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Original Scientific Paper

COMPARISON OF CORNEAL DENSITOMETRY AND VISUAL ACUITY REFRACTIVE RESULTS AFTER ALCOHOL-ASSISTED AND MECHANICAL (ROTATING BRUSH) EPITHELIUM REMOVAL TECHNIQUES IN MYOPIC PHOTOREFRACTIVE KERATECTOMY

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SUMMARY – The aim was to compare corneal densitometry, haze development, visual and refractive results after photorefractive keratectomy (PRK) performed with different epithelial removal techniques. This study included 42 patients (84 eyes) who underwent PRK with one eye de-epithelialized with 20% ethanol solution (PRK-a group) and another one with rotating brush (PRK-b group). The procedures were performed by the same surgeon on the same laser platform after comprehensive preoperative assessment. Follow up examinations of the patients were scheduled on postoperative day 4, then 1, 3 and 12 months postoperatively. Faster recovery of visual acuity was achieved in the PRK-b group during 12-month postoperative period but differences were statistically nonsignificant. Haze was significantly less present in the brush group measured 12 months after surgery. Also, eyes in the PRK-b group returned close to its basal corneal densitometry values faster than those that underwent PRK-a. Short-term visual recovery occurred faster in the PRK-b group. Less haze development and better corneal transparency were achieved in the PRK-b group throughout the 12-month follow-up period. However, both procedures showed great results and patient satisfaction was high regardless of the de-epithelialization method.

Keywords: *Photorefractive keratectomy; Myopia; Cornea; Epithelium removal*

Introduction

In the late 1980s, laser refractive surgery was introduced, and since then millions of people have undergone the procedure[1]. Some advantages of laser surgery compared to previous methods of solving refractive errors, such as wearing soft and rigid gas-permeable contact lenses, are avoidance of major difficulties such as compliance rate, infrequent lens exchange, or improper lens cleaning[2]. Corneal shape remodeling with a laser beam results in targeted and predicted visual acuity[3]. In photorefractive keratectomy (PRK), the upper layer of the cornea, i.e., the epithelial layer, must be removed in order to modify the curvature of the cornea[4]. The PRK procedure involves loosening of the corneal epithelium with 20% ethanol solution which is then removed with a microsponge[1,5]. There

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are different possible mechanical techniques by which the epithelium may be removed, e.g., alcohol solution, blunt spatula, surgical blade, motorized epithelial separator, and laser assisted removal in 'transepithelial' PRK. Rotating brush is a device investigated in this study. Due to the fact that its use avoids any possible chemical irritation by ethanol, and there is less compression on the eyeball and consequently less eye pressure increase, this method might be beneficial for clinical use. Differences between epithelial removal methods may contribute to postoperative discomfort and pain intensity, haze development, recovery speed, or cause postoperative healing that may influence final visual outcome[6,7].

Photorefractive keratectomy has remained a popular procedure despite the usual postoperative discomfort that patients frequently experience in the first few days after the surgery[8]. Discomfort happens because incision and corneal flap formation are avoided. Consequently, the potential flap-related complications such as epithelial defects, limbal hemorrhages, interface debris, abnormal flap creation, gas bubble interferences, flap button holes, free caps, and corneal perforations (which may be seen in laser assisted *in situ* keratomileusis, LASIK) are avoided[9-11].

Corneal de-epithelialization with diluted ethanol (ranging from 10% to 30%), however, has been shown to be as effective and safe in multiple earlier studies and slightly better in terms of re-epithelialization and visual speed recovery when compared to manual scraping either by sharp or blunt blade[12].

However, rotating brush has been shown to be faster compared to other debridement methods, requiring mean time of approximately five seconds to remove the epithelium, hence minimizing corneal dehydration[13]. Some other studies, e.g., Griffith *et al.* identified rotating brush as less invasive and producing less damage to Bowman`s membrane[14].

Materials and Methods

This prospective study was conducted between April 2019 and August 2020, and it included 42 myopic patients (84 eyes) in which one eye (right) was de-epithelialized with 20% ethanol solution (PRK-a group), while the contralateral (left) eye de-epithelialization was performed with a rotating brush (PRK-b group). Patient age ranged from 23 to 35 years. Comprehensive preoperative and postoperative assessments (1, 3, and 12 months after the surgery) were performed.

Exclusion criteria were other eye conditions such as glaucoma, maculopathy, amblyopia, squint, abnormal binocular vision, visual field defects, and abnormal preoperative parameters measured in preoperative assessment.

Ethics

This study received approval by the Ethics Committee of the Knezović Polyclinic and was adherent to the tenets of the Declaration of Helsinki. Written informed consent was obtained at the time of the first study visit.

Preoperative assessment

Preoperatively, each patient underwent a detailed ophthalmic examination including uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), automatic refraction (Auto refractometer Accueref K 9001, Shin-Nippon, Japan) before and after cycloplegia induced by tropicamide 1% applied twice, along with cycloplegic refraction, intraocular pressure (IOP) measurement (PASCAL Dynamic Contour Tonometer, Ziemer Group and Goldman applanation tonometry), slit lamp examination (Haag Streit slit lamp, Mannheim, Germany), pupil size measurement in different light conditions (photopic, mesopic and scotopic; 40, 4 and 0.4 lux, respectively), performed on a CSO Antares Topographer, corneal topography and aberrometry (CSO Antares Topographer, CSO, Florence, Italy), corneal tomography and densitometry (Allegro Oculyzer, Wavelight AG, USA-Germany) and noninvasive tear break-up time test (TBUT) performed on a CSO Antares topographer (CSO, Florence, Italy) which measures average time of a tear film break-up after patient has been asked not to blink as long as possible.

Surgical technique

All procedures were performed by the same surgeon, Igor Knezović, MD, PhD. Before the surgery, topical anesthetic, oxybuprocaine chloride (Benoxi 0.4%, Unimed Pharma, Bratislava, Slovak Republic) was applied two times at five-minute interval. On the right eye, 20% ethanol solution was applied for 40 seconds. The cornea was then irrigated with balanced salt solution 0.9%, and the rest of the epithelium was removed with a 'hockey blade'. On the left eye, epithelial removal was performed mechanically with a rotating brush. This step took from four to five seconds. We used atraumatic, disposable brush, triangularly shaped with 28 soft silicone extensions specially designed for this research. Diameter of the removed epithelium was 7 mm on both eyes. After removing the epithelium, excimer laser ablation was performed using the Alcon/WaveLight Allegretto Eye-Q 400Hz Excimer Laser platform (Alcon Laboratories, Ft Worth, Texas, USA), followed by irrigation of the cornea with cooled balanced salt solution (BSS, 2-3 °C) for two minutes. In all patients, mitomycin C 0.02% was applied to cornea for 40 seconds.

After washing out mitomycin C 0.02%, a silicone hydrogel high oxygen transmissible soft contact lens (Night&Day, Alcon, Geneva, Switzerland) previously soaked for two minutes in additive-free diclofenac solution was applied. All procedures were performed in the same conditions in terms of temperature (19 °C) and humidity (mean humidity 48%, humidity range 25%-68%).

The same postoperative medication treatment was used in all patients, and it included ofloxacin 3 mg/mL (Uniflox, Unimed Pharma, Bratislava, Slovak Republic) five times a day for seven days; on postoperative day 3, dexamethasone (Maxidex, Alcon, Geneva, Switzerland) eyedrops were introduced three times a day for the next ten days. During the following ten-day period, it was recommended to be used twice a day, and finally, for the last ten days, eyedrops were used once a day. Frequent application of preservative-free artificial tears was prescribed for four weeks in all patients. Soft contact lens was removed from the eye on a postoperative day 4.

Outcome measurements

Patient follow-ups were scheduled on day 4 after the surgery, then at 1, 3 and 12 months postoperatively. UDVA, CDVA, and corneal densitometry were determined. Corneal densitometry was assessed on a corneal tomographer (Allegro Oculyzer, Wavelight AG, USA-Germany) and expressed as percentage of corneal transparency, 0% denoting completely transparent medium and 100% denoting completely opaque optic media. Data collected during 12 months after surgery were analyzed.

Statistical analysis

Statistical data analysis (MedCalc Software, Ostend, Belgium) was conducted using a MedCalc version 17.2. Kolmogorov-Smirnov test was used to examine the normality of distribution of quantitative variables. Nonparametric Mann-Whitney statistical test was used to compare measurements between the left and right eye since most of the groups of numerical variables deviated from the normal (Gaussian) distribution, and the number of subjects was less than 30. The level of statistical significance was set at $p<0.05$.

Results

Demographic and clinical data are presented in Table 1, showing equal age and sex distribution of the ethanol and rotating brush groups. There was no statistically significant difference in clinical characteristics between the groups ($p>0.05$).

Visual acuity

Compared to preoperative values, there was a significant visual acuity improvement at the first postoperative month in both groups, PRK-a ($p=0.0002$) and PRK-b ($p=0.0001$). Visual acuity significantly improved after three and 12 months ($p=0.0001$ all) in both groups compared to preoperative value (Fig. 1).

Corneal densitometry

Compared to preoperative values, there was a significant increase in corneal densitometry at the first postoperative month in PRK-a group ($p=0.0017$), whereas PRK-b group did not show significant increase ($p=0.4548$). The corneal densitometry values were significantly increased at three months postoperatively in PRK-a group ($p=0.0166$), whereas PRK-b group had a statistically nonsignificant decrease in corneal densitometry compared to preoperative values ($p=0.9032$). In addition, at 12 months postoperatively, the corneal densitometry values in PRK-a group were still significantly higher compared to

Table 1. Preoperative characteristics of patients undergoing ethanol-assisted and brush-assisted photorefractive keratectomy

	Ethanol-assisted group (42 patients, 42 eyes)	Rotating brush group (42 patients, 42 eyes)	p-value*
Age (years)	28.2±8.4	28.2±8.4	>0.05
Gender	54% female	54% female	>0.05
UDVA (decimal)	0.15±0.12	0.16±0.13	>0.05
CDVA (decimal)	0.99±0.04	0.98±0.02	>0.05
Manifest spherical equivalent	-3.78±1.94	-4.13±1.96	>0.05
Cylinder (diopters)	-0.82±0.69	-0.86±0.59	>0.05
Mean keratometry (diopters)	44.15±1.38	44.30±1.32	>0.05
Central corneal thickness (μm)	546±26	544±27	>0.05

*Statistically significant difference if $p<0.05$; data are presented as mean ± standard deviation (range); UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity

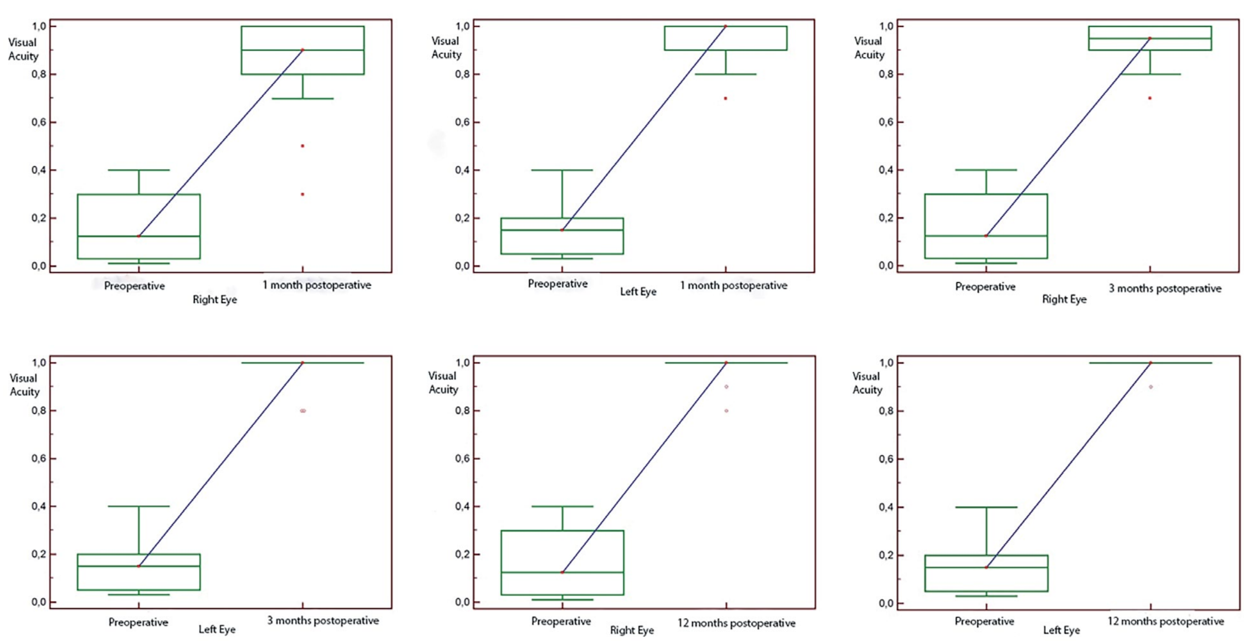


Fig. 1. Visual acuity after PRK-a and PRK-b at 1, 3 and 12 months postoperatively in comparison to preoperative values.

preoperative values (p=0.0067), whereas PRK-b group had a statistically nonsignificant drop in corneal densitometry compared to preoperative values (p=0.2166) (Fig. 2).

Comparison of visual acuity between PRK-a and PRK-b

The PRK-b group patients had higher values of visual acuity throughout the 12-month period (Fig. 3). Even though PRK-b group showed better results in

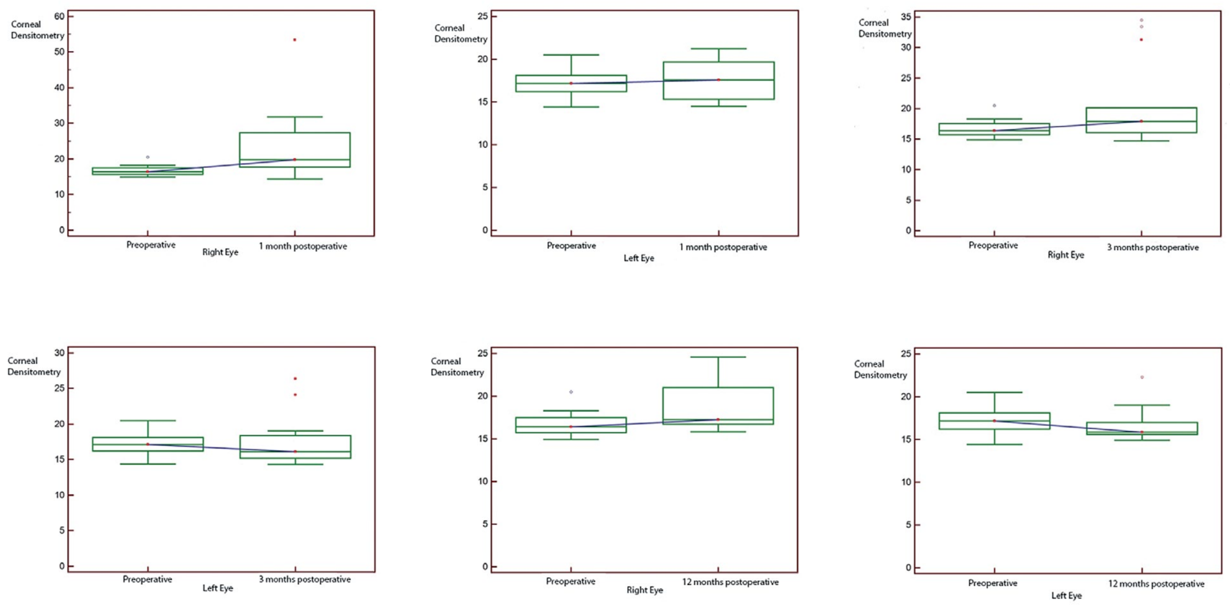


Fig. 2. Corneal densitometry after PRK-a and PRK-b at 1, 3 and 12 months postoperatively compared to preoperative values.

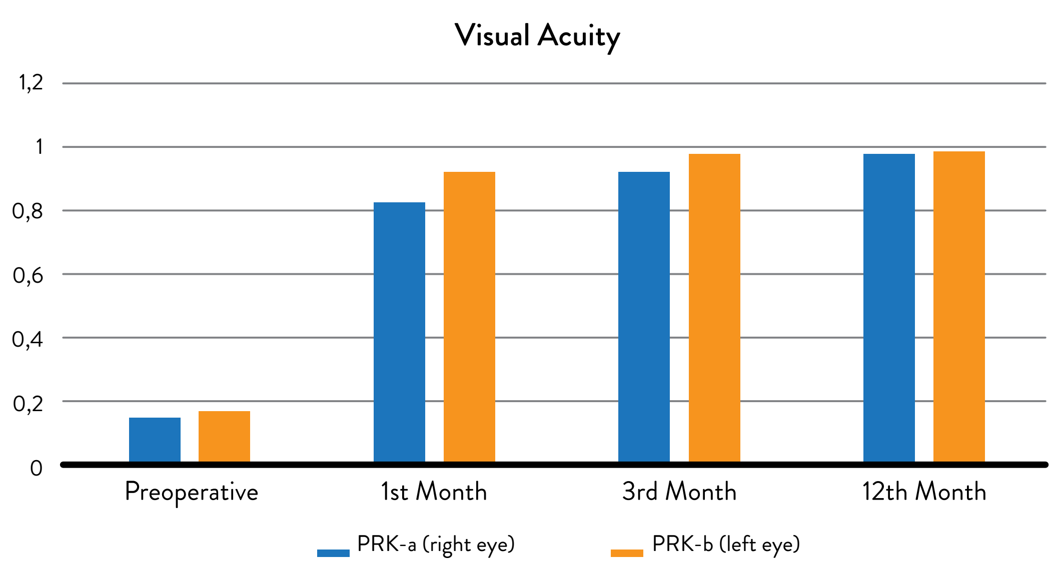
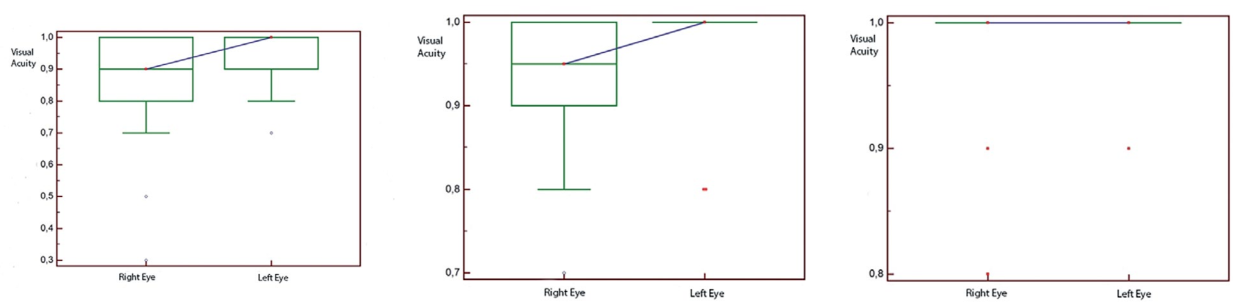


Fig. 3. Visual acuity in PRK-a and PRK-b groups measured preoperatively, and at 1, 3 and 12 months postoperatively.

visual acuity, difference between the procedures throughout the study period was not statistically significant. Mann-Whitney test at the first postoperative month yielded p=0.1383. The same test yielded p=0.0959 at three months and p=0.5713 at 12 months postoperatively (Fig. 4).

Comparison of corneal densitometry between PRK-a and PRK b

At one month postoperatively, the group of patients having undergone PRK-b surgery showed less haze development in comparison to PRK-a group. This trend continued throughout the 12-month period (Fig. 5). However, difference between the two procedures at the first and third month was not statistically significant (p=0.0695 and p=0.1611, respectively). However, at 12



Visual acuity values between two procedures at 1 month postoperatively

Visual acuity values between two procedures at 3 months postoperatively

Visual acuity values between two procedures at 12 months postoperatively

Fig. 4. Mann-Whitney test of independent samples: visual acuity values between two procedures at 1, 3 and 12 months postoperatively.

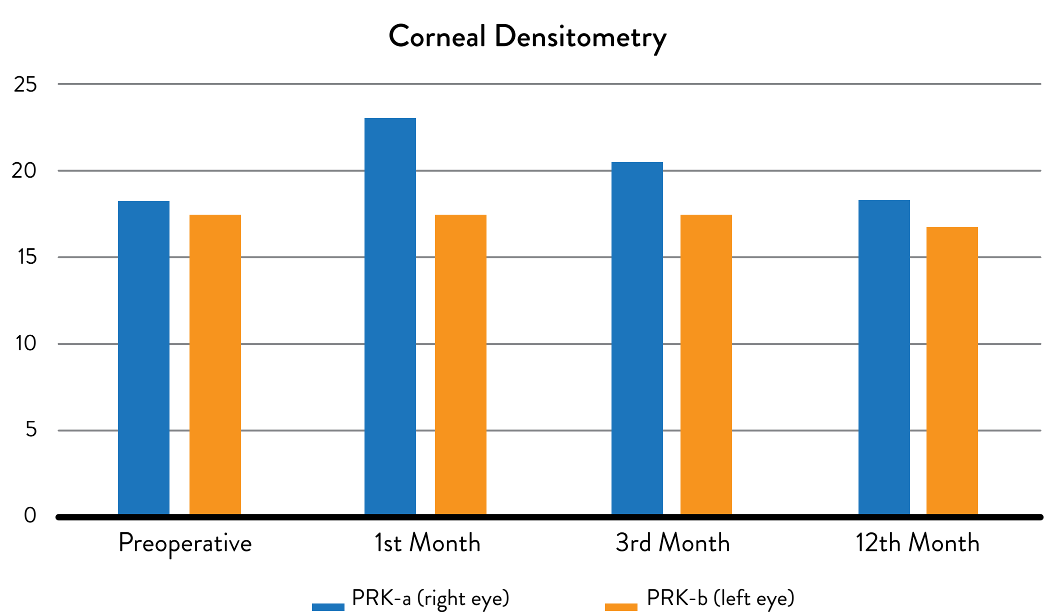
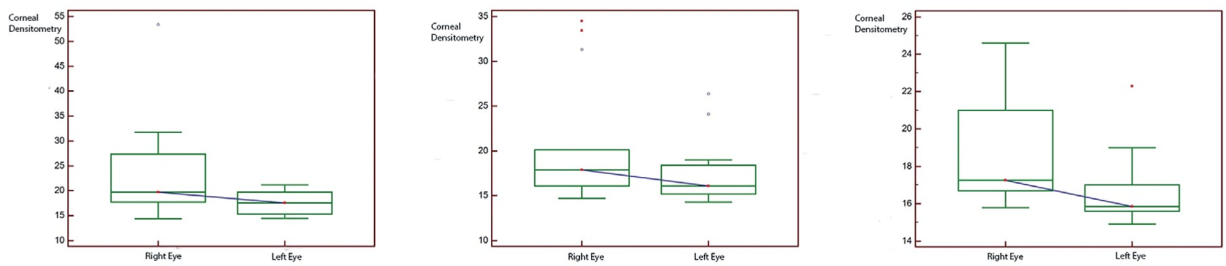


Fig. 5. Corneal densitometry in PRK-a and PRK-b groups measured preoperatively and at 1, 3 and 12 months postoperatively.



Corneal densitometry values at 1 month postoperatively

Corneal densitometry values at 3 months postoperatively

Corneal densitometry values at 12 months postoperatively

Fig. 6. Mann-Whitney test of independent samples: difference in corneal densitometry values between two procedures at 1, 3 and 12 months postoperatively.

months postoperatively, differences between the groups were statistically significant (p=0.0169) (Fig. 6).

Discussion

The aim of this study was to compare visual and refractive outcomes following two different epithelial debridement techniques performed by the same surgeon, using the same nomogram, same laser platform and follow-up periods while having one different variable in the process, i.e., debridement method. Our intention was to compare the impact of only one surgical modality, i.e., the method of epithelial removal, on the outcomes after photorefractive keratectomy. During our regular clinical practice, we have noticed certain benefits of silicone brush usage for corneal de-epithelialization and in this regard we have tried to quantify and express it in numbers to see if there are clinical data we can quantify to support this clinical observation.

Conventional PRK is associated with complications such as postoperative pain and discomfort, corneal haze, and regression of myopia. PRK techniques and procedures have been modified in many different ways in an attempt to avoid these problems. In this regard, laser transepithelial de-epithelialization, Epi-Clear epikeratome and rotating brush have been used as a method of epithelial removal[12].

Comparison of different techniques and their outcomes have still remained controversial in identification of ‘the best’ method since there are a lot of various refractive nomograms, laser platforms and different surgeons performing the procedures. Alternatively, in this study, we found that PRK-b procedure had few benefits over PRK-a.

We assume there is less haze development in PRK-b group since chemical reaction of alcohol and underground tissue, i.e., Bowman’s membrane, is avoided. Moreover, edges of the epithelium after PRK-b are smoother, which may contribute to better postoperative results.

Poyales *et al.*[15] conducted a study on corneal densitometry after PRK, LASIK, and small-incision lenticule extraction. They found that corneal densitometry was not negatively affected by any of the refractive surgical procedures under evaluation. Moreover, corneal densitometry can be used as an objective metric to assess corneal response to refractive surgery, and to monitor patients over time. The mean postoperative total corneal densitometry values were 16.53±1.94 for the LASIK-FS group, 15.53±1.65 for PRK, and 16.10±1.54 for ReLEx SMILE. When corneal densitometry was analyzed for specific corneal areas, the values corresponding to the 0-2, 2-6-, and 6-10-mm annuli were similar across the three surgical techniques. The only region in which differences were found was peripheral area ($p<0.05$), but these variations across techniques were not statistically significant[15].

In conclusion, in our research, none of the patients in either group had postoperative problems with re-epithelialization or other corneal issues. There is a vast number of factors that determine final visual outcome after PRK, including the nature of patient refractive error and patient selection, biological tissue 'quality' (cases of basal membrane dystrophy, patients prone to haze development, etc.). Our findings lead to a conclusion that both PRK-a and PRK-b potentiate safe and desirable outcomes. However, PRK-b showed relatively superior outcomes in comparison to PRK-a, especially in corneal densitometry measurements during the 12-month follow up period.

Value statement

What was known:

It is known that there are different ways of removing epithelium in PRK methods such as alcohol, laser ablation (phototherapeutic keratectomy), mechanical way, or rotating brush. So far, it has not been proven which of these methods gives better quality of vision and visual acuity.

What this paper adds:

- PRK-brush group showed superior results and statistically significant difference in terms of less haze formation and improved corneal densitometry measurements 12 months after surgery; and
- visual acuity results were slightly better in PRK-brush group but statistically nonsignificant throughout the 12-month postoperative period.

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Sažetak

USPOREDBA REZULTATA DENZITOMETRIJE ROŽNICE I REFRAKCIJSKIH VRIJEDNOSTI VIDNE OŠTRINE UPORABOM TEHNIKA UKLANJANJA EPITELA ALKOHOLOM I MEHANIČKI (ROTIRAJUĆIM ČETKICAMA) KOD FOTOREFRAKTIVNE KERATEKTOMIJE MIOPSKIH BOLESNIKA

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Cilj studije bio je usporediti denzitometriju rožnice, zamućenja rožnice, vidne i refrakcijske rezultate nakon fotorefraktivne keratektomije (PRK) izvedene različitim tehnikama uklanjanja epitela. Ovo istraživanje uključilo je 42 bolesnika (84 oka) koji su podvrgnuti zahvatu PRK s jednim okom deepiteliziranim 20% otopinom etanola (skupina PRK-a) i drugim okom rotirajućom četkicom (skupina PRK-b). Zahvate je izvodio isti kirurg na istoj laserskoj platformi nakon sveobuhvatne prijeoperacijske procjene. Kontrolni pregledi bolesnika zakazani su 4. poslijeoperacijskog dana, zatim 1, 3 i 12 mjeseci nakon operacije. Brži oporavak vidne oštrine postignut je u skupini PRK-b tijekom 12-mjesečnog poslijeoperacijskog razdoblja, ali razlike nisu bile statistički značajne. Zamućenje je bilo značajno manje prisutno u skupini PRK-b mjereno 12 mjeseci nakon operacije. Također, oči u skupini PRK-b vratile su se blizu vrijednosti bazalne denzitometrije rožnice brže od onih u skupini PRK-a. Kratkotrajni vidni oporavak uslijedio je brže u slupini PRK-b. Manji razvoj zamućenja i bolja prozirnost rožnice postignuti su u skupini PRK-b tijekom 12-mjesečnog razdoblja praćenja. Međutim, oba postupka pokazala su izvrsne rezultate i zadovoljstvo bolesnika bilo je visoko bez obzira na metodu deepitelizacije.

Ključne riječi: *Fotorefraktivna keratektomija; Miopija; Rožnica; Uklanjanje epitela*