Original Article

Long-Term Visual and Refractive Stability and Ocular Biometric Changes after Laser-Assisted Subepithelial Keratomileusis for Correction of Myopia: An 8-Year Follow-Up

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Abstract

Purpose: To assess the long-term visual and refractive stability and ocular biometric changes in low to moderate myopic subjects treated by laser-assisted subepithelial keratomileusis (LASEK).

Methods: It is a prospective, interventional study. Included were 70 eyes of 35 patients who underwent LASEK for correction of ≤6 diopters (D) myopia. The uncorrected and corrected distance visual acuity (UDVA and CDVA), manifest refractions, and ocular biometric indices (by Lenstar-LS900, Haag-Streit AG, Koeniz, Switzerland) including keratometry, anterior chamber depth (ACD), aqueous depth (AD), axial length (AL), central corneal thickness (CCT), and lens thickness (LT) were assessed preoperatively and after 6 months and 8 years.

Results: Mean preoperative spherical equivalent was −3.99 (standard deviation [SD] =1.38) D which improved to 0.02 (SD = 0.27, $P < 0.001$) D and −0.10 (SD = 0.31, $P < 0.001$) D at 6 months and 8 years, respectively. The preoperative AL was not different from postoperative measures at 6 months ($P = 0.15$) and 8 years ($P = 0.47$). The ACD and AD decreased during 8 years, while LT increased (all $P \leq 0.001$). The changes of LT inversely correlated with changes of ACD ($r_s = -0.67$, $P = 0.001$ at 6 months and $r_s = -0.87$, $P < 0.001$ at 8 years) and AD ($r_s = -0.76$, $P < 0.001$ at 6 months and $r_s = -0.86$, $P < 0.001$ at 8 years). The CCT and keratometry values reduced at 6 months postoperatively (all $P < 0.001$) and then did not change up to 8 years ($0.21 \leq P \leq 0.87$).

Conclusions: The post-LASEK myopic regression is 0.1 D over 8 years. Ocular biometric values like keratometry, CCT, ACD, AD, and LT have been changed for a long period after LASEK in low to moderate myopia except AL.

Keywords: Biometry, Laser-assisted subepithelial keratomileusis, Lenstar, Low myopia, Optical biometry

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Introduction

With the increasing demand for perfectly clear vision in today's modern life, refractive surgery modalities have made tremendous advances in this regard. However, the challenge of predicting the refractive stability and long-term outcomes of excimer laser ablation has remained as an important area of research in this issue. Some studies reported the one- or two-decade results of photorefractive keratectomy (PRK) and laser *in situ* keratomileusis (LASIK) showing mild regression in subjects without postsurgery ectasia.[1-7] However, no study has evaluated the efficacy and safety of excimer laser-assisted subepithelial keratomileusis (LASEK) in the long-term.

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Accurate biometry is of the utmost importance in refractive surgery. Advancement in ablation profiles and modalities of treatments have drawn renewed interest in detecting the correlation between corneal changes and ocular biometric parameters with refractive stability; nevertheless, discrepancies still exist.[1,2,8,9] Despite some studies that evaluated short-term changes in ACD and AL, there is still uncertainty in terms of long-term changes in ocular biometry parameters after LASEK.[8,9]

Therefore, the purpose of the current study was to report long-term visual and refractive outcomes and ocular changes in biometric parameters following LASEK for correction of low to moderate myopia. In this context, we used an optical biometer (Lenstar LS900, Haag-Streit AG, Koeniz, Switzerland) to compare the subsequent changes and investigate the associations between these changes.

Methods

This is a prospective interventional study on patients with myopia who underwent LASEK between 2008 and 2009 at a single private outpatient center. Informed consent, institutional review board approval, and ethics committee approval were obtained (IR.IUMS.REC 1398.545). The study adhered to the tenets of the Declaration of Helsinki.

Included were patients with mild to moderate myopia ranging −1.0 to −6.0 diopters (D) and up to −5.0 D of astigmatism. Patients with previous ocular surgery, any systemic disease that may interfere with wound healing such as diabetes and collagen vascular disease, any optical opacities, severe dry eye, keratoconus, irregular astigmatism, and participants who had a follow-up of fewer than 8 years were excluded from the study.

Each study participant underwent a comprehensive ophthalmic evaluation, including manifest and cycloplegic refraction, uncorrected distance visual acuity (UDVA) based on Snellen chart, spectacle-corrected distance visual acuity (CDVA) based on Snellen chart, and slit-lamp biomicroscopy at preoperative and postoperative visits.

Ocular biometric parameters were measured by Lenstar-LS900 (Haag-Streit AG, Koeniz, Switzerland) which include corneal dioptric power in the flattest meridian (flat keratometry), corneal dioptric power in the steepest meridian (steep keratometry), mean corneal power (mean keratometry), axial length (AL), anterior chamber depth (ACD), aqueous depth (AD), central corneal thickness (CCT), and lens thickness (LT) preoperatively, as well as 6 months, and 8 years postoperatively. At least five measurements were captured for each patient under mesopic conditions (3 candelas/m^2), and the mean of these was used in the final analysis. The users of soft and/or hard contact lenses stopped wearing contact lenses for at least 2 days and 2 weeks before measurements, respectively. Furthermore, the efficacy index was defined as the ratio of the postoperative UDVA to the preoperative CDVA. The safety index was calculated as the ratio of the postoperative CDVA to the preoperative CDVA. Visual acuities changed to Snellen to calculate safety and efficacy ratios.

All surgical procedures were performed by the first author (S.J.H.) under topical anesthesia using 0.5% tetracaine eye drop (Anestocaine; Sina Darou, Tehran, Iran). Prep and drape were done by povidone-iodine (BacterBye 10% povidone iodine; Kishmedipharm, Kish, Iran) after blepharostat placement and followed by conjunctival sac irrigation using normal saline. Alcohol 20% diluted in balanced salt solution (BSS) was instilled inside an 8.5 mm trephine which was centered on the pupil and left for 20 s. A cellulose sponge was used to remove alcohol, and the ocular surface was irrigated copiously with BSS. After that, the cornea was dried with a surgical sponge, and the epithelial flap was peeled back with spatula leaving a hinge at the 12 o'clock position. After drying the stromal bed with a sponge and setting the eye tracker at the center of the pupil, ablation was performed with TECHNOLAS 217P Excimer Laser (Bausch and Lomb Inc., Rochester, NY, USA) using Advanced Personalized Technology nomogram. The optical zone was 6.5 mm in all cases. Then a surgical sponge soaked in mitomycin C 0.02% was inserted over the ablated zone of the stroma for 15 s cautiously to prevent any leakage of the mitomycin C. After copious irrigation of the stromal bed with BSS, the epithelial flap was replaced. Postoperatively, a bandage contact lens (AIR Optix AQUA; Base Curve: 8.6, Diameter: 14.2; CIBA VISION) was fitted. Ciprofloxacin 0.3% eye drop (Sina Darou, Tehran, Iran) was administered four times a day for 5 days. Fluorometholone 0.1% eye drop (Sina Darou, Tehran, Iran) was administered four times a day in the 1st month, tapering to three times a day in the 2nd month, two times a day in the 3rd month, and once daily in the 4th month. Artificial tears (Artelac™, Hypromellose; Bausch and Lomb, Montpellier, France) were administered every 4 h for 12 weeks. The bandage contact lens was removed when epithelial healing was complete (3–5 days postoperative).

Statistical analysis

Statistical analyses were performed with SPSS for Windows software version 22.0 (SPSS Inc., Chicago, IL, USA). Quantitative data were described with means (standard deviation [SD]) and percentages in continuous and numerical data, respectively. Snellen visual acuity was converted into logMAR for statistical analysis. Generalized mixed model analysis was used to account for the inclusion of both eyes from each patient, which was performed to evaluate the changes of the main outcome measures including visual acuity, refraction, and biometric values after LASEK. Laterality (right and left eyes) and time-point (preoperative, 6 months, and 8 years) variables were used as repeated measures. The linear type was selected for mixed model analysis because the distribution of all target variables in time-points was normal based on Shapiro–Wilk test (all $P > 0.05$). In model, laterality and time-point were considered for random effects and fixed effects. $P < 0.05$ were considered statistically significant.

Results

In total, 90 patients were included at the beginning of the study, among them, 35 patients (70 eyes) completed both follow-ups whose mean preoperative age was 27.63 (SD = 7.25) years (range, 19–45). The majority of patients were female (80%, 28/35).

The mean preoperative CDVA was 0.01 (SD = 0.04) logMAR which improved to 0.00 (SD = 0.00) logMAR at 6 months (P = 0.02) and 0.00 (SD = 0.02) logMAR at 8 years (P = 0.02). The postoperative UDVAs were 0.00 (SD = 0.01) logMAR and 0.02 (SD = 0.07) logMAR at 6 months and 8 years, respectively. Figures 1 and 2 show the cumulative postoperative CDVA and UDVA at 6 months and 8 years after LASEK compared with the preoperative CDVA. Nearly 90% of the eyes had no change of CDVA, postoperatively at 6 months and 8 years [Figure 3]. There were significant reductions in the spherical equivalent from −3.99 (SD = 1.38) D to 0.02 (SD = 0.27) D at 6 months (P < 0.001) that had a mild myopic shift to −0.10 (SD = 0.31) D at 8 years (P = 0.02). Although the cylindrical refraction remained stable from 6 months to 8 years (P = 0.62), the spherical refraction changed from 0.11 (SD = 0.27) D at 6 months to 0.01 (SD = 0.31) D at 8 years (P = 0.03) [Table 1].

The efficacy index was 1.02 (SD = 0.07) and 0.98 (SD = 0.13) at 6 months and 8 years after LASEK, respectively. To specify, LASEK achieved 102% of baseline spectacle corrected distance visual acuity at 6 months and 98% at 8 years. The safety index was 1.03 (SD = 0.09) at 6 months and 1.02 (SD = 0.09) at 8 years indicating 103% and 102% increase in visual acuity, respectively.

Table 1 shows the parameters related to ocular biometry. All parameters changed significantly, 6 months after LASEK except AL (P = 0.22), AD (P = 0.06), and LT (P = 0.09). Sphere (P = 0.03), spherical equivalent (P = 0.02), and LT (P = 0.01) continued to change between 6 months and 8 years after surgery. The changes of LT inversely correlated with changes of ACD (r_s = −0.67, P = 0.001 at 6 months and r_s = −0.87, P < 0.001 at 8 years) and AD (r_s = −0.76, P < 0.001 at 6 months and r_s = −0.86, P < 0.001 at 8 years). Both flat and

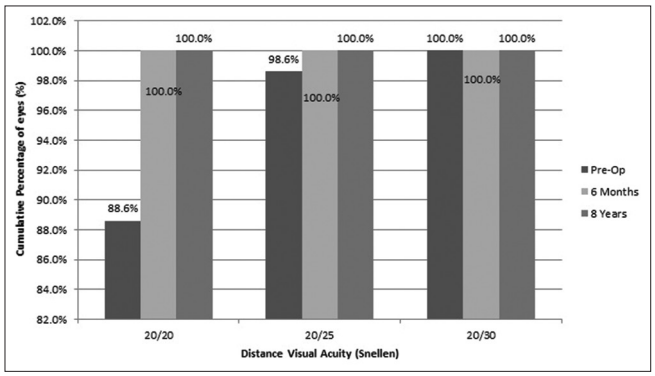

Figure 1: Cumulative preoperative and postoperative spectacle corrected distance visual acuity in laser epithelial keratomileusis

Table 1: Refractive outcome and ocular biometric measurements of 70 eyes (35 patients) at preoperative, 6 months, and 8 years following laser-assisted subepithelial keratomileusis

Variables	Baseline, mean (SD)	6 months			8 years			
		Mean (SD)	Coefficient (95% CI)§	P*,†	Mean (SD)	Coefficient (95% CI)§	P*,†	P*,‡
Refractive error								
Sphere (diopter)	−3.62 (1.35)	0.11 (0.27)	3.73 (3.41 - 4.06)	<0.001	0.01 (0.31)	3.62 (3.30 - 3.95)	<0.001	0.03
Cylinder (diopter)	−0.75 (0.68)	−0.19 (0.29)	0.56 (0.39 - 0.74)	<0.001	−0.22 (0.32)	0.54 (0.36 - 0.71)	<0.001	0.62
Spherical equivalent (diopter)	−3.99 (1.38)	0.02 (0.27)	4.01 (3.68 - 4.35)	<0.001	−0.10 (0.31)	3.90 (3.67 - 4.24)	<0.001	0.02
Flat keratometry (diopter)	42.87 (1.54)	40.24 (1.95)	−3.35 (−3.93 - −2.76)	<0.001	40.28 (1.62)	−3.15 (−3.70 - −2.60)	<0.001	0.51
Steep keratometry (diopter)	43.99 (1.46)	41.00 (2.00)	−2.98 (−3.92 - −2.04)	<0.001	41.13 (1.71)	−2.84 (−3.37 - −2.31)	<0.001	0.77
Mean keratometry (diopter)	43.42 (1.46)	40.62 (1.96)	−2.80 (−3.73 - −1.87)	<0.001	40.70 (1.66)	−2.72 (−3.24 - −2.20)	<0.001	0.87
CCT (µm)	549.30 (28.25)	467.05 (32.47)	−82.25 (−97.86 - −66.65)	<0.001	476.94 (29.94)	−72.31 (−82.03 - −62.60)	<0.001	0.21
AL (mm)	24.92 (0.96)	24.64 (0.92)	−0.28 (−0.74 - 0.18)	0.22	24.91 (0.92)	−0.01 (−0.32 - 0.30)	0.96	0.23
ACD (mm)	3.80 (0.30)	3.63 (0.30)	−0.23 (−0.37 - −0.08)	0.004	3.54 (0.31)	−0.25 (−0.36 - −0.15)	<0.001	0.71
AD (mm)	3.25 (0.30)	3.17 (0.30)	−0.14 (−0.29 - 0.00)	0.06	3.06 (0.31)	−0.18 (−0.28 - −0.08)	0.001	0.60
LT (mm)	3.59 (0.23)	3.69 (0.26)	0.11 (−0.02 - 0.23)	0.09	3.86 (0.27)	0.28 (0.19 - 0.36)	<0.001	0.01

*Generalized mixed model linear analysis *post hoc* test with estimated marginal means, †Comparing postoperative with preoperative, ‡Comparing 6 months and 8 years postoperative follow-ups, §Estimates of fixed effects (time-points) based on generalized mixed model. CI: Confidence interval, SD: Standard deviation, ACD: Anterior chamber depth, AD: Aqueous depth, AL: Axial length, LT: Lens thickness, CCT: Central corneal thickness, D: Diopter

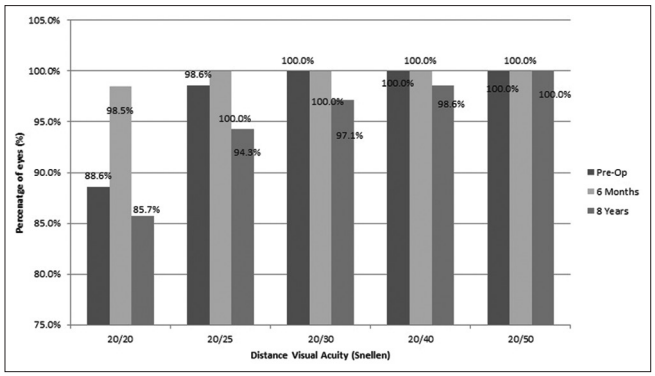

Figure 2: Cumulative preoperative spectacle corrected distance visual acuity and postoperative uncorrected distance visual acuity in laser epithelial keratomileusis

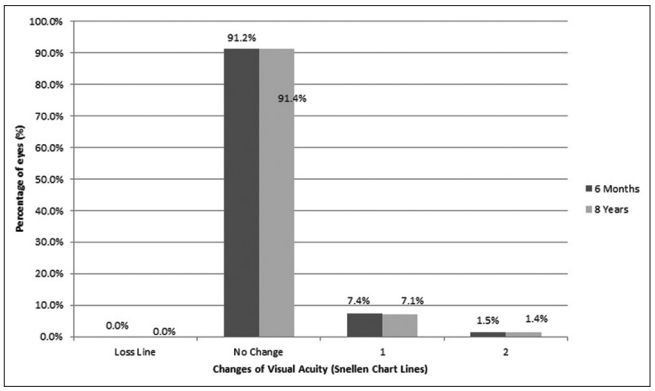

Figure 3: Changes in spectacle corrected distance visual acuity at 6 months and 8 years after laser epithelial keratomileusis

steep keratometries decreased at 6 months' follow-up, while keratometry values did not have a statistically significant change since postoperative 6 months to 8 years [Table 1]. The changes of CCT did not correlate with changes of steep (P = 0.70), flat (P = 0.06), and mean (P = 0.33) keratometries. Moreover, the amount of regression of spherical equivalent between 6 months and 8 years correlated with neither steep (P = 0.60), flat (P = 0.77), mean (P = 0.82) keratometries nor CCT (P = 0.13).

No surgical complication occurred. In addition, neither infectious keratitis nor stromal haze was observed during the follow-up.

Discussion

In this prospective study, 70 eyes with low to moderate myopia having undergone bilateral LASEK were followed for 8 years to assess the long-term stability of refractive and ocular biometric parameters. The AL was the only stable biometric parameter. The AD and ACD decreased at 8 years which correlated to the increase of LT. On the other hand, the keratometry values and CCT declined at the early postoperative phase (6 months) while they remained stable till 8 years. Similarly, the sphere value of refraction had myopic shifted between 6 months and 8 years despite significant corrections, 6 months postoperatively. However, the efficacy and safety of LASEK remained nearly 100% during 8 years.

Limited studies reported long-term (one-decade or more) results of excimer laser surface ablation procedures including LASIK and PRK for the correction of myopia.[1-7] In a 12-year study of LASIK for moderate-to-high myopia, Ikeda *et al*.[1] found a refractive regression of 0.7 D from 3 months to 12 years, postoperatively. They found a significant correlation of refractive regression with the changes in keratometry, but not with the changes in CCT from 3 months to 12 years.[1] The safety index was 1.09, 12 years after the surgery.[2] In a long-term observational case series conducted by O'Brart *et al*.[2] to evaluate the 20-year efficacy and safety of PRK, all eyes underwent −3.00 or −6.00 D corrections. The efficacy index at 20 years was 0.49, and the safety index was 0.97.[2] Similarly, a recent retrospective study reported the safety of 1.00 and the efficacy of 0.63 at a 20-year follow-up after PRK.[7] Rajan *et al*.[3] evaluated long-term refractive stability for myopic PRK and reported stability of refraction at 12 years, with no significant change in mean spherical equivalent between 1, 6, and 12 years and no late regression in the long-term.[3] Other studies of myopic refractive surgeries with PRK have also shown mild regression of <0.5 D at 10–16 years.[4-6,10] The refractive regression, efficacy, and safety of our patients were 0.1 D, 0.98, and 1.02 at 8 years, postoperatively. We did not observe any correlation between refractive regression, CCT and keratometry values. There is no other study about the long-term refractive results of LASEK to compare.

Ocular biometry is crucial in cataract and refractive surgery. Few studies investigated ocular biometry following LASEK which did not have long follow-ups.[8,9] Winkler Von Mohrenfels *et al*.[8] conducted the first study on changes of AL after LASEK using intraocular lens (IOL) Master in which no significant change of AL occurred at 1 month, postoperatively.[8] No other parameter was assessed in this study.[8] In a retrospective study, Fu *et al*.[9] did not find the significant change of mean AL (by IOL Master) in 76 eyes with high myopia and thin corneas at 3 years after LASEK. However, the CCT became thicker from 3 months to 3 years, postoperatively.[9] They did not evaluate ocular biometric parameters of the anterior chamber. Our results with longer follow-up times agreed with previous studies regarding the stability of the AL after LASEK while some reported the possible correlation between ablation depth and transient reduction of AL after corneal refractive surgery.[8,9,11,12] On the other hand, O'Brart *et al*.[2] reported two-decade results of PRK. They observed a significant increase of 0.8 mm AL (measured by IOL Master) and consequently myopic shift, at 20 years after PRK.[2] Furthermore, there was a statistically significant decrease in ACD, which was similar to the current study.[2] Stability of AD at 6 months implies that there is a bias in the measurement of the ACD with Lenstar that measures the depth from the epithelium to the anterior lens surface. Therefore, excimer ablation would lead to a false impression of a drop of ACD at

the early postoperative time, and AD would be more accurate than ACD by eliminating the effect of CCT.

The epithelium has tremendous capacity for remodeling and does so in response to underlying stromal pathology or changes in anterior corneal curvature.[13] The epithelial thickness increased 10%–20% through the remodeling process after LASIK and PRK.[13,14] This thickens the CCT, postoperatively. Our results were also in agreement with previous studies, which observed the increase of CCT after LASEK,[8] LASIK,[13] and PRK[13] ranged between 10 and 40 μm in long-term follow-ups although the changes were not statistically significant in our study.

The epithelial hyperplasia can also induce a reduction of postoperative refractive effect and regression of myopia.[13,14] The myopic shift of refraction of our patients between 6 months and 8 years might be caused by epithelial remodeling because we did not detect any subject with corneal ectasia. However, the 0.1 D of refractive regression and <0.2 D keratometry regression were not clinically important [Table 1]. Lenticular components could play an additional role in changes of refraction in the current study due to a nearly one-decade duration.

This study has some limitations. One limitation could be the small number of patients. The inclusion of mild to moderate myopia prevented the generalizability of the results to patients with high degrees of myopia with higher ablation depth which may lead to different keratometry and refractive changes. We did not have more follow-ups between 6 months and 8 years which might be helpful to draw a better picture of changes of parameters by time. Insufficient data about the epithelial thickness map limited more evaluation about the long-term epithelial remodeling and its effect on CCT, keratometry values, and regression.

In conclusion, the present study showed nearly 100% safety and efficacy of LASEK in mild to moderate myopia over an 8-year follow-up. All ocular biometry parameters changed after LASEK except AL.

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Conflicts of interest
There are no conflicts of interest.

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