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Goblet cell response after photorefractive keratectomy and laser in situ keratomileusis

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Abstract

PURPOSE—To determine whether patients without dry eye preoperatively have an altered conjunctival goblet cell density and mucin secretion postoperatively and to explore what factors affect changes in goblet cell density and mucin secretion.

SETTING—The former Walter Reed Army Medical Center, Washington, DC, USA.

DESIGN—Prospective nonrandomized clinical study.

METHODS—Impression cytology was used to determine conjunctival goblet cell density before and 1 week, 1 month, and 3 months after photorefractive keratectomy (PRK) or laser in situ keratomileusis (LASIK). The McMonnies questionnaire, Schirmer test, tear breakup time, corneal sensitivity, rose bengal staining, and computerized videokeratoscopy were also performed to assess tear-film and ocular-surface health.

RESULTS—The ratio of goblet cell to total cells changed postoperatively from baseline in both groups ($P < .001$). The most significant change was a median 29% decrease 1 month postoperatively. However, there were no significant differences between groups over time ($P = .772$). The ratio of filled goblet cell to total goblet cell did not change significantly over the same

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time period ($P = .128$), and there were no significant differences between the PRK group and the LASIK group over time ($P = .282$).

CONCLUSIONS—Patients without apparent dry eye had altered conjunctival goblet cell population after PRK or LASIK. The conjunctival goblet cell population tended to decrease in the early postoperative period after either surgery and was most affected by preoperative goblet cell density. The changes in the tear film and ocular surface did not seem to affect goblet cell mucin secretion after either procedure.

Maintaining a healthy ocular surface is important because its disruption can adversely affect vision. To protect and sustain the health of the ocular surface, a stable and functional tear film is required. Tears contain lipids, mucins, proteins, electrolytes, and water and are produced by the lacrimal functional unit.¹ Any significant disturbance in the tear film or the lacrimal functional unit can result in debilitating ocular surface diseases, including dry eye.

Keratorefractive surgery is a risk factor for tear dysfunction, and both photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK) impair the corneal sensory nerves that drive tear secretion, resulting in dry eye.^{2–4} In PRK, the corneal epithelium is removed to allow photoablation of the stromal layer, damaging nerve endings that terminate in the anterior stroma and epithelium. In LASIK, a flap is created into the anterior stroma, damaging nerves in the periphery as they enter the cornea and deeper during photoablation.⁵ Although many nerves regenerate after both procedures,^{6,7} some studies suggest a percentage never return to their original state.^{7,8} The signs and symptoms of dry eye are most severe immediately after surgery and slowly improve over a 3- to 6-month period.⁹ In a subset of patients, they may persist.¹⁰ Because symptoms of dry eye are common, ranging from mild to severe, and are experienced by patients postoperatively, an study of factors contributing to dry eye is warranted.

Goblet cells and nonkeratinizing stratified squamous cells, the main cell types in the conjunctiva, are responsible for a major portion of the mucins in the tear film.¹¹ There are 2 types of mucins; that is, membrane spanning and secreted. Conjunctival stratified squamous cells are decorated on their apical membranes with membrane-spanning mucins that extend into and form the glycocalyx. The goblet cells produce the secretory mucins, notably the mucin MUC5AC, which is a large gel-forming mucin that is the major constituent of the inner mucous layer of the tear film.¹¹ In addition, both cell types secrete electrolytes and water that contribute to the aqueous layer of the tear film. Goblet cell mucin secretion is regulated by a neural reflex arising from the sensory nerves on the cornea and conjunctiva that activates the efferent parasympathetic nerves surrounding the goblet cells.^{12,13} Multiple types of compounds stimulate goblet cell secretion, including the parasympathetic neurotransmitters acetylcholine and vasoactive intestinal peptide; epidermal growth factor; proinflammatory mediators including prostaglandin D; leukotrienes LTB₄, LTC₄, LTD₄, and LTE₄; and the allergic mediator histamine.^{12,13} Cytokines also stimulate goblet cell secretion including interferon γ and IL-4, both of which are elevated in dry eye.^{14,15} Thus, in both types of refractive surgery, the mechanical aspects of the procedures (eg, epithelial debridement, suction ring application), as well as the inflammatory and dry-eye responses that follow, and the loss of functioning nerves could alter goblet cell secretion.

Current methods of identifying goblet cells do not measure the entire goblet cell population. When goblet cells secrete, they release all over their secretory granules. Traditional methods of identifying goblet cells depend on markers of the secretory product including alcian blue–periodic acid-Schiff reagent¹⁶ and the lectins UEA-1 and Helix pomatia agglutinin (HPA).^{17,18} These methods measure goblet cells that have not secreted. A decrease in the number of goblet cells as measured by these traditional techniques could indicate that goblet cells have secreted or that they are not present. In the present study, we added a second marker of goblet cells, cytokeratin 7, that indicates the cell bodies. Our use of both cytokeratin 7 and HPA allowed us to measure the entire goblet cell population; that is, secreted (empty: stain only with cytokeratin 7)¹⁹ plus nonsecreted (filled: stained with cytokeratin 7 and HPA).

The purpose of the present study was to determine whether patients with no apparent dry eye preoperatively had altered conjunctival goblet cell density and mucin secretion and subsequently suffered from dry eye postoperatively. This study also explored what factors affected the change in goblet cell density and mucin secretion after PRK or LASIK.

PATIENTS AND METHODS

The former Walter Reed Army Medical Center Institutional Review Board (IRB) granted approval for the study. Each participant provided informed consent, and all research adhered to the tenets of the Helsinki Declaration. This trial was registered with the National Institutes of Health Clinical Trials.^A

After IRB approval, active duty United States Army participants were enrolled in the study, with equal numbers having PRK and LASIK. Each patient had to meet all inclusion and exclusion criteria in both eyes, as previously described by Bower et al.,¹⁰ to be considered eligible for enrollment in the study.

Surgical Technique and Postoperative Regimen

Two surgeons (K.S.B., R.D.S.) performed all PRK and LASIK procedures. All photoablations were done with the Wavelight Allegretto Wave Eye-Q 400 Hz excimer laser system (Alcon Surgical, Inc.). The optical zone for myopic treatments was 6.50 mm with a transition zone of 0.30 mm. For eyes with myopia and astigmatism, the ablation zone was 6.50 mm with a transition zone of 1.25 mm. For PRK, epithelial removal was accomplished using a rotary brush (Amoils Epithelial Scrubber, Innovative Excimer Solutions, Inc.). After the laser ablation, the cornea was immediately irrigated with a chilled balanced salt solution. Prophylactic mitomycin-C (0.01 mg/mL) was applied to the stromal bed for 30 seconds in all cases with an ablation depth of 70 μ m or greater. An omafilcon A bandage contact lens (Proclear, Coopervision, Inc.) was used in all cases postoperatively and left in place until complete reepithelialization, typically between 4 and 7 days. Early postoperative were performed at 1 day and then at 4 or 5 days to remove the bandage contact lens. If the epithelium was not completely healed, the bandage lens was replaced and the patient was seen every 1 to 2 days until complete reepithelialization. The postoperative regimen included topical moxifloxacin hydrochloride 0.5% ophthalmic solution (Vigamox) 4 times daily for 1 week, a 10-week course of topical fluorometholone 0.1% ophthalmic solution (4 times daily

for 4 weeks, 3 times daily for 2 weeks, twice daily for 2 weeks, then once daily for 2 weeks), topical ketorolac tromethamine 0.4% ophthalmic solution (Acular-LS) up to 4 times daily during the first 48 hours as needed for pain, frequent lubrication with preservative-free artificial tears, and oral vitamin C 500 mg twice a day for 3 months.

For the LASIK procedure, a superior hinged 9.0 mm diameter, 120 μ m thick flap was created using an Intralase femtosecond laser (Abbott Medical Optics, Inc.). After laser ablation, the flap was carefully returned to its original position and refloated into position using a balanced salt solution. Early LASIK postoperative visits were at 1 day and 1 week postoperatively. The LASIK postoperative regimen included topical moxifloxacin 4 times a day for 1 week, prednisolone acetate 1.0% ophthalmic suspension every 2 hours for 24 hours and then 4 times a day for 1 week, topical ketorolac up to 4 times daily during the first 48 hours as needed for pain, and frequent preservative-free artificial tear supplements.

Diagnostic assessments were performed preoperatively and repeated 1, 3, 6, and 12 months postoperatively as previously described¹⁰ and included (in order of evaluation) a psychometric questionnaire (McMonnies dry-eye questionnaire²⁰) to assess subjective symptoms of dry eye, computerized videokeratoscopy (TMS-4, Tomey Corp.) to topographically evaluate the regularity of the ocular surface, Cochet-Bonnet esthesiometry to measure corneal sensation, slitlamp biomicroscopy with fluorescein staining and tear breakup time (TBUT) to evaluate tear-film stability, rose bengal staining to evaluate epithelial damage of the cornea and conjunctiva, and the Schirmer test with anesthesia to measure the rate of basal tear secretion. In addition, conjunctival impression cytology was performed in the left eye preoperatively and 1 week, 1 month, and 3 months postoperatively.

Goblet Cell Conjunctival Impression Cytology

Conjunctival impression cytology specimens were obtained from the temporal interpalpebral and superior bulbar conjunctiva of the left eye. A strip of nitrocellulose membrane was placed on the superior conjunctiva, and even pressure was applied to the membrane. The membrane was placed cell side down on a slide and gently pressed unidirectionally onto a slide with a glass ball. This process was repeated across the slide using the same membrane. A new membrane was placed on the temporal conjunctiva and the process was repeated.

The slides were fixed in 100% methanol and frozen. The conjunctival impression cytology slides were rinsed in 1X phosphate-buffered saline (PBS), blocked for 30 minutes in PBS containing bovine serum albumin 2.0%, and Triton X-100 2.0%. Primary antibody to cytokeratin 7 (a-CK RCK 105, MP Biomedicals, LLC) was added and incubated overnight at 40°C followed by incubation with fluorescein isothiocyanate-conjugated secondary antibody and the HPA lectin directly conjugated to rhodamine (Sigma-Aldrich Co.). Cytokeratin 7 specifically stains goblet cells compared with conjunctival stratified squamous cells and stains the cell body compared with the secretory product, which is stained by lectin HPA.

Coverslips were mounted with polyvinyl alcohol mounting medium with 1,4-diazabicyclo[2.2.2]octane containing 4' 6-diamidino-2-phenylindole dihydrochloride (DAPI) to indicate cell nuclei. Cells from 5 random fields on each slide were counted using a Eclipse 80i fluorescent microscope with a Spot camera (Nikon) or an IX51 fluorescent

microscope with a DP71 camera (Olympus), both at a magnitude of $\times 400$. The highest counts and lowest counts from each superior and temporal 5-field counts were excluded, and the remaining fields were combined and averaged. The number of DAPI-positive cells indicates the total number of cells (blue fluorescence). The number of cytokeratin 7-positive cells indicates the total number of goblet cells (filled and empty) (green fluorescence). The number of HPA-positive cells indicates the number of goblet cells containing their mucin secretory product, filled nonsecreting goblet cells (red fluorescence). The ratio of total number of goblet cells to the total number of cells and the ratio of filled goblet cells to the total number of goblet cells were calculated and presented as percentages (percentage goblet cells and percentage filled goblet cells, respectively). The lower the percentage of filled goblet cells, the more goblet cell secretion (mucin secretion) had occurred.

Statistical Analysis

Demographic and baseline clinical characteristics were compared using a 2-sample *t* test for continuous data and the Fisher exact test for categorical data. Only data from the left eye were used for analysis. To take into account the variability in each outcome given the number of eyes included in each group, 95% confidence intervals (CIs) were added to several figures in lieu of the standard deviation to assist in interpretation of the results.²¹ The Wilcoxon signed-rank test was used to compare preoperative to 3-month postoperative continuous clinical outcomes, while the McNemar test was used to compare categorical data.

Changes in the percentage of goblet cells and percentage of filled goblet cells for each treatment were examined using a generalized estimating equations model, with time as the within-subjects factor and surgical method (PRK versus LASIK) as the between-subjects factor. A *P* value less than 0.05 was considered statistically significant. A Bonferroni correction was applied for post hoc comparisons of the percentage of goblet cells and the percentage of filled goblet cells between timepoints (preoperative; 1 week, 1 month, 3 months postoperative), with *P* values less than 0.017 signifying statistical significance.

Linear regression analysis was performed to explore significant associations between patient and surgical factors, such as age, sex, ablation depth, refractive error, and postoperative percentage of goblet cells and percentage of filled goblet cells. Spearman rho bivariate correlations were used to examine the relationship between clinical outcomes, dry-eye status, the percentage of goblet cells, and the percentage of filled goblet cells at each visit. Dry-eye status was determined for each patient at each visit as described by Bower et al.¹⁰ The Fisher exact test was used to compare dry-eye status between groups.

RESULTS

Of the 146 participants (73 men, 73 were women) enrolled in the study, 97 had complete goblet cell studies and clinical assessment preoperatively and 1 week, 1 month, and 3 months postoperatively. These 97 patients comprised the study population; 53 were enrolled in the PRK group and 44 in the LASIK group. Table 1 shows the demographic and preoperative characteristics. The LASIK group was significantly older than the PRK group ($P = .03$) and had significantly higher central corneal thickness ($P = .002$), which can be expected given corneal thickness is a determining factor when selecting the appropriate

surgical procedure. No other preoperative characteristic was significantly different between the 2 groups.

Table 2 shows the medians and interquartile ranges for PRK and LASIK clinical outcome measures preoperatively and 3 months postoperatively. There was a significant increase in the McMonnies questionnaire from preoperatively to 3 months postoperatively in both groups ($P < .001$ for PRK; $P = .012$ for LASIK). Videokeratoscopy in the PRK group showed a significant decrease in the surface regularity index (SRI) ($P = .007$), while the irregular astigmatism index (IAI) increased significantly ($P < .001$). In the LASIK group only the IAI increased significantly ($P < .001$). Corneal sensitivity measured with Cochet-Bonnet esthesiometry did not change significantly in the PRK group; however, the percentage of eyes with maximum sensitivity (0.40g/mm^2) decreased significantly in the LASIK group ($P = .003$). This trend was also apparent in TBUT measurements and rose bengal staining in the LASIK group, in which the TBUT decreased significantly from preoperatively to postoperatively ($P = .001$) and the percentage of eyes with no staining (scale of 0 no staining to 4 maximum staining) decreased significantly from preoperatively to 3 months ($P = .031$). There were no significant changes in TBUT or rose bengal staining in the PRK group. However, there was a significant decrease in the median basal tear secretion from preoperatively to 3 months postoperatively ($P = .013$). There was no significant difference in the Schirmer score in the LASIK group. There were some clinical changes on the ocular surface over time in both groups.

Figure 1 shows images of goblet cell counts over time for PRK and LASIK. Figure 2 and 3 shows the ratio of goblet cells to total cells and Figure 3, the ratio of filled goblet cells to total goblet cells, indications of whether PRK and LASIK had an effect on goblet cell population and its mucin secretion. The percentage of goblet cells in the PRK group and the LASIK group changed significantly over time ($P < .001$) (Figure 2). There were significant differences between 1 week and 3 months in the PRK group ($P = .001$). In the LASIK group, there were significant differences between 1 week and 3 months ($P = .012$) and 1 month and 3 months ($P = .001$). There were no significant differences in the percentage of goblet cells between PRK and LASIK ($P = .772$). The percentage of filled goblet cells did not change significantly over time in either group ($P = .128$) (Figure 3). Comparing PRK and LASIK, filled goblet cells to total goblet cells over time showed no significant differences between groups over time ($P = .282$). Based on our analysis, the changes seen after either procedure were in goblet cell density, but not goblet cell secretion activity.

At 1 month, 3.7% (2/53) of PRK eyes and 10% (4/44) LASIK eyes were considered to have probable dry eye. At 3 months, 7.8% (4/51) PRK eyes and 4.5% (2/44) LASIK eyes were considered to have probable dry eye. There were no cases of definite dry eye based on the study criteria at the 1-month or 3-month postoperative visits. There were no significant differences in incidence of dry eye at 1 month $P = .41$ or 3 months $P = .68$ between PRK versus LASIK. The smaller sample size of dry-eye cases limited additional analysis.

A linear regression performed to explore the relative importance of the various patient and surgical factors on conjunctival goblet cell number and function showed that the percentage of goblet cells 3 months postoperatively was not significantly influenced by age, sex, type of

surgery (PRK or LASIK), ablation depth, refractive error (mean spherical equivalent[SE]), or preoperative percentage of goblet cells ($R^2 = 0.163$, $P = .094$). However, and examination of the association of age, sex, ablation depth, mean SE, type of surgery (PRK or LASIK), and preoperative percentage of filled goblet cells on the percentage of filled goblet cells 3 months postoperatively, only the preoperative percentage of filled goblet cells was significant ($R^2 = 0.248$, $P = .001$).

Bivariate correlations to examine the relationship between clinical outcomes of videokeratoscopy (SRI, IAI, surface asymmetry index), dry-eye status, and percentage of goblet cells and the percentage of filled goblet cells at each visit showed no significant correlations in the PRK group or LASIK group ($P > .063$). There was a significant negative correlation between the 3-month postoperative SRI and the 3-month percentage of filled goblet cells ($r_s = -0.469$, $P = .002$) in the PRK group but not in the LASIK group ($P > .09$). A higher SRI might indicate an increase in goblet cell secretion in the PRK group, while a lower SRI might indicate a decrease in secretion.

DISCUSSION

The change in any component of the tear film can result in a decrease in tear-film quality and degradation in visual quality, especially in the early postoperative period. Goblet cells are critical in maintaining homeostasis in the tear film by regulating mucin production and secretion, especially MUC5AC. In turn, changes in the tear film can affect goblet cell density and mucin including MUC5AC secretion. Qualitative and quantitative goblet cell changes in ocular surface diseases have been studied using methods such as conjunctival impression cytology,^{22–27} and numerous studies have shown that conjunctival goblet cells can indicate the status of the ocular surface.^{26–29}

In the present study, along with clinical changes in the tear film, changes in goblet cell density after PRK or LASIK were observed. The percentage of goblet cells decreased, although not significantly, the first week after either surgery. There was a significant change in the percentage of total goblet cell population in the PRK group between 1 week and 3 months and in the LASIK group between 1 week and 3 months and between 1 month and 3 months postoperatively. Studies of rabbit eyes examining the effects of topical eyedrops with benzalkonium chloride (BAK)^{30–32} found significant goblet cell loss. In this study, both the LASIK and PRK treatment groups were prescribed BAK-preserved steroid eyedrops (PRK = 10 week course of topical fluorometholone 0.1% ophthalmic solution; LASIK = prednisolone acetate 1.0% ophthalmic suspension every 2 hours for 24 hours and then 4 times a day for 1 week). The remaining topical regimen was the same. There was a significant difference in the percentage of goblet cells over time. However, because BAK eyedrops were used in both groups, the difference in the percentage goblet cell recovery might not be the result of the eyedrop regimen. The PRK group recovered quicker than the LASIK group despite longer topical steroid use. Because there was no significant difference in filled goblet cells as a percentage of the total goblet cells over time for either procedure, eyedrops might not affect impression cytology results.

Clinical examination reflected the changing corneal surface, with significant changes from preoperatively in the results of the videokeratoscopy, Schirmer test, and McMonnies questionnaire²⁰ 3 months postoperatively. A study by Moore et al.²³ showed goblet cells can tolerate up to a threshold of ocular-surface disruption, as shown by clinical examination, before they exhibit changes. Furthermore, regression analysis in this study showed the postoperative goblet cell density to be most influenced by the preoperative goblet cell density. There was a significant negative correlation between the SRI and the percentage of filled goblet cells in the PRK group. A lower SRI indicates a more regular surface. The negative correlation between the SRI and the filled goblet cells in the PRK group might indicate the ongoing ocular surface changes resulting from the cytokine-activated wound-healing response in keratocytes, fibroblasts, the basement membrane, and lacrimal glands after PRK.^{32,33}

The wound-healing response after PRK might affect the goblet cell feedback response so goblet cells remain filled, even though the surface is aggravated, as suggested by Ang et al.⁵ The transient nature of ocular-surface disruption after PRK described by Bower et al.¹⁰ might also limit goblet cell changes. A study by Albietz et al.² found that ocular-surface therapy mitigated the damage caused by a decreased goblet cell density after LASIK in dry-eye patients. Of note, there were not enough dry-eye patients in this population to evaluate dry eye as a factor for a change in postoperative goblet cell density. The close follow-up and dry-eye management in the population in the present study might have moderated the damaging effects of dry eye and the inflammatory response to the ocular surface.

Our findings after LASIK were similar to those after PRK except that the ratio of goblet cells to total cells did not recover until after 1 month postoperatively. The qualitative findings indicative of a change in tear film after LASIK suggest corneal nerve injury during LASIK flap creation, and the alteration in corneal nerve function after surgery might suppress neural stimulation of goblet cell mucin secretion.³⁴ This finding is supported by previous reports of delayed recovery in LASIK compared with PRK.³⁵ This finding is reinforced by the loss of goblet cells during the application of the suction ring during LASIK, as shown by Rodriguez et al.⁴ The reason for the loss of goblet cells in surface ablation is not as readily apparent but might be related to loss of trophic factors secondary to corneal nerve injury or factors related to mechanical epithelial debridement. Even though the 2 refractive surgery procedures are different in terms of stress on the ocular surface, the conjunctival goblet cells are resilient and return to normal.

To our knowledge, this is a new approach to assessing goblet cells by impression cytology using ratios of goblet cells to total cells (percentage of goblet cells) and filled goblet cells to total goblet cells (percentage of filled goblet cells). Studies^{25,27} have shown that measurement of the goblet cell population might be affected by sampling area selection, specifically exposed conjunctiva (temporal/nasal) versus covered conjunctiva (superior/inferior). To minimize variability, samples in this study were pooled from both the superior temporal interpalpebral and superior bulbar conjunctiva. Furthermore, in a review by Doughty,²⁶ goblet cell counts based on high-powered magnification were critiqued for the reliability of field representation. The inclusion of the total cell count to determine the ratio of goblet cells to total cells increases the reliability of the counts in our study.

The purpose of the present study was to determine whether there is reduced mucin secretion by conjunctival goblet cells in patients after refractive surgery and whether this change in mucin secretion is associated with the development of dry eye after refractive surgery. Our study found that the total number of goblet cells changed significantly over time after PRK and after LASIK. However, mucin secretion by conjunctival goblet cells did not change over time after either procedure. In our study, both types of refractive surgery affected the total number of goblet cells but not goblet cell function because there were no significant changes in the filled goblet cell to total goblet cell ratio. Factors such as age, sex, type of refractive surgery, refractive error, and the preoperative percentage of filled goblet cells might affect goblet cell mucin secretion but might not be observed given the tolerance to ocular-surface disruption. The ocular surface, with appropriate therapy, might be able to withstand the stress of refractive surgery without a significant long-term change in the goblet cell population.

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WHAT WAS KNOWN

- A significant disturbance in the tear film or the lacrimal functional unit might result in debilitating ocular surface disease, including dry eye.
- Goblet cells and the nonkeratinizing stratified squamous cells, the main cell types in the conjunctiva, are responsible for a major portion of the mucins in the tear film.
- Current methods of identifying goblet cells do not measure the entire goblet cell population.

WHAT THIS PAPER ADDS

- Traditional methods of identifying goblet cells only measure goblet cells that have not secreted. Adding a second marker of the goblet cells, cytokeratin 7, to indicate cell bodies and HPA allowed measurement of the entire goblet cell population.
- The total number of goblet cells changed significantly over time after both PRK and LASIK. However, mucin secretion by conjunctival goblet cells did not change over time after either procedure.
- Both types of refractive surgery affected the total number of goblet cells but not goblet cell function.

Figure 1.

Images of preoperative and postoperative goblet cells in the PRK group and LASIK groups at each time point. Impression cytology samples taken from superior and temporal conjunctivae were stained with anti-cytokeratin-7 (K7) to identify filled and empty goblet cells (*green*), and HPA for goblet cell secretory product (*red*) was visualized using a fluorescent microscope with a camera or a fluorescent microscope with a camera (both original magnification $\times 400$) (LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy).

Figure 2.

The mean ratio of goblet cells (filled and empty) to total number of cells by treatment group. Bars indicate the 95% CI. In the PRK group, samples from 48 patients were counted preoperatively and from 49, 45, and 43 patients 1 week, 1 month, and 3 months postoperatively, respectively. In the LASIK group, samples from 35 patients were counted preoperatively and from 34, 33, and 38 patients 1 week, 1 month, and 3 months postoperatively, respectively. A red asterisk indicates statistically significant differences in both PRK and LASIK groups; a purple asterisk indicates statistically significant differences in LASIK group (LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy).

Figure 3.

The mean ratio of filled goblet cells to total goblet cells by group. Bars indicate the 95% CI. In the PRK group, samples were counted from 43 patients preoperatively and from 45, 41, and 42 patients 1 week, 1 month, and 3 months postoperatively, respectively. In the LASIK group, samples from 33 patients were counted preoperatively and from 29, 32, and 38 patients 1 week, 1 month, and 3 months postoperatively, respectively (LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy).

Table 1

Baseline characteristics.

Parameter	PRK (53 Eyes)	LASIK (44 Eyes)	P Value [*]
Mean age (y) $\pm$ SD	29.0 $\pm$ 5.3	31.3 $\pm$ 5.1	.03 [†]
Male/female (n)	25/28	22/22	.84 [‡]
Mean manifest SE (D) $\pm$ SD	-3.48 $\pm$ 1.89	-3.87 $\pm$ 1.92	.32 [†]
Mean ablation depth (μ m) $\pm$ SE	58.2 $\pm$ 22.8	60.7 $\pm$ 25.5	.62 [†]
Mean CCT (μ m) $\pm$ SD	538.9 $\pm$ 40.7	562.3 $\pm$ 31.5	.002 [†]
Mitomycin-C use (% of eyes)	24.5	—	—

CCT = central corneal thickness; LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy; SE = spherical equivalent

^{*} $P < .05$, statistically significant[†] t test[‡] Fisher exact test

Table 2

Clinical outcome measures at preoperatively and 3 months postoperatively.

Parameter	PRK			LASIK		
	Preop (53 Eyes) [*]	3 Mo Postop (51 Eyes) [*]	P Value [†]	Preop (44 Eyes) [*]	3 Mo Postop (44 Eyes) [*]	P Value [‡]
McMonnies questionnaire			<.001 [‡]			.012 [‡]
Median	5.0	7.0		6.0	8.0	
IQR	3.0, 7.0	5.0, 11.0		4.0, 9.0	6.0, 10.0	
Videokeratoscopy			.007 [‡]			.285 [‡]
Median	0.10	0.07		0.15	0.18	
IQR	0.07, 0.26	0.06, 0.16		0.06, 0.33	0.07, 0.47	
Surface regularity index			.247 [‡]			.832 [‡]
Median	0.38	0.34		0.34	0.36	
IQR	0.26, 0.50	0.26, 0.41		0.26, 0.45	0.28, 0.52	
Irregular astigmatism index			<.001 [‡]			<.001 [‡]
Median	0.35	0.39		0.35	0.44	
IQR	0.30, 0.40	0.36, 0.42		0.30, 0.41	0.38, 0.52	
Cochet-Bonnet esthesiometry (0.40 g/mm ²) (%)	84.9	84.3	.99 [§]	88.6	63.6	.003 [§]
Tear breakup time (s)			.054 [‡]			.001 [‡]
Median	13.0	11.0		12.5	9.0	
IQR	9.5, 22.0	8.0, 16.0		9.3, 21.5	6.0, 15.0	
Rose bengal staining, score 0 (%)	98.1	90.2	.219 [§]	97.7	84.1	.031 [§]
Schirmer with anesthesia (mm)			.013 [‡]			.339 [‡]
Median	23	16		23	17	
IQR	12, 32	9, 31		10, 33	10, 31	
Mean manifest SE (D) ± SD	-3.48 ± 1.89	0.25 ± 0.38	<.001 [‡]	-3.87 ± 1.92	0.05 ± 0.25	<.001 [‡]

LASIK = laser in situ keratomileusis; PRK = photorefractive keratectomy; SE = spherical equivalent

^{*} Data available for analysis[†] $P < .05$, statistically significant[‡] Wilcoxon signed-rank test

§ McNemar test

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