



# Relationship between central corneal thickness and optic nerve head parameters in primary open-angle glaucoma

Naseh Hakimzadeh <sup>1,2</sup>, Sakineh Kadivar <sup>1</sup> and Mohammad Reza Panjtan Panah <sup>1</sup>

<sup>1</sup> Ophthalmology Department, Guilan University of Medical Sciences, Rasht, Iran

<sup>2</sup> Ophthalmology Department, Lorestan University of Medical Sciences, Khorramabad, Iran

## ABSTRACT

**Background:** Primary open-angle glaucoma (POAG) is an ocular entity that causes optic neuropathy. Thin central corneal thickness (CCT) in patients with POAG correlates with changes in various optic nerve head structural parameters. Additionally, racial differences exist in CCT and optic disc parameters. Herein, we assessed the potential relationship between CCT and optic nerve head parameters in treatment-naive patients of Persian ethnicity who were diagnosed with POAG of varying severity levels.

**Methods:** This hospital-based analytical cross-sectional study recruited patients of Persian ethnicity diagnosed with treatment-naive POAG. Participants underwent detailed optometric and ophthalmic examinations. Visual field testing was performed using a Humphrey perimeter. Spectral-domain optical coherence tomography (OCT) was performed using a Cirrus OCT device to record optic nerve head parameters: disc area, rim area, vertical cup-to-disc ratio, average cup-to-disc ratio, cup volume, and average retinal nerve fiber layer thickness (RNFLT). The CCT was measured using an ultrasonic pachymeter.

**Results:** We recruited 168 eyes of 84 patients with POAG with a mean (standard deviation) age of 60.30 (12.50) years, comprising 33 (39.29%) men and 51 (60.71%) women. While weak but statistically significant inverse correlations of CCT with the vertical cup-to-disc ratio ( $r = -0.19$ ;  $P < 0.05$ ), average cup-to-disc ratio ( $r = -0.17$ ;  $P < 0.05$ ), and cup volume ( $r = -0.17$ ;  $P < 0.05$ ) were found, other optic nerve parameters showed no significant correlations with CCT (all  $P > 0.05$ ). Stepwise multiple linear regression analysis indicated that, for each unit increase in the vertical cup-to-disc ratio, the CCT decreased by 54.98  $\mu\text{m}$  ( $P < 0.05$ ).

**Conclusions:** The CCT in eyes with treatment-naive POAG of varying severity levels in a Persian ethnic group was weakly but statistically significantly inversely correlated with the vertical cup-to-disc ratio, average cup-to-disc ratio, and cup volume. For every unit increase in the vertical cup-to-disc ratio, the CCT decreased by 54.98  $\mu\text{m}$ . Our findings indicate that in patients with POAG, CCT correlates with some changes in structural optic nerve head parameters, including the cup volume and vertical/average cup-to-disc ratios. Further longitudinal studies including individuals from various racial backgrounds and POAG severity levels are needed to verify the relationship between CCT and optic nerve parameters at different time points of disease progression.

## KEYWORDS

primary open angle glaucoma, optical coherence tomography, early detection of disease, corneal thickness measurement, corneal pachymetric measurement, optic nerve head

**Correspondences:** Naseh Hakimzadeh, Ophthalmology Department, Lorestan University of Medical Sciences, Khorramabad, Iran. Email: [drhakimzadeheye@gmail.com](mailto:drhakimzadeheye@gmail.com). ORCID iD: <https://orcid.org/0009-0005-1841-8522>

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## INTRODUCTION

Primary open-angle glaucoma (POAG) is a condition characterized by optic neuropathy and leads to irreversible blindness if left untreated [1]. As the disease is often asymptomatic, its diagnosis may be delayed [2, 3]. Currently, the most effective treatment for POAG involves controlling intraocular pressure (IOP) [4, 5]. The accuracy of IOP measurement is affected by central corneal thickness (CCT) [6]. A thin CCT is also an independent risk factor for POAG, a finding first reported in the Ocular Hypertension Treatment Study [7, 8].

Functional and structural tests are essential for diagnosing and assessing POAG progression [9]. A perimetry test is a functional assessment of the visual field, but visual field defects may not be noticeable in the early stages of the disease [9, 10]. However, changes in the structure of the optic nerve head and thickness of the retinal nerve fiber layer (RNFLT) may occur before any detectable visual field defects are noticeable on perimetry, and could predict future visual field changes. Therefore, a thorough structural examination may provide valuable information in the early stages of the disease [9, 10].

In patients with POAG, a thin CCT correlates with various changes in structural optic nerve head parameters, including the vertical and horizontal cup-to-disc ratios, disc area, and loss of the neuroretinal rim area [11, 12]. Patients with open-angle glaucoma or ocular hypertension and a thin CCT also demonstrate greater shallowing of the optic cup after IOP reduction [13]. Additionally, racial differences in the CCT and optic disc parameters, as determined using Cirrus optical coherence tomography (OCT), have been reported [14-16]. We investigated the potential relationship between CCT and optic nerve head parameters in treatment-naïve patients of Persian ethnicity diagnosed with POAG of varying severity levels.

## METHODS

This hospital-based analytical cross-sectional study recruited consecutive patients of Persian ethnicity diagnosed with treatment-naïve POAG from among individuals who were referred to a tertiary referral center over the course of one academic year. All participants were diagnosed by a subspecialist glaucoma consultant at the glaucoma clinic located in Amir Al-Momenin Hospital, Rasht City, Iran. The study protocol was approved by the Research Ethical Committee of Guilan Medical University in Rasht and adhered to the principles of the Declaration of Helsinki. Before enrollment, all participants were fully informed about the study details and provided written informed consent for participation.

We included both eyes of individuals of Persian origin [17], aged 30 years and older, who had best-corrected distance visual acuity (BCDVA) of 20/40 or better, IOP of 21 mmHg or higher, open-angle on indirect gonioscopy examination, and repeatable visual field defects evident in two consecutive reliable perimetry tests that were consistent with glaucomatous visual field loss and changes in the optic disc indicative of glaucoma. Individuals were excluded if they had other types of glaucoma; myopia > -5 diopters (D); astigmatism of  $\geq 3$  D; a history of any ocular surgeries, laser therapy, or trauma; systemic comorbidities, such as diabetes mellitus; retinal, choroidal, or optic nerve lesions or neurological disorders that could affect retinal RNFLT; poor quality OCT [18]; wore contact lenses; or were lactating or breast feeding.

Participants underwent detailed optometric and ophthalmic examinations. Initially manifest refraction was performed using an autorefractor (KR-8000 autorefractor, Topcon, Tokyo, Japan) with subjective refraction, followed by determination of BCDVA using the Snellen E-chart at a 6-m distance. For all participants, a single subspecialist glaucoma consultant performed detailed anterior segment examination using a slit-lamp (Haag-Streit AG, Koniz, Switzerland), IOP measurement using a Goldmann applanation tonometer (AT 900, Haag-Streit), indirect gonioscopy using a Goldmann three-mirror lens (Volk Optical, Inc., Mentor, OH, USA), and posterior segment examination with optic nerve head assessment under a slit-lamp through an accessory lens of 78.0 D (Volk Optical, Inc.).

An expert optometrist using static automated white-on-white threshold perimetry (SITA Standard 24-2, Humphrey Field Analyzer; Carl Zeiss Meditec, Inc., Dublin, CA) performed visual field testing. Two reliable perimetry assessments were conducted consecutively for each eye [19, 20] and a subspecialist glaucoma consultant interpreted results. Spectral-domain OCT (Cirrus HD-OCT, software version 5.0; Carl Zeiss Meditec, Inc., Dublin, CA) imaging was performed [21] by an expert optometrist. If good quality scans were obtained [18], data of optic nerve head parameters, i.e., disc area, rim area, vertical cup-to-disc ratio, average cup-to-disc ratio, cup volume, and average RNFLT, were extracted for each eye [18, 22, 23]. CCT measurements were conducted by an expert optometrist using an ultrasonic pachymeter (UP-1000, Nidek Co., Tokyo, Japan) after instilling tetracaine 0.5% eyedrops (Anestocaine, Sina Daru Co., Tehran, Iran) in each eye 2 min prior to the procedure. All measurements were taken between 10:00 AM and 2:00 PM, at least 2 h after the patient woke up. The patient was instructed to sit and focus on a light target while the ultrasound probe was positioned perpendicularly to the center of the cornea. Five consecutive measurements were taken, and the mean value of these measurements was recorded.

Data were collected and analyzed using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Kolmogorov – Smirnov test. Continuous and categorical variables are reported as means (with standard deviations [SD]), along with the minimum and maximum values, or as frequencies (with percentages), respectively. To evaluate the correlation between the CCT and optic nerve head parameters, Pearson's product-moment correlation was used for parameters with a normal distribution, while Spearman's rank correlation was applied for parameters with a non-normal distribution. Stepwise multiple linear regression analysis was conducted to identify significant CCT predictors, with CCT considered as the dependent variable and optic nerve head parameters as the independent variables [24]. A *P*-value < 0.05 was deemed statistically significant.

RESULTS

Table 1. Demographic and clinical characteristics of patients of Persian origin with treatment-naive POAG

Variable	Value
Age (y), Mean ± SD (Range)	60.30 ± 12.50 (30 to 84)
Sex (Men / Women), n (%)	33 (39.29) / 51 (60.71)
CCT (µm), Mean ± SD (Range)	548.22 ± 36.84 (470 to 650)
IOP (mmHg), Mean ± SD (Range)	28.14 ± 5.55 (22 to 50)
Disc area (mm <sup>2</sup> ), Mean ± SD (Range)	2.15 ± 0.43 (1.40 to 3.77)
Rim area (mm <sup>2</sup> ), Mean ± SD (Range)	0.99 ± 0.28 (0.27 to 1.55)
Vertical CDR, Mean ± SD (Range)	0.68 ± 0.13 (0.24 to 0.92)
Average CDR, Mean ± SD (Range)	0.70 ± 0.12 (0.23 to 0.93)
Cup volume (mm <sup>3</sup> ), Mean ± SD (Range)	0.47 ± 0.31 (0.01 to 1.53)
Average RNFLT (µm), Mean ± SD (Range)	82.93 ± 12.82 (48 to 115)

Abbreviations: POAG, primary open angle glaucoma; y, years; SD, standard deviation; n, number of patients; %, percentage; CCT, central corneal thickness; µm, micrometres; IOP, intraocular pressure; mmHg, millimetre of mercury; mm<sup>2</sup>, square millimetre; CDR, cup-to-disc ratio; RNFLT, retinal nerve fibre layer thickness. Note: Range expressed by writing minimum to maximum.

Table 2. Correlation between the CCT and optic nerve head parameters in eyes with treatment-naive POAG

Variables	CCT (µm)	
	r	P-value
Disc area (mm <sup>2</sup> )	- 0.13*	0.085
Rim area (mm <sup>2</sup> )	+ 0.09**	0.238
Vertical CDR	- 0.19**	<b>0.014</b>
Average CDR	- 0.17**	<b>0.025</b>
Cup volume (mm <sup>3</sup> )	- 0.17*	<b>0.028</b>
Average RNFLT (µm)	+ 0.07**	0.386

Abbreviations: CCT, central corneal thickness; POAG, primary open angle glaucoma; µm, micrometers; mm<sup>2</sup>, millimeter of square; CDR, cup-to-disc ratio; RNFLT, retinal nerve fiber layer thickness. Note: P-values < 0.05 are shown in bold; r, \*Spearman or \*\*Pearson correlation coefficients value.

Table 3. Stepwise multiple linear regression analysis results for optic nerve head parameters predictive of CCT in eyes with treatment-naive POAG in patients of Persian origin

Model	Independent variables	Unstandardized coefficients	Standard error of estimate	Standardized coefficients	95% CI	Significance value
1	Constant	665.46	60.57	-	545.84 – 785.08	< 0.001
	Disc area	16.51	19.41	0.19	-21.83 – 54.85	0.396
	Rim area	- 45.84	39.90	- 0.35	- 124.64 – 32.96	0.252
	Vertical CDR	- 92.44	69.72	- 0.32	- 230.13 – 45.24	0.187
	Cup volume	- 4.99	23.17	- 0.04	- 50.74 – 40.76	0.830
	Average RNFLT	0.02	0.34	0.01	- 0.65 – 0.70	0.946
	Average CDR	- 62.86	96.70	- 0.20	- 253.83 – 128.11	0.517
2	Constant	666.13	59.57	-	548.50 – 783.77	< 0.001
	Disc area	16.27	19.05	0.19	- 21.34 – 53.89	0.394
	Rim area	- 44.65	35.73	- 0.34	- 115.21 – 25.19	0.213
	Vertical CDR	- 93.16	68.72	- 0.32	- 228.85 – 42.54	0.177
	Cup volume	- 4.63	22.50	- 0.04	- 49.06 – 39.79	0.837
	Average CDR	- 61.61	94.65	- 0.19	- 248.51 – 125.29	0.516
	3	Constant	663.18	57.65	-	549.34 – 777.03
Disc area		13.51	13.47	0.16	- 13.09 – 40.10	0.317
Rim area		- 40.19	28.34	- 0.31	- 96.15 – 15.77	0.158
Vertical CDR		- 93.62	68.48	- 0.32	- 228.84 – 41.59	0.173
Average CDR		- 57.91	92.65	- 0.18	- 240.85 – 125.04	0.533
4	Constant	639.50	43.37	-	553.87 – 725.13	< 0.001
	Disc area	8.45	10.74	0.10	- 12.76 – 29.65	0.433
	Rim area	- 29.63	22.71	- 0.23	- 74.47 – 15.21	0.194
	Vertical CDR	- 117.99	56.19	- 0.41	- 228.94 – -7.04	<b>0.037</b>
5	Constant	620.82	36.24	-	549.26 – 692.38	< 0.001
	Rim area	- 16.47	15.34	- 0.13	- 46.75 – 13.81	0.284
	Vertical CDR	- 82.92	34.13	- 0.29	- 150.30 – -15.53	<b>0.016</b>
6	Constant	585.51	15.25	-	555.40 – 615.61	< 0.001
	Vertical CDR	- 54.98	22.10	- 0.19	- 98.62 – - 11.34	<b>0.014</b>

Abbreviations: CCT, central corneal thickness; POAG, primary open angle glaucoma; CI, confidence interval; CDR, cup-to-disc ratio; RNFLT, retinal nerve fiber layer thickness. Note: CCT is a single dependent variable in this model; Stepwise multiple linear regression analysis was run to detect the significant predictors of CCT; P < 0.05 was considered significant.

We recruited 168 eyes of 84 patients with POAG, with a mean (SD) age of 60.30 (12.50) years. The cohort comprised 33 (39.29%) men and 51 (60.71%) women. Table 1 summarizes demographic and clinical characteristics of study participants.

Table 2 shows the results of the correlation analysis between the CCT and optic nerve head parameters. While weak but statistically significant inverse correlations were found between the CCT and the vertical cup-to-disc ratio ( $r = -0.19$ ;  $P < 0.05$ ), average cup-to-disc ratio ( $r = -0.17$ ;  $P < 0.05$ ), and cup volume ( $r = -0.17$ ;  $P < 0.05$ ), other parameters showed no significant correlation with CCT (all  $P > 0.05$ ).

Table 3 shows the results of stepwise multiple linear regression analysis, which indicated that for each unit increase in the vertical cup-to-disc ratio, the CCT decreased by  $54.98 \mu\text{m}$  ( $P < 0.05$ ).

## DISCUSSION

We investigated eyes diagnosed with treatment-naive POAG of varying severity levels in patients of Persian ethnicity [17]. We found a weak but statistically significant inverse correlation between the CCT and the vertical cup-to-disc ratio, average cup-to-disc ratio, and cup volume. However, no significant correlations were observed between the CCT and other parameters. Stepwise multiple linear regression analysis indicated that for every unit increase in the vertical cup-to-disc ratio, the CCT decreased by  $54.98 \mu\text{m}$ .

Mokbel et al. [11] conducted a study involving 80 eyes from 50 patients with medically controlled POAG, including 42 eyes with a thick CCT ( $\geq 540 \mu\text{m}$ ) and 38 eyes with a thin CCT ( $< 540 \mu\text{m}$ ). The CCT measurements were taken using ultrasonic pachymetry, and optic nerve head topography was assessed with the Heidelberg Retina Tomograph II, a confocal scanning laser ophthalmoscope. Perimetry was performed using a static automated Humphrey visual field analyzer with program 24-2. They found a negligible but significant positive correlation between the CCT and the rim area, as well as the vertical and horizontal cup-to-disc ratios, and a weak but significant inverse correlation with the disc area. However, no significant correlation was found between the CCT and cup area [11]. In contrast, the CCT did not correlate with the rim or disc area in our study, whereas it showed a weak but significant inverse correlation with the cup volume and vertical/average cup-to-disc ratios.

Pakravan et al. [12] conducted a study involving 212 eyes from 137 patients diagnosed with POAG. They measured the CCT using ultrasonic pachymetry and assessed the optic nerve head using the Heidelberg Retina Tomograph II. Among the 72 eligible eyes in their analysis, they discovered a weak inverse correlation between the CCT and the disc area that was both statistically and clinically significant [12]. Nevertheless, we did not detect such a correlation among eyes with treatment-naive POAG. Prata et al. [25] studied 42 patients diagnosed with treatment-naive POAG. They found a weak, inverse correlation between the CCT and the mean cup depth; however, they found no correlation of the CCT with the cup-to-disc ratio. The authors concluded that, among treatment-naive patients with newly diagnosed POAG, those with thinner corneas and lower values of corneal hysteresis exhibited a larger cup-to-disc ratio and a deeper cup, regardless of the IOP values and the disc size [25]. In contrast to the non-significant results found by Prata et al. [25], when we similarly investigated eyes with treatment-naive POAG, we found a weak but statistically significant inverse correlation between the CCT and the vertical or average cup-to-disc ratio. The discrepancies between the outcomes of the current and previous studies [11, 12, 25] could have arisen from differences in instruments used to measure optic nerve parameters, the ethnic background of the participants, or the severity levels of glaucoma. Further studies are needed to verify these proposed reasons.

Akkaya et al. [26] conducted a prospective study involving 101 eyes with POAG, including 60 from patients with and 41 from patients without diabetes. They used an ocular response analyzer to measure corneal hysteresis and the corneal resistance factor, while the Heidelberg Retina Tomograph-III was used to assess optic disc parameters. Additionally, the Spectralis OCT was used to measure RNFLT. The researchers found that the group with diabetes had significantly higher mean corneal resistance factor, mean rim area, and rim volume values than did the group without diabetes. However, the cup area, cup volume, and cup shape showed a significantly weak direct correlation with glycated hemoglobin levels. The difference in mean RNFLT between the two groups was not statistically significant. These results raise questions about whether diabetes provides a protective effect against glaucomatous optic nerve damage in POAG patients, from various perspectives [26]. Considering the above findings [26], we excluded individuals who had diabetes or other systemic comorbidities in order to detect the actual effect of POAG on optic nerve parameters.

Lesk et al. [13] studied 32 patients with open-angle glaucoma or ocular hypertension. The patients underwent optic nerve head topography using Heidelberg Retina Tomograph evaluation, perimetry testing using a static automated Humphrey visual field analyzer with program 24-2, and CCT measurements using ultrasonic pachymetry. The results showed that patients with thinner corneas experienced significantly greater reductions in both mean and maximum cup depth. However, these reductions did not differ significantly between patients with open-angle glaucoma and those with ocular hypertension [13]. These findings indicate that our results in patients with POAG could be compared to those of Kaushik et al. [27], who included 51 eyes with ocular hypertension and 35 normal eyes. Ultrasonic pachymetry was used to measure the CCT and a Zeiss Stratus OCT device was used to measure the average, inferior average, and superior average RNFLT, as well as optic nerve parameters. In eyes with ocular hypertension, the CCT had a direct significant correlation with all three retinal nerve fiber layer (RNFL) measurements, the rim area, and the horizontally integrated rim width, and an inverse significant correlation with the cup-to-disc ratio and the cup area [27]. Likewise, we observed a statistically significant

inverse correlation between the CCT and the cup-to-disc ratio. However, our other outcomes were not similar to those of Kaushik et al. [27].

The pathogenesis of POAG varies between Asian populations and those of other ethnicities [28]. It is therefore particularly important to consider the racial background of participants with diseases with strong racial and ethnic differences in presentation and severity, such as open-angle glaucoma [29, 30]. People of African descent are disproportionately impacted by POAG [30]. Furthermore, extensive evidence shows the effect of racial background on ocular parameters measured in healthy [16, 31–33] or diseased eyes [15, 28, 31, 34]. In this study, we exclusively included individuals of a single (Persian) ethnicity [17]. In Badr et al.'s study [15] the CCT was measured using optical low-coherence reflectometry in 1512 eyes of 929 patients diagnosed with various types of glaucoma across different ethnicities. They found that African Americans had the thinnest mean CCT, at 518.62  $\mu\text{m}$ , followed by Asians, at 539.29  $\mu\text{m}$ . The relatively thin CCT among Asians may partially explain the high rates of normal-tension glaucoma observed in this group. Among Asians, the Chinese had the thinnest mean CCT, at 537.66  $\mu\text{m}$  [15]. In a multivariable analysis of ocular biometrics involving 7601 phakic participants (7225 without and 376 with POAG), significant risk factors for POAG were identified as Latino ethnicity, refractive myopia, and longer axial length [31]. In the current study, individuals of Persian ethnicity with treatment-naive POAG had a mean CCT of 548.22  $\mu\text{m}$ , indicating a thicker CCT in this specific Asian ethnic group. Stepwise multiple linear regression analysis of our participants' data revealed that, for each unit increase in the vertical cup-to-disc ratio, the CCT decreased by 54.98  $\mu\text{m}$ .

The current study employed a Cirrus OCT to measure RNFLT and optic nerve parameters in eyes with treatment-naive POAG in patients of Persian ethnicity [17]. Racial differences in the optic disc area, the average cup-to-disc-ratio, vertical cup-to-disc ratio, cup volume, and RNFLT measured by the Cirrus OCT, were reported in an assessment of 284 normal individuals aged 18–84 years of European, Chinese, African, or Hispanic descent [14]. Using a Zeiss Stratus OCT device, Samarawickrama et al. [33] assessed the optic nerve head and RNFL parameters of 4118 children, aged 6–12 years, of both European Caucasian and East Asian ethnicities. They found that East Asian children had larger mean cup-to-disc ratios, a thicker average RNFL, and thicker non-nasal RNFL quadrants than those of their European Caucasian counterparts. The authors concluded that these anatomical differences may help to explain some racial variations in glaucoma susceptibility, which could account for the lower prevalence of open-angle glaucoma observed in Asians [33]. The average RNFLT in our participants was 82.93  $\mu\text{m}$ , ranging from 48 to 115  $\mu\text{m}$ .

Peripapillary RNFLT and macular ganglion cell-inner plexiform layer parameters in eyes with or suspected of having glaucoma differed significantly among various racial and ethnic groups stratified by glaucoma severity [35]. Comparing the optic disc size measured by the Heidelberg Retinal Tomograph II in glaucomatous eyes from individuals across different ethnic backgrounds showed that white Americans had a smaller disc size than did all other races [34]. Disparities in POAG risk by race and ethnicity may exist in individuals with myopia [36]. Blacks are more likely than Whites to report glaucoma [37]. In comparison to Whites, healthy eyes in Black individuals exhibited larger optic disc areas, as measured by the Heidelberg Retina Tomograph, a thicker RNFL both superiorly and inferiorly when evaluated by OCT, a slightly higher IOP as measured by Goldmann applanation tonometry, and a thinner CCT as assessed by ultrasonic pachymetry. These findings indicate that race significantly influences optic disc topography and the measurements of superior and inferior RNFLT in healthy eyes [32]. Using a Cirrus OCT device, the mean (SD) disc area, rim area, and cup volume among our participants of Persian ethnicity [17] and POAG were measured as 2.15 (0.43), 0.99 (0.28), and 0.47 (0.31)  $\text{mm}^2$  with an average RNFLT of 82.93 (12.83)  $\mu\text{m}$ .

The need for race-adjusted interpretation of data from the Cirrus device has previously been highlighted, due to observed structural differences in peripapillary RNFLT in the eyes of healthy Black Americans [38]. Addis et al. further indicated that reclassification using color coding suggested that the current Cirrus database may not accurately assess glaucomatous nerve changes in patients of African descent [38]. The diagnostic accuracy of two spectral-domain OCT devices in patients with POAG revealed that Spectralis RNFLT measurement varied significantly between individuals of African descent and those of European descent. In contrast, the performance of the Cirrus RNFLT measurement was consistent across both races. These findings remained unchanged even after adjusting for factors, such as age, CCT, IOP, axial length, disc area, and visual field mean deviation [39]. Measuring RNFLT and Bruch membrane opening minimum rim-width revealed that the Spectralis OCT demonstrated consistently lower diagnostic performance in individuals of African descent than in those of European descent [40]. These findings highlighted the importance of assessing optic nerve parameters across various racial backgrounds, both with and without ocular comorbidities. Moreover, it emphasizes the importance of our findings concerning CCT and optic nerve parameters in individuals of Persian ethnicity [17] who were diagnosed with treatment-naive POAG.

This study reported the mean values for CCT and various optic nerve parameters, revealing an association between the CCT and some optic nerve metrics in patients of Persian descent with treatment-naive POAG across different severity levels. However, the study had some limitations. First, the cross-sectional design of the study limited our ability to assess changes in these parameters or the strength of their associations over time, particularly in relation to disease progression and responses to IOP-lowering medications. Additionally, the absence of a control group hindered comparisons between the mean values and the strength of the associations observed in treatment-naive POAG eyes and those of healthy individuals from the same

ethnic background. Future longitudinal studies with larger sample sizes in the same ethnic group should stratify glaucomatous eyes based on severity levels and should compare these parameters with those of healthy individuals. This will help to verify our preliminary findings and provide more robust data on this specific type of glaucoma in patients of Persian ethnicity. Finally, deep learning methods are being developed for the automated detection of open-angle or angle-closure glaucoma using images from anterior segment OCT [41-45]. Future research could focus on utilizing images obtained from a Cirrus OCT in eyes with POAG to create an artificial intelligence-based method for the accurate and early detection of this potentially blinding condition. Such research could lead to improved management strategies for individuals with POAG.

## CONCLUSIONS

We observed a weak but statistically significant inverse correlation between the CCT and the vertical cup-to-disc ratio, average cup-to-disc ratio, and cup volume in eyes with treatment-naïve POAG of varying severity levels in the Persian ethnic group. For every unit increase in the vertical cup-to-disc ratio, we found a corresponding decrease of 54.98  $\mu\text{m}$  in the CCT. Our findings indicate that in patients with POAG, CCT correlates with some changes in structural optic nerve head parameters, including the cup volume and vertical/average cup-to-disc ratios. Further longitudinal studies including individuals from various racial backgrounds and different stratifying severity levels of POAG, are needed to provide strong evidence on the relationship between the CCT and optic nerve parameters at different time points of disease progression.

## ETHICAL DECLARATIONS

**Ethical approval:** The study protocol was approved by the Research Ethical Committee of Guilan Medical University in Rasht and adhered to the principles of the Declaration of Helsinki. Before enrollment, all participants were fully informed about the study details and provided written informed consent for participation.

**Conflict of interests:** None.

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## REFERENCES

- Weinreb RN, Leung CK, Crowston JG, Medeiros FA, Friedman DS, Wiggs JL, Martin KR. Primary open-angle glaucoma. *Nat Rev Dis Primers*. 2016 Sep 22;2:16067. doi: 10.1038/nrdp.2016.67. PMID: 27654570.
- Kwon YH, Fingert JH, Kuehn MH, Alward WL. Primary open-angle glaucoma. *N Engl J Med*. 2009 Mar 12;360(11):1113-24. doi: 10.1056/NEJMra0804630. PMID: 19279343; PMCID: PMC3700399.
- Soh Z, Yu M, Betzler BK, Majithia S, Thakur S, Tham YC, Wong TY, Aung T, Friedman DS, Cheng CY. The Global Extent of Undetected Glaucoma in Adults: A Systematic Review and Meta-analysis. *Ophthalmology*. 2021 Oct;128(10):1393-1404. doi: 10.1016/j.ophtha.2021.04.009. Epub 2021 Apr 16. PMID: 33865875.
- Sheybani A, Scott R, Samuelson TW, Kahook MY, Bettis DI, Ahmed IIK, Stephens JD, Kent D, Ferguson TJ, Herndon LW. Open-Angle Glaucoma: Burden of Illness, Current Therapies, and the Management of Nocturnal IOP Variation. *Ophthalmol Ther*. 2020 Mar;9(1):1-14. doi: 10.1007/s40123-019-00222-z. Epub 2019 Nov 15. PMID: 31732872; PMCID: PMC7054505.
- Garg A, Gazzard G. Treatment choices for newly diagnosed primary open angle and ocular hypertension patients. *Eye (Lond)*. 2020 Jan;34(1):60-71. doi: 10.1038/s41433-019-0633-6. Epub 2019 Nov 4. PMID: 31685971; PMCID: PMC7002706.
- Ko YC, Liu CJ, Hsu WM. Varying effects of corneal thickness on intraocular pressure measurements with different tonometers. *Eye (Lond)*. 2005 Mar;19(3):327-32. doi: 10.1038/sj.eye.6701458. PMID: 15258603.
- Belovay GW, Goldberg I. The thick and thin of the central corneal thickness in glaucoma. *Eye (Lond)*. 2018 May;32(5):915-923. doi: 10.1038/s41433-018-0033-3. Epub 2018 Feb 15. PMID: 29445115; PMCID: PMC5944650.
- Brandt JD, Beiser JA, Gordon MO, Kass MA; Ocular Hypertension Treatment Study (OHTS) Group. Central corneal thickness and measured IOP response to topical ocular hypotensive medication in the Ocular Hypertension Treatment Study. *Am J Ophthalmol*. 2004 Nov;138(5):717-22. doi: 10.1016/j.ajo.2004.07.036. PMID: 15531304.
- Lucy KA, Wollstein G. Structural and Functional Evaluations for the Early Detection of Glaucoma. *Expert Rev Ophthalmol*. 2016;11(5):367-376. doi: 10.1080/17469899.2016.1229599. Epub 2016 Sep 14. PMID: 28603546; PMCID: PMC5464747.
- Schrems WA, Schrems-Hoesl LM, Mardin CY, Laemmer R, Kruse FE, Horn FK. Can Glaucomatous Visual Field Progression be Predicted by Structural and Functional Measures? *J Glaucoma*. 2017 Apr;26(4):373-382. doi: 10.1097/IJG.0000000000000628. PMID: 28118204.
- Mokbel TH, Ghanem AA. Correlation of central corneal thickness and optic nerve head topography in patients with primary open-angle glaucoma. *Oman J Ophthalmol*. 2010 May;3(2):75-80. doi: 10.4103/0974-620X.64231. PMID: 21217900; PMCID: PMC3003855.
- Pakravan M, Parsa A, Sanagou M, Parsa CF. Central corneal thickness and correlation to optic disc size: a potential link for susceptibility to glaucoma. *Br J Ophthalmol*. 2007 Jan;91(1):26-8. doi: 10.1136/bjo.2006.106039. Epub 2006 Sep 14. PMID: 16973656; PMCID: PMC1857558.
- Lesk MR, Hafez AS, Descovich D. Relationship between central corneal thickness and changes of optic nerve head topography and blood flow after intraocular pressure reduction in open-angle glaucoma and ocular hypertension. *Arch Ophthalmol*. 2006 Nov;124(11):1568-72. doi: 10.1001/archophth.124.11.1568. PMID: 17102003.

14. Knight OJ, Girkin CA, Budenz DL, Durbin MK, Feuer WJ; Cirrus OCT Normative Database Study Group. Effect of race, age, and axial length on optic nerve head parameters and retinal nerve fiber layer thickness measured by Cirrus HD-OCT. *Arch Ophthalmol*. 2012 Mar;130(3):312-8. doi: [10.1001/archophthalmol.2011.1576](https://doi.org/10.1001/archophthalmol.2011.1576). PMID: 22411660; PMCID: PMC5536837.
15. Badr M, Masis Solano M, Amoozgar B, Nguyen A, Porco T, Lin S. Central Corneal Thickness Variances Among Different Asian Ethnicities in Glaucoma and Nonglaucoma Patients. *J Glaucoma*. 2019 Mar;28(3):223-230. doi: [10.1097/IJG.0000000000001180](https://doi.org/10.1097/IJG.0000000000001180). PMID: 30624387.
16. Chansangpetch S, Huang G, Coh P, Oldenburg C, Amoozgar B, He M, Lin SC. Differences in Optic Nerve Head, Retinal Nerve Fiber Layer, and Ganglion Cell Complex Parameters Between Caucasian and Chinese Subjects. *J Glaucoma*. 2018 Apr;27(4):350-356. doi: [10.1097/IJG.0000000000000889](https://doi.org/10.1097/IJG.0000000000000889). PMID: 29394205; PMCID: PMC9982653.
17. Hashemi H, Khabazkhoob M, Fotouhi A. Topographic Keratoconus is not Rare in an Iranian population: the Tehran Eye Study. *Ophthalmic Epidemiol*. 2013 Dec;20(6):385-91. doi: [10.3109/09286586.2013.848458](https://doi.org/10.3109/09286586.2013.848458). Epub 2013 Oct 29. PMID: 24168025.
18. Sung KR, Na JH, Lee Y. Glaucoma diagnostic capabilities of optic nerve head parameters as determined by Cirrus HD optical coherence tomography. *J Glaucoma*. 2012 Sep;21(7):498-504. doi: [10.1097/IJG.0b013e318220dbb7](https://doi.org/10.1097/IJG.0b013e318220dbb7). PMID: 21637115.
19. Newkirk MR, Gardiner SK, Demirel S, Johnson CA. Assessment of false positives with the Humphrey Field Analyzer II perimeter with the SITA Algorithm. *Invest Ophthalmol Vis Sci*. 2006 Oct;47(10):4632-7. doi: [10.1167/iovs.05-1598](https://doi.org/10.1167/iovs.05-1598). PMID: 17003461.
20. Tan JCK, Yohannan J, Ramulu PY, Kalloniatis M, Crabb DP, Crowston J, Phu J. Visual field testing in glaucoma using the Swedish Interactive Thresholding Algorithm (SITA). *Surv Ophthalmol*. 2025 Jan-Feb;70(1):141-152. doi: [10.1016/j.survophthal.2024.09.005](https://doi.org/10.1016/j.survophthal.2024.09.005). Epub 2024 Sep 29. PMID: 39349186.
21. Leung CK, Chiu V, Weinreb RN, Liu S, Ye C, Yu M, Cheung CY, Lai G, Lam DS. Evaluation of retinal nerve fiber layer progression in glaucoma: a comparison between spectral-domain and time-domain optical coherence tomography. *Ophthalmology*. 2011 Aug;118(8):1558-62. doi: [10.1016/j.ophtha.2011.01.026](https://doi.org/10.1016/j.ophtha.2011.01.026). Epub 2011 Apr 29. PMID: 21529954.
22. Moghimi S, Hosseini H, Riddle J, Lee GY, Bitrian E, Giaconi J, Caprioli J, Nouri-Mahdavi K. Measurement of optic disc size and rim area with spectral-domain OCT and scanning laser ophthalmoscopy. *Invest Ophthalmol Vis Sci*. 2012 Jul 9;53(8):4519-30. doi: [10.1167/iovs.11-8362](https://doi.org/10.1167/iovs.11-8362). PMID: 22577077.
23. Mwanza JC, Durbin MK, Budenz DL; Cirrus OCT Normative Database Study Group. Interocular symmetry in peripapillary retinal nerve fiber layer thickness measured with the Cirrus HD-OCT in healthy eyes. *Am J Ophthalmol*. 2011 Mar;151(3):514-21.e1. doi: [10.1016/j.ajo.2010.09.015](https://doi.org/10.1016/j.ajo.2010.09.015). Epub 2011 Jan 13. PMID: 21236402; PMCID: PMC5457794.
24. Roustaei N. Application and interpretation of linear-regression analysis. *Med Hypothesis Discov Innov Ophthalmol*. 2024 Oct 14;13(3):151-159. doi: [10.51329/mehdiophthal1506](https://doi.org/10.51329/mehdiophthal1506). PMID: 39507810; PMCID: PMC11537238.
25. Prata TS, Lima VC, Guedes LM, Biteli LG, Teixeira SH, de Moraes CG, Ritch R, Paranhos A Jr. Association between corneal biomechanical properties and optic nerve head morphology in newly diagnosed glaucoma patients. *Clin Exp Ophthalmol*. 2012 Sep-Oct;40(7):682-8. doi: [10.1111/j.1442-9071.2012.02790.x](https://doi.org/10.1111/j.1442-9071.2012.02790.x). PMID: 22429725.
26. Akkaya S, Can E, Öztürk F. Comparison of the corneal biomechanical properties, optic nerve head topographic parameters, and retinal nerve fiber layer thickness measurements in diabetic and non-diabetic primary open-angle glaucoma. *Int Ophthalmol*. 2016 Oct;36(5):727-36. doi: [10.1007/s10792-016-0191-x](https://doi.org/10.1007/s10792-016-0191-x). Epub 2016 Feb 9. PMID: 26857822.
27. Kaushik S, Gyatsho J, Jain R, Pandav SS, Gupta A. Correlation between retinal nerve fiber layer thickness and central corneal thickness in patients with ocular hypertension: an optical coherence tomography study. *Am J Ophthalmol*. 2006 May;141(5):884-890. doi: [10.1016/j.ajo.2005.12.026](https://doi.org/10.1016/j.ajo.2005.12.026). Epub 2006 Mar 20. PMID: 16546106.
28. Belamkar A, Harris A, Oddone F, Verticchio Vercellin A, Fabczak-Kubicka A, Siesky B. Asian Race and Primary Open-Angle Glaucoma: Where Do We Stand? *J Clin Med*. 2022 Apr 28;11(9):2486. doi: [10.3390/jcm11092486](https://doi.org/10.3390/jcm11092486). PMID: 35566612; PMCID: PMC9099679.
29. Berkowitz ST, Groth SL, Gangaputra S, Patel S. Racial/Ethnic Disparities in Ophthalmology Clinical Trials Resulting in US Food and Drug Administration Drug Approvals From 2000 to 2020. *JAMA Ophthalmol*. 2021 Jun 1;139(6):629-637. doi: [10.1001/jamaophthalmol.2021.0857](https://doi.org/10.1001/jamaophthalmol.2021.0857). PMID: 33885724; PMCID: PMC8063130.
30. Salowe R, Salinas J, Farbman NH, Mohammed A, Warren JZ, Rhodes A, Brucker A, Regina M, Miller-Ellis E, Sankar PS, Lehman A, O'Brien JM. Primary Open-Angle Glaucoma in Individuals of African Descent: A Review of Risk Factors. *J Clin Exp Ophthalmol*. 2015 Aug;6(4):450. doi: [10.4172/2155-9570.1000450](https://doi.org/10.4172/2155-9570.1000450). Epub 2015 Jul 31. PMID: 26664770; PMCID: PMC4671514.
31. Zhou S, Burkemper B, Pardeshi AA, Apolo G, Richter G, Jiang X, Torres M, McKean-Cowdin R, Varma R, Xu BY. Racial and Ethnic Differences in the Roles of Myopia and Ocular Biometrics as Risk Factors for Primary Open-Angle Glaucoma. *Invest Ophthalmol Vis Sci*. 2023 Jun 1;64(7):4. doi: [10.1167/iovs.64.7.4](https://doi.org/10.1167/iovs.64.7.4). PMID: 37261385; PMCID: PMC10241311.
32. Racette L, Boden C, Kleinhandler SL, Girkin CA, Liebmann JM, Zangwill LM, Medeiros FA, Bowd C, Weinreb RN, Wilson MR, Sample PA. Differences in visual function and optic nerve structure between healthy eyes of blacks and whites. *Arch Ophthalmol*. 2005 Nov;123(11):1547-53. doi: [10.1001/archophth.123.11.1547](https://doi.org/10.1001/archophth.123.11.1547). PMID: 16286617.
33. Samarawickrama C, Wang JJ, Huynh SC, Pai A, Burlutsky G, Rose KA, Mitchell P. Ethnic differences in optic nerve head and retinal nerve fibre layer thickness parameters in children. *Br J Ophthalmol*. 2010 Jul;94(7):871-6. doi: [10.1136/bjo.2009.158279](https://doi.org/10.1136/bjo.2009.158279). Epub 2009 Oct 12. PMID: 19822916.
34. Seider MI, Lee RY, Wang D, Pekmezci M, Porco TC, Lin SC. Optic disk size variability between African, Asian, white, Hispanic, and Filipino Americans using Heidelberg retinal tomography. *J Glaucoma*. 2009 Oct-Nov;18(8):595-600. doi: [10.1097/IJG.0b013e3181996f05](https://doi.org/10.1097/IJG.0b013e3181996f05). PMID: 19826388; PMCID: PMC2836908.
35. Gallo Afflitto G, Swaminathan SS. Racial-ethnic disparities in concurrent rates of peripapillary & macular OCT parameters among a large glaucomatous clinical population. *Eye (Lond)*. 2024 Oct;38(14):2711-2717. doi: [10.1038/s41433-024-03103-3](https://doi.org/10.1038/s41433-024-03103-3). Epub 2024 May 4. PMID: 38704424; PMCID: PMC11427570.

36. Yao M, Kitayama K, Yu F, Tseng VL, Coleman AL. Association Between Myopia and Primary Open-Angle Glaucoma by Race and Ethnicity in Older Adults in the California Medicare Population. *JAMA Ophthalmol.* 2023 Jun 1;141(6):525-532. doi: [10.1001/jamaophthalmol.2023.1007](https://doi.org/10.1001/jamaophthalmol.2023.1007). PMID: [37103940](https://pubmed.ncbi.nlm.nih.gov/37103940/); PMCID: [PMC10141276](https://pubmed.ncbi.nlm.nih.gov/PMC10141276/).
37. Grant A, Roy-Gagnon MH, Bastasic J, Talekar A, Miller G, Li G, Freeman EE. Exploring ethnic and racial differences in intraocular pressure and glaucoma: The Canadian Longitudinal Study on aging. *Heliyon.* 2024 Mar 26;10(7):e28611. doi: [10.1016/j.heliyon.2024.e28611](https://doi.org/10.1016/j.heliyon.2024.e28611). PMID: [38586381](https://pubmed.ncbi.nlm.nih.gov/38586381/); PMCID: [PMC10998131](https://pubmed.ncbi.nlm.nih.gov/PMC10998131/).
38. Addis V, Chan L, Chen J, Goodyear K, Pistilli M, Salowe R, Lee R, Sankar P, Miller-Ellis E, Cui QN, Maguire MG, O'Brien J. Evaluation of the Cirrus High-Definition OCT Normative Database Probability Codes in a Black American Population. *Ophthalmol Glaucoma.* 2022 Jan-Feb;5(1):110-118. doi: [10.1016/j.ogla.2021.05.002](https://doi.org/10.1016/j.ogla.2021.05.002). Epub 2021 May 23. PMID: [34033949](https://pubmed.ncbi.nlm.nih.gov/34033949/); PMCID: [PMC8608902](https://pubmed.ncbi.nlm.nih.gov/PMC8608902/).
39. KhalafAllah MT, Zangwill LM, Proudfoot J, Walker E, Girkin CA, Fazio MA, Weinreb RN, Bowd C, Moghimi S, De Moraes CG, Liebmann JM, Racette L. Racial Differences in Diagnostic Accuracy of Retinal Nerve Fiber Layer Thickness in Primary Open-Angle Glaucoma. *Am J Ophthalmol.* 2023 Oct 27;S0002-9394(23)00436-1. doi: [10.1016/j.ajo.2023.10.012](https://doi.org/10.1016/j.ajo.2023.10.012). Epub ahead of print. PMID: [39491122](https://pubmed.ncbi.nlm.nih.gov/39491122/).
40. El-Nimri NW, Moghimi S, Nishida T, Yarmohammadi A, Zangwill LM, Hou H, Proudfoot J, Walker E, Fazio MA, Girkin CA, Liebmann JM, Weinreb RN. Racial Differences in Detection of Glaucoma Using Retinal Nerve Fiber Layer Thickness and Bruch Membrane Opening Minimum Rim Width. *Am J Ophthalmol.* 2023 Feb;246:223-235. doi: [10.1016/j.ajo.2022.10.010](https://doi.org/10.1016/j.ajo.2022.10.010). Epub 2022 Oct 29. PMID: [36662535](https://pubmed.ncbi.nlm.nih.gov/36662535/).
41. Heidari Z, Baharinia M, Ebrahimi-Besheli K, Ahmadi H. A review of artificial intelligence applications in anterior segment ocular diseases. *Medical hypothesis, discovery & innovation in optometry.* 2022 Sep 30;3(1):22-33. doi: [10.51329/mehdiopometry146](https://doi.org/10.51329/mehdiopometry146)
42. Liu P, Higashita R, Guo PY, Okamoto K, Li F, Nguyen A, Sakata R, Duan L, Aihara M, Lin S, Zhang X, Leung CK, Liu J. Reproducibility of deep learning based scleral spur localisation and anterior chamber angle measurements from anterior segment optical coherence tomography images. *Br J Ophthalmol.* 2023 Jun;107(6):802-808. doi: [10.1136/bjophthalmol-2021-319798](https://doi.org/10.1136/bjophthalmol-2021-319798). Epub 2022 Jan 28. PMID: [35091438](https://pubmed.ncbi.nlm.nih.gov/35091438/); PMCID: [PMC10313952](https://pubmed.ncbi.nlm.nih.gov/PMC10313952/).
43. Fu H, Xu Y, Lin S, Wong DWK, Baskaran M, Mahesh M, Aung T, Liu J. Angle-Closure Detection in Anterior Segment OCT Based on Multilevel Deep Network. *IEEE Trans Cybern.* 2020 Jul;50(7):3358-3366. doi: [10.1109/TCYB.2019.2897162](https://doi.org/10.1109/TCYB.2019.2897162). Epub 2019 Feb 15. PMID: [30794201](https://pubmed.ncbi.nlm.nih.gov/30794201/).
44. Fu H, Baskaran M, Xu Y, Lin S, Wong DWK, Liu J, Tun TA, Mahesh M, Perera SA, Aung T. A Deep Learning System for Automated Angle-Closure Detection in Anterior Segment Optical Coherence Tomography Images. *Am J Ophthalmol.* 2019 Jul;203:37-45. doi: [10.1016/j.ajo.2019.02.028](https://doi.org/10.1016/j.ajo.2019.02.028). Epub 2019 Mar 6. PMID: [30849350](https://pubmed.ncbi.nlm.nih.gov/30849350/).
45. Xu BY, Chiang M, Chaudhary S, Kulkarni S, Pardeshi AA, Varma R. Deep Learning Classifiers for Automated Detection of Gonioscopic Angle Closure Based on Anterior Segment OCT Images. *Am J Ophthalmol.* 2019 Dec;208:273-280. doi: [10.1016/j.ajo.2019.08.004](https://doi.org/10.1016/j.ajo.2019.08.004). Epub 2019 Aug 22. PMID: [31445003](https://pubmed.ncbi.nlm.nih.gov/31445003/); PMCID: [PMC6888901](https://pubmed.ncbi.nlm.nih.gov/PMC6888901/).