A 14-Year Follow-up of Photorefractive Keratectomy

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ABSTRACT

PURPOSE: To evaluate the long-term outcome of myopic photorefractive keratectomy (PRK).

METHODS: This prospective study included 31 patients (49 eyes) who underwent PRK between 1991 and 1993. A Summit UV200 excimer laser was used. Patients were divided into two groups—low myopia: preoperative ≤6.00 diopters (D) (range: −1.50 to −5.75 D) (n=19); and high myopia: preoperative ≥6.00 D (range: −6.00 to −13.00 D) (n=12). Long-term postoperative follow-up was every 2 years up to 14 years. Refraction, visual acuity, corneal status, and intraocular pressure (IOP) were evaluated. At 14 years, corneal topography and endothelial cell count were performed.

RESULTS: At last follow-up, manifest refraction spherical equivalent (MRSE) for the low myopia group was −0.17±0.8, uncorrected visual acuity (UCVA) logMAR was −0.06±0.55, and best spectacle-corrected visual acuity (BSCVA) logMAR was −0.11±0.55, and BSCVA logMAR −0.03±1.00. At 14 years, BSCVA for most eyes was at least equal to preoperative BSCVA. In both groups, haze increased between 3 and 6 months, then declined in the first year. A temporary increase of IOP was seen in 4 eyes. Complications were minor haze (2 eyes), transient anisocoria (9 eyes), and intraepithelial hemosiderin deposits (4 eyes). No abnormalities in endothelial cell count or morphology, astigmatism, or ectasia were noted. Three patients reported night vision disturbance, but the majority of patients were satisfied with the outcome based on subjective questionnaire (low myopia group: 84%; high myopia group: 75%).


The development of excimer laser technology over the past two decades has heralded a new era in refractive surgery.1-6 Excimer laser–based photoablation of the cornea is the most widely used procedure for the correction of myopia. Photorefractive keratectomy (PRK) has been performed since the late 1980s7 and LASIK since the 1990s.8 Originally, excimer laser surgery was used to treat low to moderate myopia and PRK was used exclusively. As the number of commercial laser systems and treatment algorithms developed, there was a progressive increase of ablation zone diameters.9-13 Some short-term problems are associated with PRK: pain in the first 48 hours, delay in visual recovery of 3 to 5 days during epithelial healing, corneal scarring, and transient loss of corneal transparency, termed haze, for a period of weeks to months after surgery.2-14,15 With any corneal refractive surgical procedure, it is essential to monitor long-term stability and efficacy. To date, long-term prospective follow-up studies with a larger number of patients are confined to PRK; the longest study published on attempted corrections up to 7.00 diopters (D) has a 12-year follow-up,16-32 whereas for higher attempted corrections the longest follow-up available is 8 years.31 The possible development of chronic stromal remodeling, progressive regression of refractive effect, and other possible long-term complications are important considerations for patients and practitioners.
tions, especially for higher degrees of corrections, cannot be excluded.

The present study evaluates 31 patients from the original cohort of 50 patients entered into a prospective clinical trial and followed for 14 years to assess the long-term outcomes of PRK. Our study aimed to determine predictability, stability, and safety of myopic PRK and not its capability to achieve emmetropia, as emmetropia was not necessarily the goal in each treated eye.

**PATIENTS AND METHODS**

Fifty patients (32 men, 18 women) who underwent myopic PRK at the Clinica Oculistica, DiNOG, University of Genoa, Azienda Ospedaliera Universitaria San Martino, Genoa, Italy from 1991 to 1993 were consecutively recruited for this study. The 14-year follow-up was attended by 31 patients (49 eyes) as 19 patients were lost to follow-up after 2 years. In this study, we used only data from these 31 patients. Patient characteristics are shown in Table 1.

All patients had stable refraction (<0.50-D change) for the previous 2 years, <2.00 D of astigmatism, and normal and transparent corneas. To minimize the number of variables in this study, patients were divided into two groups—low myopia group and high myopia group—based on preoperative myopia (Table 2).

Mean correction of −3.30±1.70 D (range: −1.50 to −5.75 D) and −7.50±1.90 D (range: −5.75 to −13.00 D) was attempted for the low and high myopia groups, respectively, with a mean difference between total refractive error and attempted correction of 0.00±0.01 D for the low myopia group and −0.04±0.01 D for the high myopia group. No undercorrections were attempted.

Preoperative examination included manifest refraction, keratometry, slit-lamp microscopy, Schirmer test tear break-up time (BUT), Goldmann applanation tonometry, and dilated fundus examination. Manifest refraction and cycloplegic refraction with cyclopentolate chloride 1% eye drops (Ciclox; Allergan S.p.A., Rome, Italy) three times every 5 minutes with an auto refractometer were determined. Corneal topography was assessed using a computerized photokeratoscope (TMS-1, Computed Anatomy Inc, New York, NY). Preoperative central corneal thickness and endothelial cell count were not performed as they were not part of the prospective protocol in 1990.

Exclusion criteria were pre-existing ocular pathology, previous anterior segment surgery, diabetes, connective tissue disorders, severe atopic disease, susceptibility to keloid scar formation, age <19 years, and pregnancy or breast-feeding.

Ethical committee approval and signed informed consent were obtained before treatment.

**SURGICAL TECHNIQUE**

Surgery was performed under topical anesthesia with 3 drops of oxybuprocaine 0.8% (Novesina; Sandoz S.p.A., Origgio, Italy) at 5-minute intervals. Two drops of pilocarpine 2% applied 20 minutes before surgery were used to constrict the pupil, as this was the standard of care recommended at that time to center the optical zone. The same surgeon (C.E.T.) performed all procedures. The central 7.0-mm diameter epithelium was scraped using a custom-made blunt spatula (E. Janach srl, Como, Italy).

The laser system used was a UV 200 excimer laser (Summit Technology Inc, Waltham, Mass) with an emission wavelength of 193 nm, fixed pulse repetition rate of 10 Hz, maximal beam diameter of 5 mm, and radiant exposure of 180 mJ/cm².
For corrections <6.00 D, we used a single optical zone (4.5±0.5 mm; range: 4 to 5 mm). For corrections from 6.00 to 9.00 D, one single optical zone was used (4.4±0.5 mm; range: 4 to 5 mm). For corrections of ≥9.00 D, two concentric optical zones were used. Sixty percent of the attempted correction was performed on the first, smaller optical zone (4.2±0.4 mm; range: 4.2 to 4.5 mm), and 40% of the attempted correction was performed with the larger optical zone (4.5±0.4 mm; range: 4.5 to 4.7 mm). No transition zone was available. Data regarding ablation depth in each group are shown in Table 3.

At the end of the procedure, 1 drop of cyclopentolate 1% (Ciclolux), dexamethasone 0.1% (Visumetazon; MSD Chibret S.p.A., Rome, Italy), and tobramycin 0.3% (Tobral, Alcon Italia S.p.A., Milan, Italy) were applied. The eye was then patched. A systemic analgesic (oral ketorolac) was prescribed for as needed. Tobramycin 0.3% eye drops were prescribed four times daily for 1 week. Dexamethasone 0.1% eye drops were prescribed three times daily starting the day after surgery for 1 month, twice daily for 1 month, and then once daily for 1 month.

**Postoperative Evaluation**

Postoperative follow-up was scheduled at 1 day; 3 to 6 days; 1, 3, 6, 12, 18, and 24 months; and every 2 years thereafter. Complete dilated eye examinations were performed with special attention to corneal status and refraction. Uncorrected visual acuity and BSCVA were measured using Snellen acuity charts. Patients were questioned regarding symptoms of foreign body sensation, dryness, and quality of night vision.

A specific semiquantitative questionnaire was created to assess night vision disturbances and patient satisfaction. In each case, a visual analog scale (1 to 5) was used with 1 = poor and 5 = full satisfaction.

Corneal haze was assessed semiquantitatively and scored from 0 to 4 using a standardized scale. A specific semiquantitative questionnaire was created to assess night vision disturbances and patient satisfaction. In each case, a visual analog scale (1 to 5) was used with 1 = poor and 5 = full satisfaction.

At last follow-up, all patients underwent corneal topography (TMS-1), pachymetry (Ultrasonic Contact Pachymeter; Quantel Medical Pocket, Clermont, France), and endothelial specular microscopy (Non-con Specular Microscope SP-9000; Konan Inc, Hyogo, Japan). For patients treated in one eye, the fellow eye was used as a control for corneal integrity.

**Statistical Analysis**

To evaluate significant changes in visual acuity and refraction during follow-up and between groups, the two-tailed Student t test was performed. Correlation between pre- and postoperative refraction was evaluated by Bravais-Pearson correlation analysis. A P value <.05 was considered statistically significant.

**RESULTS**

Eight (30%) patients (14 [31%] eyes) in the low myopia group and 11 (48%) patients (16 [47%] eyes) in the high myopia group were lost to follow-up after 2 years. The last follow-up at 14 years was attended by 19 patients (31 eyes) and 12 patients (18 eyes), respectively, for a total of 49 eyes. Eighteen patients (12 from the low myopia group and 6 from the high myopia group) received bilateral PRK, whereas 13 patients (7 from the low myopia group and 6 from the high myopia group) received unilateral treatment. During follow-up, patients from both groups achieved best correction of their refractive defects within 6 months after PRK and remained stable thereafter (Fig 1). At the end of follow-up, manifest refraction spherical equivalent (MRSE) was −0.17±0.80 D in the low myopia group and −0.67±1.40 D in the high myopia group. These values differ significantly from preoperative (P<.001); there were no significant differences between groups postoperatively (P=.22). As a rule, an early hyperopic shift was observed. The hyperopic shift was largest at 1 month after PRK, and regressed until stabilization occurred within 6 months, with higher corrections usually taking longer to correct. The shift was generally higher when the preoperative refraction, expressed as spherical equivalent refraction, was closest to emmetropia.

Results of MRSE, mean UCVA, and mean BSCVA at last follow-up for the two groups are shown in Table 4. At 14 years postoperative, 30 (97%) eyes in the low myopia group and 17 (94%) eyes in the high myopia group had BSCVA better than or equal to preoperative. As expected, postoperative UCVA increased significantly from preoperative (P<.001); postoperative differences between the groups were not significant (P=.31). Taken together, these data show that refraction and visual acuity were not statistically different between groups; but as expected, the standard devia-
tion of visual and refractive outcomes increased with an increase in attempted correction. At 14 years, no patient treated with unilateral PRK had myopic progression in the unoperated eye.

Correlation between pre- and postoperative refraction was evaluated by Bravais-Pearson correlation analysis. One month after PRK, a significant positive correlation was observed in the low myopia group ($r=0.49$, $P<.01$), whereas the high myopia group showed a nonsignificant negative correlation ($r=-0.031$, $P>.05$). Considering our entire sample, the correlation was not significant, with an $r$ coefficient close to zero (data not shown). At 3 and 6 months and 14 years, the correlation was not significant ($P>.05$). These data confirm stabilization of the postoperative refraction within 6 months after PRK. No significant differences emerged when comparing refraction at 3 and 6 months, 3 months versus 14 years, or 6 months versus 14 years, either within each group or between the two groups ($P>.05$, two-tailed $t$ test).

To verify whether preoperative ametropia could predict long-term refraction, we first calculated the difference between total ametropia (TA) and attempted correction (AC) for each patient, subtracted it from final refraction (FR) at 14 years and considered the result as a “final error” (FE) that characterized the long-term refractive endpoint of PRK. That is,

$$FE = FR - (TA - AC).$$

The mean final error was $-0.22\pm0.65$ D for the low myopia group and $-0.53\pm0.9$ D for the high myopia group. To study the correlation between the attempted correction and this error, Bravais-Pearson correlation analysis was performed, which demonstrated a nonsignificant correlation in both groups (low myopia group: $r=0.235$, $P>.05$; high myopia group: $r=-0.001$, $P>.05$) (Fig 2).

The loss of corneal transparency (haze) was noted in all treatment groups in the early postoperative period. In both groups, haze increased between 3 and 6 months, then declined over the course of the first year, and there was little further change up to 14 years; the mean score was 0.9 for the low myopia group and 1.0 for the high myopia group at 1 month. At 3 months, mean score was 0.6 for the low myopia group and 0.7 for the high myopia group and declined to 0.5 for the low myopia group and 0.6 for the high myopia group at 12 months. No significant differences between groups ($P=.79$) were noted. At the end of follow-up, 30 (97%) eyes of the low myopia group and 17 (94%) of the high myopia group had clear corneas. At last follow-up, 1 eye of each group showed 0.5 haze without loss of BSCVA.

Anisocoria, defined as a difference of at least 1 mm, was noticed in 7 (23%) eyes of the low myopia group and in 2 (11%) of the high myopia group 2 months.
(range: 4 to 90 days, mean: 66 days) after PRK; in all cases the treated eye had the larger pupil. Anisocoria disappeared within 8 months (range: 5 to 18 months; mean: 235 days) and did not appear to be predictive of visual outcome. An increase in intraocular pressure (IOP) was recorded in 4 (22%) eyes of the high myopia group (27.5±4.4 mmHg; range: 25 to 34 mmHg), which was observed 1 to 3 months after surgery but returned to normal after discontinuation of topical steroids. These four patients also showed temporary anisocoria during follow-up. At 14 years, no patient had developed glaucoma or ocular hypertension. Central corneal thickness measurement was performed at 14 years in all treated eyes (mean: 515.6±32.3 µm; range: 435 to 580 µm).

A permanent decrease in IOP recorded with Goldmann applanation after PRK was observed in all groups, which was not significant for photoablations <6.00 D ($P=.108$) and showed a $P$ value of .057 for photoablations ≥6.00 D. In unilaterally treated patients, the difference between the two eyes was statistically significant ($P<.0001$).

At last follow-up, we performed an endothelial cell count on all treated eyes (n=49) and on fellow eyes (n=13). No abnormality was observed and no significant difference between treated eyes and untreated fellow eyes was noted (paired $t$ test $P>.5$ for cell density, coefficient of variation, and hexagonality).

Corneal topographic analysis showed an evident oblate contour with no irregular astigmatism or ectasia (surface regularity index = 0.32±0.28).

Potential visual acuity ranged from 20/20 to 20/25, which was in agreement with our clinical findings.

At slit-lamp examination, the integrity of the cornea was well preserved in all eyes. None had epithelial stippling or history of recurrent corneal erosions. Intracellular epithelial hemosiderin deposits were apparent in 1 (3%) eye of the low myopia group and in 3 (17%) eyes of the high myopia group. Visual acuity was unaffected. One patient from the low myopia group and 2 from the high myopia group showed evidence of age-related nuclear sclerosis, but none had developed retinal tears or macular pathology. Two (11%) patients from the low myopia group and 4 (33%) patients from the high
myopia group reported use of tear substitutes without evidence of dry eye or ocular surface inflammation. At last follow-up, 13 (68%) patients from the low myopia group and 7 (58%) patients from the high myopia group indicated full satisfaction (score 5) regarding night vision disturbances; 5 (26%) patients from the low myopia group and 3 (25%) patients from the high myopia group indicated high satisfaction (score 4). One (5%) patient from the low myopia group and 2 (17%) patients from the high myopia group reported night vision disturbances described as halos around bright lights at night or dusk. The age range of symptomatic patients was 36 to 48 years at final follow-up, and scotopic pupil size averaged 6.6 ± 0.35 mm (range: 6 to 7 mm). No patient used pilocarpine or other miotic agents to relieve symptoms.

At last follow-up, 16 (84%) patients from the low myopia group and 9 (75%) from the high myopia group were extremely satisfied with the outcome of PRK.

**DISCUSSION**

Refractive surgery is an evolving field of ophthalmology. Owing to the permanent nature of the procedure, adequate patient selection and counseling is critical. With increased media exposure regarding the extreme precision of refractive surgery, it is not surprising that many refractive surgery candidates have high expectations. A patient may meet all the medical and surgical requirements for refractive surgery but may not be a good candidate because of unrealistic expectations or inadequate knowledge about the procedure, its risks and benefits, or alternatives.

To achieve uniform satisfaction and safety, newer refractive surgical procedures must be validated continuously through controlled and well-designed scientific investigations. A large number of studies have been conducted in various patient groups with varying lengths of follow up. Results are generally consistent but there is some variation in the predictability of treating patients with high degrees of myopia.

Preliminary results of PRK for myopia, demonstrating short-term safety and efficacy, were presented in 1993 by Weinstock and Machat. In 1994, Sher et al showed that PRK can correct high amounts of myopia with reasonable stability after 6 months. Rosa et al and Mardelli et al demonstrated that there is no long-term damage of endothelial cells after PRK, even in highly myopic eyes.

In 1996, Kim et al concluded that a 6.0-mm diameter optical zone seems to produce better outcomes than one of 5.0 mm, without night vision problems and photoblation decentration. In 1997, Kim et al demonstrated that UCVA better than 20/25 was achievable in a high proportion (62.4%) of eyes and that myopic regression continued for up to 5 years after PRK, with the most important predictive factor of myopic regression being preoperative refraction.

Photorefractive keratotomy for corrections >10.00 D was reported as unstable 2 years after treatment and not predictable. Long-term follow-up was not available. However, Spadea et al suggested that PRK is a safe and relatively effective alternative for treating highly myopic eyes (range: −8.00 to −17.00 D) with stable effects up to 2 years. Keskinbora evaluated the 4-year refractive outcomes of multizone PRK in eyes with high myopia and concluded that PRK was effective in treating myopia between −6.00 and −10.00 D, which stabilized without significant regression between 6 and 9 months after surgery.

In 1998, a 6-year follow-up study showed there was stabilization after 1 year and a decrease of corneal haze over time with no intraocular or retinal side effects noted. Night halos remained a significant problem in a small number of patients treated with a 4-mm ablation zone. In 1997, Pioveilla et al evaluated multiple optical zone corneal ablation (4, 5, and 6 mm) in highly myopic eyes (range: −5.75 to −24.50 D) and concluded that a multiple zone technique achieved long-term, stable reduction of myopia, although perception of halos was noted by 16 of 44 patients.

In 1998, Steinert and Hersh compared PRK and LASIK for the correction of myopia between −6.00 and −12.00 D. Long-term efficacy outcomes were similar but improvement in UCVA and BSCVA was faster with LASIK. Predictability was better for smaller corrections (up to −8.90 D) with both procedures. Sporadic loss of BSCVA, observed in the PRK eyes, was not noted in the LASIK eyes.

Four long-term studies confirmed the efficacy and stability of PRK. Honda et al treated patients with low to moderate myopia (range: −3.00 to −9.00 D), and after 5 years found little regression in the first year. Rajan et al found that refractive stability was maintained up to 12 years postoperative with no evidence of hyperopic shift, diurnal fluctuation, or late regression. Patients with attempted corrections up to −7.00 D were included. Night halos remained a significant problem in a subset of patients due to the small ablation zone size. Pietilä et al demonstrated the stability and safety of PRK in patients with myopia <−10.00 D in an 8-year follow-up study. In 2006, O’Connor et al concluded that PRK showed good refractive stability from years 2 to 12 in patients with low to moderate myopia.

Recently, Shortt et al reviewed the literature for LASIK and PRK correction of myopia. They concluded that LASIK is slightly but consistently superior to PRK.
in efficacy and safety. However, the differences were small and both techniques have improved since those clinical trials.

Our results confirm previous findings of a permanent decrease of Goldmann applanation IOP readings after PRK. Due to the scatter of values and sample size, the difference was highly significant only when comparing IOP between the two eyes of unilaterally treated patients.

We confirm that PRK is a safe technique in respecting corneal endothelium because at the end of follow-up no patients showed signs of endothelial failure or abnormalities; however, it was not possible to compare pre- and postoperative cell counts because specular microscopy was not part of our prospective protocol. The number of patients in whom the fellow untreated eye was used as a control is small (n=13), which does not allow a conclusive statement.

At 14 years, our study has the longest follow-up of any prospective study published to date. Similar to a number of other investigators, we found PRK to be a safe and effective procedure for the treatment of myopia, with final results less predictable and less stable where the correction is greatest. No published follow-up data for longer than 8 years are available for corrections above 7.00 D.

Corneal haze decreased with time, without sequelae. This finding suggests that most cases of corneal haze could be followed with observation before resorting to phototherapeutic keratectomy. Smaller optical zones were used to limit total ablation depth due to the fear of removing larger areas of Bowman’s layer and to the unknown long-term consequences of deeper stromal ablation; a technical limitation of the excimer delivery systems then available was also a factor influencing the choice of a smaller optical zone. Despite the relatively small diameter of the optical zone, few patients had persistent night vision disturbances.

At 14 years postoperative, this study has the longest published follow-up of a group of eyes that underwent PRK for the treatment of myopia. Our results confirm other shorter term studies and demonstrate the efficacy and safety of myopic PRK, even when performed with the technology available in 1991 to 1993. Refractive status achieved at 6 months was maintained up to 14 years with no evidence of late regression for both low and high myopia. No late complications were found in this study.

AUTHOR CONTRIBUTIONS

Study concept and design (S.C., C.E.T.); data collection (G.B., R.S., S.C.); interpretation and analysis of data (G.B., R.S., M.M., C.E.T.); drafting of the manuscript (G.B., R.S., M.M., C.E.T.); critical revision of the manuscript (G.B., M.M., S.C., C.E.T.); statistical expertise (G.B., M.M., C.E.T.)

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