Original Article

Study on change in corneal biomechanics and effect of percent tissue altered in myopic laser-assisted *in situ* keratomileusis

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Purpose: To evaluate corneal biomechanical changes and their correlation with the percentage of tissue altered (PTA) in myopic femtosecond (FS)-flap LASIK. **Methods:** Prospective longitudinal observational study of 80 eyes of FS LASIK. Demographic details, LASIK parameters, preoperative and postoperative (day 1, month 1, 3, and 6), UCVA, BCVA, refraction, corneal topography, corneal hysteresis (CH), and a corneal resistance factor (CRF) were noted. Change in CH and CRF and its correlation with PTA were analyzed. Data were analyzed in three subgroups [subgroup 1: PTA 23 to <27%; subgroup 2: 27 to <33%; subgroup 3: 33 to <40%]. **Results:** FS LASIK for MRSE -3.5D ± 1.6D with mean PTA of 31.6 ± 4.4% (range 23.8–39.8%), showed statistically significant decrease in CH and CRF. Mean CH decreased from a preoperative value of 10.4 ± 1.9 to 8.1 ± 1.1; mean CRF from 10.5 ± 1.6 to 7.5 ± 1.3 at 6-months postoperative period, respectively. Mean preoperative CH decreased by 25%, 24%, 23%, and 21% and mean preoperative CRF decreased by 34%, 28%, 28%, and 28% at postoperative day 1, month 1, 3, and 6 follow-ups. Mean CH and CRF showed a significant negative correlation with PTA (CH: r = - 0.33 [*P* = <0.0001], CRF: r = -0.34 [*P* = <0.001]. Subgroup analysis noted greater decrease in CRF and CH in eyes with higher PTA (subgroup 3). **Conclusion:** Myopic FS LASIK causes a decrease in corneal biomechanics with a significant negative correlation with PTA indicating a greater decrease in corneal biomechanics with higher PTA.

Key words: Ablation depth, biomechanics, CH, cornea, cornea resistance factor, correlation, CRF, flap thickness, hysteresis, laser ablation, LASIK, myopia, PTA, resistance

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Myopic laser-assisted *in situ* keratomileusis (LASIK) has been known to cause a reduction in corneal biomechanical strength as measured by the Ocular Response Analyzer (ORA) (Reichert, Inc, Depew, NY): corneal hysteresis (CH) and a corneal resistance factor (CRF).[1-11] ORA records two applanation pressure measurements, P1 (pressure at which the cornea moves inward) and P2 (pressure at which the cornea moves outward from the dynamic air pulse), the average of which is the Goldman intraocular pressure (IOPg), while IOPcc (corneal compensated IOP) is less influenced by corneal properties than other tonometry measurements[12] Corneal elastic properties are indicated by CH (representative of viscous damping capabilities) and CRF (representative of overall corneal elastic resistance).[13] Both CH and the CRF were noted to be significantly reduced in both femtosecond flap LASIK (FS-LASIK) and small incision lenticular extraction (SMILE) at postoperative 1-month period.[11] Studies have noted a nonsignificant decrease in CH and CRF, indicating that thinner flaps in LASIK did not play a role in decreasing corneal biomechanics.[14,15] Percent tissue altered (PTA) is a metric of the percentage of anterior corneal tissue that is modified in laser refractive surgery. It is hypothesized that there is an integral relationship between preoperative corneal thickness, ablation depth (AD), and flap thickness (FT) in determining the relative amount of biomechanical change that occurs after laser ablation for refractive correction surgery. PTA of over 40% in LASIK is reported to be significantly associated with the development of post-LASIK ectasia. Estimation of PTA has been incorporated into preoperative assessment and screening protocols for eligibility for laser refractive surgery with values above 40% considered as exclusionary.[16] This study was undertaken to evaluate these effects further, by examining changes in corneal biomechanics in LASIK with PTA lesser than 40% and correlation of PTA with corneal biomechanics alteration.

Methods

This prospective observational longitudinal study evaluated data of 40 patients undergoing bilateral myopic LASIK with a 6-months follow-up. Myopic patients of 18 years or above with refractive stability (not more than a ± 0.5D change in refraction in the last 6 months), without other corneal morbidity and consent to participate in the study, were included in the study. Patients younger than 18 years of age, pregnant or lactating, having dry eye disease, prior history of herpetic keratitis, glaucoma, glaucoma suspects, ocular hypertension, uveitis, autoimmune

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diseases, unstable refractive error, corneal thickness less than 480 µm, corneal ectasia, and any other corneal pathology were excluded from the study. The research adhered to the tenets of the Declaration of Helsinki and approval from the institutional ethics committee was obtained. Written informed consent was taken from the study participants. The preoperative assessment included uncorrected and best-corrected visual acuity (UCVA, BCVA), IOP by non-contact tonometry, comprehensive slit-lamp biomicroscopy, fundoscopy, indirect ophthalmoscopy, cycloplegic refraction, Scheimpflug's corneal topography (Pentacam, Oculus, Wetzlar, Germany), and corneal biomechanics measure (Ocular Response Analyser, Reichert, Inc, Depew, NY). FS-LASIK surgical procedure was performed under topical anesthesia using proparacaine 0.5%. FS laser flap was done with an FS laser system (1053 nm wavelength) with a 500 kHz repetition rate, 120 µm flap creation with superior hinge, and stromal ablation with 400 Hz Allegretto excimer laser system (WaveLight Laser Technologies AG, Germany). Pupil-centered wavefront-optimized ablation with 6.5 mm optical zone, ablation zone of 7.1 mm - 8.5 mm, and transition zone of 1.0 mm for target refraction to be within ± 0.25D were done. Postoperative follow-up was done on day 1, month 1, 3, and 6, and UCVA, BCVA, refraction, IOP, corneal topography, and ORA imaging were repeated.

Corneal biomechanics (CH, CRF), IOPg and IOP cc values using the ORA, and Scheimpflug's corneal topography (Pentacam HR [Oculus, Wetzlar, German]) for corneal elevation, corneal curvature - K1, K2, K max, and Q value were noted preoperatively and on all postoperative visits. Demographic details of the patients and FS-LASIK parameters (AD, FT, PTA, residual stromal bed thickness [RSBT]) were noted on a predesigned proforma. PTA was calculated by the sum of total AD and FT divided by preoperative CCT.

Statistical Analysis: Statistical analysis was performed using SPSS statistical software (version 19.0, Chicago, USA). The normality of all data samples was checked with the Shapiro-Wilk test. Categorical data expressed as frequency and percentage. Quantitative data followed normal distribution expressed as mean ± SD. Quantitative data followed skewed distribution expressed as median (min, max). Chi-square/Fisher's exact test was used to check the association between categorical variables. Repeated measure ANOVA followed by Bonferroni correction was used to check the statistical significance over a period for those variables that followed a normal distribution. Friedman test followed by Wilcoxon signed-rank test was used to check statistical significance within the group for skewed variables. Kruskal-Wallis test or one-way ANOVA was used to compare variables among the three PTA subgroups (subdivided following a range of PTA; subgroup 1: 23 to <27%, subgroup 2: 27 to <33%, subgroup 3: 33 to <40%). Spearman's correlation coefficient was used to check the correlation between continuous variables followed by normal and skewed distribution, respectively. P value <0.05 was considered statistically significant.

Results

Data of 80 eyes of 40 patients of mean age 22.6 ± 2.8 years (range 19–31 years) who underwent FS-LASIK for a mean manifest refractive spherical equivalent (MRSE) correction of -3.5 ± 1.6D (range -0.75 D to -6.25 D, mean PTA 31.6 ± 4.4% (range 23.8–39.8%), were analyzed. Data was also analyzed in three subgroups in accordance to PTA ranges with 14 eyes in subgroup 1 (mean PTA 24.8 ± 0.90 [range 23.7 to 26.9%]), 36 eyes in subgroup 2 (mean PTA 30.5 ± 1.9 [range 27.0 to 32.9%]), and 30 eyes in subgroup 3 (mean PTA 36.0 ± 2.1 [range 33.00 to 39.8%]).

The study data categorized into three subgroups is elaborated in Table 1. Details of clinical characteristics are given in Tables 2A and 2B. Distribution of CH and CRF values in study eyes are depicted in Figs. 1 and 2. Details of corneal biomechanical parameters at all follow-up period of postoperative day 1, month 1, 3, and 6 are elaborated in Table 2B and Fig. 3. The percent decrease in CH, CRF, and IOP from preoperative values are depicted in Tables 3A, 3B and Fig. 4. There was a statistically significant change in mean CCT (P < 0.05), IOP by NCT (P = 0.0001), IOPcc (P = 0.0001), and IOPg (P = 0.0001) [Table 2A].

The change in corneal biomechanical parameters (CH and CRF) measured by the ORA was statistically significant on all follow-up visits [Table 2B]. In the entire study sample of 80 eyes, a decrease by 25%, 24%, 23%, and 22% from preoperative CH values and decrease of 34%, 28%, 28%, and 28% from preoperative CRF values were noted at postoperative day 1, month 1, 3, and 6 follow-ups, respectively in all study eyes following myopic FS LASIK within the recommended range of 40% PTA.

On subgroup analysis, in 14 eyes with PTA ranging from 23.79– 26.99% (subgroup 1), the decrease noted from preoperative mean CH values was 17%, 16%, 18%, and 18%,

Table 1: Details of the FS-flap LASIK parameters in the study subgroups

Subgroups (PTA%)	No of Eyes	Mean ± SD (range)			
		PTA (%)	MRSE (D)	AD (µm)	RSBT (µm)
SUBGROUP 1 (23 to <27%)	14	24.8±0.9	-1.4±0.4 (-2.0 to -0.8)	21.1±8.0 (9.8-35.8)	388.9±35.4 (324-432.8)
SUBGROUP 2 (27 to <33%)	36	30.5±1.9	-3.1±1.0 (-5.3 to -1.3)	42.2±14.3 (22.8-78.0)	370.7±30.0 (321.5-432.0)
SUBGROUP 3 (33 to <40%)	30	36.0±2.1	-4.9±1.1 (-6.3 to -2.3)	69.1±11.6 (48.3-87.8)	339.2±25.6 (295.0-382.5)
TOTAL	80	31.6±4.4 (23.9-39.8)	-3.5±1.6 (-6.3 to-0.8)	48.6±21.5 (9.8-87.8)	362.1±34.7 (295-432.8)

LASIK – laser-assisted in situ keratomileusis; PTA – Percentage tissue altered; SD – Standard deviation; MRSE – mean refractive spherical equivalent; AD – ablation depth; RBT – residual stromal bed thickness (Decimals corrected to first place value)

Table 2A: Clinical Characteristics of the study participants

Subgroups	Preoperative mean±SD	Postoperative Period				*P
		Day 1 mean±SD	Month 1 mean±SD	Month 3 mean±SD	Month 6 mean±SD	
UCVA						
Group 1	0.65±0.23	-0.01±0.25	-0.16±0.03	-0.04±0.35	-0.05±0.29	0.001
Group 2	0.94±0.24	0.0005±0.05	-0.01±0.04	-0.02±0.03	-0.03±0.03	0.001
Group 3	1.27±0.26	0.06±0.10	0.02±0.07	-0.02±0.03	-0.03±0.03	0.001
Total	1.01±0.33	0.21±0.08	-0.002±0.06	-0.02±0.03	-0.03±0.03	0.001
BCVA						
Group 1	0.002±0.05	-0.02±0.03	-0.05±0.29	-0.05±0.03	-0.06±0.02	0.001
Group 2	0.03±-0.16	0.002±0.07	-0.04±0.03	-0.03±0.03	-0.04±0.04	0.001
Group 3	0.05±0.14	0.06±0.11	-0.01±0.09	-0.28±0.34	-0.04±0.04	0.001
Total	0.03±0.14	0.02±0.09	-0.03±0.06	-0.03±0.03	-0.04±0.04	0.001
CCT						
Group 1	560.50±22.36	533.79±28.19	533.79±22.66	531.43±21.42	537.64±24.59	0.001
Group 2	537.61±33.86	492.25±24.52	484.69±30.42	486.86±25.35	488.58±26.71	0.001
Group 3	526.20±22.70	461.23±32.45	446.07±27.60	449.80±27.88	454.20±24.01	0.001
Total	537±30.3	487.8±37.8	478.8±41.6	480.7±38.4	484.2±38.5	0.0001
NCT						
Group 1	16.71±2.58	12.64±2.13	12.79±2.19	13.29±1.54	13.36±1.78	0.002
Group 2	15.92±2.79	11.36±1.71	11.75±1.71	11.69±1.92	12.58±1.84	0.001
Group 3	15.47±2.52	9.90±2.38	11.37±2.76	12.20±3.07	11.73±2.42	0.001
Total	15.8±2.6	11.0±2.2	11.7±2.2	12.1±2.4	12.4±2.1	0.0001
IOPcc						
Group 1	16.62±1.75	14.27±2.08	16.42±1.67	14.85±1.95	14.7±2.16	0.001
Group 2	16.94±2.52	14.14±2.47	15.07±2.93	14.86±2.78	14.71±2.60	0.001
Group 3	16.45±3.06	14.64±2.86	15.86±2.41	15.88±2.63	14.98±2.54	0.027
Total	16.7±2.6	14.3±2.5	15.6±2.5	15.2±2.6	14.8±2.4	0.0001
IOPg						
Group 1	17.55±2.63	11.98±2.17	14.22±2.81	12.35±2.63	12.39±2.95	0.001
Group 2	16.29±2.64	11.47±2.39	12.30±2.66	12.08±2.49	12.17±2.65	0.001
Group 3	15.92±3.94	10.32±3.17	11.89±3.11	11.96±3.17	10.46±2.27	0.001
Total	16.3±3.2	11.1±2.7	12.4±2.9	12.8±2.7	11.5±2.6	0.0001
PD						
Group 1	3.52±1.1	3.09±0.55	3.20±0.55	3.16±0.55	3.14±0.53	0.03
Group 2	3.40±0.60	3.07±0.51	3.18±0.57	3.10±0.48	3.12±0.49	0.001
Group 3	3.37±0.95	2.93±0.49	2.95±0.49	2.95±0.49	2.96±0.49	0.006
Total	3.4±0.8	3.0±0.5	3.1±0.5	3.0±0.4	3.0±0.5	0.0001

UCVA- Uncorrected visual acuity; BCVA- best-corrected visual acuity; CCT- central corneal thickness; NCT- noncontact tonometry; IOPcc- corneal compensated intraocular pressure; IOPg- Goldmann correlated intraocular pressure; PD – pupil diameter; *repeated measure ANOVA

and decrease from preoperative mean CRF was 25%, 22%, 29%, and 27% at postoperative day 1, month 1, 3, and 6 follow-ups, respectively; in the 36 eyes with PTA ranging from 27.00–32.99% (subgroup 2), the decrease noted from preoperative mean CH values was 24%, 25%, 23%, and 20% and decrease from preoperative mean CRF was 29%, 27%, 25%, and 23% at postoperative day 1, month 1, 3, and 6 follow-ups, respectively; in the 30 eyes with PTA ranging from 33.00– 39.8% (subgroup 3), the decrease noted from preoperative mean CH values was 30%, 28%, 21%, and 26% and decrease from preoperative mean CRF was 42%, 33%, 32%, and 33% at postoperative day 1, month 1, 3, and 6 follow-ups, respectively. The decrease in corneal biomechanics metrics of CH and CRF was observed to be higher in eyes requiring a higher PTA [Table 3A].

Correlation analysis (Spearman's correlation coefficient) between PTA and corneal biomechanics observed a negative correlation between PTA and corneal biomechanics [Table 4 and Figs. 5, 6], denoting that increase in PTA results in a decrease in corneal biomechanics parameters of CH and CRF. There was no correlation of IOP changes in the postoperative period (months 1, 3, and 6) with preoperative CCT, corneal biomechanical parameters (CH and CRF), and PTA on multiple linear regression analysis [Table 5].

Discussion

It is well-known that the various types of laser refractive surgery affect a biomechanical alteration documented by a decrease in

Table 2B: Corneal Hysteresis and Corneal Resistance Factor in the study subjects

CORNEAL HYSTERESIS						
	PREOPERATIVE		POSTOPERATIVE			
PTA Subgroups	Mean±SD (range)	Day 1 Mean±SD (range)	1 month Mean±SD (range)	3 months Mean±SD (range)	6 months Mean±SD (range)	***P*
1	11.06±1.36 (9.4 to 13.6)	9.18±1.31 (5.6 to 11.3) Δ17%	9.21±0.07 (7.6 to 11.8) Δ 16%	9.06±1.01 (7.4 to 11.5) Δ 18%	9.08±0.91 (7.8 to 11) Δ18%	0.001
2	10.54±2.33 (5.5 to 17.4)	7.98±1.51 (5.8 to 12.6) Δ 24%	7.89±1.24 (6.0 to 11) Δ25%	8.11±1.01 (6.6 to 0.1) Δ 23%	8.39±1.11 (6.8 to 1.2) Δ 20%	0.001
3	10.15±1.47 (7.9 to 14.8)	7.06±0.79 (5.5 to 8.5) Δ 30%	7.29±0.06 (5.6 to 9.7) Δ 28%	7.97±1.01 (5.5 to 9.6) Δ 21%	7.42±0.86 (6.2 to 9.2) Δ 26%	0.001
**P*	0.32	0.000	0.000	0.000	0.000	
TOTAL (*n*=80 eyes)	10.4±1.9 (5.5 to 17.4)	7.8±1.4 (5.5 to 12.6) Δ 25%	7.9±1.3 (5.6 to 11.8) Δ 24%	8.0±1.1 (5.5 to 11.5) Δ 23%	8.1±1.1 (6.2 to 11.2) Δ 22%	

CORNEAL RESISTANCE FACTOR						
	PREOPERATIVE		POSTOPERATIVE			
PTA Subgroups	Mean±SD (range)	Day 1 Mean±SD (range)	1 month Mean±SD (range)	3 months Mean±SD (range)	6 months Mean±SD (range)	***P*
1	11.85±1.99 (8.8 16 to 16)	8.92±1.31 (7.2 to 11.9) Δ 25%	9.19±1.48 (7.1 to 12.6) Δ 22%	8.45±1.44 (5.7 to 10.6) Δ29%	8.63±0.99 (6.9 to 10.3) Δ 27%	0.001
2	10.23±1.42 (8.3 to 14)	7.22±1.42 (5.3 to 10.2) Δ 29%	7.43±1.28 (5.1 to 9.8) Δ 27%	7.61±1.19 (5.6 to 10.2) Δ 25%	7.83±1.14 (5.2 to 10.2) Δ 23%	0.001
3	10.23±1.35 (7.3 to 16)	5.96±1.37 (3.7 to 11.9) Δ42%	6.91± 1.60 (4.2 to 12.6) Δ 33%	6.96±1.38 (4.4 to 10.6) Δ32%	6.81±1.33 (4.7 to 10.3) Δ33%	0.001
**P*	0.0023	0.000	0.0000	0.003	0.0000	
TOTAL (*n*=80 eyes)	10.5±1.6 (7.3 to 16)	7.0±1.7 (3.7 to 11.9) Δ 34%	7.5±1.6 (4.2 to 12.6) Δ 28%	7.5±1.3 (4.4 to 10.6) Δ 28%	7.5±1.3 (4.7 to 10.3) Δ 28%	

Δ – percentage decrease from preoperative value; *one-way ANOVA, **Repeated measure ANOVA

CH and CRF.[14,17-20] Decrease in CH and CRF following LASIK surgery is well documented.[5,20-23] An interesting observation in a study analyzing the changes in CH and CRF following individual steps such as flap elevation, repositioning, and laser ablation in FS-LASIK procedure, did not attribute flap creation to be the cause of the reduction in CH and CRF noting laser ablation to be responsible for the decrease in corneal biomechanics.[24] While flap creation does influence corneal biomechanical characteristics by reducing corneal stiffness, it is also likely that both CH and CRF are perhaps not able to accurately reflect the corneal biomechanical influences of flap creation.[24] Experimental animal studies on the influence of flaps of varying thicknesses on corneal biomechanical properties observed no significant change in CH and CRF after thin flaps.[15]

Corneal biomechanical alterations of decreased CH and CRF affected by FS-flap creation, photoablation pattern, and residual stroma geometry are complex interactions that are intensively researched.[16,25-29] CH and CRF, being combinations of the same two pressure measurements are not explicit measures of temporal and other features of ocular response that are comprehensively reflective of the biomechanical change in corneal refractive surgery.[16] They are, therefore, felt to be not entirely descriptive of all characteristics contained in the ORA waveform signal that can yield additional information about biomechanical differences between normal corneas and diseased corneas.[30,31] The behavior of ORA enumerated biomechanical descriptors (CH and CRF) after myopic FS LASIK, and comparable levels of PRK ablation has been

Table 3A: Percent change in Corneal Hysteresis and Corneal Resistance Factor in the study participants

PTA SUBGROUPS	D1-PREOP Median (range)	M1-PREOP Median (range)	M3-PREOP Median (range)	M6-PREOP Median (range)
		Percent change in CH		
1	-0.16 (-0.4 to -0.01)	-0.14 (-0.32-0)	-0.16 (-0.32 to -0.06)	-0.17 (-0.29-0.06)
2	-0.23 (-0.63-0.38)	-0.22 (-0.64-0.32)	-0.20 (-0.62-0.23)	-0.2 (-0.6-0.74)
3	-0.30 (-0.59 to -0.13)	-0.24 (-0.59 to -0.1)	-0.27 (-1.3 to -0.06)	-0.26 (-0.52 to -0.05)
*P**	0.004	0.01	0.02	0.01
Total	- 0.24 (-0.63-0.38)	- 0.24 (-0.64-0.32)	- 0.21 (-1.3-0.23)	- 0.22 (-0.6-0.74)
		Percent change in CRF		
1	-0.25 (-0.38-0)	-0.18 (-0.42 to -0.1)	-0.27 (-0.49 to -0.07)	-0.24 (-0.44 to -0.08)
2	-0.29 (-0.48 to -0.04)	-0.28 (-0.5-0.06)	-0.28 (-0.44-0.02)	-0.24 (-0.66-0)
3	-0.44 (-0.65-0.03)	-0.33 (-0.62-0.19)	-0.30 (-0.5-0.02)	-0.32 (-0.52-0.08)
*P**	0.0001	0.005	0.14	0.007
Total	-0.34 (-0.65-0.03)	- 0.28 (-0.62-0.19)	- 0.28 (-0.5-0.02)	- 0.27 (-0.66-0)

*Kruskal-Wallis test. D1-Preop=percent change from preoperative to postoperative day 1, M1- Preop=percent change from preoperative to postoperative month 1, M3 - Preop=percent change from preoperative to postoperative month 3, M4 - Preop=percent change from preoperative to postoperative month 6

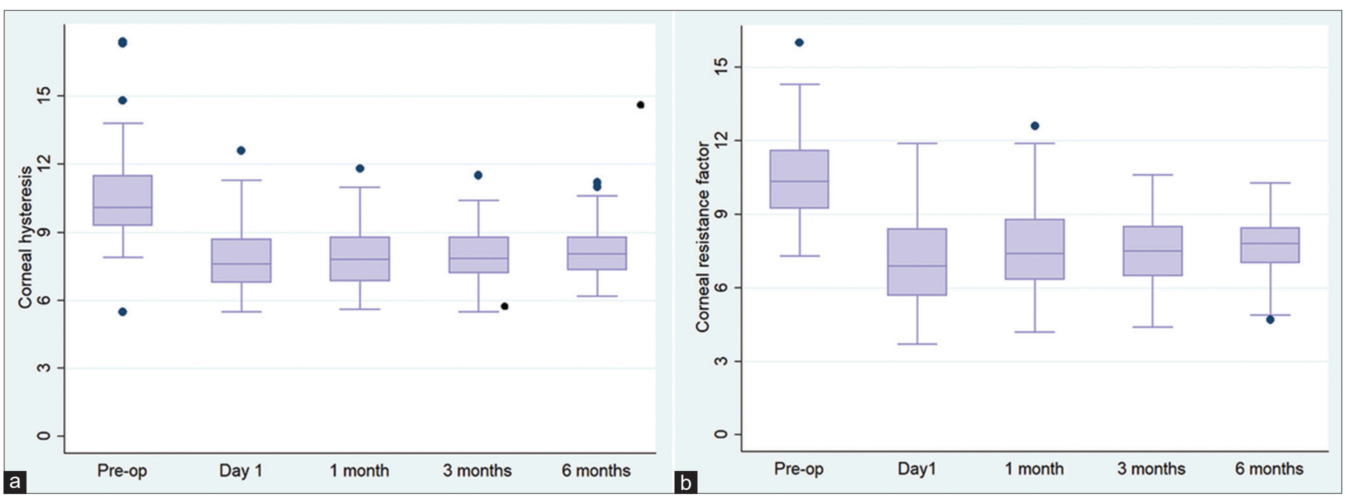

Figure 1: Box and whiskers plots depicting the distribution of corneal hysteresis (a) and a cornea resistance factor (b) in the study group's pre- and post-myopic FS LASIK ablation

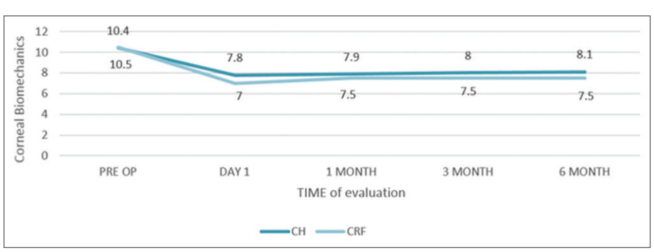

Figure 2: Graph depicting corneal hysteresis and corneal resistance factor in the study participants in the follow-up period after myopic FS-LASIK ablation

exhaustively elaborated by Santhiago *et al.*[16] They assessed the preoperative metrics of custom biomechanical variables derived from CH and CRF and the effects of FS LASIK on these variables to study their changes and correlation with CCT, AD, RSBT, and PTA at 1-month postoperative period. Their analysis of the custom variables (computed as mathematical derivation) derived from the ORA dynamic bidirectional applanation waveforms showed that LASIK and PRK-induced corneal changes result in altered resistance to deformation. The effect of laser ablation induced corneal changes on several customs derived ORA variables reflect as increased depth

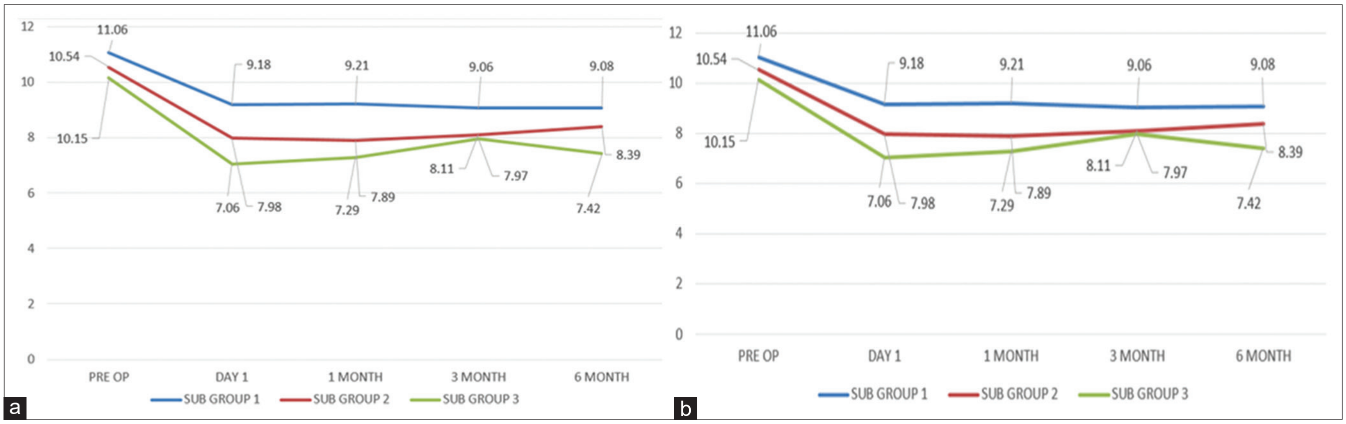

Figure 3: Graph depicting corneal hysteresis (a) and a corneal resistance factor (b) in the subgroups in the follow-up period after myopic FS-LASIK ablation

Table 3B: Percent change in IOP (IOPcc and IOPg) in the study participants

Subgroups	Day 1 Median (range)	Month 1 median (range)	Month 3 median (range)	Month 6 median (range)
Percent change in IOPg				
1	-0.29 (-0.56 to -0.16)	-0.14 (-0.58 to 0.14)	-0.28 (-0.63 to0.04)	-0.27 (-0.61 to -0.02)
2	-0.3 (-0.88 to 0)	-0.21 (-0.53 to -0.25)	-0.26 (-0.55 to 0.33)	-0.25 (-0.52 to 0.19)
3	-0.34 (-0.63 to 0.09)	-0.25 (-0.5 to 0.26)	-0.23 (-0.47 to 0.17)	-0.32 (-0.54 to 0.43)
	**P*=0.23	**P*=0.3	**P*=0.81	**P*=0.27
Total (*n*=80 eyes)	- 0.32 (-0.88-0.09)	- 0.22 (-0.58-0.26)	- 0.26 (-0.63-0.33)	- 0.29 (-0.61-0.43)
Percent change in IOPcc				
1	-0.16 (-0.25-0.07)	-0.025 (-0.22-0.26)	-0.15 (-0.28-0.2)	-0.12 (-0.37-0.24)
2	-0.13 (-0.56-0.15)	-0.09 (-0.54-0.27)	-0.09 (-0.57-0.42)	-0.12 (-0.53-0.39)
3	-0.08 (-0.46-0.41)	-0.05 (-0.28-0.5)	-0.02 (-0.32-0.51)	-0.04 (-0.38-0.28)
	**P*=0.64	**P*=0.18	**P*=0.22	**P*=0.69
Total (*n*=80 eyes)	- 0.13 (-0.56-0.41)	- 0.05 (-0.54-0.5)	-0.065 (-0.57-0.51)	- 0.085 (-0.53-0.39)

*Kruskal-Wallis test

Table 4: Correlation Analysis between PTA and corneal biomechanics (CH and CRF) and IOP

Study Variable	Postoperative period			
	Day 1 **r* (*P*)	1 month **r* (*P*)	3 months **r* (*P*)	6 months **r* (*P*)
CH	-0.39 (0.001)	-0.29 (0.008)	-0.27 (0.01)	-0.33 (0.002)
CRF	-0.58 (0.001)	-0.41 (0.001)	-0.22 (0.04)	-0.34 (0.001)
IOPg	-0.18 (0.10)	-0.10 (0.33)	0.04 (0.66)	-0.12 (0.26)
IOPcc	0.18 (0.10)	0.07 (0.48)	0.23 (0.03)	0.10 (0.36)

**r* (Spearman's correlation co-efficient); *P* (*P*)

of corneal deformation, decreased applanation pressures, more rapid onset of maximum deformation with slower recovery, and reductions in a more comprehensive analog of hysteresis (described as the hysteresis loop area), which correlated with the percentage of tissue depth altered and AD.[16] The ORA custom dynamic bidirectional applanation device variables and percentage of tissue depth altered (PTDA) are recommended as much stronger predictors of LASIK-induced

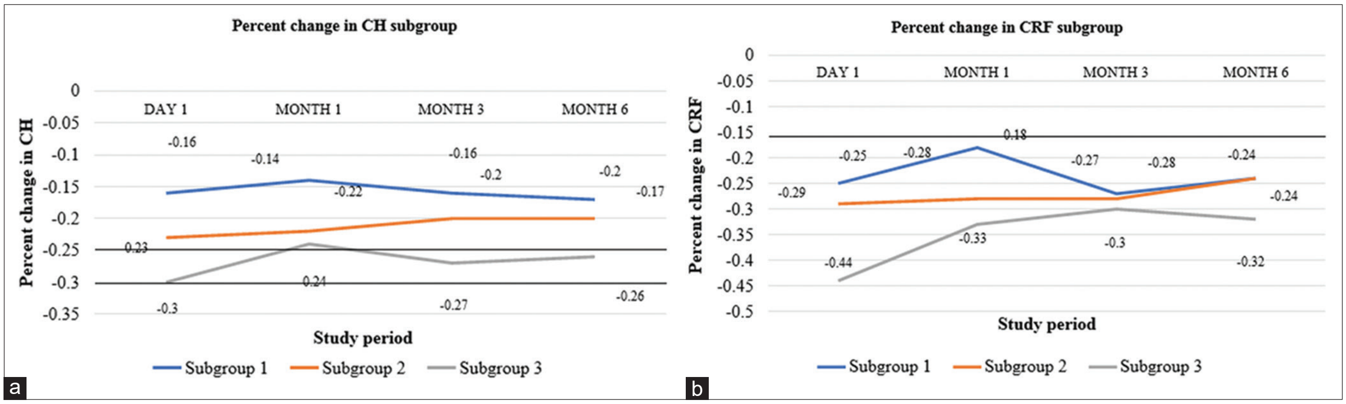

Figure 4: Graph depicting the data of percent change in corneal biomechanics: CH (a) and CRF (b) in the study subgroups

Table 5: Multiple Linear Regression Analysis for correlation between IOPg and IOPcc with preoperative study parameters (CCT, CH, CRF, and PTA)

Study variable	Day1 *r (P)	Month 1 *r (P)	Month 3 *r (P)	Month 6 *r (P)
IOPcc				
CCT	0.01 (0.23)	0.002 (0.84)	-0.001 (0.9)	-0.004 (0.7)
CRF	-0.19 (0.49	-0.17 (0.56)	0.002 (0.99)	0.24 (0.42)
CH	-0.33 (0.12)	0.003 (0.98)	-0.08 (0.71)	-0.24 (0.3)
PTA	-0.14 (0.07)	-0.07 (0.4)	-0.18 (0.04)	-0.07 (0.4)
IOPg				
CCT	0.01 (0.33)	-0.002 (0.87)	-0.006 (0.6)	-0.01 (0.2)
CRF	0.37 (0.18)	0.52 (0.12)	0.55 (0.1)	0.58 (0.08)
CH	-0.16 (0.44)	-0.35 (0.16)	-0.11 (0.66)	-0.17 (0.9)
PTA	0.08 (0.27)	0.06 (0.52)	-0.15 (0.87)	0.06 (0.4)

*r (correlation co-efficient); P (P)

biomechanical changes than the CCT, RSBT, or AD.[16,28] Hence, we evaluated the correlation of PTA to the change in ORA corneal biomechanical parameters of CH and CRF.

Chen *et al.*[27] noted a significant fall in CH and CRF at the 1-month postoperative period following LASIK. They noted a significant positive correlation of higher MRSE and ablation depth to the change in CH and CRF, however, there was no significant correlation with preoperative CCT, which suggested that CRF is perhaps a more useful indication to evaluate post-LASIK corneal biomechanical changes than CH. A comparative study on corneal biomechanical properties before and after SMILE (187 eyes) and FS LASIK (79 eyes) for myopic correction for ≤-6.00 D and >-6.00 D, noted a significantly greater decrease in CH and CRF in LASIK eyes with >6.0 D myopia, as compared to the SMILE eyes.[32] CH and CRF were observed to cause a significant decrease by 20.7% and 33.0%, respectively, after SMILE, with tissue removal of <140 μm and PTA of <25% being recommended as safe in SMILE.[33] A recent study by Khamar *et al.* described flap creation to result in more weakening as compared to the cap when measured intraoperatively. However, it was observed that the biomechanical differences between LASIK and SMILE eyes were similar after ablation for tissue removal and ongoing wound healing.[34] The decrease in corneal biomechanical parameters of CH and CRF following LASIK and PRK (with and without mitomycin C) has been reported to be similar.[35] A significant weak negative correlation between the amount of myopic correction and corneal biomechanical change has been documented after PRK and SMILE.[36] This retrospective study noted a larger biomechanical change in SMILE as compared to PRK.[36]

Most of the corneal biomechanical changes after FS-LASIK have been observed to occur within the first postoperative week, with corneal biomechanics noted to stabilize thereafter.[37] About 10% of the decrease in biomechanical parameters seems to recover by 3 months after surgery.[22] Santhiago *et al.*[16,38] described a rapidly increasing risk of post-LASIK ectasia with a PTA >35%. While high PTA values have been suggested to be consistently associated with the risk of post-LASIK ectasia in eyes with normal preoperative corneal topography, lower PTA values may be adequate to induce ectasia in eyes with a topographic abnormality.[38]

Our study explores the changes in corneal biomechanics within the recommended limit of 40% PTA and any corresponding relation between these two known effects of the intervention. It has further explored if, even within the accepted range of corneal thickness alteration, there is any differential effect depending on the quantum of change in PTA. This prospective longitudinal observational study of 80 eyes undergoing FS-flap LASIK for low to moderate myopia within the recommended range of 40% PTA, analyzed the postoperative changes in corneal biomechanics (CH and CRF) throughout 6-months follow-up (postoperative day 1, month 1, 3, and 6) and its correlation to PTA. A significant decrease in both CH and CRF noted on postoperative day-1 by 25% and 34%, respectively, persisting into the follow-up of 6 months, with CH observed to be stabilizing from the third postoperative month onwards and CRF stabilizing around the first postoperative month onwards. A greater reduction in postoperative CH and CRF (by 30% and 42%) was observed in 30 eyes (subgroup 3) which underwent FS-LASIK with the higher PTA range of 33.0–39.8% as compared to that in 14 eyes (subgroup 1) with PTA range of 23.8–26.99% (17% and25% reduction) and 36 eyes (subgroup 2) with PTA 27.00–32.99% (24% and 29% reduction). This signifies that post FS LASIK, CH, and CRF decrease is greater in myopic ablation resulting in a higher PTA that approaches closer to 40%.

Subgroup analysis in our study, noted that the corneal biomechanical alterations of both CH and CRF remain stable over

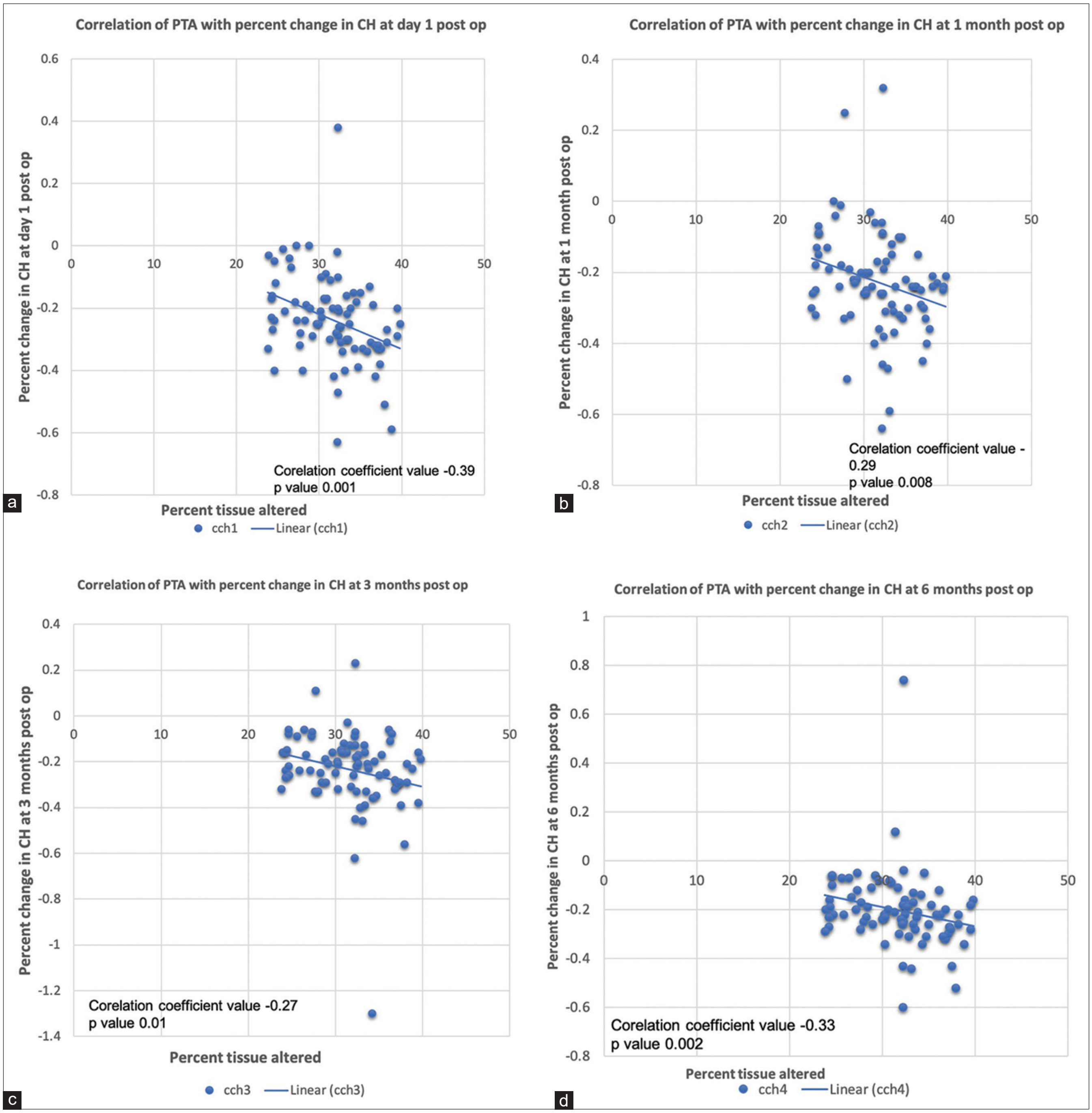

Figure 5: Graph depicting correlation analysis between percentage tissue altered and corneal hysteresis at postoperative day 1 (a), month 1 (b), month 3 (c), month 6 (d) after myopic FS LASIK ablation

the follow-up period of 6 months from first postoperative day in eyes with lower PTA (<33%; [both subgroups 1 and 2]) as opposed to eyes with high PTA approaching closer to 40% (subgroup 3) which show recovery at the first postoperative month that tends to stabilize thereafter. Though our study eyes were observed over a longer follow-up (6-months post-LASIK), as compared to those reported in the literature, a further longer follow-up would perhaps be able to throw more light on the recovery of corneal biomechanical alterations in eyes which have PTA ranges closer to 40%. With mean preoperative CCT noted to be varying significantly between the three PTA subgroups, it was interesting to note that CH values were not significantly differing while CRF was observed to show a significant difference. Our observations seem to indicate CRF, a measure of the corneal resistance to deformation, to be a better indicator of corneal biomechanics, given the display of a greater alteration postoperatively, as was reflected by Chen *et al.* as well.[27] Both CH and CRF correlated negatively with PTA (CH: [Spearman's correlation coefficient] r = -0.33, *P* = 0.002; CRF: r = -0.34, *P* = 0.001) indicating a larger decrease in corneal biomechanics with higher PTA. Clinical implications of this weak negative correlation over long-term corneal biomechanical alterations that can occur over several

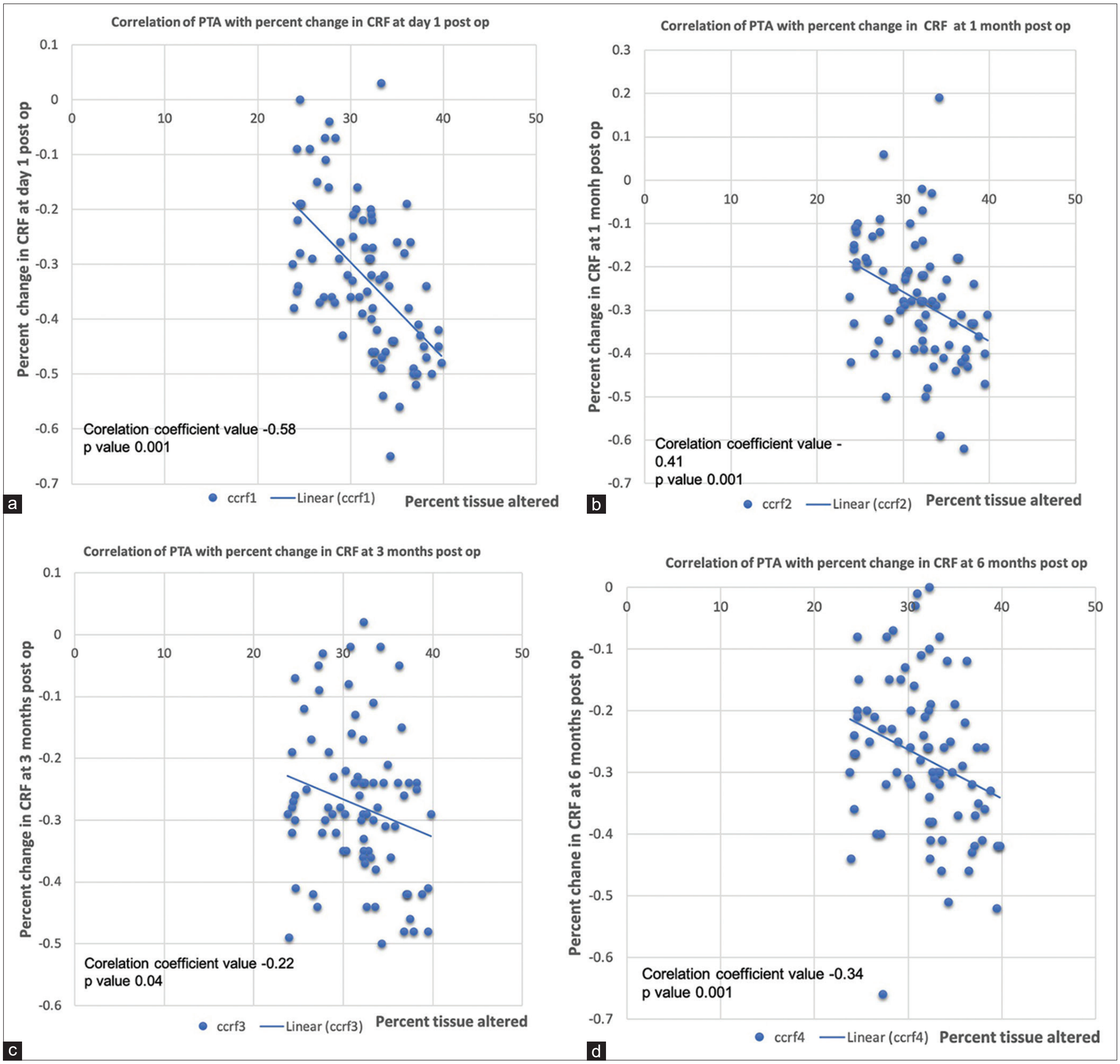

Figure 6: Graph depicting correlation analysis between percentage tissue altered and corneal resistance factor at postoperative day 1 (a), month 1 (b), month 3 (c), month 6 (d) after myopic FS LASIK ablation

years need to be further studied. However, though both CH and CRF in our study showed a higher magnitude of alteration postoperatively in eyes that had higher PTA required for larger ablations, correlation analysis in the subgroups was not possible given the smaller sample size of the subgroups.

It is becoming more evident that apart from preoperative corneal biomechanics, factors such as the amount and spatial pattern of the laser stromal ablation seem to influence the corneal resistance and viscous dissipative properties.[37] Given that PTA (flap creation and laser ablation) considers the integral relationship between CT, RSBT, and tissue altered by laser ablation and flap creation, it currently is considered to be a more customized measure of biomechanical change following corneal laser refractive procedures.[17] In eyes with normal preoperative corneal topography, high PTA seems to be the most predictive risk factor for ectasia after LASIK.[17] PTA $\geq$ 40 in LASIK is described as the single most significant independent variable with the occurrence of post-LASIK ectasia in eyes with normal corneal topography.[16]

The relationship between corneal biomechanical strain and PTA has been further explored recently with the adaption of the risk variable of PTA – percent stromal tissue altered (PTSA), which is advocated as a suitable clinical metric for risk in higher myopic treatments than in lower myopic corrections, astigmatism, and hyperopic treatments.[39] Currently, available clinical evaluation of corneal biomechanical characteristics is limited to the CH and CRF measure by the ORA and more recently available CORVIS-ST[40] which measures the corneal stiffness parameter. CRF seems to correlate with the corneal stiffness parameter.[41] It is now recognized that depending upon refractive correction required and the diameter of the optical zone used, the volume of tissue ablated can differ significantly for the same depth of ablation. Percent volume altered (PVA), a 3-dimensional metric that constitutes the theoretical volumes of the flap and tissue ablation altered during LASIK ablation is now being experimented upon as predictors scoring over PTA in influencing post-laser ablation corneal biomechanical alterations.[42]

Our prospective longitudinal study of 80 eyes of 40 patients undergoing myopic FS-LASIK with 120 μm flap for correction of mean MRSE of -3.50 ± 1.59D, observed a statistically significant decrease in corneal biomechanics (CH and CRF) with PTA ranging from 23%–39.8% (mean 31.6 ± 4.4%) with a significant weak negative correlation between PTA and CH and CRF, reflective of a greater decrease in CH and CRF with higher PTA. This study highlights the change in CH and CRF following FS-LASIK over a postoperative period of 6 months and analyzes its correlation to PTA. It provides insight with the corneal biomechanics alterations in cases of myopic LASIK ablation with PTA within the recommended safe range of 40%. It is communal knowledge that PTA >40% is predictive of the occurrence of ectasia following laser ablation, indicating a biomechanical change in the cornea that is detrimental in terms of the long-term corneal structural strength. Therefore, a long-term follow-up study with a larger sample size can perhaps throw more light on-trend of change in CH and CRF in FS-LASIK ablations with PTA >33% and its clinical implications.

Though ORA derived CH and CRF have been used in several studies, the ORA still suffers from limitations in principle as it measures the load-induced deformation at a single site of the corneal apex, which is perhaps not reflective of the entire complex corneal mechanical characteristics, such as viscoelasticity (varying stiffness with the rate of loading), anisotropy (varying stiffness with orientation), nonlinearity (varying stiffness with load), and heterogeneity (varying stiffness with location).[43] ORA measurements show good short-term repeatability in normal eyes[44] and have been described to give reproducible corneal biomechanical and IOP measurements in non-operated eyes.[45] CH and CRF are seen as poor predictors for discriminating between mild keratoconus and normal corneas (CH optimal cut-off point of 9.64 mmHg, with 87% sensitivity and 65% specificity [test accuracy, 74.83%]; CRF best cut-off point of 9.60 mmHg, with 90.5% sensitivity and 66% specificity [test accuracy, 76.97%]).[46] The hysteresis of the cornea is now being considered to be reflected in the shape of the deformation of a cornea following the application of air pulse as measured by the Corneal Visualization Scheimpflug Technology tonometer (Corvis ST tonometry: CST; Oculus, Wetzlar, Germany), that allows quantitative and visual assessment of the biomechanical properties of the central cornea. A comparative study on corneal biomechanics with ORA and CORVIS-ST concluded that both document decrease in corneal biomechanics following keratorefractive procedures.[47]

The recent Corvis ST software (version 1.3r1538) enables detailed assessment of the shape of the corneal deformation employing 37 raw parameters and by the adoption of corneal geometrical information represented by new summary parameters: deformation amplitude (DA) ratio, integrated radius, Ambrosio relational thickness to the horizontal profile (ARTh), SP A1, and Corvis biomechanical index (CBI).[43] The use of the newer evolving technology with the CORVIS-ST Scheimpflug-based dynamic measurement parameters for corneal biomechanics will also be helpful.

Conclusion

Myopic FS LASIK causes a decrease in corneal biomechanics with a significant negative correlation with PTA indicating a greater decrease in corneal biomechanics with higher PTA.

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Conflicts of interest

There are no conflicts of interest.

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