Clinical Optometry

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ORIGINAL RESEARCH

Corneal Hysteresis in Thais and Variation of Corneal Hysteresis in Glaucoma

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Purpose: To collect the normal value data of corneal hysteresis in Thais and study the variation of corneal hysteresis in glaucomatous eyes.

Methods: Retrospective cross-sectional study of corneal hysteresis (CH) in healthy non-glaucomatous and glaucomatous eyes. Demographic data, type and staging of glaucoma, Goldmann applanation tonometry (GAT) and ocular response analyzer parameters; CH, corneal-compensated intraocular pressure (IOPcc) and Goldmann-correlated intraocular pressure (IOPg) were collected.

Results: Data from one eye of 465 normal participants were included for the normal value data of CH. Mean CH, IOPcc and IOPg were 10.18 ± 1.48, 15.01 ± 3.04 and 14.16 ± 3.06 mmHg, respectively. Average age was 57.21 ± 14.4 years. CH at the fifth percentile was 8.0 mmHg. Women had significantly higher CH than men (10.29 ± 1.46 vs 9.90 ± 1.49 mmHg, p=0.009). Moderate negative correlation was found between age and CH, $r = -0.338$, p<0.001. There were 695 glaucomatous eyes from 429 patients including primary-open angle glaucoma (POAG), primary close-angle glaucoma (PACG), normal tension glaucoma (NTG) and ocular hypertension (OHT). CH in each glaucoma type and severity stage (early, moderate and severe) were as follows: POAG: 8.74 ± 1.52 mmHg (9.22 ± 1.47, 8.74 ± 1.23 and 7.92 ± 1.40 mmHg, p<0.001), PACG: 9.09 ± 1.72 mmHg (9.85 ± 1.45, 9.04 ± 1.68 and 8.45 ± 1.74 mmHg, p= 0.004), NTG: 9.55 ± 1.67 mmHg (9.47 ± 1.38, 9.75 ± 2.42 and 9.77 ± 1.34 mmHg, p 0.525) and OHT: 10.10 ± 1.40 mmHg.

Conclusion: Compared with normal value data of corneal hysteresis, CH in glaucomatous eyes was lower. The more advanced glaucoma stage was associated with lower CH. Arising from normal value data, a low percentile of CH could be applied as the deviation value from normal and this dynamic property of CH could represent a glaucoma predictor in an effort to improve glaucoma care.

Keywords: corneal hysteresis, CH, corneal-compensated intraocular pressure, IOPcc, Goldmann-correlated intraocular pressure, IOPg, glaucoma, normative database, ocular biomechanics

Introduction

Causes of glaucoma apart from intraocular pressure–related optic nerve head damage were studied: for example, ocular microcirculation and perfusion impairment, lower cerebrospinal fluid pressure–related optic nerve damage, translaminar pressure gradient and ocular biomechanics–related optic neuropathy.[1–6] The variation of the ocular biomechanical properties is highlighted as one of the potential optic nerve damage pathologies. This property may fill the gap of knowledge among cases with different disease progression despite similarity in other risk factors.[7,8]

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Received: 29 June 2021
Accepted: 16 September 2021
Published: 1 October 2021

Corneal hysteresis (CH) is an easily measurable ocular biomechanical parameter. It refers to the property of corneal tissue absorbing and dispersing energy applied by a force. This dynamic property is shown as the cornea recoiling its shape. Measuring the corneal hysteresis is applicable and repeatable. Variation of corneal hysteresis is found among different races and ages.[9–11] Detry-Morel et al reported lower CH in those of African descent compared with European descent.[9] In younger European groups, Bueno-Gimeno et al found higher CH compared with older groups,[10] similar to the result from Kamiya et al who studied those of Asian descent.[11] Lower CH in glaucomatous eyes and keratoconic eyes than in normal eyes was also reported.[12–14]

This study aims at collecting the normal value data of corneal hysteresis and comparing corneal hysteresis between different glaucoma types and severity in Thai glaucoma patients.

Materials and Methods

This was a retrospective cross-sectional study of ocular hysteresis approved by the Mettapracharak (Wat Rai Khing) research ethics committee in accordance with the International Conference on Harmonization Good Clinical Practice (ICH-GCP) COA No 003/2563. Patients' consent to review their medical records was not required by the ethics committee. All privacy data including hospital number, name, and date of birth were masked and kept confidentially in compliance with the Declaration of Helsinki. The data of patients who visited the ophthalmology clinic and glaucoma clinic of Dr KR at Mettapracharak (Wat Rai Khing) hospital from January to March 2020 were included. Corneal hysteresis was measured by the Reichert® Ocular Response Analyzer® G3, non-contact air puff tonometer. Three results were reported: ocular response analyzer parameters; corneal hysteresis (CH), corneal-compensated intraocular pressure (IOPcc), and Goldmann-correlated intraocular pressure (IOPg). The data were excluded if the waveform score (WS) was below 3.5 suggesting too low reliability of the measurement.[15,16]

The inclusion criteria for normative data were the right eye or the only reliable eye of patients who presented with ocular diseases; for example, dry eye syndrome, refractive errors and senile cataracts whose visual acuity was better than 20/70, healthy optic nerve appearance and intraocular pressure below 22 mmHg. The exclusion criteria for normative data were glaucomatous optic neuropathy, glaucoma suspected optic disc, primary angle closure suspect, corneal pathology and post-refractive surgery eyes. In glaucomatous groups, data were collected from both eyes of patients. The inclusion criteria were primary open-angle glaucoma (POAG), primary close-angle glaucoma (PACG), ocular hypertension (OHT), and normal tension glaucoma (NTG). The exclusion criteria were corneal pathology and post-refractive surgery eyes. Demographic data from both groups were collected, for example, age, sex, type of glaucoma and severity staging of glaucoma classified by the visual field's mean deviation (MD) into early, moderate, and severe following Hodapp-Parrish-Anderson glaucoma staging.[17,18]

Statistical Analysis

The data were analyzed by JASP 0.14.1. Descriptive statistics were applied to describe demographic data and results. Categorical data such as the differences of sexes between normal and glaucomatous groups, and within the glaucoma severity group, were tested by Chi-squared test, whereas continuous data such as age, method of treatment, and amount of anti-glaucoma medication were tested by one-way analysis of variance (ANOVA) and post hoc analysis by Bonferroni test. Differences of ocular response analyzer parameters in normative data between men and women were tested by Student's *t*-test. The Pearson correlation coefficient was applied to test the correlation of ocular response analyzer parameters between age and both eyes of the same person. The association between age and CH was tested by linear regression analysis. The generalized estimating equation (GEE) was applied to assess the difference of ocular response analyzer parameters and GAT between different types and severity of glaucoma. Statistical significance was set as $p<0.05$.

Results

A total of 465 eyes from 465 normal participants met the inclusion criteria for the normative data of ocular response analyzer parameters (Table 1). Average age was 57.21 ± 14.4 years, range between 14 and 87 years. Although women were predominantly included, mean ages between women and men were not different. Average CH, IOPcc, and IOPg were 10.18 ± 1.48 mmHg, 15.01 ± 3.04 mmHg, and 14.16 ± 3.06 mmHg, respectively. The corneal hysteresis showed a normal distribution (Figure 1A), CH at the 2.5th and 5th percentile were 7.4 and 8.0 mmHg, respectively. The IOPcc and IOPg also showed a normal distribution (Figure 1B and C), IOPcc at the 97.5th and the 99th percentile were 21.00 and 22.1 mmHg, and IOPg at the

Table 1 Demographic and Normative Data of Ocular Response Analyzer Parameters in Thais

	Women 327 Persons	Men 138 Persons	p value, 95% CI for Mean Difference
Eyes -Right (426 eyes) -Left (421 eyes)	465 Eyes 426 39		
Age (years)	57.21 ± 14.43 (14–87)		
	56.51 ± 14.92 (14–87)	58.88 ± 13.09 (26–85)	p=0.16 [−5.25, 0.5]
Corneal hysteresis (CH) (mmHg) −1st, 2.5th and 5th percentile −95th, 97.5th and 99th percentile	10.18 ± 1.48 (5.2–16.80) 6.7, 7.40 and 8.0 12.58, 13.10 and 13.94		
	10.29 ± 1.46	9.90 ± 1.49	p=0.009 [0.10, 0.69]
Corneal-compensated intraocular Pressure (IOPcc) (mmHg) −1st, 2.5th and 5th percentile −95th, 97.5th and 99th percentile	15.01 ± 3.04 (6.50–23.10) 8.36, 9.50, 10.40 20.08, 21.00, 22.1		
	14.9 ± 3.03	15.27 ± 3.04	p=0.229 [−0.98, 0.23]
Goldmann-correlated intraocular pressure (IOPg) (mmHg) −1st, 2.5th and 5th −95th, 97.5th and 99th	14.24 ± 3.24 (5.80–24.10) 6.73, 7.70, 8.60 18.90, 19.54, 20.50		
	14.18 ± 3.08	14.11 ± 3.00	p=0.827 [−0.54, 0.68]
Waveform score (WS)	6.6 (1.78)		

Note: Student's *t*-test.

97.5th and the 99th percentile were 19.54 and 20.50 mmHg, respectively. Women had significantly higher CH than men at 10.29 ± 1.46 vs 9.90 ± 1.49 mmHg, p=0.009, 95% CI [0.10, 0.69] while IOPcc and IOPg between sexes were not different (Figure 2).

Moderate negative correlation was found between age and corneal hysteresis analyzed by Pearson's correlation coefficient $r = -0.338$, p<0.001, 95% CI [−0.416, −0.255] (Figure 3A). Meanwhile, the correlation between age and IOPcc (r =0.110, p=0.024, 95% CI [0.020, 0.199]) and age and IOPg (r=−0.064, p= 0.139, 95% CI [−0.155, 0.027]) was not detected. Regression analysis between CH and age was CH = 12.162–0.035 (age). Ocular response analyzer parameters between eyes of the same person were similar (CH: r = 0.667, p<0.001, IOPcc: r=0.655, p <0.001. IOPg: r=0.698, p<0.001). Regression analysis between ocular response analyzer was IOPcc = 13.35 + 0.86 (IOPg) – 1.02 (CH). IOPcc and IOPg correlated highly positively, r=0.835, p<0.001. IOPcc was significantly higher than IOPg, and the mean difference was 0.97 mmHg, p<0.001, 95% CI [0.854, 1.086]. IOPcc and CH showed strong negative correlation, r=−0.459, p<0.0001, 95% CI [−0.510,-0.404] while IOPg and CH did not, r=0.067, p=0.057, 95% CI [−0.00, 0.134] (Figure 3B).

There were 695 eyes from 429 patients including primary open-angle glaucoma (POAG) 434 eyes from 272 patients; primary close-angle glaucoma (PACG) 74 eyes from 48 patients; normal tension glaucoma (NTG) 143 eyes from 79 patients; ocular hypertension (OHT) 44 eyes from 30 patients. The OHT group was the youngest group, while the average ages between OAG, ACG, and NTG were similar. Following risk factors of specific glaucoma type, women were observed more frequently than men in the PACG and NTG groups. Glaucoma treatment options were also different between groups. All patients in the POAG and NTG groups received treatments and the most frequently prescribed anti-glaucoma medication was prostaglandin analogues. Phacoemulsification was performed in 29 of 74 eyes (39.2%) of the PACG group. Average numbers of anti-glaucoma medications were between 1.12 and 1.36.

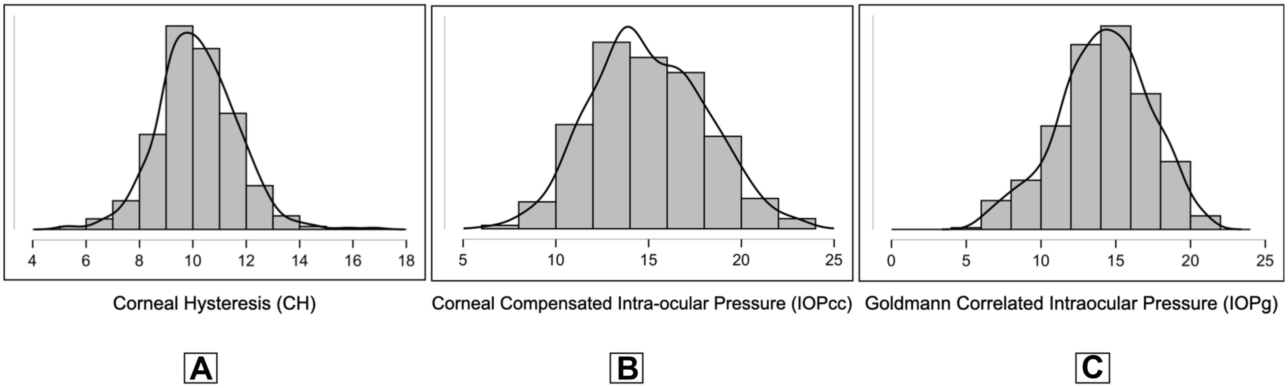

Figure 1 Frequency distribution graph of ocular response analyzer parameters. (**A**) Frequency distribution graph of corneal hysteresis (CH). (**B**) Frequency distribution graph of corneal-compensated intraocular pressure (IOPcc). (**C**) Frequency distribution graph of Goldmann-correlated intraocular pressure (IOPg).

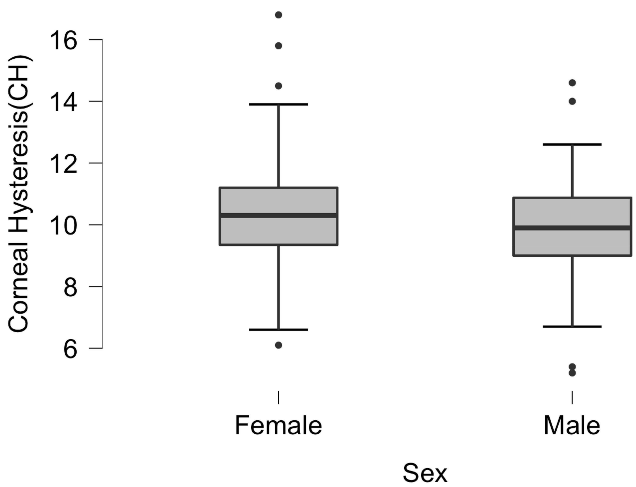

Figure 2 Box-plots of corneal hysteresis between women and men.

Following from Tables 2 and 3, the lowest CH was in the POAG group, 8.74 ± 1.52 mmHg, followed by the PACG group, 9.09 ± 1.72 mmHg, and the NTG group, 9.55 ± 1.67 mmHg, while the highest was OHT, 10.10 ± 1.40 mmHg, p<0.001. Post hoc analysis comparing CH between glaucoma types was applied, and the mean CH of POAG was significantly lower than NTG and OHT (p<0.001). Mean CH of PACG was lower than OHT (p<0.001) while mean CH between PACG and POAG and between PACG and NTG were comparable, p=0.42 and p=0.25. The OHT group had the highest IOPg and IOPcc, while the lowest was NTG, p<0.001 which corresponded to the natural history of diseases.

The difference of CH between glaucoma severity was found to be negatively correlated with the more advanced glaucoma stage in the POAG and PACG groups. The average CH in early, moderate, and severe groups of POAG was 9.22 ± 1.47, 8.74 ± 1.23, and 7.92 ± 1.40 mmHg, p<0.001, respectively. The average CH of PACG in the severe stage was significantly lower than in the early stage (8.45 ± 1.74 vs 9.85 ± 1.45 mmHg, p=0.004) and lower than the moderate stage (9.04 ± 1.68 mmHg, p=0.295) but this was statistically insignificant (Figure 4) Interestingly, among the NTG group, CH between different severity was not statistically different. Average IOPg, IOPcc, and GAT in the NTG group were the lowest compared with POAG and PACG (Table 4).

Discussion

Variation in ocular biomechanics is one of the possible glaucoma pathophysiologies.[19] There have been studies of biomechanics in various parts of the eye, for example, cornea, sclera and lamina cribrosa of the optic nerve. Anterior scleral rigidity of glaucomatous eyes measured by Schiotz tonometer was lower than in normal eyes.[20] The lowest ocular rigidity estimated by ocular pulse amplitude from pulsatile choroidal blood flow was for glaucomatous eyes when comparing between glaucoma eyes, normal, and ocular hypertension eyes.[21] Lamina cribrosa of the optic nerve deformation was observed in glaucomatous eyes.[22] Quantitative measurements of the ocular biomechanical properties of the sclera and the lamina cribrosa were developed in experimental studies but have not yet been applied in normal clinical practice.[23]

The quantifiable ocular biomechanical parameters in clinical-based practice were corneal properties, for example, corneal thickness and corneal hysteresis. The association between corneal thickness and glaucomatous risk development had been studied. Thinner corneal thickness groups had a higher risk of developing glaucoma in the case of ocular hypertension patients than the thicker

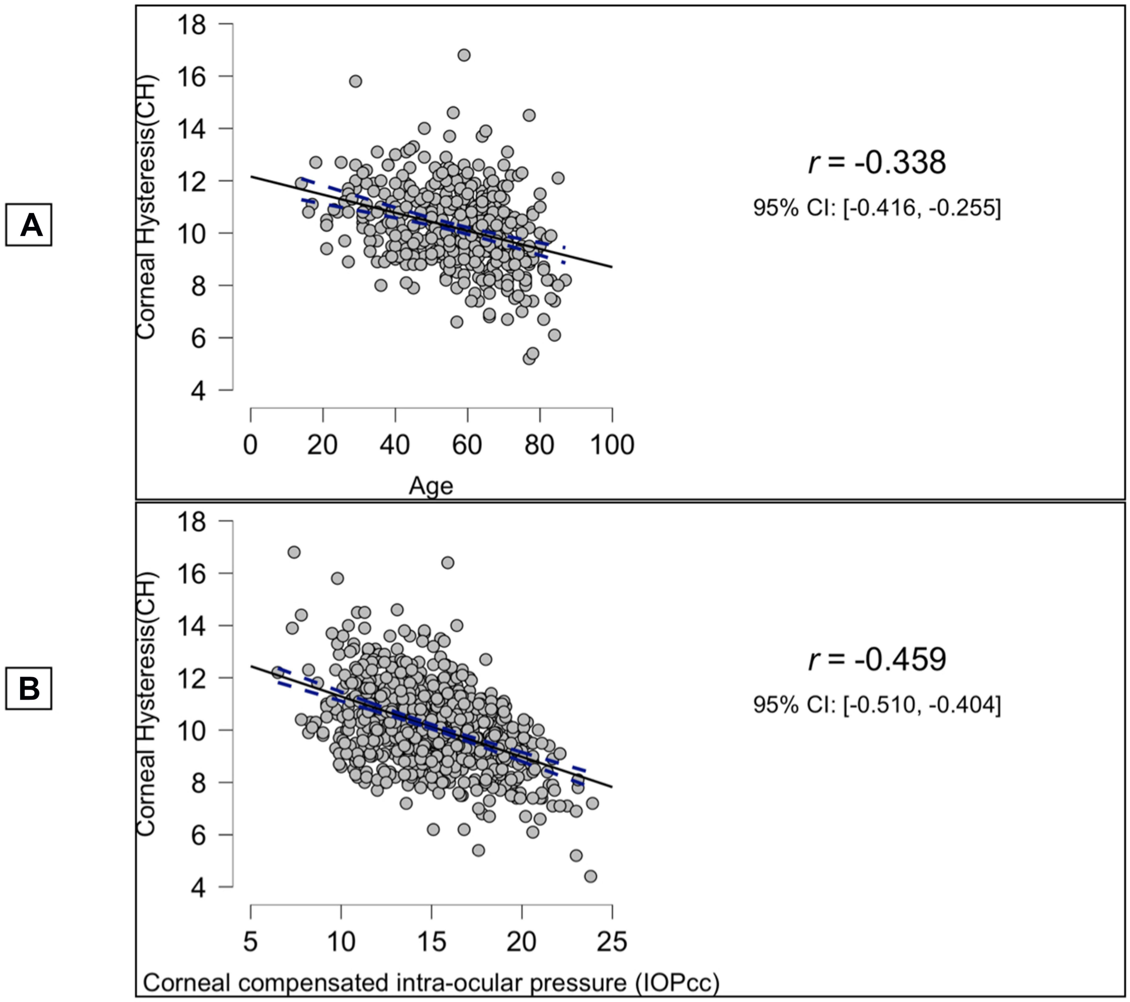

Figure 3 Scatter plot between ocular response analyzer parameters. (**A**) Scatter plot between corneal hysteresis (CH) and age. (**B**) Scatter plots between corneal-compensated intraocular pressure (IOPcc) and corneal hysteresis (CH).

groups.[24,25] Furthermore, actual intraocular pressure measurement was confounded by central corneal thickness as out-of-range central corneal thickness was associated with under or overestimated IOP.[26,27] Ocular response analyzer, a non-contact air puff tonometer and ocular hysteresis measuring device, is widely used in ophthalmology and optometry clinics. Corneal hysteresis refers to a dynamic property of the cornea, which performs as shock absorbance and is inversely associated with intraocular pressure. High reliability and high reproducibility of this device could be observed.[15,16,28] Normative databases of corneal hysteresis had been studied internationally, and the results varied narrowly among different ethnicities as shown in Table 5. Caucasians in the younger age group had higher CH than in older groups (12.12 mmHg vs 10.00 to 10.44 mmHg)[10,29–31] while the lowest CH was in those of African descent, at 9.2 to 9.70 mmHg.[9,32] CH in Asian and Middle Eastern groups were comparable, while the younger ages had higher CH similar to Caucasians (10.7 to 11.78 mmHg vs 10.1 to 10.25 mmHg).[33–38] Our results were similar to other Asians. Our proposed regression model equations between age and CH revealed that increasing age showed negative correlation with CH, corresponding to the findings of Foster et al, as CH decreased by 0.34 mmHg per decade.[31] Age-related ocular biomechanical property degeneration associated with glaucoma was observed in cornea, trabecular meshwork, and lamina cribrosa.[39–42] For instance, a decrease in collagen would enhance compliance at the lamina cribrosa that worsens the health of the optic nerve head and leads to retinal ganglion cell death. Aging affected the stiffness of corneal tissue from the alteration of the corneal structural composition: collagen fibers, glycosaminoglycans, and proteoglycans. CH

Table 2 Demographic Data and Ocular Response Analyzer Parameters in Different Glaucoma Type

	Primary Open-Angle Glaucoma (POAG)	Primary Close-Angle Glaucoma (PACG)	Normal Tension Glaucoma (NTG)	Ocular Hypertension (OHT)	p-value#
Number of eyes/ Number of patients	434 Eyes/272 patients	74 Eyes/48 patients	143 Eyes/ 79 patients	44 Eyes/30 patients	
Male Female	177 95	11 37	25 54	16 14	<0.001[abe]
Age (years)	68.07 ± 10.04	68.48 ± 10.43	65.88 ± 11.66	59.39 ± 9.78	0.002[cef]
Treatment -Medication -Selective laser trabeculoplasty -Trabeculectomy -Phacoemulsification	 421 8 5 -	 45 – – 29	 143 – – –	 24 – – –	<0.001[ac]
Anti-glaucoma medication (No.) -Prostaglandin analogues -Carbonic anhydrase inhibitors -Alpha agonist -Beta blockers	1.36 ± 0.5 414 67 4 89	1.32 ± 0.5 46 – – 16	1.12 ± 0.4 141 7 – 12	1.2 ± 0.4 24 2 – 3	<0.001[b]
Corneal hysteresis (CH) mmHg	8.74 ± 1.52	9.09 ± 1.72	9.55 ± 1.67	10.10 ± 1.40	<0.001[bce]
Corneal-compensated intraocular pressure (IOPcc) mmHg	17.19 ± 4.62	16.65 ± 4.28	13.94 ± 2.82	19.92 ± 4.95	<0.001[bcdef]
Goldmann-correlated intraocular pressure (IOPg) mmHg	14.82 ± 4.73	14.62 ± 4.32	12.30 ± 2.93	19.75 ± 4.83	<0.001[bcdef]
Waveform score (WS)	6.88 ± 1.79	6.85 ± 1.89	6.35 ± 1.89	6.64 ± 1.61	0.361
Goldmann applanation tonometry (GAT) mmHg	15.15 ± 4.32	15.30 ± 3.95	12.70 ± 2.78	19.51 ± 3.14	<0.001[b]

Notes: #One-way ANOVA for continuous data and chi-square test for categorical data. #Generalized estimating equation (GEE) for ocular response analyzer parameters. [a]Significant difference between OAG and ACG, [b]Significant difference between OAG and NTG, [c]Significant difference between OAG and OTH, [d]Significant difference between ACG and NTG, [e]Significant difference between ACG and OTH, [f]Significant difference between NTG and OTH.

of women in our study was significantly higher than in men similar to the results from other studies.[31,39] However, the average ages of women and men in this study were approximately 56.51 ± 14.92 vs 58.88 ± 13.09 years, p=0.16. Apart from aging, the estrogen hormone plays an important role in ocular biomechanical changes. Estrogen receptors presented in many ocular tissues and are associated with the growth of collagen fiber which affects corneal hysteresis as well as neuroprotection in glaucoma pathophysiology.[43,44]

Several studies had tried to apply CH as a predictor of developing glaucoma and a predictor of glaucoma progression. Schweitzer et al found moderate and severe glaucoma were 2.9 times more likely to have CH below 10mmHg, which was similar to the finding from Park et al, in which 67% risk of progression was found in eyes with CH below 10.1 mmHg.[45,46] Following the normal distribution plot of CH, the low percentiles of CH normative data could be applied as the deviation value (lower than average) from normal, for example CH at the 5th percentile was 8.0 mmHg, which was lower than 95% of normal and CH at the 1st percentile was 6.7 mmHg., which was lower than 99% of normal. This value could be a potential cut-off point of discrimination between normal and deviations from normal (lower than average) CH in Thais.

Among IOPcc, IOPg, and GAT, exactly which value would be the best to represent the true IOP is still under

Table 3 Post Hoc Comparisons of Corneal Hysteresis (CH), Corneal-Compensated Intraocular Pressure (IOPcc) and Goldmann-Correlated Intraocular Pressure (IOPg) Between Primary Open-Angle Glaucoma (POAG), Primary Close-Angle Glaucoma (PACG), Normal Tension Glaucoma (NTG) and Ocular Hypertension (OHT)

Corneal Hysteresis (CH)							
			95% CI for Mean Difference				
		Mean Difference	**Lower**	**Upper**	**SE**	**t**	**p bonf**
POAG	PACG	−0.359	−0.867	0.149	0.197	−1.820	0.415
	NTG	−0.815	−1.202	−0.427	0.150	−5.416	<0.001
	OHT	−1.367	−2.006	−0.728	0.248	−5.511	<0.001
PACG	NTG	−0.456	−1.032	0.121	0.224	−2.035	0.253
	OHT	−1.008	−1.777	−0.240	0.298	−3.378	0.005
NTG	OHT	−0.552	−1.247	0.142	0.270	−2.047	0.246
Corneal-Compensated Intraocular Pressure (IOPcc)							
			95% CI for Mean Difference				
		Mean Difference	**Lower**	**Upper**	**SE**	**t**	**p bonf**
POAG	PACG	0.598	−0.829	2.025	0.554	1.079	1.000
	NTG	3.221	2.132	4.309	0.423	7.620	< 0.001
	OHT	−2.671	−4.466	−0.876	0.697	−3.832	< 0.001
PACG	NTG	2.623	1.002	4.244	0.629	4.168	< 0.001
	OHT	−3.269	−5.428	−1.109	0.839	−3.898	< 0.001
NTG	OHT	−5.892	−7.844	−3.939	0.758	−7.770	< 0.001
Goldmann-Correlated Intraocular Pressure (IOPg)							
			95% CI for Mean Difference				
		Mean Difference	**Lower**	**Upper**	**SE**	**t**	**p bonf**
POAG	PACG	0.158	−1.261	1.577	0.551	0.287	1.000
	NTG	2.539	1.457	3.622	0.420	6.041	< 0.001
	OHT	−4.913	−6.698	−3.128	0.693	−7.089	< 0.001
PACG	NTG	2.381	0.770	3.993	0.626	3.806	< 0.001
	OHT	−5.071	−7.218	−2.924	0.834	−6.082	< 0.001
NTG	OHT	−7.452	−9.394	−5.511	0.754	−9.886	< 0.001

Notes: P-value and confidence intervals adjusted for comparing a family of four estimates (confidence intervals corrected using the turnkey method).

debate.[47–49] The gold standard of IOP measuring is the GAT, whose accuracy is limited when applied in out-of-the range central corneal thickness (CCT), for example, in post-refractive surgery and thinner or thicker than normal average CCT. IOPcc is less affected by corneal properties as a CCT independent IOP measurement.[49] Ehrlich et al showed better sensitivity and specificity to identify glaucoma using IOPcc compared with GAT. Applying an optimal GAT threshold at 20.9 mmHg, GAT showed area under curve (AUC) = 0.78, while

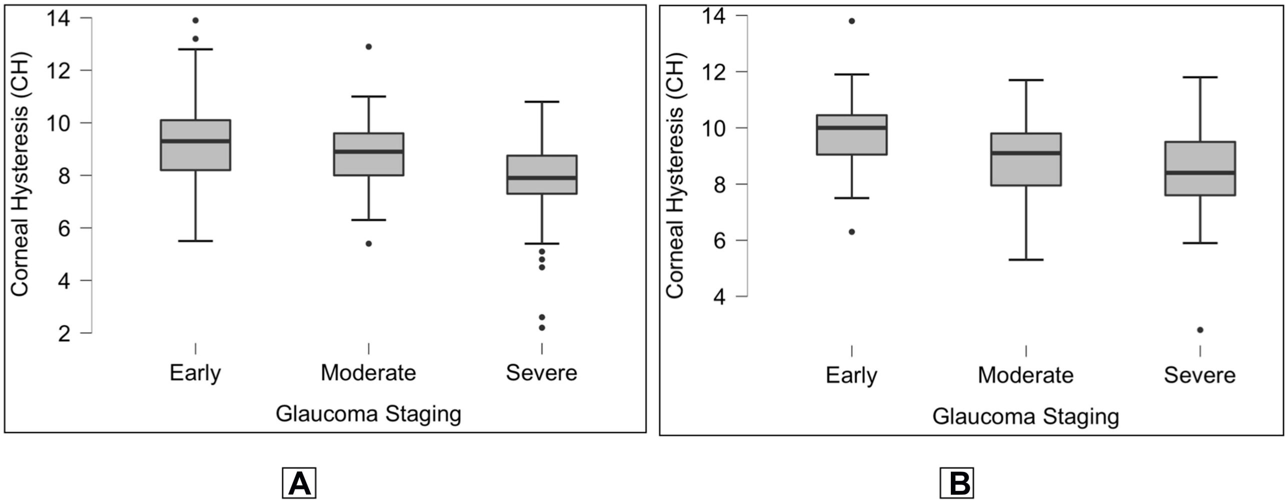

Figure 4 Box-plot of corneal hysteresis of primary open-angle glaucoma (POAG) and primary close-angle glaucoma (PACG) in different glaucoma severity. (**A**) Primary open-angle glaucoma (POAG). (**B**) Primary close-angle glaucoma (PACG).

using an IOPcc threshold at 18.4 mmHg, IOPcc showed AUC = 0.93, p<0.001.[50]

Our data for IOPcc were significantly higher than IOPg, 15.01 ± 3.04 vs.14.24 ± 3.24 mmHg, p<0.001. This value was also higher than the normative data study of GAT by Bourne et al at 13.3 ± 3.2 mmHg.[51] Compared with other ethnic groups, IOP was similar to other Asians but lower than Caucasians.[51–53] We could apply the 97.5th percentile of IOPcc (20.08 mmHg) and IOPg (19.54 mmHg) as the proper cut-off point IOP for glaucoma diagnosis, which is more accurate than the traditional criteria.[54]

Corneal hysteresis had been studied as a predictor for glaucoma progression. For example, each 1 mmHg lower CH was associated with a 21% increase in the risk of developing glaucoma in the glaucoma suspected group (95% CI [1.04–1.41], P = 0.013). Each 1 mmHg lower CH was associated with a faster rate of deterioration of the retinal nerve fiber layer (RNFL), 0.13 μm/year faster, and each 1 mmHg lower CH was associated with a 0.25%/year faster rate of visual field index (VFI) decline over time (P < 0.001).[55–58]

Our results of CH in different glaucoma types were comparable with previous studies that reported corresponding CH between PACG and POAG, while average CH of NTG was higher than both POAG and PACG (POAG 9.0–10.03 mmHg, PACG 9.1mmHg, and NTG 9.6–9.88mmHg).[9,12,59–61] When comparing between severity levels of glaucoma, our findings were similar to others in that the more advanced stages of glaucoma correlated with lower CH.[13]

One limitation of our study was that the average CH in glaucoma might not represent the original CH, because all patients' IOP were already controlled with anti-glaucoma treatment.

Several studies showed the relationship between IOP and CH; lowering IOP can increase CH, and likewise increasing IOP is associated with lowering CH. Increasing CH can be both directly and indirectly caused by topical prostaglandin analogues. Firstly, topical prostaglandin analogues alter the structure of the cornea at the level of the extracellular matrix by increasing keratocyte density in corneal stroma.[62] Secondly, topical prostaglandin analogues as well as any anti-glaucoma treatment indirectly increase CH as a result of decreasing IOP.[63,64]

The second limitation was a retrospective cross-sectional study design with lack of data to compare in the long term. The third limitation was the generalizability of the corneal hysteresis parameter results as the reference value. Our future development plan was to include more participants of various age groups to generate a normative database for the Thai population.

Conclusion

Corneal hysteresis is a reliable and repeatable value of ocular biomechanics that can be measured in clinical practice. The more advanced glaucoma stage in POAG and PACG had the lower CH. Compared with the normal value data, low percentiles of CH can be set as a cut-off point of discrimination between normal

Table 4 Demographic Data and Ocular Response Analyzer Parameters in Different Glaucoma Severity

	Primary Open-Angle Glaucoma (POAG)	Primary Close-Angle Glaucoma (PACG)	Normal Tension Glaucoma (NTG)	p-value[#]
Glaucoma Stage				
-Early	225 (51.85%)	27 (36.48%)	91 (63.64%)	1.00
-Moderate	74 (17.05%)	14 (18.92%)	32 (22.38%)	0.049[a]
-Severe	135 (31.10%)	33 (44.60%)	20 (13.98%)	<0.001[a]
Age (years)	68.07 ± 10.04	68.48 ± 10.43	65.88 ± 11.66	0.38
-Early	65.75 ± 9.89	68.78 ± 8.64	62.27 ± 11.02	0.188
-Moderate	68.76 ± 9.90	71.13 ± 4.85	71.81 ± 10.09	0.188
-Severe	71.23 ± 9.50	65.95 ± 12.52	77.60 ± 7.96	0.189
Corneal hysteresis (CH) mmHg	8.74 ± 1.52	9.09 ± 1.72	9.55 ± 1.67	<0.001[a]
-Early	9.22 ± 1.47	9.85 ± 1.45	9.47 ± 1.38	0.055
-Moderate	8.74 ± 1.23	9.04 ± 1.68	9.75 ± 2.42	0.095
-Severe	7.92 ± 1.40	8.45 ± 1.74	9.77 ± 1.34	<0.001[a]
p-value[#]	<0.001[cde]	0.004[de]	0.525	
Corneal-compensated intraocular pressure (IOPcc) mmHg	17.19 ± 4.62	16.65 ± 4.28	13.94 ± 2.82	<0.001[ab]
-Early	16.58 ± 4.07	16.38 ± 4.42	14.15 ± 2.67	<0.001[ab]
-Moderate	16.77 ± 3.89	16.86 ± 2.94	13.21 ± 3.27	<0.001[ab]
-Severe	18.61 ± 5.90	16.73 ± 4.70	14.05 ± 2.76	<0.001[ab]
p-value[#]	0.001[de]	0.910	0.379	
Goldmann-correlated intraocular pressure (IOPg), mmHg	14.82 ± 4.73	14.64 ± 4.37	12.30 ± 2.93	<0.001[ab]
-Early	14.63 ± 4.09	15.27 ± 4.47	12.41 ± 3.14	<0.001[ab]
-Moderate	14.27 ± 4.22	14.81 ± 3.70	11.75 ± 2.30	<0.001[ab]
-Severe	15.46 ± 5.88	14.05 ± 4.60	12.57 ± 2.79	0.002[a]
p-value[#]	0.241	0.565	0.399	
Goldmann applanation tonometry (GAT), mmHg	15.15 ± 4.32	15.30 ± 3.95	12.70 ± 2.78	<0.001[ab]
-Early	14.54 ± 3.72	15.90 ± 3.93	12.79 ± 2.79	<0.001[ab]
-Moderate	15.25 ± 4.14	15.33 ± 3.75	12.55 ± 2.14	<0.001[ab]
-Severe	16.11 ± 5.29	14.83 ± 4.25	12.50 ± 3.65	0.003[a]
p-value[#]	0.023d	0.678	0.898	

Notes: [#]One-way ANOVA for continuous data and chi-square test for categorical data. [#]Generalized estimating equation (GEE) for ocular response analyzer parameters. [a]Significant difference between OAG and NTG, [b]Significant difference between ACG and NTG, [c]Significant difference between early and moderate stage, [d]Significant difference between early and severe stage, [e]Significant difference between moderate and severe stage.

and deviations from normal. Following from its dynamic property, CH could serve as a glaucoma predictor to improve glaucoma care, for example, following the response to treatment, and identifying risk or predictive values for developing glaucoma in suspected groups.

Table 5 Corneal Hysteresis (CH) in Different Ethnics

Ethnics and Authors	Number	Corneal Hysteresis (CH)	Age (Years)
Caucasian, Spain Bueno-Gimeno et al[10]	293 Eyes 293 Participants	12.12 ± 1.71 mm Hg	6–17 years
Caucasian, London, United Kingdom Carbonaro et al[29]	264 Eyes from twin pairs	10.24 ± 1.54 mm Hg	54.1 (16–78)
Caucasian, Birmingham, United Kingdom Shah et al[30]	207 Eyes 105 Participants	10.7 ± 2.0 mm Hg (6.1–17.6)	62.1 ± 18.1 (18.1–87.1)
Caucasian, United Kingdom Foster et al[31]	4184 Participants	10.00 ± 1.64 mmHg Women 10.18 ±1.58 mmHg Men 9.79 ±1.69 mmHg, $P < 0.001$	48–91
African and Caucasians, Brussels Detry-Morel et al[9]	30 African 25 Caucasians	9.2 ± 1.5 mmHg 10.8 ± 1.6 mmHg	43.9 ± 11.4 58.4 ± 14.7
African and Caucasians, San Diego, USA Leite et al[32]	46 Eyes/ 37 blacks 135 Eyes/ 82 whites	9.70 ± 1.72 mmHg 10.44 ± 1.6 mmHg	58.41 ± 15.7 66.00 ± 11.9
Middle easterner, Iran Sedaghat et al[33]	506 Eyes 253 Participants	10.07 ± 1.61 mm Hg	28.43 ± 6.36 (18–35)
Middle easterner, Egypt Ali[34]	194 Eyes 98 Participants	10.25 ± 0.12 mmHg (6.5–14.4) 11.1 ± 0.14 mmHg 9.8 ± 0.21 mmHg	45 years Younger age (19–40 years) Older age (40–71 years)
Asian, Singapore Lim et al[35]	271 Eyes from 186 Chinese, 50 Malay, 33 Indian, and 2 other	11.78 ± 1.55 mmHg (6.93–16.53)	13.97 ± 0.89
Asian, rural Chinese secondary school children. Song et al[36]	1233 Eyes from 1293 participants	10.7 ± 1.6 mmHg	14.7 ± 0.8
Asian, Seoul, Korea Hwang et al[37]	958 Eyes from 958 patients	10.1 ± 1.4 mmHg (7.1–17.2)	26.7
Asian, Taipei, Taiwan Wang el al[38]	292 Healthy eyes/ 292 person	10.16 ± 1.55 mmHg (8–14)	66.51 ± 12.12 (33–87)
This study	465 Eyes from 465 participants	10.18 ± 1.48 mmHg (5.2 to 16.80) Women 10.29 ± 1.46 mmHg Men 9.90 ± 1.49 mmHg, $p=0.009$	57.21 ± 14.43 (14–87)

Abbreviations

CH, corneal hysteresis; IOPcc, corneal-compensated intraocular pressure; GAT, Goldmann application tonometry; POAG, primary open-angle glaucoma; PACG, primary close-angle glaucoma; NTG, normal tension glaucoma; OHT, ocular hypertension; WS, waveform score.

Acknowledgments

Thanks to Dr Puwat Charukamnoetkanok for proofreading this article.

Disclosure

The author reports no conflicts of interest in this work.

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