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REVIEW

Transepithelial Photorefractive Keratectomy for Hyperopia Correction: An Uncharted Territory

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Abstract: Transepithelial photorefractive keratectomy (Trans PRK) is a relatively new technology for refractive surgery and has shown promising results in myopia correction. The data on hyperopia correction by this method are limited. In this review, we have attempted to understand the outcomes of this technology on hyperopic eyes. There are comparable results with conventional PRK and laser in situ keratomileusis (LASIK) as far as refractive stability, regression rate, predictability, and post-operative complications are concerned. The best results have been obtained in lower hyperopic corrections. In moderate to higher hyperopia, the limited data available show higher regression, unstable visual outcomes, and increased stromal haze. There is a need to evaluate the technology further to understand its success for hyperopic refractive surgery.

Keywords: refractive surgery, visual outcome, annular, regression

Introduction

Corneal refractive surgery has come a long way from the days of radial keratotomy to the advent of excimer laser in 1983, leading to usage of techniques such as laser in situ keratomileusis (LASIK), femtosecond LASIK, conventional photorefractive keratectomy (PRK), small incision lenticule extraction (SMILE), and transepithelial PRK (Trans PRK).[1–3] Surface corneal ablation technology is popular amongst patients with thinner corneas, high myopia, epithelial basement membrane disease, and re-surgery for residual refractive error.[4,5] Conventional PRK is the most prominent amongst surface ablation surgeries.[6] However, due to the need of epithelial removal in conventional PRK, there was a need for a no-touch technique for surface ablation.[7] This led to the development of the Trans PRK method.[8]

The advantages of this method have been cited as minimum surgical time, zero contact of laser machine with corneal surface, shorter time for surface healing and visual correction, and decreased post-operative discomfort and dry eyes.[9] These advantages have been scientifically proven in multiple studies of Trans PRK in myopia and myopic astigmatism correction.[10,11] Surprisingly, the scientific literature of the role of Trans PRK in hyperopia correction is limited. As conventional PRK has been proven to be beneficial in hyperopia correction, we have attempted to review the data on the outcome of Trans PRK in hyperopia correction.[12] We have also tried to understand the causes of lower acceptance of this procedure amongst surgeons and the outcomes in patients.

Historical Perspective

The advent of conventional PRK in 1987 by Dr Stephen Trokel was widely appreciated by refractive surgeons and became popular.[1] However, this procedure involves removal of the central corneal epithelium, either mechanically, by diluted alcohol instillation, or by rotating brush. This can lead to asymmetrical stromal hydration and uneven ablation, increased post-operative pain, and longer healing time of the epithelium, leading to delayed visual rehabilitation.[13] The surgical time is also increased while completing a proper epithelium removal. To avoid this initial step, Trans PRK was developed.

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There was an attempt to incorporate excimer laser in the process of epithelial removal as a two-step surgery way back in the 1990s.[14] However, this innovation was overshadowed by the soaring popularity of LASIK and also due to the absence of a clear nomogram for avoiding over- or under-correction. The need to shift from a PTK mode to a conventional PRK mode, leading to potential stromal dehydration, compounded with modification of the excimer laser by around 0.75 diopter to avoid hyperopic shift, made the entire process time-consuming.[14,15]

In 2009, Amaris laser (Schwind eyetech solutions) started the single-step Trans PRK with a predetermined PRK and PTK software (ORK CAM version 4.3.15) on their excimer laser platform.[8] With shorter operating time, ablation depth based on normative data of the population for epithelial thickness, and faster recovery rate, this new technology has slowly gained the confidence of refractive surgeons worldwide. The SmartPulse Allocation laser technology with 7D eye tracking system introduced by Schwind is aimed at making the final corneal surface smoother and aberration free.[16,17] These innovations are applicable for the correction of myopia, hyperopia, and astigmatism, as claimed by the manufacturers. The iRes excimer laser (iVisTechnologies, Taranto, Italy) is another such technology for Trans PRK using Corneal Interactive Programmed Topographic Ablation software (CIPTA®2, iVIS Technologies, Taranto, Italy).[18,19] The StreamLight PRK software in WaveLight EX500 Excimer Laser (WaveLight; Alcon Laboratories, Fort Worth, TX, USA) is the latest technological advancement in this field. It is a one-step procedure in which the epithelium ablation by phototherapeutic keratectomy (PTK) is immediately followed by PRK by the WaveLight EX500 excimer laser. The size and location of epithelial treatment zone are aligned with the PRK ablation profile, and centration is only required once.[20,21]

Eligibility Criteria

The indications for the use of Trans PRK for hyperopia correction are similar to those for conventional PRK surgery.[22] As mentioned by Moghaddam et al, refractive error from +0.5 diopter to +6.0 diopter, with or without astigmatism of up to −3.0 diopter, can be corrected by this technique.[23] They further classified the patients into low hyperopia (hyperopia ≤3.00 D) and moderate hyperopia (hyperopia >3.00 D).

Abdel-Radi et al included patients with hyperopic cycloplegic spherical equivalent (SEQ) between +2.0 and +4.5 D (maximum sphere +3.0 D and/or maximum cylinder +3.0 D). They also included parameters of pachymetry >500 microns and steep keratometry <46 diopters in their selection criteria.[24]

Ortueta et al have used this method for correction of residual myopia and hyperopia after clear lens extraction in a range of −1.0 to +1.75 diopter.[17] Goggin et al attempted hyperopia correction till +2.58 diopters on the iRes excimer laser platform.[19] They required a repeatable PrecisioTM topography of 8 mm corneal diameter or more, for the pre-operative as well as for 3-month follow-up post-operative evaluation. However, there is no further scientific literature on the range of hyperopic correction that can be attempted with Trans PRK.

Contraindications

The contraindications for Trans PRK and conventional PRK surgery are similar, including high astigmatism of more than 3.0 diopter, corneal ectasias, sight-threatening ocular disease, severe dry eyes, systemic diseases which can affect vision or surgical recovery, eventful ocular surgery, and retinal pathologies.[7,19,22,23] None of the studies mentioned any specific contraindication for hyperopia correction by this technology. Soft contact lenses have to be discontinued for a week and hard contact lenses for 4 weeks before baseline examination of the eyes. In the study by Abdel-Radi et al, patients with large angle kappa (chord mu >0.3 mm) and with unilateral or bilateral hyperopic amblyopia (corrected distance visual acuity <0.2 logMAR) were also excluded.[24]

Anatomical and Physiological Changes

The anatomical and physiological changes induced by Trans PRK do not vary much from a conventional PRK, except for the changes in the epithelium and Bowman's membrane level.[5,7,9] These changes can be subdivided into the following steps.

Epithelial Changes

The epithelium is completely removed by either alcohol or mechanical debridement in conventional PRK. After the procedure, epithelial cells from the limbus and basal epithelial layer multiply and migrate centrally to restore the corneal

surface.[13,25] The cells are elongated with increase in superficial cell numbers, leading to a thicker epithelium. Studies have shown that epithelial thickness increases by 15% to 20% after conventional PRK, which can cause regression of refractive correction.[25,26]

In Trans PRK, similar findings have been reported in myopia correction. Most studies have shown increase in epithelial thickness from 6 to 12 months post-operatively, leading to similar regression of myopic correction.[27,28] However, the epithelial regeneration process after Trans PRK in hyperopia correction has not been studied to date. Complete re-epithelialization has been reported to be faster in Trans PRK compared to conventional PRK (average 2 to 3 days in Trans PRK versus 3 to 5 days in conventional PRK).[3,9,11] One hypothesis is that the area of epithelial ablation in Trans PRK is smaller compared to the area of epithelial removal in standard PRK. Moreover, the lower degree of pain perceived in Trans PRK might induce lower inflammation in the cornea, leading to faster epithelialization compared to conventional PRK, as shown in studies comparing the two techniques.[9,27] Fadlallah et al reported a pain score at 48 hours in Trans PRK of 2.00 ± 1.39 versus conventional PRK of 4.12 ± 1.40.[29] Similarly, Naderi et al found a shorter epithelial healing time for the Trans PRK group compared to the conventional PRK group post-operatively ($P = 0.01$). The pain score was also lower in the Trans PRK group as compared to the conventional PRK group ($P < 0.01$ for both comparisons).[30]

Stromal Changes

The stromal changes after ablation in conventional PRK and Trans PRK are similar as per studies.[5,13] In both procedures, there is keratocyte apoptosis underlying the ablated area due to stress exposure. The keratocyte population in anterior stroma is affected maximally, followed by middle and posterior stroma. This decline has been found to continue till 3 years after surgery.[13] Moreover, in the first 24 hours, there is an influx of inflammatory cells into the stroma to remove apoptotic keratocytes and damaged extracellular matrix (ECM). The keratocytes at the margins of the operated area then get activated to lay down new ECM, mitosis of keratocyte population with myofibroblast, and new collagen fibres formation. Studies have shown that keratocyte levels return to normal by 6 months after surgery.[13,31]

Corneal Innervation Changes

In Trans PRK, there is no literature available on the difference in recovery of corneal innervation for hyperopic correction compared to myopic correction. For myopia correction, one study has shown that the density and length of corneal sub-basal nerves decreased immediately after surgery and then returned to pre-operative levels at 1 year.[31] The corneal sensitivity, however, reduced only for a month post-operatively.

Pre-Operative Evaluation

Patient evaluation for the surgery is similar to other corneal refractive surgeries. A thorough history taking and systemic evaluation is done, followed by determining uncorrected and best corrected visual acuity for both eyes. Manifest and mandatory cycloplegic refraction is done along with pupillometry (in photopic and mesopic conditions). Slit lamp biomicroscopy, corneal topography, tonometry, and dilated fundus evaluation are mandatorily done for every patient. Moghaddam et al have used ultrasound pachymetry along with Placido-based corneal topography in their series.[23] Abdel-Radi et al included Pentacam (Oculus GmbH, Germany) for keratorefractive assessment and anterior segment ocular coherence tomography (AS-OCT, Heidelberg, GmbH, Germany) for epithelial mapping in their study subjects.[24]

Surgical Technique

The pre-operative preparation for the surgery includes application of local anesthetic drops, placement of lid speculum, and usage of cold balanced salt solution (BSS) before starting the laser ablation. Pre-operative usage of non-steroidal anti-inflammatory medications was mentioned by Ortueta et al.[17] In the Amaris platform, pupil-centered corneal ablation was done, except in pupillary offset, where the ablation was based on the corneal vertex.[23]

The ablation was done in a continuous manner to reshape the stroma followed by the epithelium for achieving an aspheric aberration-free optimized profile.

Moghaddam et al used a population-based epithelium pachymetry profile of 55 µm centrally and 65 µm peripherally, followed by individual adjustment of the epithelial ablation rate for an even corneal surface.[23] The authors used an an optical zone range of 6.8 to 7.6 mm in Iran, whereas in Germany the zone was 6.8 to 7 mm. Ortueta et al has mentioned usage of 1050 Hz infrared eye tracker centred on corneal vertex with torsion tracking, which had a response time of 1.7 milliseconds as the patients focused on a green fixation light.[17]

In the study by Abdel-Radi, after choosing the StreamLight profile, the authors used epithelial mapping to plan epithelial ablation depth between 45 and 65 µm, with epithelial optical zone (OZ) in hyperopic corrections being 8.0 mm as a default setting. The stromal ablation OZ was 6.5 mm. The total ablation zone was finally adjusted to 8.9 mm for epithelial-stromal ablation matching.[24]

Goggin et al performed the procedure in a similar manner, with the area of epithelial removal exactly fitting into the area of stromal ablation.[19] The post-operative management regime has not been mentioned by these authors. Moghaddam et al and Abdel-Radi et al used Mitomycin C 0.02% solution placed with a soaked sponge over the ablated area for maximum 30 to 60 seconds after ablation, followed by irrigation with 100 mL chilled BSS.[23,24] Ortueta et al did not use Mitomycin C in their surgeries.[17] A bandage contact lens was placed at the end of the treatment.

The post-operative regimen included topical antibiotic and lubricant in all studies.[17,19,23] Topical steroid was used by Ortueta et al and the Iranian patients subset of Moghaddam et al.[17,23] The German patients in Moghaddam's study did not use steroid after surgery, except a single drop of dexamethasone immediately after surgery. Vitamin C effervescent tablets (500 mg) were prescribed once daily for a month in the same study.[23]

Ortueta et al and Goggin et al conducted post-operative follow-up of patients till 3–7 months, while Moghaddam et al and Abdel-Radi et al had a follow-up till 12 months.[17,19,23,24]

Visual Outcomes

The visual outcomes of Trans PRK for hyperopia correction in different studies have been summarized in Table 1.

Table 1 Visual Outcomes of Trans PRK in Hyperopia Correction

Study	Moghaddam et al[23]	Ortueta et al[17]	Goggin et al[19]	Abdel-Radi M et al[24]
Range of hyperopic correction	+0.5 D to +6 D	−1 D to +1.75 D	−2.08 D ± 2.17 D	+3.21 D ± 0.61 D
Technology used	Amaris	Amaris	iVis	StreamLight EX500
Length of follow-up	12 months	3 months	3 months	12 months
UCVA (pre-operative)	0.54 ± 0.45 (logMAR)	Not mentioned	Not mentioned	0.53 ± 0.02 (logMAR)
UCVA (post-operative)	0.15 ± 0.03 (logMAR)	Not mentioned	Not mentioned	0.08 ± 0.01 (logMAR)
SE (pre-operative)	2.56 ± 1.90 D	−1.0 to +1.75 D	7.30 ± 2.58 D	3.21 ± 0.61 D
SE (post-operative)	0.05 ± 0.13 D	−0.5 to +0.75 D	Not mentioned	0.41 ± 0.04 D
Pre-operative astigmatism	−0.94 ± 0.12 D	−3.25 D to 0 D	Not mentioned	0.93 ± 0.11 D
Post-operative astigmatism	−0.71 ± 0.12 D	−0.75 D to 0 D	Not mentioned	0.39 ± 0.04 D
Stability (regression at last follow-up)	−0.75 D to +0.5 D	Close to 1 D	Not mentioned	+3.21 D to +0.5 D
Predictability	76.2%	91%	Not mentioned	79%
Complications	Peripheral corneal haze in moderate hyperopia group	None reported	None reported	None reported

Abbreviations: PRK, photorefractive keratectomy; Amaris, Amaris 500-Hz excimer laser (SCHWIND eye-tech-solutions, GmbH, Kleinostheim, Germany); iVis, iVis Suite platform (iVis Technologies, Taranto, Italy) with 1 kHz excimer laser IRESTM; StreamLight EX500, StreamLight PRK® software in WaveLight EX500 Excimer Laser (WaveLight; Alcon Laboratories, Fort Worth, TX, USA; D, diopter; SE, spherical equivalent; UCVA, uncorrected visual acuity; logMAR, logarithm of the minimum angle of resolution.

Uncorrected Visual Acuity (UCVA)

The UCVA of 55 eyes in the study by Moghaddam et al improved significantly from pre-operative UCVA of 0.54 ± 0.05 logMAR (mean ± standard error [SE]) to 0.18 ± 0.03 at 3 months after surgery till 0.15 ± 0.03 at 12 months.[23] The outcomes were better for patients younger than 45 years of age (0.07 ± 0.03 vs 0.21 ± 0.06). The cumulative percentage of eyes with UCVA of 20/25 or better at 12 months was 64.2%. Ortueta et al have reported a similar finding in their subset of 43 eyes, where the sphere reduced from a mean of 0.42 diopter (D) to a mean of 0.11 D (range −0.5 to +0.75 D).[17]

In the study by Abdel-Radi et al, mean pre-operative logMAR UCVA significantly improved from 0.53 ± 0.02 to 0.08 ± 0.01 at 12 months ($P < 0.001$). All eyes in this study achieved a UCVA of 20/40 or better at 12 months' follow-up.[24]

Best Corrected Visual Acuity (BCVA)

In the study by Moghaddam et al, there was an initial myopic overcorrection at 1 month, leading to a decrease from 2.56 ± 0.19 (mean ± SE) to −1.1 ± 0.21 D ($P < 0.001$).[23] However, this improved to 0.05 ± 0.13 D at 12 months. A significant finding in this study was that, at last visit, there was no loss of two or more lines of BCVA in any eye.[23]

Abdel-Radi et al reported a non-significant change in BCVA over the 12 months' follow-up ($P = 0.135$). There was no loss of Snellen lines of BCVA, and two eyes gained one line (4.2%) at the last follow-up.[24]

Refractive Outcome

The final SEQ was found to be significantly more towards hyperopia in the age group of 45 years or older. Ortueta et al showed a SEQ of under 0.5 diopter in 91% eyes, and 100% had under 1 D.[17] Repeat Trans PRK was done for two cases, and the SEQ and astigmatism were under 0.5 D in both cases, with no eye losing two or more Snellen lines.

The mean cycloplegic SEQ in the study by Abdel-Radi et al was reduced from 3.21 ± 0.61 D pre-operatively to 0.41 ± 0.04 D post-operatively at 12 months ($P < 0.001$). The authors reported that at 12 months the accuracy of the cycloplegic SEQ within ±0.5 D of emmetropia was achieved in 72.9% eyes.[24]

Astigmatism

In the study by Moghaddam et al, pre-operative astigmatism of −0.94 ± 0.12 D improved to −0.49 ± 0.08 D at 3 months, but reverted to 0.71 ± 0.12 D at the end of 12 months.[23] This increase was present in the moderate hyperopia subset and the German subset of patients. In the Iranian patients, the astigmatism decreased from −0.86 ± 0.22 D to −0.0.3 ± 0.04 D. In the low hyperopia group, the astigmatism reduced from −0.97 ± 0.19 D to −0.40 ± 0.09 D. Ortueta et al reported a decrease of astigmatism from the mean pre-operative value of 1.2 D to 0.22 D after 3 months.[17] Abdel-Radi et al reported a significant improvement of mean pre-operative cycloplegic cylinder from 0.93 ± 0.11 D to 0.39 ± 0.04 D at 12 months following surgery, with 79.1% eyes having a post-operative cycloplegic cylinder of 0.5 D or less at final visit.[24]

Stability

Moghaddam et al reported rate of regression for mean ± SE between post-operative 1 and 6 months as 0.17 ± 0.03 D per month for the total number of eyes.[23] This rate was higher as compared to the next 6 months of follow-up, which was up to 0.004 ± 0.01 D per month. The moderate hyperopic subset had a non-significant regression rate compared to the low hyperopic group. In the last 6 months, the change of mean ± spherical equivalent within all subgroups was not statistically significant. Ortueta et al reported an efficacy of 0.8 when comparing pre-operative BCVA with post-operative UCVA, while for Abdel-Radi et al the efficacy was 0.87.[17,24]

Complications

Moghaddam et al reported peripheral corneal haze in 5 eyes at 3 months of various grades, which cleared at 1 year in one eye.[23] The remaining eyes had BCVA of 20/25, with no difficulty in quality of vision. All these cases were from eyes with moderate hyperopia correction. The authors did not find any other complication in their patients. Ortueta et al, Goggin et al, and Abdel-Radi et al did not report any side effects of the procedure in any of their patients.[17,19,24]

Comparison of Trans PRK with Other Refractive Procedures

Although there are studies comparing Trans PRK with LASIK, SMILE, and conventional PRK in myopia correction, there is no literature available on these comparisons for hyperopia correction. A meta-analysis comparing Trans PRK with conventional PRK for outcomes of efficacy, predictability, safety parameters, and visual and patient-reported parameters reported comparable outcomes for all parameters.[11] However, the selected articles were based on myopia correction. Trans PRK had comparable visual outcomes and safety parameters compared to Femtosecond LASIK, SMILE in the limited data available currently.[3] All these studies were based on myopia correction surgery.

Discussion

The journey of hyperopia correction started with the use of peripheral thermokeratoplasty to steepen the central cornea more than a century back.[32] This was followed by other attempts such as hexagonal keratotomy, keratophakia, lamellar keratoplasty, and epikeratoplasty.[33] However, all these surgeries lacked precision, and had poor post-operative visual predictability and safety concerns, along with formation of excessive peripheral corneal haze. After the advent of LASIK and conventional PRK, good outcomes were obtained for mild to moderate hyperopia removal by these technologies.[34,35] Femtosecond LASIK is also popular recently for hyperopia correction.[36,37]

Trans PRK has offered a unique technique of reshaping the cornea for refractive correction by a "reversed single-step" method, wherein the stromal ablation is done first, followed by epithelial reshaping.[5] Although this technology has proven to be comparable to previous refractive surgeries for myopia and astigmatism correction in visual outcome and safety issues, the challenge remains for hyperopia correction. This is because regression and unpredictability has been reported when ablation is done at the mid-periphery for central corneal steepening to remove hyperopia.[33,38] The four studies published to date have reported good outcomes with Trans PRK for hyperopia correction.[17,19,23,24] Peripheral haze has been reported by Moghaddam et al, but it was not found to have any adverse effect on the visual acuity after surgery.[23] The same authors also reported minimal regression in few cases at 6 months. There is a need for further studies on this methodology to better understand the outcomes and safety profile in hyperopic eyes.

A difference in treatment plan in these studies was the application of a larger optical zone (>6.5 mm) for ablation. Previous studies for LASIK or conventional PRK in hyperopia removal had used smaller optical zones, which might have resulted in unpredictable post-operative vision and higher regression.[33,35,39,40] The sudden transition area from ablated to unablated surface, leading to uncontrolled tissue regeneration, is thought to cause such unpredictability.

The treatment outcomes in moderate to high hyperopia have been unsatisfactory in previous studies using conventional PRK and LASIK.[33,35,37] A similar outcome was noted on using Trans PRK in these eyes. The predictability is around 80% in moderate hyperopia at 1 year compared to 90% in low hyperopia eyes.[23] Similarly, regression is also found to be higher in moderate hyperopia as compared to lower hyperopia. One study reported a satisfactory rate of regression of 0.004 diopter/ month in the low hyperopia group till 1 year.[23] Another study by Kaluzny et al, using 10 mm zone of epithelium removal and 6.5 mm zone of ablation, had attempted to analyze the 3-year outcome for conventional PRK for moderate to high hyperopia correction. The authors reported good outcome in refractive stability at 3 years, with 78% of eyes being within ±0.50 D of the attempted spherical equivalent correction.[35] However, there was poor epithelial healing of >7 days in 15.7% eyes, which took 2 weeks to heal. The authors have also commented in the same article that ablating up to 10 mm of cornea leaves a very minimal distance from the ablation edge to the limbus. Moreover, there is increased risk of corneal haze formation due to the higher targeted ablation volume within the large ablation area of the corneal tissue. Longer follow-up data in this group of patients are needed to know the predictability and rate of regression at 5 to 10 years.[12]

Post-operative pain is reported to be lower in Trans PRK versus conventional PRK in myopia correction.[8,9,11,31] However there are no such comparative studies for hyperopic eyes. Similarly, post-operative stromal haze is also reported to be decreased in Trans PRK as compared to conventional PRK in myopic corrections. Further data on this technology for hyperopia correction are much wanted in view of the encouraging results in the myopic subset of patients and the outcomes in our review.

Conclusion

Trans PRK technology has shown promising results in hyperopia correction in the limited scientific literature available to date. There is an opportunity to further evaluate this technology for surgery on lower hyperopia in longer follow-up period. The correction of moderate to high hyperopia with inclusion of larger ablation zone will need further refinement of the technology to obviate the risks of regression, unpredictable outcomes, and corneal haze, observed to date.

Summary

This review was undertaken to understand the data on the outcome of Trans PRK in hyperopia correction and find the causes of lower acceptance of this procedure amongst surgeons and the outcomes in patients. As there are no in-depth analyses of this procedure in hyperopic patients, this review shows that the outcomes of the surgery are good in patients with lower range of hyperopia.

Disclosure

The authors report no conflicts of interest in this work.

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