

Incidence and quantification of corneal haze by Pentacam Scheimpflug densitometry following photorefractive keratectomy for myopia in virgin and post corneal transplant eyes with dark irides

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Abstract:

PURPOSE: To assess the incidence and quantification of corneal haze after myopic photorefractive keratectomy in virgin and post corneal transplant eyes with dark irides.

METHODS: In this retrospective study at the tertiary eye hospital, the corneal haze was evaluated by slit-lamp and quantified by Pentacam Scheimpflug densitometry after myopic photorefractive keratectomy with mitomycin C in virgin eyes (group I) and post corneal transplant eyes (group II) with dark irides over 12 months.

RESULTS: Group I comprised 126 eyes from 77 patients (35 males and 42 females) aged 31.31 years (24.11–36.18 years), and group II comprised 44 eyes from 33 patients (18 males and 15 females) aged of 32.25 years (26.15–36.66 years). The incidence of corneal haze was 9.5% (95%CI: 5.0%–16%) and 6.8% (95%CI: 1.4–18.7%) in group I and II respectively ($P = 0.587$). The corneal densitometry was 22.69 ± 8.28 GSU preoperatively and 17.98 ± 3.13 GSU at 12 months postoperatively ($P = 0.010$) in group I. The corneal densitometry was 21.86 ± 6.22 GSU preoperatively and 21.23 ± 4.29 GSU at 12 months postoperatively ($P = 0.815$) in group II. High corneal maximal densitometry was associated with the thin central corneal thickness ($P = 0.027$), the presence of haze ($P = 0.028$), post-keratoplasty ($P = 0.004$), steep keratometry ($P = 0.035$).

CONCLUSION: The incidence of corneal haze was comparable in virgin and post corneal transplant eyes. The Pentacam Scheimpflug densitometry can be helpful in the diagnosis of corneal haze; however, the cutoff values need to be studied further in larger studies.

Keywords:

Corneal haze, corneal transplant, myopia, photorefractive keratectomy, scheimpflug system

INTRODUCTION

Loss of corneal clarity after photorefractive keratectomy (PRK) due to corneal haze can lead to problems like loss of vision, regression and irregular astigmatism. Corneal haze is a more common complication after PRK compared to laser in situ keratomileusis (LASIK) and laser epithelial keratomileusis (LASEK).^[1,2] Corneal haze occurs due to abnormal deposition of collagen and decreased corneal refractivity. Most of the time corneal haze is clinically insignificant;

however, on the contrary, it may require a corneal transplant for vision rehabilitation.^[12,19]

Corneal haze could be assessed qualitatively using slit-lamp biomicroscope, confocal microscopy and anterior segment optical coherence tomography and quantitatively using Scheimpflug photography.^[3,4] In this study we analyze the incidence of post-PRK haze in a large population with a myopic refractive error of over -4.00 D. We collected similar data for post corneal transplant patients that underwent myopic PRK. Scheimpflug images were used to quantify the change in optical density after PRK in the two groups.

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METHODS

This retrospective study was conducted at the tertiary eye hospital. Patients with no previous eye surgery and patients that had previously undergone penetrating keratoplasty (PKP) or deep anterior lamellar keratoplasty (DALK) between November 2013 and May 2017 were included in the study. Patients were divided into two groups. In the first group (group I) patients who underwent PRK and no history of previous eye surgery were included. In the second group (group II) post-keratoplasty patients who underwent PRK for the correction of post-graft refractive error after complete suture removal were included. The study was performed by adhering to the Declaration of Helinski.

Patients

Data were collected on age at surgery, gender, operated eye, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), keratometry, central corneal thickness, refraction, corneal maximal densitometry preoperatively and 1, 3, 6, and 12 months postoperatively. The safety index was calculated as the postoperative BCVA acuity divided by the preoperative BCVA. The efficacy index was calculated as the postoperative UCVA divided by the preoperative BCVA. Surgically induced refractive change that is achieved refraction was calculated using the Holladay method.^[5,6] The preoperative refraction was considered the planned refraction. Then spherical and astigmatic corrections were determined.

Scheimpflug camera system

All examinations were performed with the Pentacam-HR system. The Pentacam-HR is a high-resolution rotating Scheimpflug camera system for anterior segment analysis. Pentacam sends a slit of light along the patient's line of sight, which is then observed by the Scheimpflug camera under an angle of approximately 45 degrees.^[7] It provides crisp images of cornea, iris and crystalline lens. It measures the anterior and posterior corneal topography and elevation, total corneal refractive power, corneal power distribution, chamber angle measurement in 360°, chamber depth and volume, corneal and crystalline lens densitometry. The same measurement procedure was used in all cases. The patient was asked to blink twice and then look at the fixation light prior to each measurement. The examiner adjusted the joystick until achieving perfect alignment. The automatic release mode of the Pentacam was employed to reduce operator-dependent variables. All scans were centered on the pupil center. The densitometry measurement is standardized from 0 to 100 grayscale units (GSU), defining a minimum light scatter of 0 (maximum transparency) and a maximum light scatters of 100 (minimum transparency). Preoperatively and 1, 3, 6, 12 months postoperative corneal maximal densitometry measurements were recorded.

Surgical technique

A standard surgical technique was used to perform PRK surgery. All surgeries were performed under topical anesthesia. The wavelight excimer laser (Optical Zone was

set at 6.5 mm and depth was variable, depending on the refractive error, approx. 14 microns per diopter) was used to treat all the patients. After informed consent was obtained, the operative eye was prepped and draped in a sterile ophthalmological manner. A lid speculum was used to open the eyelids. Cyclotorsional alignment was obtained prior to the procedure. An 8 mm circular microsponge was soaked in 30% alcohol and placed on the cornea for 30 seconds. The eye was irrigated thoroughly with a balanced salt solution (BSS) to wash out any residual alcohol. The loosened epithelium was then removed with weck cel sponges. The excimer treatment was performed according to the individual refractive error. Another 8 mm circular microsponge soaked in 0.02% Mitomycin C (MMC) was placed over the cornea for 30 seconds in normal corneas and 45 seconds in corneal transplants. The eye was then immediately washed with BSS to remove any residual MMC from the eye. A bandage contact lens was then placed over the cornea. A steroid and antibiotic eye drops (Moxifloxacin 0.05% and prednisolone 1%) were then used in the operative eye. Preservative-free artificial tears were also prescribed for all the patients. All patients were given written post-op instructions after the procedure.

Post-operative care

All patients were seen one day after the procedure in the eye clinic. The patients were seen again in 1 week. The contact lens was removed and complete epithelial healing was ensured. When the epithelium was completely healed, the antibiotic was stopped and the steroid eye drops were tapered over the next three weeks by decreasing the frequency of the eye drops every week. All patients were instructed to use frequent preservative-free artificial tears. These patients were then seen again at 1 month, 3 months, 6 months and then at 1 year. Serial post-op-refractions and scheimpflug images were obtained at these appointments. Any presence of haze noted on slit lamp exam was documented. Post-PRK haze was staged according to the stages of post-PRK corneal haze described by Fantes *et al.* [Table 1].

Statistical tests

Statistical tests were performed using SPSS software (version 22.0, SPSS, Inc.). Corneal maximal densitometry values were compared using the Student t-test. Linear regression was performed to evaluate the effect of various factors on corneal maximal densitometry. A p-value less than 0.5 was considered statistically significant.

Table 1: Corneal haze stages according to Fantes *et al.*

Stage	Description
0	No haze, completely clear cornea
0.5	Trace haze seen with careful oblique illumination
1	Haze not interfering with the visibility of fine details of the iris
2	Mild obstruction of iris details
3	Moderate obstruction of the iris and lens
4	Complete opacification of the stroma in the area of the scar, anterior chamber is totally obscured

RESULTS

Data were collected from patients who had myopic PRK between 2013 and 2017. Group I comprised 126 eyes from 77 patients (35 males and 42 females) with a median age of 31.31 years (24.11–36.18 years), and group II comprised 44 eyes from 33 patients (18 males and 15 females) with a median age of 32.25 years (26.15–36.66 years).

The PRK improved visual acuity, decreased myopia, reduced astigmatism, flattened keratometry, and reduced corneal thickness in both study groups. Table 2 summarizes preoperative and postoperative refractive and topographic parameters in groups I and II. The safety index of PRK was 1.00 (0.90–1.29) and 1.00 (0.97–1.13) in groups I and II respectively; the efficacy index for PRK was 0.67 (0.48–1.00) and 0.89 (0.63–1.00) in groups I and II respectively. The spherical correction was 91% (61–105) and 50% (16–93%) in group I and group II respectively ($P = 0.002$). The cylindrical correction was 116% (100–161%) and 87% (52–126%) in group I and group II respectively ($P < 0.001$). This is because PRK was performed in group II (post-keratoplasty eyes) to reduce mainly astigmatism.

The incidence of corneal haze measured subjectively by slit-lamp was 9.5% (95%CI: 5.0–16%) and 6.8% (95%CI: 1.4–18.7%) in group I and II respectively ($P = 0.587$). The corneal maximal densitometry was high in the presence of haze [Table 3]. The incidence of corneal haze was positively associated with the presence of dryness (Spearman’s rho = 0.204, $P = 0.008$).

The mean and variance of corneal maximal densitometry decreased after PRK; this decrease was more in group I compared to group II [Table 4 and Figure 1]. The corneal densitometry

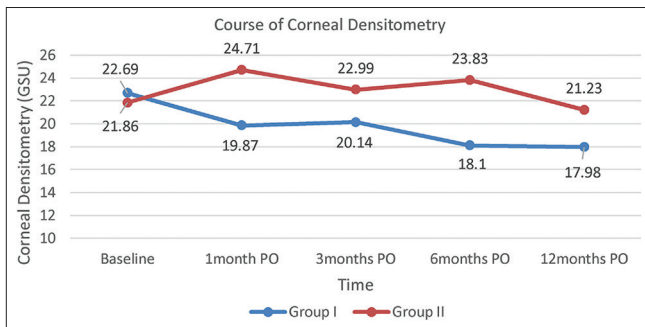


Figure 1: Course of corneal densitometry over time in the group I and II

was 22.69 ± 8.28 GSU preoperatively and 17.98 ± 3.13 GSU at 12 months postoperatively ($P = 0.010$) in group I. The corneal densitometry was 21.86 ± 6.22 GSU preoperatively and 21.23 ± 4.29 GSU at 12 months postoperatively ($P = 0.815$) in group II. High corneal maximal densitometry was associated with the thin central corneal thickness ($P = 0.027$), the presence of haze ($P = 0.028$), post-keratoplasty ($P = 0.004$), steep keratometry ($P = 0.035$).

In order to find the cutoff value of corneal maximal densitometry that indicates the presence or absence of haze, the receiver operating characteristic (ROC) curves were constructed [Figure 2]. The corneal densitometry curve with an area under the curve of 0.663 ($P = 0.063$) lies close to the diagonal line indicating that corneal maximal densitometry is fair at discriminating between the presence and absence of haze. The cutoff value by the ROC curves is 17.95GSU with 92% of sensitivity and 45% of specificity. Hence, corneal densitometry value lower than the cutoff value rules out the presence of haze; but densitometry value higher than the cut-off value rule in the presence of haze. With the above sensitivity and specificity, corneal densitometry is suitable for screening for but not diagnosing haze.

DISCUSSION

In this study, the presence of corneal haze eyes after PRK was evaluated with slit-lamp and measured with densitometry

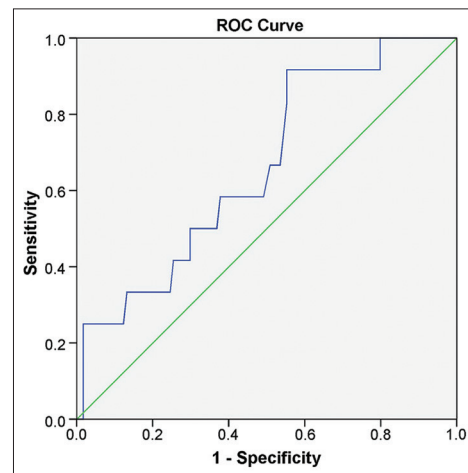


Figure 2: Receiver Operating Characteristic curve for corneal densitometry

Table 2: Preoperative and postoperative refractive and topographic parameters in group I and II

Parameter	Group I				Group II			
	Preoperative		Postoperative		Preoperative		Postoperative	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
UCVA (LogMAR)	0.56	0.4	0.21	0.2	0.58	0.3	0.42	0.3
BCVA (LogMAR)	0.11	0.2	0.1	0.1	0.23	0.2	0.21	0.2
Spherical Equivalent (D)	-4.12	2.6	-0.75	1.2	-3.79	2.8	-1.95	3.1
Average Keratometry (D)	43.3	2.2	40.6	2.8	45.6	3.2	43.9	3.2
Refractive Cylinder (D)	-1.77	1.4	-0.84	0.7	-3.34	1.4	-2.07	1.3
Corneal Astigmatism (D)	1.82	1.7	1.24	1.1	4.73	2.8	3.23	2.1
Corneal Thickness (mm)	527	41	456	59	535	65	459	73

SD, standard deviation; UCVA, uncorrected visual acuity; BCVA, best corrected visual acuity

Table 3: Corneal densitometry in presence of haze in groups I and II

Group	Haze		P	n (Present/Absent)
	Present	Absent		
Corneal Densitometry				
I	29.17±2.05	22.76±8.37	0.039	12/114
II	21.22±3.55	19.22±3.60	0.204	Mar-41

Table 4: Corneal densitometry over time in groups I and II

Time	Corneal Densitometry			
	Group I		Group II	
	Mean	SD	Mean	SD
Preoperative	22.7	8.3	21.9	6.22
1 month PO	19.9	3.8	24.7	12.2
3 months PO	20.1	3	23	7.48
6 months PO	18.1	4	23.8	5.16
12 months PO	18	3.1	21.2	4.29

PO, postoperative; SD, standard deviation

function of Pentacam Scheimflug System in virgin myopic eyes and eyes that had a corneal transplant. Corneal densitometry values in myopic patients without previous eye surgery was 22.69 ± 8.28 GSU and 21.86 ± 6.22 GSU in patients that underwent corneal grafting. These values decreased to 17.98 ± 3.13 GSU and 21.23 ± 4.29 GSU respectively at 12 months. We found higher preoperative densitometry values in the first group which could be explained by the loss of Bowman layer and anterior stroma as a result of PRK. This finding was studied and explained well by Rosema *et al.*^[7,17]

Corneal haze had been a significant complication of PRK procedure; however, with the use of Mitomycin C, the occurrence of post-PRK haze has reduced significantly.^[9-12] On the contrary, Hofmeister *et al.* suggested that Mitomycin-C may not be needed to prevent haze after modern PRK with a 4-month steroid taper as there was no clinically significant difference in haze formation between MMC eyes and control eyes.^[24] In our study population, the incidence of clinical haze was 9.5% in group 1 and 6.8% in group 2. This haze was comparable between the two groups and the maximum degree of haze was grade 2 as measured by the clinical grading system described by Fantes *et al.* We did not see any increased incidence of post-PRK haze in the keratoplasty group as compared to the virgin eyes group. As to the course of corneal haze, Lee *et al.* reported that corneal haze increased significantly after surgery, peaked at 3 months, and then decreased at 6 months.^[10] Alternately, Lipshitz reported that late-onset corneal haze had occurred in 18 eyes of 17 patients (incidence, 1.8%), appearing 4 to 12 months after PRK and resulting in decreased visual acuity and regression.^[11] As to the distribution of haze, Maldonado reported that corneal haze appeared fairly uniformly distributed within the ablation zone, but a more heterogeneous distribution was found with a longer follow-up time. Furthermore, later postoperative examinations disclosed a clear trend toward diminishing central opacification relative to peripheral regions over the entrance pupil.^[12]

After PRK, the early-onset corneal haze has been found associated with high myopia, astigmatism, and brown irides when late-onset corneal haze associated with ultraviolet radiation.^[8,22,23] However, it has been found that older age was a protective factor against the development of corneal haze after PRK.^[22] Myopia and astigmatism were associated with increased severity of haze, and older age was protective against early corneal haze development after PRK in an Asian population.^[22] Preoperative astigmatism was significantly associated with the development of corneal haze after conventional PRK without MMC. We used Mitomycin C in all patients irrespective of the magnitude of the correction. Our study comprised of Saudi population in the eastern region. 100% of our patients had brown irides. The indoor lifestyle most likely decreased the effect of ultraviolet irradiation in causing corneal haze in our study population. Previously, Tabbara *et al.* reported an incidence of the corneal haze of 28.9% in brown eyes and 5% in blue eyes.^[8]

In our study, we found that high maximal corneal densitometry was associated with the presence of haze, thin steep corneas, and after keratoplasty. Maldonado *et al.* correlated degree of haze with maximal corneal densitometry. Mean differences between scarred and clear areas for haze grade 0.5, 1.0, 2.0, 3.0, and 4.0 were 16.9, 26.6, 42.6, 60.4, and 76.4 gray levels, respectively ($r = 0.96$; $P < 0.001$).^[12] Boulze-Pankert *et al.* found a mild increase of 2GSU in maximal densitometry in presence of 0.5 haze.^[17] Kim *et al.* who found that thin corneas were associated with higher densitometry.^[15]

Corneal densitometry program of pentacam provides a good objective measurement of corneal haze;^[16] however it's specificity is only 45% in our study. Corneal densitometry value higher than the cutoff value rule in the presence of haze; but densitometry value lower than the cutoff value does not rule out the presence of haze reliably. When densitometry was divided by radial zone, densitometry values were lowest in the central zone and highest in the periphery. When divided by depth, the anterior layer displayed the highest densitometry reading.^[13] Lopes *et al.* reported that the densitometry map reveals that light backscatter was higher in the central portion of the anterior keratoconic cornea than in the normal cornea.^[14]

Evaluation of haze by slit-lamp and maximal corneal densitometry have other applications. Pahuja *et al.* suggested consequent to the low repeatability in post-corneal crosslinking eyes, densitometry should be used with caution to gauge the response to treatment and visual outcomes in treated keratoconus eyes.^[18] Nonetheless, the haze after corneal crosslinking is different from that after PRK. The former is a dust-like change in the corneal stroma or a mid stromal demarcation line, whereas the latter has a more reticulated subepithelial appearance.^[19] Chan *et al.* reported that thinning of the cornea was seen only when the haze was detectable after cross-linking.^[20] Otri *et al.* concluded that maximal corneal densitometry can be used as an objective measure of the corneal response to infection and to monitor response to therapy.^[21]

One limitation of our study was that densitometry was measured over a 4.0 mm central image of the cornea and along only 1 meridian. This study contribution was that maximal corneal densitometry was reduced after PRK and was associated with thin steep corneas.

In conclusion, densitometry function of Pentacam Scheimpflug System can be helpful in the diagnosis of corneal haze; however, the cutoff values need to be studied further in larger studies.

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Conflicts of interest

There are no conflicts of interest.

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