ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.5336/ophthal.2022-95060

Comparison of Ocular Surface Changes Following Laser-Assisted in Situ Keratomileusis and Photorefractive Keratectomy: Cross-Sectional Study

Lazer Yardımlı İn Situ Keratomileusis ve Fotorefraktif Keratektomi Sonrası Oküler Yüzey Değişikliklerinin Karşılaştırılması: Kesitsel Çalışma

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ABSTRACT Objective: To compare the ocular surface changes following Femtosecond laser in situ keratomileusis (Femto-LASIK) and photorefractive keratectomy (PRK). **Material and Methods:** TThis prospective study included 74 eyes of 37 patients: 34 were in the Femto-LASIK group, and 40 were in the PRK group. Schirmer test, tear break-up time, and conjunctival impression cytology (CIC) were used to determine ocular surface changes before and 1 month, and 3 months after PRK or Femto-LASIK. **Results:** There were no significant differences between PRK and LASIK group in mean CIC scores in the first month ($p > .05$, for each). However, a significant difference observed at goblet cell density (GCD) at the third month between PRK and LASIK group ($p = 0.008$). Comparing of the CIC scores between first month and the third month of PRK group showed significant improvements in the GCD and epithelial cell sheet ($p = 0.005$, $p = 0.001$, respectively). However, no significant changes occurred in the Femto-LASIK group between first month and the third month ($p > .05$, for each). **Conclusion:** We observed histopathological changes in the perilimbal conjunctiva in the PRK and LASIK groups at the first month after surgery. It was observed that these changes continued in the 3rd postoperative month. Although GCD improved significantly in the PRK group, it was still lower than preoperatively. We can say that these changes play a primary role in the pathogenesis of dry eye and even cause a more severe course of DED in LASIK patients.

Keywords: Conjunctival impression cytology; Femto-LASIK; PRK; Schirmer test; Tear break-up time

ÖZET Amaç: emtosaniye lazer in situ keratomileusis (Femto-LASIK) ve fotorefraktif keratektomi (PRK) sonrası oküler yüzey değişikliklerini karşılaştırmak. **Gereç ve Yöntemler:** Bu prospektif çalışmaya Femto-LASIK grubunda 34, PRK grubunda 40 olmak üzere toplam 37 hastanın 74 gözü dahil edildi. PRK veya Femto-LASIK öncesi, 1. ay ve 3. aydaki oküler yüzey değişikliklerini belirlemek için Schirmer testi, gözyaşı kırılma zamanı ve konjonktival impresyon sitolojisi (KİS) kullanıldı. **Bulgular:** PRK ve LASIK grubu arasında, ortalama KİS skorlarında birinci ayda anlamlı fark yoktu (her biri için $p > .05$). Ancak üçüncü aydaki goblet hücre dansitesinde (GHD) PRK ve LASIK grubu arasında anlamlı bir fark gözlendi ($p = 0.008$). PRK grubunun birinci ay ile üçüncü ay arasındaki KİS skorlarının karşılaştırılması, GHD ve epitel hücre tabakasında anlamlı iyileşmeler gösterdi (sırasıyla $p = 0.005$, $p = 0.001$). Ancak Femto-LASIK grubunda birinci ay ile üçüncü ay arasında anlamlı bir değişiklik olmadı (her biri için $p > .05$). **Sonuç:** Ameliyat sonrası 1. ayda PRK ve LASIK gruplarında perilimbal konjonktivada histopatolojik değişiklikler gözlemledik. Ameliyat sonrası 3. ayda bu değişikliklerin devam ettiği görüldü. GHD, PRK grubunda önemli ölçüde iyileşmesine rağmen, yine de preoperatif dönemden daha düşüktü. Bu değişikliklerin kuru göz patogenezinde birincil rol oynadığı ve hatta LASIK hastalarında kuru göz hastalığının daha ağır seyretmesine neden olduğu söylenebilir.

Anahtar Kelimeler: Konjonktival impresyon sitolojisi; Femto-LASIK; PRK; Schirmer testi; gözyaşı kırılma zamanı

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Peer review under responsibility of Turkiye Klinikleri Journal of Ophthalmology.

Received: 24 Dec 2022 ***Received in revised form:*** 14 Apr 2023 ***Accepted:*** 22 May 2023 ***Available online:*** 26 May 2023

Femtosecond laser in situ keratomileusis (Femto-LASIK) and photorefractive keratectomy (PRK) are the 2 most widely used corneal refractive surgeries.[1] With advancements in technology, both are safe, effective, and highly satisfactory for patients.[2] The surgical method selection is primarily determined by the patient's degree of refractive error and corneal morphology.

Despite high patient satisfaction and high success rates following both procedures, complications such as dry eye disease (DED) can occur.[3,4] DED, encompassing aqueous deficiency, meibomian gland dysfunction, and blepharitis, is the most encountered complication after corneal refractive surgery.[3-5] Dry eye is an adverse effect of keratorefractive surgery, which damages the corneal sensory nerves responsible for driving tear production.[3-5] Post refractive surgery, DED can significantly impair quality of life, disrupt daily activities, and even cause refractive regression.[3-5] Its reported incidence is high immediately after refractive surgery procedures and diminishes over time. Recovery can occur, but in some cases, the preoperative state cannot be reached even after a year.[4,5]

The effect of refractive surgery on the ocular surface can be demonstrated by conjunctival impression cytology (CIC).[6,7] Ryan et al. studied goblet cell density (GCD) and mucus secretion following LASIK and PRK, finding significant changes in the GCD after both. The authors found no difference in goblet cell mucin secretion.[7] However, they did not evaluate the cell-to-cell adhesion, morphology of conjunctival goblet cells and inflammatory cells, nuclear changes (type and frequency), tendency to keratinization, or degree of squamous metaplasia (nucleo/cytoplasmic correlation).

The primary purpose of this investigation was to evaluate the early postoperative impacts of Femto-LASIK and PRK on the ocular surface parameters of epithelial integrity, epithelial keratinization, squamous metaplasia, nuclear changes, GCD, and mucus morphology via CIC. This study also evaluated the recovery of these parameters over 3 months.

MATERIAL AND METHODS

This cross-sectional, prospective clinical study was implemented on patients who underwent Femto-LASIK or PRK in the department of ophthalmology of a tertiary hospital between June 2018 and June 2021. Written informed consent was obtained from the patients before enrollment. The study was conducted following the Declaration of Helsinki. The Bezmiâlem Vakıf University Clinical Research Ethics Committee (date: October 7, 2020, no: 71306642-050.05.04-) authorized the study.

Patients with a myopic refractive status who underwent either Femto-LASIK or PRK were included in the study. Patients with any of the following conditions were not eligible: cornea, conjunctiva, or eyelid abnormality; uveitis; nystagmus; strabismus; secondary ocular or systemic disease causing DED; history of any systemic disease; chronic ocular drug use; previous ocular surgery or trauma; use of topical medication or receipt of radioactive iodine treatment within the previous 4 months and 1 year, respectively. Those who did not cooperate fully throughout the evaluations were also excluded.

PRK and Femto-LASIK were performed under topical anesthesia with proparacaine hydrochloride 0.5% by the same surgeon (KO). For PRK, the epithelium was removed with alcohol, and excimer ablation was then carried out using the WaveLight EX500 excimer laser (Alcon Laboratories, Inc., Fort Worth, TX, USA). A drop of antibiotic and diclofenac 0.1% was administered, and a therapeutic contact lens was placed on the eye after the procedure. To perform the LASIK procedure, a WaveLight FS-200 femtosecond laser (Alcon Laboratories, Inc., Fort Worth, TX, USA) was used to create a flap with a superior-hinged 9.0-mm diameter and a thickness of 120 mm. After laser ablation, the flap was carefully repositioned and refloated using a balanced salt solution. The patients were then evaluated during the postoperative first week, first month, and third month.

Each patient underwent a comprehensive ophthalmologic examination, which included a measurement of their best corrected visual acuity using the Snellen chart, intraocular pressure measurement, biomicroscopic anterior segment examination, and

fundoscopic evaluation. An automatic refractor keratometry (Canon RFK2, Japan) was used to measure the refraction.

Preoperatively and at the 1-month and 3-month postoperative intervals, the tear breakup time (TBUT) was tested and analyzed, followed by the Schirmer test with topical anesthesia, and then CIC specimens were collected. The tests were separated by an hour so that they would not interfere with one another.

To evaluate the TBUT, a fluorescein strip was applied to the lower fornix with a drop of physiological saline. The patient was requested to blink, then situated for slit lamp examination and requested not to blink while staring straight ahead. During the cobalt blue corneal observation, the amount of time that had passed since the last blink before the cornea reached its initial dry point was measured to calculate the TBUT. We recorded the mean of three consecutive measurements. Ten seconds or less was considered favorable for DED. After applying a 0.5% proparacaine hydrochloride drop (Alcaine, Alcon, USA), the Schirmer test was conducted. After 3 minutes, a piece of filter paper (5 mm x 30 mm) was positioned over the intersection of the temporal and medial thirds of the lower eyelid margin to prevent the conjunctival fornix from touching the cornea. The patient looked upward throughout the examination if possible, allowing normal blinking. Wetting was measured in mm 5 minutes after the paper insertion.

CIC was applied according to Nelson et al.[8] The temporal bulbar conjunctiva was sampled. Each sample was pretreated with 0.5% proparacaine. Three minutes after anesthetic instillation, tiny plates of filter paper made of cellulose acetate with 0.025-mm pores were carefully positioned on the corneal limbus-adjacent conjunctiva. The obtained filter paper was rapidly preserved in a 95% alcohol/1% formalin fixation solution. The samples were then assessed cytologically at the university hospital's histology and embryology department. Under a light microscope (Leica DM6000B, Leica, Germany), hematoxylin and periodic acid-Schiff-stained (Merck Millipore PAS staining kit, M101646.0001) CIC samples were examined. A Leica DC 500 camera (Leica DC 500, Leica, Germany) was subsequently used to transfer the images to a computer. Five randomly selected areas were photographed from each sample. Following the study of Haller-Schober et al., under 40x magnification in 5 different locations, the following ten morphological parameters were evaluated, and their severity was independently rated on a scale from 0 (normal) to 3 (highly pathological): degree of squamous metaplasia (nucleo/cytoplasmic correlation), quality of cell-to-cell adhesion (epithelial cell sheet confluent or not), nuclear changes (type and frequency) and morphology, tendency to keratinization, and inflammatory cell and conjunctival GCD.[9]

To standardize the tests and eliminate the possibility of diurnal variation, all the tests were conducted under identical physiological conditions and by a single physician. The evaluations were performed in a room with controlled humidity, temperature, airflow, and dim lighting to avoid ocular surface stress.

STATISTICAL ANALYSIS

The data were studied on a computer using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Mean±standard deviation (minimum-maximum) was used to describe the data. Categorical variables were analyzed using Pearson's chi-square test and the one-sample chi-square test. Visual (histogram and probability graph) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests) were employed to examine the variables' adherence to the normal distribution. Independent sample t-tests were performed on normally distributed data to compare the LASIK and PRK groups, and the Mann-Whitney U test was performed on non-normally distributed data. A paired t-test was used to compare the preoperative and postoperative data of each group. A p-value of <0.05 was considered statistically significant.

RESULTS

This study included 74 eyes of 37 patients: 34 were in the Femto-LASIK group, and the remaining 40 were in the PRK group. The mean age of the PRK and Femto-LASIK patients was 25.9±2.9 years and 23.3±4.8 years, respectively. Both groups had similar refractive errors, ages, gender balances, and mean corneal thickness values ($p>0.05$ for each). Table 1 contains information regarding the demographics and clinical manifestations of the patients.

TABLE 1: Demographic and clinical characteristics of the participants.

	PRK group (n=40)	LASIK group (n=34)	p value
Age, years (X̄±SD)	25.4±2.9	23.3±4.8	0.119*
Female/male (n/n)	8/12	4/13	0.319**
Refractive error, SE, D (X̄±SD)	-3.11±-0.66	-3.23±-0.66	0.589*
Central corneal thickness, µm (X̄±SD)	543.2±23.0	546.2±24.7	0.702*

*Independent sample t-test; **Chi-square test; PRK: Photorefractive keratectomy; LASIK: Laser in situ keratomileuses; SD: Standard deviation; SE: Spherical equivalent; D: Diopters.

Table 2 and Table 3 present a comparison of the Schirmer score and TBUT between groups and the changes in these results. Despite no statistically significant differences between the groups preoperatively or at the postoperative first or third month (p>0.05 for each), the Schirmer score and TBUT of PRK and LASIK were significantly reduced at the first and third month compared to the preoperative values (p<0.05 for each). A significant improvement was observed in Schirmer values between the postoperative first and third months for the PRK and LASIK groups (p=0.041, p=0.041, respectively). The TBUT values also significantly improved (p=0.035, p=0.025, respectively).

Table 4 shows a comparison of CIC parameters between groups and the changes in these scores over 3 months. No significant differences in mean CIC scores existed between the PRK and LASIK groups in the first month (p>0.05 for each). However, a significant difference was observed in GCD at the third month between the PRK and LASIK groups (p=0.008). Comparing the CIC scores of the PRK group between the first and third month showed significant improvements in the GCD and epithelial cell sheet (p=0.005, p=0.001, respectively). However, no significant changes occurred in the Femto-LASIK group between the first and third month (p>0.05 for each). The preoperative and postoperative CIC samples in the Femto-LASIK and PRK groups are presented in Figure 1, Figure 2, and Figure 3.

DISCUSSION

Post-refractive surgery DED has become important because these procedures are now so common. A

TABLE 2: Comparison of Schirmer's and TBUT parameters between groups.

	PRK group (n=40)			LASIK group (n=34)			p value		
	Preoperative	Postoperative 1st month	Postoperative 3rd month	Preoperative	Postoperative 1st month	Postoperative 3rd month	P1*	P2*	P3*
Schirmer test, mm (X̄±SD)	14.21±3.27	7.21±2.16	8.55±3.52	14.12±5.12	7.55±2.80	8.90±3.15	0.752	0.598	0.688
TBUT, sn (X̄±SD)	13.13±3.23	7.18±3.97	9.28±3.11	12.98±3.27	7.35±2.25	9.50±1.20	0.698	0.725	0.791

P1: Comparison of preoperative results between groups; P2: Comparison of postoperative 1st-month results between groups; P3: Comparison of postoperative 3rd-month results between groups; *Independent samples t-test, p<0.05 is statistically significant; TBUT: Tear break up time; PRK: Photorefractive keratectomy; LASIK: Laser in situ keratomileuses; SD: Standard deviation; sn: seconds.

TABLE 3: Change of Schirmer's and TBUT parameters in both groups.

	Preoperative	Postoperative 1st month	Postoperative 3rd month	p value P1*	P2*	P3*
PRK group (n=40)						
Schirmer test, mm (X̄±SD)	14.21±3.27	7.21±2.16	8.55±3.52	**0.001**	**0.005**	**0.041**
TBUT, sn (X̄±SD)	13.13±3.23	7.18±3.97	9.28±3.11	**0.001**	**0.015**	**0.035**
LASIK group (n=34)						
Schirmer test, mm (X̄±SD)	14.12±5.12	7.55±2.80	8.90±3.15	**0.001**	**0.042**	**0.041**
TBUT, sn (X̄±SD)	12.98±3.27	7.35±2.25	9.50±1.20	**0.001**	**0.031**	**0.025**

P1: Comparison of preoperative- postoperative 1st month results at each group; P2: Comparison of preoperative- postoperative 3rd month results each group; P3: Comparison of postoperative 1st month-postoperative 3rd month results in each group; *Paired t-test, p<0.05 is statistically significant; TBUT: Tear break up time; PRK: Photorefractive keratectomy; SD: Standard deviation; sn: Seconds; LASIK: Laser in situ keratomileuses.

TABLE 4: Comparison of conjunctival impression cytology parameters between groups.

	PRK group (n=40)			LASIK group (n=34)			p value			
	Preoperative	Postoperative 1st month	Postoperative 3rd month	Preoperative	Postoperative 1st month	Postoperative 3rd month	P1*	P2*	P3¥	P4¥
Epithelial cell sheet	---	0.82±0.63	0.41±0.50	---	0.60±0.75	0.30±0.47	0.341	0.492	**0.001**	0.080
Degree of squamous metaplasia 1/4 nucleocytoplasmic ratio (N/C)	---	0.52±0.79	0.29±0.46	---	0.30±0.57	0.15±0.36	0.317	0.302	0.102	0.261
Degree of keratinization	---	0.58±0.50	0.41±0.50	---	0.75±0.55	0.65±0.48	0.362	0.156	0.080	0.337
Nuclear changes frequency	---	0.35±0.60	0.17±0.39	---	0.30±0.57	0.15±0.36	0.786	0.833	0.181	0.268
Nuclear changes type	---	0.29±0.58	0.17±0.39	---	0.35±0.67	0.15±0.36	0.791	0.833	0.160	0.215
Goblet cell density	---	1.88±0.99	1.00±0.70	---	1.85±0.74	1.60±0.59	0.911	**0.008**	**0.005**	0.566
Goblet cell morphology	---	0.04±0.04	0.01±0.01	---	0.30±0.92	0.20±0.61	0.190	0.190	0.156	0.602
Mucus amount	---	0.11±0.33	0.17±0.39	---	0.05±0.22	0.05±0.022	0.466	0.228	0.330	0.890
Mucus morphology	---	0.05±0.05	0.01±0.01	---	0.04±0.05	0.01±0.05	0.941	0.952	0.141	0.665
Inflammatory cells	---	0.08±0.10	0.02±0.10	---	0.20±0.41	0.10±0.30	0.053	0.190	0.222	0.160

*Independent samples t-test; ¥Paired t-test, p<0.05 is statistically significant; P1: Comparison of postoperative 1st month results between groups; P2: Comparison of postoperative 3rd month results between groups; P3: Comparison of postoperative 1st month-postoperative 3rd month results in PRK group; P4: Comparison of postoperative 1st month-postoperative 3rd month results in the LASIK group; PRK: Photorefractive keratectomy; LASIK: Laser in situ keratomileuses.

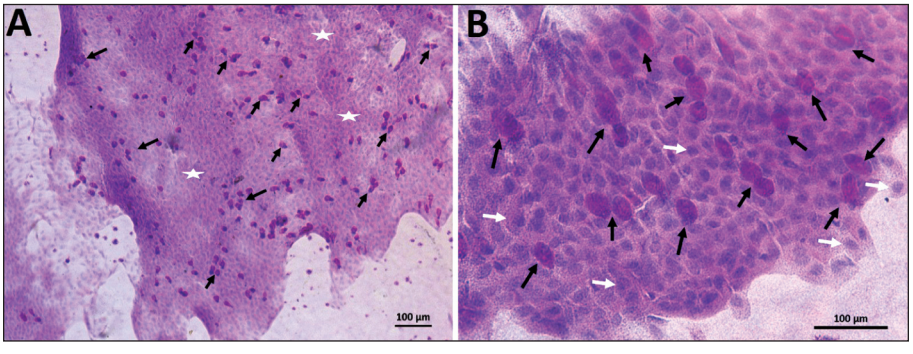

FIGURE 1: Preoperative LASIK group; **A:** Black arrows: goblet cells (normal number and morphology), stars: intact epithelial cell layer, **B:** black arrows: goblet cells (in normal number and morphology), white arrows: epithelial cells (PAS+Hematoxylin, A: X10, B: X40).
LASIK: Laser in situ keratomileuses; PAS: Periodic Acid-Schiff.

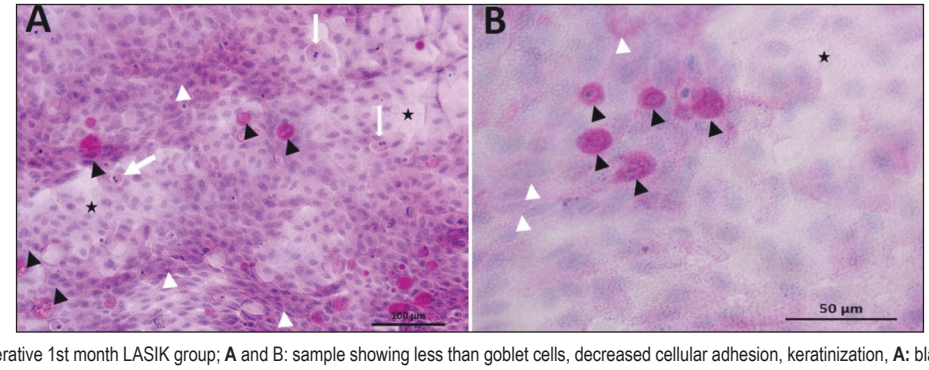

FIGURE 2: Postoperative 1st month LASIK group; **A** and B: sample showing less than goblet cells, decreased cellular adhesion, keratinization, **A:** black star: cellular area with reduced adhesion, black arrowheads: abnormal goblet cells, white arrowheads: epithelial cell area with a low degree of cakes; **B:** black arrowheads: abnormal goblet cells, white arrowheads: epithelial cell area that is low-level keratinized, black star: the cellular area where adhesion is reduced (PAS+Hematoxylin, A and B: X20).
LASIK: Laser in situ keratomileuses; PAS: Periodic Acid-Schiff.

multifactorial ocular surface disorder associated with inflammation and hyperosmolarity, DED may impair the patient's life severely in the early postoperative period.[10] It has been shown that 95% of DED symptoms are seen on the first day post LASIK, and 85% of patients continued to experience symptoms during

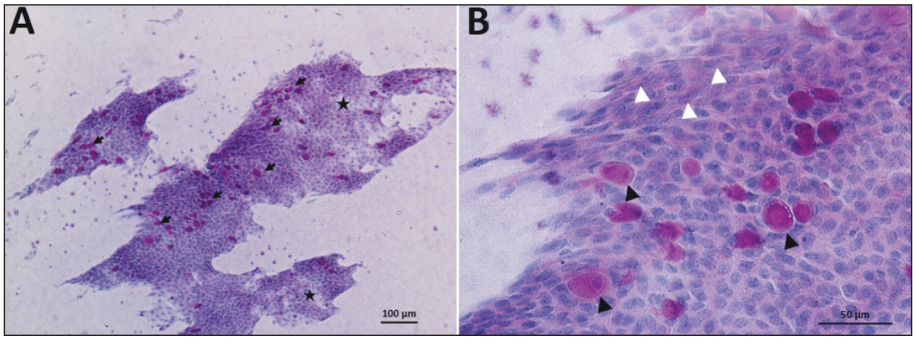

FIGURE 3: Postoperative 1st month PRK group; **A** and **B**: sample with fewer goblet cells with decreased cellular adhesion. **A:** black star: cellular area with reduced adhesion, black arrows: goblet cells; **B:** black arrowheads: abnormal goblet cells, white arrowheads: poorly keratinized epithelial cell area (PAS+Hematoxylin, **A:** X10, **B:** X40). PRK: Photorefractive keratectomy; PAS: Periodic Acid-Schiff.

the first postoperative week.[11] At the first postoperative month, 60% of patients complain of DED. Symptoms decrease over time, with prevalence ranging from 12% to 48% at 6 months.[11-13] Similar results have been reported for patients undergoing PRK, except in the early postoperative period, which causes severe ocular surface discomfort.[14,15] In this prospective study, we evaluated tear production, stability (using the Schirmer test and TBUT), and ocular surface parameters in patients who underwent Femto-LASIK and PRK.

DED can result from deficient tear secretion by the lacrimal and accessory glands and decreased stability of tears on the ocular surface. Damage to the corneal nerve bundles impairs tear secretion via denervation of the lacrimal gland.[16,17] Reduced GCD is also associated with decreased ocular surface stability.[18-20] Schirmer and TBUT values are indirect estimations of tear secretion and tear stability, respectively. According to studies evaluating these tests, 60% of LASIK patients experienced a significant decrease in Schirmer values during the first month compared to preoperative values.[11] A significant decrease in the TBUT at the first week and first month post procedure has also been detected.[11] Ozdamar et al. showed significantly lower Schirmer and TBUT values, by 28% and 31%, respectively, when comparing the operative eye with the inoperative eye in unilateral PRK patients.[21] Similarly, Siganos et al. demonstrated a reduction in Schirmer and TBUT values that remained unchanged over a 1-, 3-, and 6-month follow-up period.[22] We also found a significant reduction in Schirmer and TBUT values in the first and third months when compared with preoperative values in both the Femto-LASIK and PRK groups. Comparing PRK and LASIK in terms of Schirmer and TBUT values has previously shown significantly lower values in post-LASIK patients at 3 months compared with post-PRK patients, with differences resolving by 6 months.[23] Comparison between Femto-LASIK and PRK patients in our study showed no significant difference in the first and third months. We did not evaluate late postoperative results, so we could not assess the patients at 6 months.

Because the cornea is highly innervated, the subepithelial nerve transection resulting from the flap creation can damage those nerves in LASIK patients. The loss of sensation impacts the corneal lacrimal gland, corneal blinking, and blinking meibomian gland reflexes, likely to result in reduced aqueous and lipid tear secretion and mucin expression.[4] Moreover, meibomian lipid secretion is mainly controlled by blinking reflexes. Loss of corneal sensitivity causes a decreased blink rate, which inhibits meibomian gland secretion and results in tear evaporation and delayed tear clearance.[4] In PRK, only nerve endings that reach the basal epithelium are ablated, so corneal sensitivity loss is seen less often compared to LASIK.[5] However, both surgeries similarly affected the Schirmer and TBUT test results in our study. This suggests that some other factors may be associated with DED in refractive surgery.

Reduced GCD and changes in other ocular surface cells are other pathologic mechanisms of DED

following LASIK and PRK. A study by Boira Cabre et al. that evaluated the CIC in patients undergoing LASIK showed an increase in the cytoplasm, a decrease in nuclear size, a change in the nucleus-cytoplasm ratio, and a significant decrease in the degree of squamous metaplasia and GCD.[20] Albietz et al. evaluated PRK, LASIK without ocular surface management, and LASIK with ocular surface management in terms of CIC.[19] They found a significant reduction in GCD, with the greatest reduction in the LASIK without ocular surface management group, and proposed that the GCD reduction could be prevented by preoperative ocular surface management. Ryan et al. also showed a reduction in the conjunctival goblet cell population in the early postoperative period after either surgery.[7] In our study, we similarly found a reduction in GCD in each surgery, but no significant difference existed between groups in the first month. In the third month, a significant improvement was seen in the PRK group compared to the Femto-LASIK group. On the other hand, we observed no differences between groups at 1 or 3 months in other ocular parameters, including the degree of squamous metaplasia, tendency to keratinization, nuclear changes (frequency and type), goblet cell morphology, mucus amount, or inflammatory cells. In the third month, the GCD and epithelial cell sheet scores improved in the PRK group, but no significant change was observed in the Femto-LASIK group. These results may be associated with several factors such as the LASIK suction ring, hinge flap width, flap thickness, ablation depth, use of femtosecond laser or microkeratome for flap creation, and preoperative GCD.[5,7]

The transient high pressure exerted on the conjunctiva by the suction ring of the femtosecond laser or microkeratome at the early stages of LASIK is believed to damage the conjunctival goblet cells.[4,5,24,25] Therefore, Femto-LASIK patients have significant goblet cell loss compared to PRK patients. However, we found significant goblet cell loss in both groups. Unlike in other studies, no difference existed between the groups in the early period. Moreover, in our study, PRK patients recovered faster in the third month than expected. This is consistent with the literature: whereas the nerves are cut permanently in Femto-LASIK, they are expected to return over time in PRK. Rodriguez et al. also reported the effect of the suction ring on goblet cell loss.[6] Additionally, they compared the effect of a femtosecond laser and a microkeratome on GCD, finding a greater reduction in GCD with the former.[6] The duration of pressure on the conjunctiva was the main reason for this result.[6] Salomão et al. found that surgery using a femtosecond laser was associated with faster normalization of the ocular surface, a faster recovery time, and fewer dry eye symptoms compared to the microkeratome group.[26] Barequet et al. also found better corneal sensitivity results with a thin, uniform femtosecond flap, and they reported no symptoms of dry eye 6 months postoperatively.[27] Sauvageot et al. highlighted similar results with a femtosecond laser on the ocular surface.[2] Our study used a femtosecond laser in the flap creation. We observed no difference compared to the PRK group in GCD or other ocular surface parameters attained by CIC, different from the literature. This could be because of the thinner and more regular flaps obtained by femtosecond laser, resulting in less iatrogenic corneal nerve damage and only at the superficial corneal level, thereby increasing the ocular surface safety of this choice. Since the pressure value in the flap-forming systems used in other studies was higher than our WaveLight FS200, we found the goblet cell loss almost the same as in PRK. However, at the third postoperative month, the GCD in the PRK group was significantly improved. Moreover, different Femto-lasers exist, such as the WaveLight FS-200 with scleral suction, and the Zeiss Visumax 500 and 800 (Carl Zeiss Meditec AG, Germany) with corneal suction. The difference in suction may also affect the results that we found. Therefore, we can state that the results we specified here are for Femto-LASIK with scleral suction. We cannot rule out other results for Femto-lasers with corneal suction, and this should be investigated in future studies.

Our study is the first to comprehensively evaluate impression cytology parameters in Femto-LASIK and PRK patients. The relatively small sample size is a limitation of the study, affecting the generalizability of the results. We also could not evaluate biochemical markers such as the osmolarity and matrix

metalloproteinase levels of tears. We could not evaluate patients' complaints with a questionnaire such as the Ocular Surface Disease Index. Another drawback of our study is the short follow-up time because we could not observe late postoperative changes in ocular surface parameters.

CONCLUSION

Our results showed a decrease in tear secretion and stabilization and a decrease in GCD after both PRK and Femto-LASIK at the 3-month follow-up. DED appeared similarly in both surgeries, and some improvements were observed in the 3 months. In both surgeries, GCD decreased at 1 month, but improvement at 3 months seemed to occur early in the PRK group compared to the LASIK group. The change in the GCD is an important reason for the poorer course of DED in the LASIK group. These results indicate that DED is an important issue after both surgeries, and proper treatments are necessary following both, particularly in the early postoperative period.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Hasan Kızıltoprak, Kemal Özülken, Emine Rümeysa Hekimoğlu, Dilara Özkoyuncu Kocabaş;* ***Design:*** *Hasan Kızıltoprak, Kemal Özülken, Emine Rümeysa Hekimoğlu;* ***Control/Supervision:*** *Hasan Kızıltoprak, Kemal Tekin, Dilara Özkoyuncu Kocabaş, Kemal Özülken;* ***Data Collection and/or Processing:*** *Hasan Kızıltoprak, Kemal Tekin, Emine Rümeysa Hekimoğlu, Dilara Özkoyuncu Kocabaş, Kemal Özülken, Merve İnanç Tekin;* ***Analysis and/or Interpretation:*** *Hasan Kızıltoprak, Merve İnanç Tekin, Kemal Tekin, Dilara Özkoyuncu Kocabaş;* ***Literature Review:*** *Hasan Kızıltoprak, Kemal Özülken, Emine Rümeysa Hekimoğlu;* ***Writing the Article:*** *Hasan Kızıltoprak, Kemal Tekin;* ***Critical Review:*** *Hasan Kızıltoprak, Kemal Tekin, Dilara Özkoyuncu Kocabaş, Kemal Özülken, Merve İnanç Tekin;* ***References and Fundings:*** *Hasan Kızıltoprak, Kemal Tekin, Dilara Özkoyuncu Kocabaş, Kemal Özülken;* ***Materials:*** *Hasan Kızıltoprak, Kemal Tekin, Dilara Özkoyuncu Kocabaş, Kemal Özülken.*

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