Femtosecond Small Incision Lenticular Extraction in comparison to Femtosecond Laser In situ Keratomileusis Regarding Dry Eye Disease

Najah Kadhum Mohammad¹, Suzan Rattan², Ahmed Shaker Ali Al Wassiti¹, Zaid Al-Attar²*

¹Department of Surgery and Ophthalmology, Baghdad College of Medicine, University of Baghdad, Baghdad, Iraq; ²Department of Pharmacology, Al-Kindy College of Medicine, University of Baghdad, Baghdad, Iraq

Abstract

BACKGROUND: The objective was comparison of femtosecond small incision lenticule extraction (FS-SMILE) versus Femtosecond laser in situ keratomileusis (FS-LASIK) regarding dry eye disease (DED) and corneal sensitivity (CS) after these refractive surgeries.

AIM: The difference between FS-SMILE and FS-LASIK regarding dry eye symptoms, signs, and corneal sensitivity post-refractive surgeries in two groups of matched patients.

METHODS: A comparative prospective study was conducted for a period of 2 years, from March 2017 to February 2019. Enrolled patients were diagnosed with myopia. Fifty patients (100 eyes) were scheduled for bilateral FS-SMILE and the other 50 patients (100 eyes) were scheduled for bilateral FS-LASIK. Both groups were followed for 6 months post surgery. The age, gender, and pre-operative refraction for both groups were matched. Complete evaluation of dry eye disease had been performed at regular intervals. The evaluation included history of symptoms according to scoring systems, investigations, and clinical examination. The authors have declared that no competing interests exist.

RESULTS: One month postoperatively and in both groups, there was significant DED (p < 0.01), although incidence was lower in femtosecond SMILE group, overall severity score (0–4): 0.3 ± 0.3 (FS-SMILE) versus 1.4 ± 0.9 (LASIK). One month postoperatively, CS was lower in FS-SMILE eyes (2.3 ± 2.2 vs. 3.6 ± 1.8, respectively, p < 0.01) and then shifted to non-statistically significant sensitivities at 6-month duration. DED was negatively correlated with CS (p < 0.01).

CONCLUSIONS: The FS-LASIK surgery had a more pronounced effect on CS and DED compared with FS-SMILE, with higher incidence of DED post-refractive surgery.

Introduction

Recently, introduced femtosecond small-incision lenticule extraction (FS-SMILE) is a procedure that gathered numerous benefits, like FS laser that is used for fashioning a corneal intrastromal lenticule that is removed manually through a small (2–7 mm length) peripheral corneal incision [1, 2]. This relatively new technique does not require a flap, which, in turn, reduces some flap related side effects of FS-LASIK, such as dislocation and related astigmatism [2, 3]. Dry eye continues to be the most frequent adverse effect after LASIK. Mild to severe ocular surface dryness symptoms are experienced by many patients, after LASIK, that are adequately controlled using artificial tears. If symptoms keep to be reported for long duration, 20–40% of patients may develop chronic dry eye disease (DED) 6 months postoperatively [4]. Proposed factors that cause DED post LASIK include corneal nerves disruption during creating the flap, in addition to damage by the excimer laser photo ablation [5]. The vast majority of factors reported to be involved in the pathogenesis of DED, such as tear secretion, quality of tear-film, healing of the epithelium of the cornea, and the rate of blinking, all could be affected post-refractive LASIK procedures [6]. The SMILE operation constitutes a minimally invasive refractive surgery for the cornea, because it merely requires a small tunnel, with less associated damage to corneal nerves, thus further protection for patients against DED [7]. Clinical studies had reported refractive results, CS, and clinical ocular surface dryness post SMILE surgeries, but nothing else has been done to estimate the overall severity of the dryness, which demands integrating objective tests along with symptoms reported subjectively by patients, as recommended by Delphi [7]. The current study aimed to investigate the difference between FS-SMILE and FS-LASIK regarding dry eye symptoms, signs, and corneal sensitivity post-refractive surgeries in two groups of matched patients.
Material and Method

Study design and setting
A comparative prospective interventional study conducted at the Refractive Surgery Center of Al Istishari Hospital, Baghdad, Iraq for a period of 20 months from March 1, 2017, to October 31, 2018.

Study population
The included patients had bilateral eyes with spherical correction range from -2 to -6 diopters and cylinder range from 0 to -3.5 diopters and seeking for management and willing to participate in this study.

Exclusion criteria
Patients presented with sign or symptom of dry eye disease (tear film breakup time (TBUT) >10 s, Schirmer I test >10 mm/5 min), corneal or conjunctival staining, Meibomian gland dysfunction, previous ocular or eye lid medical or surgical treatment, and pregnancy and chronic systemic disorder were excluded from the study.

Sample size
The sample size was calculated according the two proportions formula:

\[ N = \frac{(Z_{\alpha/2} + Z_\beta)^2(p_{\text{SMILE}}(1-p_{\text{SMILE}}) + p_{\text{LASIK}}(1-p_{\text{LASIK}}))}{(p_{\text{SMILE}} - p_{\text{LASIK}})^2} = 80.38 \]

where \( Z_{0.025} \) equals 1.96 for confidence level of 95%, \( Z_{0.1} \) equals 1.28 for a power of 90%, and \( p_{\text{SMILE}} \) and \( p_{\text{LASIK}} \) were the expected prevalence of dry eye after 6 months in corresponding groups and were reported by Denoyer et al. (2015) to be 20% and 43% [8], respectively. The estimated sample size was increased to 100 eyes in each group to avoid dropouts and increase study power. Patients were assigned into two age, gender, and spherical equivalent matched equal groups:

- FS-SMILE Group: 100 eyes of 50 patients who underwent bilateral FS-SMILE.
- FS-LASIK Group: 100 eyes of 50 patients underwent bilateral FS-LASIK.

Study outcomes
All patients participated in this study attended the follow-up periods of 1 and 6 months post-refractive surgery. Outcomes were assessed using Ocular Surface Disease Index (OSDI) (0-100), Tear Break-Up Time (TBUT) (in seconds), Schirmer I test (ST-1) (in mm/5 min), Oxford score (0-5), and Dry Eye Workshop (DEWS) scale (0-4).

Ethical considerations
After the approval of Ethical Committee of Al-Istishari Hospital, informed written consent was gained from each participant, which included adequate information regarding the aim and methods of the current study.

Materials
Anterior segment spectral-domain OCT was done by (Canon, HS 100, TOKYO, JAPAN), Corneal esthesiometry, slit lamp, Fluorescein paper, and Whitnall paper.

Method/Evaluation of Dry Eye Disease

Clinical examination
All the examinations were performed 1 week preoperatively, 1 and 6 months after the surgery. The post-operative clinical examination was done by another ophthalmologist, who was masked to type of performed procedure and administered the OSDI for all patients for assessing the exact impact of DED on vision and related quality of life [9]. DEWS severity was evaluated according to an overall index (from 0 to 4) and including symptoms and signs [1], [10].

Corneal esthesiometry was performed 1 and 6 months postoperatively. The sensitivity of the cornea was measured using contact nylon thread [Cochet, Bonnet esthesiometer]. Measurements were taken and data reported as the mean of three measurements at the center of the cornea.

Investigations
1. Anterior segment OCT was done 6 months after the date of surgery. Two images of each cornea were acquired with apex measurement of corneal thickness, epithelial thickness, and the interface depth.
2. Slit-lamp examinations were conducted in a defined sequence [11] and included three TBUT measurements and their calculated mean, and the Oxford score which incorporated fluorescein staining and graded from 0 to 5.
3. ST-1 in mm per 5 min, without topical anesthesia.

Surgical technique
All surgeries were performed by single experienced surgeon under topical anesthesia [Tetracaine eye drop 0.5%] using the following technique:
Results

This study enrolled a total of 200 eyes that underwent refractive correction with no adverse effects reported among them. No statistically significant differences were found between the two study groups regarding age, sex, spherical equivalent myopia, and morphologic parameters as total corneal thickness (TCT), epithelial thickness, and the interface depth, as shown in Table 1.

DED 1 and 6 months postoperatively

Preoperatively, there were no statistically significant differences regarding DED between the two study groups. After 6 months, OSDI and DEWS scale were significantly lower in FS-SMILE group than that in FS-LASIK group (8.0 vs. 5.8, p < 0.01, respectively), while TIBUT was significantly higher in FS-SMILE group than that in FS-LASIK group (0.07 ± 0.1 vs. 0.07 ± 0.1, p < 0.05) (Table 2).

The distribution of the severity of dry eye disease 1 and 6 months after SMILE versus LASIK is detailed in Table 3. One month after the surgery, there was not statistically difference between the two groups p > 0.05.

Six months postoperatively, quality of life and tear film quality were significantly better in the FS-SMILE group compared with the FS-LASIK group. Worse scores of DED were found in FS-LASIK group p <0.05 (Tables 2 and 3). Seventy six percent of patients in FS-SMILE group stopped using any eye drops at 6 months postoperatively compared to 52% in FS-LASIK group. No patients in FS-SMILE group needed any tear substitutes 6 months after surgery versus 18% of the FS-LASIK group who needed four times daily instillation of artificial tears even gels (Figure 1).
Corneal sensitivity postoperatively

Corneal sensitivity was reduced in both groups 1 month after the surgery, but FS-LASIK eyes showed lower sensitivity than FS-SMILE eyes (p < 0.01). Six months postoperatively, there was no statistical difference between the two groups, and both returned to normal, p > 0.05 (Table 4).

Table 4: Corneal sensitivity postoperatively as measured by the Cochet-Bonnet esthesiometer

| Corneal sensitivity (cin) | Study group | P value |
|-------------------------|-------------|--------|
|                         | SMILE       | LASIK  |
| One month postoperatively | 3.6 ± 1.8   | 2.3 ± 2.2 | <0.01>0.05 |
| Six months postoperatively | 5.8 ± 0.2   | 5.6 ± 0.3 |

Discussion

The present study was designed comprehensively regarding the approach to DED following the two refractive surgical modalities, demonstrating an increment in symptoms (OSDI score), and signs (TIBUT) 6 months postoperatively in both FS-SMILE and FS-LASIK groups. Thus, there were lower values on these scales in patients treated with FS-Lasik compared to FS-SMILE for 6 months postoperatively, as some authors have reported [12], [13], [14], although ocular signs are often found to be highly variable, as pointed out by Feng et al. [6] Using a self-reported symptoms, questionnaire reported that 40% of the patients after LASIK believed that their eyes became dryer than before the surgery, Shah et al. [15] Recently, Li et al. [16] compared FS-Smile and FS-Lasik for ocular surface dryness and reported a better TIBUT and OSDI in eyes treated with the former compared with eyes treated with the latter, also reported that the patients who had LASIK used eye drops more frequently for prolonged times, which might negatively affect the quality of life and the costs of these drops in this young population. In LASIK, flap creation and damage to sub-basal nerves contributes as a main, but not exclusively as a cause for ocular dryness. While, in SMILE procedures, more innervation in protected as it creates only a 40°–60° – wide penetrating corneal tunnel, in comparison to about 300° in LASIK. From the starting of refractive surgeries, studies had reported a significant decrement in CS following LASIK, which probably lasts for months or even years, even if the flap was created by femtosecond laser [17], [18], [19], [20], [21]. Recent clinical studies reported that SMILE preserved CS in comparison to LASIK [16], [22], [23], [24]. In the present study, CS significantly decreased compared to pre-operative values at 1 month postoperatively after LASIK, which went back to normal at 6 months in both groups, these were comparable to results of Demirok et al. [23].

Labbé et al. [25] reported that after 6 months, the CS was not different compared to healthy controls that suggest a stepwise recovery of the normal physiology in both procedures. In LASIK, there was reduced nerve density in the cornea over the long-term [17], [26], [27], while SMILE preserved the density as reported in the previous studies [8], [28].

The post-operative corneal reinnervation is highly variable, and the duration ranges from 3 months to 5 years according to different studies[29]. Another factor in LASIK might be the pathological increment in tear osmolarity, which seems not to occur in SMILE [29], [30], this might suggest that the post-operative dryness is usually a combination of neurogenic and inflammatory mechanisms [31].

Increased density of ocular surface dendritic cells was found 6 months after Lasik, which further support the role of inflammatory process in DED [8]. Tear cytokine measurement as inflammatory mediator could be better way for analyzes these inflammatory processes [31].

Epithelial thickness assessment by OCT at the center of the cornea did not show any difference between FS-SMILE and FS-LASIK groups 6 months post-operative. In the present study, bilateral surgery for each patient was performed using similar technique; thus, it was possible to perform inter-individual comparisons. Patients undergone LASIK or SMILE, which were matched and paired by age, gender, and refraction, this design might create a limitation compared with a paired-eye approach (one eye operated by SMILE and their fellow eye operated by LASIK). Good understanding of the pathogenesis involved in ocular dryness after corneal photorefractive surgery is a vital issue for two important reasons. First, to know the severity and impact of post-operative ocular dryness on quality of life and influenced the development of novel refractive procedures such as SMILE. Second, for determining the risk factors for post-operative DED and further comprehending the indications for each refractive procedure.

Limitations of the study

The present study reported significantly lower CS in the FS-LASIK group in comparison to the FS-SMILE group at 1 month following the surgery but not at 6 months, although some improvement to the outcomes of the study could be done by optimizing how to assess CS, like, incorporating a non-contact esthesiometer, and by recording the blinking rate and tear clearance, but the lack of appropriate equipment made it not possible. Other limitations were small sample size and the relatively short follow-up period of 6 months. The approach in the present study may be regarded as a limitation since the paired eye approach may be more disguised method for comparison, but it is not easily accepted by most patients.
Conclusions

This study demonstrated that FS-SMILE significantly decreased the incidence of ocular dryness disease in comparison to FS-LASIK in comparable samples postoperatively with normal pre-operative ocular surfaces. A time-dependent recovery of the normal ocular surface variables in the two procedures had been noticed 6 months post-operative.

References

1. Sekundo W, Kunert KS, Blum M. Small incision corneal refractive surgery using the small incision lenticule extraction (SMILE) procedure for the correction of myopia and myopic astigmatism: Results of a 6 month prospective study. Br J Ophthalmol. 2011;95(3):335-9. https://doi.org/10.1136/bjo.2009.174284 PMid:20601657

2. Ivarsen A, Asp S, Hjortdal J. Safety and complications of more than 1500 small incision lenticule extraction procedures. Ophthalmology. 2014;121(4):822-8. https://doi.org/10.1016/j.ophtha.2013.11.006 PMid:24365175

3. Piñero DP, Teus MA. Clinical outcomes of small-incision lenticule extraction and femtosecond laser-assisted wavefront-guided laser in situ keratomileusis. J Cataract Refract Surg. 2016;42(7):1078-93. https://doi.org/10.1016/j.jcrs.2016.05.004 PMid:27492109

4. Chao C, Golebiowski B, Stapleton F. The role of corneal innervation in LASIK-induced neuropathic dry eye. Ocul Surf. 2014;12(1):32-45. https://doi.org/10.1016/j.joso.2013.09.001 PMid:24439045

5. Calvillo MP, McLaren JW, Hodge DO, Bourne WM. Corneal reinnervation after LASIK: Prospective 3-year longitudinal study. Invest Ophthalmol Vis Sci. 2004;45(11):3991-6. https://doi.org/10.1167/iovs.04-0561 PMid:15505047

6. Feng YF, Yu JG, Wang DD, Li JH, Huang JH, Shi JL, et al. The effect of hinge location on corneal sensation and dry eye after LASIK: A systematic review and meta-analysis. Graefes Arch Clin Exp Ophthalmol. 2013;251(1):357-66. https://doi.org/10.1007/s00417-012-2078-5 PMid:22722222

7. Behrens A, Doyle JJ, Stern L, Chuck RS, McDonnell PJ, Azar DT, et al. Dysfunctional tear syndrome: A Delphi approach to treatment recommendations. Cornea. 2006;25(8):900-7. https://doi.org/10.1097/01.ico.0000214802.40313.fa PMid:17102664

8. Denooyer A, Landeman E, Trinh L, Faure JF, Aucelin F, Baudouin C. Dry eye disease after refractive surgery: Comparative outcomes of small incision lenticule extraction versus LASIK. Ophthalmology. 2015;122(4):669-76. https://doi.org/10.1016/j.ophtha.2014.10.004 PMid:25458707

9. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the ocular surface disease index. Arch Ophthalmol. 2000;118(5):615-21. https://doi.org/10.1001/archopht.118.5.615 PMid:10815152

10. The definition and classification of dry eye disease: Report of the definition and classification subcommittee of the international dry eye workshop (2007). Ocul Surf. 2007;5(2):75-92. https://doi.org/10.1016/s1542-0124(12)70081-2 PMid:17508116

11. Smith J, Nichols KK, Baldwin EK. Current patterns in the use of diagnostic tests in dry eye evaluation. Cornea. 2008;27(6):656-62. https://doi.org/10.1097/QAI.0b013e3181e05b95 PMid:18580256

12. Toda I, Asano-Kato N, Komai-Hori Y, Tsubota K. Dry eye after laser in situ keratomileusis. Am J Ophthalmol. 2001;132(1):1-7. https://doi.org/10.1016/s0002-9394(01)00959-x PMid:11438046

13. Lee JB, Ryu CH, Kim J-H, Kim EK, Kim HB. Comparison of tear secretion and tear film instability after photorefractive keratectomy and laser in situ keratomileusis. J Cataract Refract Surg. 2000;26(9):1326-31. https://doi.org/10.1016/s0886-3350(00)00566-6 PMid:11020617

14. Battat L, Macri A, Dursun D, Pfugfelder SC. Effects of laser in situ keratomileusis on tear production, clearance, and the ocular surface. Ophthalmology. 2001;108(7):1230-5. https://doi.org/10.1016/s0161-6420(01)00623-6 PMid:11425680

15. Shah R, Shah S, Sengupta S. Results of small incision lenticule extraction: All-in-one femtosecond laser refractive surgery. J Cataract Refract Surg. 2011;37(1):127-37. https://doi.org/10.1016/j.jcrs.2010.07.033 PMid:21183108

16. Li M, Zhao J, Shen Y, Li T, He L, Xu H, et al. Comparison of dry eye and corneal sensitivity between small incision lenticule extraction and femtosecond LASIK for myopia. PLoS One. 2013;8(10):e77797. https://doi.org/10.1371/journal.pone.0077797 PMid:24204971

17. Linna TU, PÉRez-Santonja JJ, Tervo KM, Sakla HF, Tervo TM. Recovery of corneal nerve morphology following laser in situ keratomileusis. Exp Eye Res. 1998;66(6):755-63. https://doi.org/10.1016/0014-4835(98)00149-x PMid:9657908

18. Benitez-del-Castillo JM, del Rio T, Iradier T, Hernández JL, Castilla A, García-Sanchez J. Decrease in tear secretion and corneal sensitivity after laser in situ keratomileusis. Cornea. 2001;20(1):30-2. https://doi.org/10.1097/00003226-200101000-00005 PMid:11188999

19. Patel SV, McLaren JW, Kittleson KM, Bourne WM. Subbasal nerve density and corneal sensitivity after laser in situ keratomileusis: Femtosecond laser vs mechanical microkeratome. Arch Ophthalmol. 2010;128(11):1413-9. https://doi.org/10.1001/archophthalmol.2010.253 PMid:21060042

20. Petznick A, Chew A, Hall RC, Chan CM, Rosman M, Tan D, et al. Comparison of corneal sensitivity, tear function and corneal staining following laser in situ keratomileusis with two femtosecond laser platforms. Clin Ophthalmol. 2013;7:591-8. https://doi.org/10.2147/OPHTA.S42266 PMid:23576858

21. Kanellopoulos AJ, Pallikaris IG, Donnenfeld ED, Detorakis S, Koufala K, Perry HD. Comparison of corneal sensation following photorefractive keratectomy and laser in situ keratomileusis. J Cataract Refract Surg. 1997;23(1):34-8. https://doi.org/10.1016/s0886-3350(97)80148-4 PMid:9100105

22. Wong AH, Cheung RK, Kua WN, Shih KC, Chan TC,
Wan KH. Dry eyes after SMILE. Asia Pac J Ophthalmol (Phila). 2019;8(5):397-405. https://doi.org/10.1097/01.APO.0000580136.80338.d0
PMid:31490199

23. Demirok A, Ozgurhan EB, Agca A, Kara N, Bozkurt E, Cankaya KI, et al. Corneal sensation after corneal refractive surgery with small incision lenticule extraction. Optom Vis Sci. 2013;90(10):1040-7. https://doi.org/10.1097/OPX.0b013e31829d9026
PMid:23939296

24. Wei S, Wang Y. Comparison of corneal sensitivity between FS-LASIK and femtosecond lenticule extraction (ReLEx flex) or small-incision lenticule extraction (ReLEx smile) for myopic eyes. Graefes Arch Clin Exp Ophthalmol. 2013;251(6):1645-54. https://doi.org/10.1007/s00417-013-2272-0
PMid:2389552

25. Sonigo B, Iordanidou V, Chong-Sit D, Auclin F, Ancel JM, Labbe A, et al. In vivo corneal confocal microscopy comparison of intralase femtosecond laser and mechanical microkeratome for laser in situ keratomileusis. Invest Ophthalmol Vis Sci. 2006;47(7):2803-11. https://doi.org/10.1167/iovs.05-1207
PMid:16799017

26. Lee BH, McLaren JW, Erie JC, Hodge DO, Bourne WM. Reinnervation in the cornea after LASIK. Invest Ophthalmol Vis Sci. 2002;43(12):3660-4.
PMid:12454033

27. Zhang F, Deng S, Guo N, Wang M, Sun X. Confocal comparison of corneal nerve regeneration and keratocyte reaction between FS-LASIK, OUP-SBK, and conventional LASIK. Invest Ophthalmol Vis Sci. 2012;53(9):5536-44. https://doi.org/10.1167/iovs.11-6786
PMid:22786909

28. Gallar J, Acosta MC, Molianen JAO, Holopainen JM, Belmonte C, Tervo TMT. Recovery of corneal sensitivity to mechanical and chemical stimulation after laser in situ keratomileusis. Journal of Refractive Surgery. 2004;20(3):229-35.

29. Rodriguez AE, Rodriguez-Prats JL, Hamdi IM, Galal A, Awadalla M, Alio JL. Comparison of goblet cell density after femtosecond laser and mechanical microkeratome in LASIK. Invest Ophthalmol Vis Sci. 2007;48(6):2570-5. https://doi.org/10.1167/iovs.06-1259
PMid:17525186

30. Kacerovska J, Kacerovsky M, Hlavackova M, Studeny P. Change of tear osmolarity after refractive surgery. Cesk Slov Oftalmol. 201874(1):18-22.
PMid:30541292

31. Leonardi A, Tavolato M, Curnow SJ, Fregona IA, Violato D, Alió JL. Cytokine and chemokine levels in tears and in corneal fibroblast cultures before and after excimer laser treatment. J Cataract Refract Surg. 2009;35(2):240-7. https://doi.org/10.1016/j.jcrs.2008.10.030
PMid:19185237