

Conventional PRK versus single-step transPRK in corneal refractive surgery with excimer laser

PRK convencional versus trans-PRK de un solo paso en cirugía refractiva corneal con excímer láser

Giuseppe Miotto-Montesinos¹, Eduardo Rojas-Alvarez^{1,2*}, Diego Torres-Piedra¹ and Natali Torres-Palacios¹

¹Exiláser Ophthalmological Center; ²Faculty of Medical Sciences, University of Cuenca. Cuenca, Ecuador

Abstract

Objective: To compare conventional alcohol-assisted PRK (aaPRK) and single-step transPRK in terms of clinical-refractive and surgical variables. **Method:** An observational, prospective, longitudinal study was carried out in 72 patients who were candidates for corneal refractive surgery with the excimer laser, with a diagnosis of compound myopic astigmatism, at the Exiláser Ophthalmological Center, Cuenca, Ecuador, from September to December 2019. Patients underwent surface surgery (transPRK or aaPRK). Data processing was performed with the SPSS program, version 21.0. For data comparison between both surgical techniques, the chi-square test was used, where $P < 0.05$ was considered statistically significant. **Results:** The average spherical equivalent was obtained for aaPRK (-0.14) and transPRK (-0.11) 3 months after the procedure ($p = 0.34$). UCVA average was 0.93 in aaPRK and 0.96 in transPRK, without statistically significant differences ($p = 0.63$). Surgical time was shorter in transPRK (720.31 s) compared to aaPRK (1080.85 s), with a statistically significant difference ($p < 0.001$). In transPRK there was less pain immediately after surgery, compared to aaPRK ($p < 0.05$). Epithelial closure was achieved on day 6.27 for aaPRK and in day 3.62 for transPRK (average values; $p = 0.02$). **Conclusions:** Single-step transepithelial PRK and aaPRK in patients who are candidates for refractive surgery showed very similar results 3 months after surgery in terms of uncorrected visual acuity, spherical equivalent and with minimal postoperative complications. TransPRK offers greater advantages to the patient regarding shorter surgical time, rapid epithelial closure and less pain in the immediate postoperative period.

Key words: PRK. Trans-PRK. Myopia. Astigmatism. Visual acuity. Spherical equivalent.

Resumen

Objetivo: Establecer una comparación entre la técnica PRK convencional, asistida con alcohol (PRKaa), y la trans-PRK de un solo paso, en cuanto a variables clínico-refractivas y quirúrgicas. **Método:** Se realizó un estudio observacional, prospectivo, longitudinal, en 72 pacientes candidatos a cirugía refractiva corneal con excímer láser, con el diagnóstico de astigmatismo miópico compuesto, en el Centro Oftalmológico Exiláser, Cuenca, Ecuador, de septiembre a diciembre de 2019. Los pacientes fueron intervenidos por técnicas de superficie (trans-PRK o PRKaa). El procesamiento de los datos se realizó en el programa SPSS, versión 21.0. Para la comparación de los datos de ambas técnicas quirúrgicas se empleó la prueba de chi cuadrado, donde se consideró $p < 0.05$ estadísticamente significativo. **Resultados:** Se obtuvo como equivalente esférico promedio para PRKaa -0.14 y para trans-PRK -0.11, a los 3 meses del procedimiento ($p = 0.34$). El promedio de agu-

Correspondence:

*Eduardo Rojas-Alvarez

Federico Proaño 4-26 y Av Remigio Crespo,
Cuenca, Ecuador

E-mail: drerojasalvarez@gmail.com

Date of reception: 15-02-2020

Date of acceptance: 17-05-2020

DOI: 10.24875/RMOE.M20000126

Available online: 01-09-2020

Rev Mex Oftalmol (Eng). 2020;94(5):183-191

www.rmo.com.mx

2604-1731/© 2020 Sociedad Mexicana de Oftalmología. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

deza visual sin corrección obtenido fue en PRKaa de 0.93 y en trans-PRK de 0.96, sin diferencias estadísticamente significativas ($p = 0.63$). El tiempo quirúrgico para PRKaa fue de 1,080.85 s y para trans-PRK fue de 720.31 s, menor en esta última con diferencia estadísticamente significativa ($p < 0.001$). En trans-PRK hubo menor dolor inmediatamente después de la cirugía, comparado con PRKaa ($p < 0.05$). El día promedio de cierre epitelial en PRKaa fue el 6.27 y en trans-PRK el 3.62 ($p = 0.02$). **Conclusiones:** La PRK-transepitelial de un solo paso y la PRKaa realizada en pacientes candidatos a cirugía refractiva producen resultados muy similares a los 3 meses de la cirugía en cuanto a AVSC, equivalente esférico obtenido y mínimas complicaciones postoperatorias. La trans-PRK ofrece mayores ventajas al paciente, referentes a menor tiempo quirúrgico, rápido cierre epitelial y menor dolor en el postoperatorio inmediato.

Palabras clave: PRK. Trans-PRK. Miopía. Astigmatismo. Agudeza visual. Equivalente esférico.

Introduction

The procedures designed to correct refractive defects through the modification of the cornea have had an evolutionary process fundamentally aimed at obtaining the greatest possibility of emmetropia, predictability, efficacy and safety. Surface techniques have not been exempt from this technological evolution. Although LASIK has been the protagonist of these improvements throughout history, surface techniques have also been the subject of research to optimize their results¹⁻³.

The original method of removing the corneal epithelium before performing excimer laser ablation was mechanical (manual) for years, and it continues to be used internationally, achieving high refractive standards. In 2003, Camellin⁴ proposed a new absolute alcohol-assisted technique called *laser-assisted subepithelial keratectomy* (LASEK) that preserves the epithelium, which is replaced after laser ablation. The laser epithelial *in situ* keratomileusis (Epi-LASIK) is another method that uses the epithelial flap, in this case with a microkeratome⁵.

In the late 1990s, transepithelial photorefractive keratectomy (trans-PRK) began to emerge as a technique in which phototherapeutic ablation of the corneal epithelium was first performed, followed by refractive ablation with excimer laser of the corneal stroma. At that time, the surgical technique did not obtain the expected superior refractive results, taking into account the longer surgical time of the procedure, the greater postoperative pain of the patient and the need to adjust treatment nomograms⁶⁻⁹.

The continuous development of refractive lasers, specifically the reduction of ablation time and the advent of fast lasers, has enabled a resurgence of trans-PRK as a refractive technique increasingly used today, where epithelial and stromal ablation is performed as a single step, reducing the surgical time and increasing patient comfort during the procedure. Considering these aspects and due to the acquisition of this technology in our institution, we decided to conduct this research.

Objective

To compare the conventional alcohol-assisted PRK technique (aaPRK) with the single-step transPRK, in terms of clinical-refractive and surgical variables.

Methods

An observational, prospective, longitudinal study was conducted in 72 patients who were candidates for corneal refractive surgery with an excimer laser, with a diagnosis of compound myopic astigmatism, at the Exiláser Ophthalmological Center, Cuenca, Ecuador, from September to December 2019.

Criteria for the selection of cases

Inclusion criteria:

- Patients over 21 years old.
- Patients with a diagnosis of compound myopic astigmatism (less than 8 diopters in the algebraic sum of sphere and cylinder).
- 2-year history of refractive stability.
- Uncorrected visual acuity of 0.5 or less.
- Corrected visual acuity in the worse eye >0.5 .
- Scheduled residual corneal bed greater than 400 μm
- Initial and final programmed mean keratometry between 36 and 48 diopters.

– Preoperative pachymetry greater than 500 μm . Exclusion criteria:

- Patients with history of ocular disorders or eye surgeries (corneal refractive surgery, corneal transplantation, herpes simplex or zoster keratitis, confirmed or suspected corneal ectasia, recurrent corneal erosions, leucomas, pannus, dystrophies, degenerations, strabismus or previous strabismus surgery, glaucoma or ocular hypertension, lens sclerosis or cataract, uveitis, monocular vision loss, retinal tears, history of retinal detachment, vitrectomy, macular degeneration, retinitis pigmentosa)

- Patients who did not attend any of the study visits.
- Patients who did not grant consent for participation in the study.
- Systemic diseases such as diabetes mellitus, epilepsy, collagen diseases, immunosuppression, psychiatric disorders, Marfan syndrome, Ehlers Danlos, psoriasis, allergies.
- Systemic infections.
- Pregnancy. Postpartum (up to 6 months).
- Alteration of the ocular annexes and of the tear film (infection, inflammation, dry eye).
- Abnormal orbital configurations (small or deep orbits, small palpebral fissure, enophthalmos, prominent superciliary arch).
- Ablation time: Total ablation time was measured in seconds; for trans-PRK, total time epithelial and stromal ablation.
- Ocular pain: It was evaluated at the end of the surgery (day 0), in a postoperative consultation at 24 hours (day 1) and the following days until the fifth day. The patient subjectively reported, on a scale of 1 to 10 (worst pain), the level of eye pain to the ophthalmologist.
- Corneal re-epithelialization time: Complete re-epithelialization time after surgery, expressed in days. Evaluated by biomicroscopy on days 1, 3, 5 or 7.
- Endothelial microscopy: Registered in cells/mm² by specular microscopy, prior to surgery, one month and 3 months postoperatively.

The 72 patients underwent a surface technique, and were assigned consecutively in a random fashion: the first 32 patients were allocated to aaPRK and the following 40 patients were allocated to trans-PRK, obtaining two groups:

- N1 = 32, patients operated with the aaPRK technique.
- N2 = 40, patients operated with the trans-PRK technique.

Study variables

- Sphere: The dynamic refraction value was selected preoperatively and 3 months postoperatively.
- Cylinder: The dynamic refraction value was selected preoperatively and 3 months postoperatively.
- Uncorrected visual acuity: Measured with a Snellen chart two times, preoperatively and 3 months postoperatively.
- Degree of corneal haze: According to the following classification, evaluated (biomicroscopy) by an ophthalmologist blinded for the surgical technique used, 3 months postoperatively.
 - Grade 0: Fully transparent cornea.
 - Grade 1: Low-density haze, only visible with indirect tangential illumination of the cornea.
 - Grade 2: Light haze, showing areas of focal confluence, visible with direct illumination of the cornea.
 - Grade 3: Clinically significant moderate haze showing areas of diffuse confluence, which partially obscure iris details.
 - Grade 4: Severe haze, an opaque cornea that prevents iris visualization.
- Surgical time: The actual time of the surgery was measured from the placement of the eyelid speculum to its removal, expressed in seconds.

Preoperative examination

Preoperative information was obtained from each patient regarding general and ocular medical history, use of contact lenses and the use of medications. Examination included uncorrected distance visual acuity (UCVA), corrected distance visual acuity (BCVA), manifest and cycloplegic refraction, slit-lamp biomicroscopy, tonometry, endothelial microscopy, pupillometry, Scheimpflug camera tomography (Pentacam), fundus examination and ocular motility evaluation.

Surgical technique

All surgeries were performed with an EX500 excimer laser (Alcon Refractive Suite). The treatments were performed by two surgeons, using an identical surgical protocol. Surgical times between surgeons did not vary significantly, with 0.12 seconds of average inter-variability. The programmed optical zones of all the treatments were of 6.50 mm. All treatments were aimed at emmetropia (0.0). Before surgery, drops of 0.5% proparacaine hydrochloride were instilled (three times in a 5-minute interval). Mitomycin C (0.02%) was used in all cases for 20 seconds.

aaPRK

A drop of topical anesthetic was instilled into the eye to be operated, followed by isolation of the surgical area with a sterile surgical field and placement of an eyelid speculum to expose the eyeball. Application of iodopovidone 5% in the conjunctival cul-de-sac for 3 minutes. Flushing of the conjunctival cul-de-sac with a balanced saline solution. Placement of the 8.5 mm alcohol container with the center in the pupil, after

corneal marking for 30 seconds. Thorough flushing with a balanced saline solution. Separation of the corneal epithelium from the edges of the marker. Laser application. Placement of a micro sponge with mitomycin C (0.02%) for 20 seconds in the stromal bed. Thorough flushing with a balanced saline solution. Placement of a soft contact lens. Instillation of one drop of moxifloxacin plus dexamethasone.

Trans-PRK

A drop of topical anesthetic was instilled into the eye to be operated. Isolation of the surgical area with a sterile surgical field and placement of an eyelid speculum to expose the eyeball. Application of iodopovidone 5% in the conjunctival cul-de-sac for 3 minutes. Flushing of the conjunctival cul-de-sac with a balanced saline solution. Instillation of refrigerated balanced saline (10 °C) in the cornea, followed by drying. Initiation of scheduled transepithelial ablation for standard 55 µm epithelium. 10-second pause and continued ablation of the corneal stroma. Thorough flushing with refrigerated a balanced saline solution (10 °C). Drying and placement of a micro sponge with mitomycin C (0.02%) for 20 seconds in the stromal bed. Thorough flushing with balanced saline solution. Placement of a soft contact lens. Instillation of one drop of moxifloxacin plus dexamethasone.

Postoperative treatment consisted of Artificial tears 1 drop every 4 hours, tobramycin plus dexamethasone, 1 drop every 4 hours for one month after surgery. Subsequently only artificial tears 2 times a day for 3 months. Postoperative controls were performed at 24 hours, 72 hours, 5 days, 7 days, one month and 3 months after the intervention. No intraoperative complications were observed. Therapeutic contact lens removal was programmed depending on epithelial closure time.

Methods for obtaining information, statistical analysis and ethical aspects

Information was obtained from the clinical records and Pentacam of each patient. SPSS version 21.0 was used for data processing. The mean of the variables studied by each surgical technique was obtained. The chi-square test was used to compare data from both surgical techniques, where a p <0.05 was considered statistically significant. The patients gave their consent to participate in the study and the research was approved by the institution’s Bioethics Committee.

Table 1. Average spherical equivalent of the sample by surgical technique. Exiláser Ophthalmological Center, September-December 2019

	aaPRK	Trans-PRK	p
Preoperative	-4.17	-3.96	0.16
Postoperative (1 month)	-0.21	-0.18	0.27
Postoperative (3 months)	-0.14	-0.11	0.34

Table 2. Average uncorrected visual acuity of the sample by surgical technique. Exiláser Ophthalmological Center, September-December 2019

	aaPRK	Trans-PRK	p
Preoperative	0.32	0.26	0.16
Postoperative (1 month)	0.87	0.84	0.55
Postoperative (3 months)	0.93	0.96	0.63

Table 3. Average surgical times by surgical technique. Exiláser Ophthalmological Center, September-December 2019

Time (seconds)	aaPRK	Trans-PRK	p
Ablation	12.34	42.48	< 0.001
Complete procedure	1,080.85	720.31	< 0.001

Results

A decrease in the spherical equivalent was obtained with both surgical techniques, with average values close to emmetropia. No significant differences were observed in the average spherical equivalent between both procedures in the two postoperative time points evaluated (Table 1).

Table 2 shows the average uncorrected visual acuity for each group. In both techniques values close to 1.0 (20/20) were obtained as a mean, without statistically significant differences between both procedures.

Regarding ablation time (Table 3), this was higher in the trans-PRK group, with a statistically significant difference, compared to the average ablation time of the sample in the aaPRK group. However, the time of the surgical procedure was longer in the aaPRK group compared to transPRK, with a statistically significant difference.

As [Figure 1](#) shows, patients reported more pain in the first postoperative hours. The pain was higher in patients of the aaPRK group, with a statistically significant difference compared to the mean pain value reported in patients of the trans-PRK group. In both surgical techniques, there was a maximum pain peak on the first postoperative day, with no differences between the two techniques. There was a progressive decrease in pain until the fifth postoperative day, with very similar behavior in both procedures ([Table 4](#)).

As [Table 5](#) shows, the patients of the trans-PRK group had an earlier epithelial closure, with a statistically significant difference compared to the aaPRK group.

In the 1-month postoperative period, the presence of corneal haze in the study patients was not confirmed by biomicroscopic examination; however, 3 months after surgery, three patients showed the presence of grade I corneal haze. No other intraoperative or postoperative complications were reported during follow-up ([Table 6](#)).

As [Table 7](#) shows, no significant variations in endothelial cell density were observed between the preoperative average value compared to the average values obtained at one month and at three months of follow-up, in both surgical techniques. There were no significant differences between both groups.

Discussion

The refractive results of both surgical techniques were satisfactory. No differences were observed between both procedures, from one month to the values obtained at three months, which shows the efficacy of both techniques in the treatment of compound myopic astigmatism. UCVA values corroborate this result, and high standards were achieved as a sample mean in the two study groups.

In the case of aaPRK, laser ablation is performed directly and solely in the corneal stroma, once the corneal epithelium has been mechanically removed, providing greater certainty in terms of the accuracy of the stromal tissue removed and its exact relationship with the number of diopters to be treated, compared to trans-PRK where a double ablation occurs: first, of the corneal epithelium, and later, of the corneal stroma.

In trans-PRK, the ablation profile is obtained from a reference epithelial thickness value, taken as the standard for the population. The thickness of the corneal epithelium of a normal cornea ranges from 55 to 65 μm in the central 4 mm. In this study, we used a reference

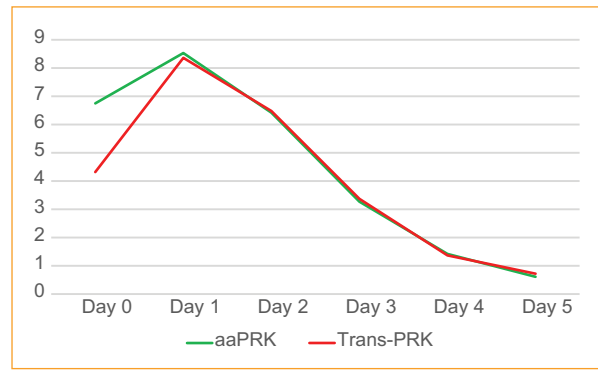


Figure 1. Average postoperative pain curves per day, with both surgical techniques. Exiláser Ophthalmological Center, September-December 2019.

Table 4. Average postoperative pain (maximum 10) after surgery. Exiláser Ophthalmological Center, September-December 2019

Days	aaPRK	Trans-PRK	p
0	6.75	4.32	< 0.05
1	8.53	8.36	0.12
2	6.42	6.48	0.23
3	3.27	3.37	0.25
4	1.42	1.37	0.19
5	0.61	0.72	0.21

Table 5. Average epithelial closure time by surgical technique. Exiláser Ophthalmological Center, September-December 2019

	aaPRK	Trans-PRK	p
Average day	6.27	3.62	0.02

Table 6. Patients with corneal haze. Exiláser Ophthalmological Center, September-December 2019

	aaPRK	Trans-PRK
Postoperative (1 month)	0	0
Postoperative (3 months)	1	2

value for the treatments of 55 μm . This fact can be controversial, considering that not all patients have the same epithelial thickness, so patients with thin epithelia

Table 7. Corneal endothelial cell density (average). Exiláser Ophthalmological Center, September-December 2019

Surgical techniques	Preoperative	Postoperative (1 month)	Postoperative (3 months)	p
aaPRK	2,431	2,422	2,425	0.36
Trans-PRK	2,426	2,409	2,432	0.42

will have more stroma ablated than that programmed. On the other hand, in patients with thick epithelia, an ablation with refractive purposes would begin with the presence of epithelium on the surface and, therefore, patients could be slightly hypo- or hypercorrected.

Different authors have reported differences in epithelial thickness along the corneal surface. Reinstein, et al.¹⁰ observed that the location of the thinnest epithelium is somewhat displaced temporarily (0.33 mm) and towards the superior cornea (0.90 mm), they showed a mean epithelial thickness of $53.4 \pm 4.6 \mu\text{m}$ at the corneal vertex using very high-frequency digital ultrasound. In addition, in their analysis of epithelial thickness maps, they observed a greater thickness of the epithelium in the inferior cornea compared to the superior cornea, and in the nasal cornea compared to the temporal cornea.

Kanellopoulos, et al.¹¹ and Sin, et al.¹² followed this line of research using spectral domain-optical coherence tomography of the anterior segment. The epithelial thickness observed in the pupillary center was of $53.28 \pm 3.34 \mu\text{m}$, in the inferior cornea of $53.81 \pm 3.44 \mu\text{m}$, and in the superior cornea of $51.86 \pm 3.78 \mu\text{m}$, so they conclude that the epithelial thickness map cannot be considered rotationally symmetrical.

Different publications agree on the high inter-individual variability of central epithelial thickness and three-dimensional epithelial maps¹³⁻¹⁵. Considering the theoretical aspects mentioned above, trans-PRK could induce worse refractive results if we take as standard a single epithelial thickness value for the procedure. However, in practice, it has not been possible to verify unsatisfactory visual results of this technique compared to aaPRK.

A determining factor for the optimal trans-PRK refractive results is the presence of an ablation profile free of spherical aberration. In addition, the laser system is adjusted to compensate for the difference between the photoablation rate of the stroma and the corneal epithelium (upper 20%). The epithelium is removed with a parallel cut profile, meaning that it is removed in the same proportion throughout the area in which the epithelium is being removed until reaching the transition

zone, where it gradually stops removing tissue. Therefore, this removal does not generate any corrective effect¹⁶⁻¹⁸.

From the beginning of the use of single-step trans-PRK, several studies showed preliminary results. Luger, et al.¹³ conducted a study in which one eye underwent trans-PRK and the fellow eye underwent aaPRK with the Amaris (Schwind) laser in 33 patients with 1-year of follow-up. Significant differences were obtained between both techniques in terms of uncorrected visual acuity. Likewise, with the Amaris platform, Fadlallah, et al.¹⁵ obtained similar visual acuity parameters with both surgical techniques. Aslanides, et al.¹⁴ conducted a study in 30 patients using a technique in each eye, and obtained similar values of visual acuity with both procedures.

Kaluzny, et al.¹⁶ performed a study in 148 patients using a more modern version of transPRK (The Amaris platform, 750 S version, sixth generation) compared to the aforementioned studies. There were no statistically significant differences between the trans-PRK group and the aaPRK group in terms of UCVA 3 months after surgery. Aslanides, et al.¹⁴ did not report significant differences in the final refraction achieved with both surgical techniques, with an equivalent safety. Ortueta, et al.¹⁹, in a more recent study, concluded that trans-PRK has refractive results similar to intrastromal techniques, with less possibility of complications. Xi, et al.²⁰ demonstrated that single-step transPRK can correct myopia effectively.

Antonios, et al.²¹ reported a majority of patients in the range of $\pm 0.50 \text{ D}$ and $\pm 1.0 \text{ D}$, one year after the procedure. Fadlallah, et al.¹⁵ reported an overcorrection trend that could be explained by corneal dehydration during the procedure. Adib-Moghaddam, et al.²²⁻²⁵ indicated that single-step trans-PRK with aberration-free mode improves visual acuity and refraction in high myopic eyes, and achieves better visual quality results compared to other refractive techniques. The single-step trans-PRK platform uses a corneal thickness population profile to calculate the amount of energy delivered to different parts of the cornea, which avoids supplying unequal amounts of energy to the central

cornea compared to the peripheral cornea. This difference could explain the better visual quality results of trans-PRK in high myopia²⁶⁻²⁹.

The duration of the surgery is another of the widely studied variables, considering its value in the effectiveness of surgical time, the usefulness of the laser parameters and the patient's comfort during the procedure. In the first instance, it could be thought that trans-PRK requires longer surgical time, considering the prolonged ablation of the corneal epithelium compared to aaPRK, where it is mechanically removed. However, the use of the absolute alcohol container, flushing with saline solution and the need for greater patient cooperation, are aspects that prolong surgical time.

An advantage of trans-PRK is the reduction in surgery time. Kaluzny, et al.¹⁶ observed a reduction (35%) of surgical time in trans-PRK compared to aaPRK. Luger, et al.¹³ stated that trans-PRK is a faster technique. Trans- and postoperative pain is related to surgical time. The surgery itself is less stressful for the patient and very comfortable for the surgeon. The topic of postoperative pain in surface refractive techniques has been evaluated by different authors. Fadlallah, et al.¹⁵ and Aslanides, et al.¹⁴ reported a decrease in postoperative pain after single-step transepithelial PRK. Kanitkar, et al.⁷ reported less pain in aaPRK compared to PRK preceded by phototherapeutic keratectomy to remove the corneal epithelium. Luger, et al.¹³ reported less postoperative pain in patients who underwent trans-PRK compared to aaPRK, as well as greater patient comfort during trans-PRK. However, Aslanides, et al.¹⁴ did not observe significant differences between the two groups on the first postoperative day, but they reported less pain in the trans-PRK group on the third day after the procedure.

In our study, the greatest difference in terms of patient-reported pain occurred immediately after the procedure, where we obtained a higher average value of pain in the aaPRK group. The absence of alcohol in transPRK, the shorter surgical time, the performance of a single-step surgery and the absence of eyeball manipulation by the surgeon, are factors that can explain these differences. On consecutive days, there were no significant differences in patient-reported pain between the two study groups. The pain on the following days is more related to the photoablation effect, the inflammatory mediators and the corneal re-epithelialization process, common to both surgical techniques.

Regarding corneal haze, it occurred with both techniques, but in a minority of cases, all grade I. They were treated with topical steroids (fluorometholone) and

without significant visual implications. The refractive defects treated in these patients with haze did not exceed 4 D in the algebraic sum of sphere and cylinder. The laser energy, among other consequences, causes a temperature increase at the corneal stroma that constitutes one of the main factors related to the presence of haze, although other factors have been cited, such as the regularity of the edges of the corneal epithelium, the magnitude of the refractive defect treated, the lack of postoperative topical steroids use, as well as the patient's own factors and healing³⁰⁻³³.

Different studies have analyzed the response of the corneal stroma to ablation and the subsequent formation of corneal haze. Helena, et al.³⁴ and Kim, et al.³⁵ argue that keratocyte apoptosis and myofibroblast activation are a key factor in stromal recovery after surface ablation procedures, and that transepithelial ablation results in lower levels of keratocyte apoptosis. Other authors report that the transepithelial removal of the epithelium produces a smooth and uniform surface, ideal for epithelial regeneration³⁶⁻³⁹. The studies by Chen⁴⁰, et al. show that the viability of the epithelial cells of the limbus is reduced with the application of alcohol, with an increase in the inflammatory response and anterior stroma keratocytes damage.

In trans-PRK, the total energy of the excimer laser is greater. Kaluzny, et al.¹⁶ reported a 163% longer mean ablation time in the trans-PRK group; however, it should be noted that most of the laser energy is delivered to the epithelium, with previous saline irrigation at 10 °C and with a 10-second pause before continuing stromal ablation, factors that attenuate the effect of increased corneal temperature in these patients.

Aslanides, et al.¹⁴ showed significant differences regarding corneal haze in the first 6 months postoperatively, with greater incidence in the aaPRK group. One year after treatment, they reported no differences between the two groups. Kaluzny, et al.¹⁶, up to 3 months after surgery, observed haze more frequently in the trans-PRK group, with no statistically significant differences compared to the aaPRK group. The non-significant differences in the intensity and presence of haze in the two groups can be explained by the use of mitomycin C, used in both techniques. The comparative analysis of haze in both techniques without mitomycin C use would be interesting to assess the real effect of ablation. This cannot be done in humans due to the obvious ethical implications.

Aslanides, et al.¹⁴ observed that on the third postoperative day, most patients in the trans-PRK group showed epithelial closure, with statistically significant

differences, compared with the aaPRK group, where most patients showed epithelial closure on the fifth day after the procedure. Fattah, et al.⁴¹ reported faster epithelial closure with trans-PRK and a lower incidence of corneal erosions compared to the aaPRK group. The main reason for the faster recovery of the corneal epithelium in trans-PRK is that the diameter of the epithelial excision coincides with the total ablation zone, reducing the wound surface and shortening epithelial closure time^{21,22}.

Regarding corneal endothelial density, we did not observe significant postoperative variations with the two procedures. We did not find scientific evidence of endothelial alteration produced by aaPRK or trans-PRK when the protocols established for these procedures are optimally followed.

One of the limitations of our study is the subjective evaluation of corneal haze by biomicroscopy, instead of using other more objective methods such as confocal microscopy or densitometry. On the other hand, in future studies would also be necessary to evaluate the differences between both techniques in terms of corneal aberrations and to perform preoperative measurements of epithelial thickness with the possibility of personalized trans-PRK ablations.

Conclusions

Single-step transepithelial PRK and aaPRK in patients who are candidates for refractive surgery produce very similar results at 3 months after surgery in terms of UCVA, spherical equivalent results and postoperative complications, which are minimal. Trans-PRK offers greater advantages to the patient, with shorter surgical times, rapid epithelial closure and less pain in the immediate postoperative period.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

The authors declare that they did not receive funding for the research.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical

research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

References

1. Kaluzny B, Cieslinska I, Mosquera S, Verma S. Single-Step transepithelial PRK vs alcohol-assisted PRK in myopia and compound myopic astigmatism correction. *Medicine (Baltimore)*. 2016;95(6):e1993.
2. Abad JC, An B, Power WJ, Foster CS, Azar DT, Talamo JH. A prospective evaluation of alcohol-assisted versus mechanical epithelial removal before photorefractive keratectomy. *Ophthalmology*. 1997;104:1566-74.
3. Dupps WJ, Jr, Kohnen T, Mamlis N, Rosen ES, Koch DD, Obstbaum SA, et al. Standardized graphs and terms for refractive surgery results. *Cataract Refract Surg*. 2011;37:1-3.
4. Camellin M. Laser epithelial keratomileusis for myopia. *J Refract Surg*. 2003;19:666-70.
5. Pallikaris IG, Katsanevaki VJ, Kalyvianaki MI, Naoumidi II. Advances in subepithelial excimer refractive surgery techniques: Epi-LASIK. *Curr Opin Ophthalmol*. 2003;14:207-12.
6. Carr JD, Patel R, Hersh PS. Management of late corneal haze following photorefractive keratectomy. *J Refract Surg*. 1995;11:S309-13.
7. Kanitkar KD, Camp J, Humble H, Shen DJ, Wang MX. Pain after epithelial removal by ethanol-assisted mechanical versus transepithelial excimer laser debridement. *J Refract Surg*. 2000;16:519-22.
8. Clinch TE, Moshirfar M, Weis JR, Ahn CS, Hutchinson CB, Jeffrey JH. Comparison of mechanical and transepithelial debridement during photorefractive keratectomy. *Ophthalmology*. 1999;106:483-9.
9. Lee HK, Lee KS, Kim JK, Kim HC, Seo KR, Kim EK. Epithelial healing and clinical outcomes in excimer laser photorefractive surgery following three epithelial removal techniques: mechanical, alcohol, and excimer laser. *Am J Ophthalmol*. 2005;139:56-63.
10. Reinstein DZ, Archer TJ, Gobbe M, Silverman RH, Coleman DJ. Epithelial thickness in the normal cornea: three-dimensional display with Artemis very high-frequency digital ultrasound. *J Refract Surg*. 2008;24:571-81.
11. Kanellopoulos AJ, Asimellis G. In vivo three-dimensional corneal epithelium imaging in normal eyes by anterior-segment optical coherence tomography: a clinical reference study. *Cornea*. 2013;32:1493-8.
12. Sin S, Simpson TL. The repeatability of corneal and corneal epithelial thickness measurements using optical coherence tomography. *Optom Vis Sci*. 2006;83:360-5.
13. Luger MH, Ewering T, Arba-Mosquera S. Consecutive myopia correction with transepithelial versus alcohol-assisted photorefractive keratectomy in contralateral eyes: one-year results. *J Cataract Refract Surg*. 2012;38:1414-23.
14. Aslanides IM, Padroni S, Arba Mosquera S, Ioannides A, Mukherjee A. Comparison of single-step reverse transepithelial all-surface laser ablation (ASLA) to alcohol-assisted photorefractive keratectomy. *Clin Ophthalmol*. 2012;6:973-80.
15. Fadlallah A, Fahed D, Khalil K, Dunia I, Menassa J, El Rami H, et al. Transepithelial photorefractive keratectomy: clinical results. *J Cataract Refract Surg*. 2011;37:1852-7.
16. Kaluzny BJ, Szkulmowski M, Bukowska DM, Wojtkowski M. Spectral OCT with speckle contrast reduction for evaluation of the healing process after PRK and transepithelial PRK. *Biomed Opt Express*. 2014;5:1089-98.
17. Adib-Moghaddam S, Arba-Mosquera S, Salimian B, Omidvari AH, Noorzadeh F. On-line pachymetry outcome of ablation in aberration free mode TransPRK. *Eur J Ophthalmol*. 2014;24:483-9.
18. Arba Mosquera S, Awwad ST. Theoretical analyses of the refractive implications of transepithelial PRK ablations. *Br J Ophthalmol*. 2013;97:905-11.
19. Ortueta D, von Rueden D. Transepithelial photorefractive keratectomy: Results and clinical experiences. *Ophthalmologie*. 2019;116(6):534-41.
20. Xi L, Zhang C, He Y. Single-step Transepithelial photorefractive keratectomy in the treatment of mild, moderate, and high myopia: six-month results. *BMC Ophthalmol*. 2018;18(1):209.
21. Antonios R, Abdul Fattah M, Arba Mosquera S, Abiad BH, Sleiman K, Awwad ST. Single-step transepithelial versus alcohol-assisted photorefractive keratectomy in the treatment of high myopia: a comparative evaluation over 12 months. *Br J Ophthalmol*. 2017;101(8):1106-12.

22. Adib-Moghaddam S, Haydar AA, Razi-Khosroshahi M, Soleyman-Jahi S, Tefagh G, Grentzelos MA, et al. Predictors of visual acuity improvement and supernormal vision after refined single-step transepithelial photorefractive keratectomy. *J Refract Surg.* 2019;35(12):771-80.
23. Adib-Moghaddam S, Soleyman-Jahi S, Adili-Aghdam F, Arba Mosquera S, Hoorshad N, Tofighi S. Single-step transepithelial photorefractive keratectomy in high myopia: qualitative and quantitative visual functions. *Int J Ophthalmol.* 2017;10(3):445-52.
24. Adib-Moghaddam S, Soleyman-Jahi S, Sanjari Moghaddam A, Hoorshad N, Tefagh G, Haydar AA, et al. Efficacy and safety of transepithelial photorefractive keratectomy. *J Cataract Refract Surg.* 2018;44(10):1267-1279.
25. Adib-Moghaddam S, Arba-Mosquera S, Walter-Fincke R, Soleyman-Jahi S, Adili-Aghdam F. Transepithelial photorefractive keratectomy for hyperopia: a 12-month bicentral study. *J Refract Surg.* 2016;32(3):172-80.
26. Shetty N, Dadacharji Z, Narasimhan R, Kundu G, Khamar P, Ahuja P, et al. Status of residual refractive error, ocular aberrations, and accommodation after myopic LASIK, SMILE, and TransPRK. *J Refract Surg.* 2019;35(10):624-31.
27. Luger MH, Ewering T, Arba-Mosquera S. Myopia correction with transepithelial photorefractive keratectomy versus femtosecond assisted laser in situ keratomileusis: one-year case-matched analysis. *J Cataract Refract Surg.* 2016;42(11):1579-87.
28. Aslanides IM, Georgoudis PN, Selimis VD, Mukherjee AN. Single-step transepithelial ASLA (SCHWIND) with mitomycin-C for the correction of high myopia: long term follow-up. *Clin Ophthalmol.* 2014;9:33-41.
29. Aslanides IM, Kymionis GD. Trans advanced surface laser ablation (TransPRK) outcomes using Smart Pulse Technology. *Cont Lens Anterior Eye.* 2017;40(1):42-6.
30. Kumar NR, Khamar P, Shetty R, Sharma A, Shetty N, Pahuja N, et al. Identification of novel predictive factors for post-surgical corneal haze. *Sci Rep.* 2019;9(1):16980.
31. Arranz-Marquez E, Katsanos A, Kozobolis VP, Konstas AGP, Teus MA. A critical overview of the biological effects of mitomycin C application on the cornea following refractive surgery. *Adv Ther.* 2019;36:786-97.
32. Kaiserman I, Sadi N, Mimouni M, Sela T, Munzer G, Levartovsky S. Corneal breakthrough haze after photorefractive keratectomy with mitomycin C: Incidence and risk factors. *Córnea.* 2017;36:961-66.
33. Ang BC, Foo RC, Lim EW, Tan MM, Nah GK, Thean LS, et al. Risk factors for early-onset corneal haze after photorefractive keratectomy in an Asian population: Outcomes from the Singapore Armed Forces Corneal Refractive Surgery Programme 2006 to 2013. *J Cataract Refract Surg.* 2016;42(5):710-6.
34. Helena MC, Baerveldt F, Kim WJ, Wilson SE. Keratocyte apoptosis after corneal surgery. *Invest Ophthalmol Vis Sci.* 1998;39(2):276-83.
35. Kim BZ, Jordan CA, McGhee CN, Patel DV. Natural history of corneal haze after corneal collagen crosslinking in keratoconus using Scheimpflug analysis. *J Cataract Refract Surg.* 2016;42(7):1053-9.
36. Reinstein DZ, Archer TJ, Gobbe M. Change in epithelial thickness profile 24hours and longitudinally for 1 year after myopic LASIK: three-dimensional display with Artemis very high-frequency digital ultrasound. *J Refract Surg* 2012;28:195-201.
37. Kanellopoulos AJ, Asimellis G. Longitudinal postoperative Lasik epithelial thickness profile changes in correlation with degree of myopia correction. *J Refract Surg.* 2014;30:166-71.
38. Raviv T, Majmudar PA, Dennis RF, Epstein RJ. Mytomycin-C for post-PRK corneal haze. *J Cataract Refract Surg.* 2000;26:1105-6.
39. Fantès FE, Hanna KD, Waring GO, III, Pouliquen Y, Thompson KP, Savoldelli M. Wound healing after excimer laser keratomileusis (photorefractive keratectomy) in monkeys. *Arch Ophthalmol.* 1990;108:665-75.
40. Chen X, Stojanovic A, Hua Y, Eidel JR, Hu D, Wang J, et al. Reliability of corneal dynamic Scheimpflug analyser measurements in Virgin and post-PRK eyes. *PLoS ONE.* 2014;9(10):e109577.
41. Fattah MA, Antonios R, Arba Mosquera S, Abiad B, Awwad ST. Epithelial erosions and refractive results after single-step transepithelial photorefractive keratectomy and alcohol-assisted photorefractive keratectomy in myopic eyes: a comparative evaluation over 12 Months. *Cornea.* 2018; 37(1):45-52.