Photorefractive Keratectomy in Keratoconus

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Key Words

Photorefractive keratectomy · Keratoconus · Refractive surgical procedures

Abstract

Purpose: To assess the efficacy and safety of topography-guided photorefractive keratectomy (PRK) for keratoconus and to estimate the subsequent risk of progression. **Methods:** This is a retrospective follow-up study. Between 1998 and 2013, 28 eyes of 23 patients (age 17–60) with grade 1–3 keratoconus received topography-guided PRK. Corrected-distance visual acuity (CDVA), keratometry, pachymetry, and corneal topography were assessed before, after 3 months, and at a late follow-up of a median of 7 years after the procedure. Postoperative complications including subsequent keratoplasty were noted. **Results:** Of the 28 eyes, 5 (18%) had undergone corneal transplantation at a median of 7 years (range 3–10) after PRK. Four eyes were not available for follow-up. In the remaining 19 eyes, CDVA was improved in 16 eyes (84.3%), reduced in 2 eyes (10.5%), and unchanged in 1 eye (5.2%). Thus, average CDVA had improved from 0.49 logMAR before PRK to 0.27 logMAR at 3 months, and to 0.24 at the long-term follow-up. The mean spherical equivalent was reduced from –6.2 to –3.7 dpt after 3 months and to –2.1 dpt at the late follow-up. Similarly, the mean cylinder was reduced from –4.2 to –3.0 dpt after 3 months and at the late follow-up. **Conclusion:** Topography-guided PRK in keratoconus may be effective for reducing myopia and astigmatism and may offer a temporary or permanent alternative to keratoplasty in contact lens-intolerant keratoconus. In the present study, we found a low risk of keratoconus progression after PRK.

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Introduction

Keratoconus is characterized by progressive corneal protrusion and thinning that leads to irregular astigmatism and impairment in visual function [1, 2]. During the past two decades, new developments in visual rehabilitation of keratoconus have been introduced, including new contact lens designs, photorefractive keratectomy (PRK), collagen cross-linking, intrastromal corneal ring segments, phakic intraocular lenses, and penetrating or lamellar keratoplasty in advanced stages [2].

Current regimes for PRK utilize topography-guided ablation profiles, intended to reduce corneal surface irregularities and improve vision. Corneal thinning disorders weaken the mechanical strength of affected corneas, suggesting that photorefractive procedures may be contraindicated in keratoconus. Few cases have been reported to confirm this hypothesis [3]. Although corneal ectasia has been described after PRK in keratoconus suspect cases [4], other studies report encouraging results using PRK alone [5–7].

Between 1998 and 2013, we treated 28 eyes of 23 keratoconus patients with PRK. The main objective was to improve visual acuity with spectacles or contact lenses, delaying or avoiding more extensive surgical interventions such as keratoplasty.

The aim of the current study was to evaluate the long-term efficacy and safety of PRK for keratoconus and to assess the risk of progression of the disease after the excimer laser procedure. As there are very few reports on this subject, we believe our study to be of interest in spite of the retrospective design and relatively small sample size.

Patients and Methods

Subjects

A total of 28 eyes of 23 patients (16 male and 7 female; median age 36 years, range 17–60) treated with topography-guided PRK between 1998 and 2013 were retrospectively identified from electronic patient records at the Department of Ophthalmology, Aarhus University Hospital, Denmark. All patients had originally been referred from a general ophthalmologist for corneal transplantation due to poor visual acuity with glasses and intolerance to contact lenses. The diagnosis of keratoconus was based on a combination of slit-lamp biomicroscopy, corneal topography, auto-keratometry, and corneal pachymetry. Preoperative and short-term postoperative data were collected from the patient's medical records. All patients had a preoperative keratoconus grade of 1–3 on the Amsler-Krumeich classification. Corneal haze was graded using the Fantes score. In 5 patients, both eyes had been treated. Two patients received one PRK retreatment, and 1 patient received two PRK retreatments. Patients were invited to a late follow-up examination in 2013–2014.

Inclusion and Exclusion Criteria

The total number of treated patients was 23 (28 eyes). When evaluating the electronic patient records, 5 patients (5 eyes) were found to have undergone keratoplasty at some time after PRK treatment. These 5 cases were classified as failed, and the patients were not invited to the follow-up visit. Two patients (2 eyes) could not be contacted because of change of address, and 1 patient (2 eyes) was not interested in participating in a long-term follow-up visit. Two patients (2 eyes) did not attend the 3-month follow-up. Thus, the statistical analyses included 26 eyes of 21 patients at the 3-month follow-up and 19 eyes of 16 patients at the long-term follow-up (fig. 1). The patient (2 eyes) who was not interested in a long-term

follow-up visit reported to be satisfied with the treatment (telephone conversation). Therefore, satisfaction data include 21 eyes of 17 patients.

Surgical Technique

Orbscan II slit-scanning (Bausch and Lomb, Rochester, N.Y., USA) topography maps were used for topography-supported planning (TOSCA) of the ablation in patients treated from 1998 to 2005 (12 eyes). Patients treated between 2005 and 2013 (16 eyes) were measured with the ATLAS topographer (Carl Zeiss Meditec, Jena, Germany) and treatment planning was performed using the CRS Master software module. PRK was performed in topical anesthesia. All patients were treated by one of two surgeons (Dr. Jesper Hjortdal or Dr. Niels Ehlers, Aarhus University Hospital). A circular corneal marker was used to define an 8-mm zone centered over the pupil. A surgical sponge was used for brief application of alcohol, followed by immediate wiping with a sponge wetted in physiological saline. Subsequently, the central epithelium was removed with a blunt Beaver knife. The excimer laser photoablation was performed with a MEL-70 (12 eyes, from 1998 to 2005) or a MEL-80 (16 eyes, from 2005 to 2013) flying spot excimer laser (Carl Zeiss Meditec). The optical zone ranged from 6.0 to 6.5 mm in diameter. The mean ablation depth was 82 μm (SD 17.8, range 45–112). Topical mitomycin C 0.02% for 20 s was applied in 3 re-treated patients (5 eyes) to minimize postoperative haze. Following the excimer laser treatment, one drop of cyclopentolate 1%, one drop of diclofenac 0.1%, and chloramphenicol ointment were applied.

Postoperative Treatment and Follow-Up

The postoperative treatment consisted of chloramphenicol eye drops 0.5% and prednisolone eye drops (0.5%) 4 times a day for 2 weeks and then 2 times a day for 2 weeks. Patients were examined preoperatively and were offered visits at 1, 3, 6, 9, and 12 months after surgery. At all visits, patients received routine clinical examination with slit-lamp biomicroscopy, determination of corrected-distance visual acuity (CDVA), pachymetry, and corneal topography with TMS-1 or TMS-3 (Tomey, Nagoya, Japan), ATLAS (Carl Zeiss Meditec), or Pentacam HR (Oculus, Wetzlar, Germany). At the late follow-up visit at a median of 7 years (range 2–14) after the procedure, patients were asked about their satisfaction with the PRK procedure in each eye, simply stating whether they were satisfied or dissatisfied. Visual acuity data were converted from Snellen equivalent to logMAR. The main outcome parameters were considered to be change in CDVA, spherical equivalent (SE) refraction, refractive cylinder, changes in keratometry (Kmax; taken from the steepest keratometer reading), as well as overall failure (need for keratoplasty or planned additional surgery). Central corneal thickness (CCT) as well as development of corneal haze were considered to be secondary parameters. Keratoconus progression was defined as an increase in the steepest keratometry measures, with concurrent changes in subjective refraction, topography, and corneal thickness between 3 months after PRK and the late follow-up visit.

Statistical Analysis

Statistical analysis was performed using Graphpad PRISM version (6.0d) software. Preoperative, early postoperative (3-month follow-up), and late postoperative parameters were compared using paired t tests. A p value < 0.05 was considered statistically significant.

Results

Keratoconus Progression

Keratoconus showed no progression in 15 out of 19 eyes (79%) at the late follow-up. Five of the total 28 eyes (18%), however, had undergone corneal transplantation during the years after PRK, and 1 patient (3%) was scheduled for implantation of intrastromal corneal ring segments (ICRS). The median age of transplanted patients at the time of PRK was 47 years (range 30–51). Three of the grafted patients had an initial effect of the topography-guided PRK treatment but had subsequent progression and developed pronounced keratoconus at a median of 7 years (range 3–10) after surgery. A fourth patient was transplanted due to development of central grade 2 haze after PRK, but keratoconus was stable. A fifth patient was transplanted because the expected results after PRK were not achieved.

Subjective Satisfaction

Long-term follow-up, a median of 7 years after PRK, showed that 13 patients (16 eyes) were satisfied and 4 patients (5 eyes) were dissatisfied with the PRK procedure. Thus, long-term satisfaction with the PRK procedure was obtained in at least 16 of the 28 eyes treated (57%).

Uncorrected-Distance Visual Acuity

Mean preoperative uncorrected-distance visual acuity improved significantly from 20/250 (1.1 logMAR) before surgery to 20/100 (0.7 logMAR) at the late follow-up visit ($p < 0.05$).

Corrected-Distance Visual Acuity

In the 26 eyes attending the 3-month follow-up, CDVA had improved by 1–7 Snellen lines in 21 eyes (81%) and was unchanged in the remaining 5 eyes (19%). In the 19 eyes attending the long term follow-up, CDVA had improved by 1–4 Snellen lines in 16 eyes (84%), was reduced by 1–2 Snellen lines in 2 eyes (11%), and was unchanged in 1 eye (5%) (table 1). The average CDVA improved significantly after topography-guided PRK, from 20/60 (0.49 logMAR) before surgery to 20/40 (0.27 logMAR) after 3 months and at the late follow-up.

Refractive Outcome

Mean SE refraction was significantly reduced by 2.5 dpt at 3 months ($p < 0.05$) and by 4.1 dpt at the long-term follow-up ($p < 0.05$; table 2, fig. 2b). In a paired comparison, SE had not changed significantly from the 3-month follow-up to the long-term follow-up visit ($p > 0.05$). The mean refractive astigmatism was significantly reduced with 1.2 dpt at 3 months ($p < 0.05$) as well as at the long-term follow-up ($p < 0.05$; table 2, fig. 2c).

Change in Corneal Thickness

Mean preoperative CCT was 484 μm (SD 45, range 410–610). CCT was significantly reduced to 440 μm (SD 43, range 337–540) at the 3-month follow-up and to 434 μm (SD 57, range 337–560) at the long-term follow-up ($p < 0.05$; fig. 3a).

Changes in Keratometry

Changes in keratometry (Kmax) were taken from the steepest keratometer reading. Mean preoperative Kmax was 50.6 dpt (SD 3.5, range 44.29–57.89), and mean postoperative Kmax was 48.92 dpt (SD 3.0, range 43.4–53.8) after 3 months, and 49.3 dpt (SD 3.3, range

44.8–56.6) at the long-term follow-up. Thus, Kmax measurements were reduced by 1.7 dpt by 3 months ($p < 0.05$) and 1.3 dpt after a median of 7 years ($p > 0.05$; fig. 3b).

Corneal Haze

By 3 months, 20 eyes had developed haze grade 1–2 and 6 eyes had developed haze grade 3–4. At the long-term follow-up, 3 eyes had no haze, 15 eyes had haze grade 1, and 1 eye had haze grade 2.

Discussion

The pathogenesis of keratoconus is not known in details, but Nielsen et al. [8] found that the protein expression is altered in the corneal epithelium with changes of the cytoskeleton, reduced extracellular matrix remodeling, altered transmembrane signaling, and modified cell-to-cell and cell-to-matrix interactions. Meek et al. [9] reported that the collagenous internal structure of the cornea is eventually altered after the PRK procedure, resulting in corneal thinning and ectasia. Cennamo et al. [6] reported a significant decrease in all keratoconus indices during 24 months of follow-up of 25 treated eyes versus an increase in indices in untreated control eyes, suggesting a possible therapeutic effect of an excimer laser treatment in keratoconus. Guedj et al. [7] treated 62 eyes of 42 patients with suspected keratoconus with PRK and found a significant improvement in visual acuity, which remained stable during a follow-up period of up to 5 years. Chelala et al. [10] also reported that in mild to moderate keratoconus PRK is a safe and effective procedure for improving uncorrected vision in patients with small refractive errors. In contrast, Kasparova and Kasparov [11] reported progression of keratoconus in 8.6% eyes in the first sixth months after surgery. Koller et al. [12] suggested corneal topography monitoring for up to 5 years to be sure that a PRK procedure does not induce keratoconus progression in corneas documented to be pre-operatively stable for years. In fact, corneal ectasia can occur even a decade after PRK [13]. Furthermore, in comparison with PRK, ICRS has the advantage of being a reversible procedure in mild to moderate keratoconus. Still, the very long-term stability of the procedure remains unknown [14].

In the current case series, all eyes had manifest keratoconus and were treated without adjunctive therapies such as collagen cross-linking, which had not been introduced into clinical use at the time of treatment of most of these eyes. We evaluated topography-based PRK, which was intended to reduce myopia and astigmatism and improve uncorrected and best-corrected visual acuity.

In the present study, keratoconus progression at a median of 7 years (range 3–10) after PRK is reported. Significant visual improvement was obtained in 84% of patients who were available for the late follow-up, and progression could not be observed in 79% of these patients. The overall risk of progression in our cohort was 6 out of 24 eyes (25%). We also observed that 3 patients who showed keratoconus progression had a median age of around 47 at the time of PRK. It is very rare to see progression at this high age, so performing a PRK procedure, which leads to further thinning of the cornea, could be an initiating factor for progression of the disease in elderly patients.

As all of these 23 patients were initially referred for corneal transplantation, the study may indicate that 4 out of 5 patients with contact lens intolerance and mild or moderate keratoconus may avoid transplantation by performing a PRK procedure. In addition, at least 3 out of 5 patients were satisfied with the procedure at the long-term follow-up.

In conclusion, although keratoconus is generally thought to be an absolute contraindication for PRK, our results indicate that topography-guided PRK may be a viable option for reducing myopia or astigmatism and improving visual acuity in selected keratoconus eyes. The present study found limited keratoconus progression after PRK.

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Statement of Ethics

The study complied with the Declaration of Helsinki, and all participants signed a written informed consent form before participation. The Central Denmark Region Committees on Health Research Ethics classified the study as a quality control study, which does not require formal ethics approval according to Danish law.

Disclosure Statement

The authors have no financial disclosures.

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Table 1. Pre- and postoperative parameters in individual patient

	Gender, age, years	Preoperative data				Postoperative data (3 months)				Postoperative data (median 7 years)			
		CDVA, decimal	Refraction, dpt	Kmax, dpt	CCT, μ m	CDVA, decimal	Refraction, dpt	Kmax, dpt	CCT, μ m	CDVA, decimal	Refraction, dpt	Kmax, dpt	CCT, μ m
1	M, 51	0.2	–3.00 –3.00 $\times$ 100	53.1	470	0.32	–1.00 –5.00 $\times$ 100	53.1	480	0.32	0.50 –3.75 $\times$ 90	49.7	373
2	M, 60	0.4	–5.0 –4.5 $\times$ 80	57.89	410	0.5	–3.0 $\times$ 80	No data	No data	0.5	+1.25 –2.75 $\times$ 69	48.2	344
3	F, 30	0.32 (LE)	–6.75 –3.75 $\times$ 165	49.85	440	0.8	–1.5 –3.0 $\times$ 30	47.73	390	ALK after 7 months 0.8	–3.0 –3.0 $\times$ 67	47.73	500
		0.4 (RE)	–1.5 –0.75 $\times$ 25	45.73	460	0.8	–3.0 $\times$ 60	46.68	400				
4	M, 51	0.63 (LE)	–7.0 –6.5 $\times$ 170	52.81	490	0.63 Retr.	–3.5 –2.0 $\times$ 166	47.87	378	0.8	–1.0 –2.0 $\times$ 163	47.9	401
		0.8 (RE)	–2.5 –7.5 $\times$ 5	49.34	490	0.80	+1.0 –4.5 $\times$ 10	52.24	490	0.63	–1.0 –3.0 $\times$ 3	47.5	458
5	M, 50	0.32	–9.5 –1.75 $\times$ 135	55.87	460	0.4	–0.5 –2.5 $\times$ 125	51.36	440	0.5	–1.5 cyl $\times$ 170	51.21	337
6	F, 36	0.5 (RE)	–3.75 –7.25 $\times$ 20	50.82	470	0.8	–2.5	49.92	420	0.8	–1.0 –0.5 $\times$ 75	46.48	433
		0.32 (LE)	–6.5 –4.5 $\times$ 170	52.00	470	0.5 sc	No data	No data	No data	0.8	–1.0 –0.5 $\times$ 77	47.48	421
7	M, 36	0.3	–2.0 –3.0 $\times$ 0	51.92	580	–	–	No data	–	0.4 hard CL	–	No data	520
8	M, 47	0.3	–5.0 –5.0 $\times$ 130	51.52	510	0.4	–0.5 –2.0 $\times$ 120	47.46	430	Absent			
9	M, 36	0.3	–10.0 –4.5 $\times$ 120	No data	No data	0.5	–2.75 –5.0 $\times$ 100	51.21	440	0.67	4.0 –4.0 $\times$ 60	53.65	423
10	F, 57	0.1	–3.75 –6.0 $\times$ 66	52.48	520	0.2	–10.0	53.82	450	0.05(due to cataract)	4.0 –4.0 $\times$ 60	55.97	423
11	M, 28	0.32	+3.5 –1.75 $\times$ 75	46.29	450	0.4	–4.5 $\times$ 156	48.28	430	0.5	+3.25 –2.5 $\times$ 90	56.62	398 ^a
12	M, 42	0.8	–2.0 –4.25 $\times$ 80	46.29	510	0.8	–3.75 –1.92 $\times$ 22	45.54	480	1.0	–3.0 –1.5 $\times$ 40	45.24	460
13	M, 39	0.25 (RE)	+3.0 –3.5 $\times$ 90	45.79	540	0.8	+2.25 –1.25 $\times$ 115	45.42	495	0.32	+3.0 –4.0 $\times$ 105	46.38	414
		0.4 (LE)	–0.5 –5.5 $\times$ 16	49.12	530	0.8	+2.0 –2.5 $\times$ 162	45.42	444	0.8	+1.0 –3.0 $\times$ 155	47.66	480
14	M, 21	0.1	–8.75 –5.75 $\times$ 17	53.23	430	0.5	–6.0 –5.0 $\times$ 150	50.90	410	Absent			
15	M, 24	0.3	–4.5 –8.5 $\times$ 125	54.26	510	0.8 Retr.	–6.0 –4.0 $\times$ 125	50.82	490	0.8	–3.75 –6.0 $\times$ 105	49.12	440
16	F, 29	0.6	–2.25 –3.0 $\times$ 59	51.44	470	1.0	–3.5 –2.0 $\times$ 5	47.80	470	1.0	–3.25 –2.5 $\times$ 27	46.87	470
17	M, 24	0.3	–7.0 –6.0 $\times$ 59	52.57	456	0.4	–6.25 –7.0 $\times$ 150	52.98	408	0.5	–3.25 –7.0 $\times$ 165	50.44	411
18	M, 51	0.1 (RE)	–1.0 –1.25 $\times$ 90	48.98	500	0.6	–2.25 –0.5 $\times$ 160	47.46	461	Absent	–	–	–
		0.16 (LE)	–0.5 –2.0 $\times$ 85	48.28	490	0.4	–0.5 –5.75 $\times$ 18	47.07	429	Absent			
19	M, 51	0.32	–9.75 –3.25 $\times$ 90	46.42	440	0.4	–9.25 sph	44.46	410	PK after 10 months			
20	F, 47	0.5	–5.5 –2.5 $\times$ 38	55.1	474	0.4	–2.5 –2.5 $\times$ 10	54.70	428	DALK after 3 months			
21	F, 48	0.4	–7.0 –5.0 $\times$ 145	51.92	480	0.63 Retr.	+0.75 –3.5 $\times$ 100	50.67	337	0.1	–0.25 –5.0 $\times$ 120	68.5	283 ^b
22	M, 36	0.8	–3.0 $\times$ 110	44.29	422	0.8	–3.25 $\times$ 130	45.18	383	0.8	+1.25 –2.5 $\times$ 115	44.76	380
23	F, 30	0.2	–1.0 –4.0 $\times$ 130	50.22	470	0.2	–2.0 –5.0 $\times$ 90	46.48	440	PK after 11 months			

^a Planned ICRS. ^b Planned PK progression and planned PK. LE = Left eye; RE = right eye; Retr. = retreated; sph = sphere; ALK = anterior lamellar keratoplasty; DALK= deep anterior lamellar keratoplasty; CL = contact lens; PK = penetrating keratoplasty.

Table 2. Changes in visual acuity and refraction

	Preoperative	3-month follow-up	Late follow-up
CDVA, logMAR	0.49 $\pm$ 0.27	0.27 $\pm$ 0.18	0.24 $\pm$ 0.28
SE refraction, dpt	6.2 $\pm$ 3.7	3.7 $\pm$ 3.1	2.1 $\pm$ 2.8
Refractive cylinder, dpt	–4.2 $\pm$ 1.9	–3.0 $\pm$ 1.8	–3.0 $\pm$ 1.7

Fig. 1. Flow diagram showing the total number of keratoconus patients treated with PRK and the number of patients available for the 3-month and long-term follow-up.

Fig. 2. **a** CDVA (logMAR) before as well as 3 months and several years (long-term) after topography-guided PRK for keratoconus. **b** Preoperative and postoperative SE refraction (D). **c** Preoperative and postoperative cylinder (D). Open circles = 3-month follow-up; closed circles = long-term follow-up.

Fig. 3. **a** CCT (μm) before as well as 3 months and several years (long-term) after topography-guided PRK for keratoconus. **b** Preoperative and postoperative Kmax (D) over the follow-up period. Closed circles = 3-month follow-up; open circles = long-term follow-up.