Trans-Epithelial Photorefractive Keratectomy in the Treatment of Myopia, Hyperopia and Astigmatism: Five-Year Results

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Received: 04 Dec. 2021; Accepted: 19 Aug. 2022

Abstract- We aimed to report the five-year results of Trans-epithelial Photorefractive Keratectomy (TPRK) in treating all kinds of refractive errors. In this retrospective cohort study, we quantitatively compared the clinical findings and assessment of optical and refractive parameters, including slit-lamp, corneal topography, Best Corrected Visual Acuity (BCVA), and Uncorrected Distance Visual Acuity (UDVA) in 172 eyes of myopic, hyperopic, and astigmatic patients before and five years after trans-PRK. The average time for post-surgery epithelial healing was 2.97±0.83 days in male and 2.94±0.87 days in female patients; the pain score in a week following the operation was 1.88±0.68 in males and 2.25±0.73 in females. Corneal haze was observed in five patients. No long-term adverse effect was reported. The pre-operative UDVA was 0.84±0.32 in male and 0.87±0.34 in female patients; while the postoperative UDVA was -0.02±0.04 in male and -0.01±0.02 in female patients. There was a highly significant correlation (P<0.001) in all indices except UDVA, which was almost near to being significant (P=0.07). In this survey, the mean safety and index were nearly 1.00. TPRK is a safe and efficient therapeutic procedure to treat all types of refractive errors, including myopia, hyperopia, and astigmatism, with no significant adverse effect. Being touchless and having a short recovery time are two main characteristics of this refractive surgery.

Acta Med Iran 2022;60(10):640-645.

Keywords: Transepithelial photorefractive keratectomy; Transepithelial photorefractive keratectomy (Trans-PRK); Myopia; Hyperopia; Astigmatism

Introduction

Refractive errors are the most common form of ocular disorders involving all age groups (1). It is estimated that more than 2.3 billion people in the world suffer from poor vision caused by refractive errors (2). Recent studies indicate that 43% of visual impairments are associated with refractive errors (3). If left untreated, it leads to decreased quality of life, poor vision, and socioeconomic complications (4). Therefore, correction is necessary when dealing with refractive errors.

Refractive errors can be corrected non- surgically with the help of eyeglasses and contact lenses and surgically with refractive surgeries (5). Prescription eyewear, including eyeglasses and contact lenses, are the most wildly used form of refractive correction (6). Although they are simple, they are not used with the proper frequency due to social misconceptions (misbeliefs), like fear of being regarded as visually handicapped (7,8). Megbalayin *et al*., claimed that only 50% of Nigerian secondary school students that were prescribed to wear spectacles by their doctor agreed to wear them (9).

Nowadays, prescription eyewear is being superseded by refractive surgeries since it can reshape the cornea of a myopic, hyperopic, and astigmatic patient and eliminate the requirement for wearing eyeglasses (10,11). Reduction in the usage of contact lenses or spectacles is

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the most common motivation for seeking refractive surgeries (12). A variety of refractive surgery methods have been found in the past years; two of the more popular refractive surgeries, both using an excimer laser, are Photorefractive Keratectomy (PRK) and Laser-Assisted in Situ Keratomileusis (LASIK) (13,14).

In LASIK, a flap of the external layer of the cornea, including epithelium, Bowman layer, and anterior stroma, is cut mechanically by a microkeratome or with laser energy by a femtosecond laser; the flap is then lifted to reveal the central part of the cornea, the stromal bed. In order to alter the shape of the stromal bed, it is ablated by an excimer laser, and finally, the flap is repositioned (5,15-17).

Trokel and colleagues developed photorefractive keratectomy (PRK) in 1983. it is used for correcting refractive errors such as myopia, hyperopia, and astigmatism (18,19). In PRK, firstly, the superficial corneal epithelium is removed mechanically, then the stroma is ablated by the excimer laser to reorganize the corneal surface. The removal of the epithelium causes corneal epithelial cells to regenerate after the procedure (20,21).

To avoid the complications of mechanical debridement and to decrease the time needed for superficial corneal epithelial removal, different techniques for the removal of the corneal epithelium were introduced. These consist of transepithelial laser ablation, alcohol-assisted debridement, and a rotating brush (22,23).

Keratocyte loss and inflammation have been reported with ethanol-assisted debridement; It may also alter stromal hydration. Transepithelial photorefractive keratectomy (TPRK) uses an excimer laser for the removal of the epithelium. TPRK was developed to reduce the complications of mechanical debridement. TPRK is less invasive in comparison to LASIK, flap-related complications due to LASIK are avoided, and the cornea is not structurally weakened. Also, the transepithelial method decreases the required time for the procedure; Therefore, it leads to less concern for stromal hydration (24-27).

In an animal study, it was reported that TPRK did not lead to keratocyte apoptosis; It is known that keratocyte apoptosis is the first step of subepithelial fibrosis; therefore, the advantages of TPRK versus PRK are more in line with faster refractive correction with reduced corneal hazing (28-30).

In this study, we evaluated the five-year clinical outcomes of TPRK in the treatment of myopia, hyperopia, and astigmatism, including qualitative and quantitative parameters.

Materials and Methods

Subjects and population

In this retrospective study, 86 patients ranging from 18 to 52 years with 172 eyes suffering from hyperopia, myopia, and astigmatism who met the inclusion criteria and received TPRK between October 2014 to March 2015 were enrolled. The inclusion and exclusion criteria have been demonstrated in Table 1. A written consent form with a thorough explanation was obtained from the patients. The study protocol was based on the Declaration tenets of Helsinki and was also approved by the ethics committee and institutional review board.

Table 1. Inclusion and exclusion criteria for enrolling patients in our study

Inclusion criteria	Exclusion criteria
1. *Informed consent achievement*	1. *Any type of ophthalmologic surgery before or after the TPRK procedure.*
2. $40 \geq Age \leq 18$	2. *Keratoconus*
3. *Fixed prescription number during the last year before the TPRK procedure*	3. *Systemic disorders with eye involvement*
	4. *Presence of other Ophthalmologic disorders*

Pre-operative examination

All 86 patients went through comprehensive ophthalmic investigations before the surgery, including corneal topography, slit-lamp examination, uncorrected distance visual acuity (UDVA), best-corrected visual acuity (BCVA), and dilated fundoscopy examination. Those patients who revealed any retinal involvement in the slit-lamp examination, including macular hole and macular cyst, were referred to a retinologist for further investigation. Retinologist treated the high-risk patient with a "Laser barrier" before the surgery.

Corneal haze was evaluated by one ophthalmologist using a slit lamp. The Fantes corneal haze grading scale was used to address the presence of any opacity in this study (31). Postoperative pain perception was evaluated using the Mcguill pain questionnaire, which delineated

pain on a five-score scale (32).

Surgical technique

All surgical procedures were accomplished by a single surgeon applying the SCHWIND Amaris 1050RS excimer laser platform (SCHWIND eye-tech-solutions GmbH, Kleinostheim, Germany). ORK-CAM software calculated the ablation algorithm. Based on the population model statistics, the epithelial thickness ablation target was 55 μ m centrally and 65 μ m peripherally in each surgery (33). We furtherly optimized ablation targeting with age adjustment; in patients aged between 18 to 25, 0.5 units were, in patients aged between 25 to 35, 0.25-unit adjustments were applied. Static Cyclotorsion Corrections (SCC) and Dynamic Cyclotorsion Corrections (DCC) were used to compensate for eye movement during the surgery.

Before the procedure, we instilled proparacaine hydrochloride 0.5% eye drops, then we located a closed-loop lid speculum, and we instilled proparacaine hydrochloride 0.5% eye drop one more time. Eventually, the whole area was comprehensively irrigated with a Balanced Salt Solution (BSS).

After the surgery, Mitomycin C (MMC) was applied and remained on the stroma for seconds, then irrigated with a Balanced Salt Solution (BSS), and a soft bandage soft lens was used for a few days. Finally, patients were prescribed 0.5% levofloxacin every six-hour for seven days and 0.1% fluorometholone eyedrop every six hours. Fluorometholone was tapered for four months.

Statistical analysis

Data were analyzed using SPSS 24.0. $P \leq 0.05$ was considered statistically significant. The Pearson correlation test was used to calculate the correlation between quantitative variables.

Safety and efficacy

The safety index is calculated through the ratio of $\frac{\text{postoperative CDVA}}{\text{pre-operative CDVA}}$. The efficacy index is defined as the ratio of $\frac{\text{postoperative UDVA}}{\text{pre-operative CDVA}}$.

Results

In this study, the five-year results of 172 eyes in 86 patients were evaluated. Thirty-four patients were male at the age of 33.56±7.26 (mean±SD), and fifty-two patients were male at the age of 28.87±6.86. The average time for post-surgery epithelial healing was 2.97±0.83 in male and 2.94 ± 0.87 in female patients, presented as mean±SD. In this study, photophobia, defined as an abnormal sensitivity to the visual perception of light, was observed in eight patients in routine postoperative visits, which gradually improved and, eventually, was removed thoroughly.

Applying the Mcguill pain questionnaire to assess postoperative pain, the score in a week following the operation was 1.88±0.68 in male and 2.25±0.73 in female patients. Using Fantes corneal haze grading scale, four patients achieved a score of "one," and one patient achieved the score of "two"; others had clear corneum with no opacity on the surface.

As demonstrated in Table 2, almost all data did not distribute in a normal pattern, except UDVA in pre-operation and post-operation evaluation. The average pre-operative sphere was -2.33±2.63 [-2.75±11] in males and -2.57±2.83 [-2.75±13.75] in female patients; while the postoperative sphere was -0.15±0.40 [-0.07±1.75] and -0.21±0.42 [-0.25±2] in male and female patients, respectively, presented as mean±SD [median±IQ range].

Table 2. Quantitative comparison of pre-operative and postoperative refractive visual indices

Time and correlation/ Indices	Pre-operation range (Mean±SD) [median]	5-year post-operation range (Mean±SD)[median]	*P* Correlation
Sphere (D)	-9.25 to +5.00 (-2.43±2.74) [-2.50]	-1.25 to +1.25 (-0.15±0.40) [0.00]	<0.001** 0.858
Cylinder (D)	-6.00 to 0.00 (-1.30±1.42) [-0.75]	-1.25 to 0.00 (-0.11±0.25) [0.00]	<0.001** 0.872
SE (D)	-9.50 to 5.00 (3.09±2.83) [-3.48]	-1.25 to 1.25 (-0.21±0.41) [-0.25]	<0.001** 0.861
BCVA (logMAR)	-0.20 to 0.00 (-0.01±0.04) [0.00]	-0.10 to 0.00 (-0.01±0.03) [0.00]	0.07 0.193
UDVA (logMAR)	0.2 to 1.70 (0.86±0.33) [0.8]	-0.20 to 0.00 (-0.01±0.03) [-0.01]	<0.001 0.997**

SE: Spherical Equivalent; BCVA: Best Corrected Visual Acuity; UDVA: Uncorrected Distance Visual Acuity;*:significant correlation; **:highly significant correlation;

The pre-operative cylinder was -1.52 ± 1.66 [-0.92±5.5] in male and -1.12±1.26 [-0.72±5.5] in female patients; whereas the postoperative cylinder was -0.13±0.32 [0.00±1.25] and -0.08±0.19 [0.00±0.75], in male and female patients, respectively. The spherical equivalent (SE) in the pre-operative evaluation was 3.09 ± 2.78 [-2.75 ± 11] in male and 3.13 ± 2.89 [-2.75±13.75] in female patients. In a five-year clinical evaluation, SE was -0.22 ± 0.43 [-0.25 ± 1.88] and -0.25 ± 0.42 [-0.25 ± 2.00] in male and female patients, respectively, as presented in mean ± SD [median ± IQ range].

The pre-operative Uncorrected Distance Visual Acuity (UDVA) was 0.84±0.32 in male and 0.87±0.34 in female patients; while the postoperative UDVA was -0.02±0.04 in male and -0.01±0.02 in female patients, presented as mean±SD. Pre-operative UDVA was the only index that had a normal distribution pattern. The pre-operative Best Corrected Visual Acuity (BCVA) was -0.01±0.04 [0.00±0.2] in both genders. The postoperative BCVA was -0.01 ± 0.03 [0.00 ± 0.1] and -0.01 ± 0.02 [0.00±0.1] in males and females, respectively, presented as mean±SD [median±IQ range]. All the aforementioned data has been depicted in Figure 1.

Using the Pearson correlation coefficient between pre-operative and five-year postoperative optical and refractive evaluation, there was a highly significant correlation (P<0.001) in all indices except UDVA, which was almost near to significant (P=0.07). In this survey, the mean safety and index were nearly 1.00.

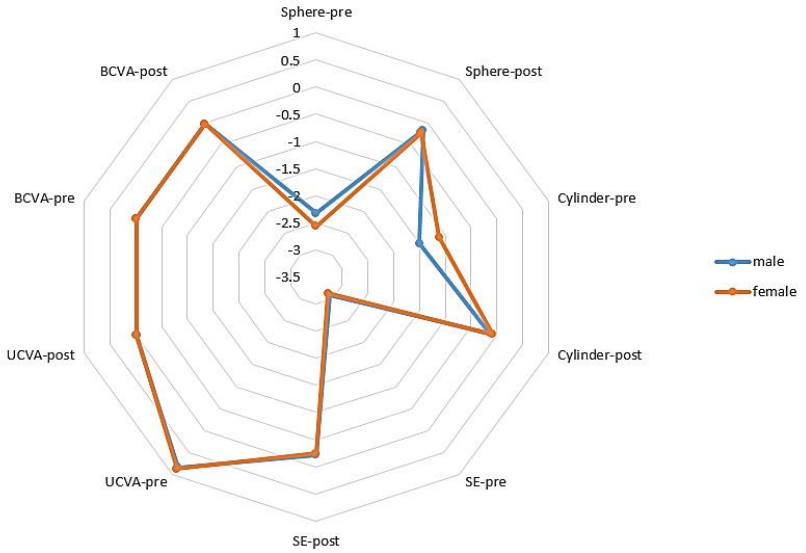

Figure 1. Comparison of refractive and visual indices in pre-operative and five-year postoperative evaluation based on gender. The unit for BCVA and UDVA is logMAR, while the rest is (D)

Discussion

In this survey, we quantitatively compared the clinical findings and assessment of optical and refractive parameters, including slit-lamp, corneal topography, BCVA, and UVDA, in 86 eyes of 172 patients before and five years after trans-PRK. PRK is a relatively new surgical method used to correct refractive errors such as myopia, hyperopia, and astigmatism. It was presented in the 1990s to reduce the accompanying issues of mechanical detriment (18,19).

In a previous study carried out by Fadlallah *et al.*, comparing the single-step TPRK and alcohol-assisted PRK using TPRK for mild to moderate myopia with or without astigmatism; TPRK was reported as safer to perform compared to conventional PRK and patients experienced less pain and the less postoperative haze and the usual healing time had decreased (34).

In 2016 a clinical study with a 12-month follow-up, consisting of 31 patients with mild to moderate hyperopia, uneven removal of the epithelium was prevented by using TPRK, and it was found efficient in correcting hyperopia (35); however, in a study performed by Lee and colleagues conventional PRK, two-step TPRK, and LASEK were compared. It was concluded that regardless of the epithelial removal technique,

similar outcomes, were reported for postoperative pain, BCVA, and subepithelial opacity in all three groups (28).

Luger *et al*., executed a study in order to compare TPRK and alcohol-assisted PRK in myopic patients; transepithelial PRK was performed in 1 eye and alcohol-assisted PRK in the other. In conclusion, TPRK was faster to perform for the surgeon, and it is a total laser procedure, leading to less stress for the patients (36).

Naderi and associates performed a study on 170 myopic patients to compare TPRK and conventional PRK. It was reported that TPRK was superior to conventional PRK in regard to postoperative pain, epithelial healing time, and visual recovery time (37).

In this study, there was a significant difference in all indices, except BDVA, between pre- and postoperative evaluation; in other words, TPRK is a safe and efficient procedure, which yielded promising outcomes in myopia, hyperopia, and astigmatism. BDVA was very near to making a significant difference, but it did not.

Although the average age of male patients was five years older than women, no remarkable difference was observed between genders, except the "postoperative pain perception." Besides, further analysis revealed that there was a remarkable difference in pre-and postoperative "Sphere Equivalent" in older and younger patients, which seems to be logical.

Photophobia, as an interesting subject to our team, was analyzed furtherly in this study. The results indicated that both pre-and postoperative Best-corrected Visual Acuity is negatively correlated with photophobia; in other words, as much the eyes are weaker, photophobia is less reported, which still has remained a conundrum for us.

This study had some limitations, which might have influenced the results, including not comparing the results in a sequential pattern; in other words, the comparison of results over different duration of time could demonstrate a detailed explanation. Moreover, we did not separately analyze the three groups, myopia, hyperopia, and astigmatism. However, we did not confront any loss to follow up. Besides, the sample size in this study was considerable enough to generalize the results.

Trans-epithelial Photorefractive Keratectomy is a safe and efficient therapeutic procedure that has no adverse effect in a five-year follow-up, despite other therapeutic procedures for refractive errors. Further studies are needed to evaluate the potential adverse effect in a longer and sequential follow-up.

Acknowledgments

We acknowledge all those medical health professionals who helped us through this long-term survey.

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