Comparison of Conventional Versus Trans-Epithelial Photorefractive Keratectomy in Hyperopia Treatment: A Contralateral Study

Hamidreza Hasani and Mohadeseh Maskan

Abstract
Background: This study was planned to compare Trans - epithelial Photorefractive Keratectomy (TPRK) and Alcohol Assisted Photorefractive Keratectomy (AAPRK) laser vision correction in hyperopia and compound hyperopic astigmatism.

Methods: This quasi-experimental study was conducted on patients with hyperopia and hyperopic-astigmatism, whose eye laterality was randomly assigned to undergo TPRK versus AAPRK using SCHWIND AMARIS 1050RS (SCHWIND eye-tech-solutions, Germany). Follow up time was 1, 3, 6 and 12 months after surgery.

Results: 112 eyes of 56 patients with mean age of 32.6 years included, of which 51.8% were female and 48.2% were male. Both TPRK and AAPRK methods were able to correct hyperopia and astigmatism safely and efficiently (p<0.05 in all cases). Postoperative vision characteristics were similar in both methods (p=0.23 for sphere, p=0.52 for cylinder, p=0.064 for axis, and p=0.35 for BCVA) postoperatively. Corneal haze was observed in 44% of the patients with a direct strong correlation with hyperopia severity (r=0.607). Post-operative pain was observed in 60% of the patients with a direct weak correlation with hyperopia severity (r=0.27). Mild photophobia was seen in 42% of the patients with a direct weak correlation between photophobia and hyperopia severity (r=0.36). Epithelial healing time lasted an average of 3.48 days and there was a direct and moderate correlation with hyperopia severity (r=0.4). Safety index in TPRK and AAPRK was 0.54 and 0.45, respectively, with no significant difference (p=0.42); Efficacy index was 0.96 and 0.9 in TPRK and AAPRK, respectively and there was no significant difference between two groups (p=0.23). No complication was observed in all of the patients.

Conclusion: TPRK and AAPRK laser vision correction are both safe and efficient in hyperopia and compound hyperopic astigmatism. There is no significant difference regarding epithelial healing time, post-operative pain and haze formation between two procedures.

Keywords: Compound hyperopic astigmatism, Conventional photorefractive keratectomy, Hyperopia, Trans-epithelial photorefractive keratectomy
Introduction

Vision is one of the indicators of health and quality of life. According to the latest estimate of the World Health Organization, 161 million people in the world have visual impairment, and the main cause of visual impairment may be refractive disorder (1). Refractive errors are the main cause of vision disorders and the second cause of blindness in the world, which affect the quality of life of millions of people of all ages, and they also put a lot of financial pressure on patients, the medical system and the society (2). These disorders have different prevalence in different races (3).

Efforts to correct refractive errors of the eye have started since 1898 and until now, various methods have been investigated to treat these errors (4). Photorefractive Keratectomy (PRK) is one of the best current methods to treat these disorders using excimer laser. This method has been used since the early 1990s due to less complications and greater safety than other common methods, such as LASIK, which can cause flap complications and iatrogenic keratectasia, and the predictability of the results (5-7). Due to the effect on the amount of hydration of the stroma during surgery and the possibility of overcorrecting the determined effect of the laser, the corneal epithelium is removed before PRK (8). There are several methods for removing the corneal epithelium in PRK, including older methods such as rotating brush, mechanical debridement, alcohol debridement (9) and the most recent, trans-epithelial laser-assisted epithelium removal (10).

In Conventional or Alcohol Assisted Photorefractive Keratectomy (AAPRK) method, alcohol is used to remove the corneal epithelium, which is a simple, fast and convenient method; but it is associated with complications such as toxicity caused by alcohol (8), inflammation and damage of keratocytes (11,12) and dehydration of the stroma (8).

In Trans-epithelial Photorefractive Keratectomy (TPRK), the removal of corneal epithelium and stroma is performed by laser, which is a safe, high-impact, predictable and fast method (13). In this method, which was invented in the 1990s, the surgeon’s hand and any device do not come into contact with the patient’s eye, which makes for a one-step process, accuracy during the operation, and greater comfort for the patient, and the size of the removed epithelium is minimized. It causes more biomechanical stability of the cornea (14,15). For this reason, TPRK is the preferred method in people with mild to moderate refractive disorders with thin corneas, recurrent erosions, and people prone to trauma such as martial artists (16,17). In the majority of studies, TPRK has shown less complications than other epithelium removal methods, including reduced surgical time, reduced post-surgical pain, reduced post-surgical haze and less recovery time, and more widely for mild cases. It is used for severe myopia and astigmatism (18-20).

In the TPRK method, due to the curvature of the cornea, the laser energy in the environment is reduced, which leads to the removal of the epithelium and ultimately irregular repair, which is one of the disadvantages of this method (14). Also, in some studies, over-correction with TPRK and under-correction with AAPRK were observed in the short term, which indicates the importance of long-term follow-up in patients who have undergone surgery (21).

Recently with the advancement of technology and the use of lasers and modern software, the complications of TPRK and AAPRK, including over or under correction, corneal healing, corneal haze, and post-operative pain have been minimized (22) and these tools lead to greater safety, reduction of final confusion and corneal biomechanical changes and for this reason, they are one of the most common surgeries today, in the correction of refractive errors (23).
without previous experience (24).

The main focus of the studies was myopia, and the majority of studies indicated the superiority of TPRK over conventional PRK in terms of postoperative pain, speed, patient comfort, epithelial repair and vision improvement (25). Considering the high prevalence of hyperopia and combined astigmatism, high financial burden and the lack of sufficient studies on other disorders except myopia, it is very important to investigate these two surgical methods to find a method with the least complications and the most benefits in people with hyperopia and combined hyperopic astigmatism (26). In this study, the purpose is to compare two surgical methods and to find the best and safest method to correct hyperopia and hyperopic astigmatism patients.

**Materials and Methods**

In this quasi-experimental study, the patients with hyperopia and hyperopic astigmatism whom randomly treated with TPRK method in one eye and conventional AAPRK in the fellow eye, according to the variables specified in pre-operative examinations and then 1, 3, 6 and 12 months after the operation were followed up. This study was conducted according to the Declaration of Helsinki after protocol approval of the Ethics Committee of Alborz University of Medical Sciences under the code of IR.ABZUMS.REC.1400.271. The latest results are reported one year after surgery.

Patients were examined in terms of information recorded in the file, including pain, corneal haze, Best Corrected Visual Acuity (BCVA), sphere, cylinder, axis, efficacy index, safety index, photophobia and corneal epithelial healing time. Pain after surgery was compared by using Visual Analog Scale (VAS) from the faces of no pain, mild pain, moderate and severe pain.

Efficacy index as the ratio of the average uncorrected distance visual acuity (UCVA) after operation to the average BCVA before operation, examines the effectiveness of the treatment method. Safety index as the ratio of the average BCVA after the operation to the average BCVA before operation evaluates the safety of the treatment method. Inclusion criteria consisted of the age between 18-50 years, the amount of hyperopia and astigmatism fixed for one year before surgery and performing pre-surgery full ocular examinations. Exclusion criteria were any ocular surgery before or after treatment, any eye or systemic diseases, keratoconus, and any post-operative complication occurrence.

Patients were examined for UCVA, BCVA in the preoperative examinations of patients. Relative Afferent Pupillary Defect (RAPD) test was performed in the patients, which should have been negative in all of them. Then, slit lamp examination, intra-ocular pressure measurement of both eyes followed by fundoscopy with complete visualization of the optic nerve, especially the macula and the central region of the retina was performed. After that, essential para-clinic tests including keratometry, corneal thickness and topographical shape were obtained by SIRIUS topography-pachymetry system (SCHWIND eye-tech-solutions, Germany). Refraction and cyclorefraction were done with Tropicamide 1% (Sinadarou, Karaj, Iran) eye drop. One drop was prescribed up to three times every five minutes, and finally 15 minutes after last drop, cyclorefraction and fundoscopy were performed. After initial examinations, conventional AAPRK surgery was performed on one eye and TPRK on the sound eye.

For AAPRK, firstly Alcohol 20% was applied for 15 seconds, then corneal epithelium was removed by hockey knife and excimer laser was applied for seconds needed to correct the refractive error, finally Mitomycin C 0.02% was used appropriate to hyperopia or hyperopic astigmatism degree. After copious irrigation, contact lens was put on the cornea.

In TPRK, excimer laser was used for epithelium removal, but the other stages were performed similar to the AAPRK.

**Sample size and sampling method**

Information related to 56 patients and 112 eyes (56 eyes in the control group and 56 eyes in the case group) who were randomly treated for hyperopia or compound hyperopic astigmatism with TPRK and conventional AAPRK methods on two eyes were used. Information of any patinas was collected from the files of patients who have inclusion criteria of study and for whom follow-up was done at specified times.

In this study, assuming the probability of type 1 error
was 5%, the probability of type 2 error was 20%, the difference in the average VAS score between the two study groups was 3 and the standard deviation was 6, the number of samples in each group was at least 43 patients (27).

**Analysis method**

SPSS 22 (IBM Corp., Armonk, New York, USA) software was used for statistical analysis of data and the significance level was considered less than 0.05. The results obtained for qualitative variables are expressed as percentages and quantitative variables are expressed as mean with standard deviation (mean±SD). To determine the parametric and normal distribution, the variables are subjected to the Kolmogorov Smirnov test, and then the pair T test and independent T test were used for comparison. Correlation between hyperopia degree and pain severity, corneal haze, epithelial healing time and severity of photophobia was determined using Pearson correlation test.

**Results**

A total of 112 eyes of 56 patients were included in the study; of which, 29 patients (51.8%) were female and 27 patients (48.2%) were male. The age of the participants was 23 to 48 years (mean= 32.68, standard deviation=5.96), whereas 27 (48.2%) of them were male and 29 (51.8%) were female. Postoperative pain was reported by the patients from the emoticon symbols as no to mild or moderate to severe pain in the first week after operation. 34 (60.7%) patients had mild pain, 20 (35.7%) people had moderate pain and 2 (3.6%) patients had severe pain. Table 1 shows correlation between hyperopia degree and pain severity. There is a direct relationship with a weak correlation between the severity of hyperopia and postoperative pain (Pearson coefficient of 0.273).

Axis specifies the astigmatism angle of 1 to 180 degrees. In this study, the eye axis was measured by keratometry before surgery and after one-year follow-up after surgery. In table 2, the average axis in two eyes of 56 participants, one eye under TPRK and the other eye under AAPRK is shown.

Paired sample T test was used to compare the results before and after operation, and independent T test was used to compare the results after operation. P-value in both tests is greater than 0.05, which indicates the lack of effect of TPRK and AAPRK on the axis and similar results after the operation.

The cylinder is a variable that determines the amount of astigmatism. Eye cylinder before surgery and after one-year follow-up was measured by keratometry. The mean and standard deviation of the cylinder are shown in table 2 in both TPRK and AAPRK groups, and Paired Sample T test was utilized to compare the

<table>
<thead>
<tr>
<th>Table 1. Correlation between hyperopia degree and pain severity, corneal haze, epithelial healing time and severity of photophobia</th>
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<tbody>
<tr>
<td><strong>Variables</strong></td>
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<tr>
<td>Pain severity</td>
</tr>
<tr>
<td>No pain</td>
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<tr>
<td>Mild pain</td>
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<tr>
<td>Moderate pain</td>
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<tr>
<td>Severe pain</td>
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<tr>
<td>Severity of corneal haze</td>
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<tr>
<td>Mild corneal haze</td>
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<td>Moderate corneal haze</td>
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<td>Severe corneal haze</td>
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<td>Epithelial healing time (days)</td>
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<tr>
<td>3</td>
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<tr>
<td>4</td>
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<tr>
<td>5</td>
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<tr>
<td>Severity of photophobia</td>
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<tr>
<td>Non photophobia</td>
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<tr>
<td>Mild photophobia</td>
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<tr>
<td>Moderate photophobia</td>
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<td>Severe photophobia</td>
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</table>
Table 2. Mean and standard deviation of axis, cylinder, BCVA in TPRK and AAPRK analyzed by T-test before and after surgery

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Number</th>
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<th>p-value</th>
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</thead>
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<td><strong>Axis in TPRK</strong></td>
<td></td>
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<tr>
<td>Before surgery</td>
<td>122.03</td>
<td>59</td>
<td>56</td>
<td>1.55</td>
<td>0.134</td>
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<tr>
<td>After surgery</td>
<td>106.48</td>
<td>68.4</td>
<td>56</td>
<td>1.58</td>
<td>0.123</td>
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<tr>
<td><strong>Axis in AAPRK</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Before surgery</td>
<td>110.17</td>
<td>61.3</td>
<td>56</td>
<td>1.58</td>
<td>0.123</td>
</tr>
<tr>
<td>After surgery</td>
<td>98.68</td>
<td>72.3</td>
<td>56</td>
<td>1.58</td>
<td>0.123</td>
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<tr>
<td>Before surgery</td>
<td>1.16</td>
<td>0.8</td>
<td>56</td>
<td>7.78</td>
<td>0.000</td>
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<tr>
<td>After surgery</td>
<td>0.37</td>
<td>0.22</td>
<td>56</td>
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<td><strong>Cylinder in AAPRK</strong></td>
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<tr>
<td>Before surgery</td>
<td>1.22</td>
<td>0.74</td>
<td>56</td>
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<tr>
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<td>0.63</td>
<td>0.520</td>
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<td></td>
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<tr>
<td>Before surgery</td>
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<td>0.083</td>
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<td>3.83</td>
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<td>After surgery</td>
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<td>56</td>
<td>3.83</td>
<td>0.001</td>
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<tr>
<td><strong>BCVA in AAPRK</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before surgery</td>
<td>0.0759</td>
<td>0.083</td>
<td>56</td>
<td>4.44</td>
<td>0.001</td>
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<tr>
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<td>0.0345</td>
<td>0.055</td>
<td>56</td>
<td>4.44</td>
<td>0.001</td>
</tr>
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</table>


results before and after the operation. Both surgical methods are used to correct astigmatism properly and there is no statistically significant difference between cylinder correction in TPRK and AAPRK.

Corneal haze is caused by surgery and is measured with a slit lamp in consecutive post-operative examinations. At the end of the one-year follow-up, the patients were divided into 4 groups: no corneal haze, mild, moderate and severe. 10 (17.9%) patients did not have corneal haze, 25 (44.6%) had mild, (33.9%) 19 had moderate, and (3.6%) 2 had severe corneal haze formation. There is a direct and strong correlation between the severity of hyperopia and corneal haze with a Pearson coefficient of 0.607 (Table 1).

Best Corrected Visual Acuity (BCVA) is the best vision the eye can have with corrective lenses as measured by the Snellen chart and Log MAR. Mean, standard deviation and analysis using paired sample T test to compare population BCVA data are shown in table 2. According to this, both methods had a high ability to correct BCVA. In comparison to BCVA after surgery in two methods done by using independent T test, there was no statistically significant difference between BCVA correction in TPRK and AAPRK.

The average and standard deviation of the sphere in the participating population are shown in table 3, before surgery and one year after surgery, and it is also compared with T test, which according to p=0.001, both AAPRK and TPRK methods are highly efficient for treatment of hyperopia and astigmatism.

Regarding the comparison of spheres after surgery in two methods analyzed by using independent T test, there was no statistically significant difference between hyperopia correction in TPRK and AAPRK. Epithelial repair is a variable that demonstrates the days it took until corneal epithelial repair after surgery and is observed with a slit lamp. Among the 56 participants, the average recovery time was 3.48 days with a standard deviation of 0.66, and recovery took a minimum of 3 and a maximum of 5 days.

After performing the Pearson correlation test, there is a direct and moderate correlation between the hyperopia degree and time of epithelial repair with a Pearson coefficient of 0.409. Table 1 indicates the relationship between the severity of hyperopia and time of epithelial repair.

Photophobia or sensitivity to light is one of the common complications of refractive surgery and was reported by the patient as having no photophobia or mild, moderate and severe in the first week after surgery. Among the 56 participants 24 (42.9%) not having photophobia, 21 (37.5%) had mild, 11 (19.6%) had moderate, and none of the patients had severe photophobia. There was a direct and weak correlation between the severity of hyperopia and the severity of photophobia with a Pearson coefficient of 0.367 (Table 1).

Safety index is defined as the ratio of average BCVA after operation to the average BCVA before operation.
According to this definition, the safety index of two methods, TPRK and AAPRK, is shown in table 4 and compared with independent T test. There was no difference between the safety index in both methods. UCV A and BCV A are reported in Log MAR unit.

Efficacy Index: It is the ratio of the average UCV A after operation to the average BCV A before operation. According to this definition, the safety index of two methods, TPRK and AAPRK, are shown in table 4. The results have been compared with the independent T test and based on the results obtained and p higher than 0.05, no difference was observed between the efficacy index in both methods.

Discussion

Refractive errors including hyperopia, myopia and astigmatism affect many people in the world and cause much more damage than the public imagines. The most important effects include damage to health, safety and beauty.

In the study conducted by Naqdi et al, the aim was to determine the refractive and vision results in patients with re-operation of photorefractive keratectomy. In the investigation of refractive results, the amount of spherical refractive error and astigmatism before reoperation was 0.80±0.67 diopters and 0.70±0.36 diopters, respectively, and after reoperation, it was 0.16±0.69 diopters, and decreased by 0.49±0.61 diopters. In the examination of visual results, the uncorrected distance visual acuity and the best corrected distance visual acuity based on Log MAR were 0.28±0.25 and 0.28, respectively before the operation. It was 0.01±0.06, which changed to 0.08±0.24 and 0.04±0.23 after the operation. In this study, they concluded that re-operation of PRK as the treatment method is useful and significantly improves far visual acuity (28).

Patients also have concerns about choosing the type of laser-assisted corrective surgery, its complications and consequences; For this reason, extensive research on the safety and efficiency of various surgical methods and their complications is necessary to help patients and physicians make better decisions (29). Current laser vision correction surgeries for refractive errors include LASIK, PRK, LASEK and Epi-LASIK, which are the most commonly used methods, respectively LASIK and PRK (30). Despite increasing the efficiency and accuracy of various surgical methods, all of them have post-operative complications and no surgical method is completely safe and predictable. Common complications of PRK include corneal haze, corneal dryness, pain, recurrence, and under or over correction (31). The more severe the refractive errors, the higher the possibility of postoperative complications, especially corneal haze and recurrence (32). Corneal epithelium removal was done mechanically and manually in the early years of PRK invention, which after some time was replaced by brush and alcohol. The latest epithelial removal method that has become very popular in recent years is the use of laser in PRK (TPRK) (33). In a study conducted by Razmjoo et al with the aim of investigating the refractive changes
after PRK to correct hyperopia above 3 diopters and accompanying astigmatism changes. In this study, it was determined that the average spherical refractive error after the operation was +1 (from -2 to +5) diopters, and the average astigmatism was -0.95 (from -0.25 to -2) diopters, and the average SE was 0.55 diopters. BCVA remained unchanged or improved in 83.4% (preoperative Log MAR 0.10 and postoperative Log MAR 0.11), but 5 eyes (16.6%) lost one or two lines. In 46.6%, refraction was within±1 diopter range and in 80% within±2 diopter range of the target value. 18 eyes (66%) had 0.5 or zero opacity, and one eye had grade 3 opacity, and none of them had grade 4 opacity. Although PRK in hyperopic treatment can improve the refractive status in a number of patients, but due to the ability the poor prediction of results in high hyperopia (above 3 diopters) is not recommended, especially in combination with astigmatism (34).

In current study, investigating the complications and finding the best corrective surgery method, the variables related to visual characteristics (sphere, cylinder, axis and BCVA) were compared in two AAPRK and TPRK methods, and the common complications of PRK surgery including post-operative pain, photophobia and corneal haze were also evaluated. Hyperopia was corrected in both methods (p=0.001); But the reduction of the sphere did not show a statistically significant difference between AAPRK and TPRK (p=0.24). Astigmatism axis changes also significantly improved after surgery with both methods (p=0.000); But the cylinder correction was also similar between two groups (p=0.52). Axis changes (astigmatism angle) after surgery were not statistically significant in this study and the final results were the same between two groups (both cases p>0.05). Corrected visual acuity (BCVA) showed slight improvement after both AAPRK and TPRK surgical procedures (p=0.001). However, no significant difference was found in the improvement of visual acuity between the two surgical methods (p=0.35). In the study of Safarian et al in 2012, examining the effect of PRK illustrated that in this group, the average hyperopia after one year was +0.42±0.72 diopters (p=0.001) and the amount of astigmatism after one year was -0.70±0.34 diopters. Uncorrected visual acuity before surgery was 0.27 ±0.02 Log MAR and after one year was 0.9±0.01 LogMAR and was associated with a significant difference (P=0.001). Examining the effect of PRK showed that the average myopia reached 0.06±0.6 diopter after 6 months, which shows a significant difference with Tukey's test (p<0.05). The average vision reached 0.99±0.012 LogMAR after 6 months and the average astigmatism level reached -0.40±0.43 diopter after six months in both eyes (p<0.05). PRK is an effective and safe method in correcting hyperopia and mild myopia (35).

Pain after surgery was observed in all the patients, but in the majority of cases, the pain was mild and tolerable, and only a very small percentage of patients experienced severe pain, and a weak correlation was also found between the severity of pain and hyperopia severity. Corneal haze was mild to moderate in the majority of patients. Fortunately, a number of patients did not experience this complication after surgery, and only a small percentage of patients suffered from severe corneal haze, and a strong correlation was also seen between the severity of hyperopia and the severity of corneal haze. It also increased among patients (r=0.609). Photophobia was also the least complication found in PRK. The majority of patients did not have photophobia and none of them experienced severe photophobia, and a weak correlation was also seen between the severity of hyperopia and the severity of photophobia. Epithelial healing time also had a direct and moderate relationship with the severity of myopia, and the greater the severity of hyperopia, the longer the time of epithelial repair (r=0.409).

Safety index and efficacy index were also calculated for both TPRK and AAPRK surgical methods, and there was no statistically significant difference between two groups (p=0.42 and p=0.23, respectively).

**Conclusion**

After one-year follow-up, no significant statistical difference was found between surgical results of the AAPRK and TPRK in hyperopia and hyperopic astigmatism correction; and both surgical methods resulted in the same visual results. Surgical complications including postoperative pain, corneal haze, and photophobia were mild in the majority of patients, and severe complications were not seen in patients. As a result, both TPRK and AAPRK surgical methods are safe, efficient with predictable results,
and each of them can be used for the treatment of hyperopia and combined hyperopic astigmatism.

**Ethics approval and consent to participate**

This study was done according to the Declaration of Helsinki after protocol approval of the Ethics Committee of Alborz University of Medical Sciences with code IR.ABZUMS.REC.1400.271. The authors thank all the colleagues of Alborz University of Medical Sciences in Karaj, Iran.

**Conflict of Interest**

The authors declare that there is no conflict of interests.

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**References**


