

Evaluation of corneal biomechanical properties following penetrating keratoplasty using ocular response analyzer

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Purpose: To evaluate corneal biomechanical properties in eyes that has undergone penetrating keratoplasty (PK). **Materials and Methods:** Retrospective observational study in a tertiary care centre. Data recorded included ocular response analyzer (ORA) values of normal and post-keratoplasty eyes [corneal hysteresis (CH), corneal resistance factor (CRF), Goldmann-correlated intraocular pressure (IOPg), and cornea-compensated intraocular pressure (IOPcc)], corneal topography, and central corneal thickness (CCT). Wilcoxon signed rank test was used to analyze the difference in ORA parameter between post-PK eyes and normal eyes. Correlation between parameters was evaluated with Spearman's rho correlation. **Results:** The ORA study of 100 eyes of 50 normal subjects and 54 post-keratoplasty eyes of 51 patients showed CH of 8.340 ± 1.85 and 9.923 ± 1.558 , CRF of 8.846 ± 2.39 and 9.577 ± 1.631 in post-PK eyes and normal eyes, respectively. CH and CRF did not correlate with post-keratoplasty astigmatism ($P = 0.311$ and 0.276 , respectively) while a significant correlation was observed with IOPg ($P = 0.004$) and IOPcc ($P < 0.001$). **Conclusion:** Biomechanical profiles were significantly decreased in post-keratoplasty eyes with significant correlation with higher IOP as compared with that in normal eyes.

Key words: Corneal biomechanics, corneal hysteresis, corneal resistance factor, intraocular pressure, keratoplasty, ocular response analyser

Corneal hysteresis (CH) characterizes the viscoelastic property of the cornea, which is expressed as a measure of its stiffness or rigidity.^[1] It is an indication of the viscous damping in the cornea and reflects the capacity of the tissue to absorb and dissipate energy.^[2,3] The electro-optical collimation detector system of the ocular response analyzer (ORA) monitors the corneal curvature in the central 3.0-mm diameter throughout the 20-millisecond applanation measurement of a precisely delivered metered air pulse. This air pulse effects an inward corneal movement (first applanation event) causing a corneal concavity. When the air pulse is shut down, the pressure applied to the eye decreases, affecting return of the cornea from concavity (second applanation event) to its normal convex curvature. The information obtained from these applanating events is depicted in graphic form with two well-defined peaks of pressure corresponding to inward and outward applanation events (peak 1: While the cornea is moving inward, p1, and peak 2: As the cornea returns from its concavity, it passes through another state of applanation, p2). CH is the difference between these two pressures peaks.^[1] The ORA also measures the Goldmann-correlated intraocular pressure (IOPg), cornea-compensated IOP (IOPcc), and corneal resistance factor (CRF). IOPg is the average of the P1 and P2 applanation pressures, while IOPcc represents the IOP that has been compensated for the corneal biomechanical properties.^[2] CRF is more strongly associated with central corneal thickness (CCT) than CH and is derived from the following formula:

$$\text{CRF} = \text{P1} - k \text{P2}$$

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Where, k is an empirically determined constant.^[2]

The normal corneal stroma comprises of lamellae of liquid crystal-like arranged proteoglycan-coated collagen fibrils. Biomechanical properties of the cornea are attributed to the regular orthogonal arrangement of these lamellae, which, in diseases like keratoconus, is significantly altered resulting in corneal weakness.^[4,5] Preliminary clinical studies have reported reduced hysteresis in the presence of corneal pathology, such as keratoconus, Fuchs dystrophy, and in conditions such as primary open-angle glaucoma and normal tension glaucoma.^[1]

The relevance of the corneal biomechanical parameters (CH and CRF) and its relationship with other parameters such as the Young's modulus of the cornea or the ocular rigidity is yet to be completely understood.^[6] Not much is known about the biomechanical properties of the cornea in eyes with altered ocular rigidity as in those which have undergone corneal grafting. The purpose of this study was to evaluate the corneal biomechanical properties in Indian eyes that have undergone penetrating keratoplasty (PK) using ORA.

Materials and Methods

Retrospective observational study of the ORA recordings of 154 eyes of 101 patients (54 eyes of 51 patients that had undergone PK and 100 eyes of 50 normal subjects as controls) was conducted. Informed consent was obtained from all participants. Eyes with active infection, intraocular inflammation, history of graft rejection or other intraocular surgeries, and ocular surface disorders were not included. ORA (Reichert Ophthalmic Instruments, Buffalo, NY, USA) recordings were performed by a single observer (MK) according to a standard protocol.^[7] Recordings were done to obtain four consecutive readings in each eye, with only the good quality measurement with two distinct peaks being included. The mean of the four measurements was used for statistical analysis. CH,

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CRF, IOPg, and IOPcc in both post-keratoplasty and normal eyes were noted. CCT was measured with ORA attached hand held ultrasonic pachymeter. Other parameters recorded included age, gender, laterality, visual, acuity, follow-up period, and topographic astigmatism (Atlas corneal topography system, Carl Zeiss). Data was entered into Excel spreadsheet, and all statistical analyses were performed with SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). The Wilcoxon signed-rank test was used to analyze the difference in each ORA parameter between the post-PK eyes and the normal eyes. Correlation between parameters was evaluated with Spearman's rho correlation and *P* value < 0.05 was considered statistically significant.

Results

The ORA graphs of 54 eyes of 51 patients of mean age 40.92 ± 18.11 years [age range: 10-73 years, males 34 (66%), females 17 (34%)] who had undergone PK with a mean follow-up period of 19.33 ± 6.42 months were evaluated. A total of 100 eyes of 50 normal subjects of mean age 36.83 ± 15.86 years [age range: 10-73 years, males 30 (60%), females 20 (40%)] without any ocular complaints was taken as controls. Demographic data of the patients is summarized in Table 1. All eyes with corneal grafting had undergone conventional PK with 16 interrupted sutures. The mean topographic astigmatism of the post-keratoplasty eyes was 8.73 ± 5.61 D, while that of the normal eyes was 0.615 D ± 0.308 D. The mean CH, CRF, IOPg, IOPcc, and CCT of the post-keratoplasty eyes and normal eyes are provided in Table 2. The CH values showed a statistically significant lower value in post-keratoplasty eyes (8.340 ± 1.85 mmHg) compared to that in normal eyes (9.923 ± 1.558 mmHg in the normal eyes; *P* < 0.0001). IOPg and IOPcc were significantly higher in eyes that had corneal grafting compared to those in normal eyes (IOPg: 15.996 ± 8.09 mmHg in the post-PK eyes and 14.104 ± 3.974 mmHg in the controls, *P* = 0.0076; IOPcc: 18.625 ± 7.97 mmHg in the post-PK eyes and 15.276 ± 4.164 mmHg in the control eyes, *P* = 0.011). CRF was lower in the post-keratoplasty eyes than in the normal eyes (8.846 ± 2.39 mmHg in the post-PK eyes versus 9.577 ± 1.631 mmHg in the normal eyes; *P* = 0.0646) and CCT was 516.29 µm ± 37.4 µm in post-keratoplasty and 530.50 ± 15.020 µm

in controls, *P* = 0.0118).

Of the 54 eyes that had undergone keratoplasty, sutures had been removed in 24 eyes, while sutures were retained in 30 eyes. The CH values of post-PK eyes without sutures and with sutures were 7.91 and 8.14 mmHg (*P* = 0.417), respectively. The CRF values of post-PK eyes without sutures and with sutures was 8.77 and 8.996 mmHg (*P* = 0.628), respectively.

No correlation was observed with the post-keratoplasty CH and CRF values with CCT (*P* = 0.580 and 0.939, respectively) [Figs. 1 and 2] and post-keratoplasty astigmatism (*P* = 0.311 and 0.276, respectively [Figs. 3 and 4] in both the groups. No significant correlation of CCT with IOPg and IOPcc [Figs. 5 and 6] was observed in the post-keratoplasty eyes.

The mean (CH – CRF) values in the post-keratoplasty eyes was -0.505 ± 2.609 mmHg, while that in the normal eyes was 0.346 ± 1.291 mmHg (*P* = 1.30). The (CH – CRF) values show good correlation with IOPg and IOPcc in both the normal and post-keratoplasty eyes [Figs. 7 and 8].

Discussion

The Reichert ocular response analyzer device enables non-invasive measurements of biochemical properties of the cornea.^[1] Several studies evaluated the corneal biomechanics factors in various ocular conditions and in following intraocular surgical procedures.^[8-18]

Despite the fact that our current understanding of the use of ORA to study the corneal viscoelastic properties in eyes that had undergone PK is still evolving, recent studies^[13] seem to provide an enhanced understanding of the influence of the various factors on transcorneal IOP measurements in these eyes.

Early accurate estimation of raised IOP in post-PK eyes is imperative to maintain the optimal function of the optic nerve and the corneal graft. It has now come to our knowledge that perhaps the role of CCT in IOP evaluations in post-PK eyes is not very convincing because of the possible effect of the lower elastic modulus of the cornea in these eyes.^[13] CH and CRF have a higher impact on IOP measurements in these eyes to a larger extent. Goldman applanation tonometry measurements have been found to be lower than IOP measurement with other tonometer techniques, revealing that the Goldman applanation tonometry may perhaps underestimate true IOP values in post-PK eyes. Fabian *et al.* studied 61 post-PK eyes with a mean follow-up of 65 months (age range: 6-206 months) and found that Goldmann applanation tonometry pressure was lesser than that with tonopen and ORA evaluation. They concluded that, within the confines of the not having used intracameral manometry estimation for IOP, CH, and CRF may have more influential role than CCT in IOP evaluations in post-PK eyes

Table 1: Demographic details of post keratoplasty and normal eyes

	Post PK eyes	Normal
No of eyes	54 eyes	100 eyes
Mean age	40.92±18.11 (10-73 years)	36.83±15.86 years (12-69 years)
Male:female	34:17	30:20
Astigmatism (D)	8.73±5.61D	0.615±0.308 D
Mean follow-up	19.33±6.42 months	-

PK: Penetrating keratoplasty

Table 2: Corneal biomechanical properties in post keratoplasty and normal eyes

	CH (mm Hg)	CRF (mm Hg)	IOPg (mm Hg)	IOPcc (mm Hg)	CCT (µm)
PostPK eyes	8.340 ± 1.85	8.846 ± 2.39	15.996 ± 8.09	18.625 ± 7.97	516.29 ± 37.44
Normal eyes	9.923 ± 1.558	9.577 ± 1.631	14.104 ± 3.974	15.276 ± 4.164	530.50 ± 15.020
p - value	< 0.0001	0.0646	0.0076	0.011	0.0118

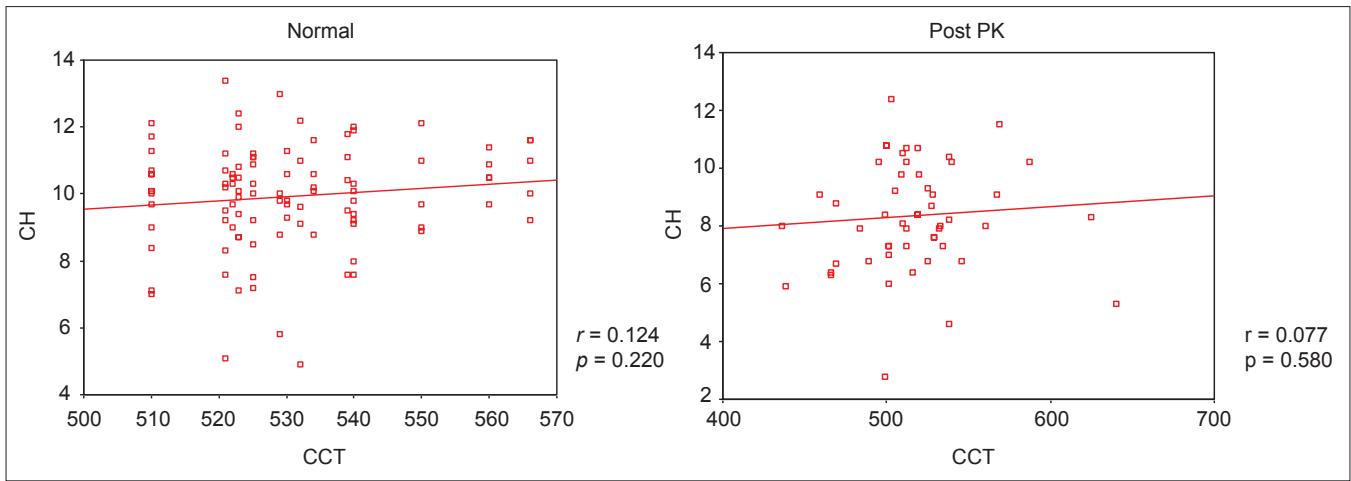


Figure 1: Correlation between CH and CCT in post PK and normal eyes

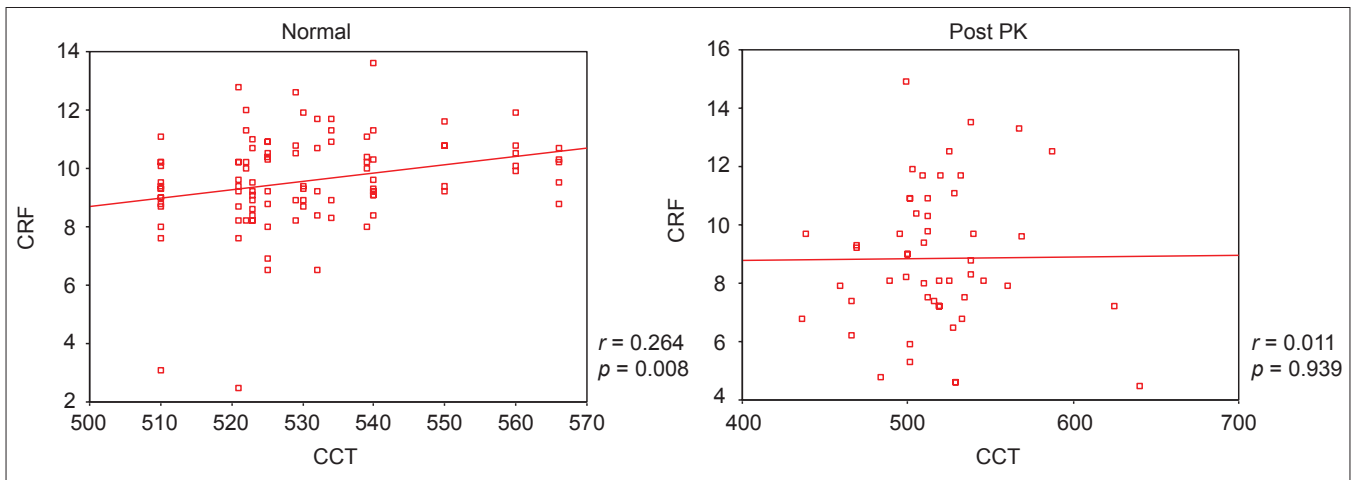


Figure 2: Correlation between CRF and CCT is post PK and normal eyes

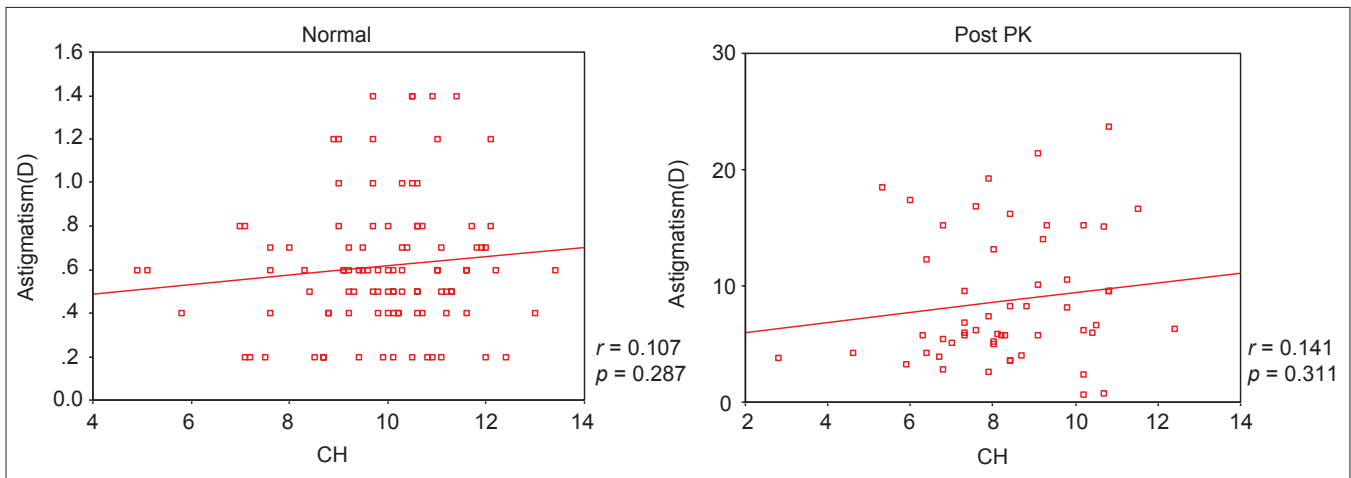


Figure 3: Correlation between CH and astigmatism in post PK and normal eyes

because of its decreased modulus of elasticity,^[13] Feizi *et al.*^[14] also showed similar results in their study of IOP evaluation in deep anterior lamellar keratoplasty eyes (DALK) with the ORA and Goldmann applanation tonometer, thereby concluding that the factors of CH and CRF that characterize

corneal biomechanics play a pivotal role in IOP determination in post-corneal grafting eyes rather than the CCT or the corneal curvature.^[14]

The variations in corneal biomechanical properties

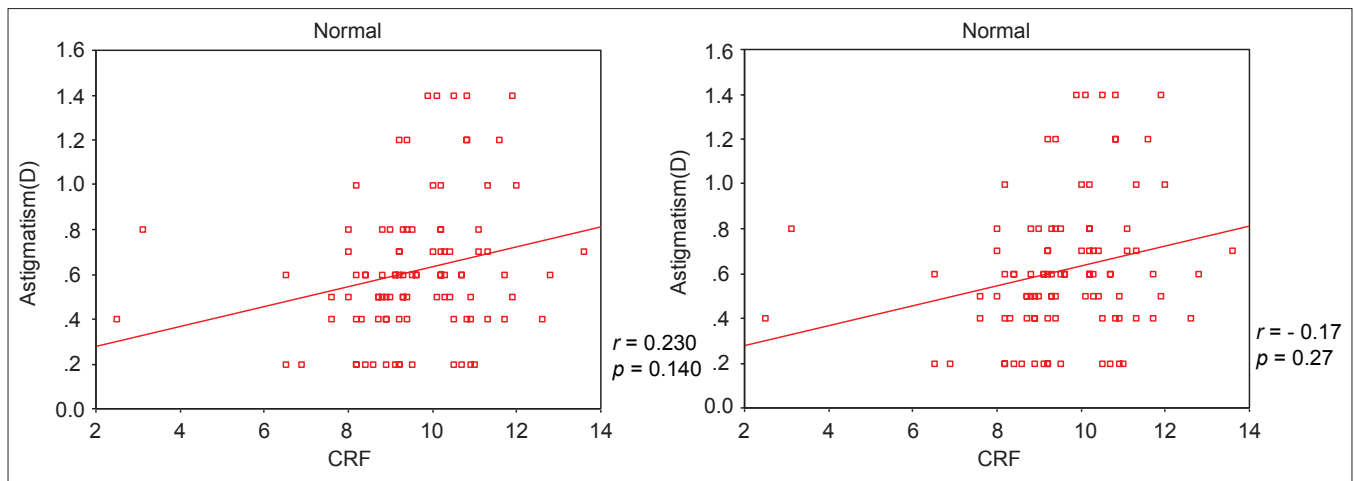


Figure 4: Correlation between CRF and astigmatism in post PK and normal eyes

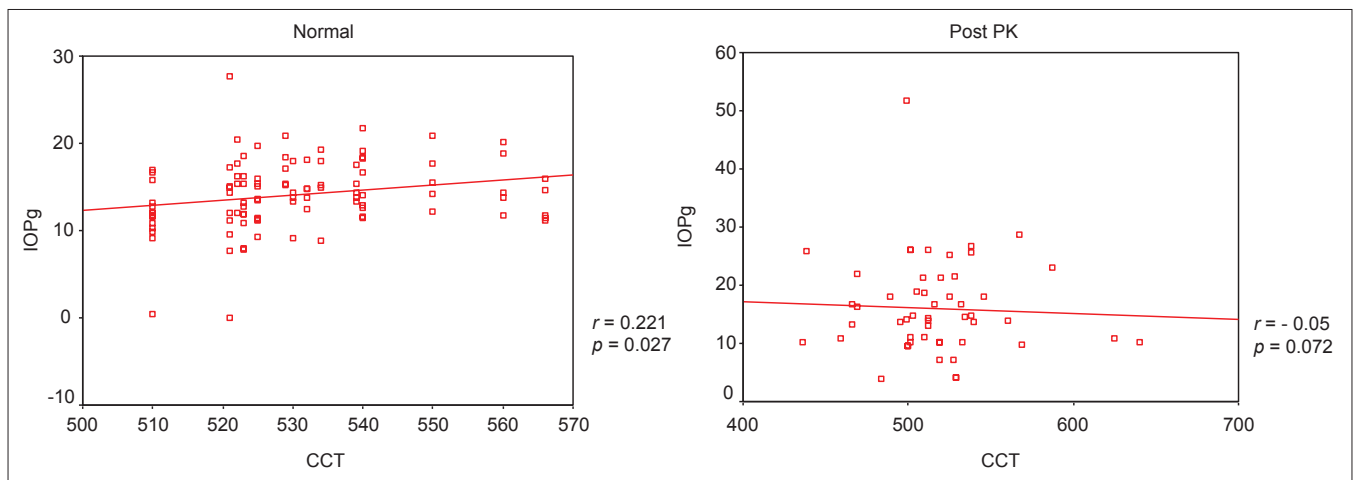


Figure 5: Correlation between IOPg and CCT in post PK and normal eyes

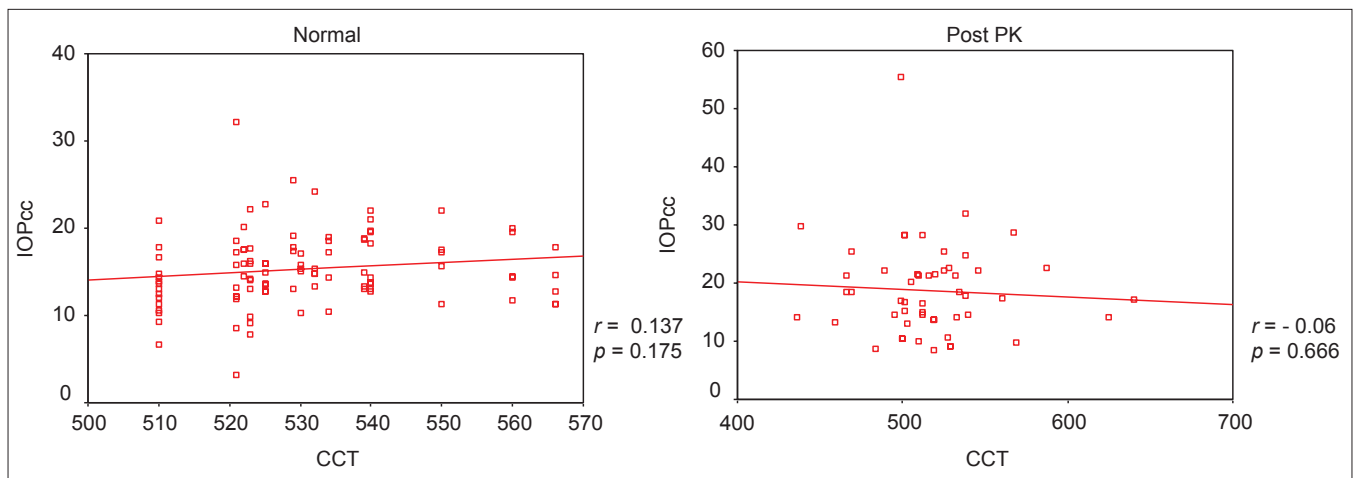


Figure 6: Correlation between IOPcc and CCT in PK and normal eyes

in corneal surgical procedures have also been recently elaborated.^[8,9,16] Stromal flap-cut in the cornea has been found to alter corneal biomechanical properties that are responsible for reduction in CH.^[8] CH was also observed to be significantly lower in eyes with descemetorhexis with endothelial

keratoplasty versus those in normal subjects. Descemetorhexis with endokeratoplasty affects reduction in CH and corneal biomechanical properties.^[9] DALK has been found to result in better corneal biomechanical characteristics that can be equated to that of the normal values.^[16] A recent experimental

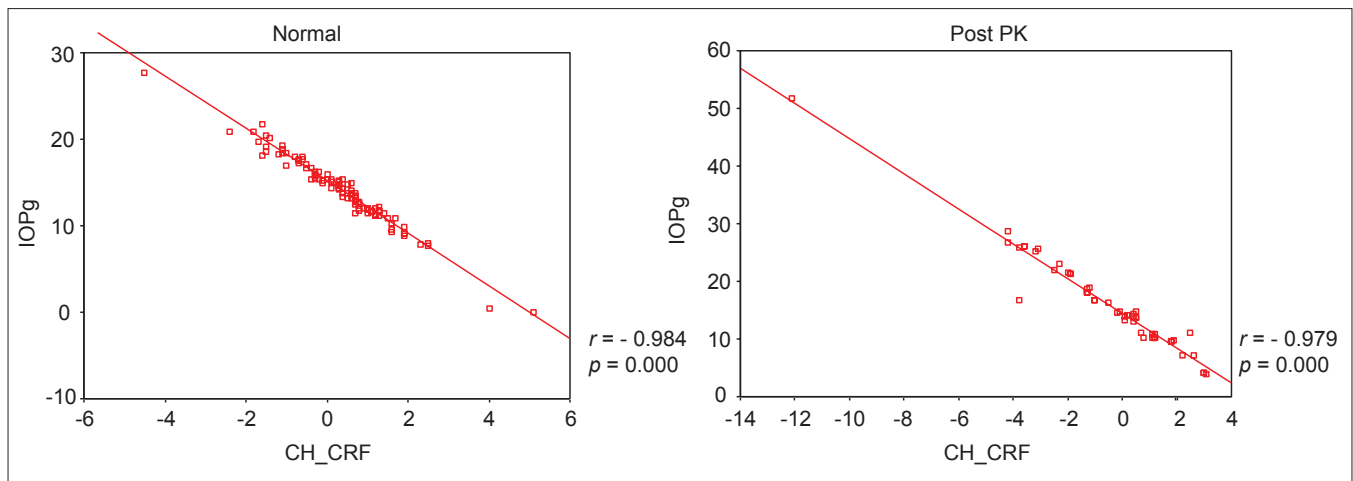


Figure 7: Correlation between IOPg and CH – CRF in postPK and normal eyes

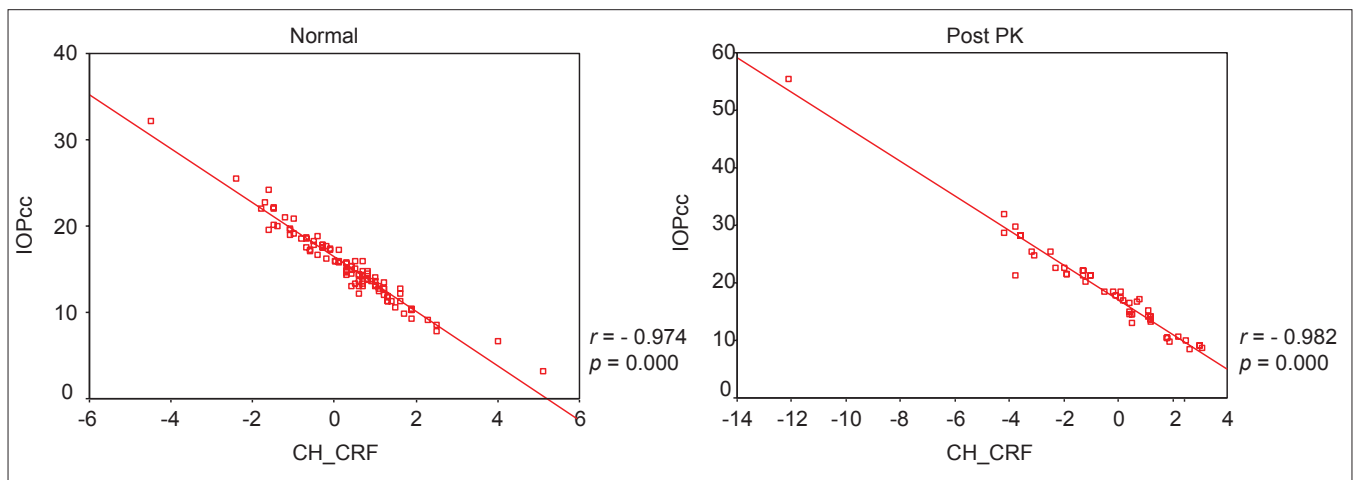


Figure 8: Correlation between IOPcc and CH – CRF in postPK and normal eyes

animal study did not note any change in CH values following a circular Descemet's incision.^[17] Rabbit eyes that had undergone a circular Descemet's incision were found to have significant decrease in mean keratometry, while no significant change was observed in CH.

Until date, there have been only few published studies that can provide an insight into the variations in corneal biomechanics in eyes that have undergone PK.^[10-12]

Shin *et al.*^[10] [Table 3] evaluated 26 post-PK eyes and compared CH, CRF, IOPg, and IOPcc with corresponding values in contralateral normal eyes. The CH and CRF values was 8.95 ± 59 mmHg and 10.26 ± 2.64 mmHg in post-PK eyes and 9.78 ± 1.45 mmHg and 9.75 ± 1.45 mmHg in normal eyes, respectively (statistically not significant). The IOPg and IOPcc were however observed to be significantly higher in the post-PK eyes as compared with those in the normal eyes. They concluded that CH decreases and CRF increases in post-PK eyes resulting in a decreasing (CH – CRF) value. Higher IOP combined with decreased CCT was hypothesized to be responsible for these biochemical changes. Our results correspond to their observations in showing a decrease in CH in post-PK eyes. In addition, the CRF values of the post-PK eyes were also found to be lower in post-keratoplasty eyes,

while the CCT values in our keratoplasty eyes were found to be comparable with those in normal eyes.

Laiquzzaman *et al.* prospective study from UK^[11] on comparative evaluation ORA values of 166 normal eyes and 34 post-PK eyes found a mean CH and CRF value of 8.9 ± 3.3 mmHg and 8.1 ± 3.3 mm, respectively, in post-PK eyes. The mean CH and CRF value was 10.6 ± 2.0 mmHg and 10.2 ± 2.0 mmHg, respectively, in the normal eyes in their study [Table 3]. The mean CCT was 541.8 ± 36.1 μ m and 556.0 ± 69.2 μ m, while the Goldmann-correlated IOP was 16.1 ± 3.1 and 12.4 ± 2.9 mmHg in normal and post PK eyes, respectively. Reduced corneal biomechanical values, despite a significantly higher CCT in post-PK eyes were an interesting finding in this study as well, which was possibly attributed to the altered corneal structure following keratoplasty.

Our current study on 100 eyes of 50 normal subjects (mean age: 36.83 ± 15.86 years) and 54 post-keratoplasty eyes of 51 patients (mean age: 40.92 ± 18.11 years, mean post-operative period: 19.33 ± 6.42 months, mean post-keratoplasty astigmatism: 8.73 ± 5.61 D) showed CH of 8.340 ± 1.85 and 9.923 ± 1.558 mmHg ($P = 0.0001$), CRF of 8.846 ± 2.39 mmHg and 9.577 ± 1.631 mmHg ($P = 0.065$), mean IOPg of 15.996 ± 8.09 mmHg and 14.104 ± 3.974 mmHg ($P = 0.0076$), IOPcc

Table 3: Comparison of corneal biomechanics data with other published studies

Study	CH		CRF		IOPg		IOPcc		CH - CRF		CCT	
	Post PK	normal	Post PK	normal	Post PK	Normal	Post PK	Normal	Post PK	normal	Post pk	Normal
Shin <i>et al</i>	8.95 ± 59	9.78 ± 1.45	10.26 ± 2.64	9.75 ± 1.45	19.22 ± 7.34	15.07 ± 3.03	20.81 ± 7.81	16.27 ± 2.49	-1.31 ± 2.32	0.03 ± 0.88	489.11 ± 90.60	556.24 ± 42.84
Laiquzzaman	8.9 ± 3.3	10.6 ± 2.0	8.1 ± 3.3	10.2 ± 2.0	12.4 ± 2.9	16.1 ± 3.1	-	-	-	-	556.0 ± 69.2	541.8 ± 36.1
M <i>et al</i>												
Our study	8.340±1.85	9.864±1.29	8.846 ± 2.39	9.385 ± 1.39	15.996 ± 8.09	13.731 ± 3.22	18.625±7.97	14.954±3.50	-0.506	0.479	516.29 ± 37.44	516.63 ± 13.9

of 18.625 ± 7.97 mmHg and 15.276 ± 4.164 mmHg ($P = 0.011$) in post-PK eyes and normal eyes, respectively. CH and CRF did not correlate with post-keratoplasty astigmatism ($P = 0.311$ and 0.276 , respectively), while a significant correlation was observed with IOPg ($P = 0.004$) and IOPcc ($P < 0.001$). Our study also corroborates with earlier reports of decreases corneal biomechanics values in post-keratoplasty eyes as compared with those in normal eyes, despite a comparable CCT.

Yenerel *et al.*^[12] retrospective observation of corneal biomechanics using the ORA in eyes with keratoconus, *Forme fruste* keratoconus before and after PK. Their study comprised of evaluation of 169 eyes—34 eyes with *forme fruste* keratoconus, 36 eyes of manifest keratoconus, 36 eyes that had undergone PK, and a control group of 63 normal eyes. Corneal biomechanics was found to be inversely proportional to the severity of keratoconus, with an improvement in the values following PK in keratoconus eyes. They have also reported significantly higher values of CH and CRF in eyes of keratoconus that underwent PK as compared with the keratoconus group. In comparison to the eyes in normal group, corneal biomechanics values were noted to be significantly lower after PK, revealing that although PK can result in an improvement in the corneal biomechanics in keratoconus, normal level cannot be attained by keratoplasty in keratoconic eyes. They attributed the residual weakened recipient corneal rim that retains the characteristics of the keratoconic cornea to be responsible for the corneal biomechanics levels not reaching normal or near normal levels in keratoconic eyes after keratoplasty. Feizi *et al.*^[19] recent study on the biomechanical properties of the corneal graft in 34 keratoconic eyes of mean age 29.6 ± 6.2 years at a mean follow-up of 82.4 ± 59.6 months (at least 6 months after complete suture removal), evaluated the relationship between donor size, donor-recipient disparity, central thickness of graft, and ocular response analyzer values. Their analysis indicated that the biomechanics of corneal grafts in keratoconic eyes approximated normal values in eyes with larger grafts and in eyes with higher donor-host disparate grafts. Among the parameters they studied, only CH, CRF, and cornea-compensated IOP had a significant positive correlation with IOP goldmann Applanation tonometry.

Few studies^[15,16] have compared the corneal biomechanical values in eyes with different techniques of keratoplasty. Hosny *et al.*^[16] evaluated the corneal biomechanics with the ORA in PK and DALK in 63 eyes in a prospective comparative study, comprising of 21 normal eyes, 21 post-PK eyes, and 21 eyes with DALK. The CH and CRF values were found to be significantly lower in the post-PK eyes as compared with the normal eyes and eyes with DALK. They did not find a significant statistical difference in the corneal biomechanics values between the normal and DALK eyes, concluding that DALK can contribute to preserve the corneal biomechanical strength. Jafarinasab *et al.*^[15] compared the biomechanical characteristics using the ORA in keratoconus eyes that have undergone PK ($n = 45$, mean age: 29.8 ± 6.1 years, follow-up of 31.4 ± 19.0 months) and DALK ($n = 23$, mean age: 27.2 ± 6.5 years, follow-up of 29.2 ± 17.3 months) using Anwar's big-bubble technique. CH was noted to be 10.09 ± 2.5 and 9.64 ± 2.1 mmHg, while CRF was 10.13 ± 2.2 and 9.36 ± 2.1 mmHg in post-PK and post-DALK eyes, respectively. No significant difference was found in the CH, CRF, IOPg, and IOPcc values between the two groups in this study. The corneal biomechanical characteristics in

keratoconus eyes achieved following DALK seem to be equivalent to that in post-PK eyes. This is in contrast to Hosny *et al.* observations suggesting that corneal biomechanics (CH and CRF) are significantly decreased in post-PK in comparison to DALK eyes or normal eyes.

Yet another new parameter that has been elaborated is the difference between CH and CRF (CH – CRF),^[19] which is considered to be more characteristic of corneal weakness and hence has been implicated in the screening of conditions such as Forme fruste keratoconus. CRF < 8 mmHg in combination with a positive (CH - CRF) has been suggested to be a better sensitive index for screening of weaker corneas than just lower CH values only.^[7] Further studies on this derivation will perhaps throw more light on its relationship to corneal weakening in the various diseases and following surgery.

Conclusions

We evaluated the corneal biomechanics in corneas that had undergone PK. Corneal biomechanical profiles were found to be significantly reduced in post-keratoplasty eyes with significant correlation with higher IOP in our study, while the corneal biomechanical profiles did not correlate with corneal astigmatism. Our evaluation also shows decrease in both CH and CRF values in post-keratoplasty eyes as compared with those in normal eyes, thereby resulting in a small negative (CH – CRF) as compared with a larger difference in normals, the significance of which remains unclear. In conclusion, biomechanical profiles of post-keratoplasty eyes are significantly lower as compared with those of normal eyes, with a significant correlation with a higher IOP than in normal eyes. Corneal astigmatism did not correlate with the biomechanical profiles of the corneas. Further studies to evaluate corneal biomechanics in eyes that have undergone anterior and posterior lamellar keratoplasty can perhaps further enhance our understanding of this evolving characteristic of the cornea.

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