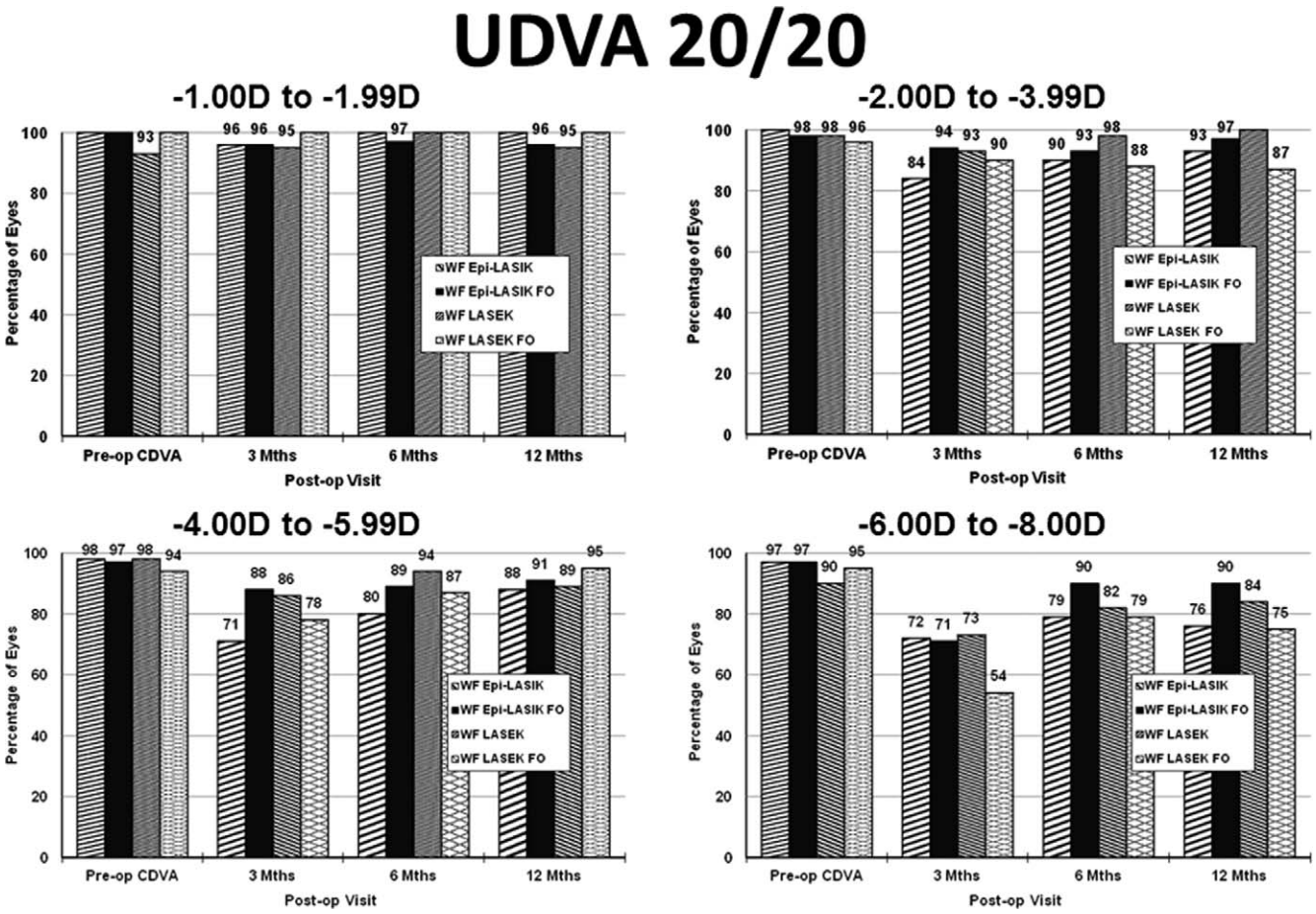

Figure 3. Uncorrected distance visual acuity (UDVA) of 20/20 (stratified by level of myopia) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO). No statistically significant difference between the groups.

postoperative CDVA/mean preoperative distance CDVA) was >1 in all four treatment groups at 12 months, with Epi-LASIK FO having statistically higher median safety than the other three groups at 12-month follow-up (Epi-LASIK = 1.16, Epi-LASIK FO = 1.26, LASEK = 1.17, LASEK FO = 1.15; standard error = 0.01–0.02, $P < 0.001$).

Efficacy

Efficacy index of a refractive procedure is reported as the ratio of the mean postoperative distance UDVA/preoperative distance CDVA. In our series, all four groups were >1.0 (Epi-LASIK = 1.08, Epi-LASIK FO = 1.19, LASEK = 1.13, LASEK FO = 1.03; SE = 0.02), with only LASEK FO showing a statistically lower efficacy ($P < 0.001$). The difference between groups was less than one line of postoperative visual acuity and was of no clinical significance.

Haze

Grading of haze severity showed that very few eyes (2%–7%) in any of the procedure groups had more than trace haze even at 1 month. At 12 months, haze was absent in nearly all eyes, and there were no statistically significant differences between procedure groups or subgroups in haze outcomes at any visit (Fig. 10).

Complications

No intraoperative or early postoperative complications were detected other than occasional intraoperative flap failure when the eye was reallocated to the flap-off category. There were no infections and no stromal incursions with the epikeratome. The corneal epithelial defect was healed in most of the eyes by day 7 (day 7 is our regular protocol for the third postoperative follow-up visit for patients undergoing refractive surgery). From clinical observation, less than 2% of our patients required an additional visit on day 10 (mostly in the "flap-on" groups), and no patient had epithelial healing delay greater than 10 days. Seventeen eyes required retreatment for undercorrection (7 eyes LASEK, 8 eyes Epi-LASIK, 1 eye Epi-LASIK FO, and 1 eye in the LASEK FO group) and achieved 20/20 UDVA at the last follow-up visit. These eyes were included in the analysis until the last follow-up visit prior to retreatment.

Discussion

The goal of our study was to determine if any of the surface ablation (LASEK, LASEK FO, Epi-LASIK, and Epi-LASIK FO) procedures outperformed the others in terms of visual or refractive outcomes for varying degrees of myopia. The results of this study, as well as those reported by other investigators, indicate that surface ablation techniques have excellent

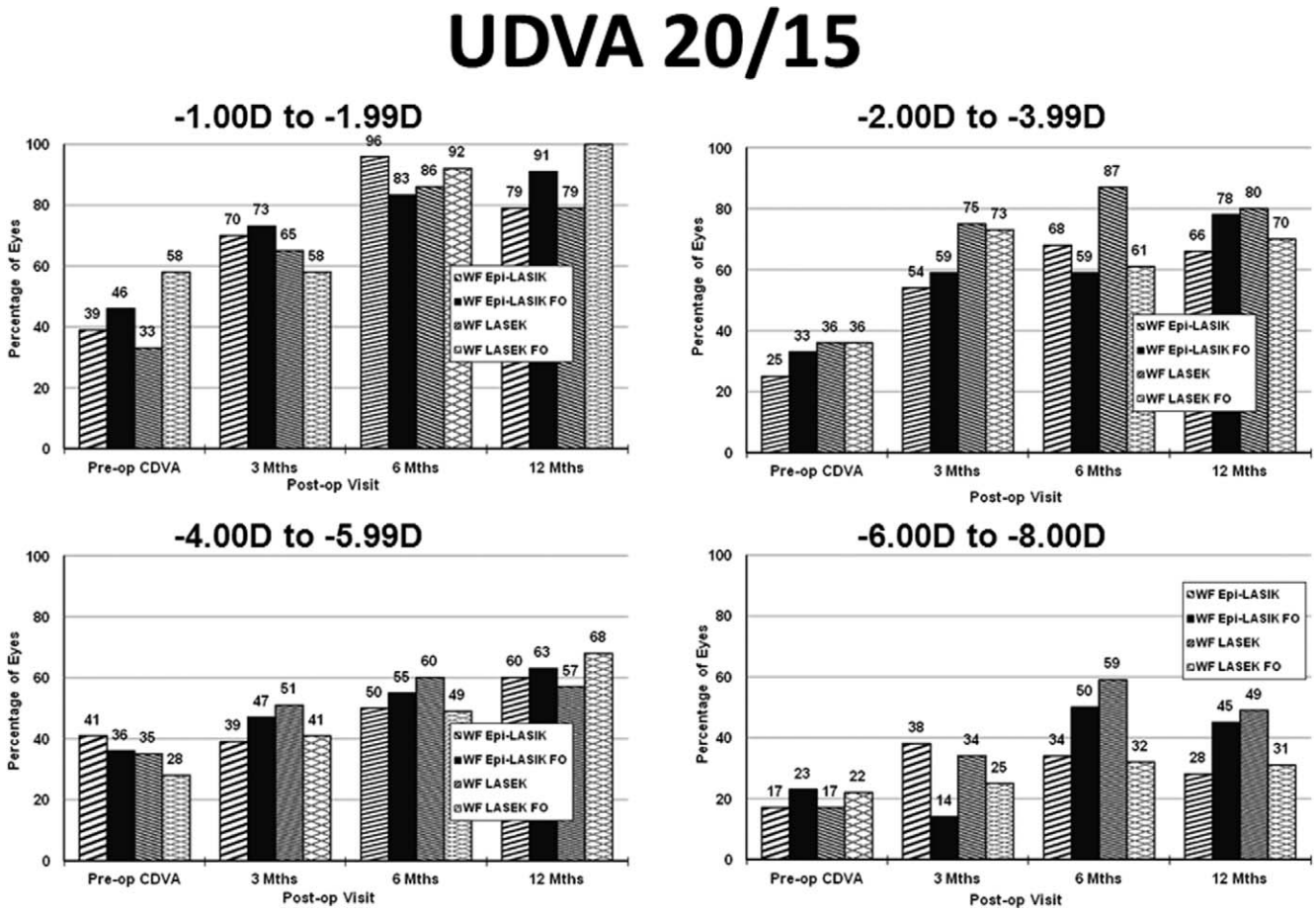

Figure 4. Uncorrected distance visual acuity (UDVA) of 20/15 (stratified by level of myopia) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO). No statistically significant difference between the groups.

efficacy, predictability, and safety profiles for correction of myopia.[8,25,26] At 12 months, irrespective of whether the flap was created mechanically or chemically and whether it was retained or discarded, we found that visual and refractive outcomes were statistically similar for all levels of myopia up to a maximum of 8.0 D SE. However, the high myopia group (Fig. 3) undergoing Epi-LASIK and LASEK FO showed less favorable UDVA outcomes compared to groups undergoing the other procedures. Although wound-healing response after laser ablation seems to be one of the prominent causes of refractive regression,[27] we believe this was not the reason for this finding in our study, as no haze was detected at the 12-month follow-up. Randomized comparative studies and meta-analysis have shown no significant differences in visual outcomes of patients undergoing PRK and LASEK,[11,14,28] PRK versus Epi-LASIK,[18,29] and LASEK versus Epi-LASIK[30–32]; thus we assume that what is noted in Figure 3 is not related to the surgical techniques per se. However, one reason could be that nine eyes in the Epi-LASIK group required retreatment for undercorrection; their MRSE at 12 months was −1.11 D, which must have contributed to lower UDVA measurement in this group. Sixteen of 17 eyes requiring retreatment for undercorrection were in the moderate to high myopia group. While the previously cited studies did not compare the procedure outcome for high myopia patients, investigations have demonstrated that the wound-healing response is more intense for high myopic corrections.[33] Randomized clinical trials with longer follow-up are needed to investigate whether any masked benefit exists for any one procedure over others and to determine the best criteria for selection of patients for each method. Another reason for the finding that high myopes undergoing Epi-LASIK and LASEK FO have poorer UDVA outcomes could be that preoperative MRSE was higher in eyes undergoing LASEK FO compared with the other groups (−4.65 D vs. −3.98 to −4.23 D, $P < 0.001$), and this might have contributed to the disparity in UDVA at 12-month follow-up. It is especially important to note that LASEK FO and Epi-LASIK FO achieved MRSE that was closer to emmetropia than the other procedures at various follow-up periods and across all categories of myopia. A third reason could be the numbers of patients lost to follow-up at 12 months postoperatively (29.6% Epi-LASIK FO, 15.3% Epi-LASIK, 20.8% LASEK, and 26.6% LASEK FO).

Although the proportion of eyes with a UDVA $\geq$ 20/15 at 3- and 6-month follow-up seemed to initially favor the LASEK group over Epi-LASIK and Epi-LASIK FO in the mild ($P < 0.001$) and high myopia subgroups ($P < 0.01$), the trend toward better UDVA did not persist at 12 months. Taneri et al.[8] found comparable UCVA at 3 months in all four surface ablation groups (in 40 patients [80 eyes]). In an earlier study of 25 patients (50 eyes), Hondur et al.[30] reported that 92% achieved 20/20 or better UCVA in Epi-LASIK and LASEK-treated eyes, and were within ±0.50 D of emmetropia at 12 months. Similarly, we found that 89% and 93%, respectively, achieved 20/20 vision and that 96% and 98% were within ±0.50 D. O'Doherty et al.[31] have also reported comparable visual and refractive results after Epi-LASIK, LASEK, and PRK in 57 patients (95 eyes).

Many contemporary studies have compared visual and refractive outcomes between mechanical and alcohol-based

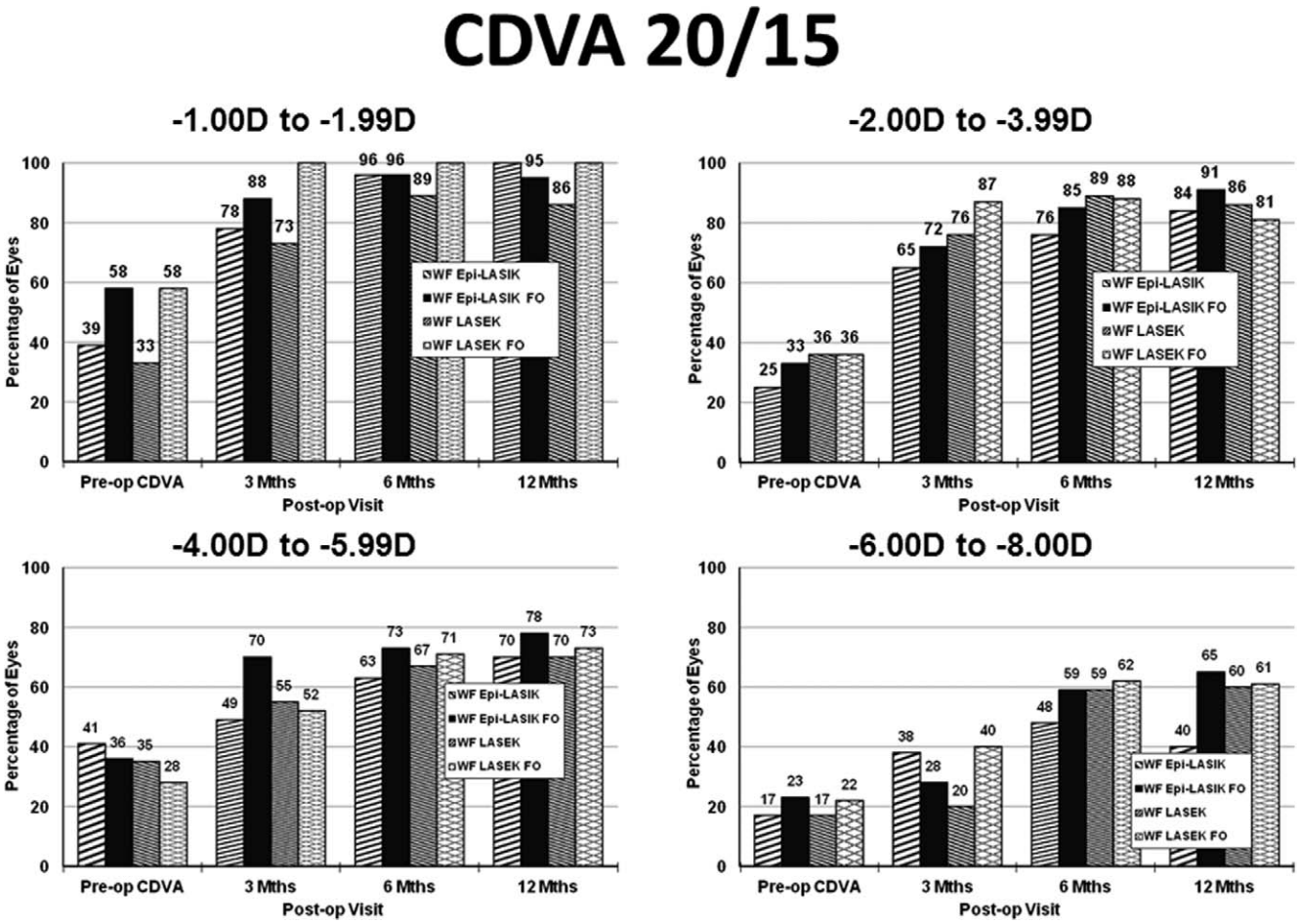

Figure 5. Corrected distance visual acuity (CDVA) of 20/15 (stratified by level of myopia) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO), with no statistically significant difference between the groups.

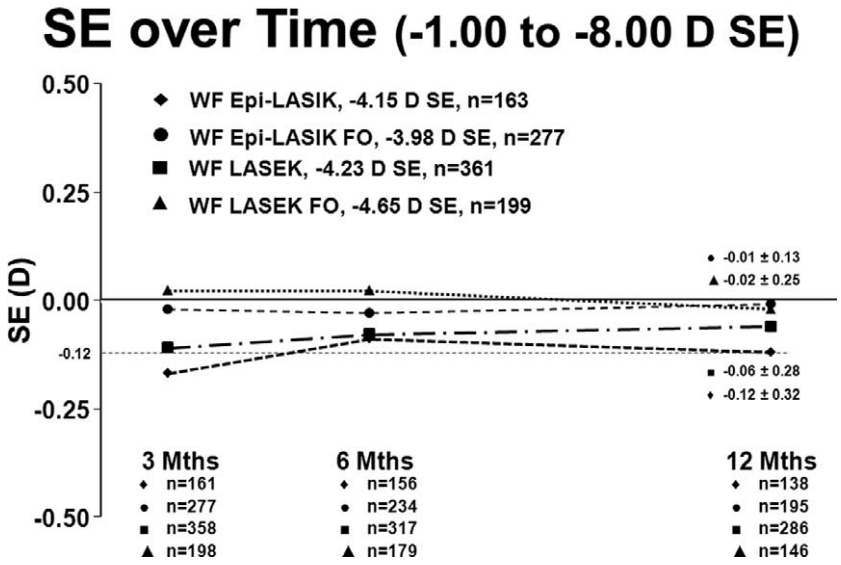

Figure 6. Mean spherical equivalent over time for treated myopia (–1.00 to –8.00 D) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO). The stability of refractive outcome at various points of follow-up is noted. No statistically significant difference was found among any of the groups in refractive outcomes at 3 or 12 months for the low myopia categories. However, LASEK FO resulted in significantly better achieved MRSE than LASEK and Epi-LASIK for the high myopia category at various follow-up periods postprocedure.

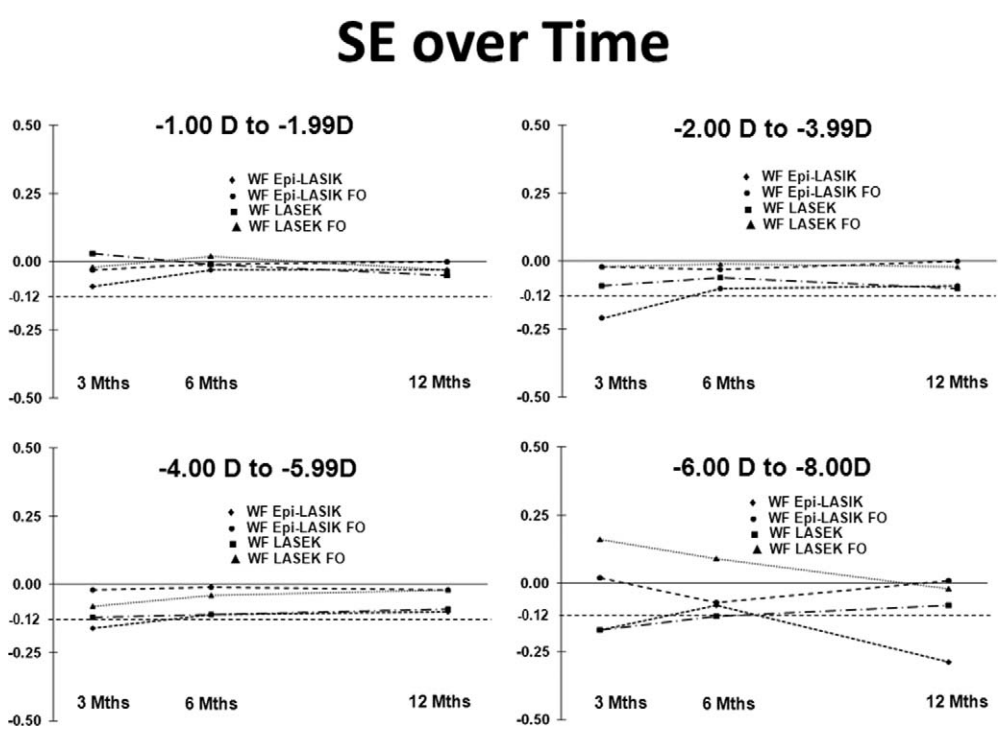

Figure 7. Mean spherical equivalent over time (stratified by level of myopia) at 3, 6, and 12 months after various surface ablation procedures (Epi-LASIK, Epi-LASIK FO, LASEK, and LASEK FO). MRSE did not change more than ±0.25 D from 3 months to 1 year postprocedure. There is no statistically significant difference between procedures at any point during the follow-up period.

flap creation techniques,[4,34–39] with arguments for and against separating flaps within or below the basement membrane and likewise for leaving the flap on versus taking it off.[4,20,29,37,38,40,41] We have also previously documented that at the 3-month follow-up, only the flap-off treatment showed a consistent correlation between the corrected aberrations and visual performance.[42]

Haze evaluation is important when one is comparing various surface ablation procedures. Javier et al.[43] have shown the advantage of retaining epithelial flaps in terms of reducing abnormal subepithelial stromal wound-healing response. It has been postulated that because the cleavage plane in Epi-LASIK is below the basement membrane, compared to within the basement membrane in LASEK, there is less disruption and inflammation within the epithelial layer and thus a more viable flap and improved healing response.[7,44] Other studies have demonstrated less haze if epithelial debridement was performed using 20% ethanol as opposed to mechanical removal.[13,45] It is speculated that quick and gentle handling of the epithelium may reduce cytokine production during de-epithelialization.[33,46–48] In addition, the epithelial flap is

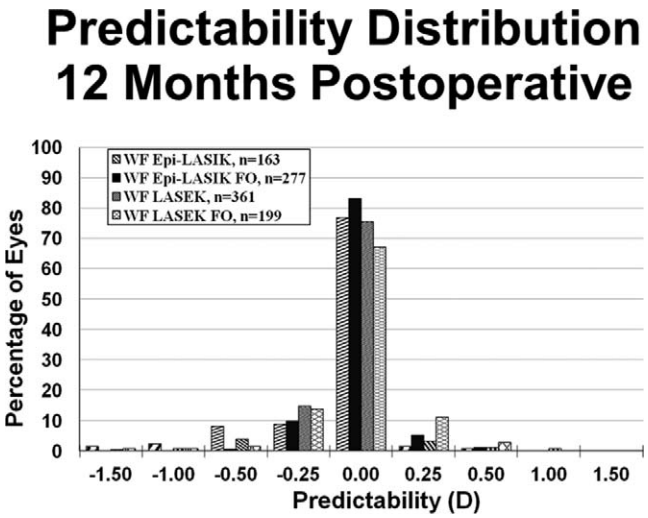

Figure 8. Predictability distribution in diopters at 12 months. Achieved MRSE was within ±0.5 D of intended in more than 95% of eyes in all treatment groups. Achieved MRSE of ±0.25 D of intended correction was attained in 86% to 97% of eyes. No statistically significant difference between the groups was found.

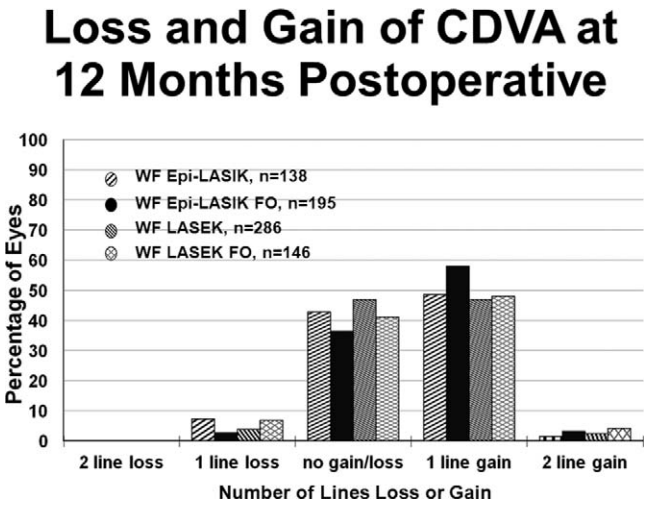

Figure 9. Changes in Snellen lines of CDVA at 12 months. No eyes in any of the groups lost more than one line of vision. No statistically significant difference between the groups was found.

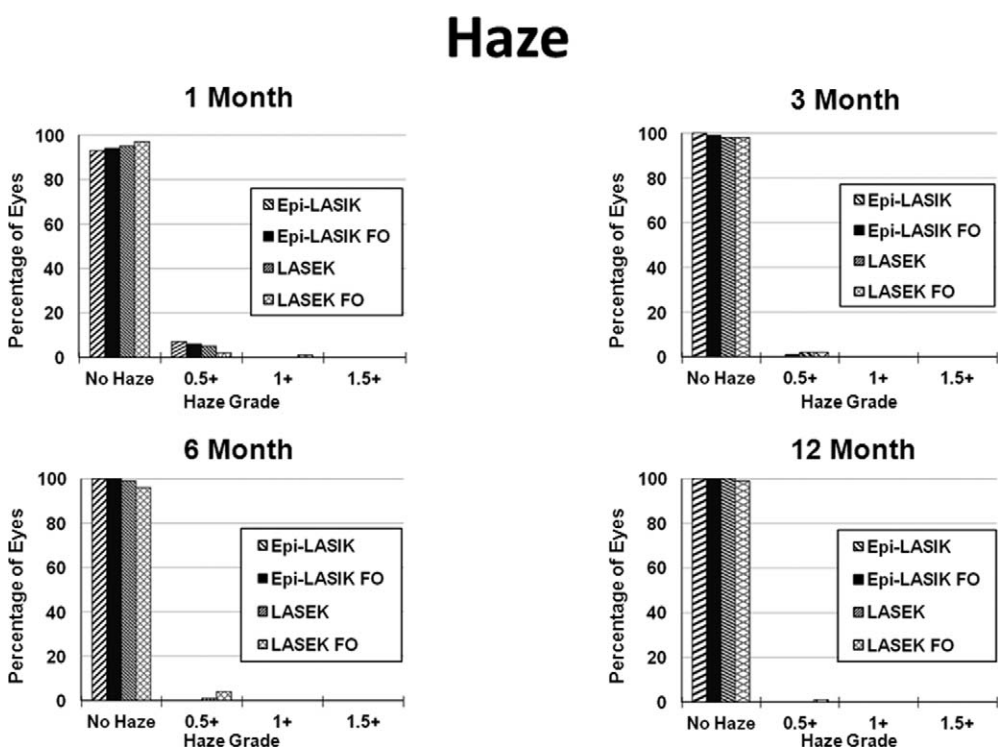

Figure 10. Comparison of haze outcomes at various points of follow-up. No statistically significant difference between the groups.

thought to be a barrier that prevents influx of inflammatory modulators toward the stroma and haze.[49,50]

In our study, no significant difference was noted in the incidence or degree of haze between any of the procedures or myopia groups at any time point in the follow-up period. Taneri et al.[8] also found no difference in haze formation between the four surface ablation techniques at 3 months. Using confocal microscopy in 55 patients (93 eyes), Chen et al.[51] showed no significant difference in stromal reaction between Epi-LASIK and Epi-LASIK FO at 1 and 2 weeks and 1, 3, and 6 months. Hondur et al.[30] found no significant difference in the incidence and degree of haze between Epi-LASIK- and LASEK-treated eyes by slit lamp and confocal microscopy at 1, 3, and 6 months. However, they did report that the incidence and severity of haze was more pronounced in the first month postprocedure.[30] This early trace haze observed at 1 month that fades by 3 to 6 months is generally attributed to the normal process of reorganization of anterior extracellular stromal matrix and deposition of new, irregular matrix material.[3]

Some authors have attributed haze formation to the preoperative degree of refractive error.[52–55] It has been proposed that with the use of newer laser technologies and smoother ablation profiles, there is less chance of haze formation.[56,57] Early PRK ablations used smaller ablation zones, with more abrupt transitions, leaving rougher surfaces that led to more haze.[58] Larger ablations with smoother transitions helped, as did variable spot scanning and variable repetition rate.[59] These result in cooler ablations with less induction of heat in the cornea.[60] In addition, MMC has been found to be effective in the prevention of corneal haze for surface ablation,[61,62] and its use is common practice among the refractive surgery community, especially for higher corrections.[47,63–67] We used MMC on 273 eyes (SE = –6.00 to –7.99 D, astigmatism $\geq$ 2.0 D) and found no significant difference either in the incidence or in the degree of haze between this group and lower myopia groups for any of the procedures.

Vitamin C prescription was also a feature of our protocol. Its positive effect on haze prevention in keratorefractive surgery has been proposed. Stojanovic et al.[68,69] have shown that ascorbate supplementation may enhance the corneal ultraviolet filtering effect and decrease keratocyte activation during and after laser treatment.

One limitation of our study is that its retrospective nature did not permit us to objectively assess epithelial healing time and patient comfort in the early postprocedure period. However, postoperative pain and slower visual recovery compared with observations after LASIK are still limiting factors for all surface ablation procedures.[20,31,70,71] Effort has been expended to overcome these by implementing various pain management strategies and optimizing surgical techniques.[40,72,73] Although ocular pain after corneal surface ablation normally ends once the epithelial defect is closed, the larger flap size (Epi-LASIK = 9 mm; LASEK = 8 mm), particularly for patients with relatively steeper corneal curvatures, has been postulated as one of the factors that might result in delayed re-epithelization.[30] Even the contact lens used may play a greater role in quicker visual recovery with less discomfort than the specific type of surface ablation in the early postoperative period.[30,74] However, the advantage of our study is that variables such as epithelial flap size, contact lens use, and surgical procedure performance were constant in this group of patients. In addition, the large sample size and the relatively long-term follow-up add further credence to our results.

In conclusion, this study demonstrates that there are no significant differences in visual and refractive outcomes at 12 months with use of four different epithelial management techniques. Notwithstanding the ongoing debates regarding the importance of retaining the flap, currently in our institution we tend to perform LASEK FO more often than the other three procedures. In our opinion, based on personal experience, the advantages are numerous. LASEK FO eliminates the use of a suction ring altogether. As a result, there is

less risk of transiently increasing intraocular pressure,[75–77] and the possibility of stromal incursion that may occur with the epikeratome[30,78] procedures is eliminated. From the patient's perspective, the procedure is appealing since the discomfort of the suction ring is avoided and the incidence of postoperative dry eye may be less because there is comparatively less damage to goblet cells[79,80] and faster re-enervation of the cornea.[3,81] From the surgeon's standpoint, the relatively easy learning curve for LASEK FO enables more fellows and residents in our teaching center to master the technique at the same time, minimizing the complication rates.

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