Lack of Association Between Corneal Hysteresis and Corneal Resistance Factor With Glaucoma Severity in Primary Angle Closure Glaucoma

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Purpose. We investigated the association between corneal hysteresis (CH) and corneal resistance factor (CRF) with glaucoma severity in primary angle closure glaucoma (PACG).

Methods. We recruited 204 subjects with PACG. Each subject underwent CH and CRF measurements using the Ocular Response Analyzer (ORA), optic nerve head topography measurement using scanning laser ophthalmoscopy, and visual field assessment. Glaucoma severity was based on the visual field mean deviation (MD) and classified as mild (71), moderate (55), and severe (78).

Results. The mean age ± SD of study subjects was 68.7 ± 8.9 years, with most being Chinese ($n = 186$; 91.2%). Corneal hysteresis and CRF were lowest in the severe PACG group (9.32 ± 1.86 and 9.50 ± 1.67 mm Hg) followed by moderate PACG (9.38 ± 1.88 and 9.73 ± 1.88 mm Hg) and mild PACG (9.47 ± 1.90 and 9.85 ± 1.75 mm Hg) respectively, but the differences were not significant ($P = 0.89$ and $P = 0.46$, respectively). There was a significant positive correlation between CH and central corneal thickness (CCT; correlation coefficient [r] = 0.26, $P < 0.001$), CRF and CCT ($r = 0.43$, $P < 0.001$), and negative correlation between CRF and vertical cup-disc ratio (VCDR; $r = -0.20$, $P = 0.004$), and CRF with cup-disc area ($r = -0.14$, $P = 0.04$). Corneal hysteresis and CRF were not correlated with MD ($r = 0.01$ for CH, $r = 0.1$ for CRF). After multivariate analyses, adjusting for age, sex, CCT, axial length, intraocular pressure, and number of glaucoma medication, no significant associations were noted between CH and CRF with MD, VCDR, disc area, rim area, or cup area.

Conclusions. Corneal biomechanical parameters measured by the ORA are not associated with severity of glaucoma in PACG.

Keywords: corneal hysteresis, corneal resistance factor, primary angle closure glaucoma

The Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY, USA) is an instrument that was developed to characterize the biomechanical behavior of the cornea in vivo.[1] Two corneal parameter measurements, namely corneal hysteresis (CH) and corneal resistance factor (CRF), are obtained from the ORA. Corneal hysteresis quantifies the viscoelasticity property of the cornea reflecting the tissue's capability to absorb and dissipate energy. Corneal resistance factor is a measurement of the overall resistance of the cornea.[1]

It has been suggested that the biomechanical characteristics of the cornea may reflect that of the sclera and optic disc.[2] Structural changes in the optic nerve head are reflective of glaucomatous damage. In an experimental study of 100 subjects, including 38 with glaucoma, Well et al.[3] evaluated the relationship between transient elevated IOP-induced optic nerve head surface deformation and CH. Optic nerve head deformation was determined from Heidelberg Retina Tomography (HRT) images as the average difference in the mean cup depth between baseline and during IOP elevation. Using a suction cup to artificially induce an elevated IOP, they showed that lower CH values were associated with greater deformation of optic nerve head in the glaucoma group.[3] The authors speculated that optic disc compliance, measured as the amount of deepening of the optic cup during the transient IOP rise, may be related to the CH. As the relationship was observed only in the glaucoma group, it, therefore, is likely that glaucoma patients have altered ocular tissue biomechanics.[3] Several studies have reported that CH is lower in eyes with glaucoma compared to normals.[4–6] Within the open angle subtypes, CH is reported to be lower in primary open angle glaucoma (POAG) compared to those with ocular hypertension (OHT) or glaucoma suspect.[5–7] However, within POAG itself, reports about CH differences between normal tension glaucoma (NTG) and high-tension glaucoma (HTG) have been variable. While Ang et al.[8] found higher CH among NTG, Shah et al.[4] reported lower CH when compared to HTG.

There is paucity of published data on the association of CH and CRF with primary angle closure glaucoma (PACG). In a

comparative study of ORA parameters, Narayanaswamy et al.[5] observed no significant differences in CH between POAG and PACG, but the CH was lower in POAG and PACG when compared to normal. Sun et al.[9] also reported lower CH in their study on 40 PACG subjects compared to normal controls. However, it is not known if these parameters are related to glaucoma severity in PACG. A better understanding of the corneal biomechanical properties in PACG may be useful clinically in the management of the disease.

The purpose of this study was to investigate whether the ORA corneal biomechanical parameters, CH and CRF, are associated with disease severity in subjects with PACG. Glaucoma severity was categorized according to the visual field–derived mean deviation (MD) value into mild, moderate, and severe disease.[10]

Methods

Subjects

Subjects with PACG were recruited from glaucoma clinics of the Singapore National Eye Center. The hospital's Institutional Review Board granted approval for the study. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all subjects before enrollment.

Exclusion criteria included eyes with a history of intraocular surgery, trauma, secondary glaucoma, such as uveitic or neovascular glaucoma, corneal decompensation or corneal abnormalities that prevented an accurate IOP measurement, and other nonglaucomatous optic neuropathies. Subjects with concurrent or prior use of glaucoma medications were not excluded. Each subject underwent a standardized ophthalmic examination, which included visual acuity assessment, slit-lamp examination, stereoscopic evaluation of the optic disc using a 78-diopter lens (Volk Optical, Inc., Mentor, OH, USA), IOP measurement with Goldmann applanation tonometry (IOP-GAT; Haag-Streit, Koniz, Switzerland), automated refraction, and keratometry (Canon RK 5 Auto Ref-Keratometer; Canon, Inc., Ltd., Tochigiken, Japan). Spherical equivalent was defined as sphere plus half cylinder. A-scan ultrasonography (Model US-800; Nidek Co., Ltd., Tokyo, Japan) was used to measure axial length (AL), anterior chamber depth (ACD), and lens thickness (LT). Optic nerve head topography were measured using scanning laser ophthalmoscopy (Heidelberg retina tomography; Heidelberg Engineering, Heidelberg, Germany). Gonioscopy was performed by an experienced examiner in the dark using a Goldmann 2-mirror lens (Haag-Streit AG) at ×16 magnification. Indentation gonioscopy was carried out using a Sussman 4-mirror lens (Ocular Instruments, Inc., Bellevue, WA, USA) to establish the presence and degree of peripheral anterior synechiae (PAS). Angle closure was defined as eyes in which at least 180° of the posterior pigmented trabecular meshwork was not visible on gonioscopy in the primary position of gaze without indentation.

We diagnosed PACG on the basis of angle closure with glaucomatous optic neuropathy[11] (defined as vertical cup-to-disc [VCDR] ratio of >0.7, CDR asymmetry >0.2, and/or focal notching), with compatible visual field loss on static automated perimetry (SITA Standard algorithm with a 24-2 test pattern; Humphrey Visual Field Analyser II; Carl Zeis Meditec, Dublin, CA, USA). This was defined as Glaucoma Hemifield Test outside normal limits; a cluster or 3 or more, nonedge, contiguous points on the pattern deviation plot, not crossing the horizontal meridian with a probability of <5% being present in age-matched normals (one of which was <1%); and an abnormal pattern standard deviation (PSD) with $P < 5\%$ occurring in the normal population, and fulfilling the test reliability criteria (fixation losses < 20%, false-positives < 33%, and/or false-negatives < 33%). Severity of glaucoma was determined from the visual field MD. Severity was categorized as mild (MD > −6 dB), moderate (MD −6.01 to −12 dB), and severe (<−12.01 dB).[10]

All participants underwent testing with the ORA (Reichert Ophthalmic Instruments).[1] The ORA uses a noncontact rapid air pulse to generate a signal. The ORA signal depicts 2 IOP measurements, P1 and P2. The average of P1 and P2 is a measure of the Goldmann-correlated IOP (IOPg). The difference between P1 and P2 is the CH, and is an indicator of the viscous properties of the cornea. The ORA also provides measurement of CRF, which is an indicator of the overall "resistance" or elastic properties of the cornea. Corneal compensated IOP (IOPcc) is generated by the software and represents IOP less influenced by corneal tissue properties. One eye of each eligible subject was evaluated; when both eyes are eligible, the worse eye based on MD value was included. Each eye had an average of 4 to 6 sequential measurements by ORA and 3 good-quality ORA signals were saved, based on the criteria set by the manufacturer (i.e., measurements with split signals, low amplitude, and asymmetrical shape were not saved). This was followed by the IOP measurements by GAT (GAT-IOP) at least 15 minutes after the ORA measurements. All PACG eyes had undergone laser peripheral iridotomy before recruitment into the study. None of the PACG eyes had undergone previous intraocular surgery.

Statistical Analysis

Statistical analysis was performed using the statistical package IBM SPSS Statistics for Windows (Version 22.0; IBM Corp., Armonk, NY, USA). One eye of each subject was analyzed. Comparisons of ocular characteristics and ORA parameters between the PACG severity subgroups were performed using 1-way ANOVA. Intergroup differences in mean values of variables were analyzed using post hoc Bonferroni tests. Correlation of continuous data variables was analyzed using the Pearson correlation test (2-sided). Multivariate linear regression analysis was performed to evaluate the association between ORA parameters (CH and CRF) with disease severity, namely visual field indices (MD, PSD), VCDR, and optic disc parameters. Significance was set at $P < 0.05$ for this study. By assuming a mean difference in CH of 1.0 mm Hg and a standard deviation of 1.7 mm Hg between confirmed and suspect glaucoma,[7] with a power of 81% and α of 5%, the sample size for a 2-sided test was 46 in each group. Additionally, for an analysis of covariance comparing 3 groups (third group mean was assumed as being intermediate of confirmed and suspect glaucoma)[7] with 6 covariates and a combined R^2 of 0.05, the total sample required is 162 with 54 in each group to achieve 81% power and α 5% to detect differences among the means.

Results

We recruited 204 subjects; 71 were categorized as having mild, 55 as moderate, and 78 as severe PACG based on MD. Most were of Chinese ethnicity ($n = 186$; 91.2%), and there were more males ($n = 106$; 51.9%). The subjects' ages ranged from 43 to 96 years, and the mean age was 68.1 years (SD, 8.9 years).

The demographic and ocular characteristics of the three groups are shown in Table 1. There was no statistical difference in the mean age ($P = 0.29$) or duration of disease ($P = 0.85$). The proportion of females was lowest in the severe PACG group ($P = 0.04$). The PSD ($P < 0.001$), VCDR ($P < 0.001$), and cup area ($P = 0.003$) were largest in the severe

Table 1. Demographics and Ocular Characteristics of Subjects With PACG, Stratified According to Severity

Characteristic	Mild PACG, $N = 71$	Moderate PACG, $N = 55$	Severe PACG, $N = 78$	*P* Value
Age, y	69.8 ± 8.0	68.2 ± 10.0	67.5 ± 8.7	0.29
Female, *N* (%)	42 (59.2)	26 (47.3)	30 (38.6)	0.04
Race (Chinese), *N* (%)	65 (91.5)	48 (87.3)	73 (93.6)	0.52
Age at diagnosis, y	66.0 ± 7.8	64.3 ± 9.6	63.5 ± 8.7	0.22
Duration of disease, y	3.77 ± 2.31	4.06 ± 2.69	3.97 ± 3.33	0.85
Spherical equivalent, D	0.65 ± 2.00	−0.17 ± 2.77	0.26 ± 2.30	0.18
Axial length, mm	22.91 ± 0.77	23.14 ± 0.95	23.09 ± 1.06	0.34
ACD, mm	2.77 ± 0.52	2.78 ± 0.50	2.72 ± 0.41	0.7
Lens thickness, mm	4.44 ± 0.87	4.35 ± 0.93	4.49 ± 0.82	0.67
Baseline IOP, mm Hg	23.81 ± 12.26	21.32 ± 7.25	27.10 ± 12.66	0.05
IOP-GAT, mm Hg	16.62 ± 4.60	16.20 ± 4.22	15.95 ± 4.18	0.64
Mean deviation, dB	−3.94 ± 1.36	−8.33 ± 1.67	−20.04 ± 6.52	<0.001
Pattern standard deviation, dB	3.82 ± 2.02	7.42 ± 2.69	10.31 ± 2.85	<0.001
Vertical cup-disc ratio	0.73 ± 0.12	0.77 ± 0.10	0.83 ± 0.11	<0.001
Disc area, mm^2	2.52 ± 0.53	2.60 ± 0.60	2.46 ± 0.44	0.33
Cup area, mm^2	1.13 ± 0.53	1.42 ± 0.75	1.44 ± 0.53	0.003
Rim area, mm^2	1.37 ± 0.42	1.16 ± 0.41	1.03 ± 0.40	<0.001
Cup-disc ratio area	0.44 ± 0.16	0.53 ± 0.19	0.57 ± 0.17	<0.001
Cup-disc ratio linear	0.65 ± 0.13	0.71 ± 0.15	0.75 ± 0.13	<0.001

PACG group. Disc area was not significantly different among the three groups ($P = 0.33$).

Corneal parameters and ORA are compared in Table 2. The IOPcc, CH, and CRF decreased with worsening severity of glaucoma, albeit not significantly ($P = 0.82$, $P = 0.89$, and $P = 0.46$ respectively). Corneal central thickness (CCT; $P = 0.35$) and corneal curvature ($P = 0.41$) were not significantly different between the three groups. Corneal hysteresis measurements also were not significantly different even after adjusting for age, sex, CCT, and IOP-GAT ($P = 0.75$).

Figures 1 to 3 are scatterplots depicting the bivariate correlation between ORA parameters (CH and CRF) versus visual field MD, VCDR, and CCT, respectively. Table 3 demonstrates the Pearson correlations of CH and CRF with the optic disc and visual field parameters in the three groups. There was a significant positive correlation between CH and CCT (correlation coefficient [r] = 0.26, $P < 0.001$), CRF and CCT ($r = 0.43$, $P < 0.001$), and negative correlation between CRF and VCDR ($r = -0.20$, $P = 0.004$), CRF and cup-disc area ($r = -0.14$, $P = 0.04$), and CRF and cup-disc ratio ($r = -0.15$, $P = 0.04$). Corneal hysteresis and CRF were not correlated with MD ($r = 0.01$ for CH, $r = 0.1$ for CRF) or PSD ($r = 0.003$ for CH and $r = 0.06$ for CRF). A negative correlation was found between age and CH and CRF; however, the correlation was not significant ($P = 0.06$ and $P = 0.38$, respectively). Men had lower mean CH (9.2 vs. 9.5 mm Hg) and CRF (9.5 vs. 9.9 mm Hg) than women, although these differences were not statistically significant.

In multivariable regression analysis adjusting for age, sex, CCT, IOP-GAT, and AL, no significant relationship was observed between the ORA parameters (CH and CRF) with visual field indices (MD and PSD), VCDR, and structural disc parameters ($P > 0.05$ for all; Table 4). The findings were similar when the analyses were performed separately for each of the three PACG severity groups (data not shown).

Discussion

In this cross-sectional study of PACG subjects, we did not detect significant associations between the corneal biomechanical parameters, namely CH and CRF, with markers of PACG disease severity, including the visual field indices, MD, and PSD, and structural optic disc features. The ORA-based corneal biomechanical parameters, although significantly lower in glaucoma eyes (including PACG) compared to normals,[4–6,8] do not appear to be related to disease severity within PACG subjects. Our findings of the significant associations between CH and CRF with CCT are comparable with the findings in eyes with POAG.[5,7,12,13]

It has been speculated that corneal biomechanical properties could reflect the structural vulnerability of the optic nerve head to develop glaucoma.[3] Corneal hysteresis, but not CCT, was observed to be associated with optic disc surface deformation during transient elevations of IOP. The authors surmised the possibility that CH could serve as a surrogate marker to assess for glaucoma risk and pathogenesis.[3] Several studies have investigated the effect of corneal biomechanical parameters on disease severity and progression, though mainly

Table 2. Comparison of ORA and Corneal Parameters in Subjects With PACG, Stratified According to Severity

	Mild PACG, $N = 71$	Moderate PACG, $N = 55$	Severe PACG, $N = 78$	*P* Value
Corneal hysteresis, mm Hg	9.47 ± 1.90	9.38 ± 1.88	9.32 ± 1.86	0.89
Corneal resistance factor, mm Hg	9.85 ± 1.75	9.73 ± 1.88	9.50 ± 1.67	0.46
IOPcc	17.65 ± 5.20	17.55 ± 4.98	17.15 ± 5.08	0.82
IOPg	16.26 ± 4.79	16.24 ± 4.68	15.50 ± 4.62	0.54
Adjusted CH*	9.52 (9.09, 9.94)	9.37 (8.89, 9.85)	9.29 (8.89, 9.70)	0.75
CCT, μm	539.91 ± 36.78	544.43 ± 36.10	534.96 ± 36.48	0.35
Corneal curvature	7.63 ± 0.24	7.68 ± 0.28	7.68 ± 0.24	0.41

IOPgL, Goldmann-correlated IOP.

* Adjusted for age, sex, CCT, and IOP-GAT (IOP by Goldmann applanation tonometry).

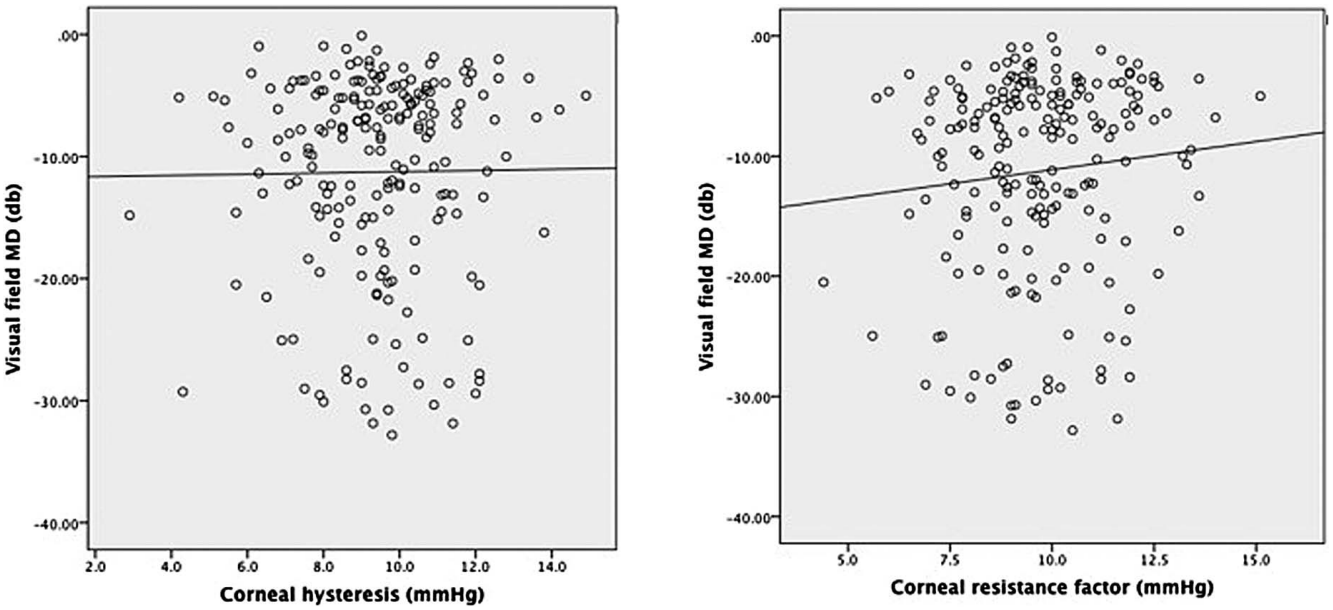

Figure 1. Correlation between corneal hysteresis and corneal resistance factor with visual field mean deviation.

in relation to open angle glaucoma.[7,14–17] In a cross-sectional study involving 151 glaucoma suspects and 148 glaucoma eyes,[7] Mansouri et al.[7] found that after adjusting for demographic and ocular parameters, only the CRF was independently associated with visual field indices, MD, and PSD, but not CH. They explained that as the CRF is an empirically derived measurement of the overall elastic property of the cornea, whereas CH represents the viscous properties, therefore, the elastic properties of the cornea are better related to glaucoma damage.[7] Anand et al.[14] explored the association between corneal biomechanical parameters and asymmetric POAG. Visual field asymmetry was defined as a five-point difference between the eyes using the Advanced Glaucoma Intervention Study (AGIS) scoring system. In contrast to the findings of Mansouri et al.,[14] they observed significant independent association between lower CH with the eye with worse AGIS scores (odds ratio, 25.9; 95% confidence interval, 10.1–66.5).[14] Several other studies also have demonstrated the association between lower CH and glaucomatous damage and disease progression, but mainly in relation to POAG and its subtypes.[15–17] We noted only modest Pearson correlations (–0.15 to –0.20) between CRF and VCDR (clinical and HRT) in our subjects. Although Vu et al.[18] showed similar weak associations ($r = -0.11$ to -0.15) of VCDR with CH, they did not report on the association with CRF. Likewise, Prata et al.[19] demonstrated significant correlations with mean cup depth ($r = -0.34$) and linear cup-disc ratio ($r = -0.41$) in their evaluation of 42 newly diagnosed POAG patients. They suggested that the reduced viscous damping of the cornea, as represented by a low CH, reflects an increased likelihood of deformability of the ONH complex.[19]

The present study on PACG eyes found no association between disease severity and either CH or CRF. Our study comprised exclusively of subjects with established glaucoma

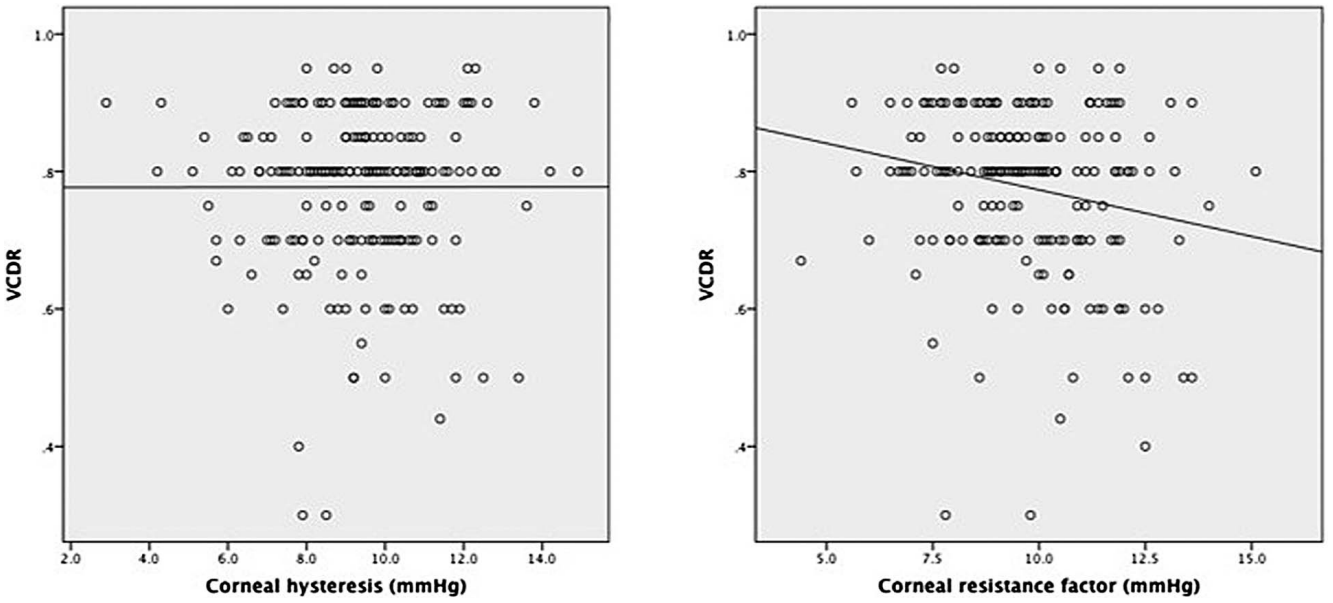

Figure 2. Correlation between corneal hysteresis and corneal resistance factor with VCDR.

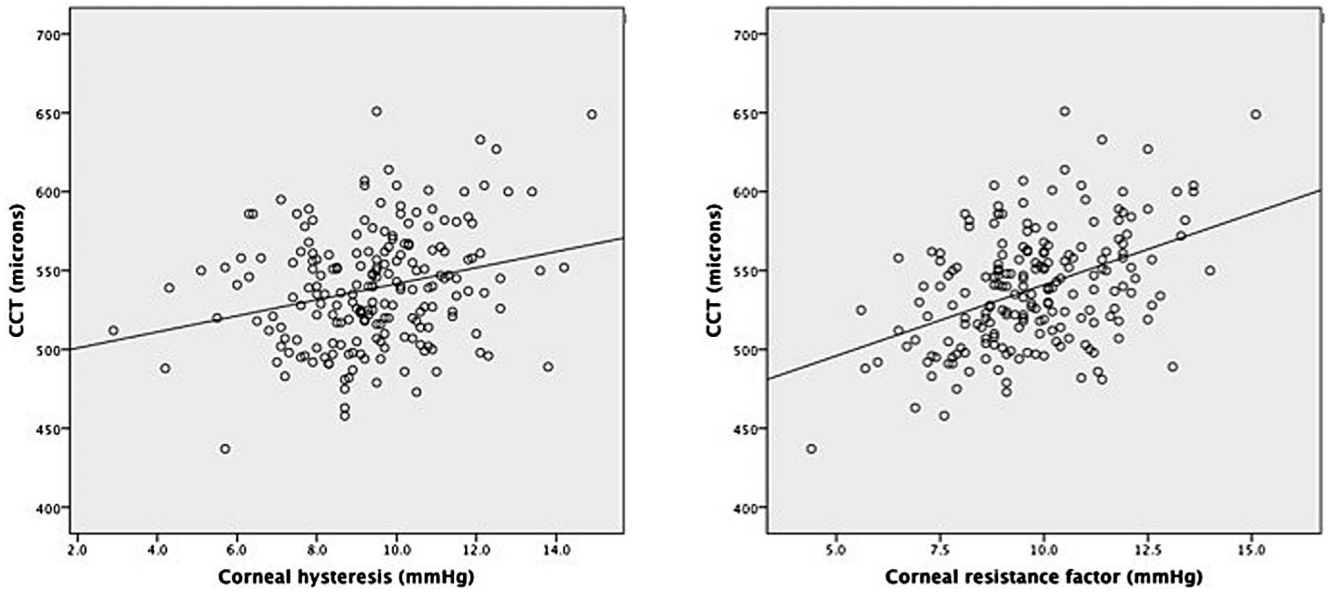

FIGURE 3. Correlation between corneal hysteresis and corneal resistance factor with CCT.

unlike the previous published studies that have included a wider range of subjects encompassing glaucoma suspects and established glaucoma.[7,14,15,18] The wider spectrum in those studies could have resulted in a higher disposition toward an association with disease severity. Therefore, it is likely that an inclusion of angle closure subjects with no evidence of optic neuropathy, such as primary angle closure suspects (PACS) and primary angle closure (PAC), may tilt our findings toward significant associations; however, the primary purpose of our study was to investigate the association of corneal biomechanical properties in PACG subjects with established optic nerve head damage. Another potential reason for the disparate findings between POAG and PACG could be the possibility of an inherent difference in the underlying mechanisms involved in the pathogenesis of glaucomatous optic neuropathy in the two disease entities. It also is likely that the same factors may influence optic nerve head vulnerability to different extents in the two disease processes. It is important to note that our and the published cross-sectional studies were only designed to assess for associations and not determine causality. Furthermore, the modest associations between CH and CRF with structural and functional characteristics suggest that other factors yet to be identified may explain a larger proportion of individual susceptibility of the ONH. Further exploratory experiments are necessary to demonstrate the existence of such factors and differences, if any, in pathogenesis of glaucomatous optic neuropathy in POAG and PACG. The ORA is the only commercially-available technology to provide some measures of corneal biomechanics in vivo.[20] Although being available for clinical use, the ORA suffers from limitations: it measures the load-induced deformation at only one single site (i.e., the apex) of the cornea; corneal viscoelasticity (indicated by the CH) and corneal rigidity (indicated by the CRF) are only evaluated each by a single-value parameter, which grossly approximates the bulk tissue behavior. The cornea is, in fact, more complex as it exhibits mechanical characteristics, such as viscoelasticity (varying stiffness with rate of loading), anisotropy (varying stiffness with orientation), nonlinearity (varying stiffness with load), and heterogeneity (varying stiffness with location). We are currently developing improved engineering-based methodologies to characterize the complex biomechanical characteristics of the cornea in vivo (Girard MJA et al. *IOVS* 2015;56:ARVO E-Abstract 1099). Such techniques will be able to be used in the near future with PACG patients.

TABLE 3. Pearsons Correlation Between CH and CRF With Other Variables

	Overall Pearson Correlation (*P* Value)		Mild PACG Pearson Correlation (*P* Value)		Moderate PACG Pearson Correlation (*P* Value)		Severe PACG Pearson Correlation (*P* Value)	
	CH	CRF	CH	CRF	CH	CRF	CH	CRF
Age	−0.13 (0.06)	−0.06 (0.38)	−0.06 (0.61)	−0.16 (0.20)	−0.33 (0.01)	−0.17 (0.22)	−0.02 (0.86)	0.03 (0.81)
Cup Area	−0.02 (0.80)	−0.13 (0.06)	−0.02 (0.90)	−0.16 (0.19)	−0.14 (0.30)	−0.28 (0.04)	0.13 (0.26)	0.07 (0.52)
Rim Area	0.06 (0.41)	0.13 (0.06)	−0.04 (0.76)	−0.02 (0.88)	0.00 (1.00)	0.18 (0.18)	0.18 (0.11)	0.22 (0.06)
Cup-disc ratio	−0.03 (0.62)	−0.15 (0.04)	0.02 (0.85)	−0.09 (0.45)	−0.08 (0.58)	−0.30 (0.03)	−0.03 (0.77)	−0.04 (0.75)
Cup-disc area	−0.04 (0.60)	−0.14 (0.04)	0.02 (0.87)	−0.08 (0.52)	−0.09 (0.52)	−0.28 (0.04)	−0.03 (0.83)	−0.05 (0.66)
MD	0.01 (0.87)	0.10 (0.16)	−0.003 (0.98)	0.10 (0.43)	0.16 (0.23)	0.09 (0.53)	−0.08 (0.47)	0.05 (0.69)
PSD	−0.003 (0.97)	−0.07 (0.34)	0.17 (0.15)	0.08 (0.53)	0.16 (0.25)	0.004 (0.98)	−0.14 (0.22)	−0.07 (0.57)
AL	0.04 (0.59)	−0.04 (0.59)	0.05 (0.65)	−0.06 (0.63)	0.17 (0.22)	0.07 (0.60)	−0.04 (0.72)	−0.08 (0.52)
CCT	0.26 (<0.001)	0.43 (<0.001)	0.22 (0.08)	0.40 (0.001)	0.37 (0.007)	0.52 (<0.001)	0.21 (0.07)	0.43 (<0.001)
IOP	−0.30 (<0.001)	0.36 (<0.001)	−0.25 (0.03)	0.40 (0.001)	−0.38 (0.005)	0.29 (0.04)	−0.32 (0.004)	0.32 (0.005)
VCDR	0.001 (0.99)	−0.20 (0.004)	0.01 (0.91)	−0.21 (0.08)	−0.04 (0.79)	−0.41 (0.002)	0.06 (0.59)	−0.05 (0.67)

Table 4. Multiple Linear Regression for Associations Between Demographics, CH, and CRF With Visual Field Indices and Optic Disc Parameters

	MD B (*P* Value)	PSD B (*P* Value)	VCDR B (*P* Value)	Disc Area B (*P* Value)	Rim Area B (*P* Value)	Cup Area B (*P* Value)	Cup-Disc Ratio B (*P* Value)
For corneal hysteresis							
CH	0.01 (0.98)	−0.15 (0.49)	−0.006 (0.45)	0.01 (0.74)	0.002 (0.88)	0.004 (0.91)	0.004 (0.65)
CCT	0.02 (0.46)	−0.02 (0.09)	0.00 (0.53)	0.001 (0.55)	0.002 (0.18)	−0.001 (0.66)	−0.001 (0.07)
IOP-GAT	0.18 (0.34)	−0.02 (0.80)	−0.003 (0.27)	−0.02 (0.23)	0.004 (0.71)	−0.02 (0.17)	−0.004 (0.27)
AL	−0.84 (0.35)	0.16 (0.67)	0.04 (0.005)	−0.04 (0.58)	−0.01 (0.85)	−0.02 (0.75)	−0.001 (0.93)
No. of medications	−2.67 (0.004)	0.25 (0.53)	0.04 (0.001)	0.06 (0.36)	−0.04 (0.42)	0.11 (0.12)	0.03 (0.06)
For corneal resistance factor							
CRF	−0.01 (0.98)	−0.01 (0.98)	−0.001 (0.84)	0.02 (0.64)	−0.003 (0.89)	0.02 (0.68)	0.004 (0.62)
CCT	−0.02 (0.04)	−0.02 (0.04)	0.00 (0.34)	0.001 (0.53)	0.002 (0.12)	−0.001 (0.58)	−0.001 (0.07)
IOP-GAT	−0.04 (0.62)	−0.04 (0.62)	−0.004 (0.15)	−0.01 (0.33)	0.004 (0.69)	−0.02 (0.21)	−0.003 (0.41)
AL	0.18 (0.64)	0.18 (0.64)	0.04 (0.005)	−0.03 (0.59)	−0.01 (0.84)	−0.02 (0.77)	−0.001 (0.94)
No. of medications	0.26 (0.50)	0.26 (0.50)	0.04 (0.001)	0.02 (0.64)	−0.04 (0.41)	0.12 (0.12)	0.03 (0.06)

Our study comprised subjects with established PACG. Hence, the CH value may have been affected by IOP lowering medications. We have tried to adjust for the medication effect in our multivariate analysis by incorporating IOP-GAT measurements and the number of current IOP lowering medications into the models. However, the possibility remains that the treatment effect may have still biased our findings.

The strengths of the study include the relatively large sample size, which was adequately powered to detect significant differences in ORA parameters based on previously published data on POAG. The study encompassed a wide range of visual field damage and the subjects were categorized into three groups based on their MD.[10] All study-related measurements of IOP, ORA, HVF, and HRT were obtained on the same day for all subjects. One of the main limitations is the cross-sectional nature of the study, which could only assess associations and not causality. Long-term prospective studies in angle closure disease are needed to better explore the relationship between baseline CH and CRF parameters and the likelihood of progression. Difference in the treatment may have affected measurements of CH and CRF. We have tried to minimize the effect by only including subjects who have not undergone any intraocular surgical procedure. The subjects were on multiple combinations of IOP-lowering medications.

In summary, this study investigated the relationship between corneal biomechanical properties CH and CRF, with markers of glaucoma severity including visual field indices and optic disc parameters in PACG subjects. The lack of association suggests that the ORA corneal biomechanical parameters may not be useful clinically in the management of PACG.

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