Transepithelial photorefractive keratectomy: Clinical results

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PURPOSE: To assess the effectiveness, safety, and comfort of transepithelial photorefractive keratectomy (PRK) using the Amaris laser platform.

SETTING: Ophthalmic Consultants of Beirut, Jal-El-Dib, Metn, Lebanon.

DESIGN: Comparative case series.

METHODS: Myopic eyes with or without astigmatism were treated by transepithelial PRK (study group) and compared with variable-adjusted eyes treated by conventional PRK (control group) during which the epithelium was removed with alcohol. Postoperative pain, epithelial healing time, uncorrected distance visual acuity (UDVA), manifest refraction, and haze were analyzed.

RESULTS: The mean subjective postoperative pain score (out of 10, indicating worst pain) at 48 hours was 2.0 in the study group (50 eyes) and 4.5 in the control group (50 eyes) (P < .02). The mean time to complete epithelial healing was 2.5 days ± 0.6 (SD) and 3.7 ± 0.8 days, respectively (P = .01). At 1 week, the UDVA was statistically significantly better in the control group; however, at 3 months, there was no statistically significant difference in UDVA, corrected distance visual acuity, or manifest refraction between the groups. Haze was significantly less in the study group (P < .01).

CONCLUSIONS: Transepithelial PRK for mild to moderate myopia with or without astigmatism was safe and easier to perform than conventional PRK, and patients had less pain, less postoperative haze, and a faster healing time. The visual outcomes with the 2 techniques were comparable.

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Photorefractive keratectomy (PRK) was first described by Trokel et al.1 in 1983 in cows’ eyes. It took until the late 1980s for it to be safely performed in human eyes with relatively normal healing of the post-laser corneas.2 In the late 1990s, PRK popularity started decreasing after the emergence of laser in situ keratomileusis (LASIK), which offered a painless spherocylindrical error correction with fast visual recovery and no clinically significant haze. However, the most feared adverse events of LASIK include flap-related complications, both intraoperatively and years later. Thus, in this respect, PRK is safer because there is no flap involved.

Even though LASIK is the dominant player in the refractive surgery market, PRK remains a useful tool in the refractive surgeon’s armamentarium. It is the first choice for eyes with mildly irregular and/or thin corneas because it preserves corneal integrity. Nevertheless, the pain, irregular epithelial healing, and corneal haze that accompany PRK remain drawbacks of the procedure. Many modifications were devised in an attempt to decrease these complications; preserving the epithelium was the cornerstone of the modified techniques. Laser-assisted subepithelial keratectomy (alcohol assisted) (LASEK) or epithelial laser in situ keratomileusis (microkeratome assisted) (epi-LASIK)
procedures emerged. Controlled studies showed mixed results with these techniques and no definite proof that they are better than conventional PRK.

In the late 1990s, a laser-assisted method for epithelial removal, termed transepithelial PRK, was introduced as an alternative to conventional PRK. Variable results were reported using different laser platforms; all are based on large-beam ablation. In studies of these platforms, epithelial removal was performed in a phototherapeutic keratectomy (PTK) mode, giving a smoother corneal surface than that achieved with mechanical ablation of the epithelium. However, because of the curvature of the cornea, the energy of the incident laser beam on the corneal periphery is reduced as a result of the oblique incidence of laser rays on the periphery and the longer distance the beam must travel. This leads to some loss of laser energy, resulting in uneven epithelial removal and, subsequently, irregular healing. Recently, a new study using the cTen nomogram of the iVis-Suite 1000 laser (iVisTechnologies) showed promising results.

The Amaris excimer laser (Schwind Eye-Tech-Solutions GmbH), which was introduced approximately 2 years ago, gives the surgeon the option of performing surface ablation using a nomogram that combines epithelial removal with sphero-cylindrical correction by delivering a varying amount of laser energy from the center to the periphery. This method would theoretically offer advantages over the conventional PTK mode of epithelial removal and allow 1-step, no-touch surgery with little trauma to the eye. To our knowledge, there are no studies in the literature reporting the results of transepithelial PRK using this nomogram.

This paper reports the first consecutive 50 myopic eyes, with or without astigmatism, that had transepithelial PRK using this laser platform. We compared surgical time, postoperative pain, healing time, visual acuity, and haze between transepithelial PRK and a variable-adjusted control group that had PRK with alcohol epithelial removal.

PATIENTS AND METHODS

This prospective study was performed at Ophthalmic Consultants of Beirut, Lebanon, between January and November 2010. Consecutive eyes with mild to moderate myopia with or without mild astigmatism that had transepithelial PRK (study group). A control group comprised myopic eyes with or without astigmatism that had conventional alcohol-assisted PRK. The 2 groups were matched for age, refractive error, keratometry (K) readings, optical zone, and central corneal thickness (CCT). Four surgeons performed the cases; 3 of them did 8 cases each, while the other 26 cases were performed by the same surgeon (S.F.). These were compared with a matched group of PRK cases from each of these surgeons.

Exclusion criteria were an unstable refraction; previous corneal or intraocular surgery; a history of any form of keratitis; current eyelid disease, including meibomian gland dysfunction; and any form of corneal dystrophy and/or degenerative disease with topographic irregularity, including keratoconus. All patients signed an informed consent form before surgery and agreed to be included in the study.

All patients had a complete preoperative eye examination including uncorrected (UDVA) and corrected (CDVA) distance visual acuities, manifest and cycloplegic refractions, slitlamp evaluation of the anterior segment and the fundus, applanation tonometry, and tear-film assessment by fluorescein tear breakup time and the Schirmer I test. The preoperative refractive workup included Scheimpflug videokeratometry (Galilei, Ziemer Ophthalmic Systems AG), ultrasonic pachymetry (Corneo-Gage Plus, Sonogage, Inc.), and ocular aberrations (Ocular Wavefront Analyzer, Schwind Eye-Tech-Solutions GmbH). Soft contact lenses were discontinued for a minimum of 3 days and hard contact lenses for a minimum of 3 weeks before examination and treatment.

Surgical Technique

The standard preoperative procedure for conventional PRK and transepithelial PRK was the same. Patients were given 5 mg of oral diazepam (Valium). One drop of proparacaine (Novocain) and 1 drop of ofloxacin (Oflox) were instilled in the eye to be treated 3 times 5 minutes apart. The eyes were then scrubbed and draped, and a closed-loop lid speculum equipped with suction was placed between the lids of the eye to be treated. The other eye was occluded.

In the study group, the epithelium and stroma were ablated in a single step using the transepithelial PRK nomogram of the Amaris laser’s ORK-CAM software. This software module, based on a spherical ablation profile, automatically considers the ablation volume of the epithelium. It takes into account the difference in epithelial thickness between the center and the periphery of the cornea and delivers different ablation energies to the epithelium and stroma.

In the control group, 20% ethyl alcohol in a 9.0 mm well was placed on the cornea for 25 to 30 seconds. The cornea was rinsed with a balanced salt solution, and a dry polyvinyl alcohol sponge (Merocel) was used to peel off the epithelium. The laser treatment was delivered using the ablation profile of the laser’s software.

In both groups, the optical zone varied between 6.00 mm and 7.00 mm. The transition zone was calculated using the nomogram based on the patient’s age, refractive error, and K readings; it varied between 0.36 mm and 2.24 mm. The laser treatment was centered on the pupillary axis; the static cyclodislocation control program was not used.

After laser ablation, a high-oxygen-content (50%) soft contact lens (Acuvue Oasys, Johnson & Johnson) was placed on the cornea and 1 drop each of a topical antibiotic agent, steroidal agent, and nonsteroidal antiinflammatory drug (NSAID) was given.

The duration of the surgery was recorded, starting with when the eyelid speculum was positioned and ending after the bandage contact lens was placed. Intraoperative pain was assessed using the Visual Assessment Pain Score (VAPS) rating, which measures subjective pain intensity on a scale of 0 (no pain) to 10 (worst pain).10

Postoperative Care and Follow-up

Patients were given prednisone drops and ofloxacin or gatifloxacin drops 4 times a day, NSAID drops 3 times a day, and preservative-free artificial tears every hour.
Epithelial healing was assessed daily at the slitlamp, with fluorescein staining when needed. It was recorded as the percentage of the original deepithelialized area. The postoperative pain was assessed daily until full epithelial healing using the subjective VAPS rating. This was administered by a third-year resident who was not present during any of the surgeries and was masked to which PRK procedure was used.

Once the epithelium had completely healed, the therapeutic contact lens was removed. The NSAIDs were then stopped; the antibiotic drops were taken for an additional 4 days, and the steroid drops were tapered progressively over the following 4 weeks.

At each follow-up visit (at 2 days, daily until the epithelium healed, at 1 week, at 1 month, and at 3 months), the UDVA, CDVA, and corneal transparency were assessed.

Haze Grading

Haze was graded using the system described in a book chapter by Fahd et al.12 Based on an article by Fantes et al., in brief, the grading was as follows: 0 = no haze; +0.5 = trace haze on oblique illumination; +1 = corneal cloudiness not interfering with the visibility of fine iris details; +2 = mild effacement of fine iris details; +3 and +4 = details of the lens and iris not discernible.

Statistical Analysis

The patients' preoperative and postoperative characteristics were analyzed using repeated-measures analysis of variance. Statistical analysis was performed using SPSS software (version 13.0, SPSS, Inc.). Correlations between preoperative and postoperative independent variables were determined using the Pearson correlation coefficient. A P value less than 0.05 was considered statistically significant.

RESULTS

The study group and the control group each comprised 50 patients. Table 1 shows the preoperative characteristics of the patients. The mean preoperative UDVA was 4.90/10 in the study group and 5.20/10 in the control group (P=.502).

Surgical Parameters

The mean optical zone was 6.81 mm in the study group and 6.70 mm in the control group (P=.225). The mean intraoperative pain score (out of 10) was 1.2 and 1.4, respectively (P=.821). The mean surgical time per eye was 205 seconds ± 77 (D) in the study group and 355 ± 84 seconds in the control group (P<.01).

Postoperative Outcomes

Table 2 shows the postoperative results. At 48 hours, the mean amount of the epithelial surface that was restored was 84% ± 13% in the study group and 56% ± 8% in the control group (P<.01). At 3 days, the mean values were 98% ± 3% and 78% ± 16%, respectively (P=.01). The mean time to complete epithelial healing was statistically significantly shorter in the study group than in the control group (P=.01). The mean subjective postoperative pain score at 48 hours was statistically significantly lower in the study group than in the control group (P=.02).

At 1 week, the mean UDVA was significantly better in the control group than in the study group (P=.04). There was no between-group difference in UDVA at the 1-month or 3-month follow-up visits. At 3 months, the 2 groups had similar CDVA (P=.401), sphere (P=.131), and cylinder (P=.090).

Subepithelial haze graded subjectively was below grade 2 in all patients at all follow-up visits (Table 3).

### Table 1. Preoperative patient characteristics.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>t-PRK</th>
<th>PRK</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Females (n)</td>
<td>17</td>
<td>18</td>
<td>.70</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td>.67</td>
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<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean CDVA</td>
<td>29.1</td>
<td>27.6</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>10.5</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Mean sphere (D)</td>
<td>.34</td>
<td>.35</td>
<td>.307</td>
</tr>
<tr>
<td>Mean cylinder (D)</td>
<td>.50</td>
<td>.60</td>
<td>.902</td>
</tr>
<tr>
<td>Mean IOP (mm Hg)</td>
<td>12.00</td>
<td>12.67</td>
<td>.595</td>
</tr>
<tr>
<td>Mean CCT (µm)</td>
<td>519</td>
<td>502</td>
<td>.201</td>
</tr>
<tr>
<td>Mean SimK1 (D)</td>
<td>43.06</td>
<td>42.99</td>
<td>.854</td>
</tr>
<tr>
<td>Mean SimK2 (D)</td>
<td>44.24</td>
<td>44.17</td>
<td>.865</td>
</tr>
<tr>
<td>Mean Schirmer 1 (mm)</td>
<td>15.68</td>
<td>16.97</td>
<td>.300</td>
</tr>
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</table>

Means ± SD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>t-PRK</th>
<th>PRK</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Schirmer 1 (mm)</td>
<td>15.68</td>
<td>16.97</td>
<td>.300</td>
</tr>
</tbody>
</table>

CCT = central corneal thickness; CDVA = corrected distance visual acuity; IOP = intraocular pressure; PRK = conventional photorefractive keratotomy; SimK1 = simulated keratometry 1; SimK2 = simulated keratometry 2; t-PRK = transepithelial photorefractive keratotomy

### Table 2. Postoperative results.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>t-PRK</th>
<th>PRK</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score at 48 hours*</td>
<td>2.00 ± 1.39</td>
<td>4.12 ± 1.40</td>
<td>.02</td>
</tr>
<tr>
<td>Epithelial healing time (days)</td>
<td>2.5 ± 0.6</td>
<td>3.7 ± 0.8</td>
<td>.01</td>
</tr>
<tr>
<td>UDVA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48 hours</td>
<td>4.23 ± 1.32</td>
<td>4.12 ± 1.25</td>
<td>.236</td>
</tr>
<tr>
<td>1 week</td>
<td>5.80 ± 1.33</td>
<td>7.10 ± 1.15</td>
<td>.04</td>
</tr>
<tr>
<td>1 month</td>
<td>8.60 ± 1.10</td>
<td>8.51 ± 0.98</td>
<td>.302</td>
</tr>
<tr>
<td>3 months</td>
<td>9.2 ± 0.99</td>
<td>9.3 ± 0.95</td>
<td>.501</td>
</tr>
<tr>
<td>CDVA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>9.39 ± 0.98</td>
<td>9.51 ± 0.96</td>
<td>.401</td>
</tr>
<tr>
<td>Sphere (D)</td>
<td>-0.21 ± 0.61</td>
<td>-0.47 ± 0.88</td>
<td>.371</td>
</tr>
<tr>
<td>Cylinder (D)</td>
<td>0.43 ± 0.62</td>
<td>0.61 ± 0.53</td>
<td>.502</td>
</tr>
</tbody>
</table>

CDVA = corrected distance visual acuity; PRK = conventional photorefractive keratotomy; t-PRK = transepithelial photorefractive keratotomy; UDVA = uncorrected distance visual acuity

*Visual Assessment Pain Score

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DISCUSSION

Studies by Camellin et al.\textsuperscript{13} and Pedrotti et al.\textsuperscript{14} report that transepithelial PRK is an effective means to correct irregular astigmatism after keratoplasty or radial keratotomy. It has also been found to be a good option for immediate retreatment of LASIK flap complications.\textsuperscript{15}

Other studies using transepithelial PRK in healthy eyes report varying results. In 1998, Clinch et al.\textsuperscript{7} using the Summit OmniMed excimer laser, compared epi-LASIK and transepithelial PRK. At all postoperative intervals, mechanical removal of the epithelium tended to yield better results than laser epithelium removal. In 2000, Kanitkar et al.\textsuperscript{16} reported 9 patients who had bilateral PRK using the Visx S3 laser, with 1 eye deepithelialized with PTK and the fellow eye deepithelialized with alcohol. All eyes healed within 3 days with no difference in healing time between the 2 groups. The postoperative pain was significantly less at 1 day in the alcohol-assisted PRK group. In 2005, Lee et al.\textsuperscript{5} compared conventional PRK, transepithelial PRK, and LASEK using the same laser system (Visx Star S3). Postoperative pain, subepithelial opacity, and the CDVA were similar in the 3 groups. Using the same nomogram, transepithelial PRK resulted in a slight overcorrection and LASEK in a slight under-correction. In 2007, Ghadhfan et al.\textsuperscript{8} reported that transepithelial PRK provided slightly better visual outcomes than LASIK or LASEK in patients with low to moderate myopia and better visual outcomes than epi-LASIK, LASIK, and LASEK in eyes with high myopia. Laser epithelial ablation was performed in a PTK mode, and all stromal ablations were performed using the Nidek EC-5000 excimer laser. In 2009, Buzzonetti et al.\textsuperscript{9} reported the results of transepithelial PRK with the Nidek CXIII excimer laser using a modified PTK mode with the Flex Scan algorithm; this ablation

At the 3-month follow-up, grade 1 or more haze persisted in 5 eyes (10%) in the study group and in 13 eyes (26%) in the control group.

<table>
<thead>
<tr>
<th>Haze Grade</th>
<th>t-PRK</th>
<th>PRK</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>30 (60.0)</td>
<td>19 (38.0)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>0.5</td>
<td>15 (30.0)</td>
<td>18 (36.0)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>1.0</td>
<td>4 (8.0)</td>
<td>10 (20.0)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>2.0</td>
<td>1 (2)</td>
<td>3 (6.0)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

PRK = conventional photorefractive keratectomy; t-PRK = transepithelial photorefractive keratectomy.

profile delivers more ablation pulses to the corneal periphery than to the central cornea to correct for the prolate shape of the cornea. They found the PTK mode to be safe and effective and state that it might offer more consistent epithelial removal than the conventional PTK algorithm. Chen et al.\textsuperscript{A} reported 40 myopic patients who had transepithelial PRK with the iVis 1000 laser and had comparable optical results, less operative pain, and faster reepithelialization than patients who had PRK with the Allegretto 400 Laser (Alcon Laboratories, Inc.). These studies used different laser nomograms, which explains the discrepancy in the results.

In all the above-mentioned studies except the last 2, the PTK mode was used for epithelial ablation, which assumes that the entire epithelium has the same thickness. Reinstein et al.\textsuperscript{17} studied the in vivo epithelial thickness in normal corneas using very-high-frequency ultrasound (Artemis) and found it to be 53 μm centrally and 65 μm at the 8.0 mm periphery. This is comparable to results in other studies that calculated the epithelial thickness using optical coherence tomography or confocal microscopy.\textsuperscript{18–20}

Our study evaluated healthy eyes that had transepithelial PRK using the Schwind Amaris nomogram. In this nomogram, the laser energy calculation is based on 2 ablation values per pulse; the first is for the epithelium (in which the laser ablates more tissue per pulse) and the other for the stroma. The epithelial ablation is based on a model that takes into account the difference in epithelial thickness throughout the cornea based on the Reinstein et al.\textsuperscript{17} study and that more energy is needed for pulses delivered to the periphery because of the oblique incidence of the laser beam and the longer distance the beam should travel to reach the periphery. If the patient's epithelial thickness matches the model, the ablation profile works perfectly. If the patient's epithelium is thinner than that in the software's database, extra tissue will be removed. If the epithelium is thicker, a part of the refractive ablation will be invested in removing epithelium, leading to a smaller achieved optical zone. If the progression of the epithelial thickness from center to periphery differs significantly from the progression of the transepithelial PRK epithelial profile, minor refractive differences could occur. The transepithelial PRK epithelium thickness profile in the Amaris database is slightly thicker than the normal epithelium, which minimizes these refractive differences.

In our study, the transepithelial PRK group (study group) and the conventional PRK group (control group) had comparable preoperative characteristics. The study group had faster epithelial healing and the patients reported less postoperative pain and discomfort than in the control group. This is probably because
in the transepithelial PRK group, the precise, smooth, and regular epithelial ablation by the laser was equal in diameter to the ablated zone and was thus smaller than the alcohol-removed epithelium. The temporary chemical toxicity of alcohol to the limbal stem cells and/or to the residual epithelial cells might be responsible for the increased pain and the slower healing time in the control group. The stromal bed was also more uniform with no epithelial islands centrally and there was a smoother peripheral progression in the study group than in the control group. Our results agree with those reported by Chen et al. Our study does not agree with results in the Ghoreishi et al. study, in which epithelial healing, postoperative pain, visual outcomes, and complications were equivalent between mechanical epithelial debridement and alcohol-assisted epithelial debridement.

The control group in our study had a better visual acuity at 1 week; however, there was no significant difference between the 2 groups at the 1-month and 3-month follow-up visits. The incidence of haze was significantly lower in the study group, which does not agree with results in many previous studies. The lower incidence of haze could be due to the longer epithelial remodeling in the transepithelial PRK group. The difference in our results could be due to the improved ablation profile of the Amaris laser we used. Laser-assisted epithelial ablation induces less keratocyte apoptosis, leading to less haze. However, this theory is controversial because some studies found a more intense inflammatory response and a greater increase in backscattering of light associated with increased keratocyte activation and myofibroblast transformation after laser-epithelial ablation.

Our study also found a significant decrease in the mean surgical time during transepithelial PRK than during conventional PRK. This shorter time decreases dehydration of the corneal stroma and is an all-laser surface ablation technique.

Our study had several limitations. A longer follow-up period (at least 6 months) is warranted to comprehensively evaluate visual acuity and haze. Although the same observer masked to surgical technique assessed epithelial healing in our study, no objective photographs were taken. Finally, the study did not include fellow control eyes.

Despite these limitations, our results show the effectiveness and safety of the Schwind Amaris nomogram for the treatment of mild to moderate myopia and mild to moderate myopia with astigmatism. The nomogram remains to be tested for hyperopia and high astigmatism. This study is underway, and the results will be reported. The nomogram may have to be modified in the future according to central pachymetry.

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