Determinants of Optical Coherence Tomography Parameters in a Population-based Study



S. RAMYASHRI, HARSHA L. RAO, GANESH BABU JONNADULA, UDAY K. ADDEPALLI, NIKHIL CHOUDHARI, SIRISHA SENTHIL, AND CHANDRASEKHAR GARUDADRI

- PURPOSE: To study the effects of age, sex, intraocular pressure (IOP), corneal thickness, axial length (AXL), disc area, and the signal strength of the scan on optical coherence tomography (OCT) parameters of normal subjects in the L V Prasad Eye Institute-Glaucoma Epidemiological and Molecular Genetic Study (LVPEI-GLEAMS), a population-based study.
- DESIGN: Cross-sectional study.
- METHODS: A total of 1,100 eyes (1,100 subjects) of normal adults aged between 40 and 80 years from LVPEI-GLEAMS underwent macular and optic nerve head imaging with spectral-domain OCT (SDOCT). Effect of age, sex, IOP, central corneal thickness (CCT) and AXL, disc area, and signal strength of the OCT scan on retinal nerve fiber layer (RNFL) thickness, rim area, and ganglion cell-inner plexiform layer (GC-IPL) thickness measurements were evaluated using univariate and multivariate regression models.
- RESULTS: Mean rim area, RNFL, and GC-IPL thickness were 1.31 mm² (standard deviation [SD] = 0.22), 93.7 μ m (SD = 9.3) and 79.6 μ m (SD = 8.7), respectively. Age had a negative association with RNFL thickness (coefficient: -0.18, P < .001) and GC-IPL thickness (-0.18, P < .001). GC-IPL thickness was significantly less in women than in men (-1.05, P < .001). AXL had a negative association with rim area (-0.05, P < .001). Disc area was positively associated with RNFL thickness (4.90, P < .001) and rim area (0.15, P < .001). Signal strength of OCT scan was positively associated with RNFL thickness (1.6, P < .001) and negatively associated with rim area (-0.02, P < .001).
- CONCLUSION: Age, sex, AXL, disc area, and signal strength of the scan were significantly associated with OCT measurements. These factors may need to be considered while interpreting the OCT parameters in

AJO.com Supplemental Material available at AJO.com.

Accepted for publication Nov 25, 2020.

From the VST Centre for Glaucoma, L V Prasad Eye Institute, Hyderabad, India (R.S., U.K.A.,N.C., S.S., C.G.); Narayana Nethralaya, Bengaluru, India (H.L.R.); and Head – Image Reading Centre, L.V Prasad Eye Institute, Hyderabad, India (G.B.J.).

Inquiries to Chandrasekhar Garudadri, L V Prasad Eye Institute, Kallam Anji Reddy Campus, Road No: 2, Banjara Hills, Hyderabad 500034, India; e-mail: gcs@lvpei.org

pathologic conditions such as glaucoma. (Am J Ophthalmol 2021;224:163–171. © 2020 Elsevier Inc. All rights reserved.)

VALUATION OF OPTIC NERVE HEAD (ONH) AND retinal nerve fiber layer (RNFL) is fundamental in diagnosing and managing glaucoma. Optic disc and RNFL can be examined both subjectively and objectively to detect the glaucomatous structural changes. A good-quality optic disc stereo photograph aids in detecting glaucomatous changes. However, optic disc examination on stereo photographs is subjective and the agreement in differentiating early glaucomatous changes from physiological variations, even among experts, is far from excellent. In

³ Moreover, glaucomatous changes in stereo photographs are nonquantifiable. Imaging techniques such as optical coherence tomography (OCT), confocal scanning laser ophthalmoscopy, and scanning laser polarimetry were developed to provide an objective and quantitative assessment of RNFL and optic disc.³

OCT is a noninvasive imaging technology that is akin to in vivo histology of tissues under study, which makes it a convenient instrument to study the layers of the retina and optic disc structure. Spectral-domain OCT (SDOCT) is the most common commercially available technology that obtains high-resolution images at a fast scanning speed. SDOCT instrument scans the ONH, macula, and peripapillary RNFL with various in-built protocols. Ganglion cell–inner plexiform layer (GC-IPL) thickness at macula determined by OCT is also shown to be significantly reduced in glaucoma.⁴

Various subject-related (age, sex, etc), eye-related (disc area [DA], refraction, axial length [AXL], etc), and technology-related (signal strength [SS] of the OCT scan) factors are known to affect the OCT measurements. ^{5–13} Understanding the factors that can affect the measurements of OCT is important to interpret the changes seen in the disease conditions meaningfully. The association between some of these determinants and OCT parameters has been studied previously. ^{5–13} However, most of these studies were hospital-based and with limited sample size.

L V Prasad Eye Institute–Glaucoma Epidemiology and Molecular Genetics Study (LVPEI-GLEAMS) is a population-based study conducted in a rural cohort in 16 villages of Guntur district in the state of Andhra Pradesh, India, in the year 2009. ¹⁴ All subjects in the study underwent OCT scanning as a part of their examination. The aim of the present study was to evaluate the effect of age, sex, intraocular pressure (IOP), central corneal thickness (CCT), AXL, DA, and SS of the OCT scan on the ONH, RNFL, and GC-IPL parameters in normal subjects of GLEAMS.

METHODS

DATA FOR THE ANALYSIS WERE OBTAINED FROM LVPEI-GLEAMS, a population-based, cross-sectional, observational study in Indian subjects aged between 40-80 years, residing in a rural setting of Andhra Pradesh, India. The study was approved by the institutional ethics committee and was conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was taken from all study participants.

Various aspects and design of LVPEI-GLEAMS are published elsewhere. 14 Relevant study design for this particular study is discussed below. All examinations were carried out by experienced optometrists and vision technicians trained in relevant diagnostic procedures. All subunderwent a comprehensive ophthalmic examination that included visual acuity and refraction, IOP, gonioscopy, CCT, dilated fundus examination, fundus photography, anterior segment optical coherence tomography (ASOCT), posterior segment OCT imaging with Cirrus high-definition OCT (model 4000, software version 6.0; Carl Zeiss Meditec Inc, Dublin, California, USA), and visual field examination with Humphrey Field Analyzer II 750i (Carl Zeiss Meditec Inc, Dublin, California, USA).

- VISUAL FIELDS: Standardized visual field testing was performed with the 24-2 Swedish interactive threshold algorithm before any contact procedures. Fields with fixation losses >20% or false-positive or false-negative response rates >33% were considered to be unreliable and were repeated a maximum of 3 times to get a reliable result. Fields with good reliability and not satisfying any of Anderson's criteria¹⁵ were labeled as normal visual fields.
- OPTIC DISC STEREO PHOTOGRAPHY: Following pharmacologic dilation of the pupils, sequential stereoscopic optic disc photographs, full-field color, red-free, and 4-field fundus photographs were obtained for both eyes of each subject using the fundus camera (TRC-NW8; Topcon, Oakland, New Jersey, USA). All photographic evaluations were performed by 2 experienced optometrists (G.B.J. and U.A.K.) on a large screen liquid crystal display monitor with a stereoscopic viewer (Screen-Vu stereo viewer; Berezin Stereo Photography Products, Mission Viejo, Califor-

nia, USA). The graders were masked to patient identification, diagnosis, and visual field status. The fundus stereo photographs not satisfying criteria of structural damage defined as intereye asymmetry in cup-to-disc ratio of ≥0.2, thinning of the neuroretinal rim in either superior or inferior temporal quadrants, localized or diffuse RNFL defects, and presence of nerve fiber layer hemorrhage or total cupping of the optic disc¹⁴ were considered as a normal optic disc. Disagreements between the observers were resolved by a glaucoma specialist (N.C.). All these eyes had to have normal and reliable visual fields to be included in the study.

- IMAGING: All subjects were pharmacologically dilated before the examination and all scans were acquired in the same session. All the participants of the study underwent 512×128 macular cube and 200×200 optic disc cube protocols.
- OCT TECHNIQUE OF SCANNING: Optic disc cube scan. In this protocol, laser scan captures a cube of data comprising of 200 A-scans with 200 linear B-scans (40,000 points) in a 6 mm × 6 mm optic disc cube area in 1.5 seconds (27,000 A-scans in 1 second). The software then defines the optic disc margin and cup in a 3-dimensional cube. The Bruch membrane opening is defined as the optic disc margin. Rim width around the entire circumference is then measured by the thickness of neuroretinal rim available as the nerve exits the Bruch membrane opening. ONH parameters of rim area (RA), DA, average cup-to-disc ratio, vertical cup-to-disc ratio, cup volume were calculated.

The square root of the ratio of the area of the cup to DA gives average cup-to-disc ratio. The ratio of cup diameter to disc diameter in vertical meridian through the cup center gives the vertical cup-to-disc ratio. Cup volume is the 3-dimensional measurement of volume between plane created 200 μm offset to the plane of cup outline at the vitreoretinal interface and the posterior surface of the ONH. ONH parameters are automatically generated by the manufacturer's automated analysis algorithm without user intervention.

The RNFL algorithm provides standard measurement within the same 3-dimensional disc cube. The central dark spot in the center of the retinal pigment epithelium is defined as the center of the optic disc and circle of data with radius 1.73 mm from the central dark spot is generated. This 2-dimensional data are processed via bilinear interpolation to get 512 A-scans. Average of these A-scans give RNFL thickness.

Macula scan. In this protocol, a 512×128 cube scan is used with a 6 mm \times 6 mm grid using a series of 128 horizontal lines, each consisting of 512 A-scans/line. A ganglion cell analysis algorithm identifies the outer boundaries for macular RNFL and inner plexiform layer.

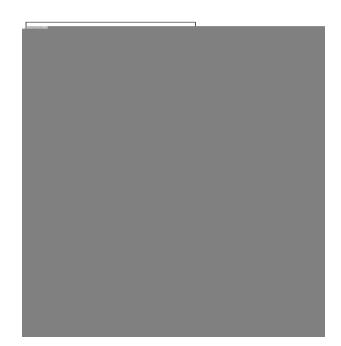


FIGURE 1. Flow chart depicting the inclusion and exclusion of study subjects.

The distance between these 2 layers is defined as macular GC-IPL thickness. Average, minimum, and sectoral (superotemporal, superior, superonasal, inferonasal, inferior, and inferotemporal) macular GC-IPL thickness measurements were calculated.

Measurement of other ocular parameters. Both unaided and aided distance and near vision measurements were performed. The IOP was measured by Goldmann applanation tonometer (Haag-Streit AT 900; Haag-Streit AG, Köniz, Switzerland) in all participants and 0.5% proparacaine eye drops (Paracain; Sunways India Pvt Ltd, Mumbai, India) was used to anesthetize the cornea and a 2% fluorescein strip to stain the tear film. CCT and AXL measurements were performed with an AL-1000 ultrasonic pachymeter (Tomey Corporation, Noritakeshinmachi, Nagoya, Japan). Both eyes were anesthetized by instilling 0.5% proparacaine eye drops into the lower fornix. One measurement was taken for each eye. If the standard deviation was more than 5 mm, the measurement was repeated. A similar procedure was followed for measuring AXL but only 5 sets of measurements were taken.

All subjects with suspicion of having glaucoma or diagnosed glaucoma (structural damage as defined above with corresponding visual field defects) and any other eye diseases that could be a confounder were excluded from the study. SDOCT scans with SS < 6 were excluded. Scanned images that did not have sharp focus and illumination, with poor centration and errors in segmentation, were also excluded from this study.

TABLE 1. Demographic and Clinical Features of the Study Subjects

Parameters	Mean	SD	Range
Age	49.5	7.6	40-85
Sex, male:female	450:651		
Right eye: left eye	761:340		
Intraocular pressure (mm Hg)	12.7	2.3	10-21
Central corneal thickness (µm)	524	32	319-630
Axial length (mm)	22.6	0.7	20-26
Signal strength of ONH scan	6.9	1.0	6-10
Signal strength of macula scan	7.8	1.2	6-10
Refractive error (diopters)	0.04	1.0	-6 to 11.5

ONH = optic nerve head; SD = standard deviation.

• STATISTICAL ANALYSIS: Baseline demographic details and ocular characteristics were expressed as mean ± standard deviation (SD) or median with interquartile range wherever applicable. Effect of age, sex, IOP, CCT, AXL, disc area, and SS of OCT scans on average RNFL thickness, RA, and GC-IPL thickness was evaluated using univariate and multivariate regression models. All associations significant at P < .05 on univariate models were evaluated in multivariate models. To account for the large sample size, P < .01 was considered to be statistically significant in the final multivariate models. Multicollinearity among the determinants were evaluated using correlation analysis, and determinants correlated with each other with Pearson r of >0.5 were considered to be collinear. However, none of the determinants was found to be collinear. As measurements from both eyes of the same subject are likely to be correlated, the standard statistical methods for parameter estimation lead to underestimation of standard errors. Therefore, the cluster of data for the study subject was considered as the unit of resampling when calculating standard errors. 16 Statistical analysis was performed using Stata (v14.2; Stata Corp, College Station, Texas, USA) software.

RESULTS

OF THE 7,666 EYES OF 3,833 SUBJECTS IN LVPEI-GLEAMS, 1,100 eyes of 1,100 subjects were included for the current analysis. Only 1 eye of each patient was included in the study. Figure 1 depicts the process of inclusion of subjects into this study. Table 1 shows the demographic and clinical features of this study population. Table 2 shows the RNFL, ONH, and GC-IPL parameters of study subjects. The RNFL was thickest in the inferior sector and thinnest in the temporal sector, while the GC-IPL was thickest in the superonasal sector and thinnest in the inferior sector.

TABLE 2. Retinal nerve fiber layer thickness, optic nerve head, and ganglion cell-inner plexiform layer parameters of the study subjects

Parameters	Mean	SD	Range
RNFL thickness parameters			
Average (μm)	93.7	9.3	64-120
Inferior sector (μm)	122	15.6	65-173
Superior sector (µm)	120	16.1	26-173
Nasal sector (µm)	74.6	11.3	22-115
Temporal sector (μm)	58.3	9.6	28-105
ONH parameters			
Rim area (mm²)	1.3	0.2	0.7-2.5
Disc area (mm²)	1.9	0.3	1.1-3.5
Average CDR	0.5	0.1	0.1-0.8
Vertical CDR	0.5	0.2	0.1-0.8
Cup volume (mm ³)	0.2	0.2	0.0-1.2
GCIPL thickness parameters			
GCIPL average (μm)	79.6	8.7	14-100
GCIPL minimum (μm)	73.76	13.0	00-96
Superotemporal quadrant (µm)	78.3	8.5	23-104
Superior quadrant (μm)	80.1	9.1	24-108
Superonasal quadrant (μm)	82.1	9.6	22-116
Inferonasal quadrant (μm)	80.7	9.4	22-115
Inferior quadrant (μm)	78.0	8.9	26-101
Inferotemporal quadrant (μm)	79.3	8.3	22-99

 $\label{eq:cdr} \text{CDR} = \text{cup-to-disc ratio}; \\ \text{GC-IPL} = \text{ganglion cell-inner plexiform layer}; \\ \text{ONH} = \text{optic nerve head}; \\ \text{RNFL} = \text{retinal nerve fiber layer}; \\ \text{SD} = \text{standard deviation}.$

TABLE 3. Univariate and Multivariate Regression Models Showing the Effect of Determinants on Average Retinal Nerve Fiber Layer Thickness

	Univariate Analysis		Multivariate Analysis	
	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value
Age	-0.18 (-0.25, -0.11)	<.001*	-0.18 (-0.26, -0.11)	<.001*
Sex	-0.79 (-1.91, 0.33)	.16		
IOP	-0.24 (-0.48, -0.001)	.05*	-0.21 (-0.44, -0.02)	.08
CCT	0.01 (-0.01, 0.02)	.44		
AXL	-0.92 (-1.72, -0.13)	.02*	-0.52 (-1.29, 0.24)	.18
Disc area	4.99 (3.44, 6.53)	<.001*	5.48 (3.95, 7.01)	<.001*
Signal strength	1.60 (1.07, 2.13)	<.001*	1.26 (0.73, 1.79)	<.001*

AXL = axial length; CI = confidence intervals; CCT = central corneal thickness; IOP = intraocular pressure. Asterisk denotes statistically significant *P* values.

Table 3 shows the associations between the determinants and RNFL thickness in univariate and multivariate analysis. Age, IOP, AXL, DA, and SS were associated with RNFL thickness in univariate analysis. Age, DA, and SS were statistically significantly associated with RNFL thickness in multivariate analysis. RNFL thickness decreased by 0.18 μm for every year increase in age. RNFL thickness increased by 4.90 μm for every 1 mm² increase in disc area. The RNFL thickness increased by

 $1.6~\mu m$ for every unit increase in SS. Figures 2-5 show the relationship of RNFL thickness with age, AXL, disc area, and SS of the scan, respectively.

Table 4 shows the associations between the determinants and RA in univariate and multivariate regression models. IOP, AXL, DA, and SS were significantly associated with RA in univariate analysis while only AXL, DA, and SS were associated with RA in the multivariate model. The RA reduced by 0.05 mm² for every 1 mm increase in

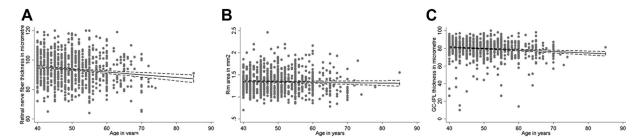


FIGURE 2. Scatterplots showing the relationship between age and retinal nerve fiber thickness (A), rim area (B), and ganglion cell-inner plexiform layer (GC-IPL) thickness (C). Univariate and multivariate regression analysis showed statistically significant negative associations between age and retinal nerve fiber thickness (coefficient: -0.18, P < .001) and between age and GC-IPL thickness (-0.17, P < .001).

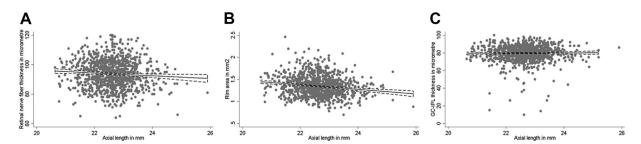


FIGURE 3. Scatterplot showing the relationship between axial length and retinal nerve fiber thickness (A), rim area (B), and ganglion cell-inner plexiform layer (GC-IPL) thickness (C). Univariate and multivariate regression analysis showed statistically significant negative association between axial length and rim area (coefficient: -0.05, P < .001).

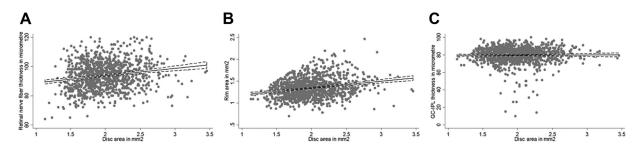


FIGURE 4. Scatterplot showing the relationship between disc area and retinal nerve fiber thickness (A), rim area (B), and ganglion cell–inner plexiform layer (GC-IPL) thickness (C). Univariate and multivariate regression analysis showed statistically significant positive association between disc area and retinal nerve fiber thickness (coefficient: 4.90, P < .001) and between disc area and rim area (0.15, P < .001).

AXL. For every 1 mm² increase in DA, RA increased by 0.15 mm². As SS increased by 1 unit, RA reduced by 0.02 mm². Figures 2-5 show the relationship of RA with age, AXL, DA, and SS of the scan, respectively.

Table 5 shows the results of univariate and multivariate analysis evaluating the associations between the determinants and average GC-IPL thickness. Age, sex, IOP and SS were associated with GC-IPL thickness in univariate

analysis. In multivariate analysis, age and sex were the only factors statistically significantly associated with average GC-IPL thickness. GC-IPL thickness decreased by an average of 0.18 μm for every year increase in age. Average GC-IPL thickness was thinner in female subjects by an average of 1.05 μm . Figures 2-5 show the relationship of GC-IPL thickness with age, AXL, DA, and SS of the scan, respectively.

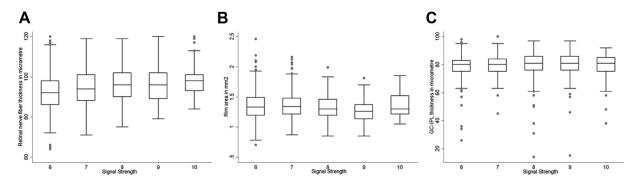


FIGURE 5. Box plot showing the relationship between signal strength and retinal nerve fiber thickness (A), rim area (B), and ganglion cell–inner plexiform layer (GC-IPL) thickness (C). Statistically significant positive association was seen between signal strength and retinal nerve fiber thickness (coefficient: 1.60, P < .001) and statistically significant negative association between signal strength and rim area (-0.02, P < .001). Horizontal line inside the box depicts the median value and the horizontal lines at the lower and upper end of the box denote the 25th and 75th percentile values, respectively.

TABLE 4. Univariate and Multivariate Regression Models Showing the Effect of Determinants on Neuroretinal Rim Area

	Univariate Analysis		Multivariate Analysis	
	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value
Age	-0.001 (-0.002, 0.006)	.21		
Sex	0.014 (-0.012, 0.04)	.29		
IOP	-0.004 (-0.01, 0.001)	.13	-0.004 (-0.01, -0.001)	.13
CCT	0.0004 (-0.0001, 0.001)	.05*	0.001 (0.0001, 0.001)	.03
AXL	-0.05 (-0.07, -0.03)	<.001*	-0.04 (-0.07, -0.03)	<.001*
Disc area	0.15 (0.11, 0.19)	<.001*	0.14 (0.10, 0.17)	<.001*
Signal strength	-0.02 (-0.03, -0.01)	<.001*	-0.02 (-0.03, -0.01)	<.001*

AXL = axial length; CI = confidence intervals; CCT = central corneal thickness; IOP = intraocular pressure. Asterisk denotes statistically significant *P* values.

DISCUSSION

IN THIS STUDY, WE REPORT THE DETERMINANTS OF ONH and RNFL parameters along with macular GC-IPL parameters measured by SDOCT in a population-based study. To the best of our knowledge, this is the first population-based study looking at OCT parameters and their determinants in an Indian population. The average RNFL thickness was $93.7 \pm 9.3 \mu m$, which was comparable to the Indian subset of a multiethnic population study¹⁷ (study subjects were aged 60.7 ± 8.1 years) and also with the Australian subjects in a study by Tariq and associates. 18 The average RNFL thickness found in our study is also comparable to that seen in 2 Indian population-based studies, 1 by Ramakrishnan and associates¹¹ (average RNFL thickness = 105 \pm 38.79 µm) and the other by Sony and associates ¹⁹ $(104.27 \pm 8.5 \mu m)$, both of which were done with Stratus OCT, and to that seen in the study by Appukuttan and associates (average RNFL thickness = $101.4 \pm 8.6 \mu m$), which was done with SDOCT. The superior and inferior sectors showed comparable thickness in our study, while other studies^{5,9,12,18,20} have reported the inferior sector to be thickest. The rim area found in our study was comparable to that reported by Cheung and associates⁷ (RA = 1.29 \pm 0.2 mm²). GC-IPL thickness was thickest in the superonasal and thinnest in the inferior sector, similar to that reported in previous studies. $^{21-23}$

Older age was associated with significantly thinner RNFL and GC-IPL thickness in our study. When we divided age into decade-wise categories, we found that the average RNFL thickness in those aged between 51 and 60 years was on average 1.85 μ m thinner than those aged between 40 and 50 years. RNFL thickness in those aged above 60 years was on average 4.2 μ m thinner than those aged between 40 and 50 years. Most previous studies 5,6,10,24,25 have also shown a reduction in RNFL thickness with advancing age ranging between 1.1 μ m/decade to approximately 2 μ m/decade. Similarly, average GC-IPL thickness in those aged between 40 and 50 years. GC-IPL thickness in those aged between 40 and 50 years. GC-IPL thickness in those aged above 60 years was on average 4.6 μ m thinner than those aged between 40

TABLE 5. Univariate and Multivariate Regression Models Showing the Effect of Determinants on Average Ganglion Cell–Inner Plexiform Layer Thickness Measurements

	Univariate Analysis		Multivariate Analysis	
	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value
Age	-0.17 (-0.22, -0.11)	<.001*	-0.18 (-0.24, -0.12)	<.001*
Sex	-1.05 (-1.97, -0.14)	.02*	-1.64 (-2.55, -0.73)	<.001*
IOP	-0.13 (-0.33, 0.06)	.18		
CCT	0.006 (-0.00, 0.02)	.36		
AXL	-0.06 (-0.70, 0.57)	.83		
Disc area	0.37 (-0.88, 1.63)	.55		
Signal strength	0.40 (0.03, 0.77)	.03*	0.15 (-0.22, 0.52)	.43

AXL = axial length; CI = confidence intervals; CCT = central corneal thickness; IOP = intraocular pressure. Asterisk denotes statistically significant *P* values.

and 50 years. Previous studies 23,26 have reported similar negative association of GC-IPL thickness with advancing age, with the GC-IPL thinning from 1 to 2 $\mu m/decade$. Age was not associated with RA in our study. In contrast to our study, previous studies 7,25 have noted age to have a negative association with RA.

Our study also found that women had significantly thinner GC-IPL thickness compared to men; GC-IPL was $1.05~\mu m$ thinner in women. RNFL thickness was also thinner in women compared to men, but this association was not statistically significant. Gupta and associates have also noted thinner GC-IPL in older age and female sex, 26 similar to our study, while some studies 12,23 have found no association between sex and GC-IPL thickness.

The AXL of the eye was negatively associated with RNFL thickness and RA, with these OCT parameters decreasing in eyes with longer AXL. Previous studies between the noted a reduction in RNFL thickness with increasing AXL ranging from 1.3 μ m to 4.79 μ m, while few studies have not seen any association of RNFL thickness with AXL. 5,10,23 Cheung and associates have reported a similar association of AXL with RNFL thickness and neuroretinal rim area, as seen in our study.

We analyzed the association of DA with RNFL thickness and RA by categorizing DA into 3 groups: small discs with (mean \pm SD) 1.63 \pm 0.13 mm² DA (range 1.13-1.8 mm²), medium discs with 1.95 \pm 0.08mm² DA (range 1.81-2.11 mm²), and large discs with 2.38 \pm 0.23 mm² DA (range 2.12-3.46 mm²). Larger DA was associated with thicker RNFL thickness and increased neuroretinal rim area. It was noted that medium-size disc had 2.7 μm and large disc had 3.8 μm thicker RNFL than the small disc. This measurement means when a fixed-diameter circle is used to measure peripapillary RNFL thickness, an artefact is created in measurement showing thicker RNFL in large discs, as the sampling is done closer to disc margin, and vice-versa in the small disc. Medium disc had 0.07 mm² and large disc had 0.12 mm² larger RA compared to the

small disc. Cheung and associates⁷ also reported DA to be independently associated with ONH measurements and that small disc has small CD, thin RA, thinner RNFL, and smaller cup-to-disc ratio.

Increased OCT signal strength was associated with thicker RNFL and reduced neuroretinal rim area. It was also positively associated with GC-IPL thickness, but this association was not statistically significant. Rao and associates¹² have shown a positive association of SS with all ONH parameters but not with RNFL and macular parameters. They found that ONH rim measurements increased and cup measurements decreased with increase in SS. Samarawickrama and associates²⁷ have reported a small but significantly increased macular thickness with increased SS. These differences between studies could be owing to different OCT devices used in these studies. Rao and associates¹³ have also demonstrated that the diagnostic ability of OCT parameters is reduced in scans with lower SS. Hence a good-quality scan with good SS is of paramount importance for longitudinal follow-up of subjects with glaucoma and other retinal pathologies.

Higher IOP was associated with thinner neuroretinal rim area, thinner RNFL thickness, and thinner GC-IPL layer, but the association was seen only on univariate analysis.

All OCT devices have in-built reference databases to flag off abnormalities in RNFL, ONH, and GC-IPL parameters. Reference databases are also used to detect progressive reduction in OCT parameters while evaluating disease progression. Currently available reference databases in OCT devices are adjusted only for age. Our study demonstrates that factors like sex, AXL, DA, and SS of the scan also affect the RNFL, ONH, and GC-IPL parameters and should be considered as determinants while detecting structural abnormalities in glaucoma and other retinal diseases.

The strengths of this study include its large populationbased sample size, which reduces selection bias, and standardized ocular examination and imaging techniques by a trained person. There are some limitations to our study. Since it is a cross-sectional observational study, the causal relationship between determinants and OCT parameters cannot be extrapolated from the data. Although we have included all subjects over 40 years of age, decade-wise clustering of age is uneven (most subjects between 40 and 60

years, and very few over 60 years), which can skew the results.

In conclusion, age, sex, AXL, disc size, and signal strength of the scan are associated with OCT parameters. These results may need to be considered while interpreting the OCT measurements in glaucoma and other retinal diseases.

FUNDING/SUPPORT: HYDERABAD EYE RESEARCH FOUNDATION, L V PRASAD EYE INSTITUTE, HYDERABAD, INDIA. FINANCIAL Disclosures: Ramyashri S, Harsha L. Rao, Ganesh Babu Jonnadula, Uday K. Addepalli, Nikhil Choudhari, and Sirisha Senthil: none; Chandrashekhar Garudadri: Allergan and Sun Pharma (Consultant), Santen Pharma (Advisory Board). All authors attest that they meet the current ICMJE criteria for authorship.

REFERENCES

- 1. Greenfield DS, Weinreb RN. Role of optic nerve imaging in glaucoma clinical practice and clinical trials. *Am J Ophthalmol* 2008;145(4):598–603.
- 2. Vessani RM, Moritz R, Batis L, et al. Comparison of quantitative imaging devices and subjective optic nerve head assessment by general ophthalmologists to differentiate normal from glaucomatous eyes. *J Glaucoma* 2009;18:253–261.
- 3. Correnti AJ, Wollstein G, Price LL, Schuman JS. Comparison of optic nerve head assessment with a digital stereoscopic camera (discam), scanning laser ophthalmoscopy, and stereophotography. *Ophthalmology* 2003;110(8):1499–1505.
- Francoz M, Fenolland JR, Giraud JM, et al. Reproducibility of macular ganglion cell-inner plexiform layer thickness measurement with cirrus HD-OCT in normal, hypertensive and glaucomatous eyes. Br J Ophthalmol 2014;98(3):322–328.
- Appukuttan B, Giridhar A, Gopalakrishnan M, Sivaprasad S. Normative spectral domain optical coherence tomography data on macular and retinal nerve fiber layer thickness in Indians. *Indian J Ophthalmol* 2014;62(3):316–321.
- 6. Bendschneider D, Tornow RP, Horn FK, et al. Retinal nerve fiber layer thickness in normals measured by spectral domain OCT. *J Glaucoma* 2010;19(7):475–482.
- 7. Cheung CY, Chen D, Wong TY, et al. Determinants of quantitative optic nerve measurements using spectral domain optical coherence tomography in a population-based sample of non-glaucomatous subjects. *Invest Ophthalmol Vis Sci* 2011; 52(13):9629–9635.
- 8. Knight OJ, Girkin CA, Budenz DL, et al. 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;130(3):312–318.
- 9. Malik A, Singh M, Arya SK, Sood S, Ichhpujani P. Retinal nerve fiber layer thickness in Indian eyes with optical coherence tomography. *Nepal J Ophthalmol* 2012;4(1):59–63.
- Mansoori T, Viswanath K, Balakrishna N. Quantification of retinal nerve fiber layer thickness using spectral domain optical coherence tomography in normal Indian population. *Indian J Ophthalmol* 2012;60(6):555–558.
- Ramakrishnan R, Mittal S, Ambatkar S, Kader MA. Retinal nerve fibre layer thickness measurements in normal Indian population by optical coherence tomography. *Indian J Ophthalmol* 2006;54(1):11–15.
- Rao HL, Kumar AU, Babu JG, Kumar A, Senthil S, Garudadri CS. Predictors of normal optic nerve head, retinal

- nerve fiber layer, and macular parameters measured by spectral domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52(2):1103–1110.
- Rao HL, Addepalli UK, Yadav RK, Senthil S, Choudhari NS, Garudadri CS. Effect of scan quality on diagnostic accuracy of spectral-domain optical coherence tomography in glaucoma. Am J Ophthalmol 2014;157(3):719–727.
- 14. Addepalli UK, Jonnadula GB, Garudadri CS, et al. LV Prasad Eye Institute Glaucoma Epidemiology and Molecular Genetic Study (LVPEI- GLEAMS). Report 1: study design and research methodology. *Ophthalmic Epidemiol* 2013;20(3): 188–195.
- 15. Anderson DR, Patella VM. Automated Perimetry. 2nd edition. St. Louis: Mosby & Co; 1999.
- Glynn RJ, Rosner B. Accounting for the correlation between fellow eyes in regression analysis. Arch Ophthalmol 1992; 110(3):381–387.
- 17. Tao Y, Tham YC, Chee ML, et al. Profile of retinal nerve fibre layer symmetry in a multiethnic Asian population: the Singapore Epidemiology of Eye Diseases study. *Br J Ophthalmol* 2020;104(6):836–841.
- 18. Tariq YM, Li H, Burlutsky G, Mitchell P. Retinal nerve fiber layer and optic disc measurements by spectral domain OCT: normative values and associations in young adults. *Eye* 2012; 26(12):1563–1570.
- 19. Sony P, Sihota R, Tewari HK, Venkatesh P, Singh R. Quantification of the retinal nerve fibre layer thickness in normal Indian eyes with optical coherence tomography. *Indian J Ophthalmol* 2004;52(4):303–309.
- 20. Ho H, Tham YC, Chee ML, et al. Retinal nerve fiber layer thickness in a multiethnic normal Asian population: The Singapore Epidemiology of Eye Diseases Study. *Ophthalmology* 2019;126(5):702–711.
- 21. Koh VT, Tham YC, Cheung CY, et al. Determinants of ganglion cell-inner plexiform layer thickness measured by high-definition optical coherence tomography. *Invest Ophthalmol Vis Sci* 2012;53(9):5853–5859.
- 22. Tham YC, Cheung CY, Koh VT, et al. Relationship between ganglion cell-inner plexiform layer and optic disc/retinal nerve fibre layer parameters in non-glaucomatous eyes. *Br J Ophthalmol* 2013;97(12):1592–1597.
- 23. Mwanza JC, Durbin MK, Budenz DL, et al. Profile and predictors of normal ganglion cell-inner plexiform layer thickness measured with frequency-domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52(11): 7872–7879.

- 24. Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. *Ophthalmology* 2007;114(6): 1046–1052.
- 25. Girkin CA, McGwin G Jr, Sinai MJ, et al. Variation in optic nerve and macular structure with age and race with spectral-domain optical coherence tomography. *Ophthalmology* 2011; 118(12):2403–2408.
- 26. Gupta P, Sidhartha E, Tham YC, et al. Determinants of macular thickness using spectral domain optical coherence tomography in healthy eyes: the Singapore Chinese Eye Study. *Invest Ophthalmol Vis Sci* 2013;54(13):7968–7976.
- 27. Samarawickrama C, Pai A, Huynh SC, Burlutsky G, Wong TY, Mitchell P. Influence of OCT signal strength on macular, optic nerve head, and retinal nerve fiber layer parameters. *Invest Ophthalmol Vis Sci* 2010;51(9):4471–4475.