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CLINICAL TRIAL REPORT

Patient-Reported Dry Eye Outcomes After Myopic Femtosecond-LASIK: A 6-Month Prospective Analysis

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Purpose: To evaluate patient-reported outcomes in relation to dry eye symptoms following femtosecond LASIK (FS-LASIK).

Methods: This study was conducted as a prospective, observational case series of patients undergoing bilateral myopic FS-LASIK at a single private practice institution. Enrolled patients were prospectively administered a standardized Dry Eye Symptom Index survey (analog score of 1 to 5 with 5 being the worst) prior to treatment and at 6-months after FS-LASIK. The following objective measurements were also recorded: objective scatter index (OSI), tear film osmolarity (TFO), and automated tear break-up times (TBUT).

Results: There were 40 enrolled patients who underwent bilateral myopic FS-LASIK and completed the 6-month study period. The Dry Eye Symptom Index score improved from 2.3 (2.0–2.6, 95% Confidence Intervals) prior to treatment to 1.3 (1.0–1.5) at 6 months ($p < 0.0001$). Subset analysis of the subjective dry eye symptoms showed improvement in "grittiness" ($p = 0.001$) but not in "light sensitivity" or "soreness" ($p = 0.13$ and $p = 0.24$, respectively). There were no significant changes in the OSI, TFO, or TBUT measurements at 6 months ($p > 0.05$ for all), and there were no adverse events or complications during the study period.

Conclusion: Patient-reported dry eye symptoms improve after 6 months following myopic FS-LASIK. This did not correlate with the objective dry eye measurement changes at 6 months.

Keywords: LASIK, tear film osmolarity, tear break-up time, patient-reported outcomes, dry eye

Introduction

Dry eye symptoms are the most frequent complication reported after LASIK and may develop transiently in almost every patient in the early postoperative period.[1,2] However, the long-term incidence has been reported quite variably with a range of <1% up to 40% at 6-months follow-up.[3,4] Preexisting dry eye symptoms prior to LASIK are the most significant risk factors for dry eye symptoms after LASIK, and preoperative questionnaires and examination findings such as tear film break-up times, Schirmer testing, corneal staining, and corneal sensation testing have been employed to assess patient risk.[5,6] However, despite numerous reports, there still exists controversy regarding the clinical significance of abnormal objective ocular surface measurements. Other risk factors for post-LASIK dry eye symptoms have been associated with larger ablation depths, history of contact lens intolerance, Asian ancestry, a superior hinge location (versus a nasal location), and mechanical microkeratome techniques which usually cut deeper flaps relative to femtosecond lasers.[7,8]

The medical sciences have increasingly acknowledged the value of patient-reported outcomes during the past two decades, and the authors concur that such outcomes allow the surgeon an opportunity to provide a more complete and holistic approach to patient care.[9,10] Limited prospective patient-reported dry eye symptom outcomes following LASIK presently exist in the literature. The Patient-Reported Outcomes with LASIK Symptoms and Satisfaction (PROWL) survey is a well-defined and validated questionnaire for evaluating patient satisfaction following LASIK.[11,12] In this study, the

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authors assess patient-reported outcomes and satisfaction in regard to dry eye symptom changes following femtosecond LASIK (FS-LASIK) using a modified PROWL survey specifically tailored for evaluating change in dry eye symptoms.

Methods

This prospective observational study was undertaken according to the tenets of the Helsinki Declaration and was compliant with the Health Insurance Portability and Accountability Act of 1996. The Panhandle Eye Group Institutional Review Board (IORG0009239; IRB00011013-13) approved the conduct of this study, and written informed consent was obtained from all participants. The study was registered at clinicaltrials.gov. (NCT04903301, last accessed May 2023) prior to subject enrollment. Participants received care from September 2021 through October 2022 at a single private practice facility in Amarillo, TX.

The criteria for inclusion were comprised of the following: 1) subject age of 21–35 years, 2) a myopic spherical equivalent ranging from −1.00 to −9.00 diopters, 3) a refractive astigmatism ranging from 0 to 3 diopters, 4) a best-corrected distance visual acuity (CDVA) of 20/20 or better for both eyes, and 5) the calculated post-treatment residual stromal bed was >300 microns. The criteria for exclusion consisted of the following: 1) the subject had a history of ocular surgery, 2) ocular surface disease, 3) corneal disease (ie dystrophy, keratoconus, scarring, etc.) was clinically evident, 4) posterior segment disease (ie diabetic retinopathy, glaucoma, etc.) was clinically evident, and/or 5) the subject had a history of systemic autoimmune disease.

Enrolled subjects underwent bilateral FS-LASIK using a standardized, on-label Contoura® Vision (Alcon Vision, LLC; Fort Worth, TX, USA) technique with the Wavelight FS200 and Wavelight EX500 laser platforms (Alcon Vision, LLC; Fort Worth, TX, USA) as reported by Stulting et al.[13] The flap parameters were all cut with a superior hinge to a depth that ranged from 90 to 110 microns and a diameter from 8.8 to 9.0 mm. Study data was collected preoperatively at baseline and then postoperatively at 1 week (+/- 2 days), 1 month (+/- 1 week), 3 months (+/- 2 weeks), and 6 months (+/- 4 weeks). All patient data was de-identified and stored on a password-protected Microsoft Excel spreadsheet.

Patients were administered a standardized Dry Eye Symptom Index survey derived from the PROWL questionnaire.[11,12] In brief, this survey consisted of a subjective analog score of 1 to 5 (with 5 indicating the most severe symptoms) and included a subset questionnaire regarding the presence or absence of “gritty”, “light sensitive”, and “sore” symptomatology. Objective dry eye measurements included the Objective Scatter Index (OSI) using the Visiometrics HD Analyzer (Keeler, Malvern, PA, USA), tear film osmolarity (TFO) using the TearLab Osmolarity System (Trukera Medical, Southlake, TX, USA), and the automated tear break-up times (TBUT) using the VX 120+ (Visionix, Bensenville, IL, USA). The OSI measures the optical quality of the eye using a double-pass technique with a laser diode. In the non-cataractous eye, it can detect subtle ocular surface abnormalities not visible at the slit lamp or on corneal topography. The VX 120+ dry eye module detects movements of Placido disc rings on the ocular surface in between blinks to determine tear break-up times without the use of fluorescein. The dry eye surveys, visual acuity measurements, and refractions were performed by the same individual in all instances (CJP).

Study Outcomes and Data Analysis

The primary outcome was change in the Dry Eye Symptom Index survey from baseline to 6-months post-LASIK. The secondary outcomes were change in OSI, TFO, and automated TBUT from baseline to 6-months post-LASIK.

A sampling of the first 10 enrolled patients completing the study’s 6-month follow-up interval produced a standard deviation of 0.5 for the Dry Eye Symptom Index. Difference to detect was determined to be 0.25 (50% of the sampling standard deviation), resulting in 36 subjects as the minimum number required to complete the study’s follow-up interval. Once 36 subjects completed the follow-up interval, enrollment ceased and the subjects already enrolled and treated were permitted to complete follow-up and therefore be included in the data analysis. The JMP 11 software from the SAS Institute (Cary, NC, USA) was used to calculate means and standard deviations. The means were compared using one-way analysis of the variance for numerical outcomes and likelihood ratios for nonparametric outcomes. Statistical significance was at an alpha level of <0.05. Snellen visual acuity was converted into logMAR for the purpose of statistical analysis.

Results

There were 52 patients encountered that met study eligibility of which 43 were enrolled and underwent bilateral FS-LASIK. Of the 43 treated patients, 40 completed the 6-month study period and therefore were included in the data analysis (93% (40/43) completion rate). The 3 treated patients not completing the study period were lost-to follow-up and could not be brought back for data collection and therefore expelled from the analysis of the data.

The baseline characteristics and demographic features of the study population are displayed in Table 1. No adverse events or intra-operative complications occurred during the FS-LASIK treatment session for each patient.

Primary Outcome

The Dry Eye Symptom Index score improved from 2.3 (2.0–2.6) at baseline to 1.3 (1.0–1.5) at 6 months follow-up ($p < 0.0001$). Subset analysis of the subjective dry eye symptoms improved in "grittiness" ($p = 0.001$) but not in "light sensitivity" or "soreness" ($p = 0.13$ and $p = 0.24$, respectively). These findings are summarized in Table 2.

Table 1 Dry Eye Outcomes After Myopic FS-LASIK. Distributions of Baseline Characteristics and Demographic Features for the Study Population

Preoperative Characteristics and Demographics (N = 40 Patients)	**Means with (Standard Deviations)**
Age (years)	30.1 (3.8) Range = 22 to 35
Gender	Male = 14 (35.0%) Female = 26 (65.0%)
Ethnicity	White = 32 (80.0%) Hispanic = 6 (15.0%) Black = 1 (2.5%) Asian = 1 (2.5%)
Contact Lens User	Yes = 30 (75.0%) No = 10 (25.0%)
Binocular Best-corrected distance visual acuity (logMAR)	−0.10 (0.05)Range = −0.2 to 0
Mean Manifest Refraction Spherical Equivalent (diopters)	−3.39 (1.58)Range = −7.88 to −0.88
Mean Manifest Refraction Refractive Astigmatism (diopters)	0.94 (0.66)Range = 0 to 2.63

Table 2 Dry Eye Outcomes After Myopic FS-LASIK. Pre- and Postoperative Comparative Analysis of the Dry Eye Symptom Index

Outcome Measure (N = 40 Patients)	**Preoperative Means at Baseline with (95% Confidence Intervals)**	**Postoperative Means at 6-Months with (95% Confidence Intervals)**	**p-value**
Dry Eye Symptom Index (patient-reported analog score of 1 to 5 with 5 being the worst)	2.3 (2.0–2.6)	1.3 (1.0–1.5)	$p < 0.0001$
Dry Eye Subset			
• Gritty?	Yes = 17.5% No = 82.5%	Yes = 0.0% No = 100.0%	$p = 0.001$
• Light Sensitive?	Yes = 22.5% No = 77.5%	Yes = 10.0% No = 90.0%	$p = 0.13$
• Sore?	Yes = 2.5% No = 97.5%	Yes = 0.0% No = 100.0%	$p = 0.24$

Secondary Outcomes

There was worsening for the OSI at the 1-week postoperative visit, but no significant change was observed at 6-months ($p = 0.20$). There were no significant changes in the TFO ($p = 0.51$) or either of the automated TBUT measurements ($p = 0.27$ and $p = 0.51$, respectively) at any of the time points assessed. These outcomes are summarized in Table 3 and are presented as a graphical representation in Figure 1.

Refractive Outcomes

The mean binocular uncorrected distance visual acuity at 6-months post-LASIK was −0.20 (0.06) logMAR (Snellen 20/12.5). All 40 patients (100%) had binocular uncorrected distance visual acuity equal to or better than 20/16 (−0.1 logMAR), 34 patients (85.0%) had binocular uncorrected distance visual acuity equal to or better than 20/12.5 (−0.2 logMAR), and 6 patients (15.0%) had binocular uncorrected distance visual acuity equal to or better than 20/10 (−0.3 logMAR). The mean preoperative binocular CDVA was −0.10 (−0.12 to −0.09) logMAR as compared to the mean 6-month postoperative uncorrected distance visual acuity of −0.20 (−0.22 to −0.18) logMAR ($p < 0.0001$). Mean 6-month postoperative absolute spherical equivalent was 0.02 (0.11) diopters, and the mean 6-month postoperative refractive astigmatism was 0.20 (0.17) diopters. There were no postoperative complications observed during the study, and no patients underwent an enhancement during the 6-month study period.

Discussion

Subjective and objective worsening of dry eye signs and symptoms following LASIK have been reported, and researchers have demonstrated that afferent sensory nerve fibers from the trigeminal nerve may be damaged during flap creation.[14–16] This neuropathy may result in a decreased blink reflex, diminished lacrimal gland function, and increased inflammation with release of cytokines and other immune mediators.[17,18] Other contributing mechanisms may include damage to goblet cells of the conjunctiva.[19] Administration of various preoperative subjective surveys and objective tests such as tear film break-up times, Schirmer testing, corneal staining, and corneal sensation testing have been reported with often conflicting results,[5,6] and controversy concerning the clinical significance of such abnormal objective ocular surface measurements exists presently. The objective dry eye measurements remained largely unchanged at the 6-month follow-up visit compared to baseline in this study. Other authors have substantiated this finding with respect to TFO,[20] but minimal data exists using OSI and automated TBUT.

To our knowledge, this is the first prospective case series reporting a net improvement in patient-reported dry eye symptoms after LASIK as opposed to merely a trend back to baseline. The significance of this finding is that the abnormal objective clinical findings of the ocular surface associated with LASIK, especially in the early postoperative period, do not correlate with overall long-term patient satisfaction and visual well-being. This has important implications when discussing the risks and benefits of LASIK with the patient. Most clinicians educate patients about the risk of dry eye symptoms and chronic dry eye conditions,[21] but the patient-reported outcomes in this study suggest that the clinician

Table 3 Dry Eye Outcomes After Myopic FS-LASIK. Pre- and Postoperative Comparative Analysis of Objective Dry Eye Assessments

Outcome Measure (N = 40 Patients)	**Preoperative Means at Baseline with (95% Confidence Intervals)**	**Postoperative Means at 6-Months with (95% Confidence Intervals)**	**p-value**
Objective Scatter Index (analog score)	0.48 (0.42–0.53)	0.52 (0.47–0.58)	p = 0.24
Tear Film Osmolarity (mOsm/L)	303.3 (300.5–306.0)	302.0 (299.2–304.7)	p = 0.51
Automated Tear Break-up Times (seconds) • First Tear Break-up Time • Average Tear Break-up Time (three consecutive measurements)	 5.7 (4.6–6.8) 8.3 (7.6–9.1)	 6.5 (5.4–7.6) 9.2 (8.4–10.0)	 p = 0.27 p = 0.15

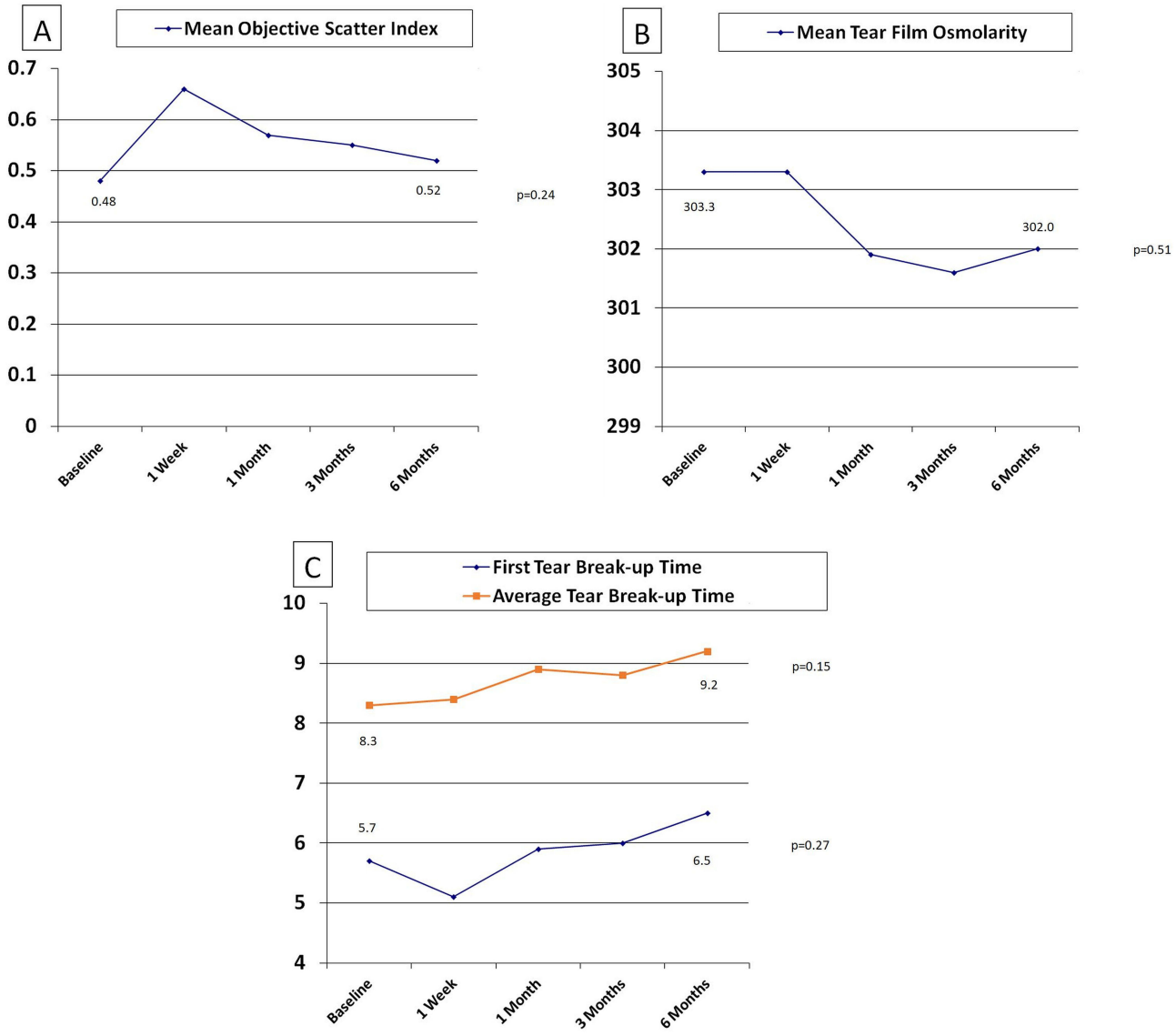

Figure 1 Objective Dry Eye Study Outcomes after Myopic FS-LASIK. (**A**) Objective Scatter Index. The line graph plots the change in objective scatter indices by analog score (Y) over time (X). (**B**) Tear Film Osmolarity. The line graph plots the change in mean tear film osmolarity in mOsm/L (Y) over time (X). (**C**) Automated Tear Break-up Times. The line graph plots the change in first and average tear break-up times in seconds (Y) over time (X).

may be able to discuss decrease of dry eye symptoms as a potential benefit of LASIK. This finding stands in stark contrast to some previous studies which suggest that symptoms for dry eye (using the McMonnies questionnaire) increased and did not recover after both LASIK and PRK.[22]

Alternative refractive treatments to LASIK such as PRK or SMILE have been associated with less abnormal dry eye findings postoperatively,[23,24] but these have not correlated well to improved patient satisfaction or enhanced quality of life. The detection and treatment of dry eye and meibomian gland disease prior to LASIK is a critical factor in the prevention of post-LASIK dry eye symptoms,[25] as any corneal refractive surgery has the potential to temporarily disrupt the tear film and result in chronic decompensation of the ocular surface. The positive patient-reported outcomes of this study were likely influenced by the eligibility criteria which included only patients with healthy ocular surfaces. The authors believe the best clinical practice is to screen out patients with unstable ocular surfaces from receiving corneal-based refractive procedures altogether.

Strengths of this report include its prospective design, its excellent subject retention following enrollment, use of automated objective measurements not prone to observer bias, being adequately powered for statistical significance, its

application of a validated patient-reported outcome survey, and its relatively long follow-up period post-refractive surgery. The major weakness of this study resides in its absence of a control or comparison cohort. Given the poor correlation of objective dry eye symptoms to patient-reported dry eye symptoms, future investigations should be performed to further validate our study's findings, and refractive surgery outcomes should focus more on patient-reported measurements to determine the most effective refractive treatments that provide the highest degree of satisfaction and quality of life with the least amount of adverse side effects. In conclusion, patient-reported dry eye symptoms improve after 6 months following myopic FS-LASIK, and these subjective outcomes correlate poorly with the objective dry eye measurement changes at 6 months.

Abbreviations

FS-LASIK, femtosecond laser in situ keratomileusis; CDVA, best-corrected distance visual acuity; UDVA, uncorrected distance visual acuity; PROWL, patient-reported outcomes with LASIK; OSI, Objective Scatter Index; TFO, tear film osmolarity; TBUT, tear break-up time.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Statement

The study was approved by the Panhandle Eye Group Institutional Review Board (IORG0009239; IRB00011013-13) in accordance with the Ethical Standards laid down in the Declaration of Helsinki.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

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Disclosure

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